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A population-based study of the effect of pregnancy history on risk of stillbirth

Sari Räisänen[1,2,*,a] | Carol J.R. Hogue[1] | Katariina Laine[3] | Michael R. Kramer[1] | Mika Gissler[4,5] | Seppo Heinonen[6]

[1]Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA

[2]Department of Obstetrics and Gynaecology, Kuopio University Hospital, Kuopio, Finland

[3]Department of Obstetrics, Oslo University Hospital, Ullevål, Oslo, Norway

[4]National Institute for Health and Welfare (THL), Helsinki, Finland

[5]Nordic School of Public Health, Gothenburg, Sweden

[6]Department of Obstetrics and Gynaecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

*Correspondence
Sari Räisänen, P.O. Box 26, 00014 University of Helsinki, Helsinki, Finland.
Email: shraisanen@gmail.com

[a]Now at the University of Helsinki.

Abstract

Objective: To examine the effect of pregnancy history on the risk of stillbirth.

Methods: In a population-based cross-sectional study, data were reviewed from all women aged at least 20 years with singleton pregnancies in Finland between 2000 and 2010. The primary outcome—stillbirth—was defined as fetal death after 22 gestational weeks or death of a fetus weighing at least 500 g.

Results: Among 604 047 singleton pregnancies, the prevalence of stillbirth was 3.17 per 1000 deliveries. Prevalence was lowest for multiparous women without previous pregnancy loss after adjusting for major pregnancy complications associated with stillbirth (placenta previa, placental abruption, and pre-eclampsia) and other confounders. Relative to these women, stillbirth prevalence was higher among multiparous women with previous spontaneous abortion and/or stillbirth (adjusted odds ratio [aOR] 1.20, 95% confidence interval [CI] 1.05–1.36), nulliparous women with no previous pregnancy loss (aOR 1.23, 95% CI 1.10–1.38), and nulliparous women with prior spontaneous abortion (aOR 1.43, 95% CI 1.18–1.74).

Conclusion: Previous pregnancy loss was found to be an independent risk factor for stillbirth, irrespective of the number of prior deliveries.

KEYWORDS

Birth; Childbirth; Population register; Pregnancy history; Pregnancy outcome; Register; Spontaneous abortion; Stillbirth

1 | INTRODUCTION

Stillbirth is a common adverse perinatal outcome: it complicates approximately 1 of every 200 pregnancies reaching 22 weeks.[1] Globally, there are an estimated 2.64 million stillbirths every year.[2] Obstetric complications, placental diseases such as abruption, and genetic or structural abnormalities are reported to be common causes of stillbirth, but the etiology remains unclear in many cases.[3,4] A recent systematic review and meta-analysis of population-based studies[5] showed that the major risk factors for stillbirth included nulliparity, obesity (body mass index ≥30 [calculated as weight in kilograms divided by the square of height in meters]), advanced maternal age (≥35 years), and smoking during pregnancy. Maternal pre-existing diabetes,[5,6] pre-eclampsia,[5] assisted reproductive technology,[5,7] small-for-gestational-age (SGA) fetus,[5] SGA in prior pregnancy,[8] and low education level[5] have also been shown to be associated with stillbirth.

A recent population-based case–control study in the USA[6] aimed to identify risk factors for stillbirth that might be identified at the start of pregnancy and reported that pregnancy history was the strongest risk factor for stillbirth (defined as fetal death at ≥20 weeks). Risk of stillbirth was lowest for multiparous women without prior spontaneous abortion or prior stillbirth, and increased progressively for nulliparous women without a previous spontaneous abortion, nulliparous women with history of spontaneous abortion, and then multiparous women with prior stillbirth.[6]

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In a large population-based study in Sweden,[9] an increased prevalence of stillbirth was associated with three or more spontaneous abortions among nulliparous women with a singleton pregnancy. A smaller population-based study in Scotland[10] reported no significant association between prior spontaneous abortion and stillbirth among nulliparous women with singleton pregnancies; however, it reported a twofold higher stillbirth rate among nulliparous women with a prior spontaneous abortion than among women with one prior live birth. Three other studies[8,11–13] reported a positive association between stillbirth in a first pregnancy and stillbirth in a second pregnancy, but none of the three studies had information on prior spontaneous abortions. It has been suggested that spontaneous abortion and stillbirth have a partly similar pathogenesis, including abnormal placentation.[14–17] Impaired placentation has also been associated with several major pregnancy complications such as pre-eclampsia, pregnancy-induced hypertension, placental abruption, and SGA—all conditions associated with stillbirth.[14,17]

