Epidemiology and knowledge of selfcare of diabetes mellitus, obesity and hypertension in Guyana and beneficial use of *Momordica charantia,* in combination with daily exercise and diet modification, to treat these non-communicable diseases.

By

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ABSTRACT

In 2018, The World Health Organization (WHO) identified chronic non-communicable diseases (NCDs) or chronic diseases (CDs) as cardiovascular diseases (CVDs), diabetes mellitus (DM) obesity, cancer, stroke, chronic respiratory diseases (CRD), cerebrovascular disease (CVD), kidney failure (KF) and dental diseases. CVDs are further classified into heart failure or cardiomyopathy, hypertension, atherosclerosis, coronary artery diseases (CAD), sudden cardiac death (SCD), arrhythmias and others. DM, obesity and hypertension are three major global health NCDs affecting people in both developed and low-and middle- income developing countries such as Guyana. These diseases are interrelated where obesity is a risk factor for DM and both obesity and DM are risk factors for hypertension. The prevalence of all three NCDs are very high, and they are also very costly to treat in Guyana. Diabetes is classified mainly into type 1 DM (T1DM) and type 2 DM (T2DM) and 85-90% of diabetics suffer from T2DM. Obesity is when someone has a basal metabolic index (BMI) of 30 and over. Likewise, hypertension (HTN) or high blood pressure (HBP) is when someone has elevated BP over20/90 mm Hg and over. Modern life- style habits including overeating but not the right food, sedentary living, stress, genetic pre-disposition and others risk factors can lead obesity, diabetes and hypertension. Guyana is cursed with the 'obese-diabetic-hypertensive time bomb'. This study investigated the epidemiology and cost-effective ways to treat these NCDs in Guyana and how knowledge of obesity and diabetic self-care management can prevent long–term complications associated with obesity and DM. In tackling the scientific problem, this study investigated the roles of regular exercise, diet modification and use of bitter melon or corilla (*Momordica charantia*), a local anti-diabetic vegetable in Guyana to treat obesity, diabetes and hypertension in newly diagnosed patients.

The main epidemiological findings in this study reveal that the three NCDs increased in prevalence gradually over the years especially among both adult males and females but significantly more so among females, especially when they reach the ages between 46 to 69 years. In addition, almost twenty five percent of adult Guyanese failed to diagnose their medical conditions and many of those who are diagnosed prefer to seek advice from a traditional healer and take herbal remedies to treat their diseases rather than taking prescribed drugs. Data also show that such NCDs as diabetes, hypertension and CVDs are responsible for more deaths in Guyana and rank high globally.

Initial time-course treatment and glucose tolerance tests (GTTs) reveal that *M charantia* consumption (5-20 grams twice daily as either a juice (weight/volume) can reduce blood sugar, blood pressure and other blood biomarkers such as total lipids (cholesterol) and triglycerides significantly ($p<0.05$) in diabetes-treated patients after 6 weeks compared to week 1 of the study (These effects were dose-dependent. The results also show that the hypoglycaemic effects were more pronounced when *M charantia* was combined with diet modification, exercise and the orthodox medicine, diamicron MR. *M charantia* had no synergistic effect on blood glucose when it was combined with dimicron MR. Measurement of blood cation levels using inductively -coupled plasma mass spectrometry (ICPMS) in plasma from diabetic and age-matched healthy control subjects reveal no significant change in the levels of the cations. Chemical analysis of *M charantia* revealed that it is rich in vitamin C, some cations, phenolic contents and antioxidant compounds

Similarly, daily intake of *M charantia* either alone or in combination with physical activity and diet modification can reduce body weight and significantly ($p<0.05$) decrease blood pressure (BP), total lipids and triglycerides in obese subjects after 6 weeks of treatment compared to the start of the study (In newly diagnosed hypertensive patients, *M charantia* either alone or combined with regular exercise and diet modification can reduce significantly ($p<0.05$) high blood pressure after 6 weeks of treatment compared to week 1 at the start of the study. *M charantia* had no significant effect on BP when it was combined with orthodox medicine, amlodipine, a calcium channel blocker).

The results also show that knowledge of the respondents using a questionnaire about T2DM self-care management was overall poor. Thus, the study concluded that the higher the level of knowledge about T2DM self-care, the less likely the diabetic patients will develop diabetes-related complications, as noted by the higher scoring of the control group. Therefore, effective health promotion and education programmes are recommended to target T2DM patients, as well as pre-diabetic and non-diabetic persons (chapter 6). However, obese patients have a good knowledge of obesity, but they were still obese. In conclusion, the results of this study have shown that *M charantia*, diet modificatio*n* and daily exercise, either alone or in combination have potential cost-effective effects in treating diabetes, obesity and hypertension and knowledge of self-care management about diabetes can delay end-organ complications.

DECLARATION

I declare that this thesis has been composed by myself while being registered as a candidate for the degree of Doctor of Philosophy (DPhil) to which this submission is made. I have not been a registered candidate for any other higher degree at this or any other University or other Institution of learning. I declare that I have participated fully in all aspects of the study. My participation included original ideas, working hypotheses, experimental designs, literature search, experimental work, analysis and interpretation of data, preparation and presentation of the data, writing, correcting and submission of the thesis.

Signature: ………………………………………

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I would also like to thank my colleagues at the University of Guyana, my friends and my family (my mother, Leontine and my three brothers, Dr Harry Hanoman, Dr Hans Hanoman and Carl Hanoman) especially my guiding companion in my profession, my late father, Dr Carl (Max) Hanoman who passed away suddenly in November 2019.

DEDICATIONS

This thesis is dedicated to my late Father, Dr Carl (Max) Hanoman MBBS, who has laid the foundation for all of my academic achievements, my entire family especially my three brothers and my mother.

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ABBREVIATIONS

Acute phase response	APR
Adenosine triphosphate	ATP
AMP-activated protein kinase	AMPKs
American Diabetic Association	ADA
Acute phase response	APR
Angiotensin-converting enzyme	ACE
Blood glucose level	BGL
Blood pressure	BP
Basal metabolic index	BMI
British Broadcasting Corporation	BBC
Cardiovascular diseases	CVDs
Caribbean Community	CARICOM
Catalase	CAT
Communicable diseases	CD
Coronary Artery disease	CAD
Chronic diseases	CD
Chronic non-communicable disease	CNCD
Chronic respiratory disease	CRD
Centre for disease control	CDC
Centre for disease control	CDC
Central Intelligent Agency	CIA
Cognitive behaviour therapy	CBT
C- Reactive protein	CRP
Diabetes mellitus	DM
Diastolic blood pressure	DBP
Excitation –contraction coupling	ECC
Fasting blood glucose levels	FBGLs
Free fatty acid	FFA
Georgetown Hospital Public Corporation	GPHC
General Practitioner	GP
Glucose tolerance test	GTT
Glucagon-like peptide	GLP-1
Glutathione S-transferase	GST
Cyclic- guanosine triphosphate	cGMP
High blood pressure	HBP
Heart Failure	HF
Injuries	Inj
Interleukin	IL
Insulin resistance	IR
High performance liquid chromatography	HPLC
Health Literacy	HL
High density lipoprotein	HDL
Hyperglycaemia	HG
Hypertension, Evaluation and Learning Programme	HELP
Hydrogen peroxide	H_2O_2
IKapa-B kinase	IKK
c-junk NH2 kinase	JNK

Kidney failure	KF
Low density lipoprotein	LDL
Methylglyoxal	MGO
Moderate releasing	MR
Non –communicable diseases	NCDs
Non-communicable diseases risk Factor collaboration	NCDRFC
Bachelor of Medicine, Bachelor of Surgery	MBBS
Oral glucose tolerant test	OGTT
Oral hypoglycaemic agents	OHA
Pan American Organization	PAHO
Sudden Cardiac death	SCD
Systolic blood pressure	SBP
Systolic and diastolic blood pressure	SDBP
Ministry of Public Health	MPH
Magnetic Resonance Imaging	MR
Methylglyoxal	MGO
Moderate release	MR
Oxygen free radical	O^-
Pan-American Human Organization	PAHO
Peroxisome proliferator-activated -receptor	PPAR-alpha
Public Health England	PHE
Proton	H^+
Reactive oxygen species	ROS
Reactive carbonyl species	RCS
Sodium Docedyl sulphate	SDS
Superoxide dismutase	SOD
Sudden Cardiac death	SCD
Transforming growth factor, beta -1	TGF-beta 1
Type 1 diabetes mellitus	T1DM
Type 2 diabetes mellitus	T2DM
United States of America Dollars	USAD
United Kingdom	UK
Vascular adhesion factor	VAP-1
Very low-density lipoprotein	VLDL
World Health Organization	WHO

FIGURE LEGENDS

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Chapter 3

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Data are mean +SEM; n=20.

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of week 1 (Figure 3.8A). However, the OGTT data in (figure 3.8B) were only significant (*p<0.05) at 60 min, 90 min and 120 min compared to the blood glucose level when 75 ml of a glucose solution was consumes at 0 min.

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Chapter 1:

GENERAL INTRODUCTION

1. Diabetes Mellitus (DM)

1.1 Historical Perspectives and classification of diabetes

Diabetes is one of the oldest metabolic disorders to inflict humans. In 3000 BC, the clinical features of diabetes were described by an Egyptian Physician (Hesy-Ra) who noticed that some patients displayed signs of polydipsia (thirst) and polyuria (excess urine output). In 1875, a British Physician by the name of Thomas Willis rediscovered the sweet taste of urine and blood of patients (first noticed by ancient Indians). He used the word mellitus (honey sweet) to describe this sweetness. The word diabetes is derived from Greek meaning siphon. Thereafter, the disorder was named diabetes mellitus (DM) which means to siphon out sugar from the body. In 1857, Claude Bernard from France established the relationship between the liver and glucose metabolism (glycogenesis). In 1889, two Austrian clinical scientists, Mering and Minkowski, discovered the role of the pancreas in the pathogenesis of diabetes by removing the pancreas from dogs. In 1921, two Canadian scientists, Dr Banting and Dr Best, with the help of John Macleod and James Collip, demonstrated the relationship between the pancreas as an insulin-producing gland and diabetes. They also isolated insulin from the pancreas and purified it. It was also established that insulin deficiency was related to diabetes which was later classified as type 1 diabetes mellitus (T1DM). Both Dr Banting and Dr Best won the Nobel Prize for their discovery. In 1936, Harold Himsworth reported that diabetes could be distinguished into two types, insulin-sensitive or type 1 DM (T1DM) and insulin-resistance (IR) or type 2 DM (T2DM) based on earlier findings by Indian and Chinese clinicians 2000 years ago. Generally, DM is now classified on its aetiology, natural history, and clinical manifestation mainly as T1DM (5-10%), T2DM (85%) and gestational DM (4-5%) (in pregnant women) (ADA, 2010). DM is not a disease, but a metabolic disorder due to elevated blood glucose (hyperglycaemia (HG)) level because of either the lack of insulin or insulin resistance (IR). The metabolic hormone insulin plays a major physiological and biochemical roles in the body to regulate blood glucose level and as such, diabetes is classified as a metabolic disorder leading to many other diseases, including hypertension, heart failure, sudden cardiac death, kidney failure, blindness (retinopathy), nerve damage (neuropathy), impotence, foot ulcers, exocrine glands insufficiencies and others (Adeghate and Schantter, 2006; D'Souza et al, 2009, 2016; Lotfy et al,. 2016; Papatheodorou et al, 2016; Harding et al, 2019).

1.2 Epidemiology of Diabetes

The current world population in 2022 is estimated to be around 7.8 billion and over 480 million people have confirmed diabetes worldwide (almost 6% of the world's population) with 90% have T2DM and 10% have T1DM and gestational diabetes. The total number of diabetics vary from one country to another globally or regionally with prevalence of almost 5-10% (lower range) compared to 25-30 % (higher range). Another 250 million people (3.2%) are undiagnosed and more than 1.5 billion people (20% of the population in the world) have pre-diabetes and insulin resistance. Several people with pre-diabetes are most likely to become diabetic later in life. Globally, it costs almost $1 trillion United States Dollars (USAD) (15% of global budgets in terms of life and demand on health budgets) to diagnose, treat and care for diabetic patients so that they can enjoy a better quality of life. It is estimated that the number of people with confirmed DM will rise to more than 700 million by 2035 thereby doubling the global health budget. In many countries of the world, almost 75% the diabetic patients, and not the Government, who pay for the health care (WHO, 2011; Guariguata et al. 2014; Diabetes, UK, 2015;2019; MPH, Guyana 2016; Zimmet, 2017). Generally, diabetes exerts tremendous burden and suffering to mankind irrespective of either age, gender, ethnicity or religion.

1.3 Risk factors of Diabetes

It is also now well established that juvenile onset TIDM is caused by autoimmune destruction of the endocrine beta cells of the pancreas. T1DM is also very common among populations which move from one country (environment) to another, like the Japanese who moved from Japan to South America. Risk factors for T2DM include high Body Mass Index (BMI) or obesity, poor diet (rich in sugar and carbohydrates and fats), genetic disposition or family history, cigarette smoking, excess alcohol consumption, lack of physical exercise, polycystic ovary syndrome, mental health conditions, pregnancy, impaired glucose tolerance, sleep disturbance, ethnicity, stress and mental conditions and others (Lotfy et al. 2016). Some of these risk factors can increase the likelihood of insulin resistance and T2DM-related complications which can be avoided if the body's blood sugar levels are kept in physiological range (3.5-4.5 mM or 90-100 mg/dl or 35-40 mol/mol HBA1c) according to the Centre for Disease Control (CDC) and the World Health Organization (WHO, 2011; WHO, 2019; Lotfy et al. 2016, Harding et al 2019). In 2015 alone, more than 3.8 million people died as a result of hyperglycaemia due mainly to cardiovascular diseases (CVDs), 80% of whom are from low- and middle- income countries including Guyana (Falcigalia et al. 2009; MPH, 2011; WHO, 2020). T2DM, also known as adult- onset diabetes, was believed to affect only adults, but more recently and what is also worrying, is its prevalence among children as young as 6-12 years of age and adolescents. All races are affected but this disorder which is most prevalent in non-white populations (Adeghate and Schantter, 2006; D'Souza et al 2009; Lotfy et al. 2016; Harding 2019, Diabetes UK, 2019).

1.4 Symptoms of Diabetes

Diabetes is associated with a number of warning signs and symptoms. These include excess thirst (poly-dispsea) and hunger (poly-phasia), frequent urination (poly urea), urinary tract infection, weight loss or gain, tired and fatigue, irritability, blurred vision, slow healing of wounds, nausea, breadth odour, skin infections, darkness of the skin in areas of body creases, ulcers, tingling or numbness in hands and feet (Kumar and Clark, 2018; ADA 2019).

1.5 Long-Term complications of diabetes

If diagnosed late or being obese and indulge in unhealthy life styles (eating unhealthy foods and do not exercise regularly) or left untreated or the patients do not take their medications (non-compliable) regularly or non-pharmacological treatment, then diabetes can lead to a number of major long-term or end–organ complications/failures including retinopathy (blindness), nephropathy (kidney damage), neuropathy (damage to nerves), cardiomyopathy (heart failure) and impotence. Some other complications that may accompany diabetes include foot ulcers, Alzheimer's disease, skin and oral ulcers, hearing defects, exocrine gland deficiencies and many others (Aparicio et al 2004; Papatheodorou et al 2016; Harding et al 2019; ADA, 2019; Diabetes UK, 2019). More than 90% of diabetic patients will subsequently die from either heart (80%) or kidney (10%) failure or both. As such, it is of paramount importance to understand how diabetes can induce heart failure or diabetic cardiomyopathy and what can be done to prevent and/or delay diabetic cardiomyopathy (Adeghate and Schantter, 2006; D'Souza et al, 2009; 2014; Lotfy et al, 2016; Papatheodorou et al, 2016; Harding et al 2019; Alomar et al, 2020)

1.6 How does diabetes affect the body?

During elevated or uncontrolled level of blood glucose (hyperglycaemia), the body produces a number of endogenous pathological compounds called oxidants which are classified as reactive oxygen species (ROS such as $2O^-$, H_2O_2 and others) or reactive carbonyl species (RCS). One particular RCS is methylglyoxal (MGO) which is elevated to high pharmacological levels. (Figure 1.1 is a flow diagram illustrating the different pathways whereby hyperglycaemic can lead to the production of and elevation in MGO level in the body. This is due to an increase in the activity of the enzyme vascular adhesion protein-1 (VAP-1) that synthesising it and a decrease in the activity of the enzyme (glyoxylase-1) that metabolising it in the vascular smooth muscle cells in the different organs of the body. Figure 1.2 is another flow diagram showing the different mechanisms by which elevated MGO can induce excitation-contraction coupling (ECC) dysfunction and subsequently to diabetic cardiomyopathy or heart failure or even sudden cardiac death. Not only in the heart, but also in the kidneys, the eyes, the nerves and other organs, MGO exerts a deleterious effects resulting in death of some cells (apoptosis), enlargement and disarray of the structure of the muscles and other tissues which are associated with an elevation of transforming growth factor beta-1 (TGF-beta-1) which in turn elicits hypertrophy of the heart and infiltration of fibrosis or stiffness of the myocardium (D'Souza et al. 2009; Alomar et al. 2016; 2020). These processes lead to a derangement in a number of contractile proteins and cation channels including cellular calcium homeostasis (elevated diastolic calcium) resulting in the development of heart failure or diabetic cardiomyopathy. As a result, remodelling of the heart occurs so that it can maintain its function to pump blood around the body but not at physiological level. With time, the heart becomes severely damaged, enlarged and weak leading to heart failure (HF) and sudden cardiac death (SCD). The question which now arises is: what can be done to prevent and also to delay the diabetes-induced hyperglycaemic and subsequently, diabetes-induced damage to different organs of the body and long- term complications. There are a few therapeutic factors including orthodox drug, gene therapy and non-pharmaceutical treatments to reduce blood sugar to almost physiological level thereby preventing organ failure in the body (D'Souza et al, 2009; 2014; Lotfy et al. 2016; Day and Bailey 2018; Janez et al 2020; Alomar et al. 2016; 2020).

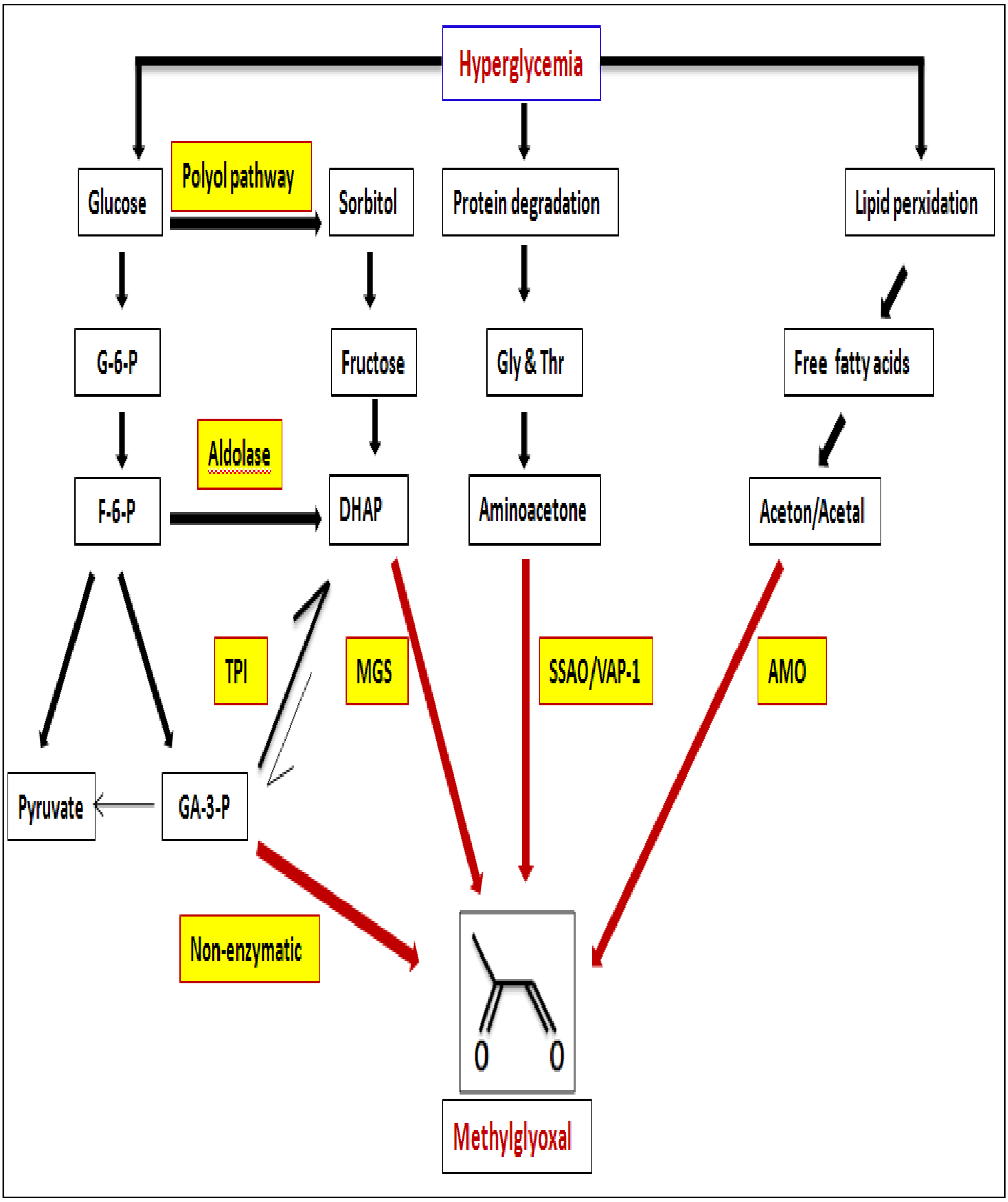


Figure 1.1: A flow diagram showing the different pathways whereby hyperglycaemic can lead to the production of and elevation in methylglyoxal (MGO) level in the body (Taken from Alomar et al. 2016).

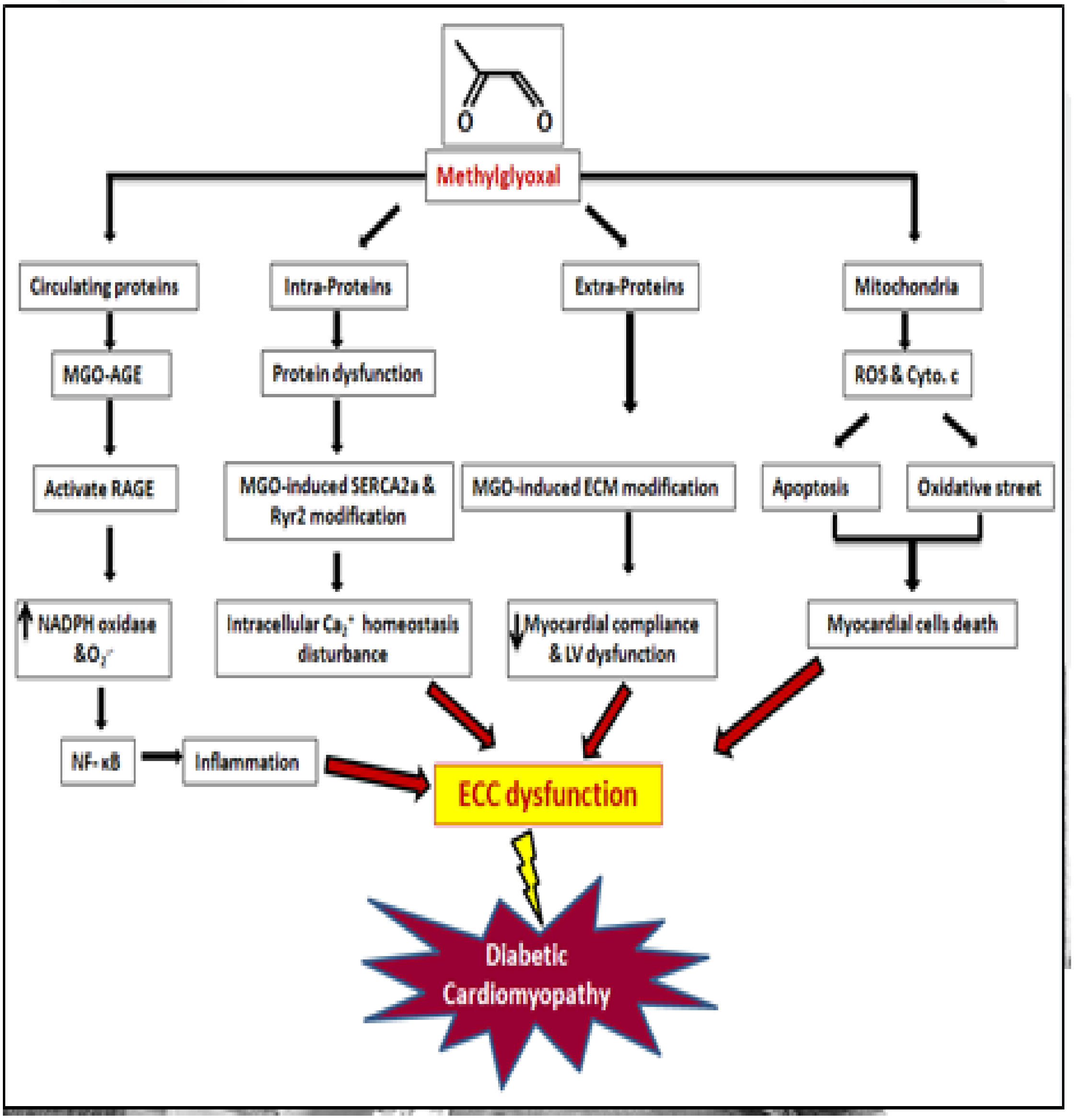


Figure 1.2: Flow diagram showing the different mechanisms by which elevated methylglyoxal can induce excitation-contraction coupling (ECC) dysfunction and subsequently to diabetic cardiomyopathy or heart failure or even sudden cardiac death (Taken from Alomar et al. 2016).

1.7 Diagnosis of DM

According to the World Health Organization (WHO, 2011), diabetes is diagnosed if the (venous) fasting plasma glucose value is ≥ 7.0 mmol/L (125 mg/dL or HBA1c of 48 mmol/mol or 6.5% and above), or the casual plasma glucose value is ≥ 11.1 mmol/L (200 mg/dL), or the plasma glucose value 2 hours after a 75 g oral load of glucose is ≥ 11.1 mmol/L (200 mg/dL) (Heisler, 2005; Diabetes UK, 2015). Universally, diabetes is now diagnosed by a well reliable **'gold'** standard test called HBA1c and value of 6.5% or 48-50 mol/mol and above confirms diabetes (Heisler, 2005; ADA, 2010; Mayo-Clinic, 2018; ADA, 2019; Diabetes UK, 2019). In terms of the value, it is equivalent to 7 mM in the United Kingdom or 125 mg /dL in the USA. Any levels just below these numbers (42-47 mol/mol or 6.0-6.4%) are classified as prediabetes, and further below are classified as either low normal, normal or high normal values (21-41 mol/mol or 4.0-5.9%). In the early days, prior to the development of diabetes diagnostic kits, clinicians and people use to taste the sweetness of the urine as a form of diagnosis (Mayo Clinic, 2018)

1.8 Management of Diabetes Mellitus

Diabetes management is achieved by lowering blood glucose to a normal glycaemic state to reduce the risk of long-term damage to organs and tissues of the body resulting from sustained hyperglycaemia (Papatheodorou et al, 2016; Mayo-Clinic, 2018; Harding et al, 2019; Diabetes UK, 2019; ADA, 2019). This strategy will indeed enable the patient to maintain as near normal healthy lifestyle as possible while ensuring an adequate control of his or her diabetes. In order that these aims are achieved, it is of paramount importance that patients are educated about their condition, receive dietary counselling, initiate a programme of regular exercise and adhere to their oral hypoglycaemic medication, non-pharmacological therapy or other agents such as insulin in addition to frequent monitoring of their blood glucose (Martinus et al, 2006; Lotfy et al. 2016; Papatheodorou et al 2016; Harding et al 2019).

There is overwhelming evidence that early detection via early screening and aggressive control of elevated blood glucose in both TIDM and T2DM can significantly reduce long-term complications such as cardiomyopathy, nephropathy, neuropathy, retinopathy and may also reduce the occurrence and severity of large blood vessel disease leading to a better quality of life for the patients (Williams and Pickup, 1998; Lotfy et al, 2016; Papatheodorou et al, 2016; Harding et al, 2019 Alomar et al, 2020).

1.9 Drug therapies

(A) Treatment of diabetes with insulin: Exogenous insulin is the main form of treatment for patients with T1DM (Shah et al, 2016). Exogenous insulin is also important in about 30% T2DM patients when blood glucose levels cannot be controlled by diet modification, weight loss, exercise, and oral medications. Insulin medication should be administered in a manner that mimics the natural pattern of insulin secretion by a healthy pancreas. The complex pattern of insulin secretion by the pancreas is difficult to duplicate. Still, adequate blood glucose control is achieved with diet modification, regular exercise, home blood glucose monitoring, and multiple exogenous insulin injections daily. Human insulin is now widely used. Insulin now comes in a variety of preparations that differ in time of onset and length of action. As a result of these differences, combinations of insulin are often used to allow for a more tailored regimen of blood sugar control. Typically, a patient may take an injection of long-acting insulin in the morning and evening to provide a baseline of insulin throughout a 24-hour period. In addition, the same patient may take an injection of short-acting insulin just before meals to cover the increase in carbohydrate load after eating (Alterman, 1997; Williams and Pickup, 1998; Bilous, 2002; Cummings et al, 2015; Lotfy et al, 2016; Papatheodorou et al 2016; Harding et al, 2019; ADA 2019; Diabetes UK, 2019; Janez et al, 2020).

1.10 Delivering insulin to the body.

Many patients with T2DM and all those with T1DM require insulin to keep blood glucose in a target range. The most common route is subcutaneous insulin injection. There are many different methods of delivering insulin to the body and the number of available insulin preparations is growing as are the methods for administering exogenous insulin (Shah et al, 2016).

(A) Pre-filled insulin pens: In the past, insulin was available only in an injection form. This involved carrying syringes (which a few decades were made of glass and required sterilization), needles, vials of insulin, and alcohol swabs. Patients often found it difficult to take multiple shots a day, and as a result, good blood sugar control was often compromised. Many Pharmaceutical Companies are now offering discreet and convenient methods of insulin delivery. A small pen-sized device holds an insulin cartridge (usually containing 300 units). Cartridges are available in the most widely used insulin formulations. The amount of insulin to be injected is dialled in by turning the bottom of the pen until the required number of units is seen in the dose-viewing window. The tip of the pen consists of a needle that is replaced with each injection. A release mechanism allows the needle to penetrate just under the skin and deliver the required amount of insulin. The cartridges and needles are disposed of after use and new ones are simply inserted. These insulin delivery devices are discreet and less cumbersome than traditional methods (Alterman, 1997; Williams and Pickup, 1998; Shah et al, 2016; ADA, 2019; Janez et al, 2020).

(B) Insulin pump: Advance in insulin delivery to diabetic patients is the insulin pump which is composed of a pump reservoir similar to that of an insulin cartridge, a battery-operated pump, and a computer chip that allows the user to control the exact amount of insulin being delivered (Allerman, 1997; Shah et al, 2016). Currently, pumps on the market are about the size of a bleeper. The pump is attached to a thin plastic tube (an infusion set) that has a soft cannula (or needle) at the end through which insulin passes. This cannula is inserted under the skin, usually on the abdomen. The cannula is changed every 2 days. The tubing can be disconnected from the pump while showering or swimming. The pump is used for continuous insulin delivery, 24 hours a day. The amount of insulin is programmed and is administered at a constant rate (basal rate). Often, the amount of insulin needed over the course of 24 hours varies depending on factors such as exercise, activity level and sleep. The insulin pump allows for the user to programme many different basal rates to allow for this variation in lifestyle. In addition, the user can programme the pump to deliver a "bolus" during meals to cover the excess demands of carbohydrate ingestion. Over 100,000 people worldwide are using the insulin pump. This number is growing dramatically as these devices become smaller and user friendlier. Insulin pumps allow for tight blood sugar control and lifestyle flexibility while minimizing the effects of low blood sugar (hypoglycaemia). At present, the pump is the closest device on the market to an artificial pancreas. Naturally, the next step would be a pump that can also sense blood sugar levels and adjust the insulin delivery accordingly. Much research is currently concentrated on this area of and possibly, even within the next few years, a prototype device will be available for trial (Alterman, 1997; Cummings et al, 2015; Shah et al, 2016; ADA 2019; Janez et al, 2020).

(C) Inhalation: Another promising route of insulin administration is through inhalation. Inhaled insulin is currently being tested but at this moment, it has not been approved by the United States Food and Drug Administration (FDA). Many devices are available that allow for other medications to be used in this manner, the best example of which is asthma therapy. Insulin is not absorbed through the bronchial tubes (airways) and must reach the air sacks at the end of the bronchial tubes (alveoli) to be absorbed. Once in the alveoli, insulin can be absorbed and enter the bloodstream. Currently, powdered inhalers and nebulisers are being studied to determine which delivery system is the most reliable. The safety of inhaled insulin is currently under research by different companies (Cummings et al, 2015; Shah et al. 2016; Papatheodorou et al, 2016; Harding et al, 2019; ADA, 2019; Janez et al, 2020).

(D) Intranasal, trans-dermal and pill: Other routes for the delivery of insulin have also been tried and intranasal insulin delivery was thought to be promising. However, this method was associated with poor absorption and nasal irritation. Trans-dermal insulin (skin patch delivery) has also yielded disappointing results to date. Insulin in pill form is also not yet effective since the digestive enzymes in the gut can break it down (Shah et al, 2016).

1.11 Treatment of T2DM patients with either non-pharmacological interventions or with conventional orthodox drugs

(A) Non-pharmacological interventions: T2DM patients should adhere to weight loss, diet modification by eating the right diet and exercise in the management of their diabetes especially if it is diagnosed at an early stage in life (Daveendra et al, 2018). Many clinicians do not like to prescribe drug therapy for T2DM during early diagnosis. In steady, they recommend that the patients should start with a healthy lifestyle to control their blood glucose level. These include losing weight if they are obese, exercise regularly and modify their normal diets to an anti-diabetic diet. They must also educate themselves about diabetes and its long-term complications and how diet modifications and regular exercise can control their diabetes. If these initial treatments do not control their blood glucose level, then medications are prescribed. Many T2DM medications work by increasing the insulin output (synthesis and release) by the beta cells of the endocrine pancreas. The challenges that remain are to determine how high-risk individuals should be identified, and how lifestyle changes of healthier diet and regular physical activity can be sustained. In order to achieve this, it may be necessary to give the diabetic patients psychological intervention training (Martinus et al, 2006; Daveendra et al, 2018; Curan et al, 2020).

1.12 Pharmacological interventions: There are several different T2DM drugs to treat the disorder. They include the following-

(A) Sulfonylureas and meglitinides: Sulfonylureas: These drugs act by increasing the endogenous insulin output by the beta cells of the endocrine pancreas. Some of these medications belong to a class of drugs called sulfonylureas. Sulfonylureas lower blood glucose levels by increasing the release of insulin from the pancreas. Older generations of these drugs include chlorpropamide and tolbutamide, while newer drugs include glimepiride (Amaryl), glipizide (Glucotrol) and glyburide (Dia Beta). These drugs are effective in rapidly lowering blood sugars but run the risk of causing hypoglycaemia. In addition, they are sulfa-compounds, and should be avoided in patients with sulfa-related allergies (Alterman, 2002; Bilous, 2002; Williams and Pickup, 1998; Cummings et al, 2015; Bailey and Day, 2018). On the other hand, meglitinides can also targets the pancreas to promote insulin synthesis and release. Unlike sulfonylureas that bind to receptors on insulin producing beta cells, meglitinides exerts its effect via a separate potassium-based channel on the cell surface. Two other drugs, nategnilide (Starlix) and repeglinide (Prandin) are short acting agents that are taken 30 minutes before meals. Unlike the sulfonylureas, which last longer in the body, Prandin and Starlix are very short acting, with peak effects within one hour. Thus, they are administered up to 3 times a day just before meals. Since these drugs also increase circulating insulin levels, they may also cause hypoglycaemia (Alterman, 1997; Bailey and Day, 2018).

(B) Drugs which act on the liver to reduce glucose release: Another group of drugs called **b**iguanides has been used for many years in Europe and Canada to control blood glucose level. One such drug is metformin (Glucophage) which reduces glucose production by the liver. Like other blood glucose lowering drug, metformin does not increase insulin level and it does not elicit hypoglycaemia. In addition, metformin tends to suppress appetite, which may also be beneficial in the treatment of T2DM. Metformin may be used by itself or in conjunction with other oral agents or insulin (Alterman, 1997; Bilous, 2002; Cummings et al, 2015; Bailey and Day, 2018)

(C) Drugs which increase insulin receptor sensitivity in cells: Another class of T2DM known as thiazolidinediones can lower blood glucose by improving target cell to respond to insulin via its tyrosine kinase receptor thereby increasing the sensitivity of the cells to insulin. Troglitazone (Rezulin) was the first of this type of drug to be introduced in the market. However, because of severe toxic liver effects, troglitazone has been taken off the market. Related compounds are now available with a better safety profile. These drugs include (Actos) Pioglitazone and (Avandia) Rosiglitazone and these drugs have been effective in lowering blood sugar level in patients with T2DM. Actos and Avandia act within 1 hour of administration and are dosed daily. It is important to note that it takes up to 6 weeks to see a drop in blood glucose levels on these agents and up to 12 weeks to see a maximum benefit (Alterman, 1997; Bilous, 2002; Cummings et al, 2015; Lotfy et al, 2016; Bailey and Day, 2018).

1.13 Incretins to mimic insulin in T2DM treatment.

(A) Incretins: Incretins are a new group metabolic hormones which are synthesised by the entero-endocrine cells within the gut (Pappachan, 2015). They can act like insulin to decrease blood glucose level. Incretins are released from the gut after eating and they augment and stimulate the release of newly synthesis insulin from endocrine pancreatic beta cells of the islet of Langerhans in the body by a blood glucose –dependent process. T2DM patients do experience progressive decreases in pancreatic β-cell function (Bulter et al, 2003) and as a result, most patients require increasingly intensive treatment, including oral combination therapies followed by insulin (Turner et al, 1999). Based on the evidence, neither oral hypoglycaemic agents (OHA) nor insulin can effectively counter the 'steady, relentless decline in pancreatic (β-cell) function associated with T2DM (Amori et al, 2007; Lofty et al, 2014a, 2014b; 2016; Bailey and Day, 2018). Interestingly, it has now been shown that regular daily exercise can improve beta cell mass and function leading to newly synthesising insulin (Curan et al, 2020).

There is also an interest in therapies that are weight neutral (or to promote weight loss in overweight/obese patients). These can minimize the risk of hypoglycaemia and exploit physiological mechanisms to modify T2DM (Van-Gaal et al, 2008). Through the coordinated actions of glucagon and insulin, the healthy endocrine pancreas can maintain glucose homeostasis by preventing both hyper- and hypoglycaemia (Porte and Kahn, 1999). As such, the use of a new form of treatment has been introduced. It employs the incretin hormone or glucagon-like peptide 1 (GLP-1) which is released by the gut in response to meal intake. In turn, this can help to maintain glucose homeostasis through coordinated effects on islet alpha- and beta-cells, which produce glucagon and insulin, respectively (Lotfy et al, 2014a; 2014b; 2016). The final response is an inhibition of glucagon output and enhancement of insulin secretion in a glucose-dependent manner. Some of the biological effects of GLP-1 include slowing gastric emptying and decreasing appetite, lower haemoglobin HbA1c, body weight, and postprandial glucose excursions in humans, all these effects leading to a significant improve beta-cell function *in vivo* (animal data). These novel incretin-based therapies offer the potential to either reduce body weight or prevent weight gain, although the durability of these effects and their potential long-term benefits need to be studied further. Moreover, patients with oral treatment experience an element of failure and it is of paramount importance to identify factors which are consistent as well as inconsistent with the use of each incretin treatment thereby delineating areas for future research (Pappachan, 2015; Lotfy et al, 2014a; 2014b; 2016; Bailey and Day, 2018).

1.14 Nondrug therapy or life-styles changes

Some non-pharmacological factors which can help to regulate blood glucose to almost physiological level include regular daily exercise, body weight reduction, diet modification, gene therapy and the use of non-orthodox medicines obtained from plants and other sources (see later). In newly diagnosed T2DM patients, many clinicians prefer to prescribe cost-effective non-pharmacological therapies as a form of treatment initially. Patients will be asked to modify their diets including eating less, cut down on sugar, carbohydrates and fast foods, stopped snacking and binging constantly, drink less fizzy and alcoholic drinks, monitor their weight loss and participate in moderate daily exercise of about 30 minutes daily. They will also be asked to monitor their blood glucose level on a weekly basis. If these non-pharmacological interventions are unable to control their blood glucose level, then the patients will be prescribed combination therapy which they must be adhere to in order to a good hypoglycaemic control (Martinus et al, 2006; Daveendra et al, 2018; Bailey and Day, 2018; Curan et al, 2020).

1.15 Combined therapy

Some of therapies can be prescribed individually or in combination. A number of clinicians support combination therapy. However, they have recommended that diabetic patients should take their prescribed medications daily, but they should also participate daily in moderate exercise, reduce their weights if their basal metabolic index (BMI) is over 25 and moreover, modify their diets to reduce sugar and carbohydrates intake (Massi-Bennedetti and Orsini-Federici, 2009). There is much evidence in the literature that in human studies with T2DM, diet modification, weight loss and regular daily exercise can reduce blood glucose level to almost physiological range. Similarly, daily consumption of a small amount (10-20 grams) of bitter melon *(Momordica charantia)* can also reduce blood glucose level *to* almost control value either with or without orthodox medications (Singh et al, 2017; Smail et al, 2018; Diabetes UK, 2019).

1.16 Exercise as a therapy for DM

Daily physical exercise is a major therapy to treat different diseases in the body including cancer, cardiovascular diseases, stress, obesity and both T1DM and T2DM. It is now universally recognised and accepted that exercise is critical in the treatment and prevention (management) of DM and this is supported by many published papers in the literature (Martinus et al. 2006; Smail et al, 2018; Hamasaki, 2016; Yani et al, 2018; Curan et al, 2020; Wagenmakers, 2020; Heiston et al, 2020). Physical activity (or prescription of exercise therapy) improves glucose control and reduces the risk of CVDs and mortality in T2DM patients. The best time to exercise is after a meal employing either aerobic or resistance exercise for 30 minutes daily or 3 hours weekly. Some forms of exercise include swimming, walking, stretching, dancing, use of the gym, cycling etc. These induce beneficial hypoglycaemic level of blood glucose. Exercise reduces the risk of CVDs, decreases daily insulin requirements, reduces stress and improved the quality of life of the patients. The question which people normally asked is: How does physical activity prevent or manage hyperglycaemia in patients with diabetes. The answer is still debatable. It is the belief that by exercising cell glucose in the body is depleted and as such the starved cells take up glucose. There is also evidence that exercise can improve beta cell mass (proliferation) and function (synthesis and secretion of new insulin), thereby increases the ability to secrete insulin from beta cells in response to a glucose stimulus (Curan et al, 2020). Exercise can also activate molecular signals that bypass defects in insulin signalling in skeletal muscles resulting in insulin -independent increase in glucose uptake. Exercise sensitizes the action of insulin (newly released) via tyrosine kinase activation. Exercise can also improve adipose-pathy (excess fat tissues) and insulin sensitivity in obese and pre-diabetic patients (Curan et al, 2020; Heiston et al, 2020; Wagenmakers, 2020).

1.17 Diet modification

Dieting and life-style changes are the cornerstone in the management of DM especially since it is important in lowering blood glucose and in preventing DM, managing existing DM and preventing or at least, slowing the rate of development of diabetes-induced-long term complications (Franz et al, 2002). Nutrition and all forms of diabetes management assisted by a strong nutrition plan for the patients can help to reduce the exaggerated risk for atherosclerotic (coronary) heart disease and long-term metabolic complications of DM. This is achieved via an improvement in lipid and glycaemic control (Franz et al, 2002). Some health therapists refer to this strategy as “medical nutrition therapy.” The goals of medical nutrition therapy include improving control of blood glucose levels, lipid profiles and blood pressure to reduce the risk of CVDs in patients with T2DM (Papatheodorou et al, 2016; Harding et al, 2019; Tapia and Defries, 2020). Medical nutrition therapy can reduce glycosylated haemoglobin (HbA1c) by at least 1% to 2% in patients with T2DM (Bantle et al 2008). It can also decease plasma level of low-density lipoprotein (LDL) cholesterol which is an important major risk factor in diabetes-induced CVDs (Yu-Poth et al, 1999). The rationale in employing diet modification is to eat low glycaemic index diets rich is fibres to reduce blood glucose. It is also important to avoid sugar intake ('time bomb') and unhealthy fast foods (cook your foods). It is recommended to adhere to the Mediterranean diet (Pandey et al, 2017). It is very important to control carbohydrates intake, especially white rice, white bread, potatoes, cassava, yams, sugar, sweets and others. Patients must follow and adhere to a diabetes-recommended diet rich in whole brown grain, cereal rich fibre products and non-oil seed pulses, vitamin E, nuts, foods rich in carotenoids, magnesium and others. It is equally important to reduce alcohol intake and non-alcoholic drinks rich in sugar. Patients must also lose weight especially if his or her BMI is 25 or over. Obesity leads to diabesity. The patients must also educate him or herself about foods and drinks with low glycaemic (sugar) effect. Patients should drink more water and stay hydrated. The patients can choose to monitor his or her blood glucose level at least 2-3 times yearly. The patients must also control his or her stress level. Patients must implement portion control (use a small plate) and also get enough quality sleep. Some therapists recommend patients to drink apple cider vinegar which lowers blood glucose and to eat small amounts of anti-diabetic herbs including cinnamon, *Momordica charantia*, berberine, fenugreek seeds and others

The current consensus for diabetic diet recommends 55 to 60 percent of energy as carbohydrate, 12 to 20 percent as protein, and less than 30 percent fat. Total cholesterol intake should be less than 300 mg per day. Fibre appears to have distinct benefits in improving glucose and lipid levels and therefore, an intake of up to 40 g per day or 15 to 25 g/1,000 kcal of food is recommended (Diabetes UK, 2019).

1.18 Vegetarian Diet

Vegetarian diets that are well planned and low in fat can also be nutritionally adequate when compared to other therapeutic diets and this should be considered for long- term use in obese and diabetic patients (Bantle et al, 2008; Barnard, 2009). Generally, vegetarian diets that low in fat are usually consisted of less saturated, monounsaturated, and trans-fat with greater amounts of fibre, vitamin C, folate, magnesium and iron, but however, low in vitamin D, calcium and zinc (Barnard et al, 2009). The potential cardiovascular benefit may be especially important for individuals with diabetes, for whom cardiovascular disease is a main cause of premature mortality. Other studies have also shown that low fat vegetarian diets have additional benefits such as reduced need for insulin and oral diabetic medications, all of which help to improve glycaemic control (Barnard et al, 2009).

1.19 High Fibre Diet

Carbohydrate quality, such as total intake of fibre is consistently been associated with a reduced risk for obesity as well as T2DM (Barclay et al, 2008; Livesey et al, 2009). In a study by Al Essa et al (2016), they reported that diets with higher fibre intake and lower starch-to-fiber intake ratio were significantly associated with lower concentrations of HbA1c in diabetes-free female subjects.

1.20 Minerals, amino acids, and vitamins

It is well known that insulin resistance and glucose uptake may be affected by deficiency of micro-nutrients. In a study by Yajnik et al, (2008), they reported that increase homocysteine levels and low maternal vitamin B_{12} and high folate status may contribute to the epidemic of adiposity and T2DM in India. Either magnesium supplementation or increased intake of magnesium-rich foods such as nuts may be seen as an important tool in the prevention of T2DM in obese children. Similarly, cations such as magnesium, calcium, potassium, zinc, chromium, and vanadium and others appear to have associations with insulin resistance or its management (Deewania and Gupta, 2006). Amino acids, including L-carnitine, taurine, and L-arginine, might also play a role in the reversal of insulin resistance. Other nutrients, including glutathione, coenzyme Q10, and lipoic acid, also appear to have therapeutic potential (Kelly, 2000).

1.21 Body weight reduction

Overweight and obesity are two risk factors for prediabetes, diabetes, and insulin resistance (IR) and as such weight loss is essential as major therapeutic objective in the management of prediabetes, diabetes and IR of the individual (Ebeling et al, 1998; Norris et al, 2005; Kelley et al, 2008; Lotfy et al, 2016). Long-term weight loss is very difficult for most people to accomplish, and this is probably due to the fact that the central nervous system plays an important physiological role in regulating energy intake and expenditure. Some studies conducted on short term basis suggested that moderate weight loss (5% of body weight) in subjects with T2DM is associated with decreased insulin resistance, improved measures of glycaemia and lipidemia and reduced blood pressure (Klein et al, 2004). There is also evidence in the literature that on a longer-term basis (≥52 weeks), using pharmacotherapy for weight loss in adults with T2DM, there was a modest reduction in weight and HBA1c (Norris et al, 2005). Other studies have shown that psychological intervention can help in adhering to lifestyle changes (Martinus et al, 2016).

1.22 Education and self-care management of diabetes

A number of studies have also shown that education (knowledge), perceptions and awareness relating to diabetes self-care management and its long-term complications can either delay or prevent several diabetes-induced diseases giving the diabetic patients a better quality of life (Brown et al, 2002; Schmid, 2002; Heisler, 2006; WHO, 2011). The incidence and prevalence of T2DM is rapidly increasing with time, as is the frequency of complications which are caused by this metabolic disorder. In 2000, approximately 350,000 persons died from diabetes in Latin America and the Caribbean. Of all the deaths in the Caribbean in 2000, 35% were caused by cardiovascular diseases, 11% by diabetes and 5% by cancer. Diabetes accounts for about 7.7% of the total annually recorded deaths in Guyana (MPH, 2006; 2009; 2016; 2017; D'Souza et al, 2009; Iqbal et al, 2013; Singh et al, 2017). A cross sectional observational study was conducted by Schillenger (2002) to examine the association between health literacy and diabetes outcomes among patients with T2DM employing 408 English and Spanish speaking T2DM patients, above the age of 30 years. The results showed that after adjusting for patients' socio-demographic characteristics, depressive symptoms, social support, treatment regimen and years with diabetes, there was a 1-point decrement on the short-form Test of Functional Health Literacy in Adults (s-TOFHLA) score and the HbA_{1c} value increased by 0.02 (P=.02). The researcher found that patients with inadequate health literacy were less likely than patients with adequate health literacy to achieve tight glycaemic control (HbA_{1c} 7.2%; adjusted Odds Ratio [OR], 0.57; 95% confidence interval [CI], 0.32-1.00; P=.05). Moreover, they were more likely to have poor glycaemic control ($HbA_{1c} \geq 9.5\%$; adjusted OR, 2.03; 95% CI, 1.11-3.73; p=.02). They also reported having retinopathy (adjusted OR, 2.33; 95% CI, 1.19-4.57; P=.01) (Shrivastava et al, 2013).

Another related study by Brown et al. (2002) was performed to investigate the effects of a culturally competent diabetes self-management intervention in Mexican Americans with T2DM. In this quantitative study, a total of 256 individuals were randomly selected, between the ages 35 and 70 with T2DM. The intervention consisted of 52 contact hours over 12 months. Ultimately, it was found that the experimental groups showed significantly lower levels of

HbA_{1c} and fasting blood glucose at 6 and 12 months and higher diabetes knowledge scores. In another study involving self-management education for adults withT2DM on glycaemic control (Schmid, 2002), it was found that on average, the intervention decreased glycosylated haemoglobin (HbA1c) by 0.76% (95% CI 0.34 –1.18) more than the control group at immediate follow-up; by 0.26% (0.21% increase - 0.73% decrease) at 1–3 months of follow-up; and by 0.26% (0.05– 0.48) at ≥4 months of follow-up. HbA1c decreased more with additional contact time between participant and educator; a decrease of 1% was noted for every additional 23.6 hours of contact (Brown et al, 2002).

It is unclear as to what extent knowledge affects T2DM but like the proposed study, evidence presented in previous studies demonstrated the importance or effectiveness of knowledge on this issue. In another study on effectiveness of self-management training in T2DM, it was reported that educational interventions that involved patient collaboration may be more effective than didactic interventions in improving glycaemic control, weight, and lipid profiles (Guariguata et al, 2014). Another study investigated the frequency and correlation of knowing one's most recent HbA_{1c} test result and whether knowing one's HbA_{1c} value is associated with a more accurate assessment of diabetes control and a better diabetes self-care management understanding, self-efficacy, and behaviours related to glycaemic control. In this cross - sectional survey, the sample size consisted of 686 adult T2DM patients from the USA. More than 66% of respondents reported that they did not know their last HbA_{1c} value and only 25% accurately reported that value.

Evidence from multivariate analysis suggests that more years of formal education and high evaluations of provider thoroughness of communication were independently associated with HbA_{1c} knowledge. Respondents who knew their last HbA_{1c} value had higher odds of accurately assessing their diabetes control (adjusted odds ratio 1.59, 95% CI 1.05–2.42) and better reported understanding of their diabetes care ($p<0.001$). Additionally, it was found that patients' HbA_{1c} knowledge was not associated with their diabetes care self-efficacy or reported self-management behaviour (Norris, 2001; WHO, 2011). Another related study by Odili, (2011) revealed the difference in the level of knowledge among certain groups found that of the 181 participants, 121 (66.9%) passed the diabetic knowledge test. There was a higher pass in the female group than in the male group, with 69.8% of the female population passing compared to 60% of the male. The overall data across the three clinics indicated a better pass by the Indian than the African population, with 75.9% of the Indian patients passed in comparison to 52.2% of the African patients. African patients had a problem with regards to their diabetes understanding, especially with T2DM and who were above the age of forty years (Murata, 2003; Strivastava et al, 2013).

In a country like Guyana where there are numerous health service providers, one would expect the prevalence of long-term complication cause by T2DM to be minimal and people should be well-informed. Nevertheless, more people still died in Guyana from DM compared to other diseases. For example, between 2000 and 2004 a total of 19,411 people died in Guyana, and they included 1,487 diabetic patients representing 16% of the deaths with equal number of males and females (Bachwani and Bach, 2002; MPH, Guyana; 2006; 2009; 2016). It is stated that a high level of knowledge or awareness among diabetics will allow for proper self-care management (Murat, 2003; Moodley and Rambiritch, 2007). Based on the literature, it can be said that knowledge indeed plays a vital role in the self-care management of T2DM. It was clearly illustrated how knowledge affects the outcome of the disease, regardless of either race or the geographic location of the various sample populations (MPH, Guyana, 2006; 2009; 2016; 2017).

Figure 2.3: Map of Guyana showing the different regions and its surrounding neighbours (Goggle map).

1.23 Noncommunicable or chronic diseases (NCDs) globally

The World Health Organization (WHO, 2018; 2021) identified chronic non-communicable diseases (NCDs) or chronic diseases (CDs) as cardiovascular (heart and blood vessels) diseases (CVDs), stroke, obesity, cancer, chronic respiratory diseases, cerebrovascular disease, kidney failure, dental diseases and diabetes mellitus (DM) (WHO, 2010; 2011; 2014; 2015; 2018; 2021). CVDs are further classified into heart failure or cardiomyopathy, hypertension, atherosclerosis, coronary artery diseases, sudden cardiac death, arrhythmias, and others (WHO, 2018; Jailobaeva et al, 2021). Chronic diseases are often viewed to affect old people primarily. Moreover, chronic diseases are among the most common, costly and preventable of all health problems, and they represent a growing burden for society globally (Ward et al, 2012). They are recognized as a growing international socio-economic and public health problem, accounting for over 36 million of the 57 million deaths worldwide in 2008 (WHO, 2011). Currently, it is estimated that NCDs kill 41 million people each year, equivalent to 71% of all deaths globally. Moreover, 15 million people die from NCDs between the age of 30-69 years of age and over 85% of these are premature deaths, especially in low- and middle- income countries throughout the world (WHO, 2021). The major risk factors for NCDs include smoking, environment pollution, alcohol intake, physical inactivity, and unhealthy diets. Detection, screening and treatment of NCD as well as palliative care are key components to reduce NCDs and or to prevent premature deaths. Metabolic risk factors for NCDs include hypertension, overweight and obesity, hyperglycaemia and hyper-lipidemia (WHO, 2018). In 2011, the WHO predicted that the proportion of the burden of NCDs is expected to increase to 75 % by the end of 2020 (WHO, 2010; 2011;2021; Jailobaeva et al, 2021).

Guyana has a growing epidemic of NCDs among its population. This is because of globalization, increased urbanization, alcoholism, smoking, physical inactivity, unhealthy diet, population ageing, behavioural, and the inadequacies of existing health promotion, disease prevention, and diagnosis and management efforts. The Ministry of Public Health reported that in 2009, NCDs accounted for over 60% of deaths amongst males and over 70% of deaths amongst females (MPH, 2009). In 2016, The Ministry of Public Health reported that NCDs account for 70 % of all deaths and with the number one cause of premature deaths before age 70 years (MPH, 2016).

1.24 Diabetes as a NCD in Guyana

Guyana was a former British colony (British Guiana) situated in upper region of the continent of South America. It is surrounded by the Atlantic Ocean from North to South with a coastline of 270 miles, Venezuela by North West, Surinam by the East and Brazil by South and South West. Guyana became an independent country in 1966. The country has an area of 83,000 square miles, the same as the United Kingdom and it divided into ten geographical regions (see Figure 2.3). In 2016, PAHO (2019) reported that Guyana had a population of about 775,000 people with about 69,000 (8.9%) reported cases of adult diabetics in 2016 (Bachwani and Back; 2005; MPH, Guyana, 2006; 2009; 2016; Singh et al, 2011; PAHO 2019). It is estimated that 25,000 cases (3.2%) were undiagnosed, and 175,000 people (22.7%) had pre-diabetes. These numbers represent about 33.47 % of the diabetes-related population comprising of Indo-Guyanese, Afro-Guyanese, Native-Amerindians, Chinese, European and people of Mixed Races.

1.25 Overweight and Obesity

In the current climate of health and nutrition, the global trend is that more than 50% of the world's population will either be obese or overweight by 2030. Obesity is also the major cause of such comorbidities as DM, CVDs, dementia, cancer and chronic pain and others (So and Yadav, 2020; Tapia and Defries, 2020; Tapia and Dhalla, 2022; Sharma et al 2022). Similar to diabetes mellitus, obesity is a major NCD, and it is also a major global health problem currently affecting more than 700 million adults and more than 2 billion people are over- weight. Both obesity and overweight are defined as an abnormal excessive fat accumulation in the body leading to diabetes, cancer, hypertension, and heart diseases over time. What is now worrying is that children as young as 5-8 years of age are either overweight or obese amounting for 40 million worldwide (Riley et al, 2005; Lopez 2012; Ng et al, 2014; Cilia et al, 2019; Tapia and Dhalla, 2022; Sharma et al, 2022). Comparing current time with 1975, over weigh has more than triple in number. Obesity and over-weight are due to an imbalance between calories (fatty food) intake and expenditure combined with sedentary lifestyle. Many people are too lazy to participate in physical activities. Obesity is defined as having a basal metabolic index (BMI) of 30 and over. Overweight is when the BMI is between 25 and 29 and normal weigh is when the BMI is between 20—24, whereas under body weight is when the BMI is less than 18. Obesity is now deemed as a major NCD leading to risk of chronic conditions, reduced quality of life and subsequently, to premature death (WHO, 2018; Tapia and Defries, 2020; Tapia and Dhalla, 2022).

In 2016, the worldwide prevalence of overweight was 39.8% and obesity was 13.1%. Within the region of America, 62% of persons were overweight and 28.6 % were obese (WHO, 2016). These values make the Americas the most overweight and obese region in the world and Guyana is one of them (PAHO, 2014). Both overweight and obesity have been on the increase in Guyana over the years. In 2016, PAHO (2016) reported that almost half (51,1%) of the adult population between the ages of 18 to 69 years at the last 2016 census was overweight and another 22% were obese. In terms of gender, 42% of males and 60% of females were overweight and 14% of males and 30% of females were obese. Moreover, people in the age range of 45 to 69 years were markedly more overweight and obese compared to adult population between 18 to 44 years. Obesity and overweight vary between genders, ethnicity, and economic status and both disorders are preventable depending on the individual (Lopez, 2012).

Some risk factors for overweight and obesity include lack of physical activity, unhealthy overeating due to constant snaking, not enough sleep, genetics, high level of stress, hypothyroidism, insulin resistance, polycystic ovary syndrome, Cushing's syndrome, some medications and others (Tapia and Defries, 2020; Tapia and Dhalla, 2022; Sharma et al, 2022).

1.26 High blood pressure or hypertension

Like obesity and diabetes, high blood pressure or hypertension is a major NCD globally affecting aver 1.2 billion people. Blood pressure is measured by 2 numbers using an equipment called a sphygmomanometer at the upper part of the hand (Elkilany et al, 2019; 2020; Mayo Clinic, 2021). The top value is referred to as the systolic blood pressure (SBP or higher number) which is the force at which the heart pumps blood around your body via the resistance arteries and arterioles. The lower number is the diastolic pressure (DBP or lower number) indicates the resistance to the blood flow in the blood vessels. Both SBP and DBP are measured in millimetres of mercury (mm Hg). The normal low-range blood pressure of a person is usually considered to be between 90/60 mm Hg (low range) and 120/80 mm Hg (normal range). High blood pressure or hypertension is considered to be mild or stage 1 at values of 140/90 mm Hg, high mild or stage 2 with values of 150/90 mm Hg. Hypertensive crisis (severe or chronic) is when systolic pressure is elevated to over 180 mm Hg and/or diastolic pressure is over 120 mm Hg, with patients needing prompt changes in medication if there are no other indications of problems or immediate hospitalization if there are signs of organ damage, especially if the person is within the age of 80 years (Roberts et al, 2017; Elkilany et al, 2019; 2020). A person is diagnosed as hypertensive when the blood pressure is measured on two different days. If the systolic blood pressure is 140 mm Hg and over and the diastolic blood pressure is 90 mmHg and over on both occasions, then the person is deemed as hypertensive (Elkilany et al, 2019; 2020; Maya Clinic, 2021).

