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Association between movement speed and instability catch kinematics and the differences between individuals with and without chronic low back pain

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Studies reported the existence of instability catch (IC) during trunk flexion in patients with chronic low back pain (CLBP). However, different movement speeds can cause different neuromuscular demands resulting in altered kinematic patterns. In addition, kinematic characterization corresponding to clinical observation of IC is still limited. Therefore, this study aimed to determine (1) the association between movement speed and kinematic parameters representing IC during trunk flexion and (2) the differences in kinematic parameters between individuals with and without CLBP. Fifteen no low back pain (NoLBP) and 15 CLBP individuals were recruited. Inertial measurement units (IMU) were attached to T3, L1, and S2 spinous processes. Participants performed active trunk flexion while IMU data were simultaneously collected. Total trunk, lumbar, and pelvic mean angular velocity (T_MV, L_MV, and P_MV), as well as number of zero-crossings, peak-to-peak, and area of sudden deceleration and acceleration (Num, P2P, and Area), were derived. Pearson's correlation tests were used to determine the association between T_MV and L_MV, P_MV, Num, P2P, and Area. An ANCOVA was performed to determine the difference in kinematic parameters between groups using movement speed as a covariate. Significant associations ($P < 0.05$) were found between movement speed and other kinematic parameters, except for Area. Results showed that L_MV significantly differed from the P_MV ($P = 0.002$) in the CLBP group, while a significant between-group difference ($P = 0.037$) was found in the P_MV. Additionally, significant between-group differences ($P < 0.05$) in P2P and Area were observed. The associations between movement speed and kinematic parameters suggest that movement speed changes can alter kinematic patterns. Therefore, clinicians may challenge lumbopelvic neuromuscular control by modifying movement speed to elicit greater change in kinematic patterns. In addition, the NoLBP group used shared lumbar and pelvic contributions, while the CLBP group used less pelvic contribution. Finally, P2P and Area appeared to offer the greatest sensitivity to differentiate between the groups. Overall, these findings may enhance the understanding of the mechanism underlying IC in CLBP.

Keywords Chronic low back pain, Trunk flexion, Kinematics, Instability catch, Inertial measurement unit

Low back pain (LBP) is a common health problem worldwide, resulting in significant disability in work performance and daily activities^{1,2}. Approximately 90% of LBP can be classified as non-specific LBP, which occurs from overuse and dysfunction of surrounding spinal tissues³⁻⁵. Although treatment algorithms for LBP have been

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established⁶, studies reported that 23% of patients with LBP would progress to the chronic stage, significantly impacting their quality of life³. There is evidence indicating aberrant movement patterns are signs of impaired motor control in individuals with chronic back pain (CLBP), which is believed to be a mechanism underlying CLBP^{7–9}. The aberrant movement patterns can cause shear force and suboptimal tissue loading resulting in recurrent episodes of LBP^{7,10,11}.

Instability catch (IC), one of the aberrant movement patterns, is defined as a momentary quiver, vibration, or shake seen in the lumbopelvic region, indicating a loss of neuromuscular control at this region^{7,12}. This impaired lumbopelvic neuromuscular control increases the risks of injury to the spinal structures and subsequently results in recurrent pain^{7,10,11}. A clinical study demonstrated that observed IC during trunk flexion is associated with LBP⁷. Although evidence supports that clinical observation of IC is useful in clinical practice, kinematic characterization is still limited. Thus, using kinematic characterization could better demonstrate quantitative information and provide objective evidence to understand the mechanism of IC in CLBP.

Although kinematic studies demonstrated differences in the quality of movement during trunk flexion, a systematic review showed differences in movement speed which would influence kinematic patterns¹³. One recent kinematic study found different movement patterns responding to changes in movement speed between individuals with and without LBP¹⁴. This would suggest the association between movement speed and aberrant movement patterns. However, no study has previously investigated the associations between movement speed and kinematic patterns specific to the IC.

A previous kinematic study using a dynamic systems approach characterized IC as a sudden change in angular velocity represented by a number of sudden decelerations and accelerations; however, the authors did not account for the amplitude and duration of shaking¹². Accordingly, incorporating peak-to-peak (amplitude) and area under the curve (amplitude and time) for each sudden change in angular velocity to kinematic characterization should better represent IC during clinical observation.