Finland is a Nordic welfare state with much publicly funded health care, such as free access to prenatal care for all women, and its prevalence of stillbirth is among the lowest in the world.[18] The aim of the present study was to examine the effect of pregnancy history including information on prior deliveries, prior spontaneous abortion, and prior stillbirth on the risk of stillbirth, taking into account several major pregnancy complications that might cause stillbirth, such as placenta previa, placental abruption, and pre-eclampsia.

2 | MATERIALS AND METHODS

In a population-based cross-sectional study in Finland, data were reviewed from all women with singleton deliveries between January 1, 2000, and December 31, 2010. The National Institute for Health and Welfare (THL) accepted the study plan and authorized use of the data, as required by the Finnish national data protection legislation (reference no. 1749/5.05.00/2011). Informed consent was not needed.

Information on all live births and stillbirths has been recorded in the Finnish Medical Birth Register (MBR) since 1987. For each delivery, information on sociodemographic characteristics, maternal reproductive history, medical history, pregnancy and delivery characteristics of the index pregnancy, and maternal and neonatal diagnoses during the first postnatal week was gathered. In addition to the MBR, information was obtained from the Population Register Centre on live births and Statistics Finland on stillbirths and deaths during the first week of life. Overall, the data covered 100% of birth events.

For the present study, MBR data were supplemented by information on maternal medical conditions such as pre-eclampsia, gestational diabetes, and maternal pre-existing diabetes mellitus, on the basis of International Classification of Diseases 10 (ICD-10) codes in the Hospital Discharge Register. This register was established in 1967 and contains information on all diagnoses, medical interventions, and surgical procedures of inpatient and outpatient care in specialized healthcare facilities in Finland. Information on major congenital anomalies defined by ICD-9-CM codes was gathered from the Register of

Congenital Malformations (established in 1963). Encrypted personal identification numbers were used to link the study women's data among the three national health registers, which are all maintained by the THL (register keeper).

For the present analysis, women younger than 20 years were excluded to allow better control of confounding factors. Additionally, multiple births were excluded owing to the higher risk of pregnancy complications. Stillbirth was defined as fetal death after 22 gestational weeks or death of a fetus weighing 500 g or more. Spontaneous abortion was defined as loss of pregnancy before 22 weeks. Maternal age was classified as 20–29 years, 30–39 years, or 40 years or older. Pregnancy history was classified as one of four groups: nulliparous women (no prior deliveries) without prior spontaneous abortion, nulliparous women with prior spontaneous abortion, multiparous women (≥1 prior delivery) without either prior spontaneous abortion or stillbirth, and multiparous women with prior spontaneous and/or stillbirth.

Pregnancy length was estimated on the basis of first- or second-trimester ultrasonography measurements or from maternal report of the date of her last menstrual period. More than 99% of pregnant women in Finland have pregnancy length estimated by ultrasonography. In vitro fertilization (IVF) included intracytoplasmic sperm injection and frozen embryo transfer. SGA was identified if the sex- and parity-specific birth weight was more than two standard deviations below the mean, as determined by the Finnish population-based birth curves for 1996–2008.[19] SGA in a prior pregnancy was defined as birth weight below the 10th percentile. Prior preterm delivery was defined as delivery before 37 weeks. ICD-10 codes were used to identify and define placenta previa (O44), placental abruption (O45), pre-eclampsia (O14 and O15), gestational diabetes (O24.4), and maternal pre-existing diabetes (O24.0 and O24.1).

Socioeconomic status was defined by maternal occupation at birth and was classified into four groups on the basis of Finland's National Classification on Socioeconomic Position, which follows international recommendations. Socioeconomic status was classified as the following five groups: upper white-collar workers, such as physicians and lawyers; lower white-collar workers, including nurses and secretaries; blue-collar workers, such as cooks and cleaners; others (women with unclassifiable occupations, including entrepreneurs, students, retired, unemployed, and housewives); and missing information. Marital status was classified as in a relationship (married or living with partner), single, or missing information. Smoking habits during pregnancy (reviewed during prenatal visits) were classified as non-smoking, smoking (quit smoking during the first trimester or continued smoking after the first trimester), or missing information.

