

Sleep Position, Fetal Growth Restriction, and Late-Pregnancy Stillbirth

The Sydney Stillbirth Study

Adrienne Gordon, FRACP, PhD, Camille Raynes-Greenow, MPH, PhD, Diana Bond, RN, Jonathan Morris, FRANZCOG, PhD, William Rawlinson, FRACP, PhD, and Heather Jeffery, FRACP, PhD

OBJECTIVE: To identify potentially modifiable risk factors for late-pregnancy stillbirth.

METHODS: This was a population-based matched case-control study of pregnant women at 32 weeks of gestation or greater booked into tertiary maternity hospitals in metropolitan Sydney between January 2006 and December 2011. The case group consisted of women with singleton pregnancies with antepartum fetal death in utero. Women in the control group were matched for booking hospital and expected delivery date with women in the case group. Data collection was performed using a semistructured interview and included validated questionnaires for specific risk factors.

From the RPA Newborn Care, Royal Prince Alfred Hospital, Sydney Medical School, Sydney School of Public Health, and the Discipline of Paediatrics and Child Health, University of Sydney, Perinatal Research, Kolling Institute of Medical Research, Sydney University, Royal North Shore Hospital, St Leonards, New South Wales, the University of New South Wales, and South Eastern Area Laboratory Services, Virology Division, Randwick, Australia.

Supported by the Stillbirth Foundation Australia.

Presented at the 2012 International Conference on Stillbirth, SIDS and Infant Survival, October 4–7, 2012, Baltimore, Maryland.

The authors thank Elizabeth Headley, Angela Carberry, and Rachel Jones for recruitment, data collection, and data entry; Deborah De Wilde, Perinatal Social Worker, for recruitment and data collection; the Principal Investigators at the recruiting hospitals: Professor Michael Peek–Nepean, Professor John Smolencic–Liverpool, Dr Antonia Shand–Royal Hospital for Women, Professor Jonathan Morris–Royal North Shore, Mater and North Shore Private, Professor Heather Jeffery–Royal Prince Alfred, Dr Janet Vaughan–Canterbury, and Dr Terry McGee–Westmead; and the families who participated in the study and contributed so much at such a difficult time.

Corresponding author: Adrienne Gordon, FRACP, PhD, RPA Newborn Care, Royal Prince Alfred Hospital, Missenden Road, Camperdown, Sydney NSW 2050, Australia; e-mail: adrienne.gordon@sydney.edu.au.

Financial Disclosure

Ms. Bond received a salary as a Research Officer during the conduct of this study that was paid for with a grant received by the Stillbirth Foundation Australia. Dr. Morris is currently chairman of the board of directors of the Stillbirth Foundation Australia and has been a director since 2008. The other authors did not report any potential conflicts of interest.

© 2015 by The American College of Obstetricians and Gynecologists. Published by Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0029-7844/15

Adjusted odds ratios (ORs) were calculated for a priori-specified risk factors using conditional logistic regression.

RESULTS: There were 103 women in the case group and 192 women in the control group. Mean gestation was 36 weeks. Supine sleeping was reported by 10 of 103 (9.7%) of women who experienced late-pregnancy stillbirth and by 4 of 192 (2.1%) of women in the control group (adjusted OR 6.26, 95% confidence interval [CI] 1.2–34). Women who experienced stillbirth were more likely to: have been followed during pregnancy for suspected fetal growth restriction, 11.7% compared with 1.6% (adjusted OR 5.5, 95% CI 1.36–22.5); not be in paid work, 25.2% compared with 9.4% (adjusted OR 2.9, 95% CI 1.1–7.6); and to have not received further education beyond high school, 41.7% compared with 25.5% (adjusted OR 1.9, 95% CI 1.1–3.5). None of the deaths to women who reported supine sleeping were classified as unexplained.

CONCLUSION: This study suggests that supine sleep position may be an additional risk for late-pregnancy stillbirth in an already compromised fetus. The clinical management of suspected fetal growth restriction should be investigated further as a means of reducing late stillbirth.

(*Obstet Gynecol* 2015;125:347–55)

DOI: 10.1097/AOG.0000000000000627

LEVEL OF EVIDENCE: II

The prevention of stillbirth is one of the greatest challenges of maternity care in the modern world, with an estimated 2.64 million fetuses stillborn each year.¹ Recent meta-analyses of population-based studies in high-income countries show that the major risk factors for stillbirth are maternal age, smoking, and obesity, with a population-attributable risk of 30%.² Unacceptably high numbers of stillbirths, however, remain unexplained, particularly in late pregnancy, and there is an urgent need to identify and target appropriate areas for research and prevention of stillbirth.^{3–6}



Recently the influence of maternal sleep practices on stillbirth has gained some attention.^{7,8} Sleep-disordered breathing in pregnancy is associated with increased risks of gestational hypertension, preeclampsia, and small-for-gestational age (SGA),^{9,10} all of which are associated with stillbirth.¹¹ Furthermore, obstructive sleep apnea has been associated with reduced fetal growth in late pregnancy.¹² However, only a single case report has described an association between sleep-disordered breathing and stillbirth.¹³ The first report of an association between maternal sleep practices and late stillbirth came from a case-control study in Auckland published in 2011.¹⁴ Women with a late-pregnancy stillbirth were found to be twice as likely to have slept in a position other than left lateral on the night of (before) the death of their fetus (adjusted odds ratio [OR] 2.03, 95% confidence interval [CI] 1.24–3.29). The population-attributable risk for non-left-sided sleep position was 37%.¹⁴

