

TOBACCO

The impact of maternal smoking during pregnancy on delivery outcome

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Background: Maternal smoking during pregnancy is associated with pre-term birth, intrauterine growth retardation, a small head circumference, a low Apgar score at 5 min and stillbirths and neonatal deaths. This study was undertaken in order to investigate the impact of maternal smoking during pregnancy when all these outcomes were considered. **Methods:** With the use of the Swedish Medical Birth Registry, infants in any one of the above mentioned outcome groups were selected from 1,413,811 infants born between 1983 and 1996 with known smoking exposure in early pregnancy. Confounders such as year of birth, maternal age, parity and educational level were controlled for. The attributable risk of maternal smoking on the various negative delivery outcomes was obtained by application of the risk estimates to population counts. **Results:** The present study confirmed the associations between maternal smoking and the miscellaneous outcomes mentioned above with high significance. The odds ratios (with 95% confidence intervals) for maternal smoking (<10 cigarettes/day and ≥ 10 cigarettes/day) for any one of the outcomes were 1.39 (1.37–1.41) and 1.65 (1.62–1.68) respectively (dose-response $p < 0.001$). The number of attributable cases caused by maternal smoking was estimated at 15,000, which represents 9% of all cases and 1% of all infants born in Sweden during the study period. **Conclusion:** Maternal smoking during pregnancy accounts for a substantial part of various negative delivery outcomes.

Keywords: attributable risk, delivery outcome, maternal smoking, registry

Maternal smoking during pregnancy is associated with pre-term birth and low birth weight,^{1–5} low birth weight for gestational age,⁶ a small head circumference,^{2,7–9} a small head circumference for gestational age,⁹ a low Apgar score at 5 min,^{10,11} and stillbirths and neonatal deaths.^{2,8,12,13} The absolute risk for each of these pregnancy outcomes is not negligible and the proportion of infants affected by any of these outcomes is considerable. The magnitude of the association between maternal smoking during pregnancy and the total