Studies indicated that different trunk movement speeds require different lumbopelvic neuromuscular demands^{14–16}. However, their results demonstrated less impact of speed on healthy individuals than patients with LBP. This could be due to healthy individuals' capability to actively control movement regardless of changes in movement speed^{14–16}. Accordingly, varying movement speeds should result in different performances between healthy individuals and patients with CLBP. However, evidence to support the effects of speed on kinematic parameters is still needed.

Based on the aforementioned research gaps, the associations between movement speed and kinematic parameters should be explored to increase the understanding of the influence of movement speed and to determine if such kinematic parameters associated with IC are able to differentiate between individuals with and without CLBP. Therefore, this study aimed to (1) determine the association between movement speed and kinematic parameters of IC during trunk flexion and (2) examine the differences in kinematic parameters between individuals with and without CLBP. It was hypothesized that movement speed would be associated with kinematic parameters. In addition, those parameters could differentiate between individuals with and without CLBP.

Methods

Study design

This study used a cross-sectional study design to determine the association between movement speed and kinematic parameters and identify kinematic parameters that could have the potential to represent IC during clinical observation. This human research followed the principles of the Declaration of Helsinki. Ethical approval was obtained from the University Institutional Review Board (COA No. MU-CIRB 2020/084.1806), and informed consent was obtained from all the participants before the beginning of the study. Informed consent for publication of identifying information/images in an online open-access publication has also been obtained.

Participants

Participants aged between 20 and 40 years were recruited using a convenience sample from Mahidol University and the surrounding area through word of mouth and posters. The inclusion criteria for individuals with no LBP (NoLBP) were (1) having no previous history of LBP that interferes with daily activities or requires treatment and (2) absence of IC during trunk flexion. The inclusion criteria for CLBP were (1) having an active episode of LBP for more than 3 months, (2) having mild (0–4) to moderate (5–6) pain on the numeric pain rating scale, and (3) the presence of IC during trunk flexion which was identified by momentary quiver, vibration, or shake seen in the lumbar region^{7,12}.

The clinical assessment of IC was conducted with the participants in a standing position, feet shoulder-width apart and exposing their lower back. The clinician was positioned directly behind the participant and instructed them to perform trunk forward bending as far as possible without bending their knees, then return to an upright position. The clinician observed the movement for any signs of shaking during the flexion, which was used to indicate the presence of IC. This procedure was repeated three times to confirm the result. Previous studies have demonstrated the predictive validity of the clinical observation of IC to identify individuals with LBP with fair to moderate inter-rater reliability ($\kappa = 0.33–0.46$)^{7,15}, while the pilot work demonstrated moderate inter-rater reliability of the clinical observation of IC ($\kappa = 0.52$).

Participants were excluded if they had (1) clinical signs of systemic disease, (2) definitive neurologic signs including neural tension, (3) weakness or numbness in the lower extremity, (4) spinal pathologies, any trunk or lower extremity condition that would potentially alter trunk movement (e.g., scoliosis, limb length discrepancy, severe hip or knee osteoarthritis, fracture), (5) vestibular dysfunction, or (6) extreme psychosocial involvement.

Sample size calculation was based on the study that aimed to compare the number of sudden decelerations and accelerations between positive and negative IC and found that the positive group (3.0 ± 1.3 occurrences)

had a significantly greater number than the negative group (5.6 ± 2.5 occurrences)¹². Mean and standard deviation values, an independent t-test (2-tailed), a 95% confidence level, and 80% power were used to calculate the required sample size. A minimum of 22 participants was required. However, to account for potential dropout (20%), the sample size was increased to 30 participants, resulting in 15 participants per group.

Instrumentation

Three Inertial Measurement Unit (IMU) sensors (Delsys Trigno, Delsys Inc., Boston, MA, USA) were attached to T3, L1 and S2 spinous processes using double-sided adhesive tape (Fixomull® Stretch, BSN medical GmbH Hamburg, Germany)¹⁷ and data were collected at 370 Hz using EMGworks acquisition software (version 4.7.8, Delsys, Boston, MA, USA). Each IMU sensor consists of a three-axis accelerometer set to ± 16 g acceleration range and a three-axis gyroscope set to ± 2000 deg/sec velocity. This system has been validated with an optical motion capture system and used in several studies^{17–19}. The study demonstrated excellent test–retest reliability using movement pattern consistency (coefficient of multiple determination = 0.85)¹⁷.