Major congenital anomalies included structural anomalies, chromosomal defects, and congenital hypothyroidisms. Hereditary diseases and diseases not associated with congenital anomalies, dysfunction of organs or tissues, developmental disabilities, congenital infections, isolated minor dysmorphic features, normal variations and common less significant congenital anomalies were not included, as per the exclusion list of the Register of Congenital Malformations.[20]

The study data were analyzed using SPSS for Windows version 19.0 (IBM, Armonk, NY, USA). Bivariate analyses were performed to

identify differences between stillbirths and live births using the χ^2 test for dichotomous and categorical variables, and Mann-Whitney U test for continuous variables. Missing data were examined for pregnancy history, socioeconomic status, marital status, smoking during pregnancy, and pregnancy history, and multiple data imputation was used.

Unadjusted odds ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals (CIs) were estimated by multivariable logistic regression using stillbirth as the dependent variable. Model 1 estimated the unadjusted association between stillbirth (referent: live birth) and pregnancy history (main exposure). Model 2 estimated the association between stillbirth and pregnancy history, adjusting for maternal age, prior SGA, prior preterm delivery, socioeconomic status, smoking, gestational diabetes, pre-existing diabetes, IVF, pre-eclampsia, placenta previa, placental abruption, and major congenital anomalies. Model 3 was a partially adjusted model without major pregnancy complications (placenta previa, placental abruption, and pre-eclampsia) to assess whether such complications mediated an association between stillbirth and reproductive history. As a sensitivity analysis, models 1 and 2 were repeated for the subpopulation of women without prior stillbirth (n=3420, 0.6%) and by using non-imputed data. Differences were taken to be significant if $P<0.05$.

3 | RESULTS

During the study period, there were 640 687 deliveries. After women younger than 20 years and multiple births were excluded, data on 604 047 deliveries were reviewed. Only 867 (0.1%) had no information on pregnancy history (Fig. 1).

Overall, there were 3.17 stillbirths per 1000 deliveries (1917/604 047, 0.3%). Stillbirth was associated with prior SGA, prior preterm delivery, IVF, pre-eclampsia, placenta previa, placental abruption, SGA, and major congenital anomalies (Table 1). Stillbirth was also associated with maternal age, pregnancy history, socioeconomic status, marital status, and smoking during pregnancy (Table 1).

For most variables, the proportion of cases with missing values was very low (Table 1); the only exception was information on socioeconomic status, which had a missing rate of 16.6% (n=100 260).

The results of unadjusted (model 1) and adjusted (models 2–3) logistic regression analyses using multiple imputed data are presented in Table 2. After adjustment for the known pregnancy complications associated with stillbirth (placenta previa, placental abruption, and pre-eclampsia) and other covariates, pregnancy history was found to be an independent risk factor for stillbirth (model 2). The prevalence of stillbirth was lowest for multiparous women without prior spontaneous abortion and/or prior stillbirth (reference group). Additionally, maternal age seemed to be an independent risk factor for stillbirth: age of 30–39 years and 40 years or more was associated with significantly higher prevalence of stillbirth as compared with 20–29 years. Prior SGA, prior preterm delivery, smoking after first pregnancy trimester, and major congenital anomalies were also independent risk factors for stillbirth. In the partially adjusted model without major pregnancy complications (model 3), the ORs of pregnancy history remained almost unchanged (Table 2).

The association between pregnancy history and stillbirth identified in the main analysis (Table 2) was consistent with the findings from a sensitivity analysis restricted to women without prior stillbirth (Table 3) and an analysis using observed rather than imputed data (Table 4).

