Smoking cessation and preterm birth in second pregnancy among women who smoked in their first

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Abstract

Introduction

The benefit of smoking cessation in reducing the risk of preterm birth is well established. Relatively less well understood is the prevalence of smoking cessation maintenance at the next pregnancy and the associated preterm risk reduction. The aim of this study was to estimate the prevalence of maintenance of smoking cessation at second pregnancy, and the associated relative risk of preterm birth.

Methods

This was a longitudinal study with retrospectively obtained records of births to multiparous women who smoked in the pregnancy of their first birth in New South Wales, 1994-2016 (N=63,195 mothers). Relative risks (RR) of preterm birth of the second child were estimated for smoking cessation with adjustment for final gestational age of the first birth, maternal age at the first birth, change in socioeconomic disadvantage between the first and second pregnancy, interpregnancy interval and calendar time.

Results

Approximately 34% (N=21,540) women who smoked during their first pregnancy did not smoke in the second pregnancy. Smoking cessation among women who smoked at first pregnancy was associated with a 26% (95% CI: 21%, 31%) decrease in risk of preterm birth at second pregnancy.

Conclusion

Despite smoking during first pregnancy, smoking cessation was achieved and maintained by more than one-third of women in their second pregnancy with encouraging levels of preterm risk reduction. It is well-established that the period after birth provides an opportunity to reduce smoking-related morbidity for both the mother and neonate. Our results indicate that this period also offers an opportunity to prevent morbidity of the future pregnancy.

What this study adds

A considerable amount of research has been undertaken on the effects of smoking during pregnancy on birth outcomes, the influence of postpartum smoking on the health of the mother and newborn child, and postpartum smoking cessation. However, follow-up of women after giving birth does not tend to be long enough to observe smoking and outcomes of subsequent pregnancies. We show that smoking cessation in the subsequent pregnancy is achievable by a large proportion of women despite smoking in their first pregnancy, which translates to clear reductions in risk of preterm birth in the subsequent pregnancy.

Introduction

Preterm birth is the single largest contributor to perinatal mortality and morbidity in high income countries, with few behavioural exposures as well-established as tobacco smoke.[1] Maternal smoking during pregnancy restricts blood flow to the placenta and uterus and leads to systemic inflammation, which are all pathways that can lead to iatrogenic and idiopathic preterm birth, and its precursors such as fetal growth restriction.[2, 3]

Tobacco smoking is a modifiable risk factor and promoting cessation prior to and during pregnancy is a clinical priority.[4] A pooled estimate from 20 prospective studies indicates that smoking during pregnancy is associated with a 27% higher odds of preterm birth.[5] These risks appear to be reversible. That is, smoking cessation, especially early in pregnancy, can reduce the risk of preterm by up to 20%.[6] However, little is known about maintenance of tobacco abstinence at and associated health benefits at future pregnancies. More specifically, few studies have estimated the prevalence of maintenance of smoking cessation in future pregnancies,[7-12] and a paucity of these studies go on to further investigate subsequent influence on risk of preterm birth.[12] Studies from New South Wales (NSW), Australia, reported that the proportion of women who smoke in their first pregnancy but do not smoke in their next pregnancy increased from 27% from the period 1994 to 2004,[12] to 34% in the period 2000 to 2010.[11] The extent to which further improvement has been achieved remains unclear and it is plausible that improvement has reached a threshold. The proportion of smokers who stop smoking in their second pregnancy appears to be consistent between cohorts from high-income countries, at 34% in Australia (NSW),[11] 31% in Norway,[10] and 33% in the US (Georgia).[8] Two previous studies have investigated associations between smoking cessation between pregnancies and risk of preterm birth but did not directly estimate expected risk reductions for women who smoked in their first pregnancy.[12, 13] Approximations, derived by taking the ratio of the odds ratios reported by studies from Australia[12] and Sweden[13] for moderate smokers (1 – 9 cigarettes per day) in first pregnancy, provides putative indication for a potential 20% and 21% reduction in the *risk* of preterm birth <37 weeks and 32 – 36 weeks, respectively. The reduction in risk of preterm birth attributable to smoking cessation among women who smoked in first pregnancy is yet to be directly estimated.