Annually, over 18 million people usually die from CVDs worldwide and this number represents a third of all global deaths which is rising yearly (Jailobaeva et al, 2021). Hypertension is the leading cause of CVDs and it kills about 10 million people per year in the world. Hypertension is a major risk factor for heart failure (HF), heart attack, stroke, kidney failure, blindness, and even premature sudden cardiac death (SCD) (Frieden and Jaffe, 2018; Elkilany et al, 2019; 2020 Mayo Clinic 2021). The disease is responsible for about 25-50% of cardiovascular mortality and morbidity leading to an enormous healthcare cost worldwide of around $375 billion USAD annually and most is this money is borne by the patients themselves (Frieden and Jaffe, 2018). If the blood pressure of many hypertensive patients is under effective control, then this can lead to premature death (Kearney et al, 2005). Some risk factors for hypertension including unhealthy diets, physical inactivity, overweight and obesity, diabetes, stress (mental disease), long-term sleep deprivation, age, family history of high blood pressure or genetics, being of African or Caribbean origin (ethnicity), pregnancy, kidney failure, consumption of excess alcohol and salt, tobacco smoking, glucose intolerance, dyslipidemia and others (WHO, 2019; 2021; Mayo Clinic, 2021).

Of the current 1.2 billion people who have hypertension globally, most of them (two thirds) are in the younger working population and living in low-and middle- income countries like Guyana rather than higher income countries (Frieden and Jaffe, 2018; WHO, 2019). In 2015, 1 in 4 men and 1 in 5 women were hypertensive worldwide and these numbers are rising daily especially in urbanised areas (crowded Cities) of the world, compared to rural areas where people are more active (WHO, 2019). Hypertension is a prominent preventable cause of premature morbidity and mortality in the world estimating at 20% of adult population between 45-60 years of their working age, especially at the time of a stressful life. People with hypertension are at high risk and as such it is of paramount to reduce their blood pressure to normal level (Saiz et al, 2018; Elkilany et al, 2019; 2020; Mayo Clinic 2021).

The incidence of hypertension in Guyana in 2016 was very prevalent taking into consideration that the country had only about 770,000 people then. According to the WHO data published in 2016, deaths from high blood pressure in Guyana reached 320 or 4.45% of total deaths. The age-adjusted death rate was 45.77% per 100,000 of the population ranking Guyana as 18th in the world for hypertension and mortality (PAHO, 2016; 2019; WHO, 2018; 2021).

In Guyana, there is a growing epidemic of hypertension among its population. This is due to the effects of globalization, increased urbanization, alcoholism, smoking, physical inactivity, unhealthy diet, population ageing, behavioural, and the inadequacies of existing health promotion, disease prevention, and diagnosis and management efforts. The Ministry of Public Health reported that in 2009, hypertension and other NCDs accounted for over 60% of deaths amongst males and over 70% of deaths amongst females (MPH, 2009). In 2016, The Ministry of Public Health reported that this number was 70 %, representing of all deaths and is the number one cause of premature deaths before age 70 years (MPH, 2016).

1.27 Traditional plant-based medicines in the treatment of diabetes mellitus (A-K)

(A) A historical perspective of *Momordica charantia (M charantia* or bitter melon)

The prevalence of T2DM is rising globally among both older adults and many young people, especially due to their overweight and obesity. Because of the rising cost of orthodox medicines, a large number of people (almost 75% of the world's population) now turn to medicinal plants (herbal medicines) for the treatment and management of their diabetes and other basic health care needs. Humans have been using herbal medicines to treat their ailments since the dawn of mankind (Platel and Srinivassan, 1997; 1999; Garau et al, 2003; Singh et al, 2011; PAHO, 2019; Hadi et al, 2022; Hanoman et al 2022). Most orthodox or conventional pharmacological medicines are derived from plants. There are more than 53,000 different species of medicinal plants described in the literature and which have been used by mankind (Lakshmi et al, 2012). Currently, herbal medicines are staging a comeback for therapy due to resistance of the body to orthodox medicines (Pan et al, 2014). Moreover, anti-diabetic medicinal plants have been used routinely to treat DM prior to the discovery of insulin in the early 1920s. In more traditional cultures, plant-based remedies continue to be the treatment of choice for diabetes. Amongst this list of plants are- *Astocarpus altillis* (Breadfruit), *Azadirachta indica* (Neem), *Bidens alba* (Spanish-needle), *Carica papaya* (Papaw), *Cassia occidentalis* (Wild coffee), *Catharan, thus roseus* (Periwinkle), *Stachytarpheta jamaicencia*

(Burr-vine), *Syzygium cumini* (Jamoon) and *Momordica charantia* (bitter melon, caryla or corilla) (Pan et al, 2014). This study employed one plant, *M charantia* or bitter melon or corilla. As such, much emphasis will be placed on *M charantia* is this thesis (Hadi et al, 2022).

(B) Structure of *M charantia* as a herb/vine

Momordica charantia (caryla/corilla or bitter gourd or melon) is a flowering vine plant belonging to the plant family Cucurbitaceae (Ahmed et al, 1999; Garau et al, 2003; Day, 1990; Singh et al, 2011; Lakshmi et al, 2012; Hadi et al 2022). It is a slender-stemmed tendril climber, the older stem often flattened and fluted, to 6 m or more long (Figure 1.4). The bright green leaves are alternate, and they are cut into 5–7 narrow based lobes where the lobes are mostly obtuse with marginal points, to about 12 cm long and as broad. Moreover, they are very thin-textured and characteristic pungent-aromatic, and tendrils laterally inserted at the petiole-base. Like the fruits, the leaves are also bitter in taste. The flowers of the mature plants are yellow, the female on short peduncles, and the male on longer ones, short-lived. The plant bears oblong-shaped, bitter fruit that ranges in colour from pale to dark green, narrowed to both ends, 8–15 cm long, with prominent tubercles on the ribs, opening when ripe, becoming softly fleshy and revealing pendulous seeds covered with red pulp. When ripe, the green fruit turns yellow in colour and the seeds are red in colour. Although the country of origin is uncertain, the plant is widely cultivated for its fruit on fences and in thickets in tropical regions of India, China, East Africa and Central, the West Indies and South America. In India, the unripe fruit is known as caryla/corilla and is a common ingredient in many curries. Caryla is found in many Asian dishes as well. The English know it as bitter gourd or bitter melon. Another local name is balsam pear. In South America and Guyana, the plant is known as caryla or wild caryla (Sharma *et al,* 1950; Lakshmi et al, 2012; Hadi et al, 2022; Hanoman et al, 2022).

In folk medicine of South Asia, Africa, South America and the West Indies, the fruits, stems and leaves of the plant have reportedly been used as hypoglycaemic agents, purgatives, emetics and abortifacients (Sharma et al, 1950; Day et al, 1990; Sharma et al, 1996; Attaruri- Rahman and Zaman, 1989; Day, 1990; Karunanayake et al, 1984; Singh et al, 2011; Lakshmi et al, 2012; Hadi et al, 2022; Hanoman et al, 2022) and the seeds therapeutically utilized against DM (Pons and Stevenson, 1943). The insulin-like hypoglycaemic activity in the seeds was attributed to charantin and momordicine, the bitter ingredients of *M charantia* (Joseph and Jini, 2013). *M charantia* is more effective as an anti- hyperglycaemic agent when eaten uncooked (raw rather than cooking} since heat can denature the active agent(s).

(C) Preparation of extract and chemical analysis of *M charantia*

Figure 1.4 shows the *M charantia* green fruits on the tree. The fruit has to be picked green when it is more active that when it becomes ripe or yellow. The green fruit is normally chopped-up and blended (weight/volume) in water to form a green juice. Most people prefer to drink the juice rather than eating the bitter fruit since the bitter taste remains in the mouth for a long time. *M charantia* is prepared in different forms to investigate it for its hypoglycaemic action. Some commercial companies or Scientists used either the green fruits after taking out the seeds and white tissues, the leaves, the seeds or the stems or the whole fruit with the seeds and internal white tissues. Generally, most scientific, and clinical studies use the whole the green fruit without the internal seeds and white tissues. Many diabetic patients eat the green fleshy fruit raw or blend it as a juice in water (weight/volume or 1 g/ 1 ml). The recommendation by the Diabetes UK (UK Diabetes, 2019) is that no one should eat 1 ounce or 28 g daily. For laboratory studies, Scientists make different water or alcoholic soluble extracts (Figure 1.5). In these studies, they employ either micro gram or mill-gram amount(s) to study its hpoglycaemic effect using the powder form (see figure 1.6A). The whole green fruit is rich in water. At industrial level, the whole fruit of *M charantia* is dried and pulverised into a powder and then made into tablets of 50 mg, 100 mg, 200 mg, 400 mg, 500 mg and 600 mg (Figure 1.6A).

(D) Composition of *M charantia*

Previous studies (and results from this study) have chemically analysed the green fruit of the plant. The results show that it contains high amounts of vitamin C, vitamin A, vitamin E, vitamins B1, B2 and B3, as well as vitamin B9 (folate). (Bakare et al, 2010). The fruit is also rich source of minerals and inorganic compounds such as potassium, calcium, zinc, magnesium, phosphorus, iron, trace elements and it is also a good source of dietary fibre. The medicinal value of *M charantia* has been attributed to its high antioxidant properties due in part to, flavonoids, isoflavones, anthroquinones, glucosinolates, triterpene, proteid, steroid, alkaloid, inorganic, lipids, several glycosides. polypeptide-p or p-insulin, vicine, charatin, alpha, beta momocharin, kaguacin-J, alkene to C3, carbohydrates, benzanoids, alkanol C5 or more, other unknown structure (eg kakara I-B, II-A and III-B, sterol and sesquiterpene, phenolic compounds and several others most of which confer a bitter taste (Taylor, 2002; Snee et al, 2010). Figures 1.6A and 1.6 B show the yellow water-soluble dried powder and alcohol soluble extract, respectively. Figure 1.6C shows dark solid extract obtained from the alcohol as shown in figure 1.6B via rota -evaporation. The solid is normally reconstituted in DMSO to study its effects on glucose uptake in muscle cells or anti-cancer properties employing different cancer cell line *in vitro* (Cummings et al 2004; Houacine et al 2021).

Figure 1.4: Diagram showing the green fruit of *M charantia (Taken from Google Images)*

Scientific name: *Momordica charantia*
Kingdom: Plantae
Division: Magnoliophyta
Family: Cucurbetaceae
Genus: *Momordica*
Species: *charantia;* **Duration**: annual

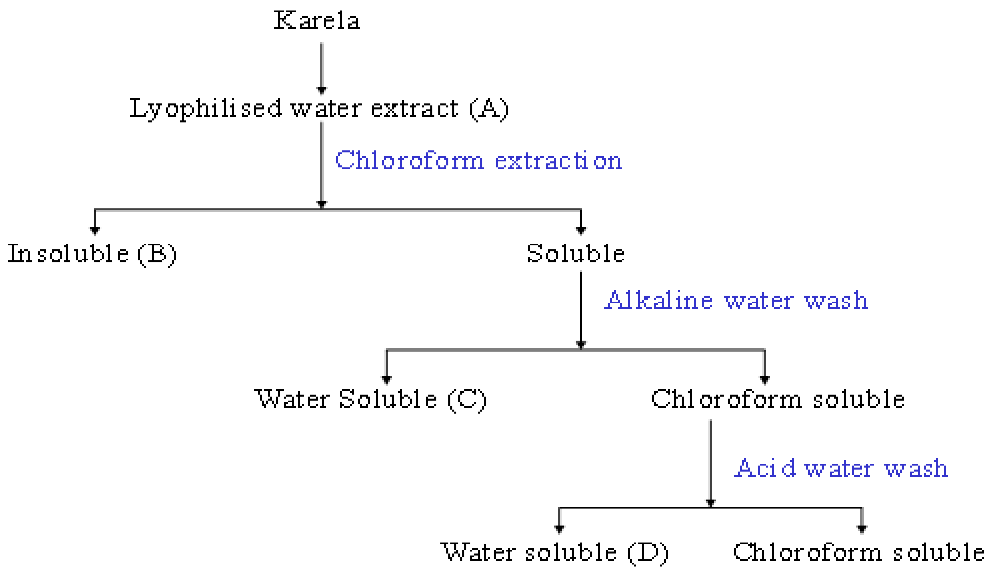


Figure 1.5: Schematic diagram showing the isolation procedures for the active ingredient(s) of *M charantia* fruit juice (redrawn from Day et al. 1990). Further purification and identification procedures employed HPLC, affinity chromatography, SDS-page, and mass spectrometry.

(A) **(B)** **(C)**

Figure 1.6: Diagrams showing (A) an example of the extracted powder of the fruit of *M charantia, (B)* an alcohol extract and (C) the solid isolated from the alcohol extract in (B) using rota-evaporation procedure.

(E) Compounds present in *M. charantia*

Currently, around 228 different medicinal compounds have been isolated from the stems, leaves, pericap, entire plant, aerial parts of the plant, endosperm, callus tissues, cotyledons and mainly the seeds and unripe fruit in different laboratories in India, Japan, USA, Thailand, Egypt, China, Taiwan, Australia, Nigeria, Pakistan, Brazil, Nepal, Philippines, and Peru (Day et al, 1990; Taylor, 2002). These different compounds have been classified into different chemical types. These include proteids, triterpenes, lipids, inorganic compounds, phenylpropanoids, carotenoids, steroids, alkalods, monoterpenes, alkene to C3, carbohydrates, benzanoids, alkanol C5 or more, other unknown structure (eg kakara I-B, II-A and III-B, sterol and sesquiterpene. Of the 228 different compounds, most of these come under the groups of proteids and triterpenes (see Taylor, 2002 for review; Hadi et al, 2022).

M charantia has many different chemical components which help medicinally either alone or when combined. One hypoglycemic agent is a steroid saponin called charantin with insulin-like chemical effect. Charantin has a molecular weight of 9.7 kDa and it is the belief that charantin is the active hypoglycemic agent of *M. char*antia. Figure 1.7 shows the chemical structures of three medicinal compounds (charantin, alpha, beta momorcharin and momordicine) extracted from *M charantia* compared to commercially available T2DM medicines and insulin (Hadi et al, 2022).

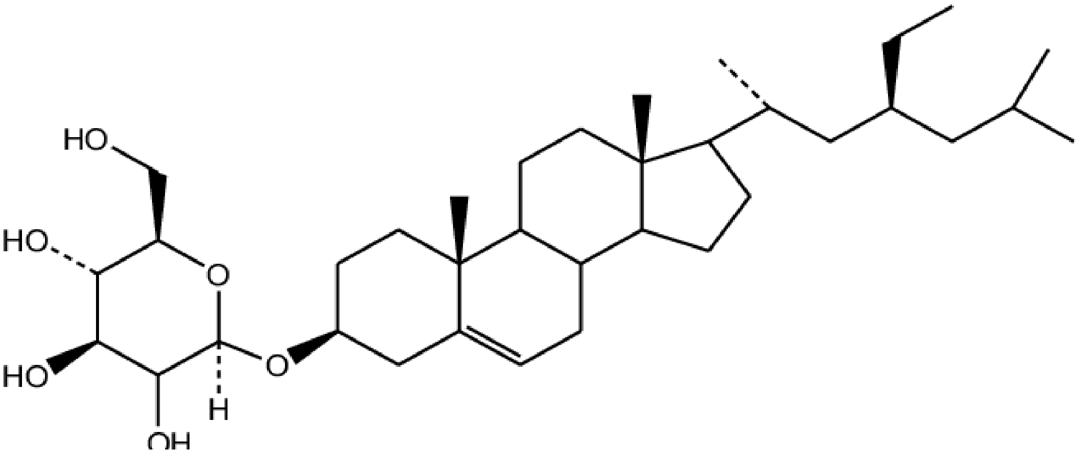
(F) Extracts and active ingredients of *M charantia*

Generally, the public used different parts of *M charantia* including the leaves, the stems and mainly the green fruits or seeds to treat their diabetes. In contrast, research scientists used the different parts of the plants to extract and to isolate anti-diabetic compounds employing different chemical extraction methods (see table 1.1). People eat the fruit raw, boil or cook the different parts (leaves, fruits, and stems) or drink the pulp of the fruit as a juice. It is believed that heat and 5boiling can denature some of the active ingredients in *M charantia*. Figure 1.5 shows a schematic diagram of the different stages of the isolation procedure for the active ingredient(s) of *M charantia* fruit employing water and organic chemicals. Initially, the fruits are chopped into small pieces and liquidized in deionized water. The green supernatant is separated from the cellulose and subsequently the water is extracted using a rota- evaporator. The residue is dried in an oven and the green powder extract is used for experimentation or for further extraction, purification and identification employing HPLC, affinity chromatography, SDS-page and mass spectroscopic methods. Two medicinal compounds extracted from *M. charantia* include, charantin, a steroidal saponin agent with insulin-like properties and momordicine, an alkaloid which is responsible for the bitterness of the fruit (Pitipanaponga et al, 2007). In laboratory and clinical *in vitro* and *in vivo* studies Scientists and Clinicians have employed different water, ethanol and ether extracts as well as other isolated biologically active phytochemicals including glycosides (momordin and charantin), alkaloids (momordicine), polypeptide-P, oils from the seeds (linoleic, stearic and oleic acids), glycoproteins (alpha–momorcharin, beta-momorcharin, lecitins and others active compounds including protein MAP30 and vicine (pyrimidine nuclease) to study their anti-cancer and hypoglycemic properties using both human and animal models (see tables 2.2-2.5; Taylor, 2002; Singh et al, 2017). Of these constituents, charantin, insulin-like peptides and alkaloids possess hypoglycemic properties. They are more effective when they are combined and they produce effects almost similar to the crude water) soluble extract (Taylor, 2002; (Singh et al, 2017).

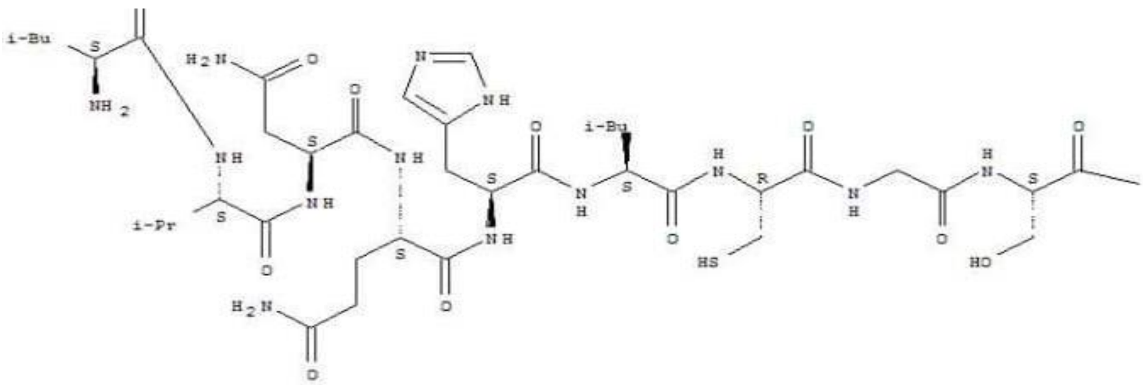
Table 1.1: Some chemical extraction procedures to prepare extracts of *M charantia* and anti-diabetic compounds (Taken from Hazarika et al. 2012).

1. *M charantia* blended with water
2. Water soluble extract,
3. Alcohol soluble extract
4. Dried pulverised powder of bitter melon (used to make tablets and capsules)
5. Charantin and vincine (isolated compound) with insulin-like properties
6. Momordenol and momordecilin (isolated compounds) with insulin –like properties
7. Polypeptide-p (isolated compound) –with insulin like properties

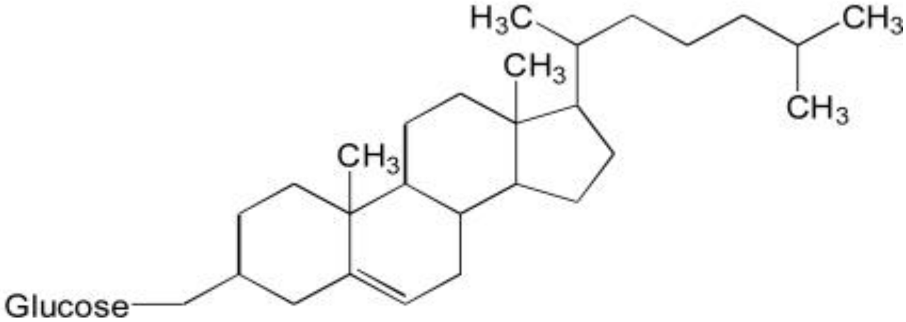
(A) Charantin



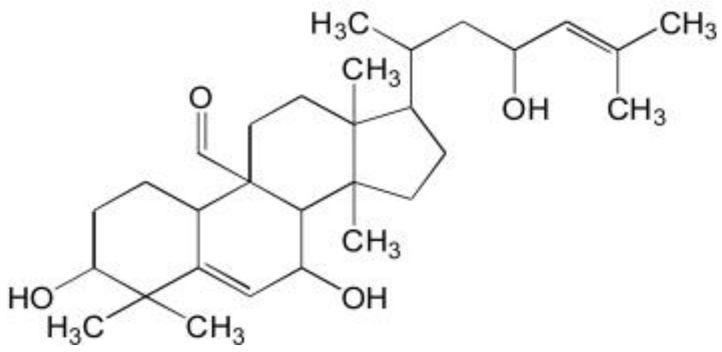
)B) Insulin



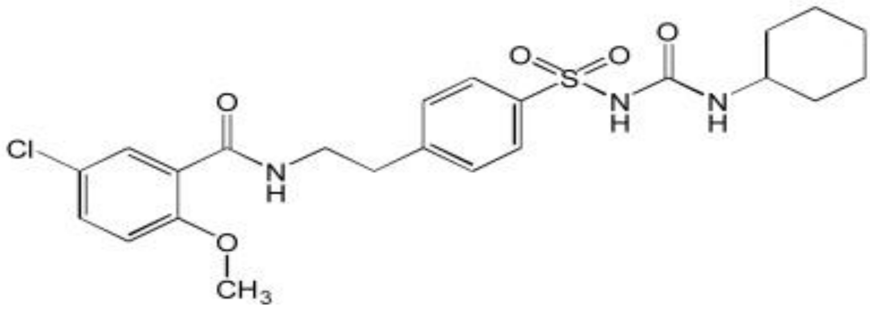
(C) Momorcharin



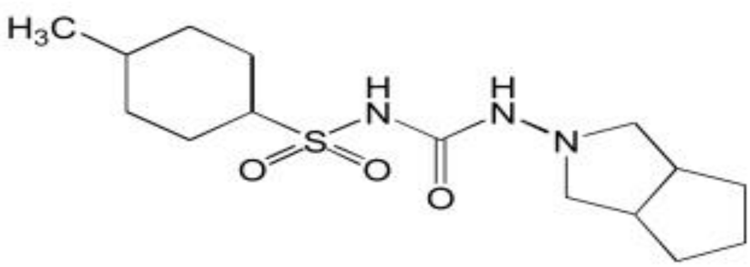
(D) Momordicine



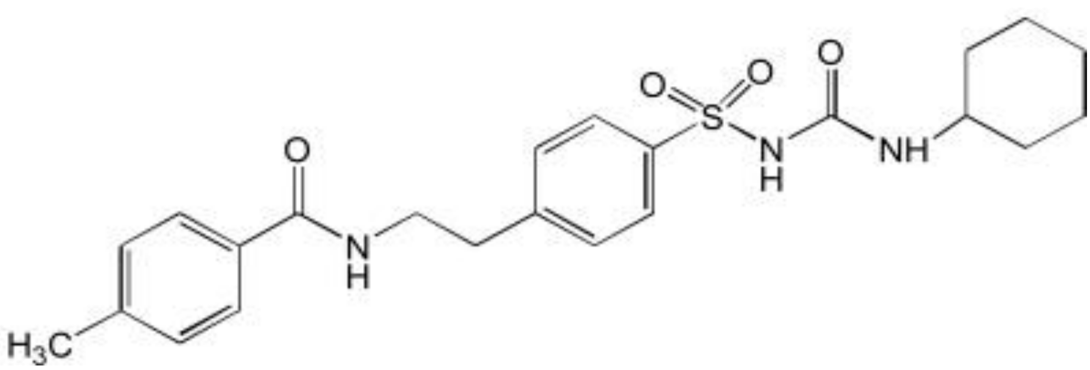
(E) Glibenclamide



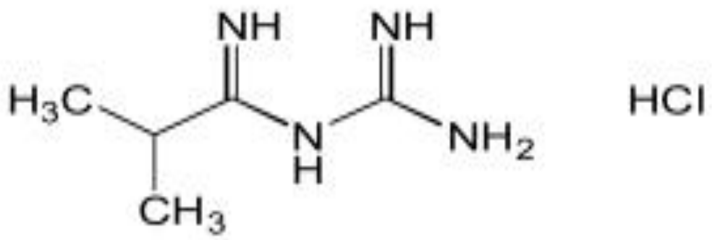
(F) Gliclazide



(G) Glipizide



(H) Metformin HCL



(I) Pioglitazone HCL

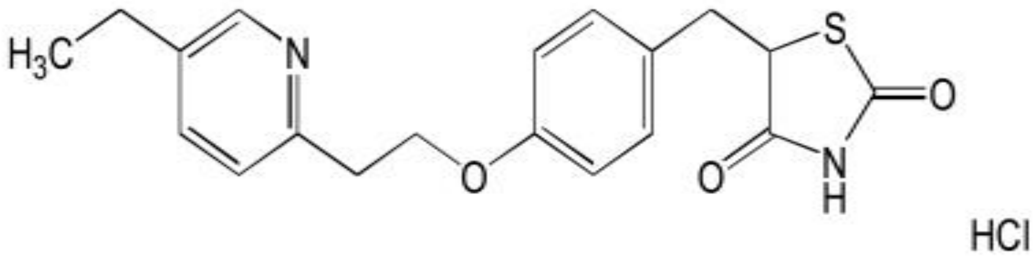


Figure 1.7: Chemical structures of (A) Charantin, (B) Insulin, (C) Momorcharin, (D) Momordicine, (E) Glibencamide, (E) Glibenclamide, (F) Glicazide, (G) Glipizide, (H) Metformin HCL and (I) Piogliazone HCL for comparison. Note some similarity in the chemical structure for insulin and related T2DM drugs to charantin and other compounds of *M charantia.*

(G) A review of previous *in vitro and in vivo* studies of different constituents of *M charantia*

It has been found that *M charantia* has a significant antidiabetic as well as hypolipidemic activity so that it can be used as an adjuvant along with allopathic treatment of medicine to treat diabetes as well as to delay the late complications of diabetes (Joseph and Jini, 2013; Singh et al, 2017; Hadi et al, 2022). Both *in vitro and in vivo* experiments employing both animal and human models have produced abundant data and hypotheses accounting for the anti-diabetic effects of *M charantia.* This literature review summarizes the hypoglycemic effects of *M charantia* using different extracts from different parts of the plant highlighting positive or negative effects. Table 1.2 shows the effects of administration of *M charantia* on diabetes mellitus using animals and human subjects. The results show that eight studies reported hypoglycemic effect compared to three which show no significant effect.

Table 1.2: Literature review showing the effects of administration of *M charantia* on diabetes mellitus using animals and human subjects.

Experimental models	Parts of Plant	Effects Demonstrated	References
Normal and diabetic rats	Whole plant	Beneficial	Leatherdale et al, (1981) Jeevathayaparan et al, (1995); Chandrasekar et al, (1989),
Diabetic rats	Ethanol extract of whole plant	Beneficial	Chandrasekar et al, (1989)
Normal and diabetic rats	Fruit juice and various extracts	Beneficial	Ali et al, (1993); Srivastava et al, (1993)
Human (T2DM)	Fruit juice/leaves	Beneficial	Welhinda et al, (1984)
Human (T2DM)	Fruit juice	No effect	Patel et al, (1968); Day et al. (1990)
Human (T2DM)	Fruit powder	Beneficial	Ahmad et al, (1996); Attar-ur-Rahman, (1989).
Normal rabbits	Fruit juice	No effect	Kulkarni et al, (1962).
Diabetic rabbits	Fruit juice	Beneficial	Akhtar et al, (1991).
Normal and diabetic rats	Fruit juice	No effect	Karunanayake et al, (1984); Platell and Srinivasan, (1999)
Normal and diabetic rats	Fruit juice	Beneficial	Srivastava et al, (1993): Karunanayake et al, (1984)
Normal and diabetic mice	Fruit juice and powder	Beneficial	Day et al. (1990); Sharma et al, (1996);

Table 1.3 (below) shows the data from four clinical studies using different pharmaceutical preparations (capsules, methanol/aqueous extract and dried fruit) of *M charantia* on human subjects. The results show that only two trials revealed positive hypoglycaemic effect using

either methanol or aqueous extract. The difference in hypoglycaemic effect may be due to form of the administration. For example, the data show that capsules exert no hypoglycaemic effect whereas extracts, fruits and other parts of the plant exert positive effects (see table 1.3).

Table 1.3: Data from four different clinical studies using *M. charantia to treat diabetic patients.*

Study designs	**Subjects**	**Form of *M. charantia* administered**	**Treatment duration**	**Outcome measured**	**Statistical significance**	**References**
Double-blind randomized controlled trial	40 with T2DM (twenty trial and twenty control subjects)	Commercial herbal supplement capsules	3 months	HbA1c	No	Dans, 2007
Controlled trial	15 with T2DM in 3 groups	Methanol extract of ground whole fruit	1 week	Fasting + postprandial blood glucose	Yes	Tongia *et al*,,2004
Randomized controlled trial	50 with T2DM (26 trial and 24 control subjects)	Tablets from dried whole fruit	4 weeks	(1) Fasting postprandial blood Glucose (2) Fructose amine	No	John *et al*, 2003
Controlled trial	Trial subjects: 9 T2DM Control subjects: 5 T2DM + 5 normal	Aqueous extract refined to subcutaneous injection (v-insulin)	Single treatment	Blood glucose	Yes	Baldwa *et al*, 1977

(H) Antioxidant effect of M charantia

M. charantia possesses potential medicinal effects on most metabolic and physiological processes in the human body. Many bioactive compounds of *M. charantia fruit* including polypeptides_flavonoids, phenols, alkaloids, triterpenoids, saponins and sterols were studied for their anti-oxidant activities (Corton *et al*, 2005; Bensinger and Tontonoz, 2008; Wang *et al*, 2008; Hadi et al, 2022). Several studies showed that *M. charantia* is a great source of antioxidant. Under experimental conditions, it was found that it possesses an activity against oxidant damage *in vitro* and *in vivo* (Dobrin *et al*, 2010; Bajpai *et al*, 2005;Thenmozhi *et a*,. 2011; Lucas *et al*, 2010;Virdi *et al*, 2005; Hadi et al, 2022). The green pulp of *M. charantia* and its extracts, followed by seed powder and its ethanol/water extracts, exhibited stronger antioxygenic activity than other solvent extracts, which were determined via several *in vitro* animal models (Padmashree *et al*, 2011). In diabetic rat, administering supplementation of *M. charantia* (13.33 g/kg) resulted in a significant rise of antioxidant (SOD, CAT and GST) activities. (Tripathi *et al*, 2009; 2010). Flavonoids are known to be one of the most effective free radical scavengers and antioxidants from *M. charantia*. The antioxidant capacity enhanced gradually with the increase of flavonoid concentration (Shan *et al*, 2012). Steroidal saponins which are an active ingredients of *M. charantia* can decrease gluconeogenesis, increase glucose metabolism and tolerance by affecting the expression of the peroxisome proliferator-activated receptors α and gamma (PPARα and PPARgamma) which may mitigate insulin resistance and a protein extract that exerted insulin-mimetic activities (Wu *et al,* 2008; Deng *et al,* 2017; Hadi et al, 2022).

(I) Other medical properties of *M. charantia*

M. charantia is a useful medicinal plant for human health and one of the most promising plants for diabetes and cancer treatment and prevention (Wang et al, 2008; Singh et al, 2019). *M. charantia* helps in the entire digestion process by stimulating the secretion of gastric juices. It is very helpful in stimulating the liver for secretion of bile juice that is very essential for metabolism of fats. *M charantia* also helps in improving the peristaltic movements and hence. it is very helpful in avoiding gastric disturbances (Jayasooriya *et al,* 2000. It was reported that charantin which is an active fraction of *M. charantia*, when it was administered to health rabbits, it produced a fall in blood sugar level. Another study found pancreatectomy was reduced, but not abolished the hypoglycaemic effect of charantin indicating a dual mechanism of action of this compound (Jayasooriya et al, 2000). It is well known that *M charantia* and its isolated compounds have direct growth-factor like effect on the pancreas and they can also stimulate glucose uptake into skeletal muscles (Ahmed et al, 2004; Cummings et al, 2004). Furthermore, it is known to have anti-lipolytic properties. A recent study reported that the extracts of *M charantia* may ameliorate high fat diet which in turn can induce obesity and hyperlipidemia in animal model. Most findings related to obesity and hyperlipidemia also showed that the plant extracts may modulate fat metabolizing kinases such as AMPKs, genes, and affected adipocyte differentiation (Wu and Ng, 2008). Moreover, *M charantia* is a very good source of all the essential vitamins, such as vitamin A, thiamine, riboflavin, vitamin C and also minerals like iron. Moreover, it is anti-inflammatory and astringent. It has specific action on the movement of bowels (Ahmad et al, 1999). it is also rich in minerals including potassium, calcium, zinc, magnesium, phosphorus, iron, trace elements and it is a good source of dietary fibre (Ahmad et al, 1999; Hadi et al, 2022).

An earlier study on the development of diabetic–induced cataracts demonstrated that blood sugar level-dependent cataract formation was slowed down by the consumption of *M charantia* fruit extract in association with better glucose homeostasis (Michael *et al*, 2006). Today, processed *M charantia* in the form of capsules or tablets is commonly advertised and sold commercially worldwide. The products are marketed under the brand name Glucobetic in Canada, India, the United Kingdom, the United States, and many Asian countries. Products can also be ordered online (Michael. et al. 2006. Compared with animal studies, clinical studies regarding the hypoglycaemic effects of *M. charantia* have been sparse and sporadic. In 1956, Lakholia, a physician, was probably the first person to document the therapeutic effect of *M charantia* in using himself as the subject (see table 1.4).

(J) Other isolated compounds from M charantia

Other major compounds that have been isolated from the pericarp and seeds of *M charantia* are phenolics and a glycol alkaloid known as vicine (Haxia et al, 2004; Horax et al, 2010). Vicine is a pyrimidine nucleoside which has been shown to induce hypoglycaemia in non-diabetic fasting rats by intraperitoneal administration (Joseph and Jini, 2013). The data reviewed in table 1.5 on *M charantia* have clearly support a beneficial role of the plant and its extracts to treat diabetes in particular, but it can be used to treat other diseases and ailments, including obesity, hypertension and cancer (Manoharan, 2013; 2014; Houacine et al, 2021).. The extracts of the plant seem to exert their beneficial hypoglycaemic, anti-obesity and anti-hypertensive effects via their antioxidant properties (Hanoman et al, 2022; Hadi et al, 2022).

M charantia is used in many parts of the world both as a functional food and as a complementary ethano-medicine for centuries to relief symptoms and debilitating conditions, especially diabetes (Hadi et al, 2022). *M charantia* is one of the most studied versatile medicinal plants worldwide for its medicinal properties to treat different diseases inflicting human due to its 228 different medicinal constituents (Taylor, 2002; Leung et al, 2009; Hadi et al, 2022). In low-and middle -income developing countries like Guyana, the concept of food as medicine is a central theme in dietetic and nutritional sciences, especially since *M charantia* is used both as cost-effective dietary supplements and ethno-medicines compared to expensive orthodox medicines. Evidence in the literature indicates that the different compounds in *M charantia* may act either separately or together in a synergistic manner to exert their medicinal effects. At least for diabetes, the charantin, an insulin-like peptide and alkaloid-like extracts seem to possess hypoglycaemic properties similar to the plant itself or its crude extracts. As described earlier, the different compounds seem to exert their beneficial effects via several mechanisms to control and treat diabetes mellitus (Joseph and Jini, 2013). In low to middle -income developing countries such as Guyana, *M charantia* is probably a feasible and potential option of remedy for people of ethnic minorities who have low income and a high prevalence of diabetes, obesity and hypertension but prefer remedy based on natural products according to their cultural beliefs.

(K) Mechanism(s) of its hypoglycaemic action

Table 1.4 shows the proposed modes of action of *M. charantia* in exerting its hypoglycemic effect. Several studies have shown that extracts of *M charantia* can block the absorption of sugar molecules in the intestine and also improves the body's ability to utilise sugar, which would help to reduce blood sugar levels (Meir and Yaniv, 1985; Shibb *et. al.* 1993; Platel and Srinvassan, 1997; 1999; Garau et al, 2003; Ahmed et al, 2004; Singh et al, 2011; Hadi et al, 2022). Other studies have shown that *M charantia* extracts (growth-like factor) can repair partially dying pancreatic islet beta cells and thus, increasing their mass (proliferation) and function. In turn, the repaired beta cells synthesise new insulin for secretion from the endocrine pancreas (Ahmed *et al*, 1998). The fruit juice or its extract can also reduce arterial blood pressure, regulate glucose uptake into jejunal vesicles, and stimulate glucose and amino acid uptakes into L6 muscle cells (Sharma et al 1999; Ahmed, 1998; Ahmed *et al*. 1999; 2004; Cummings, 2000; 2004). The uptake of glucose into L6 muscle cells can be blocked by wortmannin, an inhibitor of the tyrosine kinase enzyme. This effect of *M charantia* is similar to that of insulin suggesting that *M charantia* is exerting the same effects as insulin and probably acting on the same receptor to stimulate glucose uptake into muscle cells (Klip and Paquet, 1990; Cummings *et al*, 2002; 2004).

1.28 Summary of introduction

This introduction reviewed the historical perspectives of DM, the epidemiology, risk factors symptoms, diagnosis, long-term complications, education about DM and its complications, drug and non -drug treatment and management of the disorder. It also highlighted the problem of diabetes in Guyana and touched on how obesity can lead to diabetes and other non-communicable diseases, especially CVDs with hypertension in particular. A comprehensive literature review is done on *M charantia* and its medicinal value, especially to treat diabetes. The introduction also briefly addresses obesity and hypertension in Guyana and the needs to treat NCDs in a cost-effective manner via the non–pharmacological prevention strategies including diet modifications, weight loss, daily physical activities and the beneficial use of *M charantia*. Further supporting information is given in chapter 7, the general discussion.

Table 1.4: Literature review showing some proposed modes of hypoglycemic action of *M charantia* in reducing blood glucose concentration in the body.

Possible modes of action(s)	References
1. Insulin secretagogue effect	Karunanayke et al, (1984); Kedar and Chakrabarti, 1982); Jeevathayaparan et al, (1995); Hazarika et al, (2012).
2. Stimulation of peripheral and skeletal muscle glucose utilisation	Day et al, (1990); Day, (1990); Cummings et al, (2004).
3. Inhibition of intestinal glucose uptake	Meir and Yaniv, (1995); Ahmed, (1999); Ahmed et al, (1999).
4. Inhibition of hexokinase activity	Meir and Yaniv, (1995).
5. Suppression of key gluconeogenic enzymes	Shibib et al, (1993).
6. Stimulation of key enzyme of HMP pathway	Shibib et al, (1993)
7. Preservation of islet beta cells and their functions	Ahmed, (1999); Ahmed et al, (1999)

1.29 Scope and Rationale of Study

This study is about three non-communicable diseases (NCDs), namely diabetes mellitus (DM), obesity and hypertension in Guyana, a former British Colony which gained its independence on 26th May 1966 from the United Kingdom. Guyana is situated in upper North-East of South America surrounded by the Atlantic Ocean, Surinam, Brazil and Venezuela (see figure 1.3). As the only English- speaking country in South America, Guyana aligns itself more with the former British Caribbean countries such as Antigua, Jamaica, Grenada, Jamaica, Bahamas, Barbados, St Lucia St Kitts, and others smaller islands. Most of the people in the former British colonies including Guyana and the Caribbean comprised of Indians, Portuguese and Chinese who indentured from India, Madeira and China, Africans who came as slaves from West Africa, the Europeans, the local or indigenous Amerindians and a sizable population of mixed race. All these different ethnic groups are prone to obesity, diabetes and hypertension and around 10-12 % of the population in these countries have diabetes and other related chronic diseases and more than 80% of the diabetics usually die from cardiovascular diseases (CVDs) and kidney failure (KF) (WHO, 2018; MPH, 2016; CARICOM, 2018; Razzaghi et al, 2019; Harding et al, 2019; Sharma et al, 2021; Tapia and Dhalla, 2022).

In the course of practising medicine as a General Practitioner, it was encountered that many patients have to pay for their medications and many of them came from poor homes and with many children. As such, it was decided to employ cost-effective ways to treat the newly diagnosed type 2 diabetic, obese and hypertensive patients using diet modifications, weight loss, physical activity, and non-pharmacological treatment employing the green fruit juice (weight /volume) from the plant *M charantia.* The rationale was to ascertain the effectiveness of individual or combined therapy to treat these three NCDs.

In tackling the scientific problem, the study was based on the following-

(A) **First**, not much work has been done on such non-communicable diseases such as type 2 diabetes, the problems of overweight and obesity and hypertension among the different ethnic groups in Guyana. Some data are found in the Ministry of Public Healthy, but they need to be analysed and reported in the scientific community and recommendations made to the Ministry of Public Health (MPH, 2009, 2016; PAHO, 2019).

(B) **Second**, the major limitation in some previous studies (see tables 1.1-1.4), using *M charantia* to treat diabetes, is the doses (some unknown) and ingredients (plant parts and preparations) used by several authors and their demonstrated effects on blood glucose levels as either positive or negative effects (see tables 1.2 and 1.3).

(C) Third, only few studies have been done on the effect of *M charantia* on obesity and high blood pressure and this was done mainly in animal models.

(D) **Fourth,** most importantly, there are only few studies investigating *M charantia* in combination with orthodox drugs on either diabetes or hypertension.

(E) **Fifth,** no study has investigated the beneficial use of *M charantia* with diet modification and regular moderate exercise. Currently, most newly diagnosed diabetics are treated mainly by a combination of life-style interventions employing either diet modification, weight loss or regular exercise or a combination of these (Martinus et al. 2006; Colberg et al. 2010; Thent et al 2013; Diabetes UK, 2015; Madden et al. 2013; Smail et al, 2018; Bailey and Day, 2018; ADA, 2019). A few key studies have shown that regular exercise can induce hypoglycaemia, thereby delaying and preventing the development of T2DM (Colberg et al, 2010; Thent et al, 2013; Smail et al, 2018; Hamasaki, 2016; Yani et al, 2018; Bailey and Day, 2018; ADA, 2018; Curan et al, 2020; Heiston et al, 2020). Exercise has other positive effects including reduction in blood lipid, blood pressure, stress level, cardiovascular events and mortality and improving the quality of life of diabetic patients. Regular exercise also reduces body weight which is an important form of treatment in obesity and T2DM and also blood pressure in hypertensive patients. Although the precise cellular mechanism(s) is not yet known, exercise can increase pancreatic beta cell mass to synthesise and secrete insulin and moreover, regulate the action of insulin in T2DM to stimulate glucose uptake into muscle cells (Ahmed, 1999; Ahmed et al, 1999; Ahmed et al, 2004; Cummings et al, 2004; Curan et al, 2020).

(F) **Sixth,** it is relevant to analyse the fruit of *M. charantia* for its different constituents

(G) **Seventh**, literacy plays a major role in understanding a disease and in preventing long-term complications and end-organ failures, especially diabetic outcomes in T2DM (Odili, 2011; Schmid, 2002; Wildead et al, 1996; Morris, 2001; Murata, 2003; Moodley and Rambiritch, 2007). A cross sectional observational study was conducted by Schillinger (2002) to examine the association between health literacy and diabetes outcomes among 408 T2DM patients over 30 years of age. The author found that patients with inadequate health literacy were less likely than patients with adequate health literacy to achieve tight glycaemic control. Similar studies have been done by other authors in different parts of the world (Odili, 2011; Schmid, 2002; Widlead et al,1996; Norris, 2001; Murata, 2003; Moodley and Rambiritch, 2007), except Guyana. As such, this study investigated any relationship between knowledge and obesity and self–care management for diabetes in Guyana for the first time.

As such, this study was designed to tackle these seven health-care issues listed above using human subjects and forming the originality and novelties of the work.

Figure 1.8 shows the format or scope of this study. Chapter 1 of the study is related to a thorough literature review in the subject area followed by the working hypothesis, main aims and specific aims/objectives. In terms of the results, each chapter was written in the format of a full manuscript, except for the abstract and references. All the results are presented in Chapters 2-6. Finally, chapter 7 contains a comprehensive and critical discussion of the findings in the five result chapters followed by conclusion, limitations, recommendations, appendices and presentations and publications.

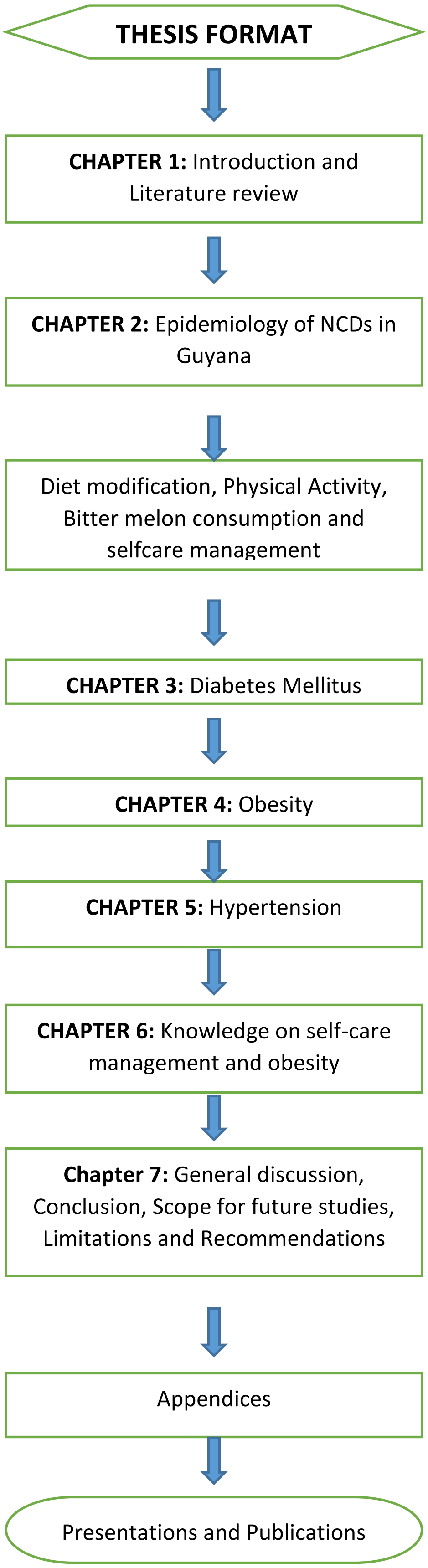


Figure 1.8: Flow diagram showing the format or scope of the thesis.

1.30 Working hypothesis.

Non-communicable diseases (NCDs) such as diabetes, obesity and hypertension are very prevalent in Guyana, but treatment is very expensive. *M charantia,* in combination with regular exercise and diet modification, is more cost-effective compared to orthodox drugs to treat diabetes, obesity and hypertension in Guyana.

1.31 Main aim

The main aim of this study was to investigate the epidemiology of diabetes, obesity and hypertension in Guyana and the use of *M charantia* either alone or in combination with diet modification and physical activity to treat these three NCDs and to undertake a study on the understanding of diabetes and obesity and the relationship between knowledge about diabetes and self-care management in delaying /preventing end-organ failures due to the disorder, using questionnaires.

1.32 Objectives of the Study

1. To undertake a search on the epidemiology of such non-communicable diseases (NCDs) as diabetes, obesity and hypertension in Guyana as undertaken and reported by Ministry of Health but funded by PAHO in 2016). The data were retrieved from the Ministry of Public Health via PAHO (2019).
2. To investigate the time-course beneficial effects of *M charantia* either alone or in combination with exercise, diet modification and an orthodox drug (diamicron- MR) in newly diagnosed diabetic patients measuring blood glucose level (FBGLs), blood pressure (BP) and changes in such blood biomarkers as total lipids and triglycerides as well cations and trace elements in blood serum.
3. To investigate the postprandial effect of *M charantia* in both healthy and diabetic subjects undertaking oral glucose tolerance test (OGTT).
4. To investigate the anti-obesity, anti-hypertensive and anti-lipidemic effects of *M charantia* either alone or in combination with diet modification and physical activity in newly diagnosed obese patients.
5. To investigate the anti-hypertensive effects of *M charantia* either alone or in combination with either diet modification, physical activity or amlodipine (an antihypertensive drug) in newly diagnosed hypertensive patients.

6. To analyse *M charantia* fruit for its phenolic contents, antioxidant activity and cation levels.
7. To investigate the understanding and knowledge of the patients about diabetes and obesity and the relationship between knowledge of diabetes and self-care management of the disorder among diabetic patients in preventing and delaying diabetes-induced long-term complications using questionnaires to obtain the data.
8. To analyse the data and write up the thesis.

Chapter 2:

Epidemiology of obesity, diabetes and hypertension, three non-communicable diseases, in Guyana

2.1 Introduction

Non-communicable diseases (NCDs) are chronic diseases of long duration which generally progress slowly over time. They include obesity, diabetes, cardiovascular diseases (CVDs), cancers, respiratory and kidney diseases and others (MPH, 2016; PAHO, 2019; WHO, 2013; 2015; 2018; 2021; Sockalingam, 2019; Sokalingam et al, 2021; Jaillobaeva et al, 2021; Sharma et al, 2021). Previously, NCDs were confined to developed countries such as Australia, Canada, USA, UK, several in Europe and other developed countries, but in recent years, NCDs now affect people in low to middle- income developing countries where more than 32 million people die from NCDs compared to 41 million who die annually from all diseases. This figure represents 71% of all deaths in the world annually (Habib and Saha, 2008; WHO, 2018; 2021; Jailobaeva et al, 2021). It is a tremendous burden on mankind and developing NCDs are their own making. NCDs occur due to combination of genetics, physiological, environmental and behavioural processes, including lifestyle factors (WHO, 2011; 2013; 2015; 2018; 2021; PAHO, 2019). NCDs kill people in their working years, between ages of 18-65 years, especially in low- and middle- income countries. CVDs account for about 50% (18 million) of all deaths due to NCDs followed by cancer (9 million), respiratory (4 million), obesity and diabetes (2 million) (WHO, 2011; 2018; 2021; Zimmet, 2017; Coates et al, 2020; Martinez et al, 2020; Jaillobaeva et al, 2021; Tapia and Dhalla, 2022).

The main risk factors for NCDs include unhealthy diet with excess fats and sugar, overeating by constant snaking and binging, smoking, alcohol abuse, physical inactivity, mental diseases including stress and anxiety, environmental pollution, urbanization and others (Habib and Saha, 2008; WHO, 2013; 2018; Martinez et al, 2020; Jaillobaeva et al, 2021; Tapia and Dhalla, 2022). NCDs affect people irrespective of ages, gender, ethnicity, religion, faith and others in different regions and countries globally. NCDs reduce the quality of life of people, especially those in their working years and almost 85% die prematurely. NCDs are driven by many natural forces including unplanned urbanisation, unhealthy lifestyles, overcrowding in urban areas, ageing population, underfunding and laziness resulting in the development of obesity, diabetes and hypertension, raised blood lipids and other physical and mental disorders which are all risks for early mortality (Coates et al, 2020). NCDs have placed tremendous burden to the National Health Services globally. In many parts of the world, the patients themselves have to bear the financial costs (WHO, 2010; 2011; 2013; 2018; 2021; Martinez et al, 2020; Jaillobaeva et al, 2021; Tapia and Dhalla, 2022).

There is no need for people to die from NCDs if they are educated about the risks, the quality of life they will experience following the development of a debilitating disease and the cost of health care. Likewise, the prevention and control of NCD are not difficult for a susceptible individual since he or she can easily avoid the risk factors and change their life-style habits (Singh et al, 2017; 2019). Managing the reduction of NCDs has to be done via Governmental programmes at all levels and for all ages. Education is still the most powerful cost-effective way and an important weapon to prevent and control NCDs. Similarly, self-care management by the patents about the danger of NCDs is another way to prevent the development NCDs, social issues, suffering and financial costs associated from NCDs (Habib and Saha, 2008; Van-Sonoorenburg et al, 2019; Coates et al, 2020; Martinez et al, 2020; Jaillobaeva et al, 2021; Tapia and Dhalla, 2022).

Guyana is a low-income developing country and epidemiological data from Ministry of Public Health (MPH) showed that there is still a high prevalence of NCDs, especially obesity, diabetes and CVDs including hypertension (MPH, 2013; 2016; PAHO,2019; Sokalingam, 2019). These NCDs have affected Guyanese population for several years leading to increased morbidity and mortality. Like many other low-income developing countries, Guyana, a former British Colony with a size of 83,000 square miles, has a growing epidemic of NCDs among its population and more than 70% of deaths are due to NCDs, the main causes of premature deaths before the age 70 years (MPH 2013; 2016; Sockalingam, 2019). In Guyana, more than 822 deaths per 100,000 individuals occurred annually and they are due mainly to CVDs. Both obesity and diabetes are major risk factors for CVDs (Sokalingam, 2019; Sokalingam et al, 2021 Martinez et al, 2020; Jaillobaeva et al, 2021; Tapia and Dhalla, 2022; Smail et al, 2022).

This study investigated the epidemiological prevalence of three NCDs, obesity, diabetes and hypertension in Guyana analysing the last published statistical data from MPH (2016) and PAHO (2019). The major objective was to undertake a brief search on the epidemiology of these NCDs during the last official census in 2016 for adult population between ages 18-69 years, retrieving available public domain data from the MPH (2026) and PAHO (2019). Obesity, diabetes and hypertension are closely interrelated, and they affect many Guyanese including families of different ethnic groups who have low income and many of them have to pay for their own medical treatment. The rationale or long- term aim was to ascertain cost-effective ways to treat these NCDs in Guyana.

2.2 Methods

2.2.1 Epidemiology data collection

This study was conducted from a General Practitioner Clinic in Guyana after retrieving the public domain published data from the Ministry of Public Health for 2016 and PAHO in 2019 (MPH, 2016; PAHO 2019). The data for the epidemiological studies were collected from the Website of the Ministry of Public Health in Guyana. Senior Staff from the Statistical Department of MPH in Guyana informed the User that the data did not need ethical clearance prior to use and analyse since they were logged into the public domain website where any one could retrieve them. The confirmed census data for NCDs in 2016 (MPH 2016) and published in 2019 (PAHO 2019) were collected from the MPH website and analysed and presented as graphs. The next set of data will be published in 2023. The delay was due to covid-19. All supporting data and graphs were also obtained from previous publications from the Ministry of Public Health and PAHO in Guyana and they were redrawn and acknowledged. This study was more interested in recent data on NCDs and how the data could help in the current research in terms of cost-effective treatment of the three NCDs, mainly obesity, diabetes and hypertension employing non- pharmacological approaches such as life-style changes and plant-based remedies (see chapters 3-5). Obesity is a main risk factor of diabetes and hypertension, and the majority of obese people might have prediabetes or fully blown diabetes and both diabetic and obese people could have a tendency in supporting the development of high blood pressure and raised blood cholesterol (Elkilany et al, 2019).

2.2.2 Conduction of Census survey for NCDs in 2016 by the Ministry of Public Health in Guyana

The Pan American STEPS Survey version 3.1 was conducted by the Ministry of Public Health in Guyana from September 28 to October 26, 2016 using digital tablets. 'The Survey was implemented as a population-based survey of adults aged 18-69 years old. The sample size and allocation were based upon the 2012 census frame and included 288 enumeration districts from both the coastal and inland regions. Moreover, 12 households were randomly selected within each enumeration district. A total of 3.456 households were selected for participation in Step 1 and a total of 50% of this sample was randomly selected for participation in Step 3. Mapping and relisting of the 288 enumeration districts was conducted in July 2016 since the 2012 census was outdated'. The total sample size was 3,456 adults and the overall response rate was 77% (2,662) for step 1 comprising of 40.1% (1,068) males and 59.9% (1,594) females. A majority

(60.1%) of both males and females represented the younger age range, ages 18-44. Each respondent was asked to complete a questionnaire to obtain demographic and behavioural information (Step 2). In addition, the waist circumference, height, weight and blood pressure were measured for each participant. For the collection of venous blood (Step 3), the total sample size was 1,728 and the overall response rate was 40%. As such, blood samples were only taken from 691 participants.

According to PAHO (2019) the sampling methodology and weighting of the data in analysis facilitated the representativeness of the results for the population in Guyana. The use of a STEP-wise approach to NCD risk factor surveillance (STEPS) as a standardized and validated tool also ensured the comparability of the results. All the data were collected, analysed and published as tables or graphs (PAHO, 2019). For the current study the relevant data on obesity, diabetes, high blood pressure and lipid profiles were selected and redrawn as graphs for comparison.

2.2.3 Defining overweight, obesity, diabetes, and hypertension.

Obesity was defined as when the body mass index (BMI) was 30 kg/m^2 and over whereas overweight was when the BMI is 25-29 kg/m^2. BMI was calculated using body mass (kg) and height (m)., Waist Circumference (WC) greater or equal to 94 cm in men and 80 cm in women was deemed obese. If a man had a WC greater than 102 cm, he was at a substantially increased risk as females with a WC greater than 88 cm. A WC greater than 120 cm for men and 110 cm for women placed these individuals at extremely high danger for obesity-related health issues (VMC. 2014). Confirmed diabetes was defined as fasting blood glucose of and above 7 mM or 126 mg/dl or HbA1c of 6.5% (48 mmol/mol). Hypertension was defined as a blood pressure of 140/90 mm Hg and over (Elkilany et al, 2019).

2.2.4 Data analysis

Statistical data analysis was done using the Statistical Package for Social Sciences (SPSS), ANOVA, EPI Info and STATA (PAHO, 2019). The data collected were compared according to the assigned groups. Data are expressed as mean percentage. A value of $p<0.05$ is taken statistically significant.

2.2.5 Ethical Considerations

The project had ethical clearance from the University of Guyana and UCLan Ethics Committees. Ethical clearance was not required from Ministry of Health in Guyana since the data were all available to the Public Domain.

2.3 Results

2.3.1 Population and deaths due to NCDs in Guyana

Figure 2.1 shows the composition of the different ethnic groups in Guyana, a multi- national and cultural country. In order of percentage population, they comprised of Indo-Guyanese (descendants from Indian indentured labourers) (39.8%), Afro Guyanese (descendants from African slaves) (29.3%), Mixed Guyanese (19.9%), Amerindian Guyanese (indigenous people) (10.5 %) and others including Portuguese from Madeira, Chinese from Hong Kong, and other Europeans (0.50 %). When the data were collected in 2016 and subsequently published in 2019, Guyana had a total population of about 770,000 compared to 780,000 in 2021. Adult male and female population represent 30% of women and 29% of men who were over the age of 20 years. (Sokalingam et al, 2021).

