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### ORIGINAL ARTICLE

# The risk factors for unexplained antepartum stillbirths in Scotland, 1994 to 2003

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**Objective:** To determine the factors contributing to unexplained antepartum stillbirth in Scotland.

**Study Design:** A 10-year birth database in Scotland was used to compare the unexplained antepartum stillbirth with other birth outcomes. The sample unit was a pregnant mother with a gestational age of 20 weeks and above and with a fetal birth weight of 200 g and above.

**Result:** Maternal age of 35 years and above, lower deprivation category, inaccessible area of residence, maternal smoking, maternal height of <160 cm and gestational age of above 39 weeks were significantly associated with unexplained antepartum stillbirth. In multivariable analysis only maternal age (adjusted odds ratio (OR): 1.8, confidence interval (CI): 1.1 to 3.0, P = 0.02), smoking during pregnancy (adjusted OR: 2.0, CI: 1.1 to 3.5, P = 0.02), and maternal height (adjusted OR: 1.4, CI: 1.1 to 1.8, P = 0.01), remain significant. Screening of pregnancies based on these three risk factors had 4.2% sensitivity and 99.4% specificity. The prevalence of stillbirth for this population was 0.2%. A positive predictive value of only 1.2% implies that only 1 in 83 women with these three risk factors will have antepartum stillbirth. The remaining 82 will suffer needless anxiety and potentially diagnostic procedures.

**Conclusion:** Advanced maternal age, maternal smoking, and shorter maternal height were associated risk for unexplained antepartum stillbirth but screening based on these factors would be of limited value. *Journal of Perinatology* (2010) **30,** 311–318; doi:10.1038/jp.2009.158; published online 15 October 2009

**Keywords:** singleton; nullipara; smoking; screening; maternal height; gestational age

#### Introduction

The stillbirth rate in Scotland is 5.7 per 1000 births for years 1996 to 2000 and 5.3 per 1000 births for the year 2005. The Scottish

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Perinatal and Infant Mortality and Morbidity Report 2004 showed that the total number of normally formed singleton antepartum stillbirths for Scotland was 237 of which 172 (72.6%) were classified as unexplained antepartum stillbirths.<sup>2</sup> Despite the importance of stillbirths, their causes remain unknown in the majority of reported cases due to an incomplete understanding of the physiology of the fetal-placental unit, inadequate diagnostic evaluation in particular the absence of placental histology and fetal autopsy and poor reporting of associated risk factors as causes.<sup>3</sup> The Confidential Enquiry into Maternal and Child Health report for 2003 showed that 70.7% of stillbirths were classified as unexplained antepartum stillbirths even when based on the extended Wigglesworth classification, supplemented by the Obstetric (Aberdeen) classification. <sup>4</sup> A study in Dundee, Scotland showed that 58% of the stillbirths in 1991 to 1992 were classified as unexplained antepartum stillbirths even though the postmortem rate for unexplained antepartum stillbirth was high (86%).<sup>5</sup> A decrease in the unexplained antepartum stillbirth rate in a population is desirable but research is needed to identify the etiology and associated risk factors. This study aims to determine the risk factors of unexplained antepartum stillbirth in Scotland from 1994 to 2003 and assess their value as a screening tool.

#### Methods

Anonymous data for all stillborn and live births in Scotland from 1994 to 2003 have been obtained with permission from the Information and Statistics Division of the National Health Service in Scotland (ISD), based on the Scottish Stillbirth and Neonatal Death Enquiry Form with linkage to the Maternity Inpatient and Day Case Record (SMRO2). The data contained all stillborn and live born infants irrespective of gestational age and all women receiving care in the obstetric specialties/health professions listed as either in-patient or day cases or also referral cases but excluded home births and births in non-National Health System (NHS) hospitals. The perinatal data collected included late fetal deaths from 20 weeks gestation. The overall database is >99% complete since the 1970s.