In March 2012 a cross-sectional study from Ghana reported an association between supine sleep position and stillbirth (OR 8.0, 95% CI 1.5–43.2; $P=.016$)⁷ and supine sleep position and low birth weight (OR 5.0, 95% CI 1.2–20.2; $P=.025$). The authors postulated that in their population, more than one-fourth of stillbirths might be avoided by altering maternal sleep position.

Such a potentially modifiable risk factor with seemingly low risk of side effects and sufficient biological plausibility merits careful consideration. When the Auckland study was published, an accompanying editorial advised caution and urgently called for further research to confirm or refute the results.¹⁵ A protocol for another 3-year case-control study in the United Kingdom has recently been published¹⁶ and a larger multicentre stillbirth case-control study in New Zealand has been recruiting since February 2012. However, pregnant women may already be adopting the health message because one state in Australia has distributed a pregnancy information leaflet advising women to sleep on their left side¹⁷ and the prevalence of non-left sleeping in New Zealand has already decreased (McCowan L. Survey of maternal sleep position in late pregnancy; unpublished data).

The main aim of the Sydney Stillbirth Study was to document risk factors for late-pregnancy stillbirth with a particular focus on those risks that are potentially modifiable. This article presents the results of this case-control study with a particular focus on the results related to maternal sleep exposure factors.

MATERIALS AND METHODS

The Sydney Stillbirth Study was a population-based matched case-control study that recruited pregnant

women at 32 weeks of gestation or greater booked into maternity hospitals in metropolitan Sydney. Ethical approval was obtained through the National Ethics Application process Study ID 0605-081M and the study was registered in the Australia and New Zealand Clinical Trial Register ACTRN12609000990224.

The study recruited progressively from a total of nine hospitals in the Sydney metropolitan area from January 2006 until December 2011. All tertiary maternity centers were included plus the two largest private hospitals and one district hospital. This represents a total annual birth cohort of 29,804 and approximately 31% of the births in New South Wales. New South Wales is the most populous state in Australia, and its 95,000 births per year account for approximately 30% of the nation's births.

The case group consisted of women with singleton pregnancies who experienced stillbirth at 32 weeks of gestation or greater. Stillbirth was defined as the death of a fetus before birth and therefore could occur antepartum or intrapartum. Women in the case group were ascertained by clinicians who provided written information to families and contacted research staff. Initial contact was then made with the family by a dedicated research team taking into consideration the sensitive situation and advice from staff caring for the mother and family. Every effort was made to contact the family during the hospitalization. An appointment for the detailed face-to-face interview (see subsequently) was made with the family at this time. Case ascertainment was checked weekly by the research team and crosschecked at the end of recruitment through recruiting hospitals' perinatal mortality review committees. Women in the control group were pregnant women at 32 weeks of gestation or greater with singleton pregnancies who were matched for booking hospital and gestation (by estimated date of delivery) and were recruited contemporaneously with women in the case group. For the seven public hospitals, women in the control group were identified through the hospital database matched for hospital and gestation then randomly selected. Two women in the control group were selected per woman in the case group. For the two private hospitals where a centralized booking system did not exist, women in the control group were matched for gestation and treating obstetrician. Secondary to smaller numbers of women per obstetrician, it was not always possible to select two women in the control group per women in the case group; therefore, women in the case group were matched to one woman in the control group if necessary. Women in the control group were contacted and invited to participate using a standardized ProForma



and an appointment for the face-to-face interview was organized. For women who declined or after two attempts did not return phone calls, the next randomly selected matched control woman was contacted.

The following were excluded from the study: 1) women who identified as Aboriginal or Torres Strait Islander, 2) fetuses that had any known lethal or chromosomal anomalies, and 3) terminations of pregnancy. Aboriginal or Torres Strait Islander women were excluded because the projected number from population data that would be expected to be recruited was only four as well as cultural sensitivities that precluded conducting an identical interview within this group of women.

An identical face-to-face interview was conducted for both women in the case group and those in the control group. For women in the case group, this was as soon as possible after the stillbirth and women in the control group at the equivalent gestation to the matched woman in the case group with the aim of interviewing within 1 week of recruitment. Interviews were held in an appropriate setting as decided by the consented family (often their home). Detailed anthropometry was performed with plotting of birth weight, head circumference, and length on Australian population-based growth charts.¹⁸ Maternal and birth data that comprise part of the New South Wales midwives data collection¹⁹ was verified by the patient medical records. Time of death was estimated where possible through clinical history of last movement, timing of diagnosis of fetal death, skin condition of the fetus at birth, and autopsy (if performed). Time of death then was classified into one of four groups: 1) day (6:00 AM to 2:00 PM), 2) afternoon or evening (2:00 to 10:00 PM), 3) overnight (10:00 PM to 6:00 AM), or 4) unknown or inestimable. Cause of death was classified using the Perinatal Society of Australia and New Zealand–Perinatal Death Classification by a multidisciplinary committee within the recruiting hospitals as per New South Wales policy and provided to the study team.²⁰