4 | DISCUSSION

Identifying which women are at high risk for adverse pregnancy outcomes such as stillbirth, SGA, or severe pre-eclampsia to optimize
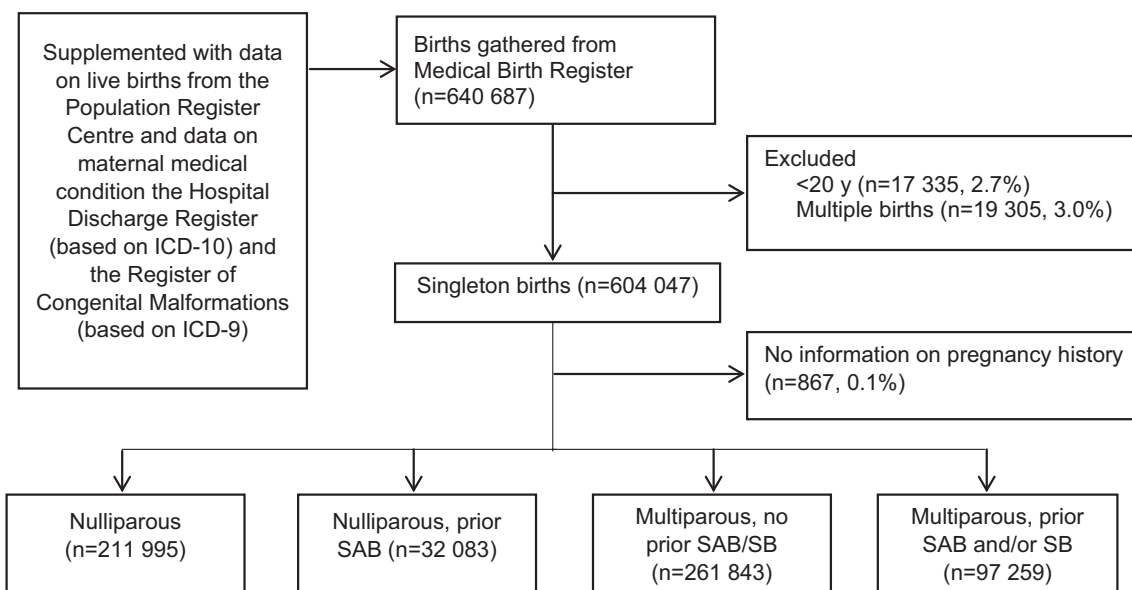

FIGURE 1 Study population. Abbreviations: ICD, International Classification of Diseases; SAB, spontaneous abortion; SB, stillbirth.

TABLE 1 Pregnancy and delivery characteristics among women with singleton deliveries (stillbirth and live births) in Finland, 2000–2010.[a]

Characteristic	Stillbirth (n=1917)	Live birth (n=602 130)	P value[b]
Maternal age, y	30.6 ± 5.7	29.8 ± 5.2	<0.001
20–29	837 (43.7)	298 605 (49.6)	
30–39	960 (50.1)	281 463 (46.7)	
≥40	120 (6.3)	22 062 (3.7)	
Pregnancy history			<0.001
Multipara, no prior spontaneous abortion or stillbirth	728 (38.0)	261 115 (43.4)	
Multipara, prior spontaneous abortion and/or stillbirth	371 (19.4)	96 888 (16.1)	
Nullipara, no prior spontaneous abortion	664 (34.6)	211 331 (35.1)	
Nullipara, prior spontaneous abortion	125 (6.6)	31 958 (5.3)	
Missing information	29 (1.5)	838 (0.1)	
Prior SGA	108 (5.6)	18 488 (3.1)	<0.001
Prior preterm delivery (<37 wk)	146 (7.6)	26 369 (4.4)	<0.001
Socioeconomic status			<0.001
Upper white-collar worker	109 (5.7)	51 556 (8.6)	
Lower white-collar worker	514 (26.8)	213 390 (35.4)	
Blue-collar worker	236 (12.3)	88 245 (14.7)	
Other[c]	354 (18.5)	149 383 (24.8)	
Missing information	704 (36.7)	99 556 (16.5)	
Marital status			<0.001
Married or cohabiting	1496 (78.0)	539 417 (89.6)	
Not married or cohabiting	125 (6.5)	35 536 (5.9)	
Missing information	296 (15.4)	27 177 (4.5)	
Smoking status			<0.001
Non-smoking	1347 (70.3)	502 072 (83.4)	
Quit smoking in 1st trimester	53 (2.8)	20 266 (3.4)	
Smoking after 1st trimester	257 (13.4)	63 951 (10.6)	
Missing information	260 (13.6)	15,840 (2.6)	
Gestational diabetes	135 (7.0)	66 124 (11.0)	<0.001
In vitro fertilization	40 (2.1)	8728 (1.4)	0.020
Pre-eclampsia	58 (3.0)	7503 (1.2)	<0.001
Pre-existing diabetes	111 (5.8)	49 086 (8.2)	<0.001
Placenta previa	15 (0.8)	1616 (0.3)	<0.001
Placental abruption	133 (6.9)	1990 (0.3)	<0.001
Pregnancy length, wk	32.5 (6.3)	39.8 (1.7)	<0.001
SGA	524 (30.6)	21 287 (3.5)	<0.001
Major congenital anomaly[d]	371 (19.4)	22 918 (3.8)	<0.001