The numeric pain rating scale (NPRS) was used to assess the pain intensity levels of the participants. It is scored from 0 to 10, where 0 indicates no pain, and 10 indicates the worst imaginable pain²⁰. A score of 0–4 indicates mild pain, 5–6 indicates moderate pain, and 7–10 indicates severe pain²⁰. To quantify the severity of disability of the participants, an 11-point Likert scale was used as a simple measure, scoring disability severity from 0 (no disability) to 10 (severe disability).

Procedure

After screening the participants for inclusion and exclusion criteria, the demographic data, including age, sex, weight, height, and clinical data (i.e., pain, disability, duration of symptoms, and frequency), were collected. Participants were asked to change their clothes to expose their lower back area without shoes and stand in a relaxed, upright position. IMU sensors were attached to the landmarks. Before data collection, the participants performed practice trials to familiarize with the testing protocol and measurements. The participants were then asked to perform active trunk flexion for three consecutive repetitions at their comfortable speed for consistency of movement while motion data were synchronously collected.

Data analysis

All kinematic data were processed and calculated using a custom LabVIEW version 2012 program (National Instrument, USA). IMU data were filtered using a second-order zero-phase low-pass Butterworth filter with a 10 Hz cut-off frequency to reduce noise¹⁷. The time-series graphs for total motion (thoracic sensor in global coordinate), lumbar motion (lumbar sensor in pelvic sensor coordinate), and pelvic motion (pelvic sensor in global coordinate) were created.

The total motion time-series graph in the sagittal plane was used to identify start and stop events using 5% of maximum angular velocity as a cut-off point. These data were further time-normalized to 101 data points that represent 100% trunk flexion. Thoracic, lumbar, and pelvic mean angular velocity in the sagittal plane (T_MV, L_MV, and P_MV, respectively) were derived.

Lumbar angular velocity was further converted to angular acceleration where the number of zero-crossings represented the number of sudden deceleration and acceleration (Num) were identified¹². Although a previous study demonstrated that Num can be used to differentiate between individuals with and without LBP¹², this did not incorporate amplitude and duration of IC in the data analysis, therefore peak-to-peak amplitude (P2P) and area under the curve (Area) of the lumbar angular acceleration graph were also identified to explore these factors. Test–test reliability for Num, P2P, and Area from The pilot work was moderate to excellent ($ICC_{2,k} = 0.95, 0.72, \text{ and } 0.91$, respectively). 95% confidence minimal detectable change values were 1.9 occurrences, 0.98 deg/sec, and 16.71 units, respectively.

Statistical analysis

Demographic data were described using descriptive statistics. Shapiro–Wilk tests were performed to determine the distribution of the data, and all parameters were found to be normally distributed: therefore, parametric tests were used.

Independent t-tests were used to compare age and body mass index (BMI), and the chi-square test was used to test sex differences between groups. The first objective of this study was to determine the association between movement speed and kinematic parameters; therefore, Pearson's correlation was performed to determine the association between total angular velocity (T_MV) and other kinematic parameters (L_MV, P_MV, Num, P2P, and Area) for each group.

A systematic review and meta-analysis demonstrated differences in movement speed between people with and without LBP, which would influence kinematic patterns, and lumbar and pelvic movements, which are not independent of each other. Therefore, a two-way mixed ANCOVA (using T_MV as a covariate) with post-hoc pairwise comparisons was used to determine segmental movement contributions (L_MV and P_MV) and between-group (NoLBP and CLBP) interactions.

In addition, a one-way ANCOVA (using T_MV as a covariate) was used to determine the differences in kinematic parameters that represent observed IC between groups. Effect size (ES) was computed and categorized according to Cohen's *d* as trivial (< 0.2), small (≥ 0.2 and < 0.5), moderate (≥ 0.5 and < 0.8), and large (≥ 0.8)²¹. All statistical analyses were performed using SPSS Software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA), and the significance level was set at 0.05.

Results

Demographic data (Table 1) demonstrated no significant difference ($P > 0.05$) in age, gender, and BMI between the NoLBP and CLBP groups. There was no report of pain medication used prior to data collection. Association results (Table 2) demonstrated that T_MV was significantly associated with L_MV, P_MV, and Num ($P < 0.05$) in the NoLBP group, while it was significantly associated with P_MV, Num, and P2P ($P < 0.05$) in the CLBP group.