The aim of this study was to estimate the prevalence of maintenance of smoking cessation at second pregnancy, and the associated relative risk of preterm birth.

Materials and methods

Study design and setting

This was a retrospective longitudinal study on smoking cessation and risk of preterm birth in New South Wales (NSW), Australia, 1994-2016. We estimated the association between smoking during pregnancy and preterm birth of the second child for women who smoked in their first pregnancy.

Participants and exclusions

Participants were women who gave birth to two singleton children. Multiple births and births with missing primary exposure (smoking status during pregnancy) or outcome (gestational age) were also excluded. Other Australian reports indicate that although late induced abortions comprise only 1% of total induced abortions,[14] their inclusion can affect preterm birth rates at these early gestations.[15] Births at gestational ages < 22 weeks and > 44 weeks were excluded to minimise the influence of late induced abortions (medical abortions ≥ 20 weeks) and gestational age errors.

Data sources

Records from the Perinatal Data Collection were obtained from the NSW Department of Health. The Perinatal Data Collection is a legally mandated database of all births in NSW public and private hospitals, as well as homebirths attended by a midwife or medical practitioner. Perinatal registrations are completed at the time of separation for all stillborn or live born neonates of ≥ 400 grams birth weight or ≥ 20 weeks' gestation. De-identified unique reference numbers for all participants enabled longitudinal matching of mothers to their babies. These reference numbers were derived by the NSW Department of Health, Centre for Health Record Linkage. For every birth the attending midwife or medical practitioner completes a form giving demographic, medical and obstetric information on the mother, and information on the labour, delivery and condition of the infant. The index of relative socioeconomic disadvantage (IRSD) was estimated at the statistical local area and obtained from the Australian Bureau of Statistics.

Outcome

In this study we used the clinical best estimate of final gestational age (completed weeks), which was predominantly estimated by ultrasound due to the recency of the cohort. Preterm birth was defined as birth before 37 completed weeks of final gestational age and was not separated into spontaneous and indicated sub-classifications because smoking can potentially elevate risk of both idiopathic and iatrogenic preterm birth.

Exposure

Self-reported smoking status during pregnancy was available for the whole study period and was the primary exposure included in this study. Associations with smoking "dose" were estimated as a secondary exposure when data was available. Specifically, dose was assessed as the number of cigarettes smoked per day (derived as 'none', '1-10 cigarettes per day', '>10 cigarettes per day', 'unknown') in the second half of pregnancy and was available until 2010, inclusive. Associations with timing of smoking in pregnancy was also assessed as a secondary exposure when data was available. From 2011, the timing of smoking in pregnancy was recorded ('smoking in the first half of pregnancy' vs 'smoking in the second half of pregnancy').

Covariates

The IRSD was categorised into quintiles for summarisation of study population characteristics. Lower IRSD scores indicate relatively more disadvantage based on a range of indicators including, but not limited to low income, unemployment, no internet connection, less than 12 years of primary plus secondary education, occupation status, low rent, single parent, disability, dwelling overcrowding, and English language proficiency.[16] Maternal age at first birth was categorised as <20 years, 20 – 24 years, 25 – 29 years, 30 – 34 years, 35 – 39 years and ≥ 40 years. Year of birth was derived from full birth dates. Interpregnancy interval was derived as the time interval between the exact date of first birth and the start of pregnancy of the next birth (birth date minus final gestational age) and was rounded to whole months. Interpregnancy interval was categorised as < 6 months, 6 – 11 months, 12 – 17 months, 18 – 23 months, 24 – 59 months, 60 – 120 months, and > 120 months.