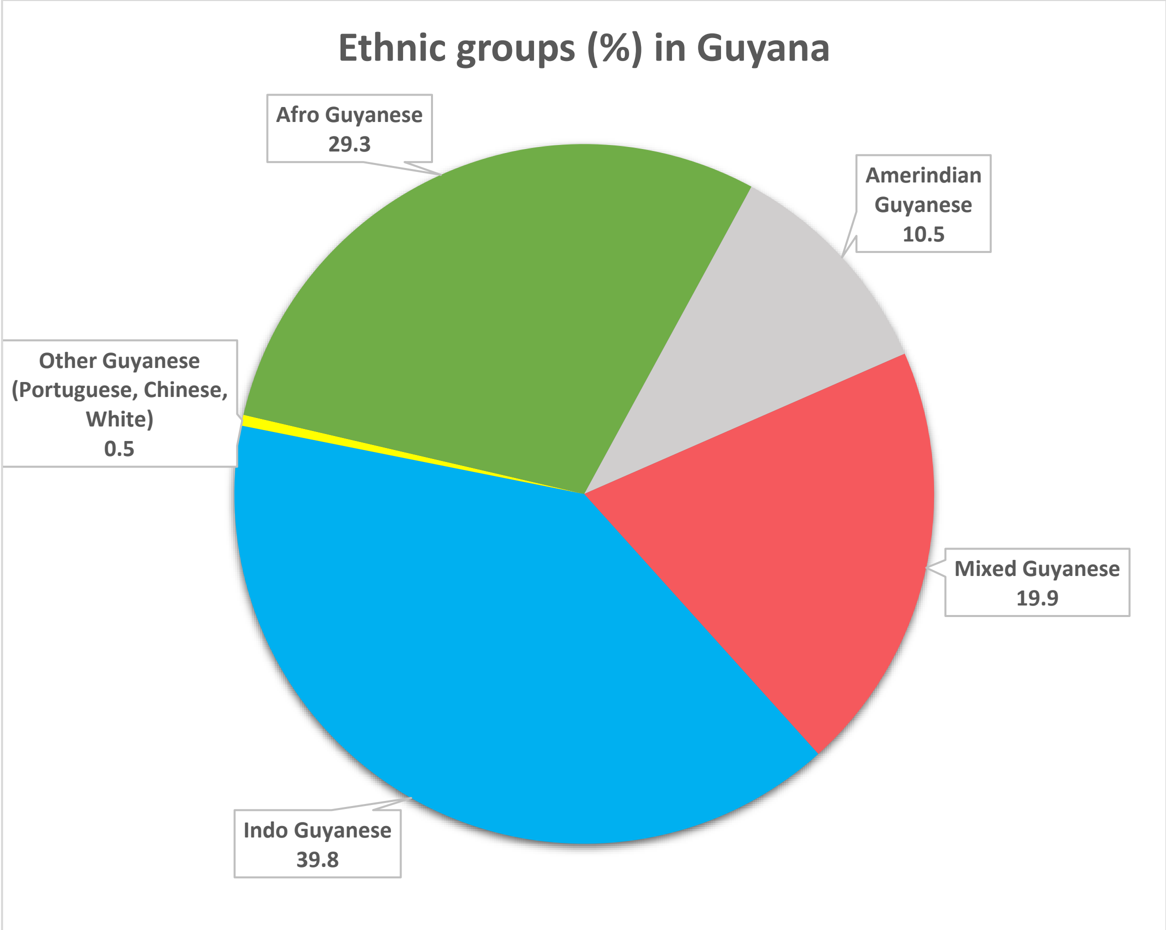


Figure 2.1: Pie chart showing the percentage population of the different ethnic groups in Guyana. Graph drawn from data available from PAHO (2019). Note that Indo and Afro Guyanese comprised of 69.2% of the 770,000 people living in Guyana in 2016.

Table 2.1: Data showing such non-communicable diseases as hypertension (HNT), diabetes mellitus (DM), strokes and coronary heart disease (CHD) in 2016 during the last census which was published in 2019. The data show the diseases, number of deaths, rate per 100,000 and world ranking (Data obtained from PAHO, 2019).

Diseases	Deaths	Percentage	Rate / 100,000	World Ranking
HTN	320	4.45	45.77	18
DM	579	8.06	82.60	14
Stroke	1022	14.22	149.26	24
CHD	1335	18.50	192.95	31

Table 2.1 shows four main NCDs in Guyana for 2016 and supported by the number of deaths, including percentage, the rate per /100,000 and world ranking. Taking into consideration the total population in Guyana and the 195 countries in the world in 2016, the data revealed that Guyana had a fairly high mortality of the four NCDs. Moreover, in 2016, Guyana had an average total annually deaths of about 7,183 and 16,000 births.

Figure 2.2 shows the mortality prevalence due to deaths from the different NCDs including. Cardiovascular diseases (CVDs), diabetes mellitus (DM), cancers, respiratory diseases and other NCDs compared to communicable diseases (CDs) and injuries (INJs) mainly from road traffic accidents in Guyana. The data plotted as percentage of total deaths for all ages during 2016. The results show that deaths from CVDs were the highest, followed by CDs, INJ including road traffic accidents, other NCDs such as kidney failure, strokes, cancer, DM and respiratory diseases (RD). These data clearly indicate that CVDs are the leading cause of deaths including hypertension, coronary heart diseases and sudden cardiac death. It is particularly noteworthy that two major risk factors for CVDs are obesity and diabetes. Over 80% of diabetic patients usually die from CVDs and renal failure and most of these are not registered as deaths due to DM.

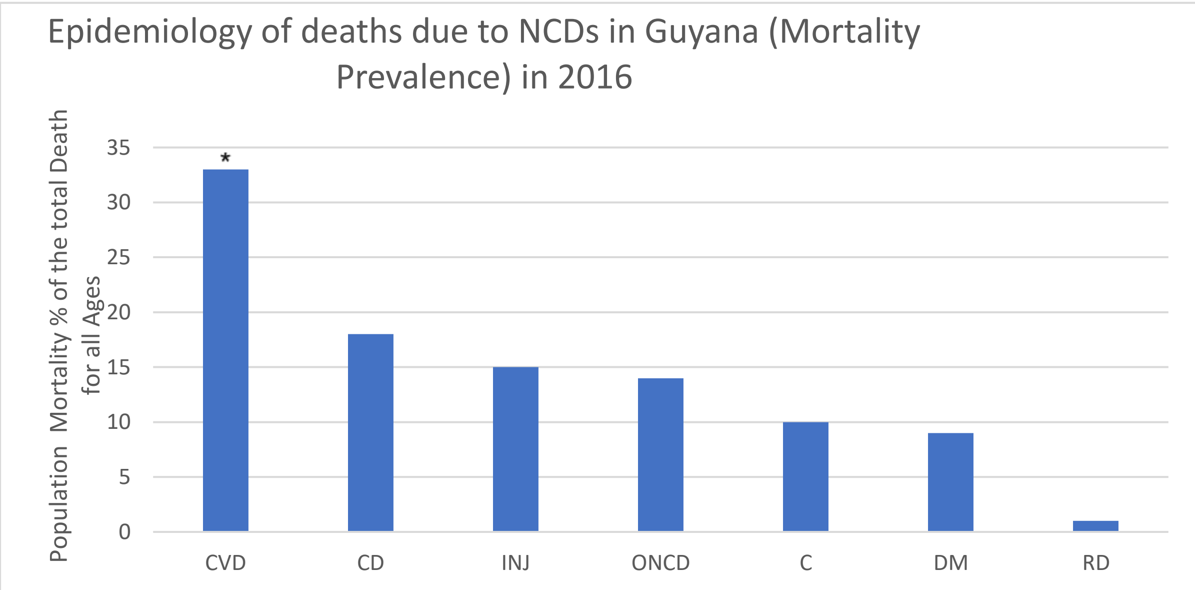


Figure 2.2: Bar charts showing the population mortality from NCDs in Guyana for 2016 compared to Communicable diseases (CD) and injuries (INJ). All the data are spread as total deaths for all ages. CVD= Cardiovascular diseases, ONCD= other non- communicable diseases; C = cancer; DM= diabetes mellitus; RD=respiratory diseases. Note that most people

died from CVDs which may be related to DM-induced mortality (Statistical data obtained from MPH, 2016 and plotted above). *p<0.05 for CVD compared to the others.

2.3.2 Epidemiology of overweight and obesity in Guyana in 2016

Previous published data from the Ministry of Public Health in Guyana revealed that overweight and obesity increased gradually from 1980 to 2014 among adult males and females, 18 years and over. Recent published data (see figure 2.3) by PAHO (2019) in the last census in 2016 reveal that 51% of adults were overweight (42 % males and 60% females). Similarly, 22% of the adult population were obese (14% males and 30% females). In 2016, Guyana had a reported adult population of around 510,000 and of this number, 260,000 were overweight and 112,000 were obese. The data presented in figure 2.3 also show that overweight and obesity among females were significantly ($p<0.005$) higher than overweight and obesity in males. It is predicted that obesity in Guyana will increase to 16% and 32% for male and female subjects, respectively by 2025 (WHO 2018). The results clearly show that the prevalence of overweight and obesity increased markedly high among both men and women in 2016 compared to previous years.

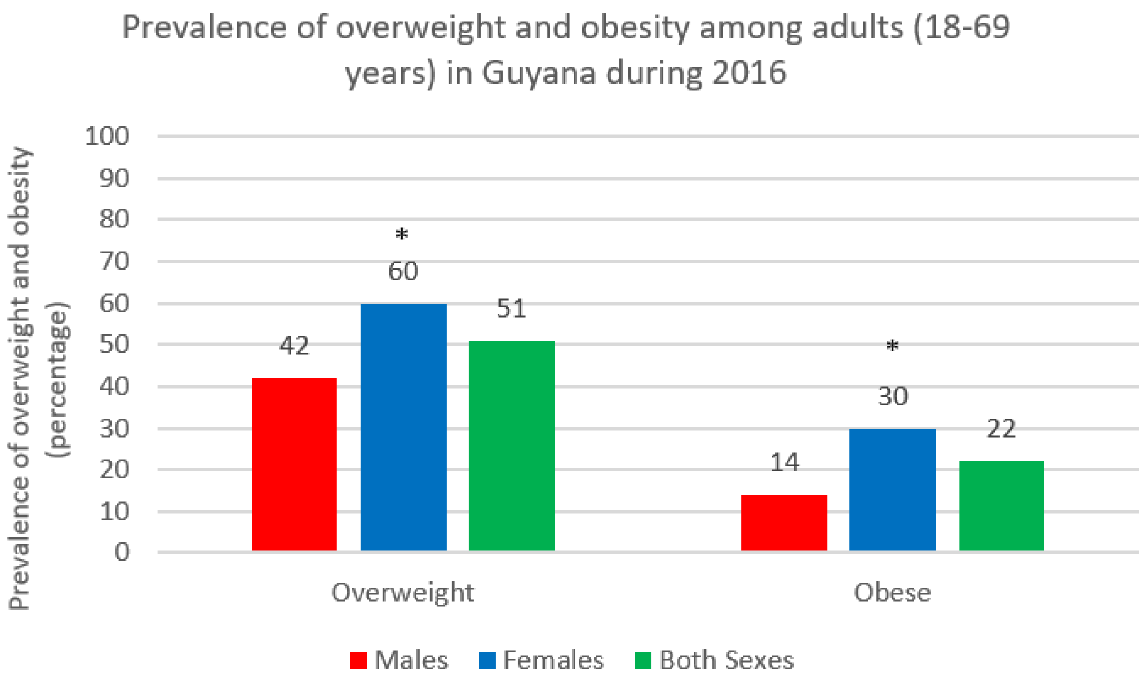


Figure 2.3: Bar charts showing the prevalence of overweight and obesity among adult males and females (ages between 18-69 years combined) in 2016 in Guyana; *p<0.05 for females

compared to males (red= males, blue =females and green =combined data). Data expressed as percentage.

Figure 2.4 shows the prevalence of overweight and obesity in Guyana in 2016 based on gender (adult males and females) for 2 different age groups, either alone or when combined for comparison. The data clearly demonstrated that significantly ($p<0.05$) more women were overweight and obese in age groups of 18-44 and 45-69 years compared to men. Moreover, women in age group of 45-69 years were significantly ($p<0.05$) more overweight and obese compared to the younger age group of 18-44 years. When the data were combined, they confirmed that adult women were significantly ($p<0.05$) more overweight and obese than adult men. Figure 3.5 show the percent data for obesity alone among adult genders and age groups based on BMI of 30 and over for comparison. The results show that females at all age groups were significantly ($p<0.05$) more obese than men for the same age groups, especially for 45-69 years.

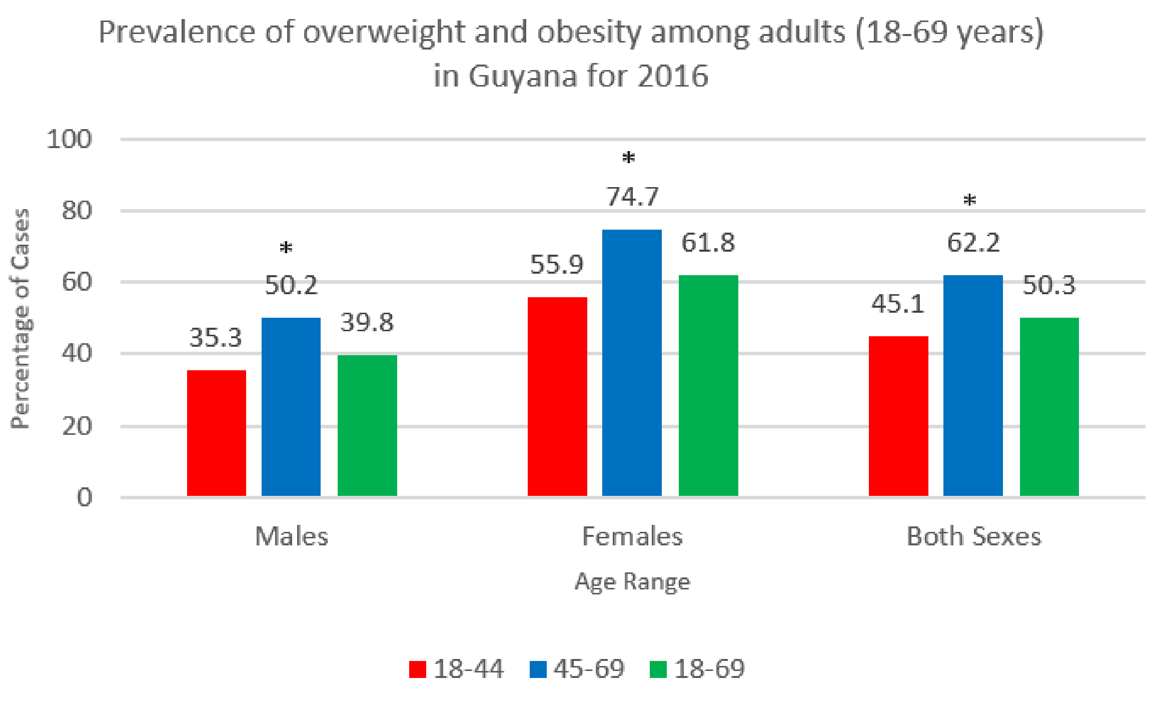


Figure 2.4: Bar charts showing the percentage of male and female adults 18-69 years old classified as overweight and obesity based on age ranges (red=18-44 years, blue =45-69 years and green = both age groups); (BMI ≥ 25 kg/m2). *$p<0.05$ for females compared to males. Note that half of adults (both sexes) were considered overweight (50.3%, range 24.6-28.9) and

males were more likely to be normal (39.8%) to marginally overweight compared to females (62.2%). Likewise, females (34%) were more likely to be considered obese than males (14%).

In addition to measuring BMI, it is possible to measure waist circumference and abdominal body fat which are other indicators of obesity. Data for waist circumference for adult Guyanese males and females for age groups 18-44 years, 45-69 years and combining the age groups are shown in figure 2.5. The data reveal that adult females had markedly a higher waist circumference compared to adult males, but these results were not significant comparing males with females at age group of 45-69 years. It has been reported abdominal obesity, which is monitored as a distribution of fat, is seldomly measured by clinicians in Guyana (Sockalingam et al, 2021).

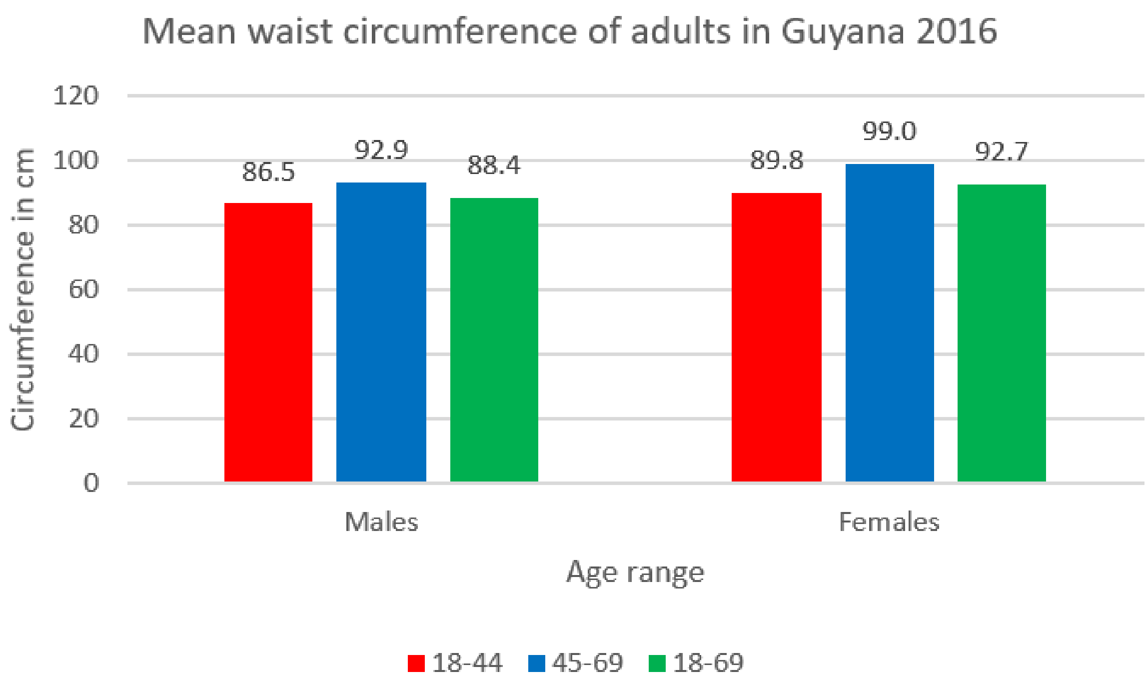


Figure 2.5: Bar charts showing mean waist circumference (data expressed as cm) among adult Guyanese males and females of age groups 18-44 years (red), 45-69 (blue) years and when the two age groups (18-69 years; green) were combined for comparison. Note than most Guyanese had larger waist size at age group of 45-69 years compared to age group of 18-45 years and women had a slightly larger waist than men.

2.3.3 Epidemiology of diabetes in Guyana in 2016

Like obesity, diabetes increased progressively from 5% and 4% in 1980 to 9% and 13% in 2014, respectively in females and males (MPH, 2016). New data for the prevalence of diabetes in Guyana for 2016 census survey are presented below based on genders, age and treatment. Data for next five years (2017-2021) on NCDs were supposed to be published in 2021 but this was delayed due to covid-19.

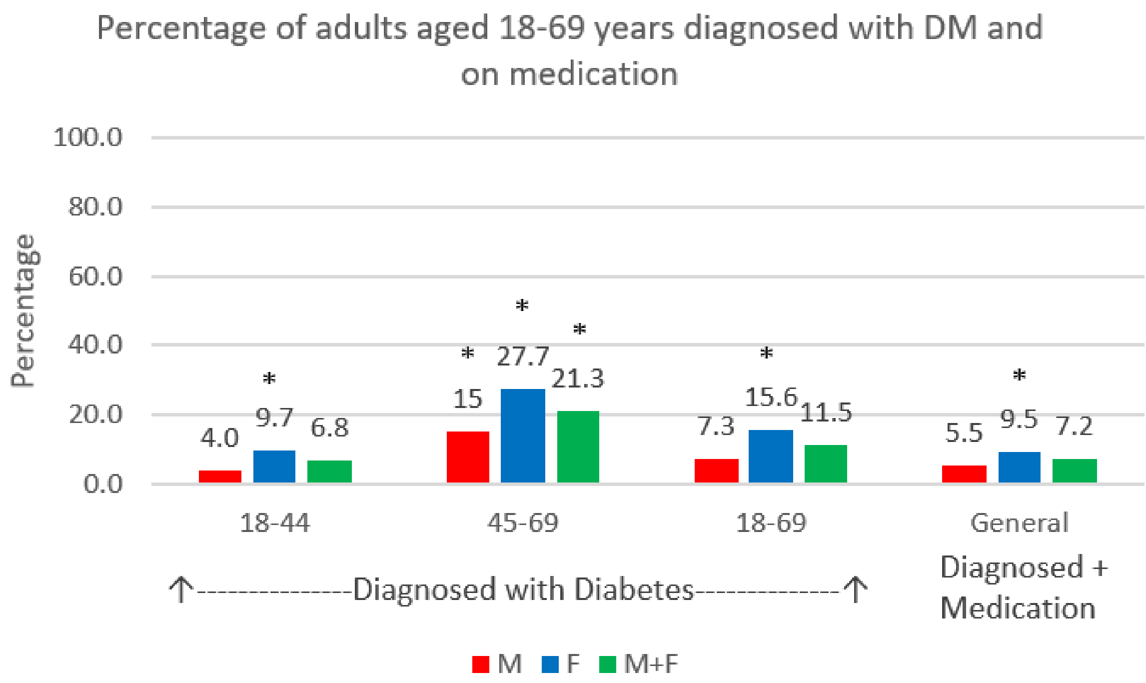


Figure 2.6: Bar charts showing the percentage of confirmed diabetes among adult males (red) and females (blue) for age groups 18-45 years, 46-69 years and when the data from the two age groups were combined (green). The data also show the prevalence of treatment with medication for the diabetic patients within each age group for comparison. *$p<0.05$ for females compared to males in all age groups as well as age group 45-69 years compared to 18-44 years

Figure 2.6 shows the percentage of confirmed diabetes among adult males and females for age groups 18-44 years, 45-69 years and when the data from the two age groups (18-69 years) were combined. The data also show the percentage of diagnosed diabetic patients treated with prescribed medication for each age group for comparison. The results show that diabetes was diagnosed in both age groups but significantly ($p<0.05$) more in age group 45-69 years compared to age group 18-44 years. Second, the results show that significantly ($p<0.05$) more women were diagnosed with diabetes mellitus compared to men in all age groups. Third, not all the diagnosed patients for both males and females were taking orthodox prescribed medication to control their blood sugar level. In terms of real figures for diabetes, 58,650 patients had developed diabetes in 2016 representing 11.5 % of the adult population of ages between 18-69 years (PAHO 2016) and with most of them developed diabetes in their working years. In terms of treatment, only 36,720 diabetic patients were taking orthodox medication to control their blood glucose level leaving 21,930 with either no treatment or with alternative treatment involving life-style changes, seeking advice from a traditional healer or using herbal remedies.

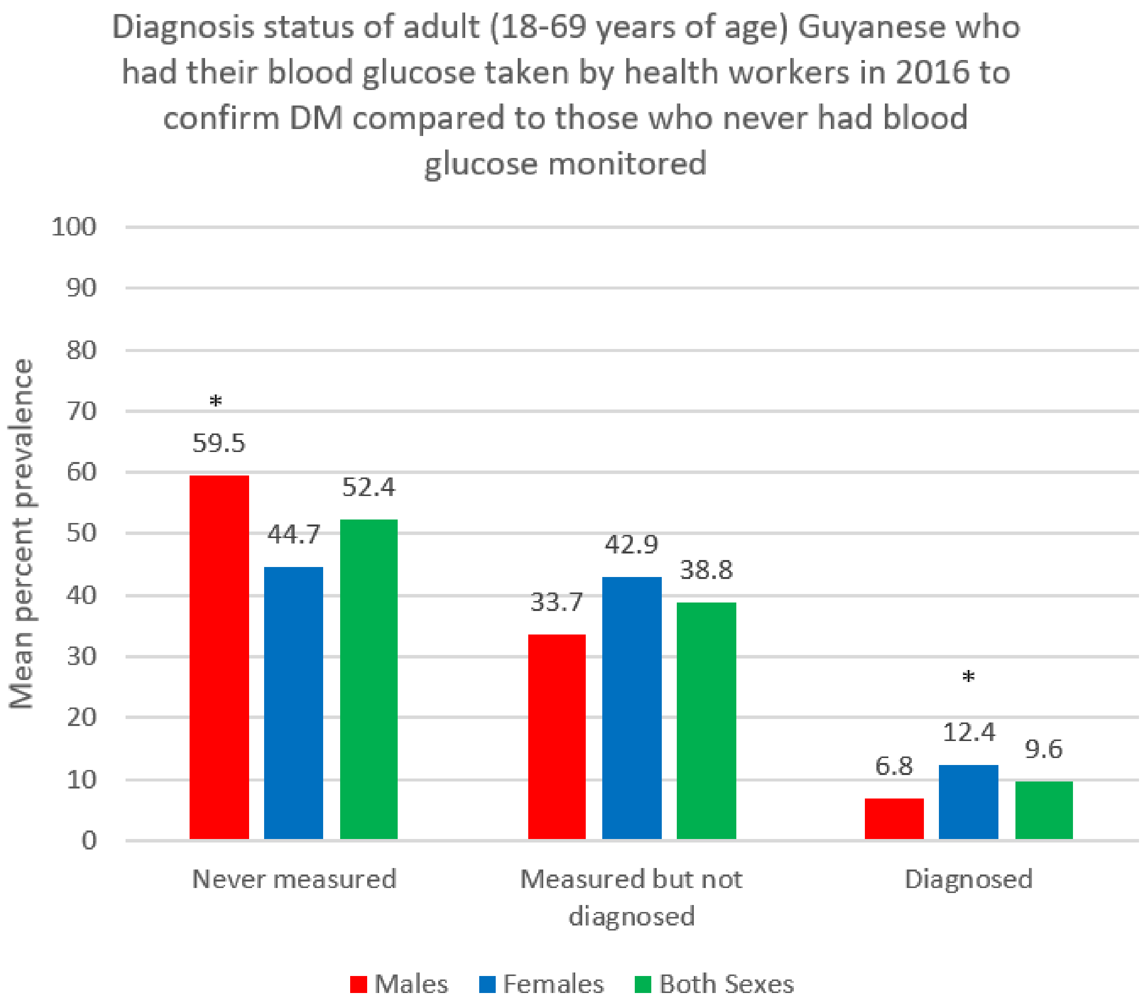


Figure 2.7: Bar chart showing the percentage of adult males (red) and females (blue) between 18-69 years and for both sexes (green) who had their blood glucose measured by a health worker to confirm diabetes compared to those who never had their blood glucose level monitored; *p<0.05 for females compared for males for diagnosed diabetes and for males compared to females who never measures their blood sugar.

Figure 2.7 shows the percentage of adult Guyanese (males and females) between 18-69 years who did or did not obtain a diagnosis of their blood glucose levels by a health worker in 2016. The results reveal that 52.4 % of the population never had their blood glucose monitored by a health worker and there were significantly ($p<0.05$) more males than females. However, almost 38.3 % of the adult population had their blood glucose measured and not diagnosed as having diabetes, The remaining 9.6% had their blood glucose measured by a health worker to confirm diabetes. These findings clearly indicated that more than half of the adult population, especially men, never bothered to ascertain if they had diabetes by monitoring their blood glucose level. This is rather worrying since undiagnosed diabetes could lead to long-term complications and a reduction in the quality of life of the individual. Second, the data confirmed that significantly ($p<0.05$) more women were diagnosed with the disorder compared to men. In addition, a sizable number of the population (38.3%) took the opportunity to find out if they had elevated blood glucose level.

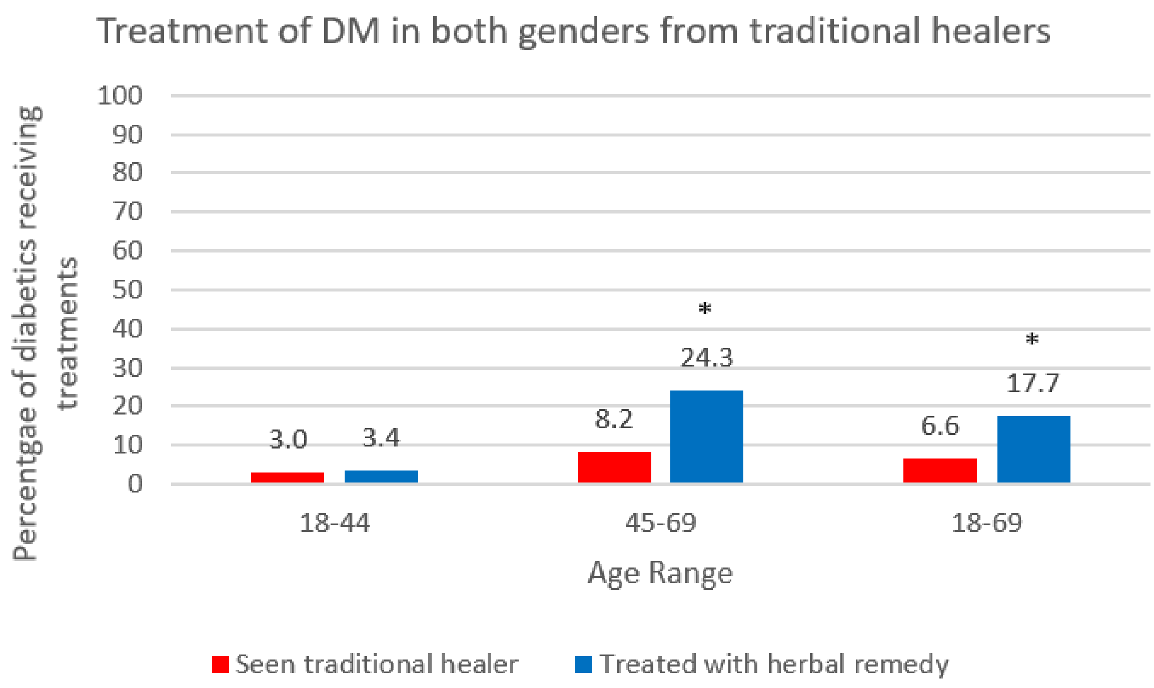


Figure 2.8: Bar charts showing the percentage of adult males and females between age groups 18-44 years, 45-69 years and when the data for both were combined (18-69 years) who sought advice and treatment for their diabetes from a traditional healer (red) or using herbal remedy (blue). *$p<0.05$ for using herbal remedy compared to advice from traditional healer for age group 45-69 years and for 18-69 years.

Figure 2.8 shows the percentage of adult diabetic patients receiving advice from a traditional healer or treated with herbal remedy based on the published data from PAHO (2019) for the year 2016 for both adult males and females of different age groups. The data show clearly that a significant ($p<0.05$) number of patients rely on herbal medicine/remedy to treat their diabetes compared to advice provided by a traditional healer. In a low- income country as Guyana, it is most likely for diabetic patients to take herbal remedy for the treatment of their condition as well as seeking advice from a traditional healer, but more patients prefer to take herbal medicine (17.7% compared to 6.6%). According to the report by PAHO (2019), adult males aged 45-69 years were most likely of all age groups to seek advice from a traditional healer or taken herbal treatment for their diabetes and most of them live in rural areas of Guyana where there are no medical centres.

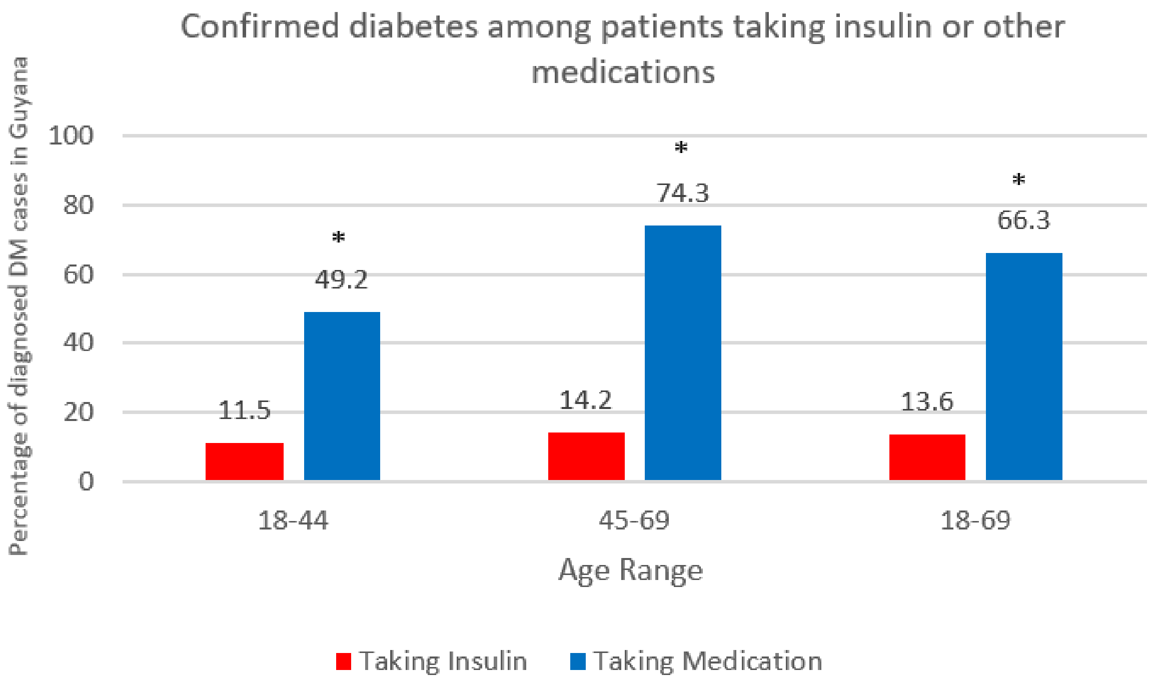


Figure 2.9: Bar charts showing the combined percentage of adult males and females in different age groups and who were treated for their diabetes with either insulin (red) or by prescribed hypoglycaemic medication (blue). *$p<0.05$ for prescribed medication compared to insulin.

Figure 2.9 shows combined data for adult diabetic male and female patients of different age groups who were taking either insulin or other prescribed orthodox medications for treating their diabetes. The data reveal that significantly ($p<0.05$) more patients took orthodox prescribed medicines compared to insulin. The results suggest that a small percentage of patients took insulin indicating that they were probably diagnosed with type 1 diabetes. In contrast, a significantly ($p<0.05$) higher percentage of patients took prescribed medication suggesting that they had type 2 diabetes. Generally, one tenth of the population have type 1 diabetes compared to 90% with type 2 diabetes. However, it is also noteworthy that about 20-30% of type 2 diabetic patients also take daily insulin.

2.3.4 Epidemiology of hypertension in Guyana

Both obesity and diabetes mellitus are risk factors in developing high blood pressure or hypertension which has been on the increase steadily from 15,0 00 diagnosed cases in 2001 to almost 28 ,000 cases in 2011 in Guyana. It then declined slightly in 2011 reaching 19,000 and then started to increase again (PAHO 2019). Among the different ethnicities in Guyana, high blood pressure was reported as the most frequent NCD among Indo- Guyanese (46%), Mixed-Guyanese (45%) and Afro-Guyanese (29.3%) for those who were over the age of 45 years and over (Sockalingam et al, 2021). Published data for 2016 show that hypertension was a major cause of morbidity and mortality in Guyana reaching 320 or 4.45% of total deaths and ranking 18 in the world of 193 countries (see table 2.1) (WHO, 2018). This study now analysed the data on the prevalence of hypertension in Guyana in 2016 when the last epidemiological census was made by the Government of Guyana (PAHO, 2019).

Figure 2.10 shows the percentage prevalence of male and female adult Guyanese, 18-69 years, who had raised systolic blood pressure (SBP) of 120 mm Hg and over in 2016. The data reveal that both adult males and females, at age group 46-69 years had significantly ($p<0.05$) raised SBP compared to age group 18-44 years of age. Moreover, mean systolic blood pressure was higher among males than females in the younger age group (125.2 mm Hg compared to 116.5 mm Hg, respectively) and it also increased slightly with age for both sexes (136.3 mm Hg). These results indicate the hypertension is an age -related medical condition occurring in the prime of life of an individual.

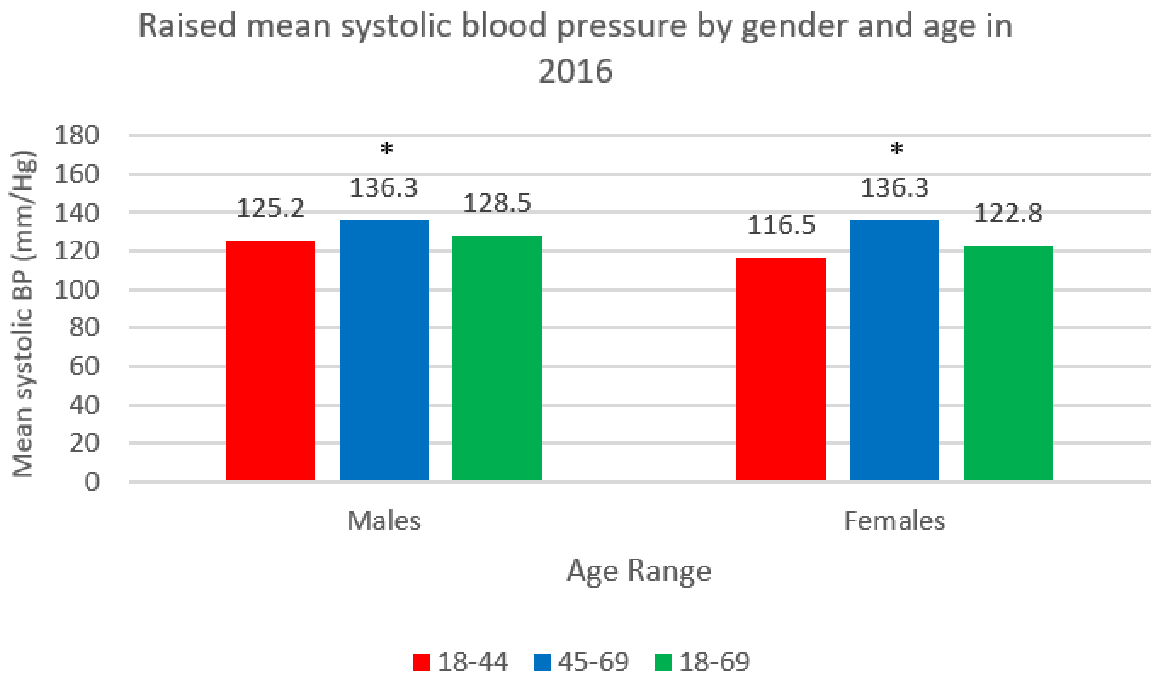


Figure 2.10: Bar charts showing mean systolic blood pressure (mm Hg) of adult males and females of age groups 18-44 years (red), 46-69 years (blue) and when the data were combined (green); *p<0.05 for females compared to males. Note that hypertension increased with age.

Figure 2.11 shows the percentage of adult males and females, 18-69 years, who either had or did not have their blood pressure measured by a health worker in 2016 at the time of the epidemiological census. The results reveal that about a quarter of the population (24.1%) never measured their blood pressure, with significantly ($p<0.05$) more males than females. Likewise, 53.4 % of them had their blood pressure taken but they were not hypertensive, and they comprised of significantly ($p<0.05$) more females than males. Regarding confirmed hypertension, 26.3% of the adult population were diagnosed with hypertension with almost same number for males and females. The data indicate that half of the Guyanese population was normotensive, a quarter was hypertensive, and another quarter failed to monitor their blood pressure to ascertain if they had high blood pressure.

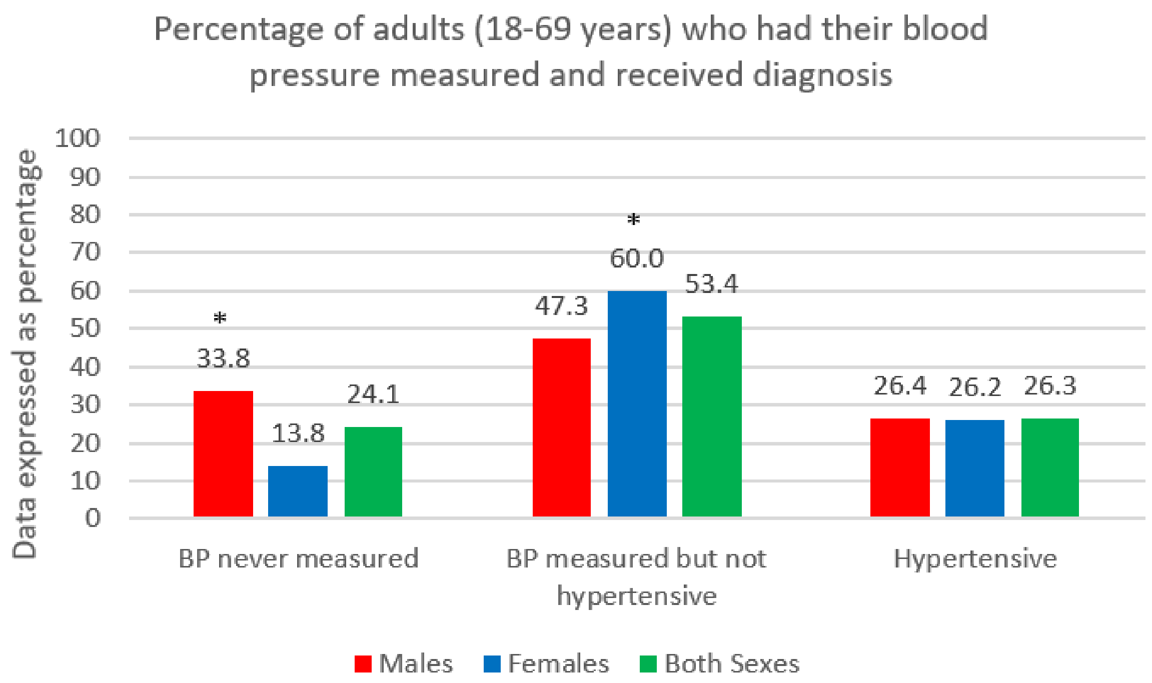


Figure 2.11: Bar charts showing the percentage of adult males (red) and females (blue) of ages 18-69 years who did not have or had their blood pressure measured by a health worker in 2016. The combined data for both sexes are also shown for comparison (green). *$p<0.05$ for males compared for females who never had the blood pressure measured and females compared who males who had their blood pressure measured but not hypertensive. Note that a quarter of the adult population had high blood pressure and another quarter failed to monitor their blood pressure for hypertension.

Figure 2.12 shows the percentage prevalence of hypertensive adult males and females (combined) who took either prescribed orthodox drugs or herbal remedies to treat their hypertension in age groups 18-45 years, 45-69 years and when the two age groups were combined. The data reveal that significantly ($p<0.05$) more hypertensive patients took herbal remedies to treat their high blood pressure compared to those who took orthodox prescribed drugs from a qualified clinician. In a country like Guyana, herbal remedies are extremely cheap and they are sold over the counter by a traditional healer who would explain to the patient as to how to use the herbal remedies.

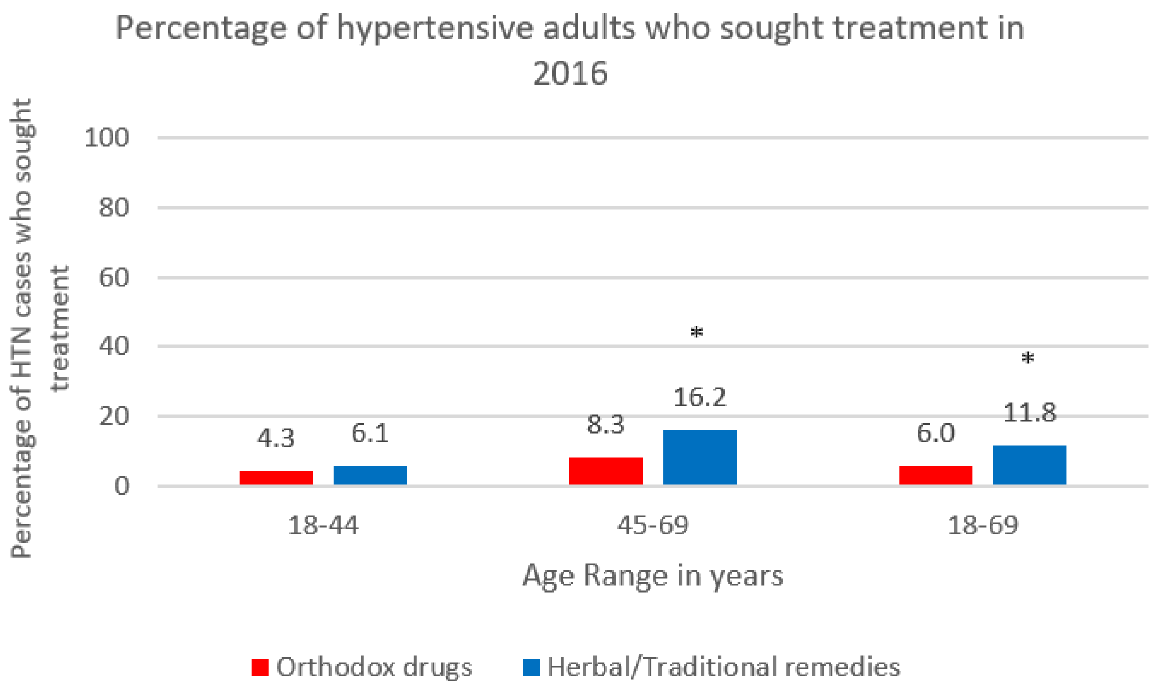


Figure 2.12: Bar charts showing the percentage of hypertensive adult males and females (combined) who took either prescribed orthodox drugs (red) or herbal remedies (blue) to treat their hypertension in age groups 18-45 years, 45-69 years and when the two age groups were combined. *p<0.05 for those patients who took herbal remedies compared to those who to orthodox/prescribed medications.

Figure 2.13 shows the percentage of adult male and female hypertensive patients currently taking antihypertensive medication as by a medical doctor to treat their high blood pressure for age groups 18-44 years, 45-69 years and when the data for the two groups were combined for comparison. The data reveal that significantly (p<0.05) more females (48.1%) took their antihypertensive medication on a regular basis to treat their high blood pressure compared to men (38.3%). Variances by age was evident with those aged 45-69 more likely to take medications compared to those 18-44 years old (58.1% compared to 23.4%, respectively).

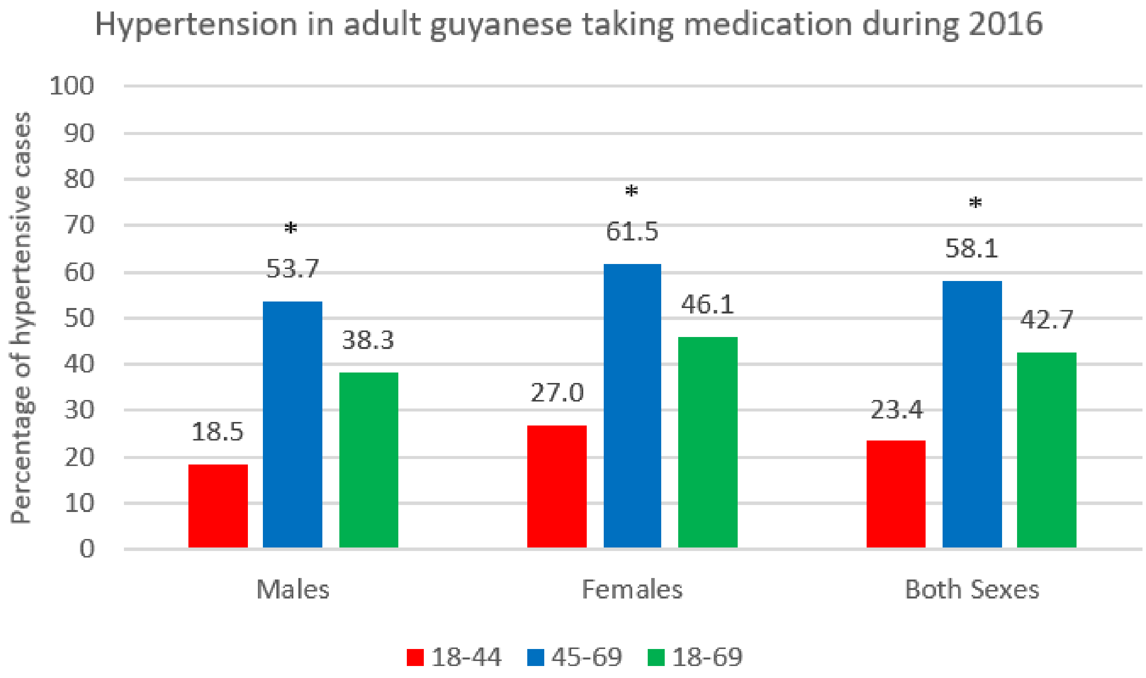


Figure 2.13: : Bar charts showing percentage of adult males and females of age groups 18-44 years (red), 46-69 years (blue) and when the data were combined (green) diagnosed with high blood pressure and currently taking antihypertensive medication as prescribed by a medical doctor. *p<0.05 for age group 45-69 years compared to age group 18-44 years for both males and females.

Since raised blood cholesterol is a major risk factor for developing CVDs and hypertension, then it was relevant to investigate the percentage of adult males and females in the two age groups who had elevated blood cholesterol. The data are presented in figure 2.14 and they show that adult males and females in age group 46-69 years had significantly ($p<0.05$) elevated blood cholesterol compared to adult males and females in age group 18-45 years. In addition, adult females (40.7%) had significantly ($p<0.05$) higher blood cholesterol compared to adult males (30.3%). These results show, just like those for hypertension, that adult Guyanese are more susceptible to hyper-cholesterolemia, a condition which is responsible for the development of CVDs,

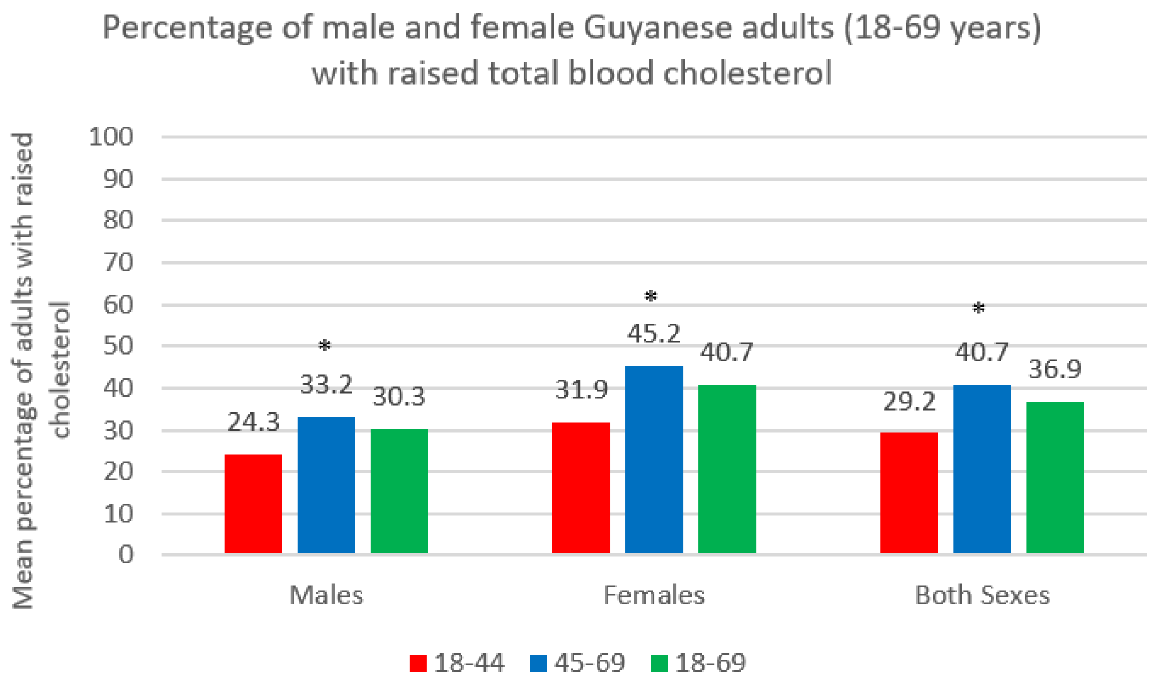


Figure 2.14: Bar charts showing the percentage of adult males and females who had raised blood cholesterol measured by a health worker and received a diagnosis for adult males and females of age groups 18-44 years (red), 46-69 years (blue) and when the data were combined (green). *p<0.05 for age group 45-69 years compared to age group 18-44 years for both males and females.

2.4 Discussion

The main objective of this study was to analyse the most recently available epidemiological data from the Ministry of Public Health in Guyana in collaboration with Pan American Health Organization (PAHO, 2019) to confirm the wide prevalence of three major NCDs, namely, overweight and obesity, diabetes and hypertension among adult males and females who are in their working years in life. The main findings reveal that the three NCDs are indeed very prevalent among both adult males and females but significantly more so among females, especially when they reach the ages between 46 to 69 years. In addition, almost twenty five percent of adult Guyanese failed to diagnose their medical conditions and many of those who are diagnosed prefer to seek advice from a traditional healer and take herbal remedies to treat their diseases rather than taking prescribed drugs. The discussion will address these findings later, but first, it is of paramount importance to understand the danger to health and economic burden of non-communicable diseases (NCDs) to human population globally (Murphy et al, 2020).

NCDs have reached pandemic proportion worldwide posing a major threat to social and economic development in many countries, especially households from low- and middle-income countries where they spend more on health care privately and as such, they are at a greater risk of excessively high expenditure leading to impoverishment (Murphy et al, 2020). As a discipline, epidemiology has improved knowledge and understanding to the forefront of global health. Moreover, epidemiological intervention has helped public health workers to appreciate the impact and burden of NCDs in widening socioeconomic disparities. Epidemiology has also contributed to the development and implementation of many preventive measures, strategies and treatments of known efficacy and safety to reduce disease burden in the world (Patel and Webster, 2016). Like many other countries globally, especially low- and middle- income countries, Guyana is experiencing a formidable disease burden of NCDs which are solely responsible for most of the deaths in the country (Coates et al, 2020; Martinez et al 2020). In 2005, more than 31 million people die from NCDs, representing 60% of all deaths globally. In 2017, the NCDs-related deaths worldwide increased to 73% compared to 60 % in 2005. Currently, seven out of ten deaths in developing countries are due to NCDS and these diseases are closely linked to Covid-19, especially among some ethnic groups (Coates et al 2020; Habib and Saha, 2009; Bello-Chavolla et al. 2020; Mc Gurnaham et al. 2020; UKNS, 2020; William et al. 2020; Martinez et al 2020).

Guyana has a unique diversification with six different ethnic groups comprising of Indo, Afro, Indigenous, Mixed Race, Chinese and European Guyanese. But the health of many Guyanese is very weak due to the prevalence and burden of NCDS. This is associated with a number of risk factors including unhealthy lifestyle habits such as excess smoking and alcohol consumption, lack of physical activity, unhealthy diets, mental health problems, suicides and others, all of which lead to the development of NCDs over time. In 2016, 68% of deaths in Guyana were due to NCDs, especially cardiovascular diseases (CVDs) (34%), cancers (8%), diabetes (8%), chronic respiratory diseases (3%) and others, The risk of chronic deaths in Guyana is 31%, especially among people in their working years (20-69 years) resulting in a negative impact on the economic productivity and health expenditure. of life (PAHO, 2019).

In 2016, the Government of Guyana, via the Ministry of Public Health (MPH) and funded by PAHO, decided to address the prevalence of NCDs. The MPH did an epidemiology study to determine the prevalence of NCDs in the country from numerous districts, households and selected respondents, collecting demographic and behavioural data using a questionnaire, measuring waist circumference, height, weight, and blood pressure as well as collecting venous blood for analysis (PAHO, 2019). The data were analysed and presented as a report on the prevalence of NCDs relating to many aetiological factors. The current study was more interested in overweight and obesity, diabetes, high blood pressure and to a lesser extent, lipid profiles. Treatment of these NCDs is very expensive and many patients usually have to pay for their treatment when using orthodox prescribed medications. Those who cannot afford prescribed commercial drugs turn to either traditional healers for advice or use herbal remedies. The long-term objective of the current study was to ascertain how life-style changes, combing with herbal treatment, could be more cost- effective for the patients and more so, the doses of the herbal medicine which can induce a significant efficacy and if it was possible to combine orthodox medications with herbal remedies without exerting any inhibition or synergistic effect on the treatment procedure. The discussion will now critically address the main findings of the PAHO (2019) report on the three NCDs comparing the data with those available globally.

As a low income developing country in South America, NCDs are very prevalent in Guyana, just like many other developing countries all over the world (Martinez et al, 2020). Although the country is low income, there is a sizable group of people who are well-educated and wealthy and as such they indulge in a modern life-style habits like many developed countries leading to the development of NCDs. Moreover, two out of three deaths globally are contributed to

NCDs annually and Guyana is one of them (Habib and Saha 2008; Kaieteur, 2018; Coates et al, 2020; Martinez et al, 2020). Many low-and middle-income countries which gained their independence from colonial powers are now emerging as semi-developed countries with more people achieving tertiary education and earning higher salaries leading to a change in their life -style habits and resulting in the development of NCDs. People now possess certain behavioural risk factors such as eating more foods but not the right ones, especially those rich in fats and sugar. They also consume more alcohol, fizzy drinks and foods rich in sugar, smoke more and exercise less, all leading to high blood pressure, overweight, obesity, diabetes, high blood cholesterol, heart failure and sudden cardiac death (Smail et al, 2020; Coates et al, 2020). Instead of walking to work or to the shop, riding or using public transport, they tend to use their car and the journey would take several hours in heavy rush hour traffic resulting in stress and muscle fatigue. In addition, many people do not have time to eat slowly enjoying their meal. Eating fast and late at night are risk factors for NCDs, especially obesity, diabetes and CVDs (Hosie, 2017; Tanner, 2017). Likewise, people do not have the time to cook their own meals of choice, but instead they eat more 'fast-foods' and many people binge and snack more often, all of which lead to NCDs. The development of overweight, obesity, diabetes, high blood pressure and raised blood cholesterol are constantly increasing in Guyana due to a number of risk factors which have synergistic effects upon our body. For example, a person who is obese, diabetic and hypertensive and does not participate in physical activity is most likely to die from sudden cardiac death (Sheldon, 2020; Smail et al 2020). The unhealthy life-style problem lies with the individual who has the ability and will-power to control it, accompanied by an element of psychological intervention to adhere to change (Martinus et al, 2006).

Compared to other parts of the world, almost 9% and 3.4% of all annual deaths are due to diabetes and hypertension, respectively in Guyana. Most annual deaths in Guyana are due to mainly to CVDs representing around 33%. Deaths from certain NCDs in Guyana rank much higher compared to other countries globally (PAHO, 2019). To date, there are no published annual data from the Ministry of Public Health in Guyana on the number people who die from obesity, but obesity is a major risk factor for diabetes and CVDs. Likewise, most diabetics usually die from kidney failure (about 10%) and mainly heart failure (about 80%). Generally, people who develop obesity tend to develop either pre-diabetes, fully blown T2DM (diabesity) or insulin resistance (IR) leading to the development of hypertension and other cardiac diseases. As such, the number of reported deaths due to CVDs is indirectly link to obesity and diabetes (Bachani and Back, 2005; Smail et al, 2022).

The results presented in this study clearly show NCDs are increasing gradually in Guyana. For example, diabetes increased gradually from 4.5% in 1980 to 7.2% in 2000, 9.1% in 2016 and 10.3% in 2017. Similarly, obesity increased from 10% in 2000 to 15% in 2010 and to 20% in 2020 for the total population. However, for adult population, obesity rates among adults in Guyana increased from 35% in 2006 to 44% in 2010 and 55% in 2015 according to Pan-American Health Organization (PAHO) (WHO, 2018). Likewise, in 2000, hypertension in Guyana was 18% and this increased slightly to 19% in 2015 and dropped slightly to 18.5 % in 2020 (WHO, 2013; 2018; Sockalingam, 2019). These three NCDs are very prevalent in Guyana and both men and women are affected especially after around 45 years of age. Moreover, some ethnic groups, especially Indo-Guyanese and Afro-Guyanese, are more susceptible in developing NCDs compared to others. In the case of Indo- Guyanese, they represent the highest number after 45 years of age for hypertension. Likewise, regarding basal metabolic index (BMI) and diabetes, more women have overweight, obesity and diabetes compared to men (WHO, 2013; 2018; Sockalingam et al, 2021). It is now known that about 2 out of 3 women die from NCDs, representing 16.8 million deaths globally. The reason(s) for this difference in susceptibility to obesity and diabetes (and possible to hypertension) is not fully known.

As such, the question which now arises is this. Why are more women developing weight gain and subsequently becoming obesity and developing diabetes and hypertension compared to men? It is apparent that women seem to eat more refined carbohydrates and those who were nutritionally deprived as children tended to put on more weight as adults. There is also evidence that women of higher socioeconomic status are significantly more likely to be obese. There may also be hormonal effects, menopausal age, more body weight fat, inactivity, working and running a home at the same time leading to stress, unhealthy eating habits and others (Bonita and Beaglehole, 2014). There is also much evidence that males participated in high levels of physical activity compared to females (PAHO, 2019). Nevertheless, regarding weight gain among some men, there is some evidence that men with higher level of education and wealth have the highest prevalence of overweight and obesity compared to those who have less education and wealth (Sockalingam et al, 2021).

What is now worrying globally is that children as young as 6 years of age are either overweight or obese amounting for 40 million worldwide (Riley et al, 2005; Lopes, 2012; Ng et al, 2014; Knosenko, 2018; Cilia et al, 2019). Obesity is when the body mass index (BMI) is 30 kg/m^2 and over whereas overweight is when the BMI is 25-29 kg/m^2 (Nuttal et al, 2015). The same is also true for Guyana where childhood overweight and obesity are growing at an alarming proportion. It is estimated that 27% boys and 34% girls between the ages of 6-16 years are obese. This is due to excess sugar consumption and most of them do not participate in daily exercise and this is more prevalent in urbanised areas. As such, overweight and obesity exert a negative impact on the children of Guyana (Kaieteur News, 2018). It is now well known that that childhood obesity is an initiator for several different NCDS including diabetes, covid-19, CVDs, respiratory ailments, kidney failure and others, thus reducing their quality of life and their life span resulting in early deaths (Bello-Chavolla et al. 2020; Mc Gurnaham et al. 2020; Sheldon 2020; UKNS, 2020; William et al, 2020; Martinez et al, 2020).