A two-way mixed ANCOVA showed an interaction trend between segment and T_MV with a medium effect size ($F_{1,27} = 3.928$, $P = 0.058$, partial $\eta^2 = 0.127$) and the significant main effect of T_MV on group with a large effect size ($F_{1,27} = 49.493$, $P < 0.001$, partial $\eta^2 = 0.647$). When taking T_MV as a covariate, a significant interaction between two groups and two segments was seen with a large effect size ($F_{1,27} = 5.106$, $P = 0.032$, partial $\eta^2 = 0.159$) and a significant main effect of segment with a large effect size ($F_{1,27} = 5.495$, $P = 0.022$, partial $\eta^2 = 0.180$). However, no significant main effect of group was found with a small effect size ($F_{1,27} = 1.142$, $P = 0.295$, partial $\eta^2 = 0.041$) when using total angular velocity as a covariate.

Post-hoc pairwise comparisons (Table 3) demonstrated that the L_MV significantly differed from the P_MV with a large effect size ($P = 0.002$, ES = 1.42) in the CLBP group after using T_MV as a covariate. In addition, a significant difference between groups was found with a large effect size ($P = 0.037$, ES = 0.82) in the P_MV after adjusting for a covariate.

A one-way ANCOVA demonstrated a significant effect of T_MV on group for Num with a large effect size ($F_{1,27} = 25.488$, $P < 0.001$, partial $\eta^2 = 0.486$) and P2P with a large effect size ($F_{1,27} = 7.719$, $P = 0.010$, partial $\eta^2 = 0.218$).

Variables	NoLBP (n = 15)	CLBP (n = 15)	P-value
Age (years)	29.5 ± 5.2	30.3 ± 5.6	0.69
Gender (%female)	80%	93.3%	0.28
BMI (kg/m ²)	22.9 ± 3.8	25.2 ± 4.7	0.16
Onset (months)	N/A	10.2 ± 7.4	N/A
Frequency of episodes (per year)	N/A	22.0 ± 33.6	N/A
Time since the last episode (days)	N/A	11.3 ± 12.7	N/A
Duration of an episode (days)	N/A	2.4 ± 2.4	N/A
Pain intensity during the episode (0 = no pain, 10 = worst pain that can be imagined)	N/A	4.1 ± 1.2	N/A
Disability during the episode (0 = not disabled at all, 10 = totally disabled)	N/A	1.87 ± 1.0	N/A

Table 1. Characteristics of NoLBP and CLBP. *NoLBP* No low back pain, *CLBP* Chronic low back pain, *BMI* Body mass index, *N/A* Not applicable.

Parameter	NoLBP		CLBP	
	r	P-value	r	P-value
L_MV (deg/sec)	0.535	0.040*	0.450	0.092
P_MV (deg/sec)	0.804	< 0.001*	0.618	0.014*
Num (occurrences)	- 0.657	0.008*	- 0.761	0.001*
P2P (deg/sec)	0.317	0.250	0.666	0.007*
Area (units)	0.172	0.539	0.464	0.082

Table 2. Association between total angular velocity and kinematic parameters by groups. *NoLBP* = no low back pain; *CLBP* = chronic low back pain; *L_MV* = lumbar mean velocity; *P_MV* = pelvic mean velocity; *Num* = number of sudden deceleration and acceleration; *P2P* = peak-to-peak of sudden deceleration and acceleration; *Area* = area of sudden deceleration and acceleration. * = significant association ($P < 0.05$).

Parameter	Unadjusted					Adjusted				
	NoLBP (Mean ± SD)	CLBP (Mean ± SD)	Diff	P-value	ES	NoLBP (Mean ± SEM)	CLBP (Mean ± SEM)	Diff	P-value	ES
L_MV (deg/sec)	26.2 ± 7.9	32.0 ± 6.6	- 5.8	0.040*	0.80	27.4 ± 1.7	30.8 ± 1.7	- 3.3	0.190	0.52
P_MV (deg/sec)	24.1 ± 10.8	22.5 ± 11.9	1.6	0.699	0.14	26.8 ± 2.2	19.8 ± 2.2	6.9	0.037*	0.82
Diff	2.1	9.5				0.7	11.0			
P-value	1.000	0.006*				0.828	0.002*			
ES	0.15	0.83				0.08	1.42			

Table 3. Unadjusted and total angular velocity (covariate)-adjusted angular velocity pairwise comparisons between groups and among different segments. *NoLBP* No low back pain, *CLBP* Chronic low back pain, *L_MV* Lumbar mean velocity, *P_MV* Pelvic mean velocity, *SD* Standard deviation, *SEM* Standard error of the mean, *ES* Effect size. * = significant difference ($P < 0.05$).