Statistical analyses

For women who smoked in first pregnancy we estimated the relative risk of preterm birth in second pregnancy for those who did not smoke compared to those who smoked in the second pregnancy. We adjusted for the final gestational age of the first birth, maternal age at the first birth, change in socioeconomic disadvantage between the first and second pregnancy, interpregnancy interval and calendar time (per 5-6 years) of first birth as continuous linear terms. Relative risk (RR) and 95% Confidence Intervals (CI) were estimated by Poisson regression with robust ('sandwich') standard errors.[17] All analyses were conducted with R v4.0.1.[18]

Results

From a starting population of 2,109,871 births, we sequentially excluded 62,511 multiple births; 602 births with missing final gestational age; 612 births with missing parity; 6,382 births with duplicate parity; and 3,052 births with gestational ages < 22 weeks or > 44 weeks. We then limited the cohort to the births of the first two children for each woman (1,001,596 births excluded). We excluded all births for women for whom smoking status was not known for one of more of these pregnancies (1,779 births excluded). We then restricted to births to women who smoked in the pregnancy of their first child (905,168 births to 452,584 women excluded). After these exclusions there were 63,195 mothers and their first two children contributing to the final study cohort for the primary analysis (N = 126,390 total births).

The prevalence of preterm birth was 7% (N=4,523) at the second pregnancy. At first birth, approximately 27% of the women were < 20 years old and 6% followed short intervals of less than 6 months (Table 1). There were more women who had their first birth earlier in the study period because of the longer follow-up time. The socioeconomic index (IRSD) for a large proportion of the study population (72%) was below the national population mean (1,000).

The proportion of women who quit smoking prior to the second pregnancy comprised more than a third of the women in the cohort (34%). This included almost half (47%) of women who quit smoking before the second half of the first pregnancy, and more than one-fifth (22%) of women who smoked throughout their first pregnancy (Table 2).

The adjusted RRs of preterm birth at the second pregnancy indicated a 26% (95% CI: 21%, 31%) lower risk for quitters than women who remained smokers and 33% (95% CI: 27%, 38%) lower risk for quitters than women who smoked more than 10 cigarettes per day in second pregnancy. For women who smoked throughout the first pregnancy, the observed preterm birth risk reductions were similar for women who quit smoking in the second half of the second pregnancy (32%, 95% CI: 7%, 51%) as women who did not smoke in the second pregnancy (30%, 95% CI: 6%, 49%). For women who stopped smoking before the second half of the first pregnancy, point estimates indicated that the observed preterm birth risk reductions were lower for women who stopped smoking in the second half of the second pregnancy (55%, 95% CI: 0%, 70%) than women who did not smoke in the second pregnancy (8%, 95% CI: -37%, 38%). Point estimates indicated that the risk of preterm birth in the second pregnancy was higher for women who resumed smoking in the second half of the second pregnancy after not smoking in the first half of the pregnancy.

The E-value for the association between smoking cessation in the second pregnancy and preterm birth was 2.04. The confidence limits for all associations for women who stopped smoking in the first half of the first pregnancy were 1. For women who smoked throughout the first pregnancy the E-values for the associations between preterm birth and smoking cessation in the second pregnancy, and smoking cessation in the first half of the second pregnancy were 2.21 and 2.30, respectively.

Discussion

For women who smoked in their first pregnancy, we estimated the association between maintenance of smoking cessation in the second pregnancy and risk of subsequent preterm birth. We found that more than a third of women who smoked during their first pregnancy did not smoke in their second pregnancy, which indicates further improvement in the same region since the last published estimate in 2008 (27%),[12] and suggests that smoking cessation is achievable for a substantial fraction of Australian women. Smoking cessation at second pregnancy was achieved by as many as half of the women who stopped smoking before the second half of their previous pregnancy. However, almost two-thirds of women who smoked during their first pregnancy continued to smoke in their second pregnancy. As our study was based on linked perinatal records we did not have information on the reasons why these women continued to smoke in their second pregnancy; however, one potential reason against smoking cessation unique to multiparous smokers is the belief that smoking confers no additional risk after experiencing a previous successful pregnancy while smoking.[19] Conversely, previous unsuccessful pregnancy is also not necessarily associated with smoking cessation. Findings based on a US cohort selected from the National Pregnancy Risk Assessment Monitoring System indicate that women who experienced a previous preterm birth were 13% more likely to smoke in pregnancy.[20] An alternative explanation for this association is that results were confounded by smoking in first pregnancy. Indeed, an earlier study from the US (Michigan) that restricted analyses to first pregnancy smokers observed that 18-24 year old women and 25 – 30 year old women were 16% and 13% less likely to smoke during pregnancy if the previous pregnancy resulted in a preterm birth.[21] Notwithstanding such factors that affect smoking behaviour, our results provide credence for targeting within-pregnancy and post-pregnancy interventions to first pregnancy smokers, for whom we observed the potential reduction in risk of preterm birth from smoking cessation is 26% compared to smoking continuation, and 33% compared to heavy smoking (< 10 cigarettes per day).