Detailed clinical history was collected using interviewer-administered questionnaires based on the Perinatal Society of Australia and New Zealand Clinical Practice Guideline clinical history checklist (see the Appendix, available online at <http://links.lww.com/AOG/A596>). Data included demographic details of the mother, father, pregnancy, labor and delivery, previous and current obstetric history, medication use, smoking and substance use, screening and diagnostic monitoring, medical conditions, and pregnancy complications. Women were classified as “suspected fetal growth restriction” if they had received extra ultrasound scans or appointments in late pregnancy specifically for concern

regarding the fetus’ growth regardless of the result of the scan or appointment. Urinary tract infection was defined by self-report of treatment for 5 days or more with antibiotics after a positive urine sample. Ethnicity was classified using the Standard Australian Classification of Countries. Maternal body mass index (BMI, calculated as weight (kg)/[height (m)]²) was calculated using first weight and height documented at the antenatal booking appointment. Additional information was collected on potentially relevant exposures that are not included on the Perinatal Society of Australia and New Zealand Clinical Practice Guideline: exercise, complementary therapies or medications, caffeine consumption, dental treatment, and symptoms of periodontal disease. For these exposures the gestational age of exposure, frequency and duration, and related health care attendances were documented.

We used several different questions to assess maternal sleep exposure variables. These included maternal sleep position, snoring, and daytime sleepiness. The Epworth sleepiness questionnaire and the Berlin Questionnaire^{21,22} were used for sleepiness and sleep-disordered breathing; both have been used in pregnant populations.²³ Women were coded as having symptoms consistent with sleep apnea if they answered “yes” to one or more of the following questions: 1) Have you or your partner noted that you choke or gasp during sleep? 2) Do you regularly wake up feeling that you have not had enough sleep? 3) Do you wake up with a morning headache? 4) Do you regularly feel so tired that you have to sleep in the afternoon? Specific questions were asked about usual sleep position when not pregnant and usual sleep position in pregnancy with a particular focus on the previous month. Sleep position was classified as supine, prone, left lateral, right lateral, both sides, combination of positions, or unsure. This information was also cross-checked with the mother’s partner if present at the interview and prompts were used if women were unsure.

Small for gestational age was the chosen risk factor for the sample size calculation secondary to the availability of robust data for both stillborn fetuses and liveborn neonates in Australia. Based on a prevalence of 10% SGA, to detect an OR of 2.5 between women in the case group and those in the control group, we estimated a sample size of 100 women in the case group and 200 women in the control group with 80% power and α set at 5%. Univariate analysis was performed using χ^2 tests for categorical data and Student’s *t* test for continuous variables. Conditional logistic regression was used to calculate adjusted ORs for a priori-specified risk factors and to account for matching within strata. Risk factors identified as



significant on univariate analysis or clearly associated with stillbirth in the literature even if nonsignificant were included in the multivariate models. If a documented previously known risk factor was present in so few participants as to make no difference to the multivariate model, it was not included. Reference categories for the multivariable models were defined as the groups likely to have the lowest risk. Population-attributable risk percent was calculated using the following formula where Px represents the population exposed in the control group: $100 \times (P_x \times [OR - 1]) / (1 + [P_x \times (OR - 1)])$. Statistical analysis was performed using IBM SPSS Statistics 21.0. Significance for all analyses was set at the 5% level.

RESULTS

There were 153 eligible women who experienced a stillbirth during the study period. One hundred nineteen women were approached by the research team to participate in the study, and 103 consented, representing 86% of approached and 67% of eligible women. Of the 34 not approached, the reasons are documented in the study flowchart (Fig. 1). In 11 cases, the main reason for refusal was preference for nonapproach by the treating clinical team (predominantly for women with mental health concerns). There were 227 randomly selected women matched for booking hospital and expected date of delivery who were eligible for the control group; 192 (84.6%)

consented. The median time between the fetal loss and interview for women in the case group was 3 days (interquartile range 1, 17). Of women who had a stillborn fetus, 62% were interviewed within 1 week of the loss. Women in the control group generally were recruited within 1 week of the matched women in the case group, and median time to interview was 13 days from the date of delivery of the matched stillborn fetus (interquartile range 6, 24).

Of the women in the case group, 98 of 103 (95%) had placental histopathology performed and 59 of 103 (57%) had a full autopsy. The three most common classifications of cause of death were unexplained antepartum death, perinatal infection, and fetal growth restriction (Fig. 2). Time of death was unknown or not able to be estimated for approximately one in four of the stillborn fetuses (23.8%). For those fetuses for which time of death was able to be determined, the majority were assigned to the overnight group (Fig. 3).