Regarding diagnosis and treatment of NCDs in Guyana among adult population, the data reveal that almost a quarter of the population was never diagnosed for either diabetes, hypertension or raised blood cholesterol. However, around fifty percent were diagnosed but with no diabetes nor hypertension, while around another quarter of the population was diagnosed with either diabetes or hypertension and they were treated for their medical conditions using either commercial prescribed drugs by health workers or seek advice from a traditional healer and taking herbal remedies (PAHO, 2019). Interestingly, the number of diabetic and hypertensive patients who seek nonpharmacological treatment almost double in number compared to those who obtained orthodox medicines. The question which now arises is: Why more adult Guyanese prefer to use non-pharmacological treatment to cure their illness compared to prescribed commercial drugs? The most likely answers is the cost for prescribed medications compared to herbal remedies which are far cheaper. Second, the use of herbal remedies for ailments has been passed down from generation to generation in Guyana and it is therefore not surprising that with the upsurge of diabetes, hypertension and CVDs, many persons may take to herbs to combat their illnesses. The beneficial uses of phyto-medicines have a long history in human lives. They are the sum- total of the knowledge, skills and practices based in theories, beliefs, and experiences of different cultures. Amerindians, black slaves from Africa, Indian indentured laborers from India, Portuguese from Madeira, Chinese from China, and European Caucasians used plants to maintain their health on a regular basis as well as in the prevention, diagnosis, improvement and treatment of physical and mental illnesses (Wheelwright, 1974; Choudhary et al, 2018; Kamyab et al, 2021).

The data presented in this study have also shown that the trend of NCDs is rising gradually in Guyana, especially among the fast- growing middle class medium earners population. As such, the Government of Guyana has to implement an aggressive plan to tackle the growing trend of NCDs which are placing financial burden on the public and private health sectors, including the patients themselves. It is now well known that NCDs are chronic diseases which have long duration, and they progress slowly with time, but they are also preventable and this depends on the individual (Srivastava and Bachani, 2011).

The question which now arises is this: What can the individual and the Government of Guyana do to reduce the number and subsequently either reduce or prevent the development of NCDs? Firstly, the Guyana Government can introduce a more aggressive campaign via schools, university, workplace, media (radio, TV, newspapers, internet etc), churches, health centres and clinics and other means to impact on the cross cutting in the modifiable risk factors associated NCDs. The interventions should focus on the abuse of alcohol, the harmful use of tobacco and its products, eating unhealthy diets which are full of sugar, fats and salt and adverse effect of physical inactivity. There is also the need to introduce legislation to cut down the amount of sugar in fizzy drinks and to implement health education for the children from an early age about the importance of maintaining healthy bodies and minds. As such, the Ministry of Public Health, in conjunction with the Ministry of Education, have to initiate health promotion programmes focusing on sensitising students about the need to eat healthy and participate in daily physical activity. This awareness message of healthy bodies and minds can be disseminated from within the school environment to the parents and guardians within the various communities. People have to develop healthy behaviours which will include regular exercise, healthy eating habits, regular health check-ups, proper use of medication and the abuse of tobacco smoking and alcohol consumption. The Guyana Government must provide such facilities as early diagnosis and screening, emphasise more on health promotion and public awareness programmes making the services universally accessible in the whole of Guyana. They should also get the health professionals to prescribe exercise as a therapy instead of medication (Kaieteur News, 2019).

2.5 Conclusion

In summary, this study has highlighted the prevalence of such NCDs as obesity, diabetes and hypertensive in Guyana and the burden which they execute to the population in Guyana. Published data from the Ministry of Public Health strongly support the rapid development of NCDs among adult population with significantly more adult women are at risk compared to adult males. Almost a quarter of the population are not diagnosed for NCDs and the majority of those who have confirmed NCDs seek advice from a traditional healer and used herbal remedies to treat their illnesses instead of prescribed commercial medications. Data also show that such NCDs as diabetes, hypertension and CVDs are responsible for more deaths in Guyana and rank high globally. Furthermore, recommendations have been suggested for the Government to implement in reducing and/ or prevent the burden NCDs.

Chapter 3:

Type 2 diabetes mellitus can be treated with *Momordica charantia,* in combination with diet modification, daily exercise and diamicron MR.

3.1 Introduction

Diabetes mellitus (DM) is one of the oldest metabolic disorders to inflict humans (Lotfy et al, 2016; Papatheodorou et al, 2016; Harding et al, 2019). Generally, DM is now classified on its aetiology, natural history and clinical manifestation mainly as type 1 diabetes mellitus (T1DM; 5-10%), type 2 diabetes mellitus (T2DM; (85-90%) and gestational (pregnant women) DM (4-5%) (ADA, 2010; Mayo-Clinic, 2018; Diabetes, UK, 2019: ADA, 2019). DM is not a disease, but a metabolic disorder due to elevated blood glucose (hyperglycaemia (HG)) level because of either the lack of insulin or insulin resistance (IR). The metabolic hormone insulin plays a major physiological role in the body to regulate blood glucose level and as such, diabetes is classified as a metabolic disorder leading to many other diseases, including blindness, neuropathy, hypertension, heart failure, sudden cardiac death, kidney failure and others (Adeghate and Schantter, 2006; D'Souza et al, 2009; Lotfy et al, 2016; Smail et al, 2020).

Currently, over 480 million people have diabetes worldwide (1 in 10% of the world's population) with 90% have T2DM and 10% have T1DM and gestational diabetes (Zimmet, 2017: ADA, 2019). The total number of diabetics vary from one country to another globally or regionally with prevalence of almost 5-10% (lower range) compared to about 20-25 % (higher range) (Danaei et al, 2011). Another 250 million people are undiagnosed, and more than 1.5 billion people have pre-diabetes and insulin resistance (IR). Several people with pre-diabetes are most likely to become diabetic later in life (Lotfy et al, 2016; Zimmet, 2017; ADA, 2019; Diabetes UK, 2019). Globally, it costs almost $1 trillion USAD (15% of global budgets in terms of life and demand on health budgets) to diagnose, treat and care for diabetic patients so that they can enjoy a better quality of life (Petersen, 2018; Diabetes UK, 2019). It is estimated that the number of people with confirmed DM will rise to more than 700 million (10%) by 2035 thereby doubling the global health budget (Wild et al, 2004). Globally, almost 75% diabetic patients and not the Government, who pay for the health care (WHO, 2011;2020; Guariguata et al, 2014; Diabetes, UK, 2019; MPH, Guyana 2016; Zimmet, 2017). Generally, diabetes exerts tremendous burden and suffering to mankind irrespective of age, gender, ethnicity or religion. Guyana has a population of about 780,000 people with about 75,000 (9.6%) reported cases of diabetes in 2016 (Bachwani and Back, 2005; MPH, 2006; 2016; Singh et al, 2011; IDA, 2014). It is estimated that 25,000 cases (3.1%) are undiagnosed and 175,000 people (22%) have pre-diabetes in Guyana. These numbers represent about 35% of the population comprising of Indo-Guyanese, Afro-Guyanese, Native-Amerindians, Chinese, European and people of mixed- race Guyanese.

Since time immemorial, mankind was trying to find medications to alleviate pain, to cure illness and to treat wounds (Sabatowski et al, 2004). The healing of the body with medicinal plants and seaweeds following diseases is as old as the existence of mankind. Throughout time, mankind has been searching for new and novel drugs in nature. Most drugs from plants have been isolated from the bark, roots, seeds, leaves and other parts of the plants. One such plant is *Momordica charantia (M charantia)* which *was* originated from India. The plant was taken to different parts of the world, including China, Southeast Asia, Africa, the Caribbean and South and Central America by Indians during colonization when the different Europeans Powers took the Indians to work in colonies as indentured labourers (Chandrasekar et al, 1989; Gopalkrishnan, 2007; Devika et al, 2015).

The main aim of this study was to investigate the potential cost-effective use of daily consumption of *M charantia* juice in conjunction with diet modification, daily exercise and the orthodox drug, diamicron MR in patients with T2DM. The first objective was to investigate the time-course and dose-dependent effects of *M charantia* either alone or in combination with exercise, diet modification and diamicron MR in newly diagnosed diabetic patients measuring fasting blood glucose level (FBGLs), blood pressure (BP) and changes in blood biomarkers including lipids and cations. The second objective was to determine the postprandial effect of *M charantia*, diet modification and physical exercise in both healthy and diabetic subjects undertaking glucose tolerance test (GTT). The final objective was to analyse M charantia for some of its biochemical contents using established analytic techniques.

3.2 Methods

3.2.1 Recruitment of Patients

Newly diagnosed T2DM patients, who visited General Practitioner (GP) clinic of the Investigator for treatment, participated in this study. They comprised of 5 male and 5 female patients. The procedure was done according to established investigative trial/study methods (Joseph and Jini, 2013; Kinoshita and Ogata, 2018). The patients, who were on no medication, were asked to participate in the programme at their own will and signed a consent form (see appendix I). They were also given a questionnaire that contained a number of questions to complete, based on their knowledge and understanding of diabetes and subsequently, returned them to the clinic for analysis (see appendix IIIA). The rationale was to ascertain how much knowledge and understanding they had on diabetes. In addition, a thorough discussion about diabetes and its long-term complication and willingness to participate in this investigative research study was done by the Investigator

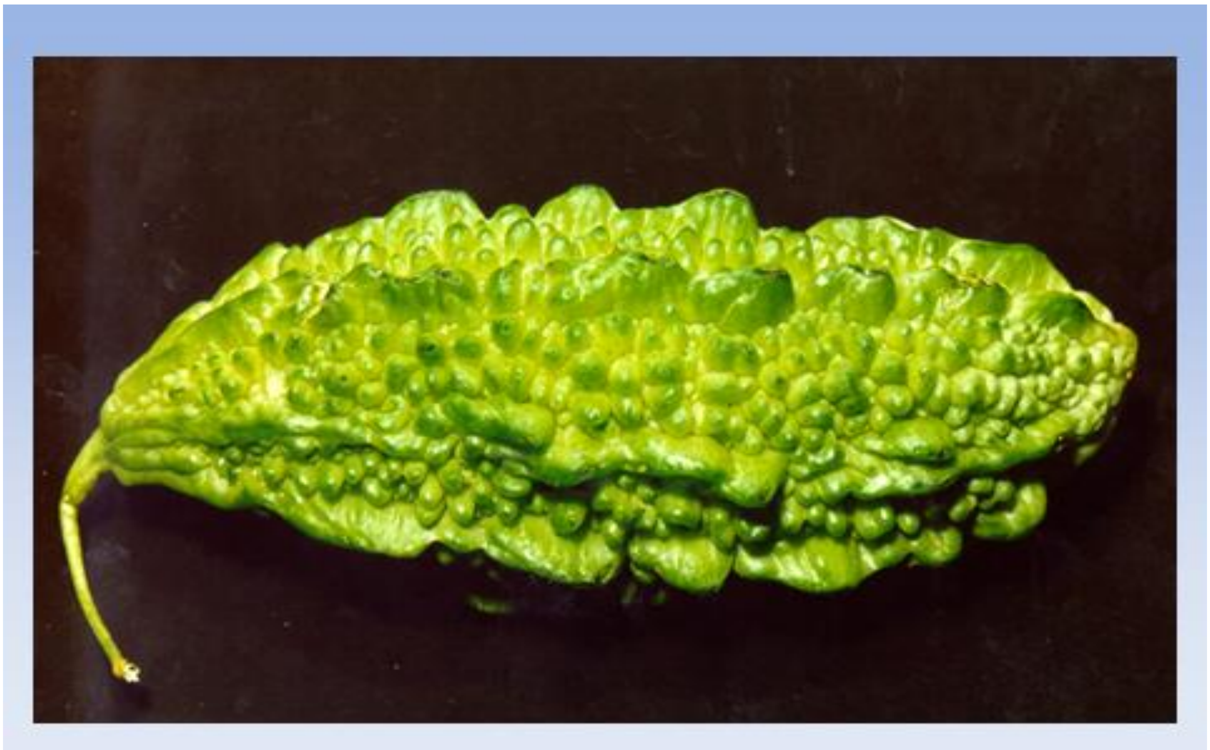
3.2.2 Diet Modification and Daily Physical Exercise

Following initial discussion with the Investigator, all patients were introduced to, and guided by a qualified Dietitian and a professional Physical Activity Instructor regarding diet modification and daily exercise, respectively aided by the Investigator at the start of the study and follow-up contacts were made every two weeks to ensure adherence (Martinus et al, 2006). Before the start of the experiments, all 10 patients in a group, were told by the trained Dietician how to modify their diets in terms of quality, reduction and what to eat as anti- diabetic, anti-obesity and anti- hypertensive meals on a daily basis. The same processes were done with all the patients who participated in the studies in chapter 4 on obesity and in chapter 5 on hypertension. They were also told about the risk of regular snaking and binging as well as eating too much fast foods regarding their health. Each patient was also asked to keep a diary of the meals they ate daily as well as monitoring their blood glucose and body weight when possible. All the patients were seen by the Investigator on a weekly basis or at convenient dates for consultation accompanied by their diary for inspection for adherence and glucose and body weight monitoring. Similarly, before the start of the daily exercise intervention, the diabetic, obese and hypertensive patients had meetings with the professional Physical Activity Instructor who explained to them the different types of daily exercise they could perform and how they could monitor progress with the aid of their mobile phone health app and a diary. Most patients were encouraged to walk or run daily for 30 minutes to an hour or ride their bicycle or the static bike. In addition, they were told how to do stretching and bending exercises for 5-10 minutes daily. Some patients, who could afford it, had access to the gym for daily exercise. Like diet modification, the patients were seen by the Investigator on a weekly basis for consultation accompanied with their diary for adherence and glucose and body weight monitoring. The patients were given oral information by the Investigator about the potential benefit in using *M charantia* to treat their medical conditions either alone or in combination with diet modification and/or exercise and with the orthodox anti-hyperglycaemic drug, diamicron MR, as in the case of diabetes. Each intervention was done over a period of 6 weeks followed by a rest period of 2 weeks and start of the other intervention for the same period of time. During the rest period, the fasting blood glucose of each patient was monitored regularly to ensure that blood sugar did not rise to pathophysiological level as a precaution.

3.2.3 Preparation of *M charantia* for consumption

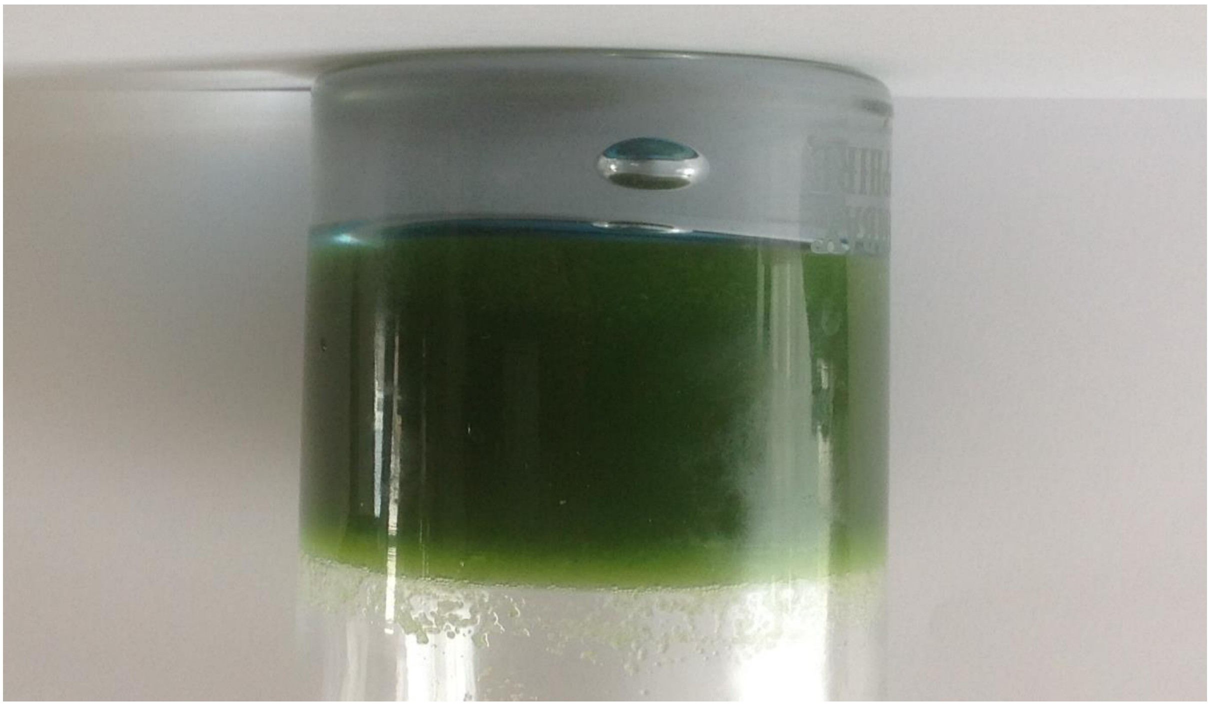
The fresh green fruit of *M charantia* was purchased from the local market almost daily as required by the patients (Figure 3.1A). The green fruit was washed, cut horizontally and the seeds and white tissues were removed with a small tablespoon. Thereafter, the fruits were cut into small pieces (see Figure 3.1B), weighed and blended with drinking water (weight to volume or 1 gram in 1 ml) to form a green juice (see figure 3.1C). The patients were given a choice to eat either the chopped fruit after weighing it or drink the juice (either 5 ml, 10 ml or 20 ml) daily. They were also asked to drink half of the volume (2.5 ml or 5 ml or 10 ml) in the morning and the other half (2.5 ml or 5 ml or 10 ml) in the afternoon about 10-15 minutes prior to their meal. Initial study up to week 1 found that the patients preferred to drink the juice rather than eating the fruit due to its bitter taste. As such, they continued in consuming the green fresh juice throughout the study. At the start of the second week, two patients withdrew from the study due to the bitter taste of *M charantia* leaving 8 patients (4 males and 4 females) to continue with the study. Figure 3D shows the ground powder of *M charantia* for chemical analysis.

(A)



(B)

(C)



(D)

Figure 3.1: Photographs showing the (A) a succulent *M charantia* green fruit from the tree, (B) the succulent green fruit cut into small circular pieces, (C) the blended green juice in water (volume/weight; for example, 100 grams in 100 ml of water) and (D) the dried ground *M charantia* as a powder.

3.2.4 Inclusion criteria: Patients with known diabetes, obesity or overweight or hypertension older than 18 years, new patients, willing to participate and were available.

3.2.5 Exclusion criteria: Patients with gestational diabetes, younger than 18 years, physical and mental illness and on any other medications.

3.2.6 Experimental protocols for blood collection and measurements of blood pressure and BMI.

Once recruited for this programme, fasting blood glucose levels (FBGLs) from the 10 newly diagnosed diabetic patients measured on a weekly basis for 6 weeks. In addition, HBA1c, lipid profiles and cation levels were measured using a small sample (1.0 ml) of blood taken from the cubital vein of either the right or left arm by veni-puncture by the Investigator (A General Practitioner) or a qualified Phlebotomist, at the start of the study at week 1 and subsequently, at week 6 on completion of the study for *M charantia* and diet modification combined with daily exercise interventions. The 1 ml blood was divided into two portions of 0.5 ml each. One portion was placed into an ethylene-diamine-tetracetic (EDTA)- coated tube to prevent clotting and it was used immediately to measure for HBA1c using established chemical diagnostic methods (see section 3.2.7). For the measurements of lipid profiles, triglycerides, cations and trace elements, the other portion of 0.5 ml was allowed to clot for 15 minutes and centrifuged at 5,000 rpm for 1-2 minutes. The supernatant or serum was decanted and placed into a small plastic tube for the immediate measurements of lipids and triglycerides. The remaining serum was covered and stored at minus 20 degrees centigrade for later analysis using the biochemical on-line technique of ICPMS to measure for cations and trace elements. For comparison, a small volume of 0.5 ml of blood was also taken from 10 healthy age-matched control subjects, allowed to clot and the serum decanted and stored at minus 20 degrees centigrade for the measurements of cations and trace elements as required. For the newly diagnosed patients, their systolic and diastolic blood pressure (SDBP) and basal metabolic index (BMI) were measured for comparison for *M charantia* alone and diet modification combined with exercise interventions only at the start at week 1 and at the end of the study at week 6 (see details below). The focus of the study was more on *M charantia* alone and diet modification combined with exercise interventions (see table 3.2). The other interventions involving *M charantia* combined with diet modification and exercise or with diamicron MR were done for comparison, especially regarding blood glucose level.

3.2.7 Measurements of fasting blood glucose level (FBGL), blood pressure, basal metabolic index (BMI), glycated haemoglobin (HBA1c) and blood total lipids and triglycerides.

Capillary blood samples were collected from each participant to measure blood glucose levels. Sterile lancets, glucose meter equipment (glucometer; ACCU-CHEK (Instants) and test strips (FreeStyle_Abbott Diabetes Care) were used in order to measure blood glucose level. This process involved the pricking of either the thumb or second finger on the right or left hand to obtain a drop of blood. A glucose-sensitive Free-Style Abbott Diabetes Care Ultra test strip was placed in the front inlet of the glucometer. As soon as a blood -drop signal was observed on the glucometer, the drop of blood from the patient was placed on the strip. After 3-5 seconds, a reading was displayed on the glucometer and recorded manually on a clinical record sheet for each patient individually. All values were expressed in mg/dl. The same process was done for each patient either once or twice weekly. All values logged on the clinical sheet were analysis later. In terms of oral glucose tolerance test (OGTT), the same process in measuring blood glucose was done just before the test and immediately following consumption of a glucose rich (75 mg dissolved in 300 ml of water) solution (zero minute). Thereafter, each subject was asked to drink *M charantia* juice (5 ml, 10 ml or 20 ml) following consumption of the elevated glucose solution, Blood glucose levels were measured at 30 min, 60 min, 90 min and 120 minutes and recorded on a clinical sheet for each patient or healthy subjects. All the data were analysed later and plotted as graphs. In relation to BMI, all the patients were weighed (mass in kg) and their heights (metre) taken. BMI was calculated by dividing the body mass by the square of the body height. Value was expressed as kg/m^2. A BMI of 25.0 -29.0 represented overweight while a BMI of 18-5-24.9 was taken as a healthy range. A BMI of 30 and over was taken as obese. Systolic and diastolic blood pressures (SDBP) were measured by the Investigator using an automated sphygmomanometer (Duronic, UK). This was done by placing a pressure monitored cuff around the upper left arm of the patient. The pressure was inflated to either 180-200 mm Hg or slightly higher and released gradually. Following deflation of the cuff, the systolic and diastolic blood pressures were recorded on a clinical sheet for each patient. This process was done twice about 2-3 minutes after another. The mean value was recorded on the clinical laboratory sheet for later analysis.

As described in section in section 3.2.6 in this chapter, a small sample (1 ml) of blood was taken from either the right or left arm of each patient by the Investigator via veni-puncture and

0.5 ml of the whole blood was used measure lipid profiles and HBA1c for each patient at the start of the study and at the end of the study at week 6 for *M charantia* and diet modification combined with daily exercise interventions.

For the measurements of total lipids and triglycerides, the blood serum sample (100ul) was dissented into a small plaster container for the measurement of total lipids (high density lipoprotein (HDL) low density lipoprotein (LDL), very-low density lipoprotein (VLDL) and cholesterol) and triglycerides. The blood serum lipid and fatty acid profiles were measured using Eon100 Auto Chemistry Analyzer (Scientific Supplies Technology). The small tube wad placed into the Chemistry Auto Analyzer which was controlled by a computer programmed to measure the level of total cholesterol, LDL, HDL, VLDL and triglycerides. The value for each was expressed mg/dl and recorded in the computer in a confidential manner for analysis later. For the measurement of HbA1c, the sample (0.5 ml) of blood was inverted 8-10 times for thorough mixing. Thereafter, 10ul of the blood was pipetted out and inserted a 2 ml plastic tube which contained 1.0 of a diluent. The content was mixed thoroughly and 100 ul was pipetted into a Getein Biotech Inc. disc. Thereafter, the disc was inserted into Getein1100 Immunology Analyzer. The Getein Biotech Machine was programmed to measure HbA1c with a duration of 5 minutes, a value for HbA1c was shown digitally. Each test was done once to each sample the value expressed in percentage.

3.2.8 Time-course of diabetes study employing four interventions.

In the first series of experiments, this study recruited 10 newly diagnosed type 2 diabetic mellitus (T2DM) patients at the inception but 2 discontinued with the study after one week due to the bitterness of *M charantia*. The remaining 8 newly diagnosed T2DM patients continued with the study from week 1 to week 6 for each intervention, followed by a rest period of 2 weeks and then continued with another intervention. The study comprised of 4 interventions over 6 weeks for each. They included (i) *M charantia* intake alone consuming 20 grams daily as a juice (weight /volume), (ii) diet modification with exercise, (iii) *M charantia* intake of 20 grams as a juice daily combined with diet modification and daily exercise and (iv) *M charantia* intake as a juice combined with diamicron MR (60 mg daily with 30 mg in the morning and 30 mg in the evening before meals). All data were expressed as time course graphs. In another series of time course experiments, diamicron MR alone (60 mg daily with 30 mg in the morning and 30 mg in the evening before meals) was administered to another cohort of 20 newly diagnosed diabetic patients for comparison.

3.2.9 Time- course effects of either 5 grams or 10 grams of *M charantia* intake alone

In two different series of experiments, twenty different patients who were diagnosed for the first time with T2DM were divided into two groups of ten patients each. Like previous experiments, all twenty patients were asked by the Investigator to participate in the study, sign the consent form and a discussion was done between the patients and the Investigator regarding the protocol. One group of patients was asked to consume 5 grams of *M charantia* daily, as a juice (volume/weight) over a period of 6 weeks. The other group of 10 T2DM patients did the same but consumed instead 10 grams of *M charantia* juice daily for 6 weeks. Their FBGLs were measured weekly by the Investigator from week 1 at the start to week 6, at the end of the study as described earlier. The rationale for this series of experiments was to ascertain if low doses of *M charantia* fruit juice could exert dose -dependent hypoglycaemic effects as the higher dose of 20 grams.

3.2.10 Oral Glucose tolerance test (OGTT)

For OGTT, both diabetic and control groups were given a high glucose solution for an oral glucose tolerance test (OGTT) immediately followed by *M charantia* juice. The patient drank either 20 grams (8 patients), 10 grams (10 patients or 5 grams (10 patients) of *M charantia* juice (volume/weight). The control healthy subjects (10 subjects) drank only 20 grams of *M charantia* juice (volume/weight) either with or without exercise. The glucose solution consisted of a glucose drink with 75 g of anhydrous D-glucose dissolved in 300 mL of water at room temperature, as prescribed by the ADA (ADA, 2010), The blood glucose levels were measured before the intervention at fasting (t0) and after 30 (t30), 60 (t60, 90 (t90) and 120 (t120) minutes after intervention in both groups. The data were recorded and analysed later as graphs.

For diabetic patients, OGTT was done at the start of the study at week one following diagnosis of diabetes and at the end of the study at week 6 of each of each intervention, For the healthy subjects, OGTT was firstly done using three interventions at the start of week 1 for *M charantia* alone. Second, this *was* followed by daily exercise alone for a week and third, after daily exercise combined with *M charantia* for another week. The healthy subjects were aided with exercise adherence with the help of a professional Physical Exercise Instructor. The data for week 1 and week 6 for diabetes and week 1 and end of week 2 for healthy controls were collected and tabulated as OGTT curves.

3.2.11 Measurements of cations in the dried powder of *M charantia*

Cation concentrations in either dried *M charantia* fruit (see figure 3.1D) or blood plasma collected from ten healthy control and eight T2DM patients upon diagnosis were measured using inductively coupled plasma mass spectrometry **(**ICPMS). This is an analytic technique. which could be used to measure elements at trace level in biological fluid samples. ICPMS is both highly sensitive and selectivity and moreover, it possessed a very good precision for the determination of many cations. The equipment is normally managed by a trained technician.

The dried powdered of *M charantia* fruit in a known amount (usually 10 mg) was dissolved in 1 ml of concentrated nitric acid. A volume of 0.1 ml was added to 0.9 ml deionized water prior to the measurement of the cations. Values were expressed as mg of cation per gram (mg/g) of *M charantia)*. Likewise, blood plasma was diluted in deionized water (0.1 ml in 9.9 ml) prior to measurement of the different cations. Values were expressed as mg/litre. The use of ICPMS was aided by senior technician who prepared the standards for each cation as well as helping in the measurement of each sample. All data were computerized and printed for analysis as graphs.

3.2.12 Measurements of proteins, phenolic content and anti-oxidant properties of the dried powder of *M charantia*

(A) Bradford protein assay

Total protein in *M charantia* was measured using the Bradford assay (Bradford). Known concentrations of albumin were prepared from a stock solution. Likewise, 1 gram of pulverised dried powder of *M charantia* was dissolved in 10 ml of deionised water. Volumes of 5 ml of Bradford Reagent were pipetted out into several test tubes. A volume of 1 ml of known concentrations of albumin solution was added to the tubes with Bradford reagent in duplicate. For blank, 1 ml of distilled water was added to two tubes containing Bradford Reagent. Similarly, 1 ml of the *M charantia* solution was added to test tubes containing Bradford reagent in triplicate. All the test tubes were rota-mixed for 15-20 seconds and this was associated with the development of a blue colour of the solution. After 5 minutes, the colour absorbance was determined against the blank at 595 nm using a spectrophotometer at room temperature. Bradford Reagent was obtained from Sigma. Following the experiment, a standard curve was plotted and the values for *M charantia* was extrapolated from the standard curve. Values were expressed as mg/100 g.

(B) Measurement of phenolic content and antioxidant properties

Phenolic contents and antioxidant activity in *M charantia* were measured by established biochemical methods described previously by Bernado et al (2015). The total phenolic concentration in the *M charantia* water soluble powder (1 gram in 10 ml water) was determined according to Folin-Ciocalteau method employing gallic acid as standard (Bernado et al. 2015). A volume of 375 uL of *M charantia* aqueous solution and 4 mL of sodium carbonate were added to 5 mL of Folin–Ciocalteau reagent. After 15 min, the absorbance was measured at 765 nm. The results are expressed as mg for gallic acid equivalent (GAE)/g of extract. For the antioxidant activity analysis, two methods were performed involving FRAP (ferric reducing antioxidant power) and DPPH (2,2-diphenyl-1-picrylhydrazyl) (Rashid et al 2022). The FRAP method was determined through a ferric reducing effect based on the blue coloured ferrous complex (Fe^{2+}) formation by electron-donating antioxidants action in 2,4,6-tri(2-pyridyl)-s-triazine (TPTZ) presence. A fresh solution was prepared by mixing 25 mL of acetate buffer (300 mM, pH = 3.6) into 2.5 mL of TPTZ solution (10 mM) in HCl (40 mM) and 2.5 mL of FeCl3-6H_2O solution (20 mM). The solution was heated at 37 degrees centigrade. Samples (150 mL) were introduced in tubes with 2850 mL of the FRAP solution and were maintained under dark conditions for 30 min. The absorbance was measured at 593 nm. Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) was used as standard and the results are expressed in _mol Trolox/L. The DPPH method was determined through 2,2-diphenyl-1-picrylhydrazyl radical scavenger. A volume of 10 mL of solution prepared (24 mg DPPH in 100 mL methanol) was added to 45 mL of methanol (= 515 nm Abs 1.1). The solutions were kept for 24 h in the absence of light. The absorbance was determined at 515 nm, and the results expressed in mol Trolox/L (Bernado et al 2015). All the experiments were performed for 3 replicates. Note that the analysis of the dried powder of *M charantia* was done by the Director of Study in collaboration with his colleagues at EGAS MONIZ University in Lisbon, Portugal. All values were expressed as the following :-phenolic content (mg/100 g), anti-oxidant activity (mg AAE/100 g (powder material), caffeic (ng/g) and celuic acid (ng/g).

3.2.13 Statistical analysis of data

Statistical data analysis was done using the Statistical Package for Social Sciences (SPSS) and ANOVA. The data were compared according to the assigned groups and expressed as mean ± SEM (either as standard error of the mean or standard deviation). A value of $p<0.05$ was taken as statistically significant.

3.2.14 Ethical Considerations

The project had ethical clearance from the University of Guyana and UCLan Ethics Committees (see appendix IIA/B). A written informed consent was obtained from each participant after given written and oral information about the study (see appendix I).

3.3. RESULTS

3.3.1 Hypoglycaemic effect of bitter melon in diabetic subjects: An initial study

Figure 3.2 shows preliminary hypoglycaemic data of the effect of 20 grams of *M charantia* juice given to ten newly diagnosed diabetic patients daily over 6 days compared to the start at day 1. The results show that *M charantia* juice can markedly (but not significant; $p>0.05$) reduce fasting blood glucose (FBG) in diabetic patients over 6 days. These initial data prompted the Investigator to undertake a longer period of the study over 6 weeks with the remaining eight diabetic patients, since two patients asked to leave the study due to the bitterness of M charantia.

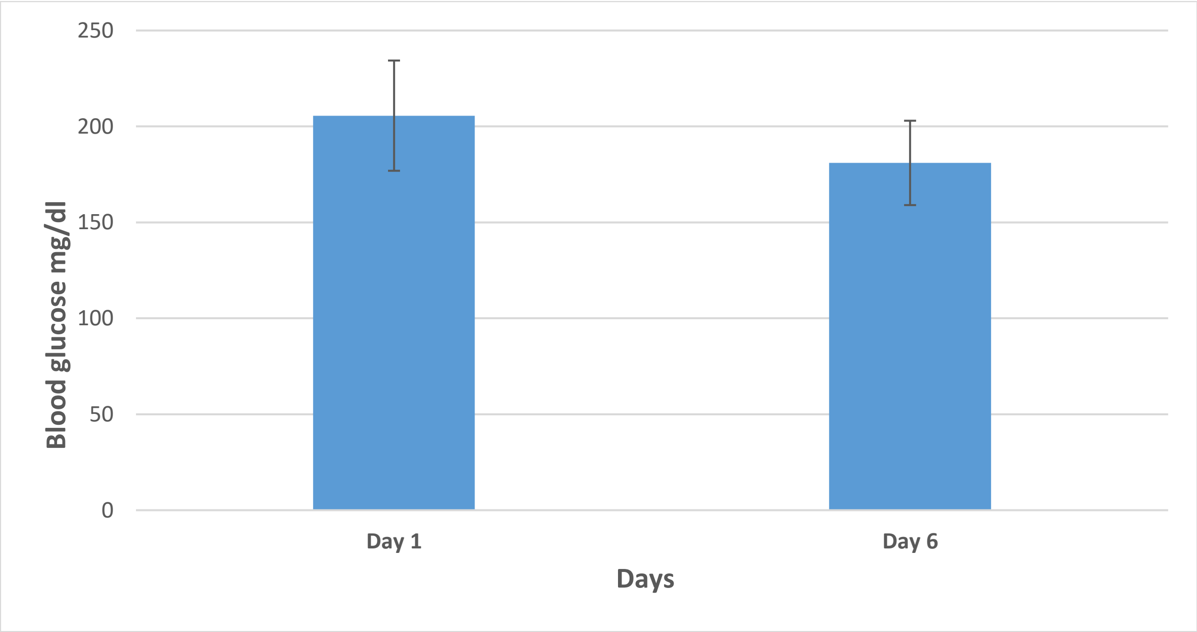


Figure 3.2: Effect of *M charantia* juice intake (10 grams twice daily) on fasting blood glucose level: Data are mean ± SEM, n=10 patients. Note that *M charantia* can exert a marked hypoglycaemic effect at day 6 compared to day 1. After this study, two patients dropped out of the study due to the bitterness of the *M charantia*. The remaining 8 continued with the study for 6 weeks.

3.3.2 Time-course hypoglycaemic effects of *M charantia*, diet modification, exercise and diamicron-MR either alone or in combination over 6 weeks in T2DM patients.

Since the data in figure 3.2 revealed that *M charantia juice* can markedly reduce FBG levels over 6 days, it was decided to undertake a full time-course study but employing different interventions. Eight diabetic patients continued with each intervention over 6 weeks. On completion of each intervention, they had a rest period of 2 weeks and then went on to the next intervention. The first intervention involved the consumption *M charantia* juice alone. This was followed by diet modification and daily exercise by the patients. The third intervention involved the consumption *M charantia* juice alone, combined with diet modification and exercise and finally, the fourth intervention involved the consumption of *M charantia* juice combined with diamicron MR. The time-course results are shown in figure 3.3 and figure 3.4 shows the percentage decrease of blood glucose level for each intervention ($p<0.05$) over 6 weeks compared to week 1 at the start of the study.

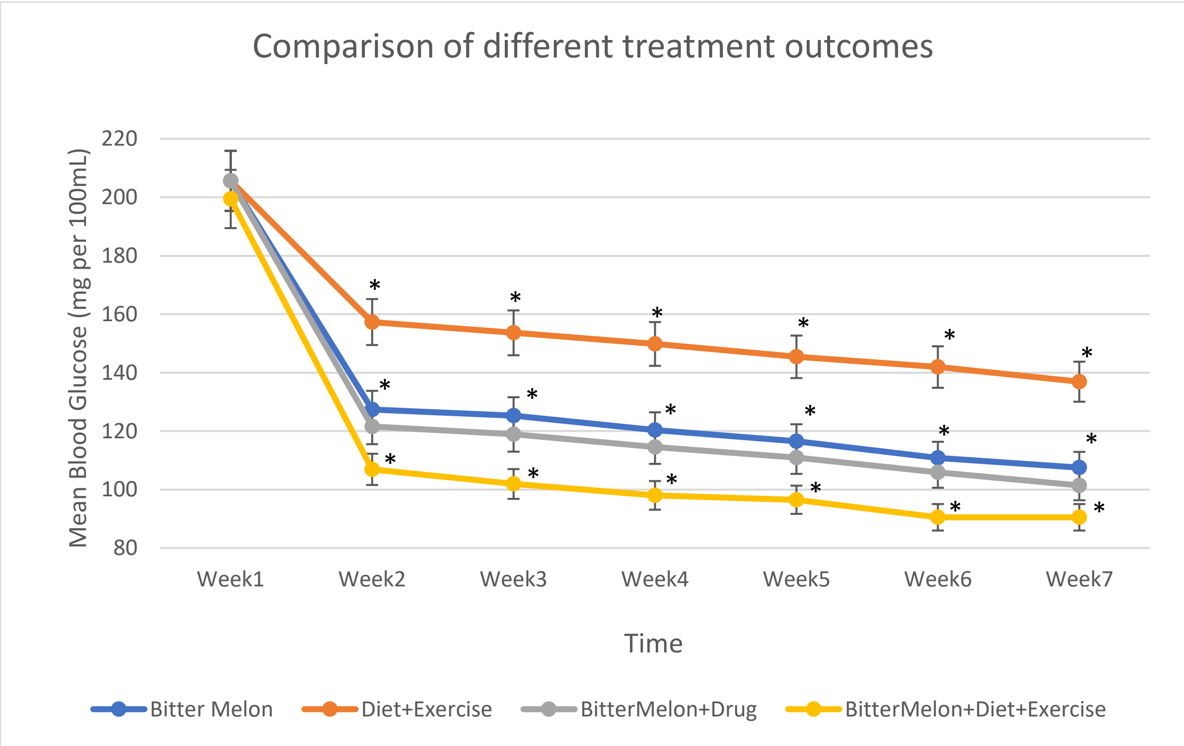


Figure 3.3: Time-course changes of fasting blood glucose levels (FBGLs) in diabetic patients during (A) *M charantia* (bitter melon*)* consumption alone (blue), (B) diet modification with exercise (orange), (C*) M charantia* consumption combined with diet modification and exercise (yellow) and (D) *M charantia* consumption combined with the drug, diamicron MR (grey). Data are mean ±SEM, n=8 patients; *$p<0.05$ compared week 1, (before *M charantia* treatment at start) to end of week 6, for each intervention.

The results in figure 3.3 demonstrated that all 4 interventions were able to decrease FBGLs steeply during week 1 and then gradually to the end of the week 6 with combined exercise and diet exerted the least effective (about 33.4%) compared to the other 3 interventions. *M charantia* was more effective in reducing (47.7%) FBGLs compared to diet and exercise alone. *M charantia* combined with diet modification and exercise reduced BGLs by around 50.6%, while *M charantia* and diamicron MR reduced FBGLs by about 50.7 % compared to the start at week 1 of the study. The best results were obtained with *M charantia* combined with diet modification and exercise or diamicron MR combined with M *charantia* (figure 3.4).

These results clearly demonstrated that newly diagnosed T2DM patients can control their diabetes-induced blood glucose levels by using cost-effective therapy involving daily *M charantia* juice consumption in combination with diet modification and exercise rather than using diamicron MR alone, which they have to purchase. Moreover, *M charantia* did not induce any synergistic effect on FBGLs when combined with diamicron MR. Figure 3.4 and table 3.1 reveal the percentage reduction in blood glucose level for each intervention and the level of significance for each. Many clinicians do not normally recommend the use of complementary medication with commercial orthodox medication, since a combination of the two may induced hypoglycaemia. As such, this is an important finding in this study. Regarding diamicron MR treatment alone (60 mg daily with 30 mg in the morning and 30 mg in the evening before meals) at the inception of diagnosis of their diabetes, the patients (n=20) had a mean fasting blood glucose value of 214.8 ± 3.9 mg/dl. Their HBA1c was 10.1% far within the diabetic range compared to normal values of 4%-5.6%). Following treatment with diamicron MR, the mean blood glucose of the patients reduced to 193.9±1.9 mg/dl, 173.8 ±1.4_mg/dl and 128.4±0.8 mg/dl at the end of weeks 2, 3-4 and 7, respectively compared to the value obtained at the start of week 1, following diagnosis (214.8 ± 3.9 mg/dl). A significant ($p<0.05$) value was obtained at week 4 and a highly significant value was obtained at week 7 compared to week 1. The time course data are presented graphically in figure 3.5.

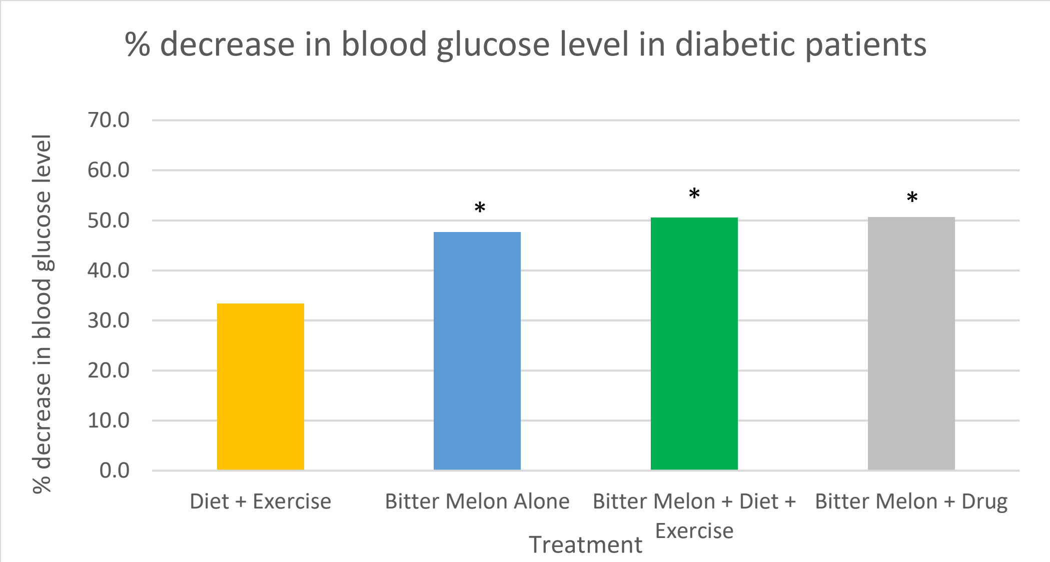


Figure 3.4: Bar charts showing the percentage decrease in FBG levels during each intervention at the end of week 6 compared to the start at week 1. Data taken from figure 3.3; diet modification and exercise (orange), *M charantia* alone (blue), *M charantia*, diet and exercise (green) and *M charantia* with diamicron MR intake alone (grey). All values are expressed as percentage (*$p<0.05$) for *M charantia* alone, *M charantia* combined with diet modification and exercise and *M charantia* combined with diamicron MR compared to diet modification and exercise). Note that diet and exercise exerted a significant ($p<0.05$) decrease in blood glucose compared to week 1, at the start of the study.

Table 3.1: Significant values were obtained in the 4 treatments comparing week 1 with week 6. Single factor ANOVA *($p<0.05$) was employed for effect of different treatments on blood sugar level of patients. (Data taken from figure 3.3).

Treatments	P values	
A. Effects of dieting and exercise on fasting blood glucose Levels in diabetic patients	6.99E-20	*Significant
B. Effects of *M charantia* juice intake (20 grams daily) and fasting blood glucose levels in diabetic patients	3.59E-21	*Significant
C. Effects of *M charantia* juice (20 grams daily) + dieting and daily exercise	3.87E-21	*Significant
D Effects of *M charantia* juice in combination with diamicron MR in diabetic patients	4.69E-10	*Significant

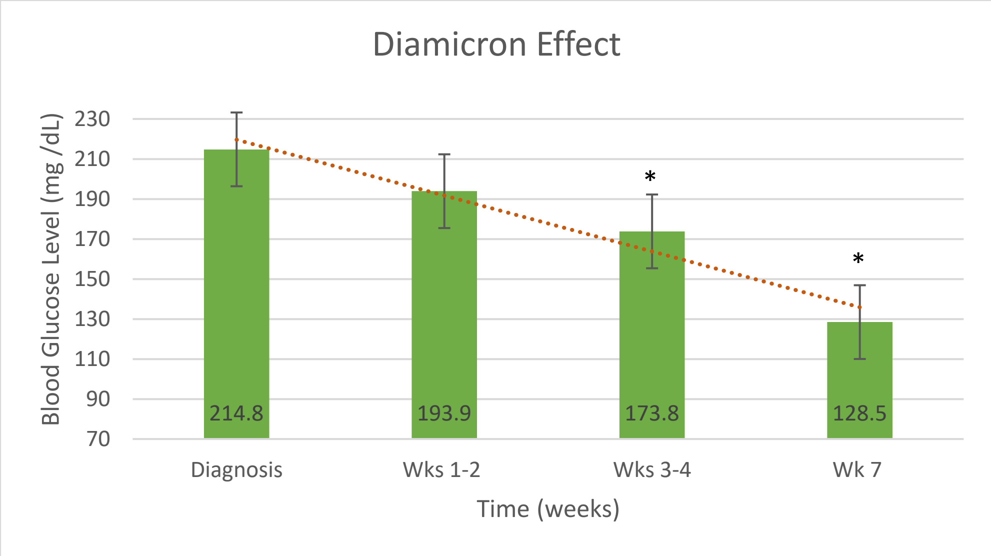


Figure 3.5: Time course effect of 60 mg (30 mg in the morning and 30 mg in the evening) of diamicron MR daily on blood glucose level over a period of 7 weeks in diabetic patients. Note than blood glucose decreased to significant (*p<0.05) level at the end of week 4 and highly significant at week 7 compared to the start at the time at diagnosis. Data are mean +SEM; n=20.

3.3.3 Oral Glucose Tolerance Test (OGTT) in diabetic patients

At the start of the study upon diagnosis of T2DM at week 1 and at the end of the study at week 6, each patient had a OGTT. The data in figure 3.6 show the time-course hypoglycaemic changes following OGTT at the beginning of the study at week 1 (green) and at the end of the study at week 6 (yellow) in patients who consumed 20 grams of *M charantia* juice. The results show that at week 1, FBGLs were in hyperglycaemic range (197.9 ±3.4 mg/dl). However, after 6 weeks of treatment with *M charantia*, BGLs decreased significantly (p<0.05) to 138.6 ±2.7 mg/dl). Regarding the OGTT on both weeks 1 and 6, *M charantia* juice consumption, immediately after consuming 75 mg glucose rich solution, was able to evoke significant (p<0.05) hypoglycaemic effects in a time–dependent manner reaching a significant decrease in blood glucose level after 120 minutes compared to the value obtained following consumption of 75 mg glucose solution at time zero minute. These results clearly demonstrated the potential hypoglycaemic action of *M charantia* to treat diabetes.

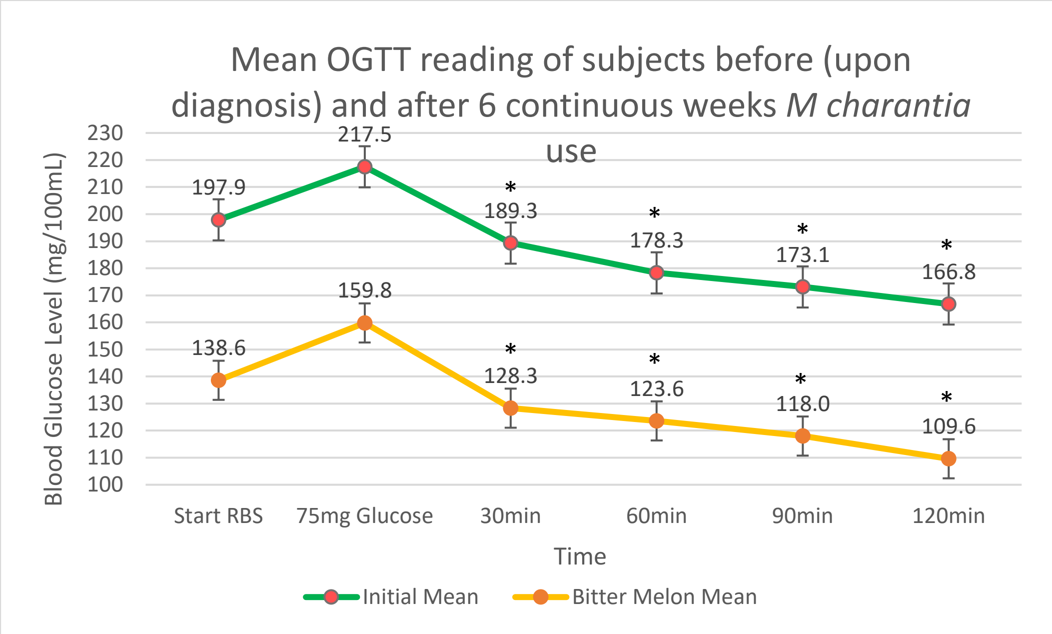


Figure 3.6: OGTT time- course effect of 20 grams of oral *M charantia* consumption as a juice on blood glucose level in the patients at week 1 (green) and at week 6 (yellow) after consuming 75 mg of glucose solution for comparison. *M charantia* juice was consumed immediately after the 75 ml glucose rich solution. Data are mean ±SEM, n=8; *p<0.05 for the presence *M charantia* compared to 75 mg of glucose consumption for both week 1 and week 6. Note also, that blood glucose level was significantly (*p<0.05) higher at week 1 compared to week 6 during the OGTT.

Table 3.2 shows the effect of either *M charantia* intake or daily exercise combined with diet modification on BMI, blood parameters (HBA1c, FBG levels, total lipids and triglycerides) and blood pressure in the T2DM patients at the start of the experiments at week 1 compared to week 6. The results show that the BMI decreased only slightly, but not significant, whereas HBA1c, FBG levels, SBP and DBP, total lipids and triglyceride decreased significantly (p<0.05) in diabetic patients after 6 weeks of treatment with either *M charantia* alone or diet modification combined with daily exercise compared to the start of the experiments at week 1 without either *M charantia* or diet modification combined with exercise.

Table 3.2: Effect of either *M charantia* intake or diet modification combined daily exercise on BMI, blood parameters (HBA1c, FBG, total lipids and triglyceride) and blood pressure in diabetic patients at the start of the experiments at week 1 compared to the end at week 6. Data are mean ±SEM; n=8 patients; *p<0.05 for end of week 6 compared to week 1, at the start. BMI = Basal metabolic index; HBA1c = glycated haemoglobin; FBS = fasting blood

glucose; SBP=systolic blood pressure; DBP= diastolic blood pressure; TGL=triglyceride. Note that *M charantia* was more effective than diet modification combined with daily exercise.

Measured Parameters	**Before *M charantia* Week 1**	**With *M charantia* Week 6**	**Before Diet modification and Exercise Week 1**	**With Diet modification and Exercise Week 6**
BMIK(g/m^2)	32.8±2.4	30.9 ± 2.75	32.8 ± 0.86	30.3 ± 0.73
HBA1c (%)	12.18± 1.47	5.58 ± 0.39*	12.19 ± 0.52	6.5 ± 0.19*
FBS (mg/dl)	200.6±11.2	125.8±11.2*	169.1 ± 6.2	150.8 ± 2.27*
SBP (mm Hg)	169.1±12.5	127.5± 7.05*	143.8 ± 4.2	128.5 ± 1.24*
DBP (mm Hg)	89.45±7.29	79.4± 10.2*	89.4 ± 2.6	82.5 ± 1.34*
Total lipids (mg/dl)	240.5±39.1	191.9±9.20*	248.0 ± 8.6	223.8 ± 8.9*
TGL (mg/dl)	187.2±20.19	139.8± 10.71*	187.9 ± 7.1	163.8 ± 5.7*

Table 3.3: General demographics of the eight diabetic patients who participated in the study from week 1 to week 6; (SS=Secondary Education; Yrs = years.

Patients	**Ethnicity**	**Sex**	**Age (Yrs)**	**Location**	**Profession**	**Education**
1	African	F	65	Georgetown	Pensioner	SS
2	East Indian	F	49	Georgetown	Cleaner	SS
3	East Indian	F	35	Lethem	Teacher	SS
4	African	F	42	Bartica	Saleswoman	SS
5	Mixed	M	52	Ituni	Security	SS
6	Mixed	M	44	Georgetown	Teller	SS
7	African	M	45	Georgetown	Businessman	SS
8	East Indian	M	60	Linden	Office Assistant	SS
	Mean		49			
	SD		9.80			

Table 3.3 shows some general demographics of the eight diabetic patients who participated in the study. They were four males and four females with an average of 49±9.8 years (range 35-65 years). They were all in their working age and came from different regions in Guyana and some of them had professional positions. In addition, they all had secondary school education.

3.3.4 OGTT in healthy human subjects

Figure 3. 7 shows the time-course hypoglycaemic changes following OGTT in age-matched healthy subjects in 3 different experimental interventions including *M charantia* alone, exercise alone and *M charantia* intake in combination with exercise. Mean fasting blood glucose level for the 10 subjects was about 115.8±2.8 mg/dl prior to the OGTT. Following intake of the 75 ml of a glucose rich solution dissolved in 300 ml of distilled water followed immediately by the consumption of 20 grams of *M charantia* juice (weight/volume), blood glucose levels decreased gradually over 2 hours on monitoring, reaching a mean value of around 112 ±1.9 mg/dl. After daily exercise for one week, the OGTT –induced blood glucose levels decreased more or less in a similar manner as *M charantia* alone. However, when exercise and *M charantia* were combined a week later, blood glucose levels decreased much faster compared to either *M charantia* or exercise alone reaching around 108 ±1.2 mg/dl. The results show that that *M charantia* juice intake combined with daily exercise can evoke significant ($p<0.05$) hypoglycaemic effects compared to either exercise alone or *M charantia* alone in decreasing BGLs following OGTT in healthy subjects.

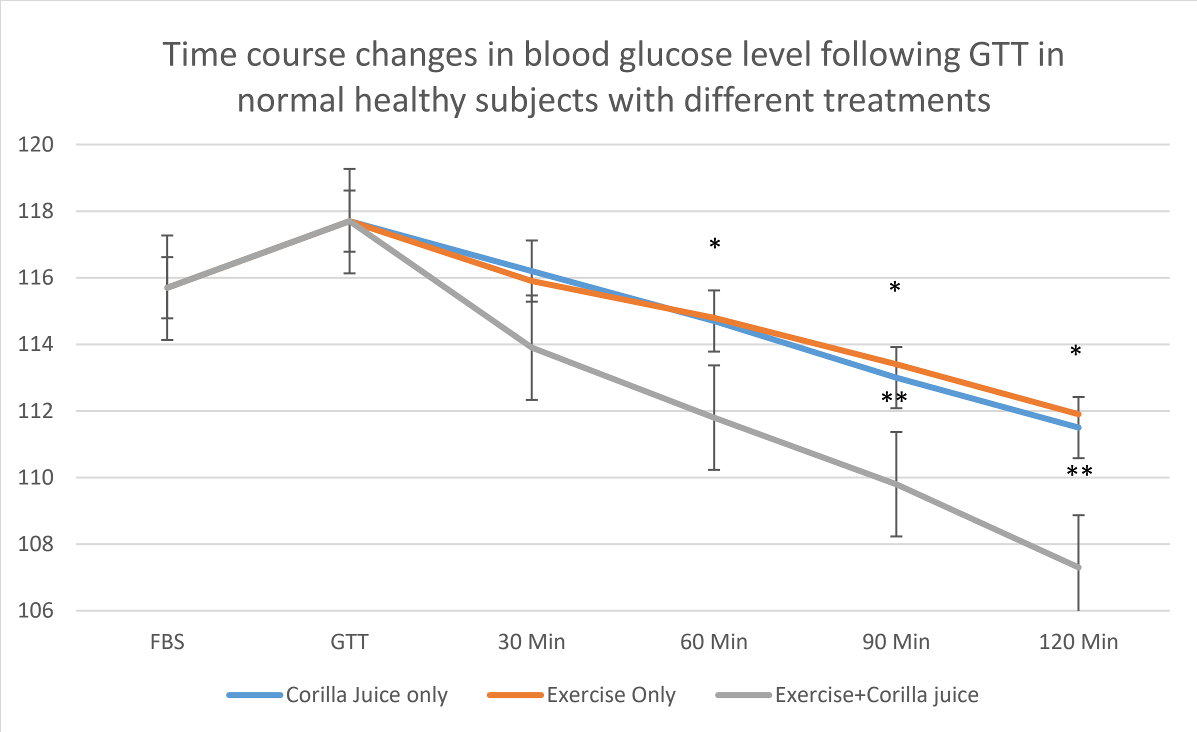


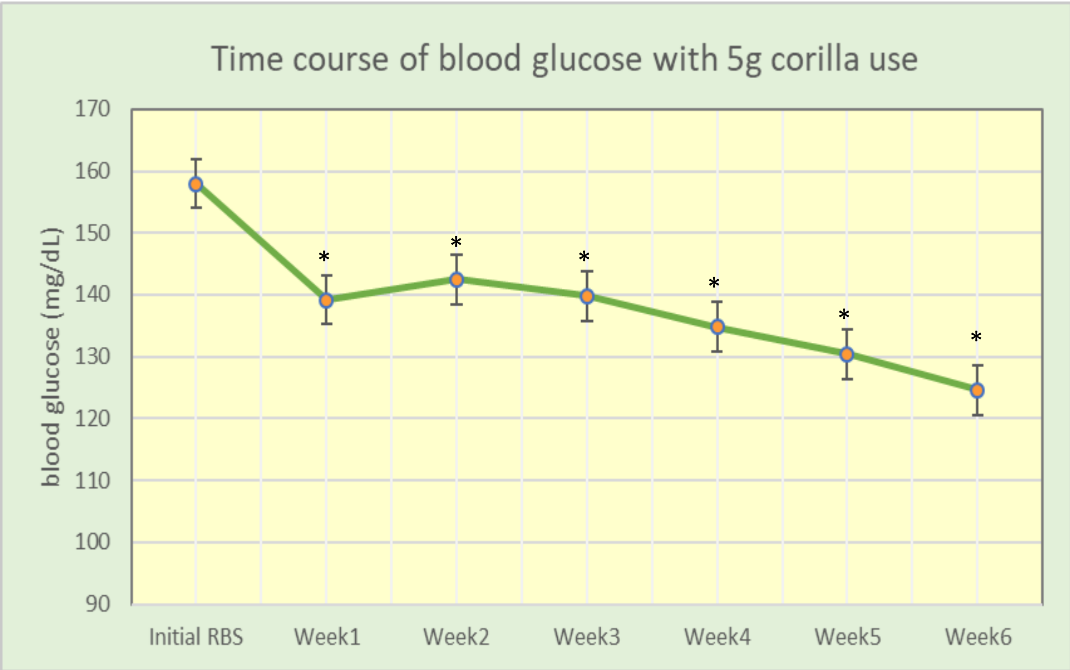
Figure 3.7: Time-course changes in BGLs following OGTT in normal healthy subjects following either *M charantia* intake or exercise only or combining *M charantia* intake with exercise. Data are mean ±SEM, n=10 patients; *p<0.05 or **0.01 comparing GTT values after drinking a glucose rich solution with values of obtained t60-120 minutes later following the intake of *M charantia*. Note that exercise combined with *M charantia* juice can elicit a better hypoglycaemic effect compared to either exercise or *M charantia* alone in these healthy human subjects.

3.3.5 Time -course effects of 5 g and 10 g of *M charantia* on BGLs and OGTT

In two different series of experiments, 20 newly diagnosed patients were divided into two groups of 10 each at the start at week 1. Their FBGLs were measured to confirmed diabetes followed by an oral glucose tolerance test (OGTT). One group consumed 5 grams of *M charantia* daily for 6 weeks and the other consumed 10 grams of *M charantia* for the same duration and their FBGLs measured on a weekly basis. At the end of 6 weeks, each group was given another OGTT and BGLs measured. The results are presented in figure 8A/B and figure 9A/B for 5 grams and 10 grams of *M charantia*, respectively.

The results in figure 8A shows that daily consumption of 5 grams of *M charantia* over a period of 6 weeks can significantly ($p<0.05$) reduce fasting blood glucose in a time-dependent manner reaching just above pre-diabetic level after 6 weeks compared to the start at week 1 of the study. Similarly, *M charantia* can reduce blood glucose level during OGTT intervention comparing week 1 with week 6 (figure 8B).