Abbreviations: SGA, small for gestational age (<2 SD mean birth weight); ICD, International Classification of Diseases.
[a]Values are given as mean ± SD or number (percentage), unless indicated otherwise.
[b]By χ^2 or Mann-Whitney U test.
[c]Included entrepreneurs, students, retired women, unemployed women, housewives, and women with unclassifiable occupations.
[d]Included all structural anomalies, chromosomal defects, and congenital hypothyroidisms identified by ICD-10 codes. Cases of hereditary and other diseases not associated with congenital malformations, dysfunction of organs or tissues, developmental disabilities, congenital infections, isolated minor dysmorphic features, normal variations, and common less significant congenital malformations were not included.

prenatal health care is a challenge in obstetrics. The present study found that prior spontaneous abortion assessed as part of pregnancy history is an independent risk factor for stillbirth even after adjustment for maternal age and major pregnancy complications associated with stillbirth.

Previous studies to determine the association between prior spontaneous abortion and stillbirth are scarce and have reported inconsistent findings. For example, a large population-based study in Sweden[9] reported a positive association between three or more spontaneous

TABLE 2 ORs for stillbirth among women with singleton deliveries in Finland in 2000–2010 (n=604 047).[a]

Characteristic	Model 1, unadjusted OR (95% CI)	Model 2, aOR (95% CI)	Model 3, aOR (95% CI)
Maternal age group, y			
20–29	1	1	1
30–39	1.22 (1.11–1.34)	1.24 (1.13–1.37)	1.27 (1.15–1.40)
≥40	1.94 (1.60–2.35)	1.86 (1.52–2.27)	1.96 (1.60–2.39)
Pregnancy history			
Multipara, no prior spontaneous abortion and stillbirth	1	1	1
Multipara, prior spontaneous abortion and/or stillbirth	1.37 (1.20–1.55)	1.20 (1.05–1.36)	1.23 (1.08–1.40)
Nullipara, no prior spontaneous abortion	1.18 (1.01–1.24)	1.23 (1.10–1.38)	1.25 (1.12–1.40)
Nullipara, prior spontaneous abortion	1.38 (1.14–1.67)	1.43 (1.18–1.74)	1.47 (1.21–1.78)
Prior SGA	1.89 (1.55–2.29)	1.52 (1.23–1.87)	1.62 (1.32–1.98)
Prior preterm delivery (<37 wk)	1.80 (1.52–2.13)	1.45 (1.21–1.75)	1.65 (1.38–1.97)
Socioeconomic status			
Upper white-collar worker	1		
Lower white-collar worker	1.08 (0.87–1.34)	–	–
Blue-collar worker	1.15 (0.93–1.43)	–	–
Other[b]	1.06 (0.89–1.26)	–	–
Not married or cohabiting	1.29 (1.10–1.53)	–	–
Smoking status			
Non-smoking	1	1	1
Quit smoking in 1st trimester	1.00 (0.76–1.32)	1.04 (0.78–1.37)	1.00 (0.76–1.33)
Smoking after 1st trimester	1.44 (1.26–1.64)	1.47 (1.27–1.70)	1.52 (1.32–1.76)
Gestational diabetes	0.61 (0.52–0.73)	0.54 (0.41–0.72)	0.53 (0.40–0.70)
Pre-existing diabetes	0.69 (0.57–0.84)	1.07 (0.79–1.45)	1.08 (0.80–1.45)
In vitro fertilization	1.45 (1.06–1.98)	1.24 (0.90–1.70)	1.25 (0.91–1.72)
Pre-eclampsia	2.47 (1.90–3.21)	1.72 (1.31–2.27)	–
Placenta previa	2.93 (1.76–4.88)	1.69 (1.29–2.21)	–
Placental abruption	22.39 (18.75–22.92)	18.13 (15.02–21.88)	–
Major congenital anomaly[c]	6.07 (5.41–6.80)	5.80 (5.17–6.49)	5.94 (5.30–6.66)