$\eta^2 = 0.222$). However, there was no significant effect of T_MV on group for Area with a medium effect size ($F_{1,27} = 3.016, P < 0.094$, partial $\eta^2 = 0.10$). Therefore, an independent t-test was used to determine between-group differences in Area. Table 4 demonstrates a significant difference between NoLBP and CLBP groups in P2P with a large effect size ($P < 0.001$, $ES = 2.13$) after using T_MV as a covariate. An independent t-test showed significant differences between groups in Area with a large effect size ($P < 0.001$, $ES = 1.80$).

Discussion

From a demographic point of view, both study groups had similar characteristics regarding age, gender, and BMI. Therefore, the results should not be confounded by these data^{14,22}. In terms of clinical data, the CLBP group had moderate pain levels and very low disability²³. The inclusion of CLBP subjects with mild to moderate current intensity pain levels was to ensure that their pain intensity levels did not influence movement patterns. The CLBP group reported that their onset was approximately a year, and they had LBP episodes almost twice a month. Each episode lasted about 2 days, and the last episode was approximately 11 days ago. These clinical characteristics could lead to suboptimal movement control, leading to shear forces and inadequate tissue loading, which may, in turn, increase the risk of re-injury and low back symptoms^{7,9,12,24}.

The present study aimed to determine the association between the speed of the movement represented by T_MV and kinematic parameters, including L_MV and P_MV, as well as Num, P2P, and Area of sudden deceleration and acceleration. Findings demonstrated that the speed of the movement was positively associated with pelvic velocity while negatively associated with the occurrence of sudden deceleration and acceleration in both groups. These findings suggest that increased speed will increase pelvic movement but decrease the number of shakings. Increased speed of the trunk flexion causes changes in neuromuscular demands^{14–16}. The clinical implication of these findings is that clinicians may consider challenging lumbopelvic neuromuscular control by instructing individuals to perform slower trunk flexion during clinical observation. By slowing down the movement, subtle instabilities or compensatory patterns that may not be apparent at higher speeds may be able to observe.

Although the CLBP group did not show a significant association between movement speed and lumbar velocity, there was a trend showing a positive association similar to the significant association in the NoLBP group. This suggests the influence of movement speed on lumbar velocity^{14–16}. In addition, the P2P of sudden deceleration and acceleration was positively associated with movement speed in the CLBP group, indicating that increased movement speed might cause a larger amplitude of sudden deceleration and acceleration in this patient population. Unlike the CLBP group, the NoLBP group is still capable of controlling movement during trunk flexion regardless of changes in movement speed. No association between movement speed and area of sudden deceleration and acceleration suggests no influence of movement speed on this kinematic parameter. Therefore, modifying movement speed may not help clinicians elicit change in movement patterns corresponding to this parameter.

Based on the two-way mixed ANCOVA, the interaction between segment and T_MV and the main effect of T_MV on the group support the influence of movement speed on segmental movement in both groups, which are consistent with the association findings. After taking T_MV into account, a significant interaction was observed between segment and group where the NoLBP group used shared contribution between lumbar and pelvic, while the CLBP group used less pelvic contribution compared with the NoLBP counterpart. In addition to statistically significant differences, the magnitude of the difference between L_MV and P_MV observed in the CLBP group, as well as between-group differences in P_MV demonstrated large effect sizes ($ES > 0.8$). These large effect sizes would help to confidently interpret the results as meaningful differences. These findings are consistent with other studies that found excessive lumbar contribution in the CLBP population^{11,17}. Excessive lumbar contribution may increase shear force or alter load distribution resulting in an increased risk of re-injury that causes recurrent or persistent LBP^{10,11}.