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Analyses were performed for singleton, pregnancies occurring at 20 completed weeks of gestation and more or occurring after the fetus reached a body mass of 200 g or more. Gestational age was calculated based on the estimated date of delivery. The cause of death was assigned and those deaths classified as unexplained antepartum stillbirths were not categorized further according to the Obstetric (Aberdeen) classification as had been done under the Confidential Enquiry into Maternal and Child Health reporting system. 4 Unexplained fetal deaths were defined as deaths occurring before labor with no evident fetal, maternal, or placental abnormality sufficient to be considered as the cause of death.8 As multiple births are at a greater risk of adverse perinatal outcome than singletons, 9 they were excluded from this study. Those cases with underlying maternal illness such as chronic hypertension or diabetes will not be grouped as unexplained fetal deaths. Cases with placental complication were not be grouped as unexplained fetal deaths such as abruption placentae. The Urban/Rural Category classification used was developed by the Scottish Household Survey that takes account of both the population (settlement size) and remoteness (measured by drive times). The deprivation classification was based on the Carstairs and Morris index developed in the 1980s using 1981 census data. The index was designed with the expectation that it would be mirrored by direct measurement of household income if that were possible by using four variables: crowdedness, male employment, social class, and own car. The maternal weight is only available from the data set for 2003; therefore, it has been analyzed separately and is not usable for further analysis. The variable on perinatal death was collected until the year 1997 and was divided into stillborn and neonatal deaths from 1997 onwards; therefore, both of them have been analyzed in a separate table. This data set does not have the data on HCG measurment and AFP. Factors such as alcohol and drug consumption were not assessed in this analysis as both variables were incomplete.

The data were analyzed using SPSS version 14.0 for Windows after data checking was completed. As this study was undertaken using data obtained from ISD Edinburgh, the original source of data cannot be checked directly but the data can be compared with the report published by the ISD. The different numbers noted in this study compared with the annual report published in the Scottish Perinatal and Infant Mortality and Morbidity Report are because of the fact that this study uses all cases obtained from the ISD, whereas the annual report uses only registered births during the period and home and private (non-NHS) deliveries were not captured in the ISD data. Overall, the consistency of the data was checked by using the SMR validation manual V1.1<sup>10</sup>

 $\chi^2$  tests were used for comparisons of categorical data. The P-values for all hypothesis tests were two-sided and significance was set at P-value <0.05. The bivariate analyses enabled identification of various potential risk factors that were significantly associated with unexplained antepartum stillbirth. The crude odds

ratios (ORs) were calculated for each explanatory variable. The confidence interval (CI) for each factor was reported together with the OR.

To control for the possibility that these factors might be confounded, all factors were entered simultaneously, using automatic selection procedures, into multivariable logistic regressions models. Adjusted ORs were obtained. Logistic regression analyses were performed to predict or estimate the probability that an individual would have an unexplained antepartum stillbirth and to make a comparison with other outcomes. Bayes' theorem of conditional probabilities was used to calculate the predictive values. These predictive values were useful in the interpretation of the relevance of a combination of the significant factors as a screening tool as they are determined by the sensitivity, specificity, and the prevalence of the outcomes studied (stillbirths and unexplained antepartum stillbirths), which may change from setting to setting. <sup>11</sup>

#### **Results**

The study includes all singleton pregnancies and assessed their outcomes comparing the unexplained antepartum stillbirth with all other outcomes (live births, explained antepartum and intrapartum stillbirth). There were 541 811 births between 1994 and 2003 including 1452 unexplained antepartum stillbirths out of a total of 2822 stillbirths. Table 1 shows the univariate analysis for cases classified as unexplained antepartum stillbirth versus others outcomes.  $\chi^2$  tests showed that maternal age, marital status, deprivation category, smoking during pregnancy, parity, previous hospital admission, maternal height, maternal weight, history of previous stillbirth, gestational age, and birth weight were significant associated factors with the unexplained antepartum stillbirths and other outcomes. However, area of residence, diabetes status, previous caesarean section or abortion and sexr were not significant. The median maternal age for unexplained antepartum stillbirth is significantly lower than the other groups  $(35 \pm \text{Interguantile range } 10 \text{ versus } 40 \pm 2, P < 0.01)$ . The risk based on gestational age was calculated using cumulative probability as shown in Figure 1 and recommended 20 years ago by Yudkin et al. 12,13 The curve increases, especially after a gestational age of 39 weeks, for stillbirth and unexplained antepartum stillbirth compared with explained antepartum stillbirths.