Associations specific to the time period of smoking in pregnancy varied considerably. Firstly, we observed a higher estimate of risk for women who did not smoke in the first half but did smoke in the second half of their second pregnancy compared to women who smoked throughout their second pregnancy. This estimate was imprecise due to the very small numbers of women. Nonetheless, the higher risk of preterm birth for women that relapse back to smoking in the second half of pregnancy might be due to stressful events,[22-24] particularly among the women who demonstrated the ability to quit smoking during the first pregnancy. Secondly, we observed that the risk of preterm birth was either similar or higher for women who stopped smoking in the second half of their second pregnancy than for women who reported that they did not smoke throughout their second pregnancy. Although it is plausible that the benefits of smoking cessation are limited to the second half of pregnancy because the exposure is encountered closer to the time of normal parturition,[25] we propose the following alternative explanations. Under-reporting of smoking during the second pregnancy might be more prevalent among women who stopped smoking during their previous pregnancy, if we assume that these women were more health conscious or are more aware of societal pressure to not smoke during pregnancy.[19] This would lead to misclassification of women who smoked in the first half of pregnancy and those who smoked throughout pregnancy, which would inflate risk estimates of those who stated that they did not smoke. Another explanation is that smoking cessation during pregnancy is a marker for broader health related behavioural improvements and that these improvements as a whole, which included but were not limited to smoking cessation, led to the reductions in risk of preterm birth.[26] Apparent *protective* associations have been observed in studies of single pregnancies that have investigated the timing of smoking or smoking cessation in pregnancy and risk of preterm birth.[6, 25] Authors of a large US study spanning multiple states observed that among mothers who smoked prior to pregnancy the risk of preterm birth was lower for those who smoked in the third trimester compared with those who did not smoke in third trimester, and posited that spontaneous abortion (left truncation) would be more prevalent among the smokers.[6] Another study from the US (Ohio) reported that the odds ratio of PTB for women who quit smoking after second trimester relative to non-smokers was higher than the odds ratio of PTB for women who continued to smoke relative to non-smokers, although this observation was not discussed.[25] A biologically plausible explanation is that smoking reduces the risk of hypertensive disorders of pregnancy such as preeclampsia,[27] which is a cause of indicated preterm birth. However, the Ohio study also reported similar *protective* associations for both indicated and spontaneous preterm births.[25] Moreover, the section of the pathway between smoking and preeclampsia might also be explained by left truncation bias.[28] It is more likely that observed protective associations between preterm birth and smoking, or adverse associations observed between preterm birth and smoking cessation are attributable to common sources of bias in perinatal studies.[29]