(A)



(B)

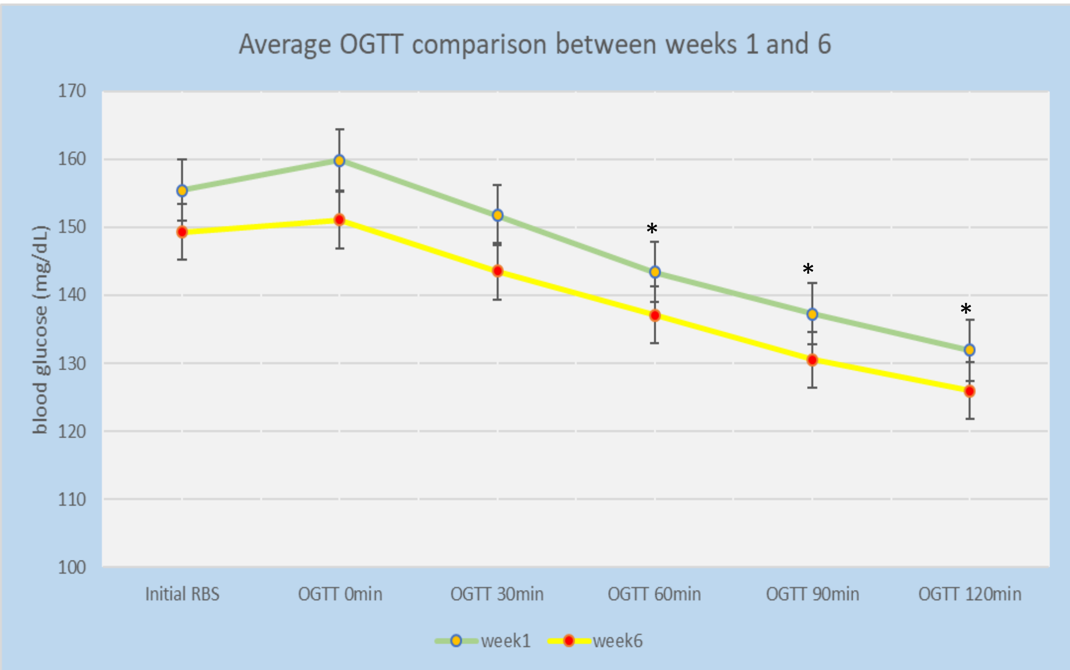
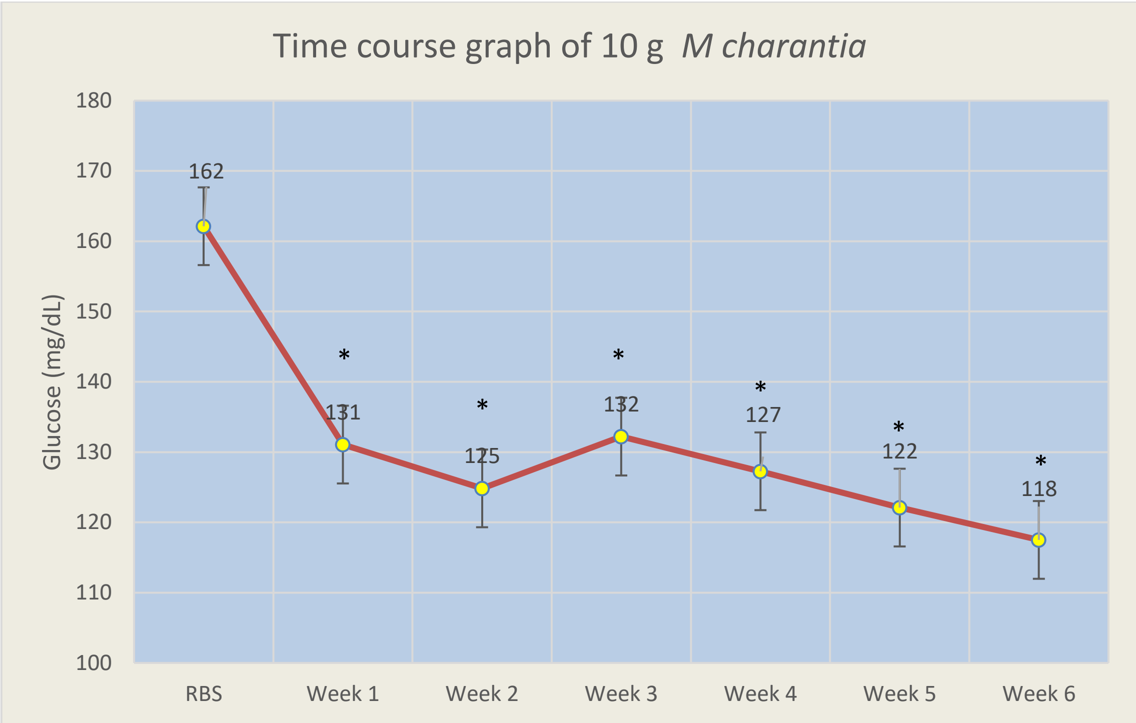


Figure 3.8: (A) Time- course effect of 5 grams of *M charantia* consumption on FBGLs for a period of 6 weeks and (B) OGTT in patients at week 1 at the start (green) and at week 6 (yellow) at the end of the study for comparison. Data are mean ±SEM; n=10; note the significant (*$p<0.05$) decline in blood glucose level up to 6 week of *M charantia* consumption compared to the start of week 1 (Figure 3.8A). However, the OGTT data in (figure 3.8B) were only significant (*$p<0.05$) at 60 min, 90 min and 120 min compared to the blood glucose level when 75 ml of a glucose rich solution was consumes at 0 min.

Figure 3.9A shows the time- course effect of 10 grams of daily consumption of *M charantia* in T2DM patients and figure 3.9B shows typical OGTT graphs at the start of the study (initial RBS measurement at week 1) compared to week 6 in the presence of 10 grams of continuous *M charantia* juice consumption. The results in figure 3.9A reveal that daily consumption of *M charantia* juice over a period of 6 weeks can reduce FBGLs from about 162 ±6.8 mg/dl to about 118 ±5.8 mg/dl (about 27.1%) significantly ($p<0.05$) in a time-dependent manner reaching almost pre-diabetic to control level after 6 weeks compared to the start of week one (RBS), at the start of the study. Similarly, *M charantia* can significantly ($p<0.05$) reduce blood glucose level during OGTT intervention comparing time 60-time 120 min to time 0 min, when the glucose rich solution was consumed (figure 3.9B).

(A)



(B)

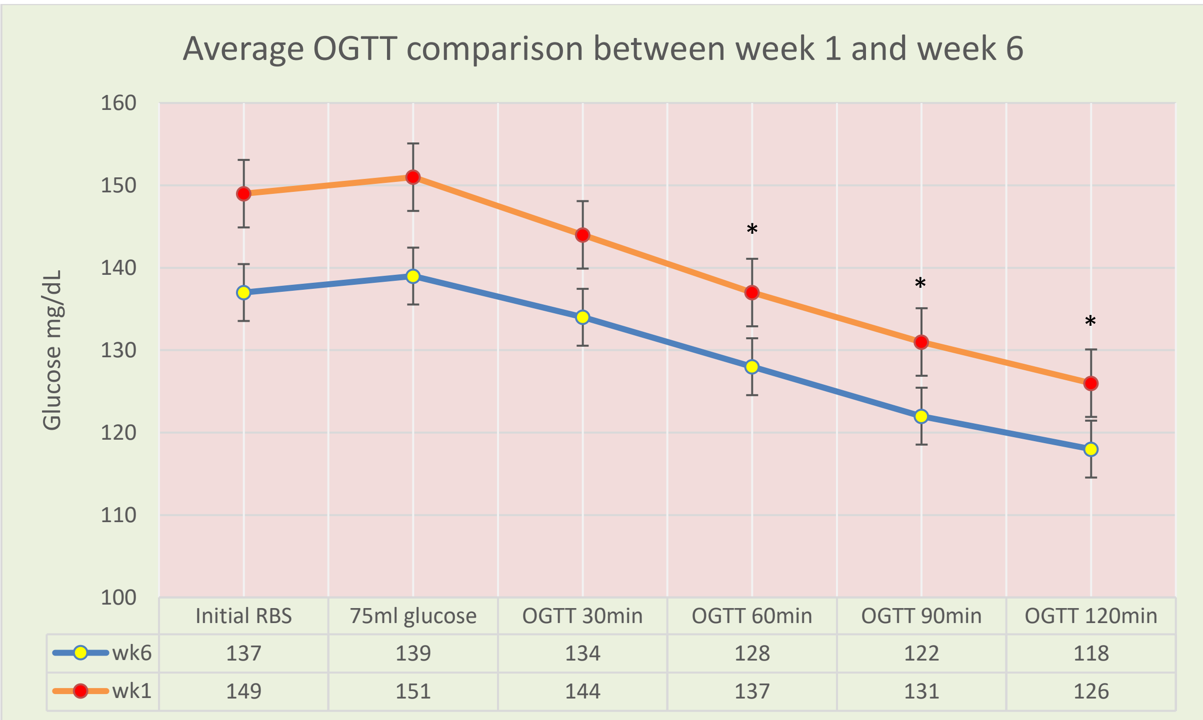


Figure 3.9: (A) Time course effect of 10 grams of *M charantia* consumption on FBGLs for a period of 6 weeks and (B) OGTT in the patients at week 1 (orange) and at week 6 (blue) for comparison. Data are mean$\pm$ SEM, n=10; note the significant (*p<0.05) declined in blood

glucose after 6 week of *M charantia* treatment compared to week 1 (Figure 3.9A). Similarly, for OGTT, blood sugar decreased significantly (*$p<0.05$) at time 60-time 120 min compared to time 0 min, when a rich glucose solution was consumed.

3.3.6 Cation levels in blood of age-matched healthy control subjects and T2DM patients

Cations play major physiological and biochemical roles in maintaining the homeostasis of the body (Al-Fartusie and Mohsson, 2017). This series of experiments investigated if diabetes could alter cation homeostasis in the body. Upon diagnosis, blood samples were taken from the initial ten recruited diabetic patients compared to ten age-matched healthy control subjects for the measurements of plasma cation contents using the technique of ICPMS. Figures 3.8A-D show the plasma levels of cations in blood taken from age-match control and diabetic patients for comparison. These results reveal no significant ($p>0.05$) changes in the different cation levels in blood plasma comparing healthy subjects with diabetic patients, except for silver and molybdenum. The data also show that the concentrations of the different cations varied significantly in plasma. The order of the concentrations is $Na^{+}>K^{+}>Ca^{2+}>Mg^{2+}>Fe^{2+}>Cu^{2+}>$trace elements.

(A)

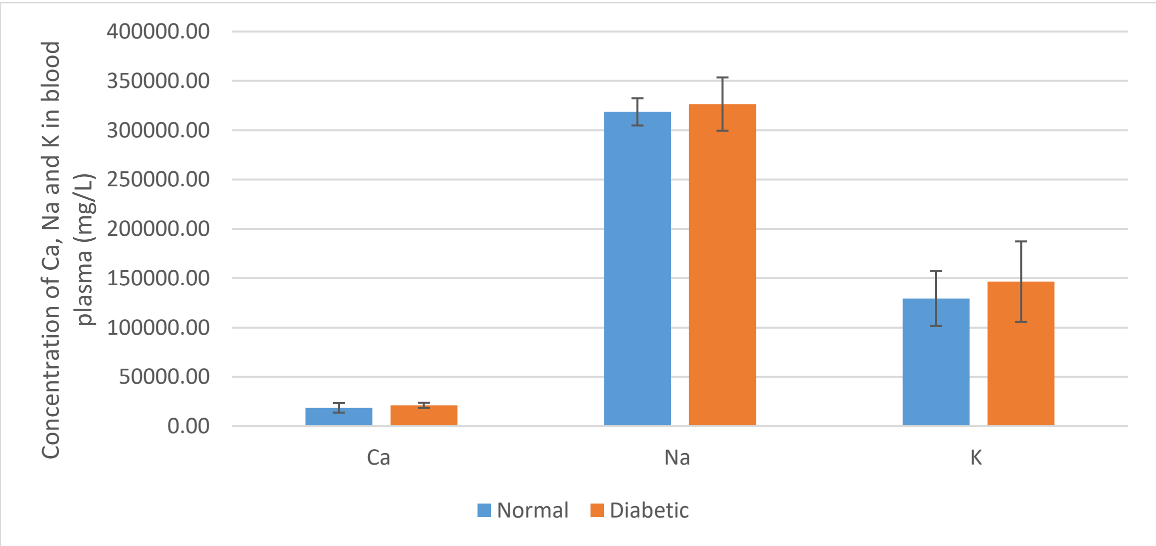


Figure 3.10 A: Bar charts showing the concentrations **of** Ca^{2+}, Na^{+} and K^{+} in blood serum samples from normal (blue) and diabetic (pink) patients: Data are Mean $\pm$ SEM, n=10 patients for each; $p>0.05$.

(B)

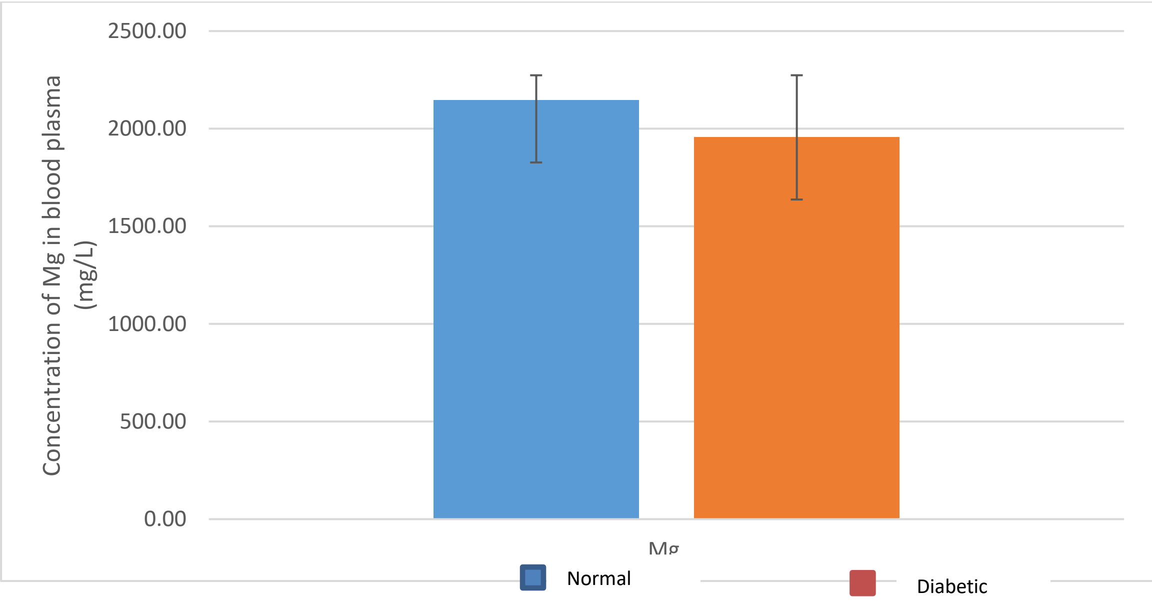


Figure 3.10B. Bar charts showing the concentration of Mg^{2+} in blood serum samples from normal (blue) and diabetic (pink) patients: Data are Mean $\pm$ SEM, n=10 patients for each; p>0.05

(C)

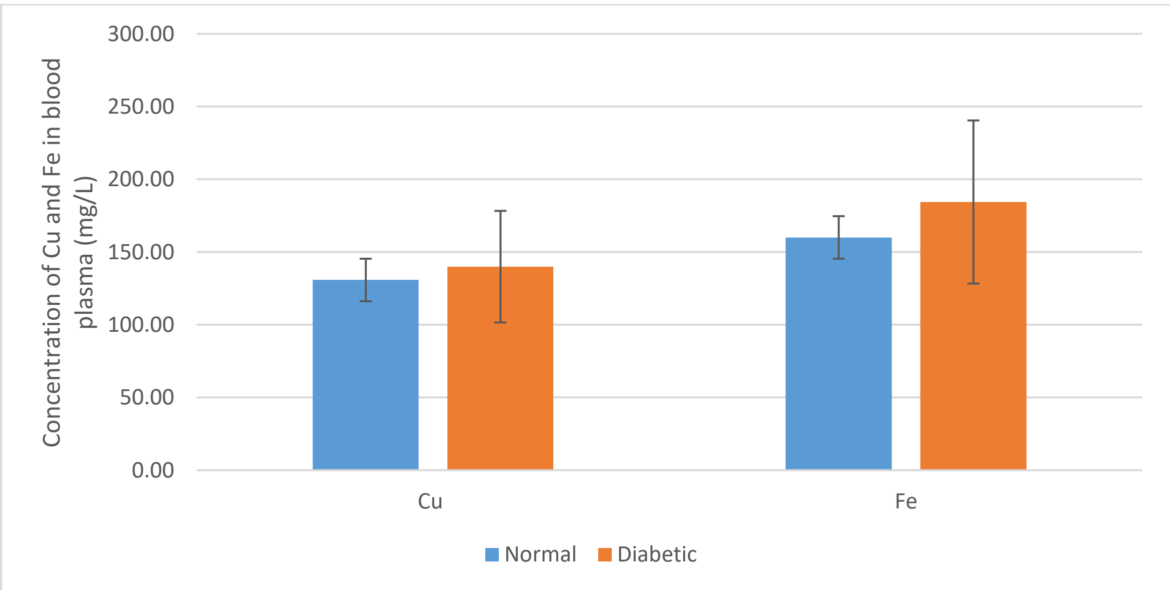


Figure 3.10C: Bar charts showing the concentrations **of** Cu^{2+} and Fe^{2+} in blood serum samples from normal (blue) and diabetic (pink) patients: Data are Mean $\pm$ SEM, n=10 patients for each; p>0.05

(D)

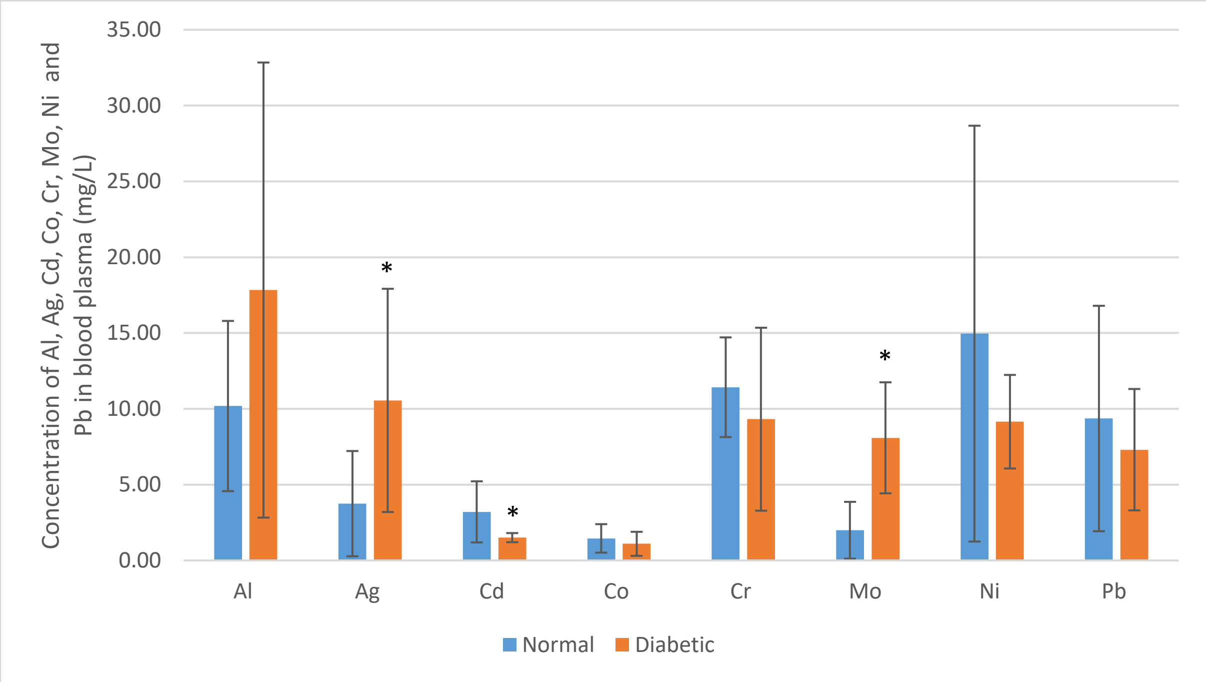


Figure 3.10D: Bar charts showing the concentrations of such trace elements as Al^{3+}, Ag^{2+}, Cd^{2+}, Co^{2+}, Cr^{2+}, Mo^{2+}, Ni^{2+} and Pb^{2+} in blood serum samples from normal healthy subjects (blue) and diabetic patients (pink). Data are mean $\pm$ SEM, n=10 patients for each. [For Ag *$p \leq 0.04$ (Significant at $p \leq 0.05$) and Mo *$p \leq 0.01$ (Significant at $p \leq 0.05$)]

3.3.7 Chemical analysis of *M charantia*

The green fruit of *M charantia* was dried and pulverised into a powder and chemically analysed for some of its chemical contents (see figure 3.1D. The data also reveal that the fruit contains a number of cations including sodium (7.76$\pm$0.51 mg/g), potassium (0.667$\pm$0.044 mg/g), calcium 28.95$\pm$2.21 mg/g), magnesium (0.443$\pm$0.0028 mg/g), manganese (0.42$\pm$0.03 mg/g), copper (0.26$\pm$0.031 mg/g) and zinc (0.99$\pm$0.03 mg/g). Among the cations, the fruit had significantly ($p<0.05$) more sodium and calcium compared to the other cations present. The results also show that the fruit is rich in proteins (2.86+0.07 mg/100 g), phenolic content (2.42$\pm$0.25 mg/100 g), and anti-oxidant activity (44.5$\pm$2.46 mg AAE/100 g (powder material), including the presence of caffeic (221 ng/g) and celuic acid (623.6 ng/g).

3.4 DISCUSSION

The main findings of this study revealed that *M charantia* can elicit significant decreases in fasting blood glucose levels (FBGLs), HBA1c, total lipids and triglycerides and both systolic and diastolic blood pressure in newly diagnosed type 2 diabetic (T2DM) patients over a period of six weeks compared to the start of the study at week one before they were diagnosed with T2DM. Similarly, diet modification combined with daily exercise can also evoke similar effects as *M charantia* but to a lesser extent. Combining *M charantia* with diet modification and daily exercise or with the commercial anti-diabetic drug, diamicron MR elicited more or less the same hypoglycaemic effect. *M charantia* can also enhance the reduction in FBGLs during oral glucose tolerance test (OGTT) in both newly diagnosed diabetic patients and healthy control subjects. The hypoglycaemic effect of *M charantia* was dose dependent. *M charantia* is rich in cations, phenolic content and antioxidant properties. In tackling the scientific problem, the study employed a number of conventional physiological and biochemical techniques including the measurement of blood pressure using the conventional sphygmomanometer, a blood glucose level employing the clinical glucometer, the biochemical auto analyser to measure total lipids, triglycerides and HBA1c in whole blood, ICPMS to measure cations and trace elements in blood serum and other biochemical parameters to analyse for the contents of *M charantia*. The discussion will now focus on the background of diabetes and the potential importance of the current results compared to those in the literature.

Diabetes mellitus (DM) is one of the oldest metabolic disorders to inflict humans. Diabetes was first recognised as a metabolic disorder about 3,000 years ago by Egyptian and the Indians Physicians. Type 2 diabetes mellitus (T2DM) is considered as one of the commonest disorder affecting millions of people globally. The symptoms can come very slowly and often very difficult to spot. Many cases are only diagnosed when people visit their GPs about other health conditions. As such, early diagnosis of T2DM is of paramount importance in delaying and preventing the risk in developing long-term complications (Lotfy et al, 2016; Papatheodorou et al, 2016; Harding et al, 2019). T2DM is associated with several factors including, age, ethnicity, genetic, diet, overweight, obesity, physical inactivity, smoking and others (Adeghate and Schantter, 2006; Danaei et al, 2011; Lotfy et al, 2016; Sami et al, 2017; Smail et al, 2018). DM can inflict tremendous burden and suffering to mankind irrespective of age, gender, ethnicity or religion with marked severity leading to a reduced quality of life, especially if left untreated or diagnosed late (WHO, 2020).

Currently, about 480 million people have diabetes globally, another 250 million undiagnosed and almost 1.5 billion with prediabetes (Zimmet, 2017). It costs almost $1 trillion USAD (15% of global budgets in terms of life and demand on health budgets) to diagnose, treat and care for diabetic patients so that they can live longer and also enjoy a better quality of life (Petersen, 2018). Moreover, more than 4 million people died annually from diabetes (WHO, 2020). Globally, almost 75% diabetic patients pay for the health care (WHO, 2011; 2020; Guariguata et al, 2014; Zimmet, 2017; Diabetes, UK, 2019;) resulting in a financial burden for the patients. As such, it is of paramount importance to look to nature for cost-effective and non-pharmacological ways to treat DM, especially T2DM. Most T2DM patients who are diagnosed early are usually treated in such cost-effective manner as weight loss, diet modification including eating less food with reduced sugar and carbohydrates and participate in daily exercise (Norris, 2010; Maden, 2013; Thent et al, 2013; Sami et al, 2017). Some patients are also given psychological intervention to encourage adherence to their lifestyle changes (Martinus et al, 2006).

The present study was designed to address the use of non-pharmacological interventions as diet modification and exercise but also in combination with bitter melon or corilla (*Momordica charantia*) to treat newly diagnosed T2DM patients. The study also investigated the effect of *M charantia* in combination with orthodox anti-diabetic medicine, diamicron MR to ascertain if there is any enhanced or inhibitory hypoglycaemic effect when a complementary medication is combined with a commercial orthodox drug. The rationale is that all three parameters are affordable for the patients, especially in low and middle –income third world tropical and sub-tropical countries like Guyana where *M charantia* is grown widely and more so, they could be substitutes for expensive orthodox anti-diabetic medicine.

The results presented in this study have shown that a combination of moderate daily exercise including walking, stretching, bicycle riding and diet modification by eating less sugar and carbohydrates, but more fruits, beans, nuts and other foods full of fibres, guided by either a dietician or a physical activity Instructor, can reduce blood glucose level slowly, but also gradually over 6 weeks. Typically, blood glucose reduced by almost 33.4% for diet and exercise intervention but remained above control level. If the patients had continued further in the study, then it was possible to see time–dependent reduction in blood sugar to almost control level. For interventions involving either *M charantia alone, M charantia* combined with diet modification and exercise or *M charantia* combined with diamicron MR, blood glucose reduced to almost control level following treatment. Currently, many General Practitioners prefer to suggest weight loss, diet modification and daily moderate exercise to treat newly diagnosed T2DM patients whose blood glucose levels are mild to moderate diabetic level. These results are consistent with what is known about the beneficial effect of exercise and diet modification to manage hyperglycaemia in diabetic patients (Paez et al, 2000; Norris, 2001; Weinstein et al, 2001; Davies et al, 2003; Madden, 2013; Thent et al, 2013; Sami et al, 2017). The importance of diet modification, as a possible therapy for T2DM, was first noticed by the Indian Physicians. They observed that rich people who ate excessively, especially foods with a lot of sugar and fats gained weight and as a result they developed T2DM. It was also observed that during a war, famine, or food shortages less people seemed to develop T2DM. As a result, it was concluded that there was a marked association between sugar and fat intake and T2DM (Khatib, 2004; Sami et al, 2017). However, those who ate moderately and with reduced sugar consumption were unlikely to become diabetic (Sudell, 1998). Generally, dietary practices are influence mainly by cultural background as well as the types of foods and their tastes viable around the culture. In addition, knowledge about T2DM and its association with foods seem to play a significant role regarding diabetic diet and dietary practices. It is now generally agreed that knowledge of both diets and their contents tends to influence the food selection and eating pattern of people (Savoca and Mitter, 2001).

Like diet modification, several studies have shown a strong association between physical inactivity, overweight, obesity and T2DM. Generally, people who do not participate in daily physical activity or living a sedentary lifestyle seem to develop T2DM (Weinstein et al, 2001; Davies et al, 2003). In contrast, people who participate and adhere to daily physical activity are unlike to develop T2DM or they could delay the development of T2DM (Martinus et al. 2006; Smail et al, 2018). The question arises now is this: How does daily physical activity protect a person either from the development of T2DM or help to treat the T2DM? To date, there are several explanations how physical activity exerts its beneficial effect in the body. Firstly, it has been suggested that physical activity increases sensitivity to the hormone insulin in the body, possible via its tyrosine kinase receptor on muscle cells (Ahmed, 1999). Second, it was suggested that physical activity is more beneficial during the early stage of the development of diabetes, especially in pre-diabetes by helping to delay and possible preventing the progression of T2DM, before insulin therapy (Colberg et al, 2010; Smail et al, 2018). Third, physical activity seems to increase pancreatic beta cell mass and function by encouraging the pancreas to produce newly synthesized insulin content, thereby producing a synergistic effect with insulin (Diabetes, UK, 2019; Curan et al, 2020). Fourth, during a prolonged session of physical activity, contracting muscle cells usually receive a healthy supply of blood and as such, they take up more glucose from the blood. Utilization of glucose by the cell due to physical activity helps to replenish glucose delivery to the cells. Fifth, physical activity can also reduce intra-abdominal fat which is risk factor for insulin resistance. It is also possible that physical activity is exerting an effect on the liver to take up more glucose which can result in hypoglycaemia (Colberg et al, 2010). Another possible explanation is that physical activity has a direct effect on K cells in the gut which in turn helps in the release of glucagon–like peptide-1 (GLP-1) into the circulation. GLP-1 can also mimic the action of insulin, or it has direct effect on the beta cells in the pancreas to release insulin (Singh et al, 2011; Lotfy et al, 2014a, 2014b; Trefts et al. 2015; Sami et al. 2017; Smail et al. 2018; Diabetes UK, 2019; Curan et al, 2020).

The results of this study have demonstrated that *M charantia* consumption either alone or combined with diet modification and exercise or with diet modification, exercise and anti-diabetic drug exert significant hypoglycaemic effect in values of around, 47.7%, 50.6% and 50.7%, respectively after 6 weeks of daily consumption compared to week 1, at the start of the study. A combination of *M charantia*, diet modification and exercise exerted the same hypoglycaemic effect as *M charantia* combined the anti-diabetic drug, diamicron MR. These data suggest that patients can control their own blood glucose level in a cost-effective manner once they are educated about adherence to diet modification, exercise and *M charantia* consumption (Joseph and Jini, 2013). These results, especially, the data obtained with the consumption of *M charantia* alone, are in total agreements with other similar human studies demonstrating its potential hypoglycaemic action (Welhinda et al, 1984; Attar-ur-Rahman, 1989; Ahmad et al, 1996; Baldwa et al, 1997; Johns et al, 2003; Tongia, 2004; Dans, 2007; ,Clinical Trials, 2017). *M charantia* is used, not only as a food, but also as traditional plant-based medicine globally (Platel and Srinivassan, 1997; 1999; Garau et al, 2003; Singh et al, 2011; Hadi et al, 2022). It is particularly noteworthy that *M charantia* exerts little or no beneficial effects when it is cooked or heated since its medicinal potential is heat-sensitive (Ahmed, 1999; Garau et al, 2003; Singh et al, 2011). This study also investigated the dose-dependent effect of *M charantia* on blood glucose level since in the literature, many workers sometimes never the mention the amount of *M charantia* they used in their studies. The Diabetes UK (2019) suggested that patients should consume no more than one ounce (28 grams) of the green fruit daily. The present study employed the consumption of either 5 grams, 10 grams or 20 grams daily and they all exerted hypoglycaemic effect in a dose–dependent manner with maximum effect obtained with 20 grams of *M charantia*. In several other studies, investigators employed either the roots, leaves, the green fruits and its juice, the stems, capsules, tablets and alcohol and water soluble powder extracts from the fruits and other parts of the plant to investigate their hypoglycaemic effects in human (Welhinda et al, 1984; Attar-ur-Rahman, 1989; Ahmad et al, 1996; Baldwa et al, 1997; Johns et al, 2003; Tongia, 2004; Dans, 2007) and animal models (Karunanayake et al, 1984; Day et al, 1990; Akhtar et al.1991; Srivastava et al, 1993: Sharma et al, 1996;). Most of the previous studies employed the fruit juice or the fruit itself, similar to the present study.

The question to be addressed now is this: How does *M charantia* exert its hypoglycaemic effect. Several workers have suggested that *M charantia* possesses a plant-like insulin which has the same effect as animal insulin (Day et al, 1990; Platel and Srinivassan, 1999; Garau et al, 2003; Singh et al, 2011). The present study has also investigated some contents of the *M charantia* fruit. The results show that it is rich in proteins, phenols, antioxidants and in some essential cations (Bajpai et al, 2005). All these different constituents are of paramount importance in protecting the body against oxidants such as reactive oxygen species (ROS) and reactive carbonyl species (RCS) (Alomar et al. 2016; 2020). In terms of its hypoglycaemic effect, several studies have suggested a few mechanisms. Firstly, *M charantia* exerts an insulin secretagogue-like effect (Kedar and Chakrabarti, 1982; Karunanayke et al, 1984; Jeevathayaparan et al, 1995; Ali et al, 1993; Hazarika et ail, 2012). Second, it stimulates peripheral and skeletal muscle glucose utilisation (Day et al, 1990) similar to insulin and the effects of both insulin and *M charantia* were blocked by wortmannin, a tyrosine kinase inhibitor (Ahmed, 1999; Cummings et al, 2004). Third, bitter melon inhibits intestinal glucose uptake (Meir and Yaniv, 1995; Ahmed, 1999; Ahmed et al, 1998; Ahmed et al, 2004). Fourth, inhibition of hexokinase activity, resulting in the suppression of key gluconeogenic enzymes that stimulates another enzyme of HMP pathway (Meir and Yaniv, 1995; Shibib et al, 1993). Fifth, it acts like a growth factor in repairing and preserving pancreatic beta cell mass and the functions of the beta cells to secrete newly synthesised insulin (Ahmed, 1999; Ahmed et al, 1998; Ahmed et al, 2004), almost like regular exercise (Curan et al, 2020). The results also show that diabetes had virtually no effect on plasma cation and trace element levels, but the disorder can elevate blood biomarkers such as lipids and triglycerides and blood pressure of the patients. Interestingly, *M charantia* treatment can significantly reduce blood pressure and total lipids and triglyceride in the blood of the patients (Ffried et al, 2014). These results clearly demonstrated that *M charantia* is a major potential therapeutic remedy to avoid cardiovascular risk in patients.

The OGTT is a routine clinical diagnostic test to confirm if a patient is diabetic (Ahmad et al, 1999; Bernado et al, 2015; Rachid et al, 2022). This study investigated the beneficial effect of *M charantia* and on the OGTT in diabetic patients at the start of the study before the consumption of *M charantia* and after of six weeks in consuming *M charantia*. The results show that in diabetic subjects, *M charantia* intake alone can exert marked hypoglycaemic effect immediately after consuming a high glucose solution over a period of two hours. The data revealed that blood glucose level declined slowly at week one compared to a rapid decrease at week six. These results show that *M charantia* can induce satisfactory hypoglycaemia in diabetic patients. Similar effects of *M charantia* were obtained in healthy age-matched subjects (Patel et al, 1968; Leatherdale et al, 1981; Ahmad et al.,1999). Together, the results of this study have revealed that people can control their blood sugar level cost-effectively by altering their lifestyle habits via diet modification and exercise and at the same time consume a small amount *M charantia* thereby enhancing their quality of life.

3.5 CONCLUSION

In the literature, most workers employed *M charantia* alone in their studies and they employed possible one dose of the fruit juice. The present study was designed to investigate the dose – dependent hypoglycaemic effect of *M charantia* alone and its combination with either diet modification or with diet modification and exercise or with the commercial anti-diabetic medicine, diamicron MR. The data clearly show that either *M charantia* alone or especially, *M charantia* combined with diet modification and exercise can exert almost the same effect compared to *M charantia* in combination with the commercial anti-diabetic medicine, diamicron MR. As such, the present study supports the assumption that newly diagnosed T2DM patients can treat and manage their diabetes in a cost-effective manner without spending money to buy expensive commercial anti-diabetic medicine. These results may have tremendous benefits for people who live in low and middle- income countries like Guyana and who cannot afford medical care for their diabetes.

Chapter 4:

Effects of *Momordica charantia,* diet modification and regular exercise in the treatment of obesity

4.1 Introduction

The World Health Organization (WHO) identified chronic non-communicable diseases (CNCDs) or chronic diseases (CDs) as cardiovascular diseases (CVDs), stroke, overweight and obesity, cancer, chronic respiratory diseases, cerebrovascular disease, kidney failure, dental diseases, diabetes mellitus (DM) and a few others (WHO, 2012; 2018). CDs are often viewed to affect mainly old people, Moreover, CDs are among the most common, costly and preventable of all health problems, and they represent a growing burden for society globally (Tapia et al, 2020; Tapia and Dhalla, 2022). The major risk factors for NCDs include smoking, environment pollution, alcohol intake, stress, physical inactivity and unhealthy diets. Detection, screening and treatment of NCDs, as well as palliative care, are key components to reduce NCDs and/ or to prevent premature deaths. Metabolic risk factors for NCDs include hypertension, overweight and obesity, hyperglycaemia and hyper-lipidemia (WHO, 2018; Tapia et al, 2020; Tapia and Dhalla, 2022; Sharma et al, 2022). This study focussed on non-pharmacological treatment of obesity, but first, it is important to understand how both overweight and obesity are developed and concurrent surgical and pharmacological treatments.

Some risk factors for the development of overweight and obesity include ageing, physical inactivity, hormone imbalance, psychological disturbances, epigenetic factors, genetic predisposition, metabolic derangements, few calories expenditure, socio-economic level, environmental factors, birth weight, excess alcohol, some medications and health conditions, lack of self-care, and more importantly excessive food intake, especially those full with fats and sugar, (Tapia et al, 2020; Tapia and Dhalla, 2022; Sharma et al 2022). In recent years, scientists have been looking for a cure of this overweight and obesity pandemic problem. These are many factors which can help in reducing the weight of our body including daily exercise, eating less, the use of daily intake of plant-based remedies, use of orthodox medicines and surgery. It is well known that that regular exercise can exert a protective role in appetite regulation via a change in eating behaviour and habits of the obese subject (Garberm, 2019; Sharma et al, 2022). A study published by Wilding et al, (2021) demonstrated that the newly developed anti-obesity drug, semaglutide could cut body weight by 20%. It is believed that the drug can mimic a hormone released by the gut to instruct the brain to send a message to the stomach that it is filled thereby reducing hunger and calorie intake. The drug also helps in reducing waist circumference, blood fats, blood sugar and blood pressure levels, all of which can help to improve longevity and the quality of life of obese patients (Wilding et al, 2021).

Another intervention is bariatric surgery which is used routinely in cases of chronic obesity to treat the disease thereby reducing CVD events in the patients (Wolfe et al, 2016).

Previous research studies have shown that the consumption of either *M charantia* juice or its extract can be used effectively in reducing weight gain and fat deposition in the body (Fan and Moon, 2019) as well as treating obesity (Alam et al, 2015). Both overweight and obesity are two complex and multifactorial major health hazards in Guyana and conventional treatment using either surgery or pharmacological medicines are very expensive. In light of this, the main objective of the current study was to investigate the hypothesis that *M charantia* could also be used to reduce body weight when combined with such life-style changes as diet modification and daily exercise. Generally, obese people develop high blood pressure, and the second objective was to investigate if life-style changes and *M charantia* can also reduce blood pressure as well as blood glucose and cholesterol for comparison.

4.2 Methods

4.2.1 Recruitment of Patients

Thirty-two male and female subjects (16 males and 16 females) were recruited from newly diagnosed overweight or obese patients who had no other illness and not on any medication and who visited the GP clinic for treatment according to established investigative trial/study methods (Alam et al, 2015). Following detailed discussion of the research project and willing to participate, interested subjects signed a consent form to join the study at their own will and they could withdraw at any time if they wanted (see Appendix I). Following recruitment, the subjects were explained thoroughly about their obesity or overweight and also about the experimental protocol which was designed to last over a period of six weeks. In addition, each patient was given a questionnaire, which contained 25 questions about obesity, to complete and returning to the clinic at their convenience (see appendix IIIB).

4.2.2 Experimental design

The thirty- two subjects, in their working years of similar ages, were divided into four different groups of eight subjects (4 males and 4 females) per group. Group 1 (diet only) was asked to modify their diets over 6 weeks with the help of a trained Dietician (see details of diet modification in section 3.3.2 in chapter 3). Group 2 (Diet and *M charantia*) did the same as group 1, but in addition, they consumed 20 grams of *M charantia* juice (vol/weight) twice daily before meals (10 ml in the morning and 10 ml in the evening) over 6 weeks (see details of the preparation of *M charantia* juice in section 3.2.3 in chapter 3). Group 3 (diet, exercise and *M charantia)* did the same as group 2 (diet plus *M charantia)* but combined with daily exercise for 6 weeks. Exercise training was done by a professional Physical Activity Instructor as described in detail in section 3.2.2 in chapter 3. In Group 4 (diet and exercise), the subjects modified their diets and participated in daily exercise over 6 weeks aided by a Dietician and a a professional Physical Activity Instructor to ensure adherence.

4.2.3 Experimental protocols (see detailed in section 3.2.7 in the methods of chapter 3)

At the start of the study at week 1, each subject was weighed and his or her height taken and recorded. Similarly, the systolic and diastolic blood pressures (SDBP) were measured using an automated sphygmomanometer. A small volume (0. 5 ml) of fasting blood was taken from either the right or left arm of each subject via veni-puncture for the measurements of fasting blood glucose (FBG), HBA1c, total lipids and triglycerides. BMI was calculated from the weight and height following weekly measurements over 6 weeks. Likewise, blood pressure was measured using automated digital sphygmomanometer on a weekly basis over the six weeks. Fasting blood glucose (FBG), HBA1c, total lipids and triglycerides were measured using a conventional clinical laboratory auto-analyser (see full details for measurements of BMI, blood pressure and blood parameters in section 3.2.7 in chapter 3).

4.2.4 Inclusion criteria: Patients with known obesity, diabetes, or hypertension older than 18 years, new patients, willing to participate and were available.

4.2.5 Exclusion criteria

Patients with gestational diabetes, younger than 18 years, physical and mental illness and on any other medications.

4.2.6 Ethical clearance

The project had the relevant ethical clearance from the University of Guyana and UCLan Ethics Committees. A written informed consent was obtained from each participant after given written and oral information about the study (see appendix IIA/B)

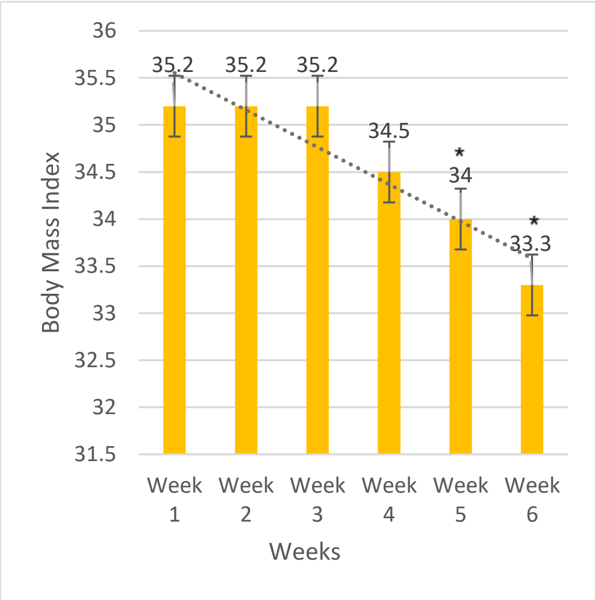
4.2.7 Statistical analysis of data

Statistical data analysis was done using the Statistical Package for Social Sciences (SPSS) and ANOVA. The data collected were compared according to the assigned groups. Data are expressed as mean ± SEM**.** A value of $p<0.05$ is taken as statistically significant.

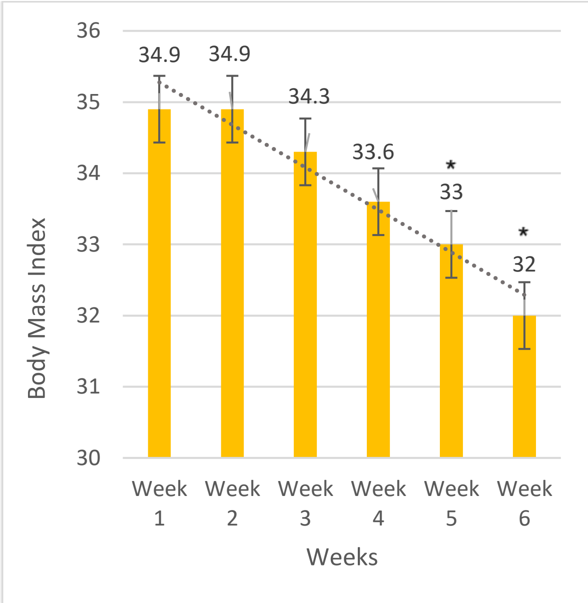
4.3 RESULTS

4.3.1 Time course of weight loss

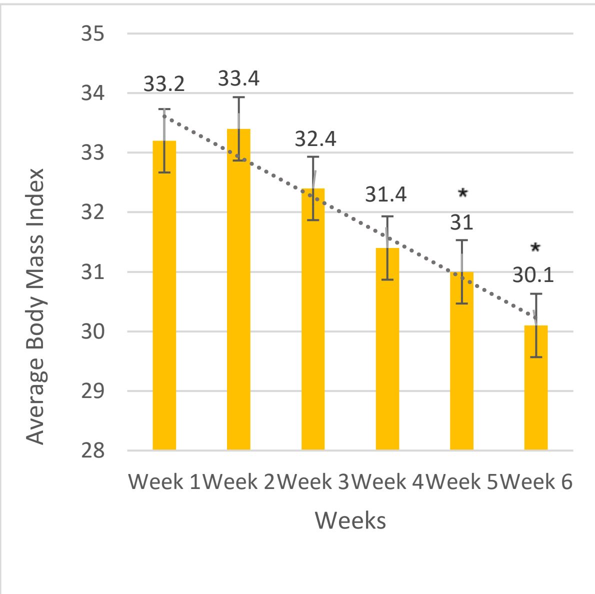
(A) Diet alone



(B) Diet and *M charantia*



(C) Diet, exercise and *M charantia*



(D) Diet and exercise

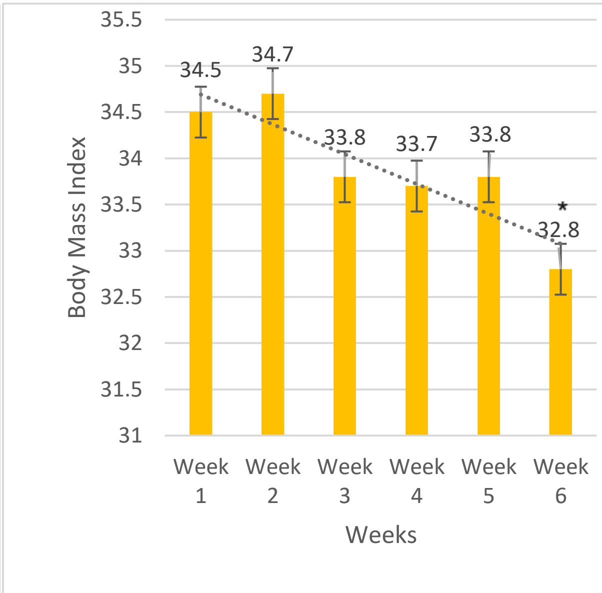


Figure 4.1: Time-dependent effects of (A) diet alone, (B) diet and daily intake of 20 grams intake of *M charantia* juice daily (10 ml in the morning and 10 ml in the evening before meals), (C) diet and both daily exercise and intake of 20 grams of *M charantia* juice and (D) diet and

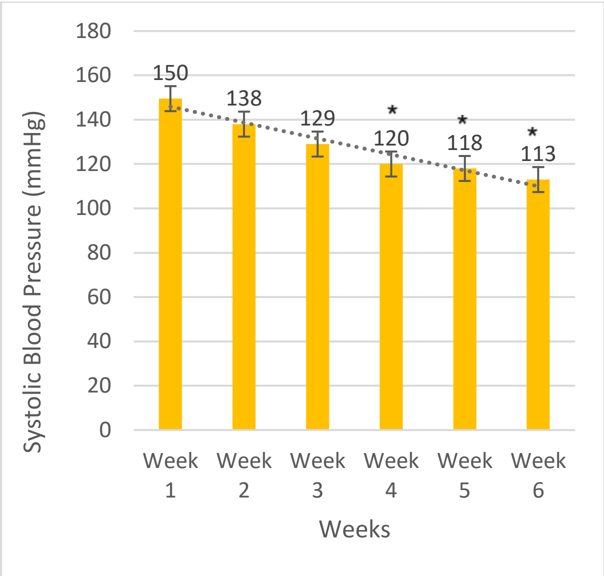
daily exercise on BMI over a period of 6 weeks in obese subjects. Data are mean ± SEM and n=8 for each measured parameter. Note that all four interventions reduced gradually BMI over 6 weeks compared to week 1 at the start of the experiment, *p<0.05 for weeks 5 -6 compared to week 1 at start of the study.

Figure 4.1 shows the time-course effects of (A) diet alone, (B) diet combined with daily intake of 20 grams of *M charantia juice*, (C) diet, exercise and daily intake of 20 grams of *M charantia* juice and (D) diet and daily exercise on BMI in obese subjects over a period of 6 weeks compared to week 1 at the start of the study, but only with significant value (p<0.05) at weeks 5-6. However, combining diet, exercise and *M charantia* produced a more pronounced effect on BMI reduction compared to the other three interventions after 6 weeks. Typically, body weight was reduced by 5.39%, 5.48%, 8.30%, and 9.33% for diet alone, diet and exercise, diet and bitter melon and diet, exercise and *M charantia*, respectively over the six weeks of the study.

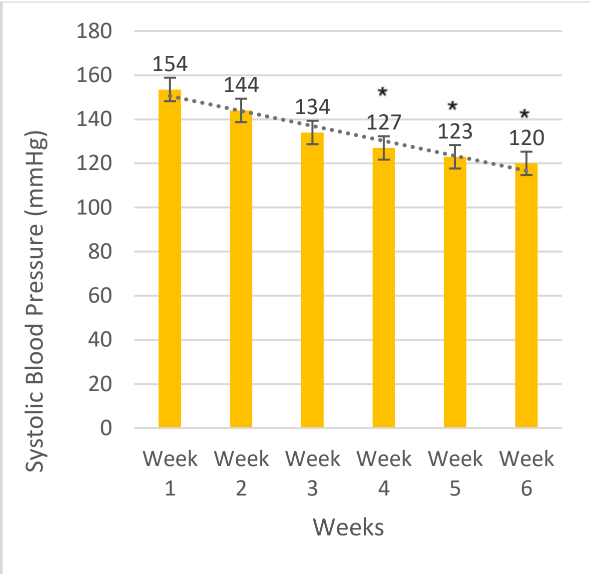
4.3.2 Time course of high blood pressure measurement

(A) (Systolic Blood Pressure)

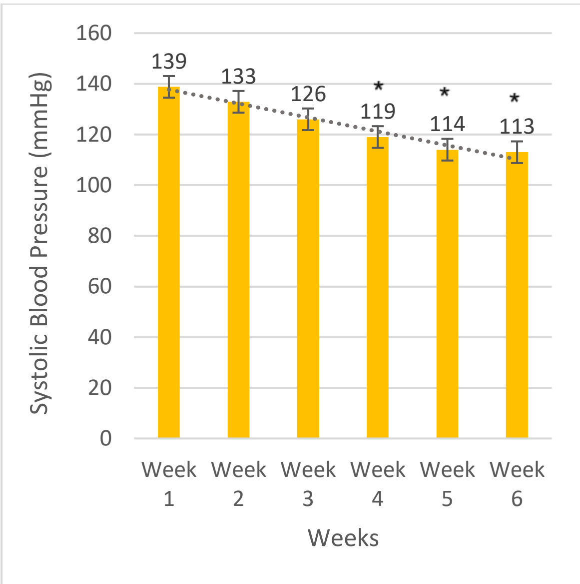
(A) Diet alone



(B) Diet and bitter melon



(C) Diet, exercise and bitter melon



(D) Diet and Exercise

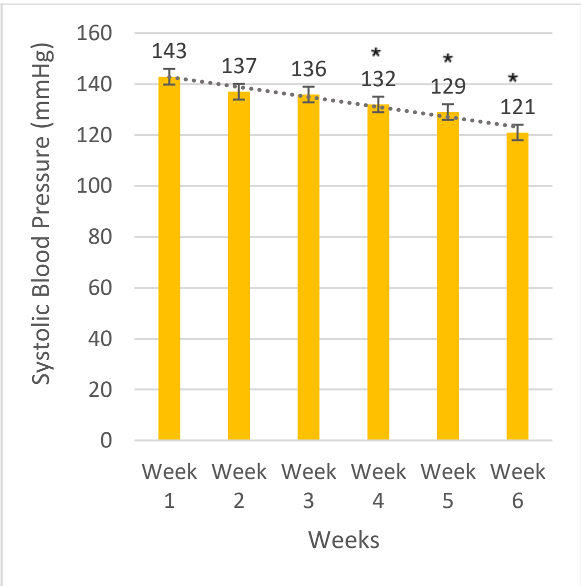


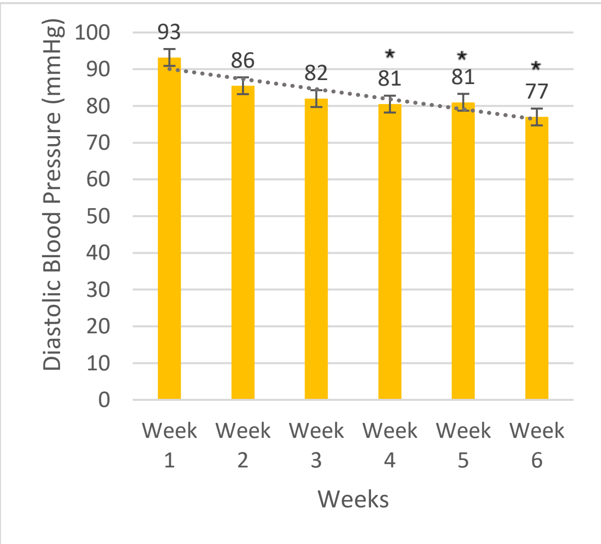
Figure 4.2: Time- dependent effect of (A) diet alone, (B) diet and daily intake of 20 grams of *M charantia juice*, (C) diet and both daily exercise and intake of 20 grams of *M charantia* juice and (D) diet and exercise on systolic blood pressure (SBP) in obese subjects over a period of 6 weeks. Data are mean ±-SEM and n=8 for each measured parameter. Note that all four

interventions reduced gradually SBP but with significant (*p<0,05) effect from week 4 to week 6 compared week 1 at the start of the experiment.

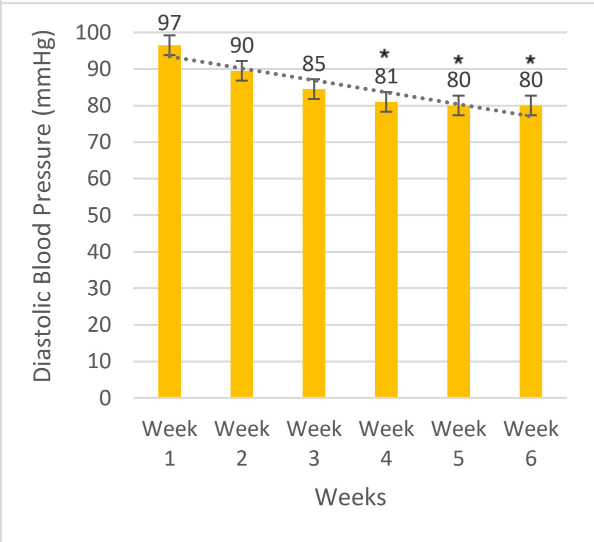
Figure 4.2 shows the time–course effect of (A) diet alone, (B) diet combined with daily intake of 20 grams of *M charantia juice*, (C) diet, exercise and daily intake of 20 grams of *M charantia* juice and (D) diet and daily exercise on systolic blood pressure (SBP) in obese subjects over a period of 6 weeks compared to week 1 at the start of the study. The data show that all four interventions involving diet modification and exercise in life style changes either individually or combined with *M charantia* juice can significantly ($p<0.05$) reduce SBP gradually in a time-dependent manner from elevated levels in week 1 to significant ($p<0.05$) levels in week 4 to week 6, reaching normal value at around week 6. Typically, SBP was reduced by 25.38%, 18.70%, 22.665 and 24.66% with diet and exercise, diet alone, diet in combination with *M charantia juice* and diet and exercise in combination with *M charantia*, respectively over the duration of the study.

(B) (Diastolic Blood Pressure)

(A) Diet alone



(B) Diet and bitter melon



(C) Diet, daily exercise and bitter melon (D) Diet and Exercise

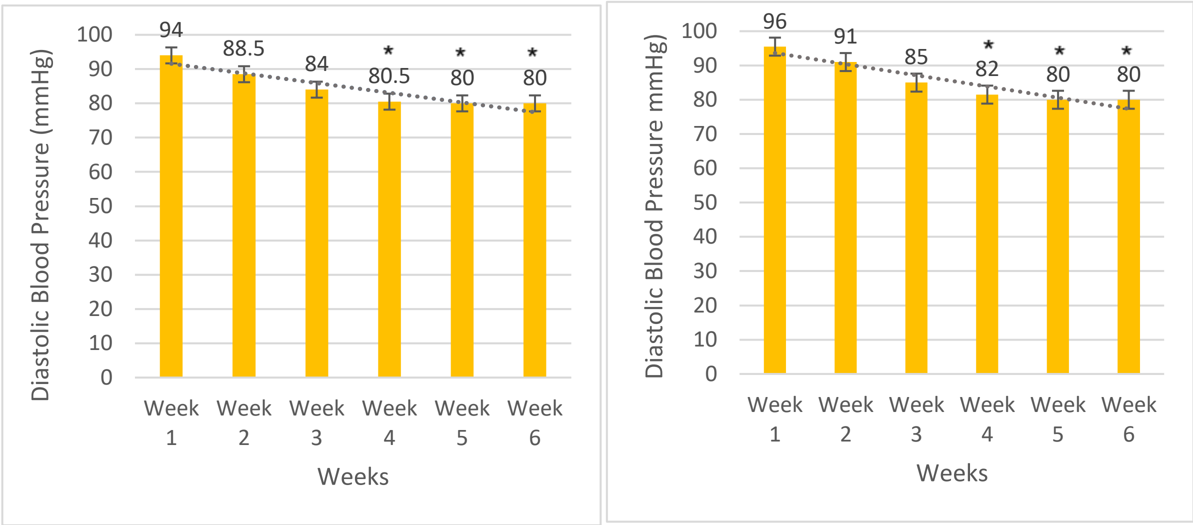


Figure 4.3: Time–dependent effect of (A) diet alone, (B) diet and daily intake of 20 grams of *M charantia* juice, (C) diet and both daily exercise and intake of 20 grams of *M charantia* juice and (D) diet and exercise on diastolic blood pressure (DBP) over a period of 6 weeks in obese subjects. Data are mean ±SEM and n=8 for each measured intervention. Note that all four interventions reduced DBP gradually over 6 weeks compared week 1 at the start of the experiment. Note also that that DBP was significantly (*$p<0.05$) reduced between week 4 to week 6 compared to week 1, at the start of the study reaching normal control levels at around week 5-6.

Figure 4.3 shows the time-course effect of (A) diet alone, (B) diet combined with daily intake of 20 grams of *M charantia juice*, (C) diet, daily exercise and 20 grams intake of *M charantia* juice and (D) diet and exercise on diastolic blood pressure (DBP) in obese subjects over a period of 6 weeks compared to week 1 at the start of the study. The data show that all four interventions involving diet modification, exercise, and consuming *M charantia* juice either individually or combined can significantly (*$p<0.05$) reduce DBP gradually in a time-dependent manner from elevated levels in week 1 to significant levels between week 4 to week 6, reaching normal value at around week 5 to week 6. Typically, DBP was decreased by 14.89%, 16.66%, 17.20% and 17.52% for diet and exercise, diet alone, diet and *M charantia* and diet, exercise, and daily *M charantia* juice intake, respectively over the duration of the study.

4.3.3 Measurements of blood biomarkers

Table 4.1: Data showing age, gender, HBA1c, fasting blood glucose (FBG), total lipids and triglycerides in the four different groups, namely (A) diet only, (B) diet, exercise and *M charantia* juice (C) diet and daily intake of *M charantia* juice and (D) diet and daily exercise in obese subjects at week 1, prior to the start of this study, compared to 6 weeks later at the end of the study. Data are mean ±SEM; n=8 for each intervention; *p<0.05 comparing week 6 with week 1.

Measured Parameters	Diet only		Diet + Exercise + *M charantia*		Diet + *M charantia*		Diet + Exercise	
	Week 1	Week 6	Week 1	Week 6	Week 1	Week 6	Week 1	Week 6
Age	42±4.5	42±4.5	43±4.6	43±4.6	42±4.7	42±4.7	44±3.8	44±3.8
Male	4	4	4	4	4	4	4	4
Female	4	4	4	4	4	4	4	4
HbA1c (%)	6±0.52	5.3±0.34	5.8±0.46	5.80±0.46	5.6±0.52	5.6±0.52	6±0.0	5.8±0.46
FBS (mg/dL)	126±1.9	122±1.4	126±1.6	122±2.0	124±1.7	122±1.8	121±2.7	115±3.9
Total lipids (mg/dL)	239.2±2.2	228.1±3.9	232.1±1.5	*186.1±1.3	241.1±2.9	*193±7.0	254±2.5	*189.1±1.7
Tryglycerides (mg/dL)	173±9.3	163±8.5	167±7.0	*138.1±6.0	165±8.5	*139±6.8	171.1±5.8	*141±8.2

Table 4.1 shows the mean age (±SEM), gender and levels of such blood biomarkers as HbA1c, fasting blood glucose (FBG), total lipids and triglycerides for the 8 subjects (4 males and 4 females) in each of the four different intervention groups namely, diet alone, diet and daily exercise combined with *M charantia* juice intake, diet combined of *M charantia* intake and diet and exercise at week 1 at the start of the study compared to week 6 at the end of the study for comparison. The results show that the subjects were in their working years of age in life. The majority of them had secondary education. Moreover, their HBA1c and FBG only reduce very slightly for each intervention. In contrast, the four interventions reduced blood total lipids and triglycerides, but with significance ($p<0.05$) only in the presence of diet and exercise, diet, exercise and *M charantia* and with diet combined with *M charantia.* The results indicate that life-style changes combined with daily intake of *M charantia* may exert an inhibitory effect on the level of total lipids and triglycerides in the body thereby reducing the risk of cardiovascular diseases among obese subjects.