Findings from the one-way ANCOVA were consistent with association findings in which the movement speed affects the number and peak-to-peak amplitude of sudden deceleration and acceleration, but no effect on the area of sudden deceleration and acceleration. However, subsequent analyses demonstrated between-group differences with large effect sizes in peak-to-peak amplitude and area of sudden deceleration and acceleration, which partially support the kinematic characterization of observed IC. These findings suggest that clinicians should consider the amplitude and timing of sudden deceleration and acceleration to capture observed IC.

No significant between-group differences were observed in occurrences of sudden deceleration and acceleration, which could be because it represents only the number of sudden deceleration and acceleration without

Parameter	Unadjusted					Adjusted				
	NoLBP (Mean ± SD)	CLBP (Mean ± SD)	Diff	P-value	ES	NoLBP (Mean ± SEM)	CLBP (Mean ± SEM)	Diff	P-value	ES
Num (occurrences)	23.9 ± 7.7	21.7 ± 6.0	2.2	0.397	0.32	22.3 ± 1.3	23.3 ± 1.3	- 1.0	0.607	0.20
P2P (deg/sec)	2.5 ± 0.8	6.4 ± 2.5	- 3.9	< 0.001*	2.10	2.8 ± 0.4	6.1 ± 0.4	- 3.3	< 0.001*	2.13
Area (units) ^a	20.6 ± 7.3	52.8 ± 24.1	- 32.2	< 0.001*	1.80					

Table 4. Unadjusted and total angular velocity (covariate)-adjusted kinematic parameter pairwise comparisons between groups. *NoLBP* No low back pain, *CLBP* Chronic low back pain, *Num* Number of sudden deceleration and acceleration, *P2P* Peak-to-peak of sudden deceleration and acceleration, *Area* Area of sudden deceleration and acceleration, *SD* Standard deviation, *SEM* Standard error of the mean, *ES* Effect size. * = significant difference; ^a = independent t-test.

consideration for the amplitude and/or timing of the IC. Small shaking (high occurrences of sudden deceleration and acceleration, but low amplitude) during active forward bending may not be detected by clinical observation. However, based on the negative association between movement speed and the number of sudden deceleration and acceleration, a decrease in movement speed can cause greater challenges for the neuromuscular system (requiring greater control of movement)^{14–16}. This may result in greater occurrences of sudden deceleration and acceleration sufficient to differentiate between groups. It appears that P2P and Area are the most sensitive kinematic parameters to differentiate between groups. Therefore, future studies may include these parameters to investigate IC between groups or pre- and post-intervention.

The present study found movement speed to be associated with kinematic parameters, which suggest that changes in movement speed can alter segmental angular velocity and IC. Thus, clinicians may consider challenging lumbopelvic neuromuscular control by modifying movement speed to elicit greater change in movement patterns. In addition, the findings demonstrated that the NoLBP group used a shared contribution between the lumbar spine and the pelvis, while the CLBP group used less pelvic contribution compared with the NoLBP counterpart. This less pelvic and greater lumbar movement contribution may be responsible for recurrent or persistent LBP. In addition, P2P and Area seem to be the most sensitive kinematic parameters representing the IC to differentiate between groups in this study. Therefore, future studies may include these parameters to investigate IC between groups or pre- and post-intervention.

Limitations

This study has some limitations, which should be considered when interpreting the findings. First, this study specifically selected extreme groups, including participants who have no previous history of LBP and no IC as a control group and participants with CLBP and presence of IC as a CLBP group. This would limit generalizability where the general population can be varied (i.e., patients with CLBP, but no IC). Second, clinical observation of IC in the present study was rated during the forward bend phase, while clinicians observe both forward bend and return to upright phases in clinical practice. Therefore, the interpretation is limited only to the forward bend phase. Future studies may include both phases to match with clinical practice.

Data availability

The datasets used and/or analyzed during this study would be available from corresponding author upon reasonable request.

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Author contributions

SK has significantly contributed to conceptualization, data curation, formal analysis, methodology, and writing-original draft. KK and NR have substantially contributed to data curation and formal analysis. RV has substantially contributed to writing-review & editing. JR has significantly contributed to formal analysis and writing-review & editing. PW has significantly contributed to conceptualization, data curation, formal analysis, funding acquisition, and writing-original draft. All authors reviewed the manuscript.

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Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Mahidol University (COA No. MU-CIRB 2020/084.1806).

Additional information

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