Our results indicated a 26% reduction in risk of preterm birth associated with maintenance of smoking cessation in the second pregnancy, which is compatible with the previously reported consensus estimate of 27% higher odds of preterm birth associated with antenatal smoking that was based on 20 prospective studies.[5] As the magnitude of bias in the use of odds ratios to estimate relative risk increases with the prevalence of preterm birth, and the prevalence of preterm birth can vary considerably between cohorts in different settings,[30] we recommend relative risk estimation for future studies on the topic. Interestingly, adjustment for potential confounders had a small influence on the estimates of effects of smoking cessation, a result that was also observed in a study on offspring psychiatric morbidity, which applied a similar design to our study.[31] Thus, conditioning on smoking status in the first pregnancy was possibly a strength of our study as it may have led to indirectly controlling for a fraction of the underlying unmeasured confounding. Based on the E-values, to explain the association observed in our study an unmeasured confounder would have to be associated with a two-fold increase in both the risk of preterm birth and smoking cessation in second pregnancy. This condition is likely to be met for the association between smoking cessation, which tends to be accompanied by other health-related behavioural changes once pregnancy is recognised. However, the associations between behaviours (such as poor diet, physical inactivity, and alcohol consumption) tend to confer a smaller risk of preterm birth. Heavy alcohol consumption in pregnancy compared to abstinence is associated with a relative risk of approximately 1.7.[32] In our opinion, it is unlikely that our results can be fully explained by unmeasured confounding. A limitation of our study was the variation in how smoking data were collected over time in the NSW Perinatal Data Collection. A further limitation of our study was that it was retrospective and relied on self-reported smoking status. Results from a validation study imply that the magnitude of the bias in the NSW Perinatal Data Collection is small, with smoking sensitivities of 82% for preterm births and 90% for term births.[33] Nonetheless, it remains plausible that smoking status is differentially under-reported by timing of smoking cessation. Biomarkers of smoking during pregnancy would provide an opportunity to separate the relative contributions to risk reductions of smoking cessation during pregnancy and other health-related behavioural improvements during pregnancy. Although these limitations affected our antenatal smoking cessation results, we are more confident in the results from our primary analysis on smoking cessation. The retrospective design is a strength of studies on post-partum smoking because longer follow-up time can be observed. Specifically, 82% of second pregnancies in our cohort would have not been included by a prospective study with a typical 12-month follow-up period. Prospective attainment of the sample size of more than one million births included in this study would be infeasible. A limitation of our study was that we were unable to ascertain the specific timing of smoking cessation during the interpregnancy interval. As the causes of smoking and associated types of antepartum interventions differ between early/late pregnancy smokers/quitters one might also expect that the timing of cessation and knowledge of relapse are also important after pregnancy.[19, 34] A challenge in the provision of post-pregnancy counselling, not well recognised in strategies to prevent subsequent preterm birth by smoking cessation,[35] is that the interval between pregnancies can be very long. For our cohort, almost half of the women had interpregnancy intervals of two years or longer. Although maintaining abstinence from smoking after pregnancy has been comprehensively investigated,[36] further studies are required with sufficient follow-up to observe subsequent pregnancies and evaluate smoking cessation both within and between pregnancies, and subsequent effects on risk of preterm birth.

Conclusion

Smoking in the first pregnancy does not necessarily imply that women will smoke in the subsequent pregnancy. For women who smoked in their first pregnancy, smoking cessation was achieved by more than a third of these women in second pregnancy, which may achieve up to 26% reductions in the risk of preterm birth. It is well-established that the period after birth provides an opportunity to reduce smoking-related morbidity for both the mother and neonate. Our results indicate that this period also offers an opportunity to prevent morbidity of the future pregnancy.

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Ethical approval

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval for this study was obtained from the Human Research Ethics Committee, Department of Health, New South Wales (#2017/HRE0705).

Disclosure statement

The authors declare no conflicts of interest

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Contributions

GP conceptualized and designed the study and conducted the statistical analyses. GP, JD, GAT and AKR contributed to interpreting results, revisions of the manuscript and approved the final version. GP is guarantor.

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Table 1. Characteristics of the study population at first birth of the study population of women who smoked in their first pregnancy and gave birth between 1994 and 2016 in New South Wales, Australia.

	N	%
Preterm birth		
No	58,344	92
Yes	4,851	8
Age		
< 20 years	17,140	27
20-24 years	22,631	36
25-29 years	14,573	23
30-34 years	6,981	11
35-39 years	1,734	3
≥ 40 years	121	< 1
Missing	15	< 1
Year of birth		
1994 – 1999	25,848	41
2000 – 2004	16,274	26
2005 – 2009	13,025	21
2010 – 2016	8,048	13
IRSD[1]		
700 – 800	69	< 1
800 – 900	4,257	7
900 – 1000	41,513	66
1000 – 1100	15,518	25
1100 - 1200	1,274	2
Missing	564	1
Interpregnancy interval		
< 6 months	3,950	6
6 – 11 months	9,425	15
12 – 17 months	10,294	16
18 – 23 months	8,639	14
24 – 59 months	22,406	36
60– 120 months	7,165	11
> 120 months	1,296	2
Missing	20	< 1

1. Index of Relative Socio-economic Disadvantage (IRSD). Lower numbers reflect relatively greater socioeconomic disadvantage. The national mean and standard deviation are 1000 and 100 respectively.