4.4 DISCUSSION

Obesity is epidemic and it can lead to substantial morbidity and mortality globally. Like many other countries, overweight and obesity are very prevalent in Guyana, and they are major risk factors for developing diabetes and cardiovascular diseases which can result in sudden cardiac death (Tapia et al, 2020). Effective strategies exist for managing obesity, but they are rarely used by physicians (Orzano and Scott, 2004; Tapia and Dhalla, 2022. This study attempted to address this issue by employing life-style changes combined with daily intake of *M charantia* to treat newly diagnosed obese subjects. In tackling the scientific problem, the study employed a number of physiological and biochemical diagnostic techniques. BMI is easily determined by measuring the height and weight of a person and then calculate its value. Measuring waist circumference is another method in determining if a person is either overweight or obese but this was not done in this study. Moreover, overweight and obese people are normally hypertensive due to the excess weight of the body. Their systolic and diastolic blood pressures can be easily determined by themselves or by a clinician using an automated digital sphygmomanometer. In addition, overweight and obese people are susceptible in developing prediabetes and confirmed diabetes over time and as such, they are at cardiovascular risk. As a result, it is vitally important to measure their blood sugar level and total lipids and triglycerides using conventional clinical diagnostic techniques. The major findings of this study demonstrated that people who are obese can be treated in a cost-effective manner by just modify their diets, participate in daily physical activities and consume the juice of *M charantia*. The discussion will now focus on the causes, epidemiology and treatment of obesity, a burden to global health resources and its risk to life. This will be accompanied by a critical discussion of the current findings of this study compared to those in the literature.

Both overweight and obesity, due to an imbalance between calories intake and imbalance, are becoming major health problems affecting almost two billion people globally at present, with almost 700 million obese (Tapia et al, 2020: Tapia and Dhalla, 2022). The results in the present study have clearly shown that daily reduction of food intake, including no snaking and binging, reduction in fast food consumption but instead consume more vegetables low in calorie can markedly reduce BMI, systolic and diastolic blood pressure, total lipids and triglycerides comparing week 6 at the end of the experiments to week 1. Dieting had little or no significant effect on HBA1c and fasting blood glucose level, but it reduced total lipids and triglyceride levels but not to significantly value through to 6 weeks of the study compared to week 1. These data are in total agreement with other similar studies (Taher et al, 2020).

M charantia originated from India and the plant was taken to different parts of the world including China, Southeast Asia, Africa, the Caribbean and South and Central America by Indians during colonization. *M charantia* has been used by many people globally as a plant remedy to treat obesity, diabetes, hypertension, heart attacks and strokes, cancer, reducing blood cholesterol and triglyceride and many other debilitating conditions ((Ivorra et al, 1989; Platel and Srinivassan, 1997; 1999; Taylor, 2002; Garau et al, 2003; Singh et al, 2011; Alam et al, 2015, Manoharan et al, 2013; 2014; Fan et al, 2018). *M charantia* is low in calories but high in fibre. It contains approximately 2 grams of fibre in each 94 grams. It can also promote the burning of fats in the body thereby leading to weight loss (Alam et al, 2015).

The results of this study have shown that when the consumption of *M charantia* juice was combined with either diet modification or exercise and diet modification there were marked decreases in BMI, systolic and diastolic blood pressure and total blood lipid and triglyceride levels in the obese subjects after 6 weeks of the intervention compared to week 1 at the start of the experimental period. Combination of *M charantia* with either diet modification or exercise and diet modification had little or no effect on HBA1c and fasting blood glucose (FBG) over the experimental period. *M charantia* combined with diet modification, either with or without exercise seems to exert a slightly better protective effect compared to diet modification alone. *M charantia* is rich in minerals, especially calcium, sodium and some trace elements, vitamins, particularly C, phenolic compounds, saponins and triterpenes, glycosides, a plant–like insulin and antioxidants. It is possible that most of these different cations and compounds can help in reducing the weight of the body by enhancing glucose and fat metabolism utilizing different mechanisms. In some cases, the different compounds act synergistically to exert their protective effects in the body (Bajpai et al, 2005; Thenmozhi and Subramanian, 2011; Fan et al. 2018). These results are in total agreement with other similar studies (Ahmed et al, 2004; Alam et al, 2015; Badhwar et al, 2020) highlighting the evaluation of the various extracts of *M charantia* in their therapeutic potentials in obesity, diabetes and the metabolic syndrome.

Regarding systolic and diastolic blood pressure in the thirty- two obese patients, the data show that *M charantia* consumption can markedly reduce both in a time-dependent manner. In a recent systematic review of the effects of *M charantia* on blood pressure, Jandaria et al, (2020) found very small decreases in systolic and diastolic blood pressure in old-age groups of 75 years and over. However, they found, significant hypotensive effect of *M charantia* in young adults who were 50 years and less, especially during short-term interventions as carried out in this present study where the subjects also had a mean age of about 42±4.8 years and more so, participated in exercise training for at least six weeks. In a study by Kumari et al, (2018), using a clinical trial on patients with type-2 diabetes mellitus (T2DM), they reported that that *M charantia* supplementation resulted in a significant reduction in SBP and DBP. Similarly, Rahman et al, (2015) found that supplementation of *M charantia* (4 g/day) was able to decrease systolic blood pressure significantly in T2DM patients. Similar results have also been obtained in animal model of HBP (Sharma et al, 1996; Ahmed, 1999; Ahmed et al, 2004).

Like *M charantia*, daily physical exercise is also a powerful cost-effective and non-pharmacological tool to prevent a number of disorders and diseases in the body including overweight, obesity, diabetes, cancer, cardiovascular and respiratory diseases, stress, mental illnesses and others (Paez and Kravitz, 2000; Martinus et al, 2006; Smail et al, 2018). Regarding weight loss, physical activity does help to increase the number of calories the body uses for energy leading to a small reduction in body weight. It is also well known that the higher the intensity of the physical activity then there will be high weight loss due to calorific deficit more so when the obese subjects adhere to the physical activity (Chambliss, 2005). In addition to weight loss, daily exercise can reduce stress and improve cardiorespiratory fitness especially when it is combined with dietary modification (Chambliss, 2005; Smail et al, 2018). The results of this study have revealed that combining diet modification with daily exercise and intake of *M charantia* can help to reduce BMI, systolic and diastolic blood pressure as well as total blood lipid and triglyceride levels, but with little or no effects of HBA1c and fasting blood glucose. The data further reveal that a combination of dieting with daily exercise and *M charantia* intake seems to induce a small enhancing protective effect, similar to dieting and *M charantia* intake when compared to diet modification alone. It is well established that combining diet modification with daily physical exercise is the best method for weight loss.

The results from the present study have now shown that the combining *M charantia* consumption with exercise and diet modification can even exert a better cost-effective health benefit in treating obesity, blood pressure and blood lipid and triglyceride levels. Regarding exercise alone, it has to be performed at a moderate intensity such as brisk walking for at least 30 minutes daily to obtain the full benefit (Ross and Jennsen, 2000; Janiszewski and Ross, 2007). Moreover, further benefits can be gained from these interventions especially if the obese subject is given some form psychological training to facilitate adherence to the measured parameters (Martinus et al, 2006; Barnes and Cassidy ,2018).

It is now well known that obesity is a major contributing risk factor for cardiovascular diseases via to the release of several pro-inflammatory mediators (Tapia et al, 2020; Sharma et al 2022, Tapia and Dhalla, 2022). The fluctuation in the levels of these mediators and adipocytokines released by the adipocytes further leads to cardiovascular dysfunctions (Behl et al, 2016). The increase in the risk of CVDs and mortality caused by obesity is due to increasing levels of atherosclerotic plaques developing in the arteries and blood vessels of the heart (Ahmed et al, 2020). It is now known that flavonoids are polyphenolic compounds which occur naturally in nature and they can be used in a cost-effective way to treat obesity. In this study, the small reduction in weight of the obese subjects may be due to the polyphenolic antioxidant compounds present in *M charantia*.

It is also worthy to note that overeating high calorific diets is the main cause for overweight and subsequently obesity leading to diabesity (Mc Naughton, 2012; Zimmet et al, 2014; Taher et al, 2020). There are also some people who have a hormonal-induced metabolic disorder which can also cause obesity (Tapia and Dhalla, 2022). During eating, many people never feel filled and satisfied and as such they continue to eat excessively, including snaking and sometimes binging. The main treatment or preventative measure for overeating is to eat less or dieting in addition to the surgical intervention or bariatric surgery whereby the size of the stomach is reduced (Athyros et al, 2011; Wolfe et al, 2016). There are also several anti-obesity drugs such as semaglutide which could cut body weight by 20% (Wilding et al, 2021). For many people without will power, it is not possible to lose weight unless they obtain psychological intervention for adherence to food intake, just like exercise (Martinus et al, 2006). Quality of food also plays a major role in the development of obesity. It is now the norm that fast foods can induce obesity whereas the Mediterranean-style diet rich in olive oil, vegetables and fish can help in the reducing the weight of the body (Singh et al, 2017).

4.5 CONCLUSION

In conclusion, the findings in this study suggest that life-style changes in combination with *M charantia* can help in reducing the weight, blood pressure and such cardiovascular risk factors as lipids and triglyceride of obese subjects. However, people do not seem to have will power over their eating habits irrespective that excess food intake can damage the body over time. As such, the best way forward in controlling obesity is to provide psychological intervention in combination with lifestyle changes in order to achieve adherence to eating habits.

Chapter 5:

***Momordica charantia*, physical activity and amlodipine, either alone or in combination, can be used effectively to treat hypertension.**

5.1 INTRODUCTION

The cardiovascular or circulatory system is made up of three parts, namely the heart, the blood vessels and the blood. The heart pumps the blood via the blood vessels throughout the body to maintain its homeostasis. Blood pressure is the force exerted by the blood pumped by the heart against the wall of the arteries of the body (Aronson et al, 2020). Blood pressure is normally recorded with 2 numbers which are referred to as the systolic blood pressure (SBP or higher/upper number) which is the force at which the heart pumps blood around the body via the resistance arteries and arterioles. On the other hand, the diastolic blood pressure (DBP or lower/smaller number) indicates the resistance to the blood flow in the blood vessels. Both SBP and DBP are measured in millimetres of mercury (mm Hg). The normal blood pressure of a person is usually considered to be between 90/60 mm Hg (low range) and 120/80 mm Hg (normal). High blood pressure or hypertension is when the values are 140/90 mm Hg (mild) or higher (or 150/95 mm Hg (high mild) or higher (moderate, severe or chronic) if the person is within the age of 75 years and over (WHO, 2015; Elkilany et al, 2019; Aronson et al, 2020). A person is diagnosed as hypertensive when the blood pressure is measured on two different days. If the SBP is 140 mm Hg and over and the diastolic blood pressure is 90 mm Hg and over on both occasions, then the person is deemed as hypertensive.

High blood pressure (HBP) or hypertension is a major global health problem currently affecting about 1.3 billion people, especially those living in over-crowded urban areas and most of them (two thirds) live in low- and middle- income countries like Guyana (Mittal and Singh, 2009; WHO, 2015; Zhou et al, 2021). In 2015, 1 in 4 men and 1 in 5 women were hypertensive and these numbers are rising daily especially in crowded urbanised and suburbanised areas of the world, but more so in urbanised areas compared to rural areas where people are more active and less stressful (WHO, 2015; Zhou et al, 2021). Hypertension is a prominent preventable cause of premature morbidity and mortality. Moreover, hypertension is a major cause of heart failure which can lead to sudden cardiac death (Elkilany et al, 2020; Mills and Stefaneseu, 2020). People with hypertension are at high risk and as such it is of paramount importance to reduce their blood pressure to normal level (Saiz et al, 2018). There are several factors that can raise risk of developing high blood pressure. They included stress, age, family history of high blood pressure or genetics, being of African or Caribbean origin, consuming a high amount of salt in your food, lack of exercise, being overweight or obese, diabetes, regularly drinking of large amounts of alcohol, smoking, long-term sleep deprivation, kidney diseases, pregnancy and others (Nguyen and Lau, 2012; WHO, 2015; Elkilany et al, 2020; Zhou et al 2021).

Prevention strategies for developing hypertension is to avoid the above-mentioned risk factors. Symptoms of hypertension include constant headache, blurred vision, kidney failure, irregular heart rhythms and others. Chronic hypertension can lead to kidney damage, blindness, strokes, heart failure and other diseases. Hypertension is normally controlled by managing and reducing the mental stress (reducing essential hypertension), checking the blood pressure regularly, treating the high blood pressure and managing the other medical conditions which are related to the hypertension in order to prevent damages to other organs of the body (Wiklund, 1995; WHO, 2015; Kit et al, 2019; Elkilany et al, 2019; Zhou et al, 2021).

Like many other countries in the world, Guyana is a low- income developing country and during the past 20-30 years, the country was infested with non-communicable diseases (NCDs) including overweight, obesity, kidney failure, respiratory diseases, diabetes, hypertension and other cardiovascular diseases (CVDs) and cancer. According to the recent WHO data published in 2018, people die from the cause of hypertension reached 234 or almost 3 4% of total deaths. The age adjusted death rate per 100,000 of the population was around 47%. Currently, Guyana ranks 5th in the world from deaths due to hypertension (MPH, 2013; WHO, 2015; PAHO, 2019).

Previous studies have shown that *M charantia* alone can be used as a cost-effective plant-based or non-pharmacological medicine to treat hypertension and related diseases in both animal (Sharma et al, 1996; Ahmed, 1999; Ahmed et al, 2004; Singh et al, 2011) and human models (Alam et al, 2015; Joseph and Jini, 2013; Singh and Hanoman, 2019). Since many people in Guyana are hypertensive and treatment is very expensive, then the main objective of this study was to investigate, in a small preliminary study, the potential cost-effective effect of either daily consumption of *M charantia* juice, daily exercise or amlodipine either alone or during combination with *M charantia* in patients with newly diagnosed hypertension.

5.2 METHODS

5.2.1 Recruitment of Patients

Forty (40) male and female subjects, between the ages of 30-50 years (mean age of 43±5.5 years), were recruited from newly diagnosed hypertensive patients who had no other illness and not on any medication and who visited a GP clinic for treatment according to established investigative trial/study methods (Jandaria et al, 2020). Systolic and diastolic blood pressure values of patients were obtained on two different occasions and recorded to confirm hypertension using an automated sphygmomanometer, a clinical equipment which was designed to measure blood pressure (see section 3.2.7 in chapter 3 for details). Thereafter, the patients were asked to participate in the programme at their own will and signed a consent form (see appendix I). Following a thorough discussion about hypertension and their complications and willingness to join this investigative research study, the patients were asked to participate in daily exercise aided by a professional Physical Activity Instructor. The exercise regime included walking, stretching or bicycle riding or a combination for 30 minutes daily for a period of 6 weeks (see section 3.2.2 in chapter 3 for details). They were also explained about the potential non-pharmacological medicinal use of *M charantia)* to treat their hypertension by consuming 20 grams daily as a juice (weight to volume) to treat their hypertension either alone or in combination with either exercise or with the orthodox medicine, amlodipine (10 mg daily), a calcium channel blocker for 6 weeks. The juice was blended as required and kept in a fridge for no more than 3-4 days at 4 degrees centigrade for consumption (see section 3.2.3 in chapter 3 for the preparation of *M charantia* fruit juice for consumption). Once recruited for this programme, the blood pressure of each patient was measured and recorded on a weekly basis from week-1 (at start) to week-6 (end of the study) using an automated sphygmomanometer.

5.2.2 Time course of hypertension intervention study

The forty patients were divided into 5 different intervention groups with 8 patients in each. They included (i) exercise alone, (ii) *M charantia* juice alone consuming 20 grams daily (weight/ volume), (iii) *M charantia* juice intake of 20 grams daily combined with daily exercise, (iv) amlodipine alone (10 mg daily) and (v) *M charantia* juice intake (20 grams) combined with amlodipine (10 mg daily).

5.2.3 Inclusion criteria

Patients with known diabetes or hypertension older than 18 years, new patients, willing to participate and were available.

5.2.4 Exclusion criteria

Patients with gestational diabetes, younger than 18 years, physical and mental illness and on any other medications.

5.2.5 Data analysis

Statistical data analysis was done using the Statistical Package for Social Sciences (SPSS) and ANOVA. The data collected were compared according to the assigned groups. Data are expressed as mean ± SEM**.** A value of $p<0.05$ is taken as statistically significant.

5.2.6: Ethical Considerations

The project had ethical clearance from the University of Guyana and UCLan Ethics Committees (see appendix II). A written informed consent was obtained from each participant after given written and oral information about the study (see appendix I).

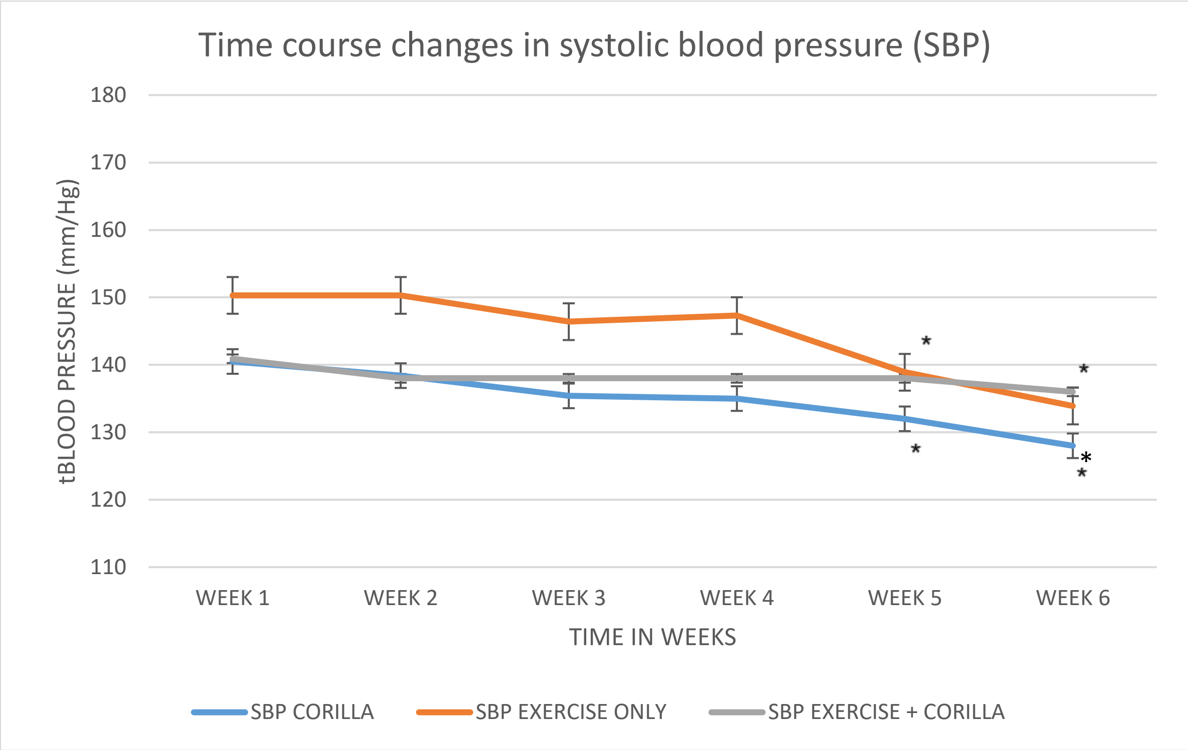
5.3 RESULTS

5.3.1 Effects of *M charantia,* exercise and amlodipine either alone or in combination on blood pressure of hypertensive patients.

Figure 5.1 (A/B) shows the time course effects of either *M charantia* juice alone, exercise lone and *M charantia* juice in combination with exercise on (A) systolic and (B) diastolic blood pressure in hypertensive patients. At the start of the study at week 1, all the subjects had severe to chronic hypertension upon diagnosis. After 6 weeks of treatment, both systolic and diastolic BP dropped significantly ($p<0.05$) compared to week 1. *M charantia* juice alone or in combination with exercise was more effective than exercise alone in reducing BP. These results demonstrated a potential therapeutic role for either *M charantia* or *M charantia* combined with daily exercise to treat both systolic and diastolic BP in newly diagnosed hypertensive patients.

In another intervention, both systolic and diastolic blood pressure was monitored in recently diagnosed hypertensive patients who were on 10 mg daily of the anti-hypertensive calcium blocking drug, amlodipine over a period of 6 weeks. The results show that the anti-hypertensive medication can reduce both systolic and diastolic blood pressure in a time-dependent manner reaching control level after 6 weeks of treatment. However, when *M charantia* was combined with amlodipine. there was virtually no significant (p>0.05) change in either systolic (A) or diastolic (B) blood pressure over the duration of the study for 6 weeks compared with the values obtained with amlodipine alone (see figure 5.2A/B).

(A)



(B)

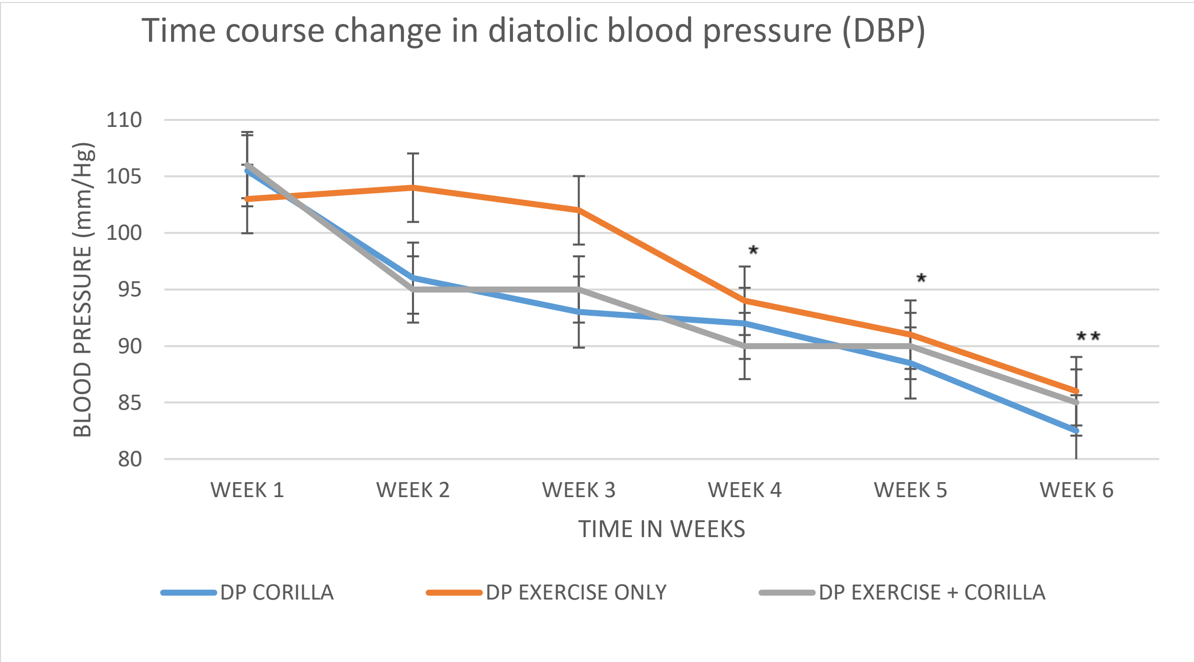
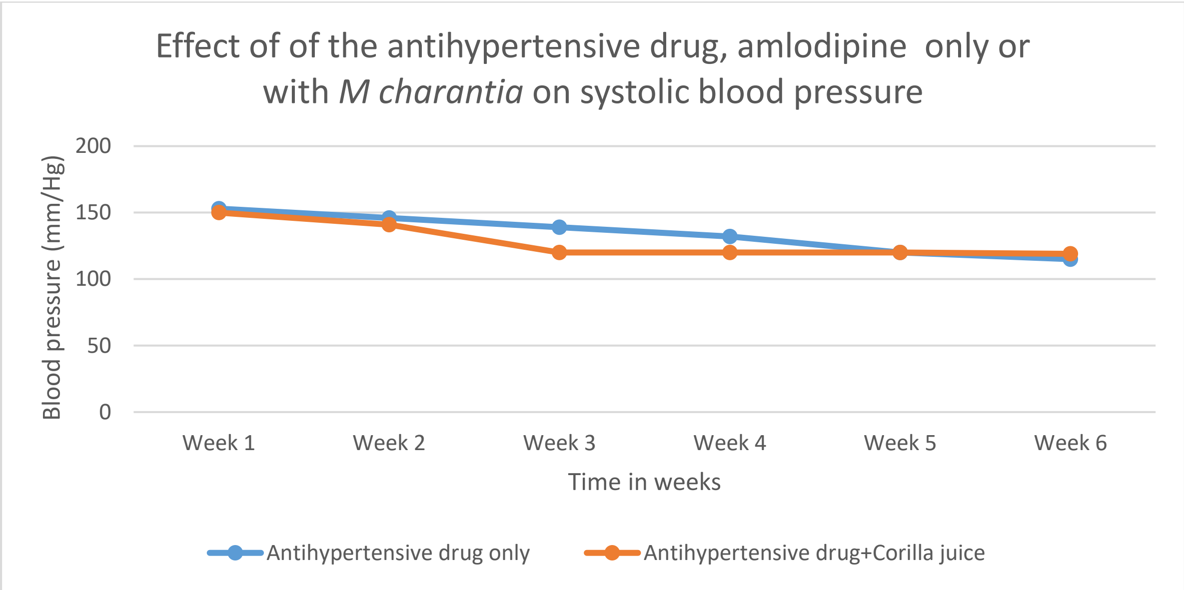


Figure 5.1A/B: Time-course graphs showing changes in (A) systolic blood pressure (SBP) and (B) diastolic blood pressure (DBP) over a period of 6 weeks following treatment with either *M charantia* juice only, exercise only or *M charantia* juice combined with exercise. Data are mean ±SEM; n=8 for each group. Note that both SBP and especially DBP reduced significantly (*p< 0.01) comparing weeks 5-6 for SBP and weeks 4-6 for DBP with week 1.

(A)



(B)

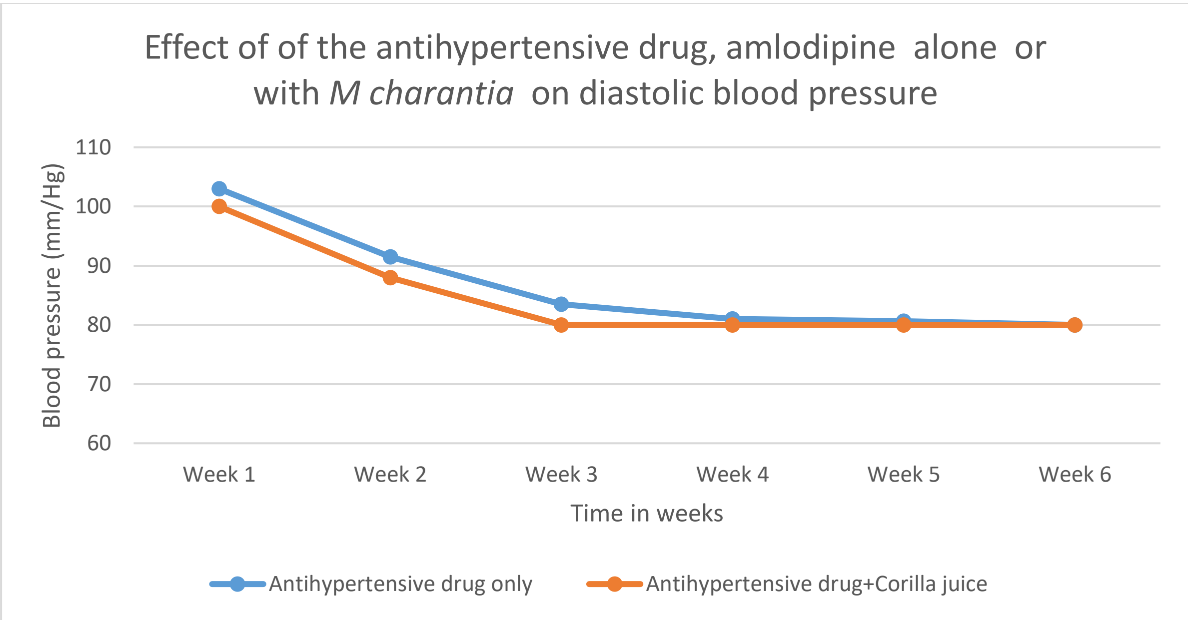


Figure 5.2 A/B: Time-course graphs showing the effects of daily intake of either the anti-hypertensive drug, amlodipine alone or in combination with bitter *M charantia* juice on (A) systolic blood pressure (SBP) and (B) diastolic blood pressure (DBP) over 6 weeks of treatment

in patients with hypertension. Data are mean + SEM, n= 8 for each group; p>0.05. Note that *M charantia* juice combined with amlodipine had either no inhibitory nor synergistic effect on either SBP or DBP when they were combined (compare blue line (amlodipine alone) with pink line (*M charantia* combined with amlodipine).

5.4 DISCUSSION

High blood pressure (HBP) or hypertension is a major global health problem in the world affecting around 1.3 billion people in both developed and low-and middle-income developing countries, and Guyana is one of them (Basu and Millett, 2013; WHO, 2015). HBP is related to the cardiovascular system due to problems with the heart, blood vessels or volume of blood and it falls under the category of non-communicable disease (NCD) (MPH, 2013; Martinez et al, 2020). Currently, most General Practitioners use an automated sphygmomanometer to measure blood pressure of a patients. The normal blood pressure of a person is usually considered to be between 90/60 mm Hg (low range) and 120/80 mm Hg (normal). HBP or hypertension is when the blood pressure is 140/90 mm Hg (mild or stage 1) or higher mild/moderate or stage 2 (150/95 mm Hg or higher (hypertensive crisis) which could be either severe or chronic (180/120 mm Hg) (Elkilany et al, 2019; Zhou et al, 2021). Hypertensive patients are a heterogeneous group of subjects who can be placed into different treatment strategies. They also show different cardiovascular risks, and these are related to the type(s) of treatment in order to provide the best benefit for the patients. At stage 1 of HBP, the doctor is likely to prescribe life- style changes involving diet modification, regular exercise or practising meditation and yoga. At stage 2 of HBP, the clinician is likely to prescribe a combination of anti-hypertensive drugs as well as life- style changes (Mar et al, 2001). During hypertensive crisis, the patient needs urgent medical attention, or it could lead to strokes, blindness, kidney damage and heart failure and subsequently premature death of many the patients (Elkilany et al, 2019; Elkilany et al, 2020; Mills and Stefaneseu, 2020; Zhou et al, 2020.

During the past 20-30 years, Guyana has become infested with NCDs including overweight, obesity, kidney failure, respiratory diseases, diabetes, hypertension and other cardiovascular diseases (CVDs) and cancer (WHO, 2015; MPH 2016). Published data by WHO (2018) and PAHO (2019) reveal that people who die from the cause of hypertension reached 234 or almost 3 4% of total deaths. The age adjusted death rate per 100,000 of the population was around

47%. Currently, Guyana ranks 5th in the world from deaths due to hypertension (WHO, 2018). The HBP problem in Guyana is due to several factors including mental health problems, especially stress and depression, smoking, alcohol consumption, physical inactivity, overcrowding environment, urbanization and unhealthy diet with excess salt and sugar, unemployment and poverty, death of a family member, marital problems, and others (Nguyen and Lau, 2012; WHO, 2013; Zhou et al, 2020). Many people are susceptible to at least three or four of these risk factors whereas some may have them all leading to a synergistic effect in the development of HBP. The prevalence of these risk factors and HBP in many developing countries, such as Guyana, particularly urban societies, are already as high as those seen in developed countries such as UK, Germany, USA and others. Prevalence may also vary from one country to another depending on many factors including environment, urbanisation, economic situation, ageing, mental illness, personal matters, smoking, ethnic group and many others (Public Health England 2017). The incidence increases with age in people of all ancestries and both sexes. Prevalence is higher in men than in women before 65 years of age, and higher in women than in men from 65 years of age. The reason for this difference is still unknown, but the hormone oestrogen and work stress may play a part. The lifetime risk is 90% for men and women who were normotensive at 55 years of age and survive to 80 years (Virani et al, 2020; Vassan et al, 2020).

Health-care system in Guyana is divided into a public sector and a private sector and each of the three counties (Berbice, Demerara and Essequibo) in the country has a publicly funded hospital, where patients receive free medical care and prescription medication. The largest and the main hospital is situated in the Capital City of Georgetown in the county of Demerara. The public sector is highly underfunded and deprived of properly trained doctors, nurses and health professionals due to low wages. As such, the highly qualified and experienced health workers migrated abroad where they received better income (Bristol, 2010). In addition, the pharmacy in each public hospital is also underfunded leading to the unavailability of essential lifesaving prescribed medicines. As a result, a large section of the Guyanese population visits private hospitals and General Practitioners (GPs) for treatment, but this is costly. Unemployment is very high in Guyana due to the closure of several sugar cane factories making over 2,500 workers unemployed affecting almost 15,000 residents (Families) (Jaayfer, 2020). In addition, people who live in far-away villages are unable to travel to the Government and private local hospitals as well as visiting GPs. As such, it is of paramount importance to look for cost-effective and non-pharmacological ways to treat their disease from home in Guyana.

The results of the present study have shown that all five interventions can reduce both systolic and diastolic blood pressure gradually over the 6 weeks of treatment compared to week 1. Typically, diastolic pressure decreased from mild to severe values (95-110 mm Hg) to almost control level (80-90 mm Hg). Similarly, systolic pressure reduced from values (140-150 mm Hg) to almost control levels (120-130 mm Hg). *M charantia* consumed as a juice, either alone or in combination with exercise, was more effective in reducing the elevated blood pressure of the patients compared to exercise alone. Combining *M charantia* with the anti-hypertensive drug, amlodipine produced the same reduction in blood pressure compared to the effect of amlodipine alone. These results from this preliminary study have indicated a therapeutic role of *M charantia* either alone or in combination with daily exercise to treat hypertension and moreover, *M charantia* had no synergistic nor inhibitory effect on the orthodox anti-hypertensive medication, amlodipine. These results for the effects of *M charantia* and exercise to treat HBP are in agreement with a number of previous studies in animal models (Sharma et al, 1996; Ahmed, 1999; Ahmed et al, 2004) and in human hypertensive subjects (Joseph and Jini, 2013; Alam et al, 2015; Rahman et al, 2015; Di-Cisare et al, 2016; Kumari et al, 2018; Singh and Hanoman, 2019; Jandaria et al, 2020).

The question which now arises is this. How does *M charantia* alone or in combination with exercise exert their anti-hypertensive effect? *M charantia* is rich in a number of chemicals including antioxidants, phenols (gallic acid, tannin, catechin, epicatechin, alkaloids, chlorogenic acid, gentisic acid, carotenoids, and sterols), flavonoids, vitamins (A, B, C and E), minerals and others. It is the consensus that the anti-hypertensive properties of *M charantia* is probably due to its chemical properties (Singh et al, 2011; Joseph and Jini, 2013; Alam et al, 2015; Kishoshita et al, 2018; Khan, 2019; Prysyazhna et al, 2019; Jandaria et al, 2020). Several bioactive components in *M charantia* have been proposed to exert Angiotensin-I Converting Enzyme (ACE) inhibitory activities which is one of the ways to treat HBP. These compounds including polysaccharides, ACE inhibitory peptides, which are mainly derived from *M charantia* seed proteins and phenolic phytochemicals, mainly flavonoids, which are derived from the green fruit of *M charantia*. Their hypotensive impact has been demonstrated in a several *in vivo* studies (Priyanto et al, 2015; Shodehinde et al, 2016; Tan et al, 2016; Lestari et al, 2017).

Like *M charantia,* exercise is a drug-free life- style change or non-pharmacological approach to lower blood pressure in hypertensive patients. Being cost-effective, it is an affordable potential physiological tool for patients who cannot afford orthodox expensive medicine in low income developing countries like Guyana. Exercise can reduce blood pressure by strengthen the cardiac muscles (physiological hypertrophy) of the heart making them stronger for the heart to pump a larger volume of blood each stroke but with less effort. This is due to a decrease in heart rate which is less detrimental to arteries in the body resulting in a lowering of blood pressure (Di-Cisare et al, 2016). During exercise, the muscle and other cells burn up adenosine triphosphate (ATP) to provide energy for the body. A major by-product of ATP is adenosine which is a powerful endogenous vasodilator. Moreover, during exercise the muscle cells in the body produce several auto-regulatory chemicals such as carbon dioxide, protons (H^+), kinins and cations, especially potassium (K^+) which are all vasodilators leading to a fall in blood pressure (Dias and Shimbo, 2013; Myo-Clinic, 2019; Aronson et al, 2020). Exercise can also increase the mass and function of pancreatic beta cells in the body leading to the synthesis and production of new insulin which induces vascular vasodilatation in the skeletal musculature in the body leading to a reduction in blood pressure (Baron, 1994; Curan et al, 2020).

The results of this study also show that *M charantia* does not seem to interfere with the action of the anti-hypertensive drug, amlodipine which is a calcium channel blocker in both cardiac myocytes and vascular smooth muscle cells (Khan et al, 2021). There was no potentiation nor reduction in blood pressure. The values were about the same in the absence or presence of *M charantia*. There is no other study in the literature on blood pressure regarding a combination of *M charantia* with anti-hypertensive drugs. However, some evidence is available that combined exercise with anti-hypertensive drug had no additive or synergistic effect on blood pressure (Pescastello et al, 2021). The current finding indicates that there is no harm in prescribing both complementary and orthodox medicines to hypertensive patients. Nevertheless, more research needs to be done in this area.

5.5 CONCLUSION

In conclusion, the results present in study on high blood pressure, have clearly supported a cost-effective therapeutic role of exercise and *M charantia*, especially when they are combined, in the treatment of high blood pressure. Moreover, the study also attempted to explain the cellular mechanism(s) of action of both exercise and *M charantia* in inducing their antihypertensive effects. Furthermore, the results reveal no synergistic effect between *M charantia* and the anti-hypertensive drug, amlodipine on blood pressure when they are combined. The concluding message is that people who are hypertensive and cannot afford to seek treatment from either public or private health sector in Guyana, then they should follow a non-pharmacological approach to treat their high blood pressure in a cost-effective manner, especially since complementary medicines for the treatment of hypertension are increasing popularly among some patients (Jandaria et al, 2020).

Chapter 6:

Assessing the knowledge and understanding of newly diagnosed patients about diabetes and obesity and on self-care management relating to long-term complications among confirmed type 2 diabetic patients in Guyana using questionnaires

6.1 INTRODUCTION

Both overweight and obese are the main modifiable risk factor for type 2 diabetes (T2DM). Globally, obese adults are five times more likely to be diagnosed with diabetes than adults of a healthy weight. Currently, 90% of adults with T2DM are either overweight or obese. People with severe obesity are at greater risk of T2DM than mild obese people with a lower Body Mass Index (BMI). Moreover, it is now known that deprivation is closely linked to the risk in developing both obesity and T2DM. Prevalence of T2DM is about 40% more common among people in the most deprived regions of the world compared with those in the least deprived regions. People from Black, Asian and other minority ethnic groups are at an equivalent risk of T2DM at lower BMI levels than white European populations (Abdulla et al, 2010; Eckel et al al, 2011; Galineau et al, 2014). Overweight, obesity and diabetes are severe public health crises globally and their prevalence is increasing steeply in both developed and in low- and middle- income developing countries (Arroyo-Johnson and Mincey, 2016). Moreover, overweight, obesity and diabetes are significant physical and mental health problems globally characterised by substantial impairment in quality of life and a high -risk factor for other chronic diseases including cardiovascular diseases (CVDs). Both overweight and obesity are generally more resistant to treatment (Mond et al, 2009) compared to diabetes. Current trends suggest that eating and weight-related health issues are increasing and are likely to present public health challenges and economic burdens for the next few decades (da-Luz et al, 2017). Obesity is also associated with bulling and adverse physical and mental health outcomes including covid-19 (Bello-Chavolla et al, 2020; Mc-Gurnahan et al, 2020; Williamson et al, 2020; Hanoman et al, 2022; Smail et al 2022). It is of paramount importance to reduce the obesity pandemic burden worldwide since it can also induce the development of diabetes and CVDs (Mond et al. 2009).

Both obesity and diabetes are highly prevalent in most Caribbean countries, including Guyana, and the number of people with these two NCDs is expected to rise as more people becomes obese at younger ages. Guyana is part of the Caribbean Community of Countries, and it is thought to have a similar high prevalence of obesity and diabetes (Hennis et al, 2002). Guyana has an adult diabetes and obesity prevalence of 15.9% and 30.5%, respectively, the second highest prevalence of any country in the Americas (McNaughton et al, 2015; PAHO, 2019). The incidence and prevalence of both NCDs are rapidly increasing with time, accompanied by the frequency of long-term complications (Tapia and Dhalla, 2022). This is probably due to a lack of health literacy.

Poor health literacy, due to lower level of education such as primary education only, is related to an inability to read and to comprehend health information and this is associated with less primary self-care management, worst clinical outcomes leading to long-term complications and increased health care costs (McNaughton et al, 2015). In term of diabetes, Schillinger (2002) conducted a cross sectional observational study to examine the association between health literacy and diabetes outcomes among patients with T2DM employing 408 English and Spanish speaking T2DM patients, above the age of 30 years. The results showed that after adjusting for patients' socio-demographic characteristics, depressive symptoms, social support, treatment regimen and years with diabetes, there was a 1-point decrement on the short-form Test of Functional Health Literacy in Adults (s-TOFHLA) score and the HbA_{1c} value increased by 0.02 (p=.02). Schillinger (2002) furthermore reported that patients with inadequate health literacy were less likely than patients with adequate health literacy to achieve tight glycaemic control. Other studies by Schmidt (2002) and Brown et al, (2006) strongly support the results of the findings of Schillinger (2002). Psychological intervention is an important tool to get people to adhere to life-style changes including self-education (Martinus et al, 2006). It is unclear as to what extent knowledge affects T2DM, but like previous studies, evidence demonstrated the importance or effectiveness of knowledge on this issue (Shrivastava et al, 2013; Diabetes, UK, 2020). In another study on effectiveness of self-management training in T2DM, it was reported that educational interventions that involved patient collaboration may be more effective than didactic interventions in improving glycaemic control, weight, and lipid profiles (Norris, 2001; Shrivastava et al, 2013; Diabetes, UK, 2020). In a previous study, Wiklead et al, (1996) reported that a high level of knowledge or awareness among diabetics could allow for proper self-care management. Based on the literature, it can be said that knowledge is indeed playing a vital role in self-care management of T2DM.

In light of the findings in the literature, the main objective of this study was to assess the level of knowledge about T2DM self-care management among T2DM patients employing a questionnaire as a tool for data collection. The second objective of the study was to assess the level of knowledge and understanding of obesity including it causes, control and prevention strategies, its association with other diseases and the health consequences which may result from the diseases among a cohort of Guyanese adults of both genders for comparison.

6.2 METHODS

6.2.1 Use of a questionnaire to collect data about diabetes and its self-care management relating to long-term complications.

(a) Description of the subjects

This study was conducted at the rural hospital clinic in Guyana. A total of 180 patients ((93 (51.9%) females and 87 (48.1%) males) with T2DM were chosen at random, based on their willingness to participate in the study. Following interviews and signing the consent form (see Appendix 1), they were placed into two groups, namely T2DM experimental group (90 patients who had developed T2DM- related complications including elevated blood glucose levels, foot and oral ulcers, partial blindness, and nerve damage) and T2DM control group (90 patients who did not develop such T2DM- related complications).

(a) Study design

The research was conducted using a prospective design questionnaire. Data for this study were collected from the patients after they had been placed into one of the two above mentioned groups. This was determined based on the patients' health status i.e, the presence or absence of complications. This study made use of a questionnaire to collect quantitative data (see appendix IIIC). The questionnaire was constructed in an examination format containing several structured questions which allowed for the easy assessment of patients T2DM self-care related knowledge in managing their diabetes. The questions contained in the questionnaire pertained to T2DM-related complications, prevention and treatment and others. Before filling out the questionnaire, the respondents were interviewed and given general ideas of what the study was about, the importance of the study and their intended role. Each participant was asked to sign a consent form once he or she had agreed to participate in the study at his or her own will and the person could withdraw at any time if they wanted (see appendix I).

(b) Variables

The independent variable in this study was the level of knowledge of T2DM-self-care and the dependent variable was the occurrence of complications.

(c) Method of measuring the variables

The questionnaire given to the participants was used as the tool for measuring the variables. The dependent variable included the occurrence of complications which was correlated with the independent variable involving the level of knowledge of T2DM self-care determining the possibility of complications occurring. Participants with 70% correct responses were considered to have passed and be adequately knowledgeable about T2DM self-care management.

(d) Data analysis

All statistical analysis was done using the Statistical Package for Social Sciences (SPSS). The data collected were tallied according to the two assigned groups; control and experiment. Each question on the questionnaire was dealt with individually and the percentage of correct responses was illustrated for each group. Next, the average test scores were calculated for the groups and given as the mean ± standard deviation (SD) and standard error of the means (SEM), along with the other measures of central tendencies. The means were used to make comparison to determine what group scored higher. The data were expressed as true values and presented percentages in table 6.1 and all the graphs.

(e) Ethical Considerations

Before the questionnaire was answered by the patients, they were all instructed to read and sign a consent form and was assured that their answers would remain strictly confidential (see Appendix 1). It was also conveyed to the respondents that their participation was entirely voluntary and if they wished to cease participation at any time, they were free to do so. The project had ethical approval from the Ethics Committees from the University of Guyana and the University of Central Lancashire) (see Appendix II).

*6.2.2 The u***se of questionnaires to collect data on the knowledge and understanding about obesity and its relationship with diabetes (follow-up from chapter 4) and on diabetes alone (follow-up from chapter 3)**

(a) Description of the subjects

This part of the study was a follow up from Chapter 4 on obesity and chapter 3 on diabetes where the subjects (32 in chapter 4 and 10 in chapter 3) were given questionnaires to complete relating to their knowledge and understanding of obesity and diabetes at the start of the investigation. The *s*tudy design relating to this research was conducted using prospective design questionnaires *(*see appendix IIIA for diabetes and IIIB for obesity). Data for this study were collected via a designed questionnaires from either the 10 newly diagnosed diabetic patients (follow-up details from chapter 3) or 32 patients after they had been interviewed about the subject area of obesity (follow-up details from chapter 4). The 32 male and female obese subjects (16 males and 16 females) were recruited from newly diagnosed overweight or obese patients who had no other illness and not on any medication and who visited the clinic for medical treatment. The study was done according to established investigative trial/study methods (Kinoshita and Ogata, 2018). All the subjects signed a consent form to participate in the study at their own will and they could withdraw at any time if they wanted.

Following recruitment, the subjects were explained thoroughly about their obesity or overweight and about the experimental protocol which was designed to last over a period of six weeks (see experimental data in chapter 4). Thereafter, they were each given a questionnaire comprising of 25 questions relevant to knowledge about obesity. This study made use of a questionnaire to collect quantitative data. The questionnaire was constructed in an examination format containing several structured questions which allowed for the easy assessment of obesity self-care management of the patients related knowledge of the disease and its relation to the development of co-morbidities. They were asked to complete the questionnaire and returned to the clinic. Only **twenty** subjects submitted the questionnaire following completion. For the newly diagnosed diabetic patients, all 10 completed the questionnaire. Each question in the questionnaire for either obesity or diabetes was analysed and the data presented in the result section of this chapter as original answers in some cases.

(a) ***Variables***

The independent variable in this study was the level of knowledge of obesity and self -care and the dependent variable was development of comorbidities due to obesity.

(c) Ethical Considerations

Before the questionnaires were completed, each respondent was instructed to read and sign a consent form and was assured that their answers would remain strictly confidential (Appendix I). It was also conveyed to the respondents that their participation was entirely voluntary and if they wished to cease participation at any time, they were free to do so. The project had ethical approval from the Ethics Committees from the University of Guyana and the University of Central Lancashire).

6.3 RESULTS

<u>Section 1</u>

(A) Knowledge on diabetic self-care management in T2DM employing questionnaire presented in Appendix IIIC.

A.6.3.1 General demographics of the 180 volunteers, recruited in two groups of T2DM subjects.

Table 6.1: General demographics of the 180 volunteers (experimental (exp) and control) recruited in two groups of T2DM subjects. Data expressed a %age; *p<0.05 for 35-45 year and 56 years and over, Indo ethnicity and secondary education.

General demographics		Exp (%)	Control (%)	Total
Gender	Male	24.1	24.1	48.1
	Female	24.1	27.8	51.9
Age (years)	25-35	8.9	12.7	21.5
	36-45	8.9	20.3*	29.1
	46-55	7.6	3.8	11.4
	56 and over	22.8*	15.2	38.0
Ethnicity	Afro-Guyanese	11.4	15.2	26.6
	Indo-Guyanese	27.8*	29.1*	57.0*
	Amerindian	6.3	2.5	8.9
	Other	2.5	5.1	7.6
Level of education	Nursery	0.0	0.0	0.0
	Primary	6.3	7.6	13.9
	Secondary	41.8*	35.4*	77.2*
	Tertiary	0.0	8.9	8.9

Table 6.1 shows the general demographics of the 180 volunteers, recruited in two groups of T2DM subjects. The study recruited 180 T2DM subjects (ages between 25-70 years; mean $\pm$SEM of 49.5$\pm$6.7 years) who were divided into two groups, one experimental (90 patients with T2DM-related complications) and the other control (90 patients with no T2DM-related

complications). In terms of gender, there were 93 (51.9%) females and 87 (48.1%) males) who were selected randomly for this study, based on the presence or absence of associated complications. A total of 86 (48.10%) of the respondents developed complications (45 females (51.9%) and 41 (48.1%) males). These included foot and oral ulcers, partial blindness, nerve damage and elevated blood glucose (diabetic level). Regarding each group, there were 24.1% males and 24.1% females in the experimental group (90 patients) and 24.1% males and 27.8% of females in the control group (90 patients). These data reveal an almost equal distribution of men and women in the two groups.

In terms of age-ranges, the subjects were divided into four age-ranges namely 25-35 years, 36-45 years, 46-55 years and 56 and above years. The rationale was to ascertain which age-range was more susceptible to diabetes-induced long-term complications. Percent of subjects in the experimental group was 8,9%, 8,9%,7.6% and 22.8% for age-ranges 25-35 years, 36-45 years, 46-55 years and 56 and above years, respectively. Similarly, for the control group, the percentage was 12.7%, 20.3%, 3.8% and 15.2% for age-ranges 25-35 years, 36-45 years, 46-55 years and 56 and above years, respectively. The data reveal that most patients in the experimental group (22.8%) were in the age-range of 56 and over compared to the control group (15.2%). Likewise, more subjects were in in the control group (20.3% compared to 8.9% in the experimental group who were in the age range of 35-45 years. This is interesting since the data suggest that as people get older, they tend to develop diabetes and they are more likely to develop long-term complications compared to subjects of younger age-range. In addition, they probably became more forgetful with ageing and less educated. In contrast, the younger age-group are more alert and possible more educated on self-care.

Regarding ethnicity, Indo-Guyanese accounted for the vast majority of respondents with 27.8% in the experimental group and 29.0% in the control group control, totalling 57% (101 subjects out of 180). This was followed by Afro-Guyanese with 11.4% in the experimental group and 15.2% in the control group, totalling 26.6% (48 out of 180 subjects). Likewise, for the Amerindian Guyanese, there were 6.3% in the experimental group and 2.5% in the control group, totalling 8.9% (17 out of 180 subjects). In the final ethnicity group (mixed, Europeans and other Guyanese), there were 2.5% in the experimental group and 5.1% in the control group totalling 7.6% (14 out of 180 subjects). The data reveal that there were significantly ($p<0.05$) more Indo-Guyanese in both experimental and control groups compared to either Afro-Guyanese, Amerindian Guyanese or other Guyanese. The order was 101 Indo-Guyanese, 48 Afro-Guyanese, 17 Amerindian Guyanese and 14 other Guyanese, all totalling 180 subjects.

Furthermore, most of the respondents (62% or 110 subjects) fell into the 25-54 years aged group (working years) compared to 38% (70 subjects) who fell into 56 years and over age-range. A total of 77.2% (137 subjects) of the respondents from the two groups (41.8% experimental and 35.4% control) had secondary education compared to 13.9% (25 subjects) who had only primary education (6.3% experimental and 7.6% control). In addition, only 8.9% (18 subjects) in the control group had tertiary (University) education compared to 0% for the experimental group. There was no patient with nursery education alone. The results show that that significantly ($p<0.05$) most of the subjects (137) had secondary education compared to 25 with primary education and 18 with tertiary education and all the those with tertiary education were in the control group.

A.6.3.2 Gender of participants and percentage average scores on the knowledge test relating to level of education on long-term complications based on, age-ranges, level of education and ethnicity of the two groups of 180 respondents.

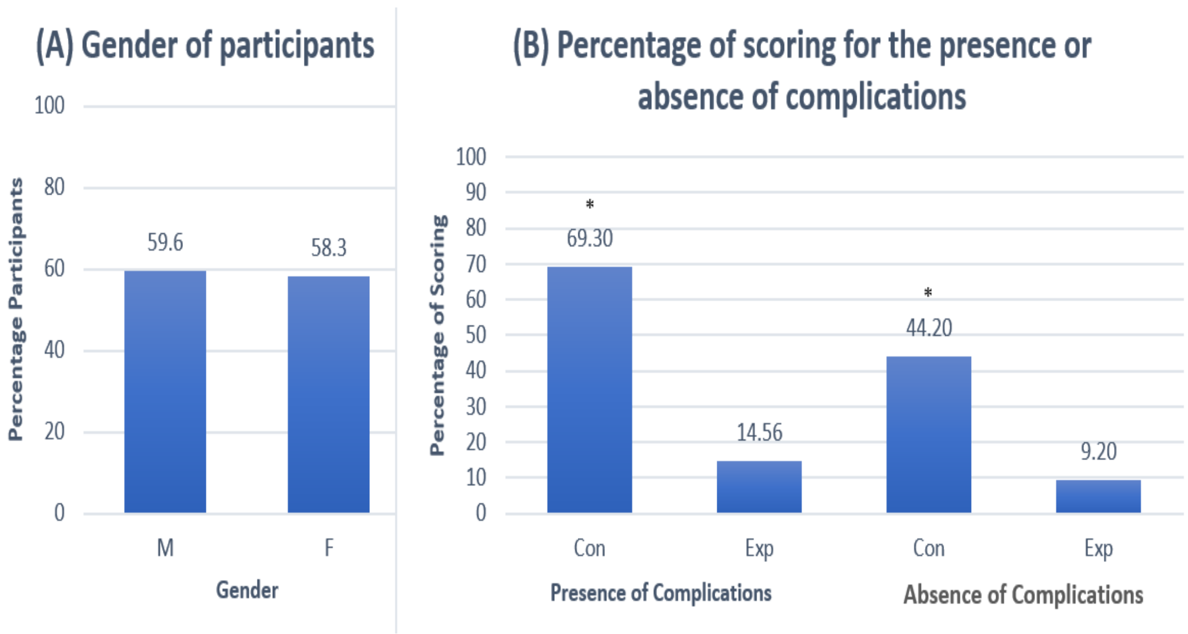


Figure 6.1: Bar charts showing (A) the percentage of males (M) and females (F) participated in the study and (B) the average percentage scores on knowledge of diabetes self-care of the control (Con) and experimental (Exp) groups for either presence or absence of complications. Data expressed as a percentage; *$p<0.05$ for control group compared to the experimental group.

Figure 6.1A shows the percentage of males and females participated in the study relating to knowledge on diabetes self-care management. The data reveal an equal number of the two genders. Figure 6.1B reveals the percentage scores obtained by the control and experimental groups for either the presence or absence of long- term complications. The data show that the control group scored significantly ($p<0.05$) higher compared to the experimental group regarding either the presence or absence of long-term complications. These findings clearly show that patients from the control group had a better understanding and knowledge about diabetes self- care management probably due to their level of education. It is particularly noteworthy that patients in the control group had both secondary and tertiary education. As such, the level of education seems to play a major role in the scoring process regarding diabetes-induced long- term complications.

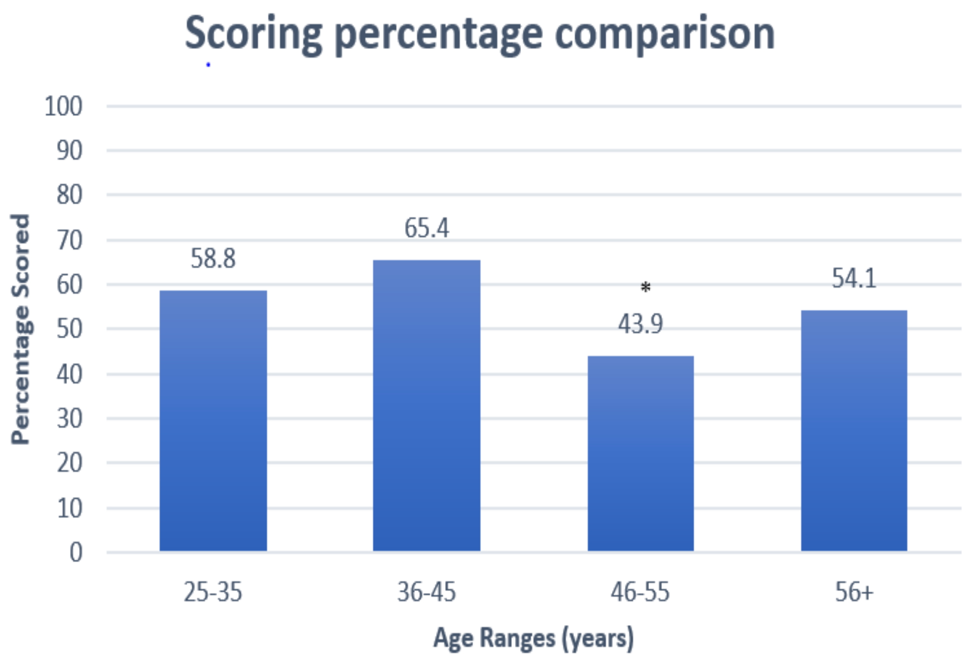


Figure 6.2: Bar charts showing the scoring percentage by the four different age-ranges. Data expressed as percentage. *$p<0.05$ age range 46-55 years compared to age ranges 25-35 and 36-45 and 56 and over years.

Figure 6.2 shows the scoring percentage for knowledge on diabetes self-care management by the four different age -ranges participated in the study for comparison. The data were combined for both control and experimental groups. The results show that the age-range which scored the lowest was 46-55 years compared to the other three age ranges who obtained significantly higher scores (p<0.05). The order of percentage scores from high to low were 36-45, 25-35, 56 and over and 45-55 years. The data suggest that younger and possibly retired patients seem to have a better knowledge about diabetes self-care management.

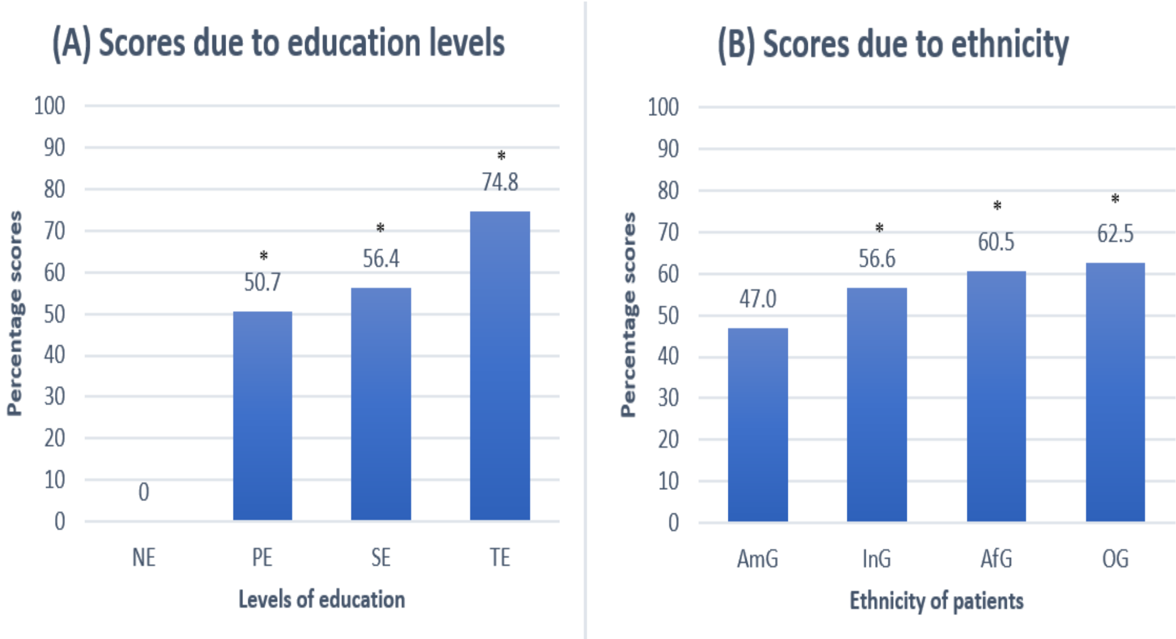


Figure 6.3: Bar charts showing the percentage scoring due to (A) the different levels of education and (B) ethnicity of control and experimental groups combined. Data are expressed a percentage and *p<0.05. Note that patients with tertiary education (TE), Secondary education (SE) and primary education (PE) education scored significantly higher (*p<0.05) compared to nursery education (NE) but with much higher score by diabetic patients with tertiary education (TE). Likewise. Indo Guyanese (InG), Afro Guyanese (AfG) and other Guyanese (OG) scored significantly higher (*p<0.05) than Amerindian Guyanese (AG).