Further analysis using multiple logistic regressions was conducted based on the significant findings of the univariate analyses. A multivariable model with automatic selection of risk variables showed that smoking during pregnancy, maternal age, and maternal height remained independently significant (Table 2). The model's goodness of fit was good with a small value of -2 log-likelihood (5984.954) and a Cox and Snell  $R^2$  of 0.100. The Hosmer and Lemeshow test also showed a high P-value indicating the goodness-of-fit between the observed and predicted number of



**Table 1** Sociodemographic factor by pregnancy outcomes, 1994–2003

| Risk factors         | Unexplained<br>antepartum ( |        | P-value | Odd ratio<br>(confidence |
|----------------------|-----------------------------|--------|---------|--------------------------|
|                      | stillbirth ( $N = 1452$ )%  | %      |         | interval)                |
| Maternal age         | group                       |        |         |                          |
| 10 - 19              | 9.5%                        | 8.2%   | < 0.001 | 1.073 (0.875-1.314)      |
| 20 - 24              | 20.0%                       | 18.4%  |         | 1.00                     |
| 25-29                | 26.6%                       | 29.9%  |         | 0.820 (0.704-0.955)      |
| 30-34                | 27.0%                       | 29.4%  |         | 0.846 (0.727-0.985)      |
| 35-39                | 14.4%                       | 12.1%  |         | 1.095 (0.916-1.309)      |
| 40-                  | 2.5%                        | 1.9%   |         | 1.215 (0.863–1.712)      |
| Marital status       |                             |        |         |                          |
| Never                | 33.7%                       | 27.9%  | < 0.001 | 1.339 (1.194-1.502)      |
| married              |                             |        |         |                          |
| Married              | 51.2%                       | 56.6%  |         | 1.00                     |
| Widowed/             | 0.9%                        | 0.6%   |         | 1.572 (0.907-2.722)      |
| divorced/            | * -                         |        |         | , ,                      |
| separated            |                             |        |         |                          |
| Other                | 8.2%                        | 8.3%   |         | 1.084 (0.892-1.316)      |
| Unknown              | 6.0%                        | 6.5%   |         | 1.010 (0.807–1.263)      |
|                      |                             |        |         |                          |
| _                    | ivation quintile            |        |         |                          |
| Quintile 1           | 13.7%                       | 19.2%  | < 0.001 | 1.00                     |
| Quintile 2           | 19.6%                       | 19.0%  |         | 1.445 (1.205–1.733)      |
| Quintile 3           | 20.9%                       | 19.7%  |         | 1.488 (1.244-1.781)      |
| Quintile 4           | 19.3%                       | 20.4%  |         | 1.327 (1.106-1.592)      |
| Quintile 5           | 26.4%                       | 21.6%  |         | 1.709 (1.439-2.029)      |
|                      | sixfold indicato            |        |         |                          |
| Large urbar<br>areas | n 41.4%                     | 40.1%  | 0.273   | 1.00                     |
| Other urbar          | n 29.8%                     | 29.8%  |         | 0.968 (0.855-1.096)      |
| Accessible           | 9.7%                        | 10.3%  |         | 0.912 (0.758-1.096)      |
| small town           | 2 (0)                       | 2.70/  |         | 1 222 (2 212 1 (//)      |
| Remote<br>small      | 3.4%                        | 2.7%   |         | 1.229 (0.918-1.646)      |
| towns                |                             |        |         |                          |
| Accessible           | 10.8%                       | 12.3%  |         | 0.855 (0.717-1.020)      |
| rural                |                             |        |         | ,                        |
| Remote               | 4.9%                        | 4.8%   |         | 0.989 (0.773-1.266)      |
| rural                | -                           |        |         |                          |
|                      |                             |        |         |                          |
|                      | ng pregnancy                | F7 00/ | -0.001  | 1.00                     |
| No                   | 44.9%                       | 57.0%  | < 0.001 | 1.00                     |
| Yes                  | 33.6%                       | 26.0%  |         | 1.642 (1.460-1.846)      |
| Unknown              | 21.5%                       | 17.0%  |         | 1.605 (1.403–1.837)      |
| Smoking histo        | -                           |        |         |                          |
| Never                | 50.8%                       | 64.5%  | < 0.001 | 1.00                     |
| Current              | 35.8%                       | 27.0%  |         | 1.685 (1.506–1.885)      |
| Former               | 2.5%                        | 2.7%   |         | 1.178 (0.846-1.640)      |