Demographic data are shown in Table 1. Women who had a stillbirth were significantly more likely to be in unpaid work and to have had high school education only. There was a trend to association with stillbirth for women who had BMIs of 30 or above that did not reach statistical significance (OR 2.1, 95% CI 0.95–4.6). Fetuses who were stillborn were no more likely to be male than female but were significantly more likely to be SGA using both less than the 10th percentile (OR 3.8, 95% CI 1.8–8.2) and less

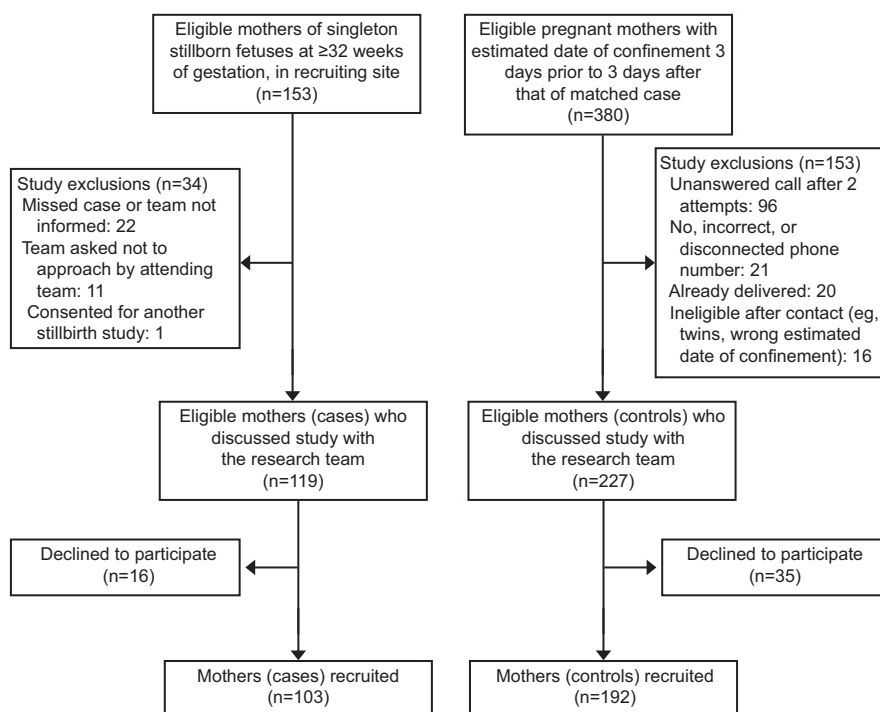


Fig. 1. Study flow chart.

Gordon. Risk Factors for Late-Pregnancy Stillbirth. *Obstet Gynecol* 2015.



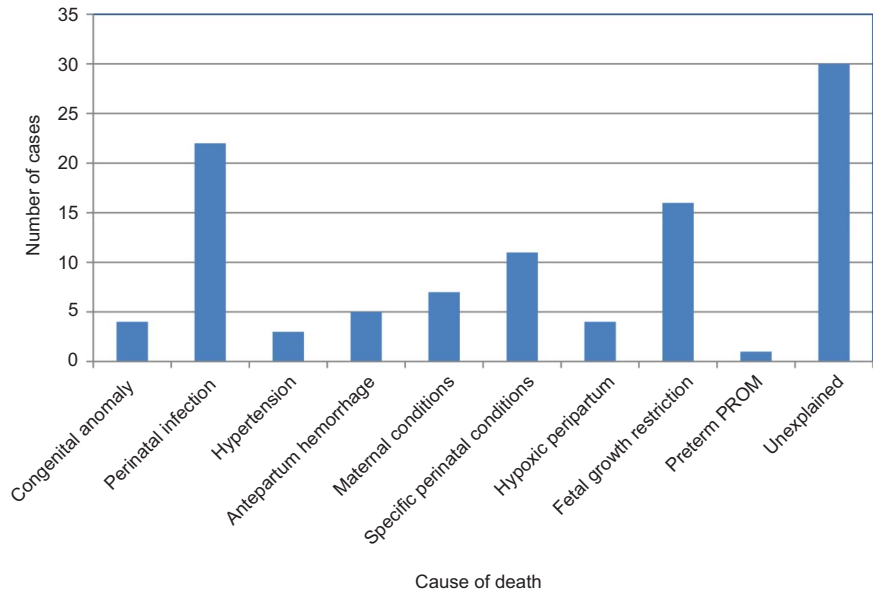


Fig. 2. Cause of death using Perinatal Society of Australia and New Zealand perinatal death classification. PROM, premature rupture of membranes.

Gordon. *Risk Factors for Late-Pregnancy Stillbirth. Obstet Gynecol* 2015.

than the third percentile (OR 3.6, 95% CI 1.2–10.9). There was no significant difference in birth length between fetuses in the case group and neonates in the control group.

Pregnancy-related conditions for women in the case group and those in the control group are shown in Table 2. The only conditions significantly associated with stillbirth on univariate analysis were suspected fetal growth restriction (OR 8.3, 95% CI 2.3–30) and supine sleeping in pregnancy over the last month (OR 5.0, 95% CI 1.5–16.5). There was a high proportion of self-reported snoring in both women in the case group, 51 of 103 (49%), and women in the control group, 87 of 192 (45%) with no significant difference seen

(OR 1.2, 95% CI 0.7–1.9). There was also no association between self-reported symptoms of sleep apnea for women who had stillborn fetuses (OR 1.2, 95% CI 0.6–2.1). Mean Epworth sleepiness score was 6.6 (standard deviation 4.3) for women who had stillborn fetuses and 5.1 (standard deviation 3.6) for women in the control group ($P=.11$).