Table 2. Unadjusted and adjusted relative risks and odds ratios for the association between preterm birth and smoking status in the second pregnancy stratified by smoking status in first pregnancy.

Smoking		Women[1]		Preterm birth in 2nd pregnancy		
1st pregnancy	2nd pregnancy	N	%	Unadjusted RR	Adjusted[2] RR	E-value (CI limit) [3]
Smoked at any time in pregnancy [4]	Did not smoke	21,540	34	0.72 (0.68, 0.77)	0.74 (0.69, 0.79)	2.04 (1.85)
	Smoked	41,655	66	Referent	Referent	NA
	< 1 cigarettes / day	19,709	34	0.65 (0.60, 0.71)	0.67 (0.62, 0.73)	2.40 (2.12)
	1-10 cigarettes / day	15,667	27	0.79 (0.73, 0.85)	0.79 (0.73, 0.86)	1.85 (1.60)
	> 10 cigarettes / day	14,758	26	Referent	Referent	NA
	Unknown	7,236	13	0.95 (0.81, 1.11)	0.95 (0.81, 1.11)	1.29 (1)
Smoked in 1st half of pregnancy only [5]	Did not smoke	822	47	0.93 (0.65, 1.32)	1.08 (0.76, 1.54)	1.37 (1)
	Smoked	925	53	Referent	Referent	NA
	Did not smoke	822	47	0.80 (0.54, 1.19)	0.92 (0.62, 1.37)	1.39 (1)
	Smoked in 1st half only	326	19	0.59 (0.34, 1.06)	0.55 (0.30, 1.00)	3.04 (1)
	Smoked in 2nd half only	56	3	1.39 (0.62, 3.11)	1.56 (0.72, 3.37)	2.49 (1)
	Smoked throughout	543	31	Referent	Referent	NA
Smoked throughout pregnancy [6]	Did not smoke	785	22	0.71 (0.54, 0.95)	0.75 (0.56, 1.00)	2.00 (1)
	Smoked	2,856	78	Referent	Referent	NA
	Did not smoke	785	22	0.67 (0.50, 0.90)	0.70 (0.51, 0.94)	2.21 (1.32)
	Smoked in 1st half only	633	17	0.69 (0.50, 0.95)	0.68 (0.49, 0.93)	2.30 (1.36)
	Smoked in 2nd half only	91	2	1.12 (0.61, 2.03)	1.05 (0.62, 1.79)	1.27 (1)
	Smoked throughout	2,132	59	Referent	Referent	NA

RR: relative risk. CI: confidence interval.

1. Total number of women included in unadjusted analyses

2. Adjusted for gestational age at first birth, maternal age at first birth, interpregnancy interval, time period of first birth and change in socioeconomic status between first and second birth.

3. E-value calculated for the adjusted RR estimates. The Confidence Interval (CI) limit of the E-value is the RR for the association between the outcome and an unmeasured confounder, and, between the exposure and an unmeasured confounder, that would be required to reduce the lower limit of the confidence interval of the adjusted RR to 1.

4. Primary analysis: N = 63,195 women who smoked at any time during the pregnancy to their first child, 1994 - 2016. Secondary analysis: Number of cigarettes smoked was available for the period 1994 to 2010 (N = 57,370 women).

5. Secondary analysis: N = 1,747 women who smoked in the first half but not the second half of the pregnancy to their first child, 2011 - 2016.

6. Secondary analysis: N = 3,641 women who smoked in both the first and second halves of the pregnancy to their first child, 2011 - 2016.