Table 1 Continued

| Risk factors                       | Unexplained antepartum (N stillbirth (N = $1452$ )% | Others<br>= 541 811)<br>% | P-value | Odd ratio<br>(confidence<br>interval) |
|------------------------------------|---|---------------------------|---------|---------------------------------------|
| Unknown                            | 10.9%   | 5.7%                      |         | 2.405 (2.025-2.857)                   |
| Parity                             |   |                           |         |                                       |
| 0                                  | 39.6%   | 35.0%                     | 0.014   | 1.00                                  |
| 1                                  | 28.6%   | 32.0%                     |         | 0.792 (0.698-0.899)                   |
| 2                                  | 16.3%   | 18.0%                     |         | 0.805 (0.692-0.937)                   |
| 3                                  | 8.8%  | 8.5%                      |         | 0.916 (0.755-1.110)                   |
| 4                                  | 3.7%  | 3.7%                      |         | 0.863 (0.651-1.144)                   |
| 5 and above                        | 3.0%  | 2.9%                      |         | 0.933 (0.686-1.268)                   |
| Previous histor                    | ry of spontaneou                                    | s abortion                |         |                                       |
| 0                                  | 78.8%   | 79.7%                     | 0.392   | 1.00                                  |
| 1                                  | 16.5%   | 15.6%                     |         | 1.075 (0.935-1.236)                   |
| 2                                  | 3.6%  | 3.4%                      |         | 1.059 (0.802-1.399)                   |
| 3 and above                        | 1.1%  | 1.3%                      |         | 0.880 (0.537-1.442)                   |
| Previous bistor                    | ry of therapeutic                                   | abortion                  |         |                                       |
| 0                                  | 88.6%   | 89.2%                     | 0.476   | 1.00                                  |
| 1                                  | 9.3%  | 9.2%                      |         | 0.728 (0.323-1641)                    |
| 2                                  | 1.7%  | 1.4%                      |         | 0.715 (0.372-1.636)                   |
| 3 and above                        | e 0.4%  | 0.3%                      |         | 0.742 (0.299–1843)                    |
| Previous histor                    | ry of caesarean                                     |                           |         |                                       |
| 0                                  | 90.2%   | 91.0%                     | 0.243   | 1.00                                  |
| 1                                  | 8.3%  | 7.7%                      |         | 1.088 (0.903-1.312)                   |
| 2                                  | 1.4%  | 1.1%                      |         | 1.252 (0.804-1.948)                   |
| 3 and above                        | 0.2%  | 0.2%                      |         | 1.016 (0.327-3.158)                   |
| Previous adm                       | ission  |                           |         |                                       |
| 0                                  | 60.2%   | 42.9%                     | 0.001   | 1.00                                  |
| ≥1                                 | 39.8%   | 57.1%                     |         | 1.107 (0.931-1.316)                   |
| Diabetes statu                     | s   |                           |         |                                       |
| Pre-existing diabetes              | 0.3%  | 0.5%                      | 0.468   | 1.00                                  |
| Gestational<br>diabetes            | 0.1%  | 0.4%                      |         | 0.622 (0.079-4.922)                   |
| No diabetes<br>during<br>pregnancy | 99.6  | 99.1%                     |         | 0.901 (0.464-1.950)                   |
| 10,                                |   |                           |         |                                       |
| Maternal beig                      |   | 20. =2/                   | 0.00    | 1 222 /1 277                          |
| <160 cm                            | 34.3%   | 29.5%                     | 0.001   | 1.223 (1.077-1.390)                   |
| 160−169 cm<br>≥ 170 cm             | 1 65.7%   | 70.5%                     |         | 1.00<br>0.927 (0.779–1.103)           |
| Maternal weis                      | ght (data for yea                                   | r 2003 only)              | )       |                                       |
| <80 kg                             | , . ( jor your                                      | 5                         | < 0.001 | 0.453 (0.207-0.990)                   |
| ≥80 kg                             |   |                           |         | 1.00                                  |