The adjusted multivariate analysis showed significant associations with late-pregnancy stillbirth and suspected fetal growth restriction, 12 of 103 women in the case group compared with 3 of 192 women in the control group (adjusted OR 5.5, 95% CI 1.36–22.5), unpaid employment status in 26 of 103 women in the case group compared with 18 of 192 women in the

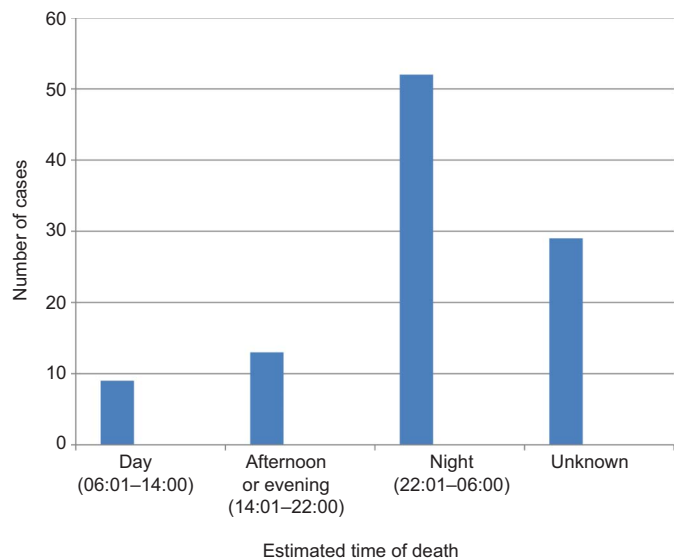


Fig. 3. Estimated time of death.

Gordon. *Risk Factors for Late-Pregnancy Stillbirth. Obstet Gynecol* 2015.



Table 1. Maternal and Neonatal Demographic Data

Characteristic	Women in the Case Group (n=103)	Women in the Control Group (n=192)	OR (95% CI)
Maternal			
Age (y)			
Younger than 35	73 (70.9)	121 (63)	Reference
35–39	22 (21.4)	53 (27.6)	0.62 (0.3–1.1)
40 or older	8 (9.4)	18 (7.8)	0.67 (0.26–1.7)
BMI (kg/m ²)			
Less than 25	62 (62.6)	129 (67.9)	Reference
25–29.9	22 (22.2)	44 (23.2)	1.1 (0.6–2.0)
30 or higher	15 (15.2)	17 (8.9)	2.1 (0.95–4.6)
Primiparous	53 (51.5)	104 (54.2)	0.9 (0.55–1.5)
Not in paid work	26 (25.2)	18 (9.4)	3.2 (1.7–6.3)
Living with partner	91 (88.3)	183 (95.3)	0.65 (0.14–2.8)
Smoking	14 (13.6)	25 (13)	1.05 (0.52–2.1)
Recreational drug use	3 (2.9)	4 (2.1)	1.4 (0.3–6.4)
Education to high school or less	43 (41.7)	49 (25.5)	2.1 (1.2–3.5)
Born in Australia	52 (50.5)	110 (57.3)	0.76 (0.47–1.2)
Neonatal			
Male	45 (43.7)	89 (46.4)	1.1 (0.68–1.8)
SGA less than the 3rd percentile	9 (8.7)	5 (2.6)	3.6 (1.2–10.9)
SGA less than the 10th percentile	21 (20.4)	12 (6.2)	3.8 (1.8–8.2)
Length less than the 10th percentile	12 (11.7)	12 (6.2)	1.9 (0.8–4.6)

OR, odds ratio; CI, confidence interval; BMI, body mass index; SGA, small for gestational age. Data are n (%) unless otherwise specified.

control group (adjusted OR 2.9, 95% CI 1.1–7.6), no further education beyond high school in 43 of 103 women in the case group compared with 49 of 192 women in the control group (adjusted OR 1.9, 95% CI 1.1–3.5), and reported supine sleep position in 10 of 103 compared with 4 of 192 (adjusted OR 6.26, 95% CI 1.2–34) (Table 3). The population-attributable risk for reported supine sleep position was 9.88% (95% CI 5.67–14.1%).

We examined the relationship between SGA birth weight and maternal BMI 25 or higher (overweight or obese) with supine sleeping during pregnancy (Table 4).