Figure 6.3A shows the influence of the level of education on the combined percentage scoring by control and experimental groups of diabetic patients relating to knowledge of diabetes self-care of diabetes on the development of long-term complications. The data clearly show that subjects with primary, secondary and tertiary education scored significantly (p<0.05) higher compared nursery education. Those patients who had tertiary education scored the highest. The order of scoring was tertiary>secondary>primary. nursery. Surprisingly, patients with secondary and primary education scored the same. Figure 6.3B shows a bar charts of the percentage scores obtained by the four different ethnic groups of diabetic patients. The results reveal that the other Guyanese diabetic patients scored significantly (p<0.05) the highest (62%)

followed by Afro-Guyanese (60.5%), Indo-Guyanese (56.6) and then Amerindians (47%). The other Guyanese are of mixed race, and some are Europeans and normally they are well educated. The order of scoring was Other Guyanese (62.7%)>Afro-Guyanese (60.5%)> Indo Guyanese (56.6%) > Amerindian Guyanese (47%).

A. 6.3.3 Percentage average scores on the knowledge test relating to diseases associated with diabetes, diabetes diets, HBA1c and normal blood glucose level for the 180 control and experimental respondents.

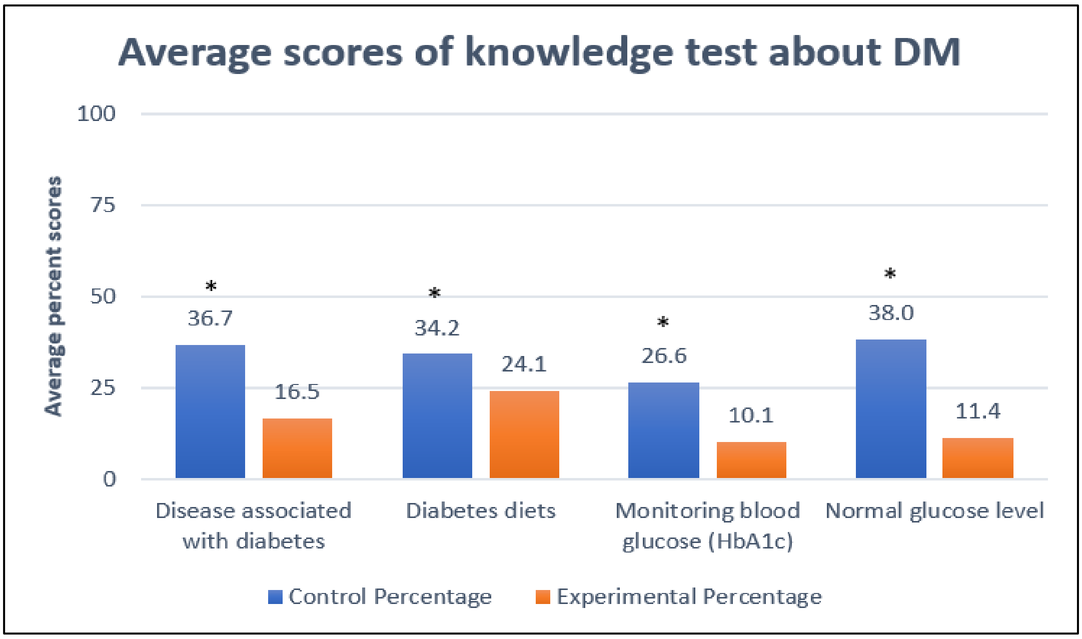


Figure 6.4 Data (expressed as percentage) showing the average scores on the knowledge test relating to diseases associated with diabetes, diabetes diets, HBA1c and normal blood glucose level for the 180 control and experimental respondents, *$p<0.05$ for control group compared to experimental group.

Figure 6.4 shows average percentage scores on the knowledge test relating to diabetes associated with diseases, diabetes diets, HBA1c and normal blood glucose level for the 180 control and experimental respondents. The data clearly reveal that the control group possessed a significantly ($p<0.05$) higher level of knowledge relating to diabetic diet, diabetes-associated diseases, the importance in regular monitoring of HBA1c and normal blood glucose level. This is an important finding since the level of HBA1c can determine the degree of diabetes-induced long-term complications. Another important finding from this study is that most of the diabetic patients in the experiment group were unable to answer the question pertaining to a normal glucose range correctly (11.4%) compared to 38% from the control group ($p<0.001$). Moreover, respondents from the experimental group were unsure of which glucose test was best to use and more accurate in determining the diabetes.

Section 2

6.3 (B) Knowledge on obesity and its relationship with diabetes

B.6.3.1 Obesity data

As outlined earlier in section 6.2.2 above, the questionnaire was given to 32 subjects (16 males and 16 females) with an average age of 42±4.6 years. They all had problems with their body weight, and they also visited the medical clinic for treatment between September 2018 and October 2019. All the patients were obese, some with prediabetes and hypertension. All the patients were explained about the study and asked about their willingness to participate voluntary in completing the questionnaire and signing the consent form. Thereafter, they were all given the questionnaire about their knowledge about obesity to complete at their convenience and then returned the questionnaire to the clinic. A total of 20 subjects completed the questionnaire individually and returned it to the clinic for analysis. The questionnaire had 25 questions relating to their knowledge about obesity, risk factors, causes, interrelationship with diabetes, hypertension and life-style habits (see Appendix IIIB for questionnaire).

The first question was: What is obesity?

From the answers for the question, it was clear that all 20 subjects had a good knowledge of obesity. The majority said that it was due to excess fat in the body or overweight or excessive overweight. Some typical answers included the following-

‘Obesity is when a person gains too much weight than a normal person’.

‘Obesity is a major health problem due to excess fat deposit in the body’.

‘Obesity is the state of being too fat or overweight’.

From the several related answers, it was clear that virtually all 20 subjects had a good knowledge of obesity and overweight, but sadly most of them were all obese.

The second question was: What are the causes of obesity? Many of them gave the following answers-

1. ‘Lack of exercise and eating too much fatty food’.
2. ‘When one’s organs are breakdown’ (probably meaning is that obesity can affect other organs in the body).
3. ‘Excess food intake and the types of food you consume daily’.
4. ‘Poor diet rich in fats and sugar’.
5. ‘Unhealthy diet such as junk foods and lack of exercise’.
6. ‘Eating too much of fatty food’.
7. ‘Overeating too much of fatty foods.
8. ‘Genetic behaviour and environmental factors.’
9. ‘Obesity is caused by eating too much and lack of exercise which lead to the built up of fats and sugar in the body over time’.
10. ‘Eating foods which are rich in cholesterol.’

From these interesting answers, it is correct to say that the subjects had a very good understanding of the causes of obesity and overweight due to eating excess food full of sugar, fats, cholesterol and lack of exercise. Two subjects mentioned that some people become obese because of genetic predisposition and environmental factors. What was amazing was that they knew the causes of obesity, but they were still obese?

Questions 3, 4 and 5 were based on obesity and health, life expectancy and weather obesity can be cured. The subjects gave the following answer-

All the subjects acknowledged ‘Yes’ to the three questions that obesity could affect their general health and shorten their life expectancy and it is possible to cure obesity. Note that they were not asked to give an explanation regarding each question.

Again, like questions 1 and 2, the subjects had a good knowledge about the danger of obesity to their health and life expectancy.

Question 6 was based on sugar. How can sugar affect your life?

Most of the subjects agreed that sugar could cause diabetes or elevated blood sugar level and other diseases such as obesity, kidney failure, blindness and as well as risks of cardiovascular diseases.

From the answers to the questions, it was understandable that that they had very good knowledge and understanding of the adverse effects of sugar in the development of obesity, diabetes and other-related diseases.

Question 7 was related to: Does obesity run in the family and what happens to our body to cause obesity?

Surprisingly, over 85% of the subjects said that obesity ran in their family. Regarding the second part of the question, most of the respondents said that obesity helped in building up fats in the body or it could lead to the storage of excess fats in the body. In turn and over time, the excess body fat would affect their liver, heart and in some cases, they would have problem in breathing.

The answers given by the respondents are correct and they indicate that their knowledge of the subject area is very good.

Question 8 was related to- What is the connection between lifestyle and obesity. The responds gave some typical answers as-

'Overweight, obesity and diabetes are very bad for the body and they are due to laziness, unhealthy life-style, not exercising regularly, snacking and binging regularly and the choice of food they ate.'

From the answers, it is fair to say that the respondents had a good knowledge that there is a strong connection between life-style habits and obesity and even the development of diabetes.

Question 9 was related to- What are the steps which people can take, both kids and adults, to break the unhealthy habits that lead to obesity?

Surprisingly, over 80% of the respondents gave the following points as answers.

'Eating healthy diet, take regular exercise, eating the right foods, dieting, stop eating a lot of fatty foods, educate yourself about obesity and its long-term complications, better to change your life-style habits before it is too late, ease up on watching TV, avoid eating junk foods, stop regular snacking and binging, try to get more sleep, do not skip breakfast, eat less sugar and starchy foods and monitor your body weight regularly'.

From these answers, the respondents knew exactly how to avoid overweight and obesity or even treat their obesity problem, but nevertheless, they were all obese.

Questions 10-19 were related to the association between obesity, diabetes, and hypertension.

(a) All the respondents answered 'Yes' for the link between obesity as a risk factor for the development of obesity and hypertension. The answers clearly indicated that they had very good knowledge and understanding about the connection between the consumption of 'junk' or unhealthy foods and the development of obesity. They also knew that obesity was a major risk factor for the development of high blood pressure by affecting blood circulation due to excess fat accumulation in the body. Regarding type 2 diabetes (T2DM), the respondent seemed to have a very good knowledge on how the consumption of excess fats and sugar can lead to the metabolic disorder.

Some other typical answers include-

(a) 'Fats can block blood vessels leading to the formation of plaques and stiffness of blood vessels resulting to hypertension'.

(b) 'Excess fats are building around and in blood vessels and as such obesity can affect the heart leading to heart failure.'
(c) 'Being obese, the body is unable to control blood sugar.'
(d) Obesity contributes to type 2 diabetes by allowing more sugar to accumulate in the blood vessel'.
(e) 'Obesity slows down the body to burn sugar'.
(f) 'Obesity is a risk factor for high blood pressure and type 2 diabetes due to excess fat and sugar and they affect the blood vessels and flow leading to heart problem'.
(g) 'Obesity adds pressure on the ability of the body to use insulin to properly control blood glucose levels, thus leading to type 2 diabetes.'

Regarding the answers for questions 10-19, on the association between obesity and diabetes and hypertension, many of the respondents agreed that obesity is a major risk factor for the development of T2DM and hypertension. Only one respondent mentioned the inability of insulin to stimulate glucose uptake into muscle cells in the body or insulin resistance. Most of the respondents had very good understanding of how obesity is associated with excess sugar in the blood and how the muscle cells in the body are unable to take up the glucose resulting to diabetes.

Question 20 is related to the side effects of obesity in the body.

Most of the respondents mentioned sleeplessness, tiredness, slow movement in breathing, delaying in the healing of wounds, development of diabetes and high blood pressure, quality of life is impaired, sudden cardiac death, arthritis, knee pain and the body is unable to function properly and the possibility of heart diseases.

From these different answers, it is evident that respondents have very good knowledge on some of the health side-effects of obesity. Nevertheless, they were all obese and they probably knew what would happen to their body if they did not control their body weight.

Questions 21- 22 were related to whether obesity is a preventable disease and how to control it.

Most of the respondents answered, 'Yes' except for one respondent who said 'No'. They also gave some answers on healthy diet, the importance of daily exercise and not to eat extra during a meal.

Regarding how to control obesity, the respondents gave such answers as regular daily exercise, eat less, modify your diet, eat the right food, eat a balance diet, change your lifestyle, and eat healthy, control your eating habits and avoid constant snaking and binging**.**

Question 24 asked for the most common causes of obesity.

The respondents gave such answers as eating unhealthy diet such as junk food rich is bad fats and sugar, eating extra food, lack of exercise, bad health management by the Government, improper diet and others.

Question 25 was related to the factors which contribute to obesity.

The respondent gave such answers as medical problems, ageing, genetics and family history, some medications, family lifestyle, eating too much food, no exercise, improper diet, over eating, late night sleep, not following the right guidelines regarding the type of healthy foods to eat and a few other answers.

<u>Section 3</u>

6.3 (C): Use of questionnaire to acquire data on knowledge about diabetes

In this study, a questionnaire was designed to acquire demographic data and understanding and knowledge about diabetes from each of the original ten diabetic patients at the inception of the study (see Appendix IIIA). The questions included information relating to age, gender ethnicity, occupation and level of education and these are given in table 3.1 in chapter 3. The data relating to knowledge and understanding of diabetes are now given below.

The questions attempted to retrieve general information as: What is diabetes? the different types, causes, diagnosis, symptoms, diabetes information, diabetic diet and eating habits, *Momordica charantia* to treat diabetes, diabetes in the family and others.

They all said that they knew what diabetes 3 patients was all about and only were able to distinguish between type 1 and type 2 diabetes mellitus. They were asked about the causes, and they all mentioned that diabetes was due to our modern life-style habits and overweight and obesity. They were also asked about diagnosis of diabetes. Two patients mentioned about elevated blood sugar, two said to discuss this with the doctor and the other six had no idea. In general, the majority had virtually no idea in diagnosing diabetes, except for two of them who knew the relationship between diabetes and elevated blood sugar. They were asked about the symptoms of diabetes. Most of them said they had no knowledge except for three patients who mentioned dizziness, unable to sleep, fainting, numbness, excess urination and constant thirst. They were also asked how they could find out if they were diabetic. They all mentioned about visiting their doctor for a test. Only two patients mentioned about getting a glucose test. They were asked about long-term complications of diabetes. Eight of them said that they did not know while two patients mentioned blindness, limb amputation and kidney problems. In the next two questions they were asked if any family member had diabetes and if they knew that they could die from diabetes. They all answer 'Yes'. They were asked about the beneficial effects of daily exercise to prevent diabetes. Nine of them answered **'yes'** whereas one answered '**no'**. They were asked about the use of *M charantia* to treat diabetes. Eight patients answered **yes** while two answered **no.**

A few questions were related to diet and diabetes. All the patients knew that fizzy drinks contained a lot of sugar. They also knew that eating foods with reduced sugar could prevent the development of diabetes. They also knew that white bread, cassava, rice and other foods rich in carbohydrates could induce diabetes, whereas diet rich in fibre (brown bread, brown rice, nuts, beans etc) can prevent diabetes. They also knew that sedentary lifestyle, overweight and obesity could lead to diabetes,

The patients knew that diabetes could reduce their quality of life and even leading to early death. They also knew that if they did not take their anti-hyperglycaemic drugs regularly and on time then they could end up with long –term complications. All the patients knew that diabetes could run in the family, and they had no idea on the cost for diagnosis, treatment and care for diabetic patients in Guyana. They also had no idea that diabetes killed more people in Guyana compared to some other diseases, except for cardiovascular diseases. They had no idea that diabetes is linked to hypertension and other heart diseases.

The patients were asked about their daily breakfast. Most of them said that they tried to eat sensible by eating whole meal bread, fruits and less starch foods in the morning. The patients were asked about snacking at night. Five of them said that they had late meals and five said no. They all cooked their own meals rather than buying ‘fast foods’. They all knew that eating a lot of vegetables can prevent the development of diabetes, whereas eating a lot of starchy food could facilitate the development of diabetes, except for one person who had no knowledge about food and its relationship with diabetes. They also knew that fruit desserts were far better that processed sugar desserts. The patients were asked if they drank herbal medicine or ate herbal plants. Eight of them said no while two of them said they drank tea with cinnamon and turmeric.

6.4 DISCUSSION

<u>Section 1</u>

6.4.1 (A): Knowledge on diabetic self-care management in T2DM

Questionnaires, as research methodological tools, are very popular and cost-effective in retrieving information from subjects globally for research purposes. Each questionnaire acts like a research instrument, and it consists of a series of questions for the purpose of information gathering from respondents. A questionnaire is like a written interview which can be done via telephone, computer, post, face to face interviews, individually and others. Questionnaires are known to provide a relatively cheap, quick and different ways in obtaining a large amount of information from small, as well as large sample of people measuring a number of parameters including behaviour, knowledge and understanding of a subject area, attitude, opinion, preference, opinion and others (Brown, 2004; Einola and Alvesson, 2021). This study employed the use of three conventional questionnaires successfully to gather information from obese and diabetic patients in Guyana relating to their knowledge and understanding of the subject areas.

The discussion will now focus on the use of questionnaires to ascertain about the knowledge of the patients relating firstly. to diabetes self-care management and second, the knowledge and understanding of the patients about obesity and diabetes.

A 6.4.1.1 Knowledge of self-care management of diabetes

Diabetes is a major global health problem currently affecting about 480 million people and this number is rising gradually (Zimmet, 2014; 2017). Moreover, the prevalence and incidence of T2DM and the occurrences of its long-term complications including heart diseases, kidney failure, blindness, nerve damage, impotence, exocrine gland insufficiencies, foot ulcers and others are also increasing worldwide (WHO, 2011; Lotfy et al, 2016; Diabetes UK, 2020). T2DM occurs as a result of several factors such as overweight, obesity, genetic pre-disposition, sedentary lifestyle and poor diet. If these risk behaviours persist after the confirmatory diagnosis of T2DM, then complications can develop. T2DM is a very devastating metabolic disorder which can negatively affect the quality of a person's life (Wiklead et al, 1996) and increase the economic burden to the patients and also to national Health and Social Services globally (McNaughton et al, 2015). A heightened awareness about T2DM can lead to better self-care management or even prevention of long-term related complications and end-organ failures as well as a reduction in health care cost by the patients by health providers (McNaughton et al,,2015; Lotfy et al, 2016; ADA, 2019; Diabetes UK, 2020). It is of paramount importance for clinicians and health care workers (professionals) to guide and educate diabetic patients, especially those who are not well educated about the disorder, about diabetes self-care management. Self-care concepts which can benefit diabetic patients include adherence to diet modification, physical activity, regular blood glucose monitoring and taking their medication on time and regularly (Martinus et al, 2006; Saleh et al, 2012; Zhao et al, 2018; ADA, 2019. Diabetes UK, 2020).

The results of this study have revealed that all the respondents (males and females combined from control and experimental groups) had a poor overall test average (12.03±4.2 or 57.3%) based on the scores from the knowledge test. In a similar study conducted in Nigeria, Odili, (2011) found that the respondents also had a very low level of diabetes knowledge based on a similar Diabetes Knowledge Test (DKT) of 14 questions (39.5% ± 16.7%). These low scores suggest that diabetic patients are lacking basic T2DM knowledge and understanding of the disorder, keeping in mind the proposed pass grade was ≥70%/15 marks. The control group demonstrated a higher level of knowledge (14.56±3.3 or 69.3%) than those from the experimental group (9.29±3.2 or 44.2%). This higher level of T2DM self-care knowledge or management among members of the control group can be stated as the reason for the absence of complications. It is well known that those patients who read about the type(s) of disease(s) or disorder(s) which they suffer from, then they tend to be more aware about long-term complications and as such, they seem to have a better control over the disease or disorder.

The present results also show that males, on average score slightly higher (12.47±4.6 or 59.4%) than their female counterparts (11.61±3.7 or 55.3%). These results agree with another related study which found that females scored far less than males on self-care management of their diabetes relating to foot ulcers, dietary practises and physical activity (Raithatha, 2014) and younger patients who are in their working years score higher (Missiriya, 2016). The reason for men scoring higher than female and younger age-group patients scoring higher is unknown. It is possible that men discuss their disorders with others compared to women and as such, knowledge could pass from one person to another. Another possible explanation is that more men had tertiary education in this study compared to women. This was substantiated by the fact that people with tertiary education scored higher compared to those with lower (primary) levels of education. Regarding younger people scoring higher, it is possible that they read more widely around the subject area compared to older people. Some of the findings are in contrast to another related study which investigated the characteristics of T2DM men and women who visit a diabetes education centre regularly and found that women to be most likely to have previous diabetes education (Odili, (2011). As such, they should have scored higher than men in such knowledge test. Therefore, it is tempting to say that current programmes available to educate women about T2DM in the Guyanese population are inadequate. It is also noteworthy that both males and females failed the test (not reaching 70%) indicating that education on self-care management in general is lacking in Guyana about T2DM and its long -term complications.

The level of education appears to play a major role as it relates to diabetes knowledge. It can be seen clearly that as the level of education increases among the respondents since it is reflected on the average test scores for primary (10.64±3.4 or 50.7%), secondary (11.85±4.2 or 56.4%) and tertiary (15.71±3.5 or 74.8%) education. So as one progresses academically in life, the desire to access information is more desirable. Contrary to this, a study conducted in Nigeria by Norris (2001) found that persons with no formal education had the highest average diabetes knowledge test (DKT) score compared to their counterparts who had primary to post graduate education ($p<0.05$). Other studies challenged this trend arguing that the level of education has to play a positive role in diabetes self-care knowledge (Murata, 2003; Moodley and Rambiritch, 2007).

Variations in the average test scores in this study were noted among people of different ethnic groups. Persons of “other” ethnic group scored higher (62.7%/13.17±4.6) than analogous ethnic groups. However, Afro-Guyanese scored higher (12.71±4.6 or 60.5%) than Indo-Guyanese (11.89±4.1 or 56.6%), who in turn scored higher than the Amerindians (9.86±4.1 or 47.0%). Studies have shown that persons with African decent are prone or more likely to develop diabetes either by lifestyle or hereditary causes. Therefore, the transfer of information among persons with African decent can be a notable cause for the higher scores as compared to Indo-Guyanese. However, a study conducted in KwaZulu-Natal (Moodley and Rambiritch, 2007), indicated a better overall pass rate in the Indian (75.9%) than African (52.2%) population in a similar knowledge test. Therefore, it can be said that knowledge variation among ethnic groups may be brought about by difference in cultural beliefs, location and strategies used to deliver information which will vary from place to place. The highest score in this study achieved by persons of “other” ethnic group may be due to economic status as well as education. This group of people are of mixed Guyanese ethnicities, Chinese and Europeans and most of they are economically stable and can afford a very good education. This is another area for future study investigating the effect of economic status on self-care management on diabetes-induced hyperglycaemia and long-term complications.

The present results also show that respondents from the experiment group had either little or no knowledge about diseases associated with diabetes and diabetic diets. For diseases associated with diabetes, the control group scored 36.7 % compared to the experimental group which scored 16.5%. Likewise, for diabetes diets, the control group scored 34.2 % compared to 24.1% by the experiment group. This lack of knowledge can be therefore attributed to the lack of dissemination of information at the place of primary health care, more specifically at the clinics where these patients attend regularly. Normally, the diabetic clinic is the main centre for interaction between the patient and the health visitor. These results clearly show that basic information fact sheets on diabetic diets and diabetes-induced long-term complications are lacking at most diabetic clinics in Guyana.

It is now well known that a better understanding of the patient’s own HBA1c and their long-term diabetes control are fundamental to self- empowerment of diabetic patients (Heisler et al. .2005; Bowler and Erde, 2014). The present results in this study have shown that knowledge of diabetes monitoring using the glycosylated haemoglobin (HbA_{1c}) test was 26.6% among the respondents from the control group compared to 10.1% from the experiment group ($p<0.01$). This finding suggests that the control group had more knowledge of glucose monitoring compared to the experimental group. This further highlights the need to provide health promotion and education about T2DM self-care management in Guyana. The majority of the members in the experiment group were unable to answer the question pertaining to a normal glucose range correctly (11.4%) compared to 38% from the control group ($p<0.001$). Moreover, respondents from the experimental group were unsure of which glucose test was best to used and more accurate in determining the diabetes. Based on these results, it can be concluded that T2DM population in Guyana, especially those from urban, suburban and rural areas, possess very little knowledge about self-care management of their illness. This in turn places them at a disadvantage in combating this major metabolic disorder effectively. Thus, input from both the health care provider (clinicians, health care workers and nurses) and the patient themselves are required to control diabetes. Furthermore, the results of this study have clearly revealed the importance and need to improve diabetic knowledge of self-care among patients via education as soon as they are diagnosed with the disorder or even earlier years in their lives when they attend schools via health education. A general health education curriculum is lacking in primary, secondary and tertiary education in Guyana (Mehta et al, 2006; Mukeshimana et al, 2015).

A 6.4.1.1 CONCLUSION

The results have clearly shown a low level of diabetic self-care management among some patients in Guyana, due to lack of effective health promotion and education programmes. From the present results, it is possible to recommend to the Ministries of Public Health and Education in Guyana that more emphasis should be placed in educating the public in general about diabetes mellitus, but specifically to patients with T2DM. They should adhere and more so compliable with their medications, diet modification, weight loss, regular physical activities and how the neglect of these can lead to long-term complications and subsequently early mortality. It is equally important to educate the whole population on diabetes on how to prevent this major metabolic disorder and how its long- term complications can affect the quality of life for diabetics. For these initiatives to be successful, the Ministry of Public Health and the Ministry of Education in Guyana have to involve all sectors of health and social care and education systems, including health care workers or professionals, the patients themselves and health care teachers in schools. It is also strongly recommended that that programmes in education be put in place that are specially tailored to suit individual socio-demographic groups. Current methods used now may only work for certain groups, but not for others. Additionally, more research needs be done around T2DM, specifically as it is related to factors that might present as barriers to knowledge and what are the most effective ways to relate information to a highly diverse population in Guyana.

<u>Section 2</u>

6.4.2 Knowledge on overweight and obesity

Overweight and obesity are major global health problems currently affecting almost 2 billion people and 800 million are fully obese (Kelley et al. 2008). These figures represent 40% of adults, 18 years and over, who are overweight and 14% with obesity. What is more worrying now is that children as young as 6 years of age are becoming overweight and obese amounting for 40 million worldwide (Riley et al, 2005; Lopes, 2012; Ng et al, 2014; Cilia et al, 2019)? It is estimated that by the year 2030, 57.8% of the world population will be obese if the prevalence rate continues at the current pace (Kelley et al, 2008). This pandemic disease is easily preventable if people take care of their health as well as the welfare and life of their children. Like similar low- and middle- income developing countries worldwide, Guyana is also faced with the same obesity burden.

The question which needs answering is this: How can the people prevent the development of obesity? Firstly, it is important to find out how much they know and understand about obesity, it causes and more importantly, its burden to life, long-term complication, association with other chronic diseases and others. The best ways to retrieve information from people involve is to use questionnaires, face to face interviews and other methods. It is well known that literacy can play a major role in understanding either a disorder or a disease and in preventing long-term complications and end-organ failure and improving the quality of life of the patient. As such, the study designed a questionnaire containing twenty-five questions based on obesity to assess their knowledge and understanding about this chronic disease. The information gained can help to understand why the subjects became obese in the first place and what help can be given to combat the disease.

The results from the questionnaire, based on the twenty questions relating to obesity, indicate clearly that most of the respondents had a very good knowledge and understanding about obesity. These include its causes, control, prevention, risk factors, its association with the development of lethal chronic disorders and more so, how this chronic disease can affect their quality of life of the individual. Surprisingly, they give virtually the correct answers to almost all the twenty- five questions including what obesity is, causes, risk factors, how it can affect their health, control and prevention techniques and its association in developing diabetes, high blood pressure and heart diseases. What is surprising is that they gave the right answers for causes, control and prevention, adverse outcomes to their health and quality of life if they continued to be obese or having excessive body weight, but they were still obese (Sinha and Kling, 2009).

In the first place, they must have a good knowledge that obesity can reduce the quality of their life and more so, resulting in long-term complications, even end-organ failure and sudden cardiac death. The next question is this: Why they did not stop eating excessively to reduce their obesity and keep it under control? In this study, there seem to be a strong association between knowledge and understanding of the obesity and the development of it. This interesting observation suggests that human behaviour is very strange and also difficult to appreciate, predict and to comprehend. It is like telling someone that if he or she crosses the busy road, then it is likely that a car would kill the person. But nevertheless, the person would still cross the road.

Regarding such chronic diseases as obesity, diabetes and hypertension which can be controlled and prevented, there is an urgent need for people to acquire some form of psychological intervention to adhere to live saving interventions as eating less, modify their diets, participate in regular physical activity, do not eat late at night or too fast, avoid binging and snaking and others (Martinus et al, 2006; Sinha and Kling, 2009). It is also well known that cognitive behavioural therapy (CBT) is established as a well-recognised therapy for binging eating, and it is a preferred intervention to treat obese patients (Castelnuovo et al, 2017). Previous studies have applied cognitive therapy, psychotherapy, relaxation therapy and hypnotherapy in obese patients to reduce their weights. However, behavioural therapy was found to obtain the best significant results, in getting patients to lose weight compared to non-obese placebo subjects. Behavioural therapy is normally used as ‘stand-alone less therapy’ (Shaw et a,. 2004). Other studies have demonstrated that the inclusion of psychological counselling/intervention in multi-disciplinary treatment for adolescent obesity can provide significant benefit in losing weight and in improving quality of life compared to subjects who received no psychological counselling/intervention (Friestas et al, 2017).

(B) 6.4.2.1 CONCLUSION

In conclusion, the results of this study have shown that obese subjects gain body's weight irrespective of knowledge about the adverse effects of the disorder although they have very good understanding about the subject area. It is possible that they have no mind control over their eating habits possible due to the taste of the food, problem with satiety or they just do not care but instead they love to eat, compete with others or other unknown reasons. A such, psychological counselling or intervention may be required to adherence.

<u>Section 3</u>

(C) 6.4.3 General knowledge on diabetes

The answers from the questionnaire suggested that most patients had limited knowledge on all aspects of diabetes including types, causes, symptoms, diagnosis, diet, blood glucose monitoring, complications and others. This is possibly due to the fact that they were diagnosed with the metabolic disorder for the first time. Apparently, they do not test their blood for diabetes especially since they lack basic understanding and knowledge of the disorder. Only when they visit their local clinic or general practitioner (GP) for other medical conditions then they are diagnosed for diabetes. Similarly, only when they displayed some symptoms of diabetes, then they would visit the clinic or GP and during when they are diagnosed. Unlike obesity, the results from the diabetic questionnaire clearly demonstrate the lack of education on diabetes in Guyana. It is concluded that diabetic education is of paramount importance at a very young age so that potential diabetic patients have basic knowledge of the disorder and self- care management can adhere in either delaying or preventing the development of the disorder (ADA, 2019; Diabetes UK, 2021).

Chapter 7:

General Discussion, Conclusion, Scope for Future Studies, Impact of Study, Limitations and Recommendations

7.1 BACKGROUND OF STUDY

This study is related to the cost-effective way to treat such non-communicable diseases as diabetes, obesity and hypertension in Guyana using life-style changes and *Momordica charantia* (bitter melon or corilla*)* combined with knowledge and understanding of diabetes and obesity and self-care management in preventing diabetes-induced long-term complications. Guyana was a British Colony for over 200 years, and it gained its Independence from the United Kingdom in May 1966 (see figure 1.3 for map of Guyana in chapter 1). Guyana has a very small population of about 780,000 people currently (around 1.7% compared to UK) comprising of Indo-Guyanese, Afro-Guyanese, Native-Amerindians, Chinese, European and people of mixed races (WIKIPEDIA, 2020). After Independence in 1966 and moving on to the 21st Century, the economic situation in Guyana changed gradually for political reasons. Sugar was one of the main export products followed by rice. The ten sugar estates employed almost 12,000 workers and many of them became unemployed during the past 6 years due for a decrease in demand for sugar in the world and closure of seven sugar factories. This led to unemployment of several workers. As such, more people moved to urbanised areas of the country to find jobs, followed by stress, anxiety, and depression (suicide due to mental diseases), changes in eating (eating more fast foods), drinking (excess alcohol consumption) and smoking habits and the development of more inactivity (laziness). These were accompanied by more smoking, drinking and environment pollution, all of which resulted in the development on such non-communicable diseases (NCDs) as cancer, obesity, diabetes, chronic respiratory diseases, kidney failure, dental diseases, hypertension and other cardiovascular diseases (CVDs) such as coronary heart disease, heart failure and arrhythmias leading to a high incidence of mortality (MPH, Guyana, 2013; 2016; WHO, 2014; 2018; PAHO, 2019). Guyana, like other low and middle- income countries, is infested with NCDs and the people have to bear the main cost in treating their diseases and illnesses (PAHO, 2020). In 2020, Oil and Gas were discovered in the adjoining Atlantic Ocean in Guyana and this newfound income/wealth may also alter not only the economic situation in Guyana but also the infection of more people with NCDs (WHO, 2020).

Guyana has two health care systems, namely public and private. The private system includes general practitioners, private clinics and clinical laboratories and private hospitals. The public system is free and it is funded by the Government of Guyana via taxation (WHO, 2018). However, there are problems with the public health and social care systems due to understaffing and underfunding, unavailability of essential medicines, bureaucracy, long waiting times for treatments, lack of trained medical and social care professionals including clinical specialists and basic diagnostic equipment. In general, Guyana has a brain drain where qualified people move abroad to earn a better salary because the salary paid by the Government is very low. As such, most people turn to the private hospitals and General Practitioners for medical and social care attention and treatment. In addition, many people are still unaware of cost-effective non-pharmacological or complementary treatment of their illnesses due to NCDs, and this may be due to the lack of knowledge of self-care management, psychological intervention to adherence or no confidence or no education of these forms of therapies (WHO, 2018). The public and private health services do not have enough time to explain to the patients of alternative treatments for the diseases. Another possible explanation is that if the people know more about costs-effective benefits of non-pharmacological therapies then some clinics will be deprived of patients as well as income.

As such, this study was designed to tackle these health and social care problems in Guyana. Firstly, it undertook a small epidemiological study relating to obesity, diabetes, and hypertension in Guyana with data retrieved from the Ministry of Public Health in Guyana (MPH, 2016; PAHO,2019). Next, it investigated the beneficial effect of diet modification, daily exercise and intake of *Momordica charantia (M charantia)* juice either alone or in combination with daily exercise and diet modification on obesity, diabetes and hypertension. It also examined any inhibitory or synergistic effect of *M charantia* with either a commercial hypoglycaemic or an anti-hypertensive commercial drug. Finally, the study undertook preliminary studies, using questionnaires to ascertain knowledge on obesity and self-care management knowledge of diabetic patients on their understanding of diabetes-induced hyperglycaemia and long-term complications, especially blindness (retinopathy) and others, such as foot and oral ulcers and neuropathy (nerve damage and loss of feeling sensation). This discussion will now focus on the results of chapters 2-6 presented in this study comparing the data with what is known in the literature and focusing on the epidemiology of such NCDs as diabetes, obesity, hypertension and knowledge about obesity and self- care management of diabetes.

7.2 Epidemiology of NCDs in Guyana

In 2016, the Ministry of Health in Guyana undertook a country wide study to investigate the prevalence of NCDs in Guyana and the data were published by PAHO in 20119.The data on overweight and obesity, diabetes, hypertension, and blood cholesterol were critically analysed graphically, discussed and presented in chapter 2 of this study. The findings have revealed that chronic diseases or NCDs, which are most common at this moment in time in Guyana and the Caribbean, seem to affect more older people, especially those who are in their later working years (45-69 years) compared to younger age group (18-45 years). This may be due to the fact that people of the senior working age have more responsibilities in life and more so, stress and life-style changes may also play a major role in inducing NCDs. In terms of obesity, diabetes, hypertension and elevated blood cholesterol and triglycerides, both genders are prone to these NCDs, but female Guyanese seem to be more susceptible compared to male Guyanese (WHO 2014; 2018; 2020; PAHO, 2019). NCDs are costly to diagnose and to treat and more so, easily preventable of all health problems, representing a growing burden for all societies and a marked reduction in the quality and duration of life for the patients globally (Hayjet and Stein, 2018). NCDs are recognized as growing international socio-economic, public health and social care problems, accounting for over 41 million (74%) of the 56 million deaths worldwide in 2021. Moreover, around 15 million people die between the ages of 30-69 years, during their working age of their lives and over 85% of these are premature deaths, especially in low and middle-income countries throughout the world and Guyana is one of them. Annual deaths from NCDs are projected to escalate to 52 million by 2030 (WHO, 2022). The largest burden (80% or 28 million) occurs in low and middle-income developing countries, and Guyana is a very good example, making NCDs a major cause of poverty and an urgent developmental issue for governments of the world to address (WHO, 2010; 2011, 2021, 2022; PAHO, 2019).

Comparing the prevalence of NCDs in a low- income developing country as Guyana with such developed countries as UK, Germany, USA, Australia, Canada and others, the current data reveal more or less the same health and social care problems relating to NCDs. More people in Guyana die from such diseases as obesity, diabetes, cancers, respiratory dysfunction, renal failure, cardiovascular diseases (CVDs) and now covid-19 which are all interrelated (Smail et al 2022; Tapia and Dhalla, 2022). It is well known that our modern life -tyle habits can lead to obesity which in turn induces diabetes (diabesity) which subsequently leads to a number of long-term complications including nephropathy, neuropathy, retinopathy, CVDs as well as others (WHO 2014; Zimmet, 2017; Al Jaberi et al, 2022; Smail et al, 2022; Sultan et al, 2022; Tapia and Dhalla, 2022; Hanoman et al, 2020; Rupee et al 2022). In addition, the data also show that adult Guyanese failed to diagnose their medical conditions and many of those who are diagnosed prefer to take herbal remedies to treat their illnesses rather than prescribed drugs.

7.3 Diabetes in Guyana and treatment

Diabetes mellitus (DM) is a metabolic heterogeneous syndrome or disorder (Srinivasan and Ramarao, 2007; Lotfy et al, 2016; Regufe, 2020) characterized by hyperglycaemia (elevated blood glucose), which results from defective insulin secretion or function (ADA, 2009; 2016, 2019 Diabetes UK, 2019). The prevalence of DM is increasing worldwide (Zimmet et al 2014; Zimmet, 2017). It is estimated that by year 2030 more than 660 million individuals will suffer from diabetes (Maiese, 2008) and type 2 diabetes mellitus (T2DM) accounts for 90-95% diabetic cases (Regufe, 2020). The increased prevalence of morbidity and mortality necessitates more research in the pathogenesis of complications, as well as efficacy of therapeutic agents (Deshpande et al, 2008; Pappachan, 2015). Diabetes is rapidly emerging as a major health-care problem in Guyana and the Caribbean, especially in urban areas where the prevalence of T2DM has been reported as around 10-12% of the adult population (MPH, 2016; PAHO, 2019). Furthermore, there is an equally large pool of people, almost 200,000 in Guyana and around 2 billion globally, with impaired glucose tolerance or prediabetes. With time, many of these people may go on to develop T2DM in the future, especially if they neglect health self-care advices such as daily exercises, diet modification, adherence to medication, use of non-pharmacological medicines and others on how to either prevent or delay the development diabetes.

Diabetes, as a metabolic disorder, is one of the most major health problems worldwide, including both developing and developed countries showing high indices of prevalence and mortality ((Harris et al, 1998; Barcelo and Rajpathak, 2001; ADA, 1997; 2019; Diabetes UK 2019). In a recent report published in JAMA (Cardiology), it was reported that early heart diseases in women were linked to T2MD, especially those who are under 55 years of age. The results show that there is a close link between life-style changes, the induction of T2DM and subsequently, the development of CVDs. The data suggest that people at younger age may die from CVDs unless they change their life-style habits (Daily Express 2021; Dugani et al. 2021). Management options for the disorder in developed countries include diet modification, daily exercise and administration of insulin, and/or hypoglycaemic agents. However, these methods may not be affordable for patients in a low- income developing countries like Guyana due to socio-economic conditions (Ducorps et al, 1996). This partly contributes to the high prevalence of non-compliance observed in minority, disadvantaged communities in industrialized countries, and rural folks in developing countries (Dyer et al, 1998).

If diagnosed late or left untreated, then diabetes can cause many long–term complications such as kidney and heart failures, hypertension, atherosclerosis, sudden cardiac death, nephropathy or severe nerve damage, retinopathy or blindness, foot ulcers, impotence and other minor complications (Defronzo et al, 1992; Chait and Brunzell, 1996; Alberti et al, 1997; Kamalakkannan et al, 2006; Papatheodorou et al, 2016; Harding et al 2019; ADA 2019; Diabetes UK, 2019). Control of DM, especially T2DM, normally involves weight reduction, regular exercise, diet modification and drug treatment, as well as the utilization of cost-effective antidiabetic plants which have attracted increasing interest (Bailey and Day, 1989; Alarcon-Aguilar et al, 1997).

The results of this study have clearly shown 20 grams *M charantia* alone as a juice or in combination with diet modification and daily exercise or with diamicron MR can reduce blood glucose (BG) from chronic level to more or less control value over 6 weeks of treatment. *M charantia* can also reduce elevated BG during glucose tolerance test (GTT) and reduce HBA1c, blood pressure (BP), total cholesterol and triglyceride levels significantly comparing week 1 with week 6. Lower doses (either 5 or 10 grams daily) of *M charantia* can also reduce elevated BG in a time-dependent manner and reduce BG during GTT. These findings are closely related to those published in the literature on human (Welhinda et al,1984; Ahmad et al, 1996; Attar-ur-Rahman, 1989; Baldwa et al, 1997; Tongia et al, 2004; Dans, 2007) and animal models (Platel and Srinivassan, 1997; 1999; Ahmed, 1999; Ahmad et al. 1999; Johns et al. 2003; Garau et al. 2003; Srinivassan and Ramarao, 2007; Singh et al, 2011; Hadi et al, 2022). The present data also reveal that *M charantia* is rich in minerals, vitamins, phenol compounds and anti-oxidants, all of which may exert a hypoglycaemic effect in the body (Joseph and Jinni, 2013).

The results from the 4 interventions employed in this study show that combined exercise and diet exerted the least effective (about 33.4%) on BG compared to the other 3 interventions. *M charantia* was more effective in reducing (47.7%) BG compared to diet and exercise alone. *M charantia* combined with diet modification and exercise reduced BG by 50.6% while *M charantia* and diamicron MR reduced BG by 50.7 %. The best results were obtained with either M charantia and diamicron MR or *M charantia*, diet modification and exercise. These results clearly have demonstrated that newly diagnosed T2DM patients can control their diabetes-induced elevated BG using cost-effective therapy involving daily *M charantia* intake in combination with diet modification and exercise rather than using diamicron MR which they have to pay for.

Most newly diagnosed T2DM patients are advised by their Clinicians or health workers to lose weight if they are obese, modify their diet, including eating less and eat heart- healthy foods which are rich in fibre and consume less sugar and carbohydrates and most importantly, participate in daily exercise for at least 3 hours per week before they are prescribed anti–diabetic medication. Many patients who adhere to these regimes are able to control their blood glucose levels for several years. It is obvious that that diet modification can reduce blood glucose since the diet itself is responsible for the diabetes. On the other hand, exercise is known to exert more energy leading to weight loss. It is assumed that since exercise is depleting the glucose within muscle cells, then by some unknown mechanism(s), glucose is transported into the starving cell. This is an area of particular interest regarding exercise-induced glucose uptake into muscle cells. Moreover, there is now strong evidence that regular exercise can increase pancreatic beta cell mass and function via the synthesis and production of new insulin in the body which can enhance glucose uptake into muscle cells after six weeks of training due to insulin sensitivity (Curan et al, 2020; Wagenmakers, 2020). The study by Curan et al, (2020) also demonstrated that moderate exercise of 120-150 minutes per week has benefits on beta cell mass and function (health), thereby helping to reduce cardiovascular risk and increasing longevity and quality of life of the patients. As such, a combination of daily exercise and diet modification is highly recommended for the treatment of diabetes by many General Practitioners and more so, it is cost-effective for the patients, especially in a country as Guyana where healthcare is expensive.

The plant Kingdom is a wide field to search for natural and effective oral hypoglycaemic or hypolipidemic agents that have little or even no side effects since they are normally consumed as food (Hadi et al, 2022). More than 450 plants with glucose-lowering potentials are now known (Ernst, 1997). Hypoglycaemic activity of nearly 100 polysaccharides from plants has been reported. Some botanical polysaccharides are considered as important bioactive components which are responsible for hypoglycaemic effect (Yuan et al, 1998; Wang and Ng, 1999). In addition, several plants are known to possess hypo-lipidemic activity (Ram et al, 1996; Sharma et al, 2003). However, there is little information about some plants and their components which can induce both hypo-glycaemic and hypo-lipidemic effects. Interestingly, this current study has reported that *M charantia* can reduce both blood glucose and lipids in diabetic patients. Nutritional factors including antioxidants have great influence in the management of DM and its complications (Alberti et al, 1997; Packer et al, 2000). An imbalance between oxidative stress and anti-oxidative defence mechanisms in diabetics can result in cell and tissue damage and accelerate inflammation and subsequently, diabetic-induced long–term complications. Administration of appropriate antioxidants could either prevent or retard diabetic complications to some extent or even repair dying islets as well as increasing their mass (Ahmed, 1999; Packer et al, 2000; Cummings et al, 2004). The same is also true for daily exercise (Curan et al, 2020). Antioxidant activity of 35 medicinal plants consumed by the indigenous peoples of the boreal forest of Canada supported the contribution of these traditional medicines in a lifestyle historically low in the incidence of diabetes (McCune and Johns, 2002).

The novelty of the study is the use of either *M charantia* alone or when it was combined with either daily exercise and diet modification or with diamicron MR. All three interventions induced more or less the same hypoglycaemic effects. Moreover, *M charantia* did not exert any inhibitory or synergistic effect when it was combined with diamicron MR, a commercial hypoglycaemic drug to reduce blood glucose levels in diabetic patients. These are interesting results for diabetic patients since it indicates that they do not have to worry in experiencing severe hypoglycaemia if they use their anti-diabetic medication in combination with a mild to moderate amount of *M charantia* and participate in moderate exercise as well.

Nevertheless, this is an area for further investigation since many General Practitioners are reluctant to recommend the two combinations as therapy since little or no data are available. Furthermore, the study supports the use of *M charantia* with an anti-diabetic drug to control blood glucose levels (Diabetes UK, 2015; 2019; ADA, 2019). As such, more experiments are required on human studies using large sample size, proper design, controls, statistical power and the dose which can exert acclaimed efficacy. Another important area is to investigate the potential medicinal effect of *M charantia* on prediabetes. One previous study among Tanzanian subjects shows that *M charantia*, employing 50 grams daily, can lower blood glucose in individuals with prediabetes. It was more pronounced in those patients who had higher blood glucose levels (Krawinkel et al, 2018).

7.4 Management of diabetes employing pharmacological and non-pharmacological therapies

Since DM is now a major health problem in developed and developing countries globally, management options for the disease is of paramount importance (NICE, 2015). Iin developed countries DM is managed by diet modification, regular exercise and administration of insulin, and a number T2DM hypoglycaemic agents. However, these methods may not be affordable for patients in low- and middle -income developing countries due to socio-economic conditions

(Ducorps et al, 1996). This partly contributes to the high prevalence of non-compliance observed in minority among disadvantaged communities in industrialized countries, and similarly, rural folks in developing countries (Dyer et al, 1998). Coupled with this, is the fact that medical centres are not always within the reach of these population groups, especially in Guyana. There is preference for traditional medications by some sections of the rural community (Musabayane et al, 2005; Muthulingam, 2005). Moreover, the rapidly increase in DM is becoming a serious threat to the health of mankind globally, especially in countries where people eat white rice or ground provisions (cassava, eddoes, yams, plantains, potatoes and other tuberous foods which are lack in fibres when overcooked). The control and treatment of diabetes and its complications mainly depend on the chemical or biochemical agents, but the fact is that it has never been reported that someone had recovered totally from diabetes. With the distinctive traditional medical opinions and natural medicines mainly originated in herbs, the traditional medicine performed a good clinical practice and in turn, it is showing a bright future in the therapy of DM and its complications. Based on a large number of chemical and pharmacological research studies, numerous bioactive compounds have been found in medicinal plants for diabetes (Ivorra et al, 1989). With the increasing number of ageing populations, consumption of calorie rich diets, obesity and sedentary lifestyles have all led to a tremendous increase in the number of patients with diabetes worldwide (Simpson et al, 2003).

The demand for the plant-derived drugs seems to increase in low–and middle-income developing countries due to their medicinal values and economic procurement. Plants have been used in a wide variety of dosage form. Traditional or conventional dosage forms include the raw fruit or leaves, stems or roots, pill, powder, semi fluid extract, tincture, decoction, medicated tea and alcoholic extracts dissolved as solution. Some modern herbal dosage forms include tablet, capsule, soluble granule and ointment which are available commercially. The advantage of modern herbal dosage form offers small dosage size and comparatively good absorption than conventional dosage form. Modern dosage form is more flexible in carrying and can be taken even in a busy schedule hence, it plays tremendous role in clinical treatment. Even after advancement, modern herbal dosage form is still showing certain limitations such as delayed therapeutic response, lack of potential of reaching the drug to the target site, requirement of relatively large quantity of drug, chances of variability in herbals and destruction of the drug (flavonoid) during its systemic passage from gastrointestinal tract to liver. These limitations can be overcome by improving the therapeutic performance of established herbal drugs by formulating them in a new dosage form for the better drug delivery, including nanotechnology (Sikarwar et al, 2008; Joseph and Jini, 2013; Dhivya and Rajasimman, 2015). This is an interesting area for future research.

M charantia has been used by mankind since ancient times as a source of herbal medicinal drug (Bajpai et al, 2005; Shunmugam and Palpandi, 2008). *M charantia* is also nutritionally valuable as fresh or dried vegetables or as ingredients in a wide variety of prepared foods (Robledo and Pelegrin, 1997; Hadi et al 2022). As shown in this and other studies, *M charantia* contains significant quantities of lipids, proteins, carbohydrates, fibres, vitamins, especially C and minerals (rich in sodium and calcium and some trace elements), phenols, antioxidants and others (Sanchez-Machado et al, 2002). Over the past several decades, *M charantia* and its water soluble and alcohol extracts have been studied as novel sources which have been shown to produce a variety of compounds and some of them have been reported to possess biological activity of potential medicinal value (Moore, 1978; Konig et al, 1994; Tutour et al, 1998; Satoru et al, 2003; Pitchakaran et al, 2011; Manoharan et al, 2013; 2014; Singh et al. 2017; Houacine et al, 2021).

Recently, much attention has been paid on the anti-tumour activity, and antioxidant activity of constituents of *M charantia* (Gauru et al 2004; Pitchakaran et al, 2011; Manoharan et al, 2013; 2014; Singh et al, 2017; Houacine et al, 2021). Consequently, antioxidant activity is intensively focused due to the currently growing demand from the pharmaceutical industry where there is interest in anti-ageing and anti-carcinogenic natural bioactive compounds, which possess tremendous health benefits. Almost, all photosynthesizing plants are exposed to a combination of light and high oxygen concentrations, which lead to the formation of free radicals and other strong oxidizing agents, but they seldom suffer any serious 12 photodynamic damage during metabolism. This fact implies that their cells have some protective anti-oxidative mechanisms and compounds (Matsukawa et al, 1997). *M charantia* is considered to be a rich source of antioxidants (Cahyana et al, 1992). Recently, the potential antioxidant compounds were identified as some pigments (fucoxanthin, astaxanthin, carotenoid) and polyphenols (phenolic acid, flavonoid, tannins). Those compounds are widely distributed in *M charantia* and are known to exhibit higher anti-oxidative activities. The activities have been reported through various methods of reactive oxygen species scavenging activity and the inhibition of lipid peroxidation (Yan et al, 1999; Heo et al, 2003; Siriwardhana et al, 2003; 2004). Many researchers have indicated that reactive oxygen species and lipid oxidation in food industry can be controlled or minimized, at least by the addition of commercial synthetic antioxidants or natural antioxidants (Gray et al, 1996; Hadi et al, 2022).

Since *M charantia* can exert a favorable hypoglycemic effect, almost like insulin and other orthodox hypoglycemic drugs, the question which now arises is this. What is its mechanism of action? Some of the chemical components of *M charantia*, especially charantin can produce a fall in blood sugar level (Jayasooriya et al, 2000). Several other studies have shown that extracts of *M charantia* may block the absorption of sugar molecules in the intestine or improve the body's ability to utilise sugar, which would help to reduce blood sugar levels (Meir and Yaniv, 1985; Shibb *et al.* 1993; Platel and Srinvassan, 1999; Garau et al, 2003; Ahmed et al, 2004; Singh et al, 2011; Hadi et al 2022). Other studies have shown that extracts of *M charantia* possess growth-like factors which can repair partially dying islet beta cells and thus, increasing their mass (proliferation). In turn, the repaired beta cells can synthesise new insulin for secretion from the endocrine pancreas (Ahmed, 1999; Ahmed *et al,* 2004). The fruit juice or its extract can also regulate glucose uptake into vesicles of the jejunum of the small intestine and stimulate glucose and amino acid uptakes into L6 muscle cells (Ahmed, 1999; Ahmed et al, 2004; Cummings *et al*, 2004). The uptake of glucose into L6 muscle cells can be blocked by wortmannin, an inhibitor of the tyrosine kinase enzyme. This effect of *M charantia* is similar to that of insulin suggesting that *M charantia* is exerting the same effects as insulin and probably acting on the same receptor to stimulate glucose into muscle cells (Klip and Paquet, 1990; Cummings *et al*. 2004).

7.5 Overweight and obesity in Guyana and treatment

Overweight and obesity are major global health problems currently affecting almost 2 billion people and 800 million are obese. These figures represent 40% of adults, 18 years and over, who are overweight and 14% with obesity. In the European countries, the numbers of obese individuals have tripled over the past 2 decades and in the United States of America (USA) nearly a third of all individuals are either obese or overweight. In the United Kingdom (UK), obesity contributes to 30,000 deaths annually and £3.5 billion ($5.4 billion USAD) in health care costs. In the USA, the annual health care costs are 36% greater for an obese person compared to a normal weight person (Riley et al, 2005; Arternbun et al, 2005; WHO, 2011; Wilhrow et a,l 2011; Philip et al, 2017; Tapia and Defries, 2020; Tapia and Dhalla, 2022; Al Jaberi et al, 2022). What is now worrying is that children as young as 5 years of age are either overweight or obese amounting for 40 million worldwide (Riley et al, 2005; Lopez, 2012; Ng et al 2014; Cilia et al, 2019). Obesity is when the body mass index (BMI) is 30 kg/m^2 and over whereas overweight is when the BMI is 25-29 kg/m^2 (Nuttal et al, 2015). It is estimated that by the year 2030, 57.8% of the world population will be obese if the prevalence rate continues at the current pace (Kelley et al, 2008). In a global scale, men with BMI ≥ 25 kg/m^2 increased from 25.4% to 38.5% accounting for a 5% percentage increase to 10.1% from the period between 1980 and 2015, and in females it was from 27.8 to 39.4% accounting for a percentage increase from 8.9% to 14.8% in the same time period (So et al, 2020). Moreover, the prevalence of obesity is more pronounced in women when compared to men. By the year 2025, the prevalence of obesity will reach 18% in men and 21% in women as predicted by the Non-Communicable Disease Risk Factor Collaboration (NCDRFC) (Di Cesare et al, 2016). Beside the BMI, other measurements that are helpful in quantifying obesity include waist circumference. Increases in waist circumference is associated with mortality even in individuals with normal BMI measurements. A review of waist circumference and mortality performed on 650,000 adults showed that increased waist circumference above normal resulted in higher mortality rate (Cerhan et al, 2014). Using a combination of both methods helps in generating accurate and clearer way to distinguish between high BMI related to increased muscle content and elevated adiposity. In addition, a more advanced method, but less commonly used for measuring body fat, is magnetic resonance imaging (MRI) and dual energy X-ray absorptiometry (Cerhan et al, 2014).

Obesity is an imbalance between calories intake and calories expenditure. In general, obesity is due to excessive eating and reduced physical activity (Tapia and Defries, 2020; Tapia and Dhalla, 2022; Al Jaberi et al 2022). Obesity is a major risk factor for such NCDs as diabetes mellitus (DM), respiratory and liver dysfunctions, sleep apnea, chronic inflammation, compromised immune system, real failure, cancers, musculoskeletal disorders, cardiovascular diseases (CVDs) and others (Ivaro et al, 1989; Field et al, 2001; Kanter an Cabellaro, 2002; Mahese, 2008; MPH, 2016; Tapia and Dhalla, 2022; Al Jaberi et al 2022). Obesity is also a major risk factor for coronavirus disease (Covid-19) which induces severe cases of pneumonia and sepsis or acute respiratory distress syndrome (ARDS) (Bello-Chavolla et al 2002; Williamson et al, 2020; UKNHS, 2020; Smail et al, 2022).

DM and obesity can lead to presence of low-grade chronic inflammation which has a harmful effect of oxidized low-density–lipoprotein cholesterol, initiating a chronic inflammatory reaction, the result of which is a vulnerable plaque, prone to rupture and thrombosis leading to sudden cardiac death (Adabag et al, 2015). Epidemiological and clinical studies have shown strong and consistent relationships between markers of inflammation and risk of future cardiovascular events (Viahal et al, 2020; Wilkerson et al, 2004; Tapia and Dhalla, 2022; Al

Jaberi et al 2022). Inflammation is widely considered to be an important contributing factor in atherogenesis and the risk of athero-thrombotic complications (Welsh et al, 2017). Baseline measurements of some inflammatory markers are well-known to be predictive risk factors for future CVD events in prospective epidemiological studies. Inflammatory markers dominant in the literature are acute phase response (APR)-associated and they include fibrinogen and C-reactive protein (CRP) (Plourde et al, 2014; Adabag et al, 2015). Elevated NF-kappa-B pathway expression in obesity and diabetes affects the immune system in such patients. Activation of the innate immune system in adipose tissue has been suggested in connection with inflammation, obesity and diabetes. Weight gain causes adipose tissue remodelling and expansion with inadequate supporting of vasculature leading to higher oxygen supply and consequently, promote inflammation state. One of the most co-existing complications of diabetes is obesity-induced insulin resistance (IR). It has a major role in ongoing inflammation, via the macrophage switching to M1 type, the release of various cytokine; especially, IL6 and TNF-alpha, increase Th1 and Th17 cells, stimulation of TLR2/4 and finally activation of IKapa-B kinase (IKK). Macrophages can also exert their inflammatory responses via C-junk-NH2 terminal kinase-1 (JNK-1) signalling, an important component of obesity-induced insulin resistance. Pro-inflammatory cytokines such as TNF-alpha and IL6, disturb the insulin action, which consequently leads to systemic and local insulin resistance. TNF-alpha impairs insulin function by IRS1 tyrosine phosphorylation blockade in adipose and muscle tissue (Plourde et al, 2014; Adabag et al, 2015; Tapia and Dhalla, 2022; Al Jaberi et al, 2022).

The results of the present study have shown that all thirty- two subjects recruited in this study had BMI values of between 33 and 36 which are classified as obese and they were both males and females in their working ages of around 42±4.6 years. The data also reveal that the four interventions involving diet only, diet and exercise, diet and *M charantia* and diet, exercise and *M charantia* were associated with marked, but not significant decreases in BMI comparing week 1 with week 6. Typically, BMI decreased by 5.39%, 5.48%, 8.30%, and 9.33% for the four interventions, respectively. However, it is tempting to predict that if the experiment had gone on for several weeks or months then there would have been significant reduction in BMI. Although all the subjects were pre-diabetics (120 mg/dl and above) all four interventions exerted very small reduction in fasting blood glucose (FBG) but with virtually no change in HBA1c compared week 1 with week 6. Again, a duration of 6 weeks of treatment may be inadequate to obtain significant reduction in FRG and HBA1c. All thirty- two four subjects had mild to moderate hypertension at the start of the study which was probably due to their obesity. The results reveal that after 6 weeks of treatment with the four interventions, both systolic and diastolic blood pressure (SDBP) returned to normal values. These changes were associated with significant ($p<0.05$) and concomitant decreases in total cholesterol and triglyceride levels comparing week 1 with week 6. The mechanism(s) for blood pressure decrease will be discussed later. These results highlight the importance of life-style changes, involving either diet alone, *M charantia* alone, diet modification and regular exercise or a combination of all three parameters. Together, they can help to reduce blood pressure, blood lipid and triglyceride levels and the weight of obese subjects leading to a better quality of life in a cost-effective and non-pharmacological manner, but the subjects have to participate in these interventions on a daily or regular basis in order to enjoy a better life- style. A previous study has shown that people who received some form of psychological intervention adhere more to life changes habits compared to those who received no training (Martinus et al, 2006).