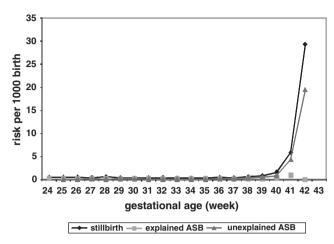


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Table 1 Continued

| Risk factors    | Unexplained       | Others     | P-value   | Odd ratio                  |
|-----------------|-------------------|------------|-----------|----------------------------|
|                 | antepartum (N     | I = 541811 | )         | (confidence                |
|                 | stillbirth        | %          |           | interval)                  |
|                 | (N = 1452)%       |            |           |                            |
| Previous stille | pirth (data from  | 1997–200   | 3 only)   |                            |
| 0               | 97.0%             | 99.1%      | < 0.001   | 1.00                       |
| 1               | 2.8%              | 0.8%       |           | 3.376 (2.283-4.994)        |
| 2 and abov      | e 0.2%            | 0%         |           | 6.179 (1.526–25.020)       |
| Previous neor   | natal death (data | a from 199 | 7-2003 or | nly)                       |
| 0               | 98.9%             | 99.4%      | 0.072     | 0.213 (0.053-0.862)        |
| 1               | 0.9%              | 0.6%       |           | 0.325 (0.068-1.542)        |
| 2 and abov      | re 0.2%           | 0%         |           | 1.00                       |
| Estimated       |                   |            |           |                            |
| gestational     |                   |            |           |                            |
| age             |                   |            |           |                            |
| 20 - 23         | 0%                | 0.0%       | 0.001     | 0                          |
| 24 - 27         | 19.3%             | 0.3%       |           | 211.660 (167.557 - 267.372 |
| 28 - 31         | 15.7%             | 0.7%       |           | 81.693 (64.390-103.646)    |
| 32 - 36         | 23.8%             | 5.0%       |           | 17.913 (14.320-22.406)     |
| 37 - 40         | 34.3%             | 67.9%      |           | 1.918 (1.546-2.380)        |
| 41-             | 6.8%              | 25.9%      |           | 1.00                       |
| Birth weight    |                   |            |           |                            |
| <2500 g         | 61.8%             | 6.0%       | < 0.001   | 1.00                       |
| ≥2500 g         | 38.2%             | 94.0%      |           | 0.039 (0.035-0.044)        |
| Gender          |                   |            |           |                            |
| Boy             | 52.8%             | 51.2%      | 0.231     | 1.067 (0.962-1.183)        |
| Girl            | 47.2%             | 48.8%      |           | 1.00                       |

cases (P = 0.994). Table 2 shows multiple logistic regression analyses, which include all singleton pregnancies and also analyses among the singleton nulliparous pregnancies only. The result showed that the adjusted OR for unexplained antepartum stillbirth increased with increased maternal age after 35 years compared with the reference age of 20 to 24 years for both analyzed groups (Table 2). The adjusted odds of unexplained antepartum stillbirth varied from category 1 (most affluent) to category 7 (most deprived). The less affluent showed increasing of risk of unexplained antepartum stillbirth (Figure 2). Smoking during pregnancy was associated with two times (OR: 1.639, 95% CI: 1.351, 1.909, P < 0.01) higher odds of unexplained antepartum stillbirth. Nulliparous pregnancies had a higher risk of unexplained antepartum stillbirth compared with multiparous pregnancies. The risk reduces with an increasing number of pregnancies. Those of a height of <160 cm showed a higher risk of having an unexplained antepartum stillbirth as compared with height above 160 cm. There was an increasing risk of unexplained



**Figure 1** Risk by week of gestation for stillbirth, explained and unexplained antepartum stillbirths, 1994 to 2003, for singleton nulliparous pregnancies. *Note*: The rate was calculated per 1000 total ongoing birth (live and still).

antepartum stillbirth if they had previous history of stillbirth (OR: 3.467, 95% CI: 2.101, 5.643, P<0.01).

Analyses among the singleton nulliparous pregnancies showed that higher maternal age increased the odds of unexplained antepartum stillbirth significantly and was 1.8 times higher (OR: 1.806, 95% CI: 1.097, 2.975, P = 0.02) for the maternal age group 35 to 39 years than those of 20 to 24 years. Smoking during pregnancy associated with two times (OR: 1.970 95% CI: 1.110, 3.495, P = 0.02) higher risk of unexplained antepartum stillbirth A maternal height of <160 cm gave a 1.3 times higher risk (OR: 1.378, 95% CI: 1.070 to 1.775, P = 0.01) of unexplained antepartum stillbirth than those with maternal height of 160 to 169 cm. Marital status and previous history of hospital admission were no longer significant in the multivariable model.