Abbreviations: OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; SGA, small for gestational age (<2 SD mean birth weight); ICD, International Classification of Diseases.

[a]Logistic regression analyses using multiple imputed data. Model 1 was unadjusted. Model 2 was adjusted by maternal age, pregnancy history, prior SGA, prior preterm delivery, smoking status, gestational diabetes, pre–existing diabetes, in vitro fertilization, pre-eclampsia, placenta previa, placental abruption, and major congenital anomaly. Model 3 was adjusted by maternal age, pregnancy history, prior SGA, prior preterm delivery, smoking status, gestational diabetes, pre-existing diabetes, in vitro fertilization, and major congenital anomaly.

[b]Included entrepreneurs, students, retired women, unemployed women, housewives, and women with unclassifiable occupations.

[c]Included all structural anomalies, chromosomal defects, and congenital hypothyroidisms identified by ICD-10 codes. Cases with hereditary diseases and other diseases not associated with congenital malformations, dysfunction of organs or tissues, developmental disabilities, congenital infections, isolated minor dysmorphic features, normal variations, and common less significant congenital malformations were not included.

abortions and stillbirth (fetal death at ≥28 weeks) among nulliparous women with singleton pregnancy, whereas a small population-based study in Scotland[10] found no association between prior spontaneous abortion (<24 weeks) and stillbirth (fetal death at ≥24 weeks) among this group of women.

The present results have confirmed that prior stillbirth is associated with stillbirth in subsequent pregnancies, as reported previously.[8,11,12] However, a direct comparison with other studies is hampered by differences in study design: in some previous investigations, the effect of prior spontaneous abortion was not studied, or the definitions of spontaneous abortion and stillbirth differed from those in the present

study. Furthermore, previous studies lacked information on several important covariates associated with stillbirth, including congenital anomalies[8–11] and adverse pregnancy outcomes such as prior SGA or preterm delivery.[8,10–12] The present results can be compared with those of a population-based case–control study conducted by the Stillbirth Collaborative Research Network[6] in the USA, which assessed risk factors identifiable in early pregnancy. That investigation had findings similar to those of the present study; however, it did not control for major pregnancy complications associated with stillbirth owing to study design. In the present study, the association between pregnancy history and stillbirth remained almost unchanged after controlling for major

TABLE 3 ORs for stillbirth among women with singleton deliveries, excluding women with prior stillbirths, in Finland in 2000–2010 (n=600 627).[a]

Characteristic	Model 1, unadjusted OR (95% CI)	Model 2, adjusted OR (95% CI)
Maternal age group, y		
20–29	1	1
30–39	1.22 (1.11–1.34)	1.25 (1.13–1.38)
≥40	1.93 (1.59–2.35)	1.87 (1.53–2.29)
Pregnancy history		
Multipara, no prior spontaneous abortion	1	1
Multipara, prior spontaneous abortion	1.30 (1.15–1.49)	1.17 (1.03–1.33)
Nullipara, no prior spontaneous abortion	1.13 (1.01–1.25)	1.23 (1.10–1.38)
Nullipara, prior spontaneous abortion	1.40 (1.15–1.69)	1.42 (1.16–1.72)
Prior SGA	1.79 (1.46–2.20)	1.52 (1.22–1.89)
Prior preterm delivery (<37 wk)	1.64 (1.37–1.98)	1.36 (1.11–1.65)
Socioeconomic status		
Upper white-collar worker	1	
Lower white-collar worker	1.09 (0.90–1.30)	–
Blue-collar worker	1.14 (0.90–1.46)	–
Other[b]	1.05 (0.88–1.25)	–
Not married or cohabiting	1.29 (1.10–1.53)	–
Smoking status		
Non–smoking	1	1
Quit smoking in 1st trimester	0.99 (0.75–1.30)	1.05 (0.79–1.39)
Smoking after 1st trimester	1.50 (1.30–1.73)	1.48 (1.28–1.71)
Gestational diabetes	0.62 (0.52–0.74)	0.54 (0.41–0.71)
Pre-existing diabetes	0.71 (0.58–0.86)	1.10 (0.81–1.50)
In vitro fertilization	1.47 (1.07–2.02)	1.26 (0.91–1.73)
Pre-eclampsia	2.50 (1.92–3.26)	1.83 (1.39–2.42)
Placenta previa	2.80 (1.65–4.74)	1.61 (0.92–2.82)
Placental abruption	22.39 (18.62–26.92)	18.34 (15.16–21.18)
Major congenital anomaly[c]	6.05 (5.39–6.79)	5.79 (5.16–6.49)