Daily physical exercise is a powerful cost-effective and non-pharmacological tool to prevent a number of disorders and diseases in the body including overweight, obesity, diabetes, cancer, Alzheimer’s, cardiovascular and respiratory diseases, stress, mental illnesses and others (Paez and Kravitz, 2000; Martinus et al, 2006; Smail et al. 2018; Curan et al, 2020; Express Newspapers, 2021). Maintaining a healthy weight via cost-effective daily exercise or diet modification can help people against the development of these NCDs, but again, people have to adhere to such life-saving interventions. The consensus almost globally is that daily exercise should be prescribed by GPs since it is both the primary and second prevention against a number of NCDs and mental health conditions. In a previous study, it was reported that regular exercise can exert a beneficial role in appetite regulation via a change in eating behaviour and habits of the obese subject (Garberm, 2019). A recent study, by Wilding et al, (2021), published in the New England Journal of Medicine demonstrated that the newly developed anti-obesity drug, semaglutide could cut body weight by 20%. It is believed that the drug mimics a hormone release by the gut to instruct the brain to send a message to the stomach that it is full thereby reducing hunger and calorie intake. The drug also helps in reducing waist circumference, blood fats, blood sugar and blood pressure levels, all of which help to improve the quality of life of the patients (Wilding et al, 2021). However, more research needs to be done to clarify the precise mechanisms behind the improvement in the short-term appetite observed with daily exercise and the long-term complications in terms of eating behaviour and weight change (Martins et al. 2008).

The consensus is that regular exercise can control weight by preventing excess weight gain and also by increasing the total energy expenditure of an obese person by helping the individual to stay in energy balance or even lose weight as long as the person can control his or her food intake. Physical activity also decreases fats around the waist and total body fat and as such slowing the development of abdominal obesity. In addition, exercise helps to combat several health conditions and NCDs. It also helps in improving moods, mental health, and memory, boosting energy levels in the body, improving sleep and other physiological benefits (Paez and Kravitz, 2000; Martinus et al, 2006; Smail et al, 2018; Express Newspapers, 2021).

M charantia is a widely used non-pharmacological food or supplement to treat several diseases including NCDs and cancers (Hadi et al, 2022). In terms of obesity, other studies, similar to the current one, have shown that *M charantia* fruit juice and extracts demonstrated useful benefit on body weight gain and fat deposition in the body (Fan and Moon, 2019). These potential health effects are probably mediated by inducing fat and lipid metabolizing gene expression and in increasing the function of AMPK and PPARs as well as other signalling agents in the body (Alam et al, 2013). *M charantia* is known to contain a number of important medicinal compounds including phenols, vitamin C, cations and antioxidants (see chapter 3) which may have direct effects on fat metabolism in the body. Data presented in this and chapters 3 and 4 of this study show that *M charantia* can reduce total cholesterol and triglyceride levels following consumption indicating that *M charantia* is a useful non-pharmacological therapeutic tool, just like the statins, to reduce the levels of cholesterol and other lipids in the body, thereby preventing heart diseases (Alam et al, 2013).

The results of this study have shown that combining diet modification, by eating a healthy diet, with daily exercise exerted the same effect on body weight loss compared to diet alone. However, when diet modification was combined with either *M charantia* or with exercise and *M charantia*, weight loss was more effective. It is possible that both exercise and *M charantia* can increase the metabolism in the body or behaving like a circadian clock to regulate how much calories an obese person can burn daily in a synergistic manner. It may also help the obese person to maintain and increase a lean body mass by increasing the number of calories an obese person burns per day (Pletcher, 2020).

The question which now arises is this. How does *M charantia* exert its anti-obesity effect? *M charantia* is rich in iron, calcium, sodium, magnesium, potassium, several trace elements, vitamin C and fibre, but low in lipids, carbohydrates and calories. It is also a main source of thiamine, riboflavin, and pantothenic acid, phenols and antioxidants. In addition to fat and lipid metabolizing gene expression (Alam et al, 2013; Fan and Moon, 2019), and its anti-obesity effect may also be linked to its anti-diabetic effect by controlling blood glucose level. *M charantia* is known to exert a plant-based insulin–like effect since it can act as a growth factor is re-paring pancreatic beta cell mass thereby increasing the synthesis of new insulin and its release thereby facilitation insulin sensitivity (Ahmed, 1999; Ahmed et al, 2004) This in turn is relevant in regulating weight management. Through its insulin–like effects, *M charantia* may prevent the storage of sugar in the body as fat and as such, helps in the weight loss process. Moreover, the fibre content of *M charantia* tends to curb hunger and reduce satiety for a longer period of time. The succulent fresh *M charantia* contains about 89 to 94% of water by weight and this may be another reason for weight loss (TTN, 2019).

In a previous study by Chen et al. (2003)) employing a rat model, they demonstrated that *M charantia* was able to reduce weight gain and body fat without affecting energy intake and apparent fat absorption in rats fed a HF diet. Moreover, *M charantia*, lowered serum insulin and leptin but raised serum free fatty acid (FFA) concentration. The impaired oral glucose tolerance that accompanied fat feeding was normalized by *M charantia* supplementation. The authors concluded that *M charantia* was altering energy balance through its effects on fat metabolism and improved insulin resistance might be secondary to a reduced visceral fat mass. These multiple effects of *M charantia* are useful dietary adjunct for the management of body weight and glucose intolerance (Chen et al, 2003). In another study in rats, it was demonstrated that *M charantia* consumption produced adiposity and energy efficiency which were mediated by a series of physiological processes involving enhanced sympathetic activity, lipolysis and fatty acid oxidation (Chen, 2011). Further experiments are required to explain at cellular and molecular levels how a combination of these three interventions can help an obese person to lose weight. Nevertheless, obesity can easily be prevented if people only attempt to help themselves. Figure 7. 1 is a flow diagram illustrating some of the major factors which can help in reducing the weight in the body thereby either preventing the development of obesity or helping to treat the disease.

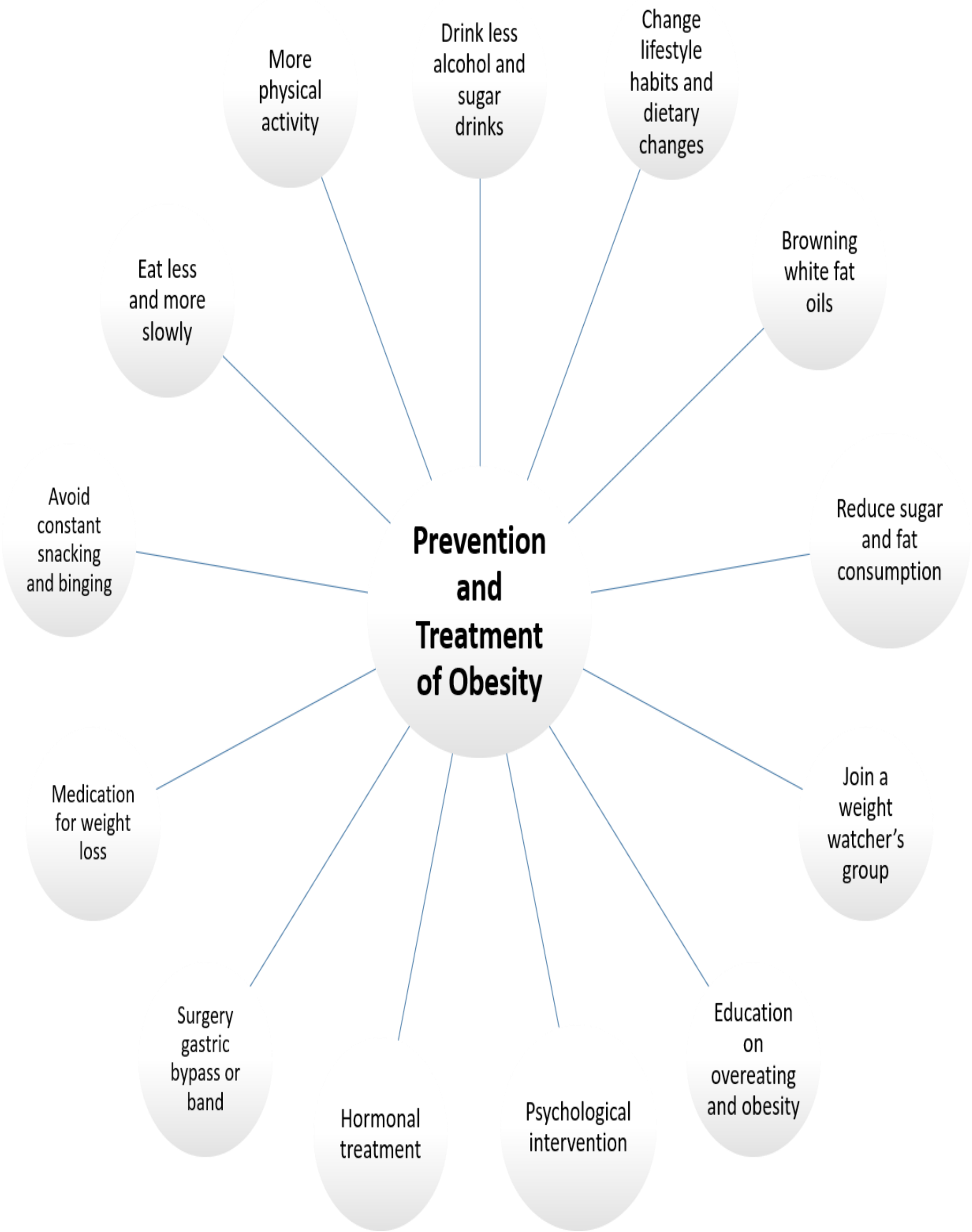


Figure 7.1: Flow diagram showing some of the major factors which can help in reducing the weight of the body thereby either preventing the development of obesity or helping to treat the disease.

7.6 Hypertension in Guyana and non-pharmacological therapy

Hypertension or high blood pressure (HBP) is the leading cause of CVDs and premature death worldwide (Mills et al, 2020). The WHO (2020) estimated that 1.3 billion people have essential or primary hypertension globally. This is when systolic blood pressure [BP] is ≥140 mm Hg and diastolic BP is ≥90 mm Hg) with most people living in low- and middle-income countries like Guyana (Basu and Millett, 2013). HBP is now an increasingly common health problem because of increased longevity and the prevalence of such contributing factors as obesity, diabetes, mental health, especially stress, smoking, alcohol consumption, physical inactivity, overcrowding environment, urbanization and unhealthy diet with excess salt and sugar (Nguyen and Lau, 2012). Many people are susceptible to at least three or four of these risk factors whereas some may have them all, making them more prone to hypertension. The prevalence of these risk factors and HBP in many developing countries, such as Guyana, particularly urban societies, is already as high as those seen in developed countries such as UK, Germany, USA and others. Prevalence may also vary from one country to another depending on economic situation and ethnic group. In England, for example, the prevalence of HBP is about 31% among men and 26% among women, affecting more than 1 in 4 adults (Public Health England, 2017) whereas the prevalence among adults in the USA is around 46%. In the USA, 116.4 million adults (age ≥20 years) have HBP. Prevalence in the USA is highest among non-Hispanic black males (58.6%) and non-Hispanic black females (56.0%). The incidence increases with age in people of all ancestries and both sexes. Prevalence is higher in men than in women before 65 years of age, and higher in women than in men from 65 years of age. The lifetime risk is 90% for men and women who were normotensive at 55 years of age and survive to 80 years (Virani et al, 2020; Vassan et al, 2020).

Like many other developing countries in the world, Guyana is a low-income country and during the past 20-30 years, the country was infested with several non-communicable diseases (NCDS) such as overweight, obesity, kidney failure, respiratory diseases, diabetes, CVDs including hypertension, cancer and others. According to the recent WHO and PAHO data published in 2018 and 2019, respectively, people die from the cause of hypertension reached 234 or almost 3 4% of total deaths (WHO, 2018; PAHO, 2019). The age adjusted death rate per 100,000 of the population was around 47%. Currently, Guyana ranks 5th in the world from deaths due to hypertension. Both interventions and recommendations by the national Government of Guyana via the Ministry of Public Health and the Ministry of Education are necessary to increase awareness that elevated or high blood pressure is a serious medical condition, despite its asymptomatic nature. The disease can lead to blindness, strokes, kidney dysfunction, constant headache, CVDs, especially heart failure and others (El Kilany, et al 2019; 2020). Prevention of hypertension is linked to the elimination of relevant modifiable risk factors and the promotion of a healthy lifestyle habits (CHEP, 2014). The Government of

Guyana, with the help of WHO, has set up a Hypertension, Evaluation and Learning Programme (HELP) which aims to provide a pharmacy-based intervention in a developing-world country as Guyana, together with education in schools and workplaces.

Guyana is the only English-speaking country in South America comprises of three major counties, Essequibo, Demerara and Berbice. The 2 largest ethnic groups are the Indo-Guyanese (43.5%), descendants of Indian indentured labourers, and the Afro-Guyanese (30.2%), who are descendants of African slaves. Mixed-raced or children from mixed ethnic groups comprise 16.7% of the population. The indigenous Amerindians make up 9.1%; and the remaining population including Portuguese, Chinese and Caucasian Europeans (1%) (CIA, 2015). Approximately one-third of Guyana's 780,000 people live below the poverty line. Most Guyanese (37.42%) are between the ages of 25 and 54 years, followed by the 15-24–year age bracket (21.26%). Only 13.25% of the population are older than 54 years (CIA, 2015; Dyal and Dolovich, 2016).

CVDs are NCDs which are responsible for the greatest number of deaths in Guyana, accounting for 526 deaths per 100,000 population (MPH, 2014). Hypertension is a major modifiable risk factor for cardiovascular mortality. It is also a global health concern, affecting approximately 20% of the adult population in most countries. Hypertension is responsible for 20% to 50% of all cardiovascular mortality and morbidity, which contributes to increased health care costs globally (WHO, 2015). In Guyana, hypertension is the leading cause of mortality among those between 45 and 64 years in their working age (WHO, 2012).

In a typical suburb community or village in Guyana almost 40% of citizens live in absolute poverty, earning less than USAD $100-250 per month and about 18% of people who reside in this area live in critical poverty, equivalent to earning less than US$100 monthly. Hypertension is inversely related to education, income and occupation and as such, higher levels of blood pressure are prevalent in lower socioeconomic groups (MPH, 2015). More recently, the former Government of Guyana closed 7-8 sugar estates/factories due to a low demand for sugar globally leading to the unemployment of over 8,000 workers affecting almost 24,000 Guyanese (families with children). As a result, the unemployed sugar workers with families live in critical poverty resulting in mental diseases, including chronic anxiety and depression leading subsequently to suicides. According to the BBC (UK), Guyana has the highest suicide rate in the world among young and working adults. Stress is a major risk factor for essential hypertension and the disease is not cheap to treat, especially if the patient has chronic stress and unable to work.

The study recruited 40 newly diagnosed hypertensive patients who were divided into five different intervention groups 8 per group) over 6 weeks for each. They included (i) exercise alone, (ii) *M charantia* alone, consuming 20 grams daily either as a juice (vol/weight), (iii) *M charantia* and intake of 20 grams daily combined with daily exercise, (iv) *M charantia* intake combined with the orthodox antihypertensive medication, amlodipine and (v) amlodipine alone. The results show that all five interventions were able to reduce both systolic and diastolic blood pressure gradually over the 6 weeks of treatment compared to week one at the start of the study. Typically, diastolic pressure decreased from mild to severe values (95-110 mm Hg) to control level (80-90 mm Hg). Similarly, systolic pressure reduced from values (140-150 mm Hg) to almost control levels (120-130 mm Hg). *M charantia* was more effective in reducing blood pressure than exercise alone. Combining *M charantia* with the anti-hypertensive drug, amlodipine, produced the same fall in blood pressure compared to amlodipine alone. These results from this preliminary study have indicated important therapeutic roles of either exercise alone, *M charantia* alone or *M charantia* in combination with exercise to treat hypertension. In addition, the data also revealed that *M charantia* had no synergistic effect on orthodox anti-hypertensive medication, amlodipine, a calcium channel blocker which can induce vasodilatation and reduce the force of contraction of the heart (Fares et al 2016). The question which now arise is this. How does exercise or *M charantia* or in combination help in reducing HBP in the patients?

It is well known that exercise is both a drug-free or non-pharmacological approach to lower blood pressure in hypertensive patient. Moreover, it is also cost-effective and as such, it is an affordable physiological tool for patients in low-income developing countries like Guyana who cannot afford orthodox expensive medicine. There are different mechanisms whereby exercise can reduce blood pressure. Firstly, exercise is known to strengthen the muscles (physiological hypertrophy) of the heart and thus, making them stronger to enable the myocardium to pump a larger volume of blood but with less effort (decrease heart rate). A decrease in heart rate is less detrimental to arteries in the body resulting in a lowering of blood pressure. Exercise is known to lower both systolic and diastolic blood pressure and not one alone since both are elevated in hypertension (Di-Cisare et al, 2016). For newly diagnosed hypertensive patients, regular exercise combined with yoga and meditation is adequate to reduce blood pressure without anti-hypertensive medication. In addition, exercise helps the muscles in the body, including the heart, to break down adenosine triphosphate (ATP) for energy expenditure and the activities of the different tissues in the body. A by-product of ATP metabolism is adenosine which is a powerful natural vasodilator substance in the body. Adenosine acts on the smooth muscle cells in the blood vessels to bring about vasodilatation thereby increasing blood flow and lowering blood pressure (Denton, 2018). In addition, exercise produces excess carbon dioxide, in addition to the elevation in several endogenous substances (H^+, K^+, kinins and others) during metabolism of glucose in the body leading to a physiological process called 'autoregulation' which helps to increase blood flow due to vasodilatation of the blood vessels. In turn, these biochemical and physiological processes result in a fall in blood pressure (Dias and Shimbo, 2013; Denton 2018; Myo-Clinic, 2019).

The results presented in chapters 3, 4 and 5 of this study have clearly demonstrated that *M charantia* consumption can markedly reduce blood pressure in diabetic, obese and hypertensive patients. In a recent systematic review of the effects of *M charantia* on blood pressure, Jandaria et al, (2020) found very small decreases in systolic and diastolic blood pressure in in old-age groups of 75 years and over. However, they found, significant hypotensive effect of *M charantia* in young adults who were 50 years and less, especially during short-term interventions as carried out in this present study where the subjects were between 30-50 years of age and participated in exercise training for at least six weeks. In a study by Kumari et al, (2018) using a clinical trial on patients with type-2 diabetes mellitus (T2DM), they reported that that *M charantia* supplementation resulted in a significant reduction in SBP and DBP. Similarly, Rahman et al, (2015) found that supplementation of *M charantia* (4 g/day) was able to decrease systolic blood pressure significantly in T2DM patients. Similar results have also been obtained in animal models of HBP (Sharma et al, 1996; Ahmed, 1999; Ahmed et al, 2004).

The question which now arises is this. How does *M charantia* exert it antihypertensive effects in the body? Currently, there is no evidence in the literature that *M charantia* possesses diuretic properties. However, it has been suggested that *M charantia* has anti-bilious and sedative properties thereby releasing stress which is a main risk factor for essential hypertension. Blocking the renin–angiotensin–aldosterone system is a pivotal treatment for hypertension (Riet et al, 2015). Several bioactive components of *M charantia* have been proposed to exert Angiotensin-I Converting Enzyme (ACE) inhibitory activities, including polysaccharides, ACE inhibitory peptides. These are mainly derived from *M charantia* seed proteins and their hypotensive impact has been demonstrated in *in vivo* studies using phenolic phytochemicals of

M charantia, mainly flavonoids (Priyanto et al, 2015; Shodehinde et al, 2016; Tan et al, 2016; Lestari et al, 2017).

It is the consensus that the anti-hypertensive properties of *M charantia* may be due to its rich chemical composition including antioxidants, phenols (gallic acid, tannin, catechin, epicatechin, alkaloids, chlorogenic acid, gentisic acid, carotenoids, and sterols), flavonoids, vitamins (A, B, C and E), minerals and others. *M charantia* can also reduce LDL cholesterol levels in the body to manage dyslipidemia. Some of the compounds of *M charantia* can also exhibit antioxidant and free radical scavenging effects to exert their antihypertensive effects (Kishoshita et al, 2018; Khan, 2019; Jandaria et al, 2020)). Flavonoids can also increase nitric oxide (NO) bioavailability, decrease endothelial cell oxidative stress and alter the activity of vascular ion channels, such as Ca^{2+}-activated K^{+} channels (Maaliki et al, 2019). In a review by Brito et al, (2013), they did a systematic investigation of supplements and foods on the reduction of blood pressure in pre-hypertensive and hypertensive patients. They provided strong scientific evidence to show that there are a number of foods, including *M charantia*, and isolated food supplements which are capable in promoting a reduction in blood pressure in obese, diabetic, hypertensive and hyper-cholesterolemic subjects. Moreover, they reported that the magnitude of the reduction in blood pressure was almost like commercially available prescribed anti-hypertensive medicines. This study provided substantial evidence to incorporate several foods and supplements into the diets of people who have NCDs, especially hypertension, obesity and diabetes in order to control their blood pressure in a cost–effective manner, especially for those people from low-income countries as Guyana.

There is much evidence in the literature than antioxidants either as isolated compounds or contents in foods can help to reduce blood pressure (Kishoshita et al. 2018; Prysyazhna et al. 2019; Jandaria et al. 2020). Studies on human hypertensive patients have shown that an antioxidant supplement by the name of pycnogenol was able to lower blood pressure by more than 30% while keeping the blood pressure to be maintain within normal range. Other studies have reported that polyphenols found in foods, especially *M charantia*, grapes, flavonoids and green tea can reduce blood pressure and blood cholesterol level, similar to the finding in this study (Warnier, 2004). Antioxidants, especially polyphenols, are known to exert their anti-hypertensive effects by oxidising cyclic guanosine triphosphate (cGMP)-dependent protein kinase alpha in vascular smooth muscles in arteries, thereby inducing vasodilatation (Prysyazhna et al, 2019).

The present study has also shown that *M charantia* does not seem to interfere with the action of the anti-hypertensive drug, amlodipine which is a calcium channel blocker. The data reveal no synergistic effect in terms of blood pressure reduction or elevation. The values were the same in the absence or presence of *M charantia*. This is an interesting finding since many clinicians are worried in prescribing orthodox medicine in combination with complementary medications to treat hypertension. This is an area which requires further investigation using varied concentrations for each.

7.7 The role of knowledge on diabetes self-care management and an understanding of obesity and diabetes in Guyana in Guyana using questionnaires.

7.7.1 Knowledge about diabetes self-care management

It is now the consensus by clinicians and health professionals that self-care management interventions are pivotal for the patients to look after or manage their health by adhering to treatment and also in delaying and preventing long-term complications induced by diabetes globally. This is also the same for Guyana during the past 8-10 years, due to high unemployment rate following the closure of several sugar factories. This led to the development of a high level of stress, mental health problems and others among Guyanese. This discussion now focuses on proper management of NCDs, especially diabetes and obesity, via self-care management since this can also save the patients a lot of money (McNaughton et al, 2015).

Self-care management in diabetic patients is crucial in both controlling and preventing associated complications. Diabetes-induced long-term complications such as blindness, foot ulcers, impotence, heart and kidney failures, nerve damage and others are still highly prevalent and most of them are attributed to the lack of self-care knowledge and practices via education by the patients even if there is a national programme for this. Many people, especially those who are less educated about the disorder, do not adhere to their treatment, including daily intake of medication or even non-pharmacological interventions such as diet modification and daily exercise. As soon as the patient feels much better, he or she stops adhering to lifestyle changes or even taking their daily medication. Diabetes education, in tandem with improvement in knowledge, attitudes and skills, can lead to a better control of the disease and it is now widely accepted to be an integral part of comprehensive diabetes own-self-care for the patients. Moreover, adequate self-care is associated with positive outcomes in slowing down the development and progression of long-term complications of diabetes (Mehta et al, 2006; Mukeshimana et al, 2015).

Literacy is believed to play a major role in understanding either a disorder or a disease and in preventing long-term complications and end-organ failure and improving the quality of life of the patient, especially diabetes-induced outcomes among patients with T2DM (Mehta et al, 2006; Mukeshimana et al, 2015). As such, this study was designed to assess the level of knowledge about T2DM self-care among T2DM patients using the information gained to determine whether the frequency of T2DM-related complications is influenced by an understanding of the disorder. This study was conducted at a clinic in Guyana. A questionnaire containing structured examination type questions were used as the primary data collection tool to assess T2DM self-care-related knowledge of diabetics employing both control without long-term complications) and experiment group (with one or more long-term complications) of T2DM patients. The results revealed that the knowledge of the respondents in the experimental group about T2DM self-care was overall poor compared to the control group.

The main conclusion from the results is that that the higher the level of knowledge and education about T2DM self-care, the less likely the diabetic patients will develop diabetes-related long-term complications especially blindness, oral and foot ulcers and nerve damage. This was confirmed by the higher scoring of the control group compared to the experimental group of patients who scored less due to a lack of knowledge of the disorders induced by diabetes. In this study, male patients scored higher than female patients and the age range scoring the highest was 35-45 years, in their working years. These results are in agreement with another related studies which found that females scored far less than males on self-care management of their diabetes relating to foot ulcers, dietary practises and physical activity (Raithatha, 2014) and younger patients who are in their working years score higher (Missiriya, 2016). The reason for men scoring higher than female and younger age-group patients scoring higher is unknown. It is possible that men discuss their disorders with others compared to women and as such knowledge could pass from one person to another. Another possible explanation is that more men had tertiary education in this study compared to women. This was substantiated by the fact that people with tertiary education scored higher compared to those with lower (primary) levels of education. The results have clearly demonstrated that participants who had good knowledge of some aspects of diabetes self-care management, possible due to their education, scored higher compared to participants who had knowledge gap due to lack of education. It may be possible that both gender and age may also play a role in adhering to self-care. These data are consistent with related studies on knowledge and self-care management of diabetes (Norris, 2001; Murata, 2003; Moodley and Rambiritch, 2007; Raithatha, 2014).

The question which now arises is this. What other factors are responsible for non-compliance or adherence to self- care management beside poor education? Poor self-care compliance can also be due to mental health including stress and anxiety, lack of resources and time, poverty, inadequate support as to how to engage in self-care and others (Mukeshimana et al, 2015). On the other hand, several studies have shown that by increasing diabetes self-care management, social support for patients, sharing information and resilience may benefit the patients in terms of self-well- being. This may also act like a psychological intervention tool to adhere to change (Zhao et al, 2018).

The results of the present study have clearly revealed the importance and need to improve diabetic knowledge among patients via education as soon as they are diagnosed with the disorder or even earlier years in their lives when they attend schools via health education. A general health education curriculum is lacking in primary, secondary and tertiary education in Guyana. Second, when a diabetic patient visits his or her private GP or public health clinics for treatment, the patient would spend no more than ten minutes in the surgery. If it is a first visit, then the consultation would probably take longer time to carry out the relevant diagnostic tests to confirm diabetes. Following the visit to the clinic, the patient is not given any reading materials or asked to make an appointment with a health-care professionals since these services are not usually available in Guyana. As such, the patient is left alone to find out for himself or herself about diabetes and its self-care management. A patient with a fairly good education and who has a computer will search the web for information about his or her disorder. Unfortunately, the person with poor education and no computer and web/internet facilities will rely on the doctor by visiting the clinic again for treatment. As a result, it is of paramount importance to bring about awareness among the patients in the right path to maintain a better quality of life ((Mehta et al, 2006; Mukeshimana et al, 2015).

The Guyana Government must establish a diabetic and information centre for teaching diabetic patients about self-care in different areas on long-term complications. The centre can also provide reading materials and videos on the problems of long-term complication. In addition, private hospitals and GPs should also provide similar facilities. Moreover, nurses and health professions can provide such service in public health centres throughout Guyana, in addition to some psychological intervention to adherence to lifestyle changes and intake of daily medication. In addition, the Government of Guyana can promote health and education programmes via radio, newspapers and television to target T2DM patients, as well as pre-diabetic and non-diabetic persons in order to bring about awareness in the right path. Interestingly, Guyana has recently introduced "The Guyana Diabetes and Foot Care Project" for surgical debridement but this used to take place either in poorly lit or unsanitary wards. Moreover, it must compete with other surgical emergencies in the operating rooms (Lowe et al, 2015). This procedure has recently been improved at the foot clinic at Georgetown Public Hospital Corporation (GPHC).

7.7.2 Understanding and knowledge of obesity using a questionnaire.

Regarding the questionnaire on obesity, the results have revealed that people seem to have a fairly good knowledge of obesity which can induce a number of long–term complications such as diabetes, CVDs and others. Nevertheless, they ignore these life–threatening outcomes completely and continue with their modern life-style habits, which in turn can lead to a reduction in the quality of life and subsequently early death. This observation suggests that current behaviour, likeness for fast foods and drinks, with little or no self-care management and self-control, as well as a lack of psychological intervention to induce adherence to an individual, seem to play major roles in the demise of people. As such, people must be strong, proactive and more so, change their behavioural pattern of life and attitude in order to change their life- styles including be more active, cook their own foods, eat less, drink and smoke less and possible participate in daily yoga and meditation in order to achieve spiritual achievement and satisfaction (Singh et al 2017; 2019). It is well known that improving support for self- care management can exert a proactive and positive outcome on the life- style and health outcomes patients. Self-care management can motivate the patients to look after themselves resulting in a reduction of long–term complications and more so giving them a better quality of life and even living longer (van-Sonoorenburg et al, 2019).

Before changing the adverse behaviour of people, then it is necessary to educate them, especially at an early stage in life at nursery, primary and secondary schools, explaining what the adverse and insulting effects of modern life-style habits can have on health and moreover, manage their lives (Tapia and Defries, 2020). Second, it is equally important to give people psychological intervention training to adhere to changes which in turn can lead to a better quality of life (Martinus et al, 2006). Overweight and obesity among young children are major problems globally. In some countries of the world, the Governments run anti-obesity programmes to tackle the problem of overweight and obesity not only among children, but also adults (Sheriff, 2005). The programme involves weighing and testing individuals regularly for their agility and balance. Those who are diagnosed as overweight or obese are referred to health care professionals for advice and counselling include dieting, avoid regular binging and snaking, reduce smoking and alcohol consumption, and participate in regular exercise (Garberm et al, 2019; Mc Cafferty et al, 2020). In some cases, home visits are made to help people, especially children to shed pounds they put on with the help of parents. In addition, people have to make a strong effort to change their eating habits. It is advisable to drink two glasses of water before a meal since water will help in reducing satiety. People are advised to cook their own foods of choice rather than buying and eating fast extra tasty foods which are really the cause of obesity. Similarly, people have to eat at least 50% of salads and non-starchy vegetables filled with fibres daily such as broccoli, beans and other green vegetables. Likewise, people have to consume daily at least 25% proteins which are heavier and tend to fill up the stomach (Barnes and Cassidy, 2018).

7.7.3 Knowledge and understanding of diabetes using a questionnaire.

In relation to the questionnaire on knowledge and understanding of diabetes, it is apparent that the majority of patients had limited knowledge and understanding on all aspects of diabetes including types, causes, symptoms, diagnosis, diet, blood glucose monitoring, complications and others. This is possibly since they were diagnosed with the metabolic disorder for the first time. Unlike obesity, the results from the diabetic questionnaire clearly demonstrate the lack of education on diabetes in Guyana. It is concluded that diabetic education is of paramount importance at a very young age so that potential diabetic patients can have basic knowledge of the disorder which in turn can help in developing self- care management and adherence which in turn can either delay or prevent the development of the disorder (ADA, 2019; Diabetes UK, 2021).

7.8 CONCLUSION OF STUDY

1. In conclusion, the results of this study have clearly demonstrated that such NCDs as obesity, diabetes and hypertension are very prevalent in Guyana.

2. Treatment of these NCDs can be done via daily diet modifications combined with daily exercise and intake of *M charantia* which in turn can help to reduce body weight, blood glucose level, blood pressure, blood cholesterol and triglyceride levels for at least for 6 weeks compared to week 1, as demonstrated in the study. *M charantia* may exert its potential plant-based

medicinal effects via its antioxidant properties. In addition to body weight loss, daily exercise can also help to improve pancreatic beta cell mass and function leading to the secretion of newly synthesised insulin.

3, *M charantia,* when combined with either diamicron MR or amlopidine, two commercial drugs to treat either diabetes or hypertension respectively, induced no synergistic nor inhibitory effect.

4. The data further reveal that knowledge (literacy) of self-care of the disorder can reduce the development of diabetes-induced long-term complications especially blindness, nerve damage oral and foot ulcers and other related complications. Moreover, obese subjects seem to possess a good knowledge of the disease but there are nevertheless, still obese. They need psychological intervention to help them with their obesity problem to adhere to their eating habits.

4. From the data of this study, it is tempting to suggest that these cost-effective and non-pharmacological interventions must be continued for a longer period of time in order to obtain better and more useful beneficial effects leading to longevity and a better quality of health and life for the patients.

5. Figure 7.2 is a flow diagram summarising the relationship between the risk factors which can lead to sudden cardiac death. The risk factors induce increased levels of lipids and triglycerides in the body resulting in weight gain and subsequently obesity which can induce diabetes, CVDs and sudden cardiac death. *M charantia,* combined with dieting and regular physical activity, can prevent and possible, treat the development of these adverse effects due to the risk factors.

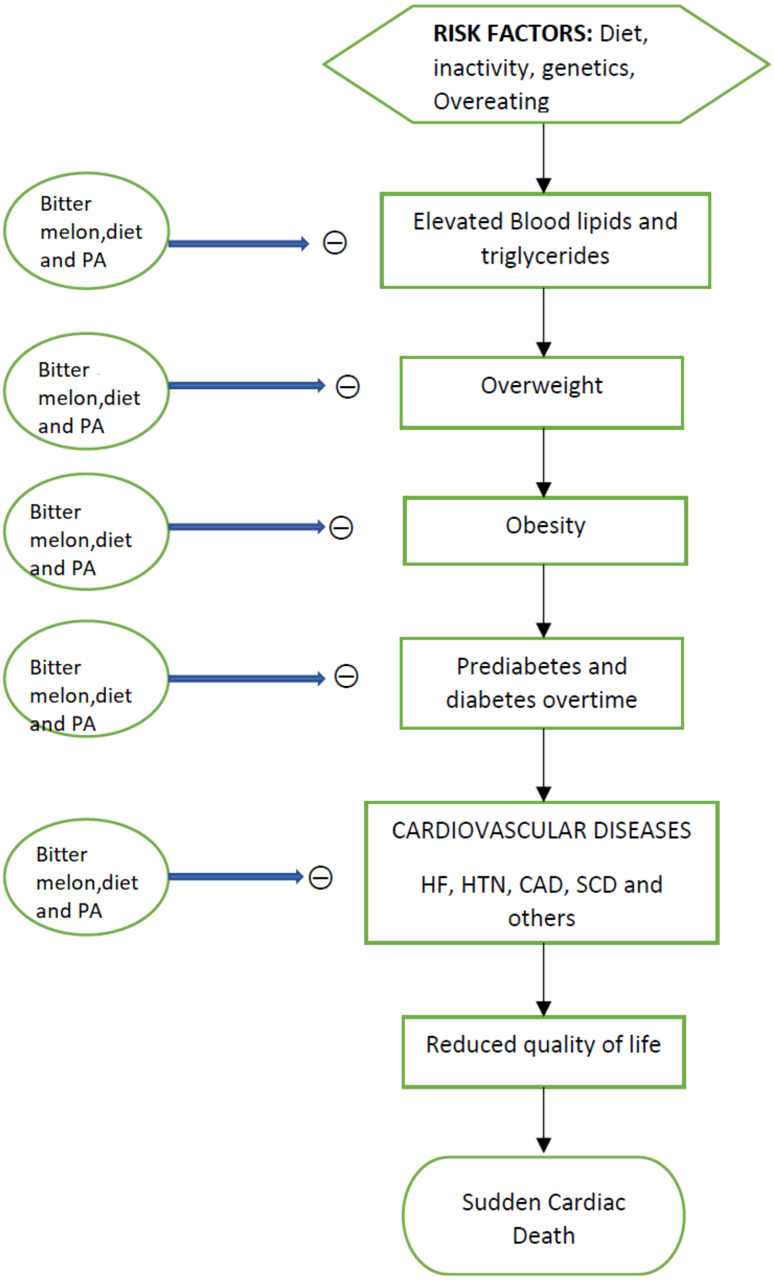


Figure 7.2: Flow diagram summarising the relationship between the risk factors for NCDs which can lead to sudden cardiac death and how *M charantia* combined with diet and physical activity (PA) can help in combating the adverse effects due to the risk factors. CVD= cardiovascular diseases; CAD= coronary artery disease; HTN= hypertension; SCD= sudden cardiac death; PA= physical activity

7.9 Scope for future Studies

1. Repeat the studies with diet modification, exercise, and *M charantia* but employed larger sample size, proper design and control, statistical power and the dose which can exert acclaimed efficacy for a longer duration, possible 3-6 months. Another important area is to investigate the beneficial effect of *M charantia*, diet modification and daily exercise on prediabetes.
2. Investigate the effects of either diamicron MR or metformin with either diet modification or exercise alone and then combine the two with either of the orthodox medicine but using a larger cohort of diabetic patients.
3. Investigate the effects of amlodipine and other anti-hypertensive drugs with either diet modification or exercise alone and then combine the two with either of the orthodox medicine but using a larger cohort of hypertensive patients.
4. Undertake the experiments involving diabetes, obesity and high blood pressure but use either charantin, a purified compound from *M charantia* or capsules which contain M charantia powder since some patients do not like the bitter taste of the juice or fruit.
5. Undertake in *vitro studies* to ascertain the effect of *M charantia* extract on glucose uptake into skeletal muscle cells.
6. Undertake further questionnaire studies, as well as face to face interviews, on economic status, barriers, knowledge and self-care of obesity, diabetes (only economic status and barriers) and hypertension in different cohorts of patients in Guyana.
7. Undertake experiments on different doses of the juice or extracts of *M charantia* delivery to target tissues.
8. Beside the BMI, other measurements that are helpful in quantifying obesity include waist circumference. Increases in waist circumference is associated with mortality even in individuals with normal BMI measurements. Using a combination of both methods helps in generating accurate and clearer way to distinguish between high BMI related to increased muscle content and elevated adiposity.
9. Undertake a study to investigate the interactions between plant-based complimentary medicine with some orthodox medicine for diabetes and hypertension.

7.10 Major Impact of Current Findings

The results from this study have provided strong evidence for the use of life-style changes in combination of non-pharmacological plant-based-medicine for the treatment of such NCDs as obesity, diabetes, high blood pressure and in reducing cardiovascular risks such as elevated blood lipids and triglycerides in a cost-effective manner. The potential benefits are suitable to all patients, but particularly to those who are from low-and middle-income developing countries as Guyana where most patients have to pay for their medical treatment. The results also demonstrated that the fruit juice of *M charantia* had no inhibitory or synergistic effect when combined with commercial drugs to treat either diabetes or hypertension. The onus for change in life-style habits lies with the patients and supported with self-care management via education about the disease or disorder and an element of psychological intervention to adhere to changes.

7.11 LIMITATIONS

The study has a few limitations including the number of patients, especially in chapter 3 where only 8 patients were employed. Future studies should employ large sample size, proper design, controls, statistical power and the dose which can exert acclaimed efficacy. In addition, it is important to continue with each intervention for more than six weeks in order to ascertain a more sustained time-course of results. Future studies should focus on one NCD, rather than three, where cellular and molecular mechanistic investigations could be done especially with the fruit juice of *M charantia.*

7.12 RECOMMENDATIONS

1. The Ministry of Health within the Government of Guyana should promote the use of diet modifications in combination with daily exercise to treat NCDs via a public health programme. The Government should also encourage clinicians to prescribe exercise as a therapy to treat NCDs.
2. Like the ‘’The Guyana Diabetes and Foot Care Project”, the Guyana Government should set up similar projects for obesity, diabetes, and hypertension or a general NCD self-care project.
3. The Guyana Government must establish a diabetic and information centre for teaching diabetic patients about self-care in different areas relating to long-term complication. Same can be done for obesity and hypertension.

4. The Guyana Government, in tandem with the University of Guyana, should train health professional workers who are specialised in specific health and social care issues such as mental health, suicide, obesity, diabetes, CVDs and even NCDs in general. They can work in different public health centres in Guyana counselling patients and provide them with reading materials.

5. People who cannot afford to pay for medication or are living in far outlining villages should be encouraged to use natural plant-based medication (for example *M charantia* and other related to anti-diabetic plants) in combination with life-style changes to treat their ailments.

6. The Ministry of Public Health and the Ministry of Education in Guyana have to involve all sectors of health and social care and education systems, including teachers in schools and lecturers in colleges, health care workers or professionals and the patients themselves about health care management of diseases. It is also strongly recommended that that programmes in education be put in place that are specially tailored to suit individual socio-demographic groups. Current methods used at the moment may only work for certain groups, but not for others.

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<u>**APPENDICES**</u>

Appendix I: Consent Form

University of Guyana

Inform Consent

Organizations:	UClan and UG
Name of Principle Investigator:	Carlin Hanoman, UClan and UG
	Professor Jaipaul Singh (UClan)
Co- Investigators:	Dr. Emanuel Cummings (UG)
	Professor Abdulla Ansari (UG)
	Dr Mohamed Sadik (UG)
Sponsors:	University of Guyana/University of Central Lancashire.

This Informed Consent Form is for men and women who attend the diabetic clinic at the Brickdam Surgery of Dr Carl Hanoman and Dr Carlin Hanoman at 7 Winter Place, Brickdam, Georgetown, Guyana, and who we are being invited to participate in this research on Diabetes mellitus in Guyana.

The title of our research project is ‘Epidemiology of diabetes mellitus in Guyana and the role of knowledge of the disorder and how regular exercise and intake of *Momordica charantia* can lower blood glucose level″

We are working for the University of Guyana (UG) and the University of Central Lancashire (UCLAN) and we are doing research on diabetes, which is very common in our country of Guyana. We are going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

Purpose of the Research

1. To find out more about the epidemiology of diabetes in Guyana relating to gender, age, ethnicity, mortality, region, economic status and others.

2. To establish a relationship other risk factors that may be associated with diabetes and its complications and how knowledge of the disorder can prevent long term complications. This will be done via a questionnaire to complete.
3. To investigate the beneficial effects of exercise and/or intake of *Momordica charantia* (corilla) can be used to treat diabetes mellitus successfully in a cost-effective way.

Participant selection

We are inviting all adults with diabetes who attend the diabetic clinic at the Brickdam Surgery (Clinic) of Dr Carl Hanoman and Dr Carlin Hanoman at 7 Winter Place, Brickdam, Georgetown, Guyana to participate in this research. We will also invite normal healthy subjects to participate in an oral glucose tolerance test (OGTT).

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will continue to benefit from services offered at this clinic. You may change your mind later and stop participating even if you agreed earlier.

1. This research will involve you participating in a questionnaire that will be administered to you by Dr Carlin Hanoman and there will be no follow up relating to the questionnaire.

2. We will ask you to participate in daily exercise by walking half to one mile. If you feel uncomfortable in walking then you must inform Dr Carlin Hanoman, immediately.

3. We will ask you to either eat or drink the juice made from *M charantia* (corilla) in the morning and afternoon before your meal.

4. We will ask you to fast the night before and come to our clinic next morning to participate in a glucose tolerance test (GTT). Dr Carlin Hanoman will explain the whole process to you.

5. We will take blood as a finger prick or from your arm using a syringe and needle during the entire research. At the end of the research (2-3 hours for the OGTT) or over 6 weeks (intake of corilla, diet modification or exercise) any left -over blood sample will be destroyed. Dr Carlin Hanoman will also monitor your blood pressure and basal metabolic Index (BMI) from time to time.

Confidentiality and data protection

With this research, something out of the ordinary is being done in your community or in our surgery. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one, but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key or stored in our computers at UClan. It will not be shared with or given to anyone.

Sharing the Results

The knowledge that we get from doing this research will be shared with you through individual meetings before it is made widely available to the public through publication or used for a thesis. Confidential information will not be shared. After these individual meetings, we will publish the results or present then as a research thesis in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here. Your treatment at this clinic will not be affected in any way.

You may also stop participating in the research at any time you choose. It is your choice, and all of your rights will still be respected. If you withdraw then we will not use your results. They will be destroyed appropriately.

Adverse / Unexpected Outcomes

We anticipate none, but if there are any adverse effects/outcomes, then we will tend to the subject urgently via our Medical Surgery/ Practice or via one of our local hospitals. Second, we will ask subjects to withdraw from the program for the sake of their health. All these will be explained to the patients at the start of the program.

Division into different groups

Dr Carlin Hanoman will explain all parts of the project to each potential participant personally. These include what the experiment involves and how it is done, who will be in which group, duration of the study, what to do, any problems and issues relating to the study if any (for example dropouts or with-drawl and what will happen to partial data), how the full data will be used and the significance and medical potential of the research (for example cost effective treatment for DM) and data presentation etc. If yes, each participant is asked to sign the consent form/sheet. Most participants normally read around the subject area.

We are happy to do what is necessary or the right approach in order to have a positive outcome of the research project and which will have tremendous benefits to poor people who cannot afford traditional medicine to treat their Diabetes.

Who you can contact.

If you have any questions, you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact Dr Carlin Hanoman at her surgery or via phone on 2275590 or 227 5217 or email her at (carlinhanoman@hotmail.com). Carlin is in constant contact with the other investigators who are involved in the project.

Certificate of Consent

I have read the foregoing information, or it has been read to me by Dr Carlin Hanoman. I have had the opportunity to ask Dr Carlin Hanoman questions about it and any questions that I have asked to have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant: ____________________________

Signature of Participant: ______________________________

Date: ____________________________

Day/month/year

If illiterate:

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumbprint as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask Dr Carlin Hanoman questions. I confirm that the individual has given consent freely.

Print name of witness: ____________________________ AND Thumb print of participant

Signature of witness: ______________________

Date _________________________

Day/month/year

Statement by the researcher/person taking consent:

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands what will be done during the research.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Signature of Researcher /person taking the consent: _________________________________

Date ____________________________

Day/month/year

Appendix II (A): UClan Ethics approval 2017

From: Alison Zelda Naylor
Sent: 16 June 2017 17:00
To: Jaipaul Singh <JSingh3@uclan.ac.uk>; Carlin Hanoman <CHanoman@uclan.ac.uk>
Cc: Research Office <ROffice@uclan.ac.uk>
Subject: STEMH 603 - approval with recommendation

Dear Jai

I am pleased to advise that **approval with recommendation** has been granted on the project - 'Epidemiology of diabetes mellitus in Guyana and the role of knowledge of the disorder and how regular exercise and intake of *Momordica charantia* can lower blood glucose level.

The Recommendation is that the new PIS (in response to condition 4c – copy attached) should be re-worded to depersonalise. For example paragraphs 1 and 6 starting "Dr Carlin Hanonman will…" were highlighted and phrasing such as "she will." were not standard phrasing for an information sheet. It was acknowledged that there may be cultural differences that make this style/wording suitable to the activity being undertaken in this project.

If you wish to address this recommendation, please provide a revised copy of the relevant PIS for our records.

Regards

Alison

Alison Naylor
Senior Research Officer

Research Development and Support Team

Greenbank Building Room 316, UCLan, PRESTON, PR1 2HE

Tel: 01772 892728   Email: AZNaylor@uclan.ac.uk

Follow @UCLanRDS

Appendix II (B):

UNIVERSITY of GUYANA

Turkeyen Campus, Turkeyen, Greater Georgetown, P.O. Box 101110, Guyana, South America
Website: uog.edu.gy

FACULTY OF NATURAL SCIENCES
Department of Biology
Tel: + (592) 6090754 E-mail: abdullah.ansari@uog.edu.gy

To whom it may concern

21st November 2016

Re: **Ethical Clearance for Research Project by Dr. Carlin Hanoman**

This is to certify that ethical clearance has been given for Dr. Carlin Hanoman to work on a research project entitled '**Epidemiology of diabetes mellitus in Guyana, the role of knowledge of the disorder and how regular exercise and intake of *Momordica charantia* can lower blood glucose levels'.**

Thank you

....

Dr. Abdullah. A. Ansari, MSc., PhD
Chairman, Ethics Committee
Faculty of Natural Sciences
University of Guyana

Appendix III (A) on basic knowledge on diabetes

Public awareness of Diabetes Mellitus in Guyana questionnaire.

The questions that were asked were the following:

1. Gender: Male or Female
2. Age
3. Ethnicity: Indo-Guyanese, Afro- Guyanese, Chinese, Amerindian, Mixed or Other
4. Place of residence and name: City, Suburbs, Countryside
5. Occupation
6. Level of education: Primary, Secondary, Tertiary
7. Marital status: Married, Single, Divorced
8. What is your current weight?
9. Do you know what Diabetes is? Yes, or no?
10. Do you know the different types of Diabetes? Yes, or no?

If yes, what are they?

11. Do you know what can cause Diabetes? Yes, or no?
12. Do you know the symptoms of Diabetes? Yes, or no?
13. If not, would you like to know more about this? Yes, or no?
14. How does a person know if he or she is diabetic?
15. What are the symptoms of Diabetes?
16. What can a person do to find out if he or she is Diabetic?
17. Do you know the long-term complications of Diabetes? Yes, or no?
18. If yes, list the long-term complications of Diabetes.
19. Do you know that you can die from Diabetes? Yes, or no?
20. Is there anyone in your family who is Diabetic? Yes, or no?
21. If yes, who?
22. Do you know that 20 to 30 minutes of exercise or brisk walking everyday can prevent Diabetes at no cost? Yes, or no?
23. Do you know that eating raw *M charantia* (corilla) or drinking half a glass of its juice daily can prevent or help to treat your Diabetes? Yes, or No?
24. Do you know that most fizzy drinks contain a lot of sugar which can lead to Diabetes? Yes or No?
25. Do you know that eating slowly can prevent Diabetes? Yes, or No?

26. Do you know that eating little or not too much food containing sugar and starch can prevent Diabetes? Yes, or no?
27. Do you know that eating whole bread, roti, bran or cereals can prevent Diabetes? Yes, or No?
28. Do you know that being top heavy or obese can cause Diabetes? Yes, or no?
29. Do you know that excessive stress can lead to Diabetes? Yes, or no?
30. Do you know that a sedentary (no exercise or walking) lifestyle can cause Diabetes? Yes, or no?
31. Do you know that if you have Diabetes your quality of life can be reduced? Yes, or no?
32. Do you know that you can die early if you have Diabetes? Yes, or no?
33. Do you know that if you become Diabetic and do not take your medication daily as prescribed by your doctor, this can lead to many long-term complications of Diabetes? Yes, or no?
34. Do you know that Diabetes can run in the family? Yes, or no?
35. Do you know how much money it costs to diagnose, treat and care for Diabetic patients in Guyana? Yes, or no?
36. If yes, how much?
37. Do you know that Diabetes kills more people than other diseases? Yes, or no?
38. Do you know that you may not get Diabetes if you know about the disorder and do all the things which can prevent it? Yes, or no?
39. What foods do you normally eat for breakfast, lunch, and dinner and how much?
40. Do you snack during the day and night? Yes, or no?
41. If yes when and what do you eat?
42. Do you cook your foods or buy prepared foods?
43. Do you know that eating a lot of vegetables can prevent Diabetes? Yes, or no?
44. Do you know that eating a high carbohydrate diet like white rice, bread and roti made with white flour, cassava, sweet potatoes or potatoes, yam, eddoes and others regularly can lead to Diabetes? Yes, or no?
45. Do you know that you can enjoy a cup of tea or coffee even better without sugar and avoid Diabetes? Yes, or no?
46. Do you know that fruits are better than sugary desserts and thus prevent you getting Diabetes? Yes, or no?
47. Do you drink any herbal medicine or eat an herbal plant at present? Yes, or no?

Appendix III (B): Questionnaire on Obesity

In the obesity questionnaire, subjects were asked twenty -five questions based on their knowledge and understanding obesity. They include the following-

1. What is obesity?
2. The causes of obesity.
3. If obesity can affect health or shorten lifespan.
4. Is there is a cure for obesity?
5. How can sugar affect someone's health?
6. Does obesity run in families?
7. What happens to our body to cause obesity?
8. What is the connection between lifestyle and obesity?

9 What steps can be taken by both children and adults to break unhealthy habits that lead to obesity?

10.Is obesity a risk factor for diabetes?

!1. Is there a link between obesity and diabetes mellitus?

12.Can obesity contribute to type 2 diabetes mellitus?

13.How does obesity contribute to type 2 diabetes mellitus?

14.Does obesity contribute to high blood pressure?

15. Can being overweight cause high blood pressure?

16.How does being overweight cause high blood pressure?

17.Can obesity lead to diabetes mellitus and hypertension?

18.Is obesity a risk factor for high blood pressure?

19.What are the side effects of obesity?

20. Is obesity a preventable disease?

21. How does a person control obesity?

22, How can obesity be prevented?

23.What is the most common cause of obesity?

24.What are the factors that contribute to obesity?

25. What are the different factors which contribute to obesity?

Appendix III (C): Questionnaires and consent form

Knowledge, attitudes and practices concerning diabetes and diabetes -induced long-term complications, especially retinopathy or blindness at hospitals in Guyana.

Questionnaire.

Date-______________________

Participant Number-_________

Section A: Demographics

1- What is your gender? a) Male b) Female

2- Which race (Ethnic group) best describes you?

a) Indo-Guyanese
b) Afro-Guyanese
c) Chinese
d) Amerindian
e) Mixed
f) Other. Please specify_____________

3- How old are you today (in years)? _________

4- Where do you live (region)? ____________

5- What is your Level of Education?

a. No formal education

b. Primary

c. Secondary

d. Tertiary (College/University)

6- What is your occupation?_________________

7- How long have you been diabetic?

a) ≤ 1year

b) 1 ≤ 2years

c) 2≤5years

d) 5 ≤10years

e) ≥10years

Knowledge of diabetes

Preliminary statement: You will be asked a few questions to test your knowledge about diabetes and its complications. These questions are asked purely to test your knowledge about diabetes.

1. **What are the tests done to diagnose diabetes (to find out if a person is diabetic)?**
    1. Blood tests√
    2. Urine tests√
2. **How can you keep diabetes under control?**
    1. Medication√
    2. Diet√
    3. Exercise√
    4. Weight reduction√
    5. Going for regular check- up√
    6. Do not know.
3. **Once diabetes is diagnosed, how long should diet control/ treatment be continued?**
    1. Till the sugar levels get under control
    2. Lifelong√
4. **Which parts of the body are affected by diabetes?**
    1. Kidney√
    2. Feet√
    3. Eyes√
    4. Nerves√
    5. Heart√
    6. Do not know.

If option 3 in Question 4 has been circled (diabetes can affect the eyes), proceed to question 5; if not, skip to Attitude section.

5. **What problems can patients with diabetes have in the eye?**
    1. Cataract√
    2. Retinopathy (damage to retina/nerve at the back of the eye due to diabetes).
    3. Infections in the eye√
    4. Defective vision√
    5. Do not know.

    If option 2 in Question 5 has been circled (patients with diabetes can have retinopathy, i.e., damage to retina/nerve at the back of the eye due to diabetes), proceed to **question 6; if not, skip to Attitude section.**

Total Score for knowledge regarding diabetes: 17

Good knowledge: score of 10 and above

Poor knowledge: score of less than 10

Knowledge of diabetic retinopathy

6. **How did you first find out that diabetes can cause retinopathy (damage to the retina/ nerve at the back of the eye due to diabetes)?**
    1. Physician at local hospital
    2. Ophthalmologist at local hospital
    3. Optometrist at local optical dispensary
    4. Physician at GPHC
    5. Ophthalmologist at Eye clinic (GPHC)
    6. Got information from media, books (specify)
    7. Got information from family/ friends.
    8. At the time of diagnosis.
7. **Can diabetic retinopathy cause blindness?**
    1. Yes
    2. No
    3. Do not know.
8. **What are the factors that cause progression/worsening of diabetic retinopathy?**
    1. Poor control of diabetes
    2. Hypertension
    3. Nephropathy
    4. Anaemia
    5. Do not know.
    6. Any other (specify)
9. **What are the treatment options available for diabetic retinopathy?**
    1. Spectacles
    2. Laser
    3. Surgery
    4. Injection into the eye
    5. Do not know.
10. **Can a person with diabetic retinopathy have normal vision?**
    1. Yes
    2. No
    3. Do not know
11. **Should patients with diabetes have a periodic/regular dilated eye check up to look for diabetic retinopathy (examination of the back of the eye after instilling dilating eye drops to look for changes in the retina due to diabetes)?**
    1. Yes
    2. No
    3. Do not know!

Total score for knowledge regarding diabetic retinopathy: 11

Good knowledge: score of 7 and above Poor knowledge: Score of less than 7

<u>Attitude</u>

Preliminary statement: These are some statements regarding your thoughts, feelings and opinions regarding diabetes and its complications. These statements are not designed to test your knowledge regarding the disease or to find out what you practice/ do. Please indicate whether you 'agree' or 'disagree' with these statements, or whether you are 'undecided'.

1. **I believe eating sweets occasionally is quite alright.**
    1. Agree
    2. Undecided
    3. Disagree
2. **Even if I forget to take my medicines on some days, it is alright.**
    1. Agree
    2. Undecided
    3. Disagree
3. **I should go for regular check -up as my doctor says, even if my sugars are under good control.**
    1. Agree
    2. Undecided
    3. Disagree
4. **<u>Even if I am not</u> able to exercise as much as my doctor tells me to, it is alright because I get enough exercise while I am doing my daily activities.**
    1. Agree
    2. Undecided
    3. Disagree

    Total score for patient's attitude towards diabetes: 12
    Positive attitude: score of 7 and above
    Negative attitude: score of less than 7.

5. **Even though eye doctors say that diabetic patients should have regular eye check up, if my diabetes is under good control, there is no real need for this.**
    1. Agree
    2. Undecided
    3. Disagree √
6. **I should not go for regular eye check- up as the eye doctor tells me, because I don't have any problem in my eyes.**
    1. Agree
    2. Undecided
    3. Disagree√

    For patients who have 'never heard of diabetic retinopathy', skip to Practice section; otherwise proceed to Question 7.

7. **Eye doctors say that good control of diabetes prevents problems due to diabetic retinopathy; but it is not possible to keep sugars under perfect control as they say.**
    1. Agree
    2. Undecided
    3. Disagree√
8. **No matter what I do, my vision may become poor/may not improve. So what is the use of doing all this treatment/follow up for diabetic retinopathy?**
    1. Agree
    2. Undecided
    3. Disagree√

Total score for patient's attitude towards diabetic retinopathy: 12
Positive attitude: score of 7 and above
Negative attitude: score of less than 7

<u>Practice towards Diabetes</u>

Preliminary statement: You will be asked a few questions to find out what you actually do regarding treatment and control of diabetes and its complications.

1. **Do you take medicines for diabetes as advised by the physician?**
    1. Yes√
    2. No
2. **Do you follow the diet schedule as advised by the physician?**
    1. Yes√
    2. No
3. **Do you take regular exercise?**
    1. Yes √
    2. No
4. **Is your diabetes under control at present?**
    1. Yes√
    2. No
    3. Do not know!
5. **Do you go for regular follow up as advised by your physician?**
    1. Yes > skip to Question 7√
    2. No > proceed to Question 6
6. **Why do you not go for regular follow up as advised by your physician?**
    1. Cannot afford.
    2. No support from family
    3. Do not think it is important.
    4. Did not find time.
    5. Checking sugar levels with glucometer at home is sufficient.
    6. Did not know that regular follow up is necessary.
    7. Any other (specify)

Total score for patient's practice pattern regarding diabetes: 5
Good practice pattern: score of 4 and above
Poor practice pattern: score of less than 4

7. **Has anyone told you that you need to go for a dilated eye check- up?**
    1. Yes (specify when: time interval in years since diagnosis of diabetes, and who, and where)
    2. No
8. **To whom do you go for your dilated eye check- up?**
    1. Optometrist at local optical dispensary
    2. Ophthalmologist at local hospital
    3. Ophthalmologist at Eye Clinic, GPHC.
    4. Eye camps
    5. Any other (DR Screening Centre).

(Options 3 or 4 or 5 may be circled; score of 1 for correct practice)

9. **Why do you go for a dilated eye check- up?**
    1. Follow up/treatment of diabetic retinopathy√
    2. To check power of glasses
    3. Been instructed to have periodic eye check- up, but do not know reason.
    4. Any other (specify)
10. **How often do you go for a dilated eye check- up?**

    (Key: correct option will depend on presence and level of diabetic retinopathy and treatment regime followed)

    1. Once in 3 months
    2. Once in 6 months
    3. Once a year√ if no diabetic retinopathy.
    4. As advised by ophthalmologist (specify)√ if treatment is needed.
    5. Any other (specify) Score of 1 for correct answer.
11. **Why have you not gone for a dilated eye check- up?**
    1. Do not trust the local doctor.
    2. Poor family support
    3. Long distance from hospital (in hours of travel by the means of transport usually utilized by the patient)
    4. Financial problems
    5. Physically unwell (specify details of physical ailment)
    6. Did not know that periodic eye check- up should be done
    7. Had good vision; so did not feel need for check up
12. **Why did you come to the eye hospital today?**
    1. For a general eye check up
    2. To check power of glasses
    3. Defective vision
    4. To have tests/treatment for diabetic retinopathy√

    If option 4 in Question 12 has been circled (patient came to have tests/ treatment for diabetic retinopathy), proceed to Question 13; if not, skip to Question 14.

13. **Who referred you for tests/treatment for diabetic retinopathy to this hospital?**
    1. Physician at GPHC√
    2. Referred from eye camp conducted by GPHC Eye clinic√
    3. Physician at local hospital√
    4. Ophthalmologist at local hospital√
    5. Optometrist at local optical dispensary√
    6. Came on my own√

    Any one of the answers is scored as 1.

14. **At what age was you first diagnosed with diabetic retinopathy? Answers in years**

15. **Were you advised to undergo treatment for diabetic retinopathy?**
    1. Yes (specify treatment) >
    2. No > Questionnaire ends.

Total score for patient's practice pattern regarding diabetic retinopathy: 5
Good practice pattern: score of 4 and above
Poor practice pattern: score of less than 4

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