On the basis of the significant findings for singleton nulliparous unexplained antepartum stillbirths, a further analysis was conducted to look for relationships between the identified determinant factors and the occurrence of unexplained antepartum stillbirths in the population. Predictions of the rates of unexplained antepartum stillbirth were calculated based on the three independently significant risk factors. Only 5 of 120 unexplained antepartum stillbirths and 413 of the total population (63 579) singleton nulliparous pregnancies) had all three risk factors present (maternal age of 35 years and more, smoking during pregnancy and height of <160 cm). On a population basis, this was a sensitivity of the screening based on the three factors of only 4.2%. The specificity (99.8%) was very high, indicating that all three risk factors were rarely present for other birth outcomes. The prevalence of unexplained antepartum stillbirth with the presence of three risk factors was very low at 0.2% of the population. The positive predictive value was also very low (1.2%) and the negative predictive value was very high (99.8%). A PPV of



**Table 2** Adjusted odds ratios and 95% confidence interval for unexplained ante partum stillbirths versus others in multiple logistic regressions, 1997–2003

| Risk factors           | odds      | pregnancies adjusted<br>ratios (95% confidence<br>intervals, P-value) | Nulliparous pregnancy<br>adjusted odds ratios<br>(95% confidence intervals,<br>P-value) |
|------------------------|-----------|---|---|
| Maternal age           |           |   |   |
| 20-24 I                | Referent  | (P < 0.01)  |   |
| 10 - 19                | 0.822     | (0.567-1.137, P=0.27)   | 1.051 (0.719 $-1.538$ , $P = 0.797$   |
| 25 - 29                | 1.091     | (0.881-1.450, P=0.48)   | 1.162 (0.821 $-$ 1.645, $P = 0.397$   |
| 30 - 34                | 1.367     | (1.119-1.848, P=0.01)   | 1.286 (0.879 $-$ 1.880, $P = 0.195$   |
| 35-39                  | 1.541     | (1.208-2.185, P<0.01)   | 1.806 (1.097 $-$ 2.975, $P = 0.020$   |
| 40-                    | 2.235     | (1.450 - 3.829, P < 0.01)   | 2.027 (0.630 - 6.524, P = 0.236)  |
| Marital status         |           |   |   |
| Married I              | Referent  | (P = 0.27)  |   |
| Never<br>married       | 1.140     | (0.935 - 1.365, P = 0.19)   | (0.639 - 1.159, P = 0.322)  |
| Carstairs depri        | ivation   | category  |   |
| Category 1 I           |           | o .   |   |
| Category 2             |           | (0.748-1.948, P=0.42)   | 1.556 (0.722 $-$ 3.351, $P = 0.259$   |
| Category 3             |           | (1.044-2.577, P=0.03)   | 2.074 (0.994 - 4.331, P = 0.052)  |
| Category 5             |           | (1.033-2.542, P=0.03)   | 1.887 (0.904 $-$ 3.939, $P = 0.091$   |
| Category 4             | 1.629     | (1.002-2.563, P=0.04)   | 1.749 (0.813 - 3.761, P = 0.153)  |
| Category 6             | 2.014     | (1.254-3.186,P<0.01)  | 1.810 (0.829 $-3.949$ , $P = 0.136$   |
| Category 7             | 1.666     | (0.968-2.710, P=0.05)   | 2.765 (1.259 - 6.073, P = 011)  |
| Smoking durin          | ng pregn  | nancy   |   |
| No I                   | Referent  | (P < 0.01)  |   |
| Yes                    | 1.639     | (1.351-1.909, P<0.01)   | 1.970 (1.110 $-3.495$ , $P = 0.021$   |
| Previous delive        | eries (pa | arity)  |   |
| 0 1                    | Referent  | (P<0.01)  |   |
| 1                      | 0.867     | (0.716-1.053, P=0.15)   | Not applicable  |
| 2                      | 0.831     | (0.661-1.045, P=0.11)   |   |
| 3                      |           | (0.520 - 0.964, P = 0.02)   |   |
| 4                      | 0.428     | (0.254-0.718, P<0.01)   |   |
| 5 and                  | 0.582     | (0.357 - 0.950, P = 0.03)   |   |
| above                  |           |   |   |
| Previous admi          |           |   |   |
|                        | Referent  | (0.550 4.005 5 5 5  | 0 ((0 (0 044 ) 0 1) 1 =   |
| At least one admission | 0.876     | (0.752 - 1.030, P = 0.09)   | $0.663 \ (0.311 - 1.414, P = 0.287)$  |
| Height                 |           |   |   |
| 160- I                 | Referent  |   |   |
| 169 cm                 |           |   |   |
|                        |           |   |   |