The analysis is not adjusted because the individual cell numbers are too small. The distribution of maternal BMI 25 or higher does not appear to differ for the supine sleepers and whether they had stillborn fetuses; however, SGA less than the 10th percentile is overrepresented in the supine sleepers as a group as well as having an association with late-pregnancy stillbirth. This finding needs to be interpreted with caution because the study was not powered to test this interaction. It may suggest that SGA less than the 10th percentile birth weight is an effect modifier on the relationship between maternal BMI and supine sleeping;

Table 2. Medical Conditions in Pregnancy

Condition	Women in the Case Group (n=103)	Women in the Control Group (n=192)	OR (95% CI)
Hypertension in pregnancy	3 (2.9)	3 (1.6)	1.9 (0.37–9.5)
Gestational diabetes	10 (9.7)	14 (7.3)	1.4 (0.6–3.2)
Treated for urinary tract infection in pregnancy	13 (12.6)	13 (6.8)	2.0 (0.9–4.4)
GBS-positive	9 (8.7)	27 (14.1)	0.6 (0.2–1.3)
Suspected fetal growth restriction	12 (11.7)	3 (1.6)	8.3 (2.3–30)
Anemia	21 (20.4)	43 (22.4)	0.9 (0.5–1.6)
Early bleeding	18 (17.5)	35 (18.2)	0.95 (0.5–1.8)
Supine sleeping	10 (9.7)	4 (2.1)	5.0 (1.5–16.5)
Snoring	51 (49)	87 (45)	1.2 (0.7–1.9)
Symptoms of sleep apnea	13 (12)	21 (11)	1.2 (0.6–2.1)

OR, odds ratio; CI, confidence interval; GBS, group B streptococcus. Data are n (%) unless otherwise specified.



Table 3. Multivariate Analysis*

Characteristic	Women in the Case Group (n=103)	Women in the Control Group (n=192)	Adjusted OR (95% CI)
Maternal age (y)			
Younger than 35	73 (70.9)	121 (63)	Reference
35–39	22 (21.4)	53 (27.6)	0.72 (0.34–1.5)
40 or older	8 (9.4)	18 (7.8)	0.81 (0.25–2.6)
Maternal BMI (kg/m ²)			
Less than 25	62 (62.6)	129 (67.9)	Reference
25–29.9	22 (22.2)	44 (23.2)	1.4 (0.72–2.7)
30 or higher	15 (15.2)	17 (8.9)	1.7 (0.7–4.4)
Primiparous	53 (51.5)	104 (54.2)	0.95 (0.52–1.72)
Not in paid work	26 (25.2)	18 (9.4)	2.9 (1.1–7.6)
Sleep apnea symptoms	13 (12)	21 (11)	1.6 (0.65–4.2)
Smoking	14 (13.6)	25 (13)	0.88 (0.35–2.1)
Suspected fetal growth restriction	12 (11.7)	3 (1.6)	5.5 (1.36–22.5)
Education to high school or less	43 (41.7)	49 (25.5)	1.9 (1.1–3.5)
Sleep position			
Left	32 (31)	48 (25)	Reference
Right	14 (13.6)	25 (13)	1.1 (0.43–2.6)
Back	10 (9.7)	4 (2.1)	6.26 (1.2–34)
Other	47 (45.6)	115 (60)	0.69 (0.36–1.3)

OR, odds ratio; CI, confidence interval; BMI, body mass index.

Data are n (%) unless otherwise specified.

* All risk factors in the table adjusted for in the multivariate model.

however, this would need to be tested in a sufficiently large study to assess interactions.

Table 5 shows cause of death classification where usual reported sleeping position in the last month was supine compared with nonsupine sleepers. None of the supine sleepers were classified as unexplained deaths. This may reflect a potential underlying reason or “vulnerability” for stillbirth.

DISCUSSION

We report an association between reported usual maternal sleeping position during pregnancy and late-pregnancy stillbirth. We postulate that our findings indicate supine sleep position may be an additional risk for a vulnerable fetus. Other risk factors identified were suspected fetal growth restriction, not being in paid work, and lower educational status.

The study further adds cause and timing of death to the literature on late-pregnancy stillbirth and has documented a relationship with SGA and supine sleep. This finding is consistent with the biological rationale that supine sleep places increased pressure on the inferior vena cava and aorta potentially reducing venous return and subsequently uterine and placental blood flow. There are several physiologic studies and a systematic review demonstrating reduced maternal cardiac output, maternal hypotension, and reduced fetal oxygenation with supine and right-sided position compared with left.^{24–26} Two systematic reviews document evidence of an association with sleep-disordered breathing and adverse pregnancy outcome,^{27,28} and there is growing interest in the importance of sleep, sleep-disordered breathing, and pregnancy complications.²⁹

Table 4. Associations Among Small for Gestational Age, Body Mass Index, and Supine Sleep

Sleep Position	Women in the Case Group	Women in the Control Group	OR (95% CI)
Supine	n=10	n=4	
SGA less than the 10th percentile	4 (40)	1 (25)	NS
Overweight or obese	3 (30)	0	NS
Nonsupine	n=93	n=188	
SGA less than the 10th percentile	17 (18.3)	11 (5.9)	3.6 (1.6–8.0)
Overweight or obese	34 (36.6)	61 (32.4)	NS

OR, odds ratio; CI, confidence interval; SGA, small for gestational age; NS, nonsignificant.

Data are n (%) unless otherwise specified.