Abbreviations: OR, odds ratio; CI, confidence interval; SGA, small for gestational age (<2 SD mean birth weight); ICD, International Classification of Diseases.

[a]Logistic regression analyses using imputed data. Model 1 was unadjusted. Model 2 was adjusted by maternal age, pregnancy history, prior SGA, prior preterm delivery, smoking status, gestational diabetes, pre-existing diabetes, in vitro fertilization, pre-eclampsia, placenta previa, placental abruption, and major congenital anomaly.

[b]Included entrepreneurs, students, retired women, unemployed women, housewives and all women with unclassifiable occupations.

[c]Included all structural anomalies, chromosomal defects, and congenital hypothyroidisms identified by ICD-10 codes. Cases with hereditary diseases and other diseases not associated with congenital malformations, dysfunction of organs or tissues, developmental disabilities, congenital infections, isolated minor dysmorphic features, normal variations, and common less significant congenital malformations were not included.

pregnancy complications, suggesting that pregnancy complications did not mediate the association between pregnancy history and stillbirth.

The present bivariate analyses showed that women with stillbirth had a higher frequency of SGA (>2 SDs lower than mean birth weight) neonates as compared with women with live birth. This finding is in accordance with previous studies to determine the timing of fetal death before stillbirth delivery.[5,21] Additionally, the present study found that prior SGA was associated with a 1.5-times higher prevalence of stillbirth as compared with women with no prior SGA, in accordance with a Swedish study.[8] In the present study, index

pregnancy information on SGA—a disorder associated with impaired placentation[14,17]—was not used as a covariate because it is a causal factor in the pathway between impaired placentation and stillbirth. Impaired placentation leads to placental dysfunction and is likely to reduce fetal growth, potentially resulting in a live-born SGA neonate or ultimately to stillbirth.

The present findings concerning risk factors for stillbirth are in accordance with previous studies confirming a positive association between stillbirth and advanced maternal age,[5] smoking during pregnancy,[5,6] IVF,[7] and major congenital anomalies.[3,4] In the present study,

TABLE 4 ORs for stillbirth among women with singleton births in Finland in 2000–2010, calculated with observed data (n=604 047).[a]

Characteristic	Model 1, unadjusted OR (95% CI)	Model 2, adjusted OR (95% CI)
Maternal age group, y		
20–29	1	1
30–39	1.22 (1.11–1.34)	1.24 (1.13–1.37)
≥40	1.94 (1.60–2.35)	1.82 (1.49–2.22)
Pregnancy history		
Multipara, no prior spontaneous abortion or stillbirth	1	1
Multipara, prior spontaneous abortion and/or stillbirth	1.37 (1.21–1.56)	1.21 (1.07–1.38)
Nullipara, no prior spontaneous abortion	1.13 (1.01–1.25)	1.27 (1.14–1.42)
Nullipara, prior spontaneous abortion	1.40 (1.16–1.70)	1.48 (1.22–1.80)
Missing information	12.41 (8.51–18.10)	4.19 (2.81–6.27)
Prior SGA	1.89 (1.55–2.29)	1.52 (1.23–1.87)
Prior preterm delivery (<37 wk)	1.80 (1.52–2.13)	1.45 (1.21–1.75)
Socioeconomic status		
Upper white-collar worker	1	–
Lower white-collar worker	1.14 (0.93–1.40)	–
Blue-collar worker	1.27 (1.01–1.59)	–
Other[b]	1.12 (0.90–1.39)	–
Missing information	3.35 (2.73–4.09)	–
Marital status		
Married or cohabiting	1	–
Not married or cohabiting	1.27 (1.06–1.52)	–
Missing information	3.93 (3.47–4.45)	–
Smoking status		
Non-smoking	1	1
Quit smoking in 1st trimester	0.98 (0.74–1.28)	1.03 (0.78–1.36)
Smoking after 1st trimester	1.50 (1.31–1.71)	1.47 (1.29–1.69)
Missing information	6.12 (5.35–6.99)	5.46 (4.75–6.29)
Gestational diabetes	0.61 (0.52–0.73)	0.55 (0.42–0.73)
Pre-existing diabetes	0.69 (0.57–0.84)	1.06 (0.78–1.44)
In vitro fertilization	1.45 (1.06–1.98)	1.28 (0.93–1.76)
Pre-eclampsia	2.47 (1.90–3.21)	1.67 (1.27–2.20)
Placenta previa	2.93 (1.76–4.88)	1.80 (1.07–3.04)
Placental abruption	22.48 (18.75–26.96)	17.24 (14.26–20.84)
Major congenital anomaly[c]	6.07 (5.41–6.80)	5.75 (5.13–6.46)

Abbreviations: OR, odds ratio; CI, confidence interval; SGA, small for gestational age (<2 SD mean birth weight); ICD, International Classification of Diseases.

[a]Unconditional logistic regression analyses using non-imputed data. Model 1 was unadjusted. Model 2 was adjusted by maternal age, pregnancy history, prior SGA, prior preterm delivery, smoking status, gestational diabetes, pre-existing diabetes, in vitro fertilization, pre-eclampsia, placenta previa, placental abruption, and major congenital anomaly.

[b]Included entrepreneurs, students, retired women, unemployed women, housewives and all women with unclassifiable occupations.

[c]Included all structural anomalies, chromosomal defects, and congenital hypothyroidisms identified by ICD-10 codes. Cases with hereditary diseases and other diseases not associated with congenital malformations, dysfunction of organs or tissues, developmental disabilities, congenital infections, isolated minor dysmorphic features, normal variations, and common less significant congenital malformations were not included.

the association between socioeconomic status and stillbirth was statistically nonsignificant in the multivariate analyses. A few studies have reported disparities in socioeconomic status for stillbirth,[5] but it is difficult to compare the data owing to differences in the definition. The association between disparities in socioeconomic status

and stillbirth has been partly explained by a lack of prenatal care; in Finland, however, all pregnant women have free access to publicly funded health care.

The present results did not confirm the positive association between maternal pre-existing diabetes or gestational diabetes and stillbirth

reported by several previous studies.[5,6,22] This discrepancy might be explained by the policies of pre-conception planning for all pregnancies among women with pre-existing diabetes and a detailed surveillance program for women with pre-existing and gestational diabetes.

A strength of the present study was the use of validated health registers[23,24] covering information on the whole population, thereby minimizing selection and misclassification biases. The information on stillbirth was highly reliable because it was gathered from the MBR and supplemented with data compiled by Statistics Finland on still-births and deaths during the first week of life. Furthermore, the data included information on the most important known risk factors for stillbirth except maternal weight (gathered since 2004) and major pregnancy complications.

The study has some limitations. The most important potential source of bias was the proportion of missing information on socio-economic status, marital status, and smoking during pregnancy. The proportion of cases with missing information was substantially higher among women with stillbirth than among women with live birth; this is understandable, because stillbirth is a sensitive situation in which some of the background information might remain unregistered. To counter this, multiple imputed data were used in the multivariable analyses.

On the basis of the present evidence, the most important reproductive risk factors for stillbirth are previous adverse pregnancy outcomes such as prior stillbirth and prior SGA. The present study also showed that a prior spontaneous abortion is an independent risk factor for stillbirth irrespective of prior childbirths. This information could also be used to select nulliparous women at high risk for close obstetric surveillance.

AUTHOR CONTRIBUTIONS

All authors designed the study, analyzed the data, and drafted the manuscript.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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