1.220 (1.028–1.449, P = 0.02) 1.378 (1.070–1.775, P = 0.01)

0.95 (0.673 - 1.341, P = 0.76)

Not applicable

0.899 (0.716-1.135, P = 0.37)

3.467 (2.101-5.643, P<0.01)

5.005 (0.695-36.473, P=0.11)

Referent (P < 0.01)

< 160 cm

≥ 170 cm

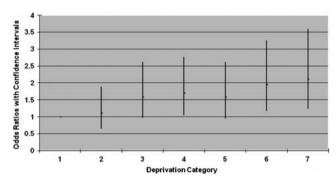
Previous stillbirth

0

1

2 and

above



**Figure 2** Odds ratios for unexplained antepartum stillbirths by Carstairs deprivation category. *Note*: Category 1 as reference.

1.2% implies that only 1 in 83 women with these three risk factors will have antepartum stillbirth. The remaining 82 will suffer needless anxiety and potentially diagnostic procedures. However, in 333 cases of 574 unexplained antepartum stillbirths and of 85 673 cases of the population with at least one of the three risk factors present, the sensitivity of the screening was increased to 58% with specificity of 55%. The prevalence remained approximately the same, but the positive predictive value decreased further to 0.4% and the negative predictive value remained at a high percentage (99.8%). This showed that with the positive predictive value of 0.4% implies that only 1 in 250 women present with at least one of three risk factors (maternal age 35 and above, smoking during pregnancy, and maternal height <160 cm) will in fact end the pregnancy as unexplained antepartum stillbirth. The remaining 249 pregnancies will suffer needless anxiety and potentially diagnostic procedures. Therefore, more identified risk factors will be able to closely predict the cases of unexplained antepartum stillbirth.

#### Discussion

The data available showed that stillbirths were the largest contributors to perinatal mortality (69.1% of total perinatal deaths). On the basis of the Obstetric (Aberdeen) classification, the data showed that unexplained antepartum stillbirths were the largest category (40.5% of total stillbirths). In the univariate analyses, sociodemographic and obstetrics risk factors were statistically significant including high maternal age group, deprivation category, area of residence, smoking, no previous admission, and height <160 cm. These findings were in accordance with previous reports that have identified these risk factors as determinants of unexplained antepartum stillbirth. 8,14–19 Nevertheless, further multiple logistic regression analysis showed that advanced age, especially 35 years old and above, smoking and shorter height were independently significant risk factors for unexplained antepartum stillbirth. Univariate



assessment of the obstetric factors among the nulliparous also showed that higher gestational age contributed to a higher risk of unexplained antepartum stillbirth. Gestational age was analyzed based on cumulative rate and showed a significant increase in risk with an increase of gestational age, especially after 39 weeks.

Smokers consistently showed higher risk, especially current smokers. The observation that the risk of unexplained antepartum stillbirths was very high at term among smokers has been reported in earlier studies. 20,21 Restricted fetal growth present in stillbirths is well known and has been reported in many studies. 3,8,22-24 and this has a relationship with smoking. However, birth weight and growth retardation were not considered in this study. Birth weight also depends closely on gestational age and is confounded by many maternal illnesses. 3,25,26 Gestational age had a very strong association with unexplained antepartum stillbirth. The finding has been consistently seen in other studies that performed the cumulative risk ratio as recommended by Yudkin et al. 12,13 Therefore, it can be suggested that in pregnancies at high risk of stillbirth, an active interruption of pregnancy near to 39 weeks of gestation may need to be considered to diminish the probability of adverse outcomes.

Advanced maternal age has been shown to be significantly associated with higher risk of unexplained antepartum stillbirth in this study as was found in two earlier studies. <sup>27,28</sup> However, a population study conducted in the United States for 1995 to 1997 did not show this association among black women. <sup>29</sup>

There was a non-significant association showing poorer outcomes among those who were not married. Social deprivation was shown to be associated with unexplained antepartum stillbirth with higher Carstairs Deprivation increasing the risk. A link was seen between adverse pregnancy outcome and lack of accessibility to health care based on urban rural classification. Deprivation and residence were no longer significant in multivariable analyses most probably because of confounding with smoking and maternal height, which remained significant within the model. A NHS Health Indicator Report 2004 also showed that under International Federation of Gynaecology and Obstetrics, the rates of stillbirth and neonatal deaths increased with deprivation from 3.4 per 1000 births for the least deprived areas (Quintile 1) to 5.3 per 1000 births for the most deprived areas (Quintile 5).30 This study has not looked at the association of a history of existing diabetes or gestational diabetes as it is known that any stillbirth with diabetes will be normally classified as an explained, rather than unexplained, antepartum stillbirth.