Table 5. Perinatal Society of Australia and New Zealand Perinatal Death Classification by Reported Maternal Sleep Position

PSANZ-PDC	Supine Sleep	Nonsupine Sleep
Congenital anomaly	0	4 (4.3)*
Perinatal infection	3 (30)	19 (20.4)
Hypertension	0	3 (3.2)
Antepartum hemorrhage	1 (10)	4 (4.3)
Maternal conditions	2 (20)	5 (5.4)
Specific perinatal conditions	0	11 (11.8)
Hypoxic peripartum	0	4 (4.3)
Fetal growth restriction	3 (30)	13 (14)
Preterm PROM	1 (10)	0
Unexplained	0	30 (32.3)

PSANZ-PDC, Perinatal Society of Australia and New Zealand Perinatal Death Classification; PROM, premature rupture of membranes.

Data are n (%).

* These congenital anomalies were unknown before the stillbirth and subsequent investigations; three cases were trisomy 21— one case with myeloproliferative disease; one case was congenital leukemia.

A recent editorial has postulated a “triple risk” hypothesis for stillbirth.³⁰ The hypothesis proposes that stillbirth results from a combination of: 1) maternal risk factors (eg, maternal age, obesity, smoking), 2) fetal and placental risk factors (eg, fetal growth restriction, placental insufficiency), and 3) a stressor (eg, venocaval compression from maternal supine sleep position). Our study supports this hypothesis.

The Sydney Stillbirth Study had significant strengths in its study design. Women in the control group were recruited contemporaneously to women in the case group and were recruited while still pregnant so as to minimize recall bias as much as possible. They were randomly selected to improve generalizability to the general pregnant population and to minimize selection bias. Both women in the case group and those in the control group were blinded to the underlying hypotheses for the study. A structured interview was performed and the research team was all trained in interview technique to ensure reliability. All interviews were recorded and qualitative data transcribed verbatim. Demographic data were validated using patient medical records and classification of cause of death was performed independently by the hospital mortality review committees. The sleep position question focused on “usual” sleep position over the past month, which should result in less differential misclassification between women in the case group and those in the control group compared with focusing on one particular night. The study was population-based, representative of

a large proportion of births in New South Wales, and had a high consent rate for both women in the case group and those in the control group, especially considering the difficult time for families.

There are, however, inherent limitations to such a study design. One is recall bias related to both the time delay between recruitment and interview and differential recall between women in the case group and those in the control group. We tried to reduce this limitation, and the average time between stillbirth and interview was relatively short. Previous research has demonstrated that families recall details related to adverse events very clearly,³¹ which could contribute to differential recall. However, we did not note any difference between women in the case group and those in the control group with respect to maternal snoring perhaps indicating a lack of this recall bias. We were unable to validate maternal sleep position in this study; however, we concurrently assessed a random sample of 20 women in late pregnancy using a device that measures position and reported a high correlation with maternal self-report and the objective measurement (70%). We did not use gold standard sleep study data to assess sleep-disordered breathing because it would not have been possible. We did however use validated scales of sleep-disordered breathing and snoring, which have been used in pregnant populations. We are unable to comment on length of sleep and any dose-response relationship, unlike a previous study.¹⁴ We did however attempt to determine timing of death and in those in whom this was possible, the majority occurred overnight. There is only one other study that has assessed timing of death for stillbirths, which is an unpublished case-series of 60 mothers of (mostly term) stillbirths who reported that the deaths mainly occurred during sleep between 12:00 AM and 7:00 AM.³² Our study was also underpowered to assess interactions between risk factors. The currently recruiting Midland and North of England (MiNESS) study aims to recruit 291 women in the case group and 582 women in the control group to detect an interaction with an OR of 2.5.

In summary we have confirmed the findings of an association between reported maternal supine sleep position and late-pregnancy stillbirth. We have added information on cause of death and shown that the stillborn fetuses of supine sleepers all had an “explained” cause. This adds weight to the “triple risk” hypothesis that maternal supine sleep position is a risk factor for an already vulnerable fetus. We are aware of two currently recruiting observational studies in the United Kingdom and New Zealand examining this association and interactions, particularly with fetal



growth restriction. The next step after completion of these studies may not be a large-scale randomized trial secondary to feasibility but rather a rigorously evaluated population-based public health intervention that is sufficiently powered to address stillbirth as well as “near miss” perinatal outcomes. Such an intervention for stillbirth prevention would need to carefully consider the way to convey the opposite message for mothers’ sleep position in late pregnancy from the back to sleep advice they receive for their newborns without creating increased anxiety. It will be imperative to ensure that interventions or campaigns are applicable, transferable, and testable in different populations.

REFERENCES

- Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. *Lancet* 2011;377:1319–30.
- Flenady V, Koopmans L, Middleton P, Froen JF, Smith GC, Gibbons K, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. *Lancet* 2011; 377:1331–40.
- Fretts RC, Boyd ME, Usher RH, Usher HA. The changing pattern of fetal death, 1961–1988. *Obstet Gynecol* 1992;79:35–9.
- Gordon A, Jeffery HE. Classification and description of stillbirths in New South Wales, 2002–2004. *Med J Aust* 2008;188:645–8.
- Silver RM, Varner MW, Reddy U, Goldenberg R, Pinar H, Conway D, et al. Work-up of stillbirth: a review of the evidence. *Am J Obstet Gynecol* 2007;196:433–44.
- Stillbirth Collaborative Research Network Writing Group. Causes of death among stillbirths. *JAMA* 2011;306:2459–68.
- Owusu JT, Anderson FJ, Coleman J, Oppong S, Seffah JD, Aikins A, et al. Association of maternal sleep practices with pre-eclampsia, low birth weight, and stillbirth among Ghanaian women. *Int J Gynaecol Obstet* 2013;121:261–5.
- Stacey T, Thompson JM, Mitchell EA, Ekeroma AJ, Zuccollo JM, McCowan LM. The Auckland Stillbirth study, a case-control study exploring modifiable risk factors for third trimester stillbirth: methods and rationale. *Aust N Z J Obstet Gynaecol* 2011;51:3–8.
- Izci-Balserak B, Pien GW. Sleep-disordered breathing and pregnancy: potential mechanisms and evidence for maternal and fetal morbidity. *Curr Opin Pulm Med* 2010;16:574–82.
- Louis J, Auckley D, Sokol RJ, Mercer BM. Maternal and neonatal morbidities associated with obstetric sleep apnea complicating pregnancy. *Am J Obstet Gynecol* 2010;202:261.e1–5.
- Franklin KA, Holmgren PA, Jönsson F, Poromaa N, Stenlund H, Svanborg E. Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. *Chest* 2000;117:137–41.
- Fung AM, Wilson D, Lappas M, Howard M, Barnes M, O’Donoghue F, et al. Effects of maternal obstructive sleep apnea on fetal growth: a prospective cohort study. *PloS One* 2013;8:e68057.
- Brain KA, Thornton J, Sarkar A, Johnson AO. Obstructive sleep apnoea and fetal death: successful treatment with continuous positive airway pressure. *Br J Obstet Gynaecol* 2001;108: 543–4.
- Stacey T, Thompson JM, Mitchell EA, Ekeroma AJ, Zuccollo JM, McCowan LM. Association between maternal sleep practices and risk of late stillbirth: a case-control study. *BMJ* 2011;342:d3403.
- Chappell LC, Smith G. Should pregnant women sleep on their left? *BMJ* 2011;342:d3659.
- Platts J, Mitchell EA, Stacey T, Martin BL, Roberts D, McCowan L, et al. The Midland and North of England Stillbirth Study (MiNESS). *BMC Pregnancy Childbirth* 2014;14:171.
- Warland J. Keeping baby SAFE in pregnancy: evaluating the brochure. *Midwifery* 2013;29:174–9.
- Roberts CL, Lancaster PA. Australian national birthweight percentiles by gestational age. *Med J Aust* 1999;170:114–8.
- Centre for Epidemiology and Evidence. New South Wales mothers and babies 2010. Sydney (Australia): NSW Ministry of Health; 2012.
- Flenady V, King J, Charles A, Gardener G, Ellwood D, Day K, et al. PSANZ clinical practice guideline for perinatal mortality. Version 2.2. Available at: <http://www.psanz.com.au/special-interest/perinatal-mortality-group/psanzcpg>. Retrieved June 1, 2014.
- Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540–5.
- Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999;131:485–91.
- Izci B, Martin S, Dundas K, Liston W, Calder A, Douglas N. Sleep complaints: snoring and daytime sleepiness in pregnant and preeclamptic women. *Sleep Med Rev* 2005;6:163–9.
- Kaupilla A, Koskinen M, Puolakka J, Tuimala R, Kuikka J. Decreased intervillous and unchanged myometrial blood flow in supine recumbency. *Obstet Gynecol* 1980;55:203–5.
- Milsom I, Forssman L. Factors influencing aortocaval compression in late pregnancy. *Am J Obstet Gynecol* 1984;148:764–71.
- Cluver C, Novikova N, Hofmeyr GJ, Hall DR. Maternal position during caesarean section for preventing maternal and neonatal complications. *The Cochrane Database of Systematic Reviews* 2010, Issue 6. Art. No.: CD007623. DOI: 10.1002/14651858.CD007623.pub3.
- Luque-Fernandez MA, Bain P, Gelaye B, Redline S, Williams MA. Sleep-disordered breathing and gestational diabetes mellitus: a metaanalysis of 9,795 participants enrolled in epidemiological observational studies. *Diabetes Care* 2013;36:3353–60.
- Pamidi S, Pinto L, Marc I, Benedetti A, Schwartzman K, Kimoff RJ. Maternal sleep-disordered breathing and adverse pregnancy outcomes: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2014;210:52.e1–14.
- Romero R, Badr MS. A role for sleep disorders in pregnancy complications: challenges and opportunities. *Am J Obstet Gynecol* 2014;210:3–11.
- Warland J, Mitchell EA. A triple risk model for unexplained late stillbirth. *BMC Pregnancy Childbirth* 2014;14:142.
- Gibbons LE, Ponsonby AL, Dwyer T. A comparison of prospective and retrospective responses on sudden infant death syndrome by case and control mothers. *Am J Epidemiol* 1993;137:654–9.
- Collins J. Umbilical cord accidents—time of death. Available at: http://www.preginst.com/case_study/case_study_3.html. Retrieved February 7, 2014.