After adjusting for the possible confounding factors, the remaining and definitive significant risk factors were increasing maternal age, especially after 35 years old; shorter maternal height; and smoking during pregnancy. Percentages of premature stillbirth (<36 weeks) were higher in unexplained antepartum stillbirth

(table not shown). However, a calculation made based on a proportional rate using the denominator of all ongoing pregnancies as recommended showed that increasing gestational age, especially after 39 weeks, contributed to a higher risk of unexplained antepartum stillbirths. About one third of those with a gestational age of >37 weeks also had a lower birth weight and were, therefore, potentially avoidable. A study done in six developing countries also showed a consistent relationship between a risk cumulative probability increase and an increase in gestational age. <sup>31</sup>

A study done at a hospital in Saudi Arabia<sup>32</sup> showed very similar findings, as follows: low socioeconomic status (OR: 1.22; 95% CI: 1.14, 2.86); maternal age 40 years or more (OR: 3.62; 95% CI: 1.22, 4.52); and maternal age of 18 years or less (OR: 1.79; 95% CI: 0.82, 2.89). However, that study did not show any significant associations between smoking, fetal sex, and post-term pregnancies and unexplained antepartum stillbirths. The difficulty in the classification of stillbirth as antepartum and intrapartum as well as in verifying the classifications is, of course, that they depend on the view of the reporting physician. There may have been a bias in the reporting: for example, fetal deaths may have been reported incorrectly as miscarriages and antepartum stillbirths may have been reported as intrapartum deaths. However, it was not possible to ascertain whether this was the case as the data obtained did not contain the relevant information.

The SMR data sets that constitute the computerized, population-based data were derived from the hospital inpatient summary (maternity inpatient and day case records SMR02) and have shown coverage of 98 percent of all births since 1976.<sup>33</sup> More than 99% of total deliveries in Scotland were hospital deliveries.<sup>7</sup> The large sample size in this study (population data) provided greater statistical power than previous work based on a smaller sample sizes. As unexplained antepartum stillbirth was noted among the low-risk deliveries, this study, with its larger number of these low-risk deliveries, was able to detect substantial differences in the outcomes.

Unexplained antepartum stillbirth was the focus of this study because it is of general public concern. Even though a study has reported that the majority of stillbirths occurred in 'low-risk' women, a significant minority had stillbirth risk factors that were recognized during their antenatal care.<sup>34</sup> However, an extensive review showed that there was suboptimal care in nearly half (45%) of all stillbirths.<sup>34</sup>

Identifying the risk factors for unexplained antepartum stillbirth is relevant for clinical practice and for the planning of future services to improve the health and well-being of mothers and their babies, especially mothers living in social deprivation. The presence of significant associations between the risk of unexplained antepartum stillbirth and maternal age, deprivation category, area of residence, smoking, and



maternal height were observed in this study. The findings for age, smoking, and height persist after adjusting for socioeconomic and reproductive factors. The importance of this study stems from the fact that it was performed in the country that started the classification of perinatal death based on unexplained and explained causes of death and involved almost 200 000 births over a 10-year period.

However, this study has its limitation as a high proportion of unknown or missing data such as alcohol and maternal diseases were not recorded during the process of care in the database system. The weight and drug misuse variables were recently included in the database in year 2003. These may have had an influence on the outcomes but were not analyzed in this study because the sample size became too small. The inter-pregnancy interval could not be measured in this study because the database obtained was anonymous and those cases with more than one pregnancy could not be assessed for their inter-pregnancy intervals. This problem also applies to an earlier history of low birth weight and earlier preterm birth. Furthermore, there is difficulty in the classification of stillbirth as antepartum or intrapartum as well as in verifying the classification as it has to depend on the clinical judgment of the reporting physician.

#### **Conflict of interest**

The authors declare no conflict of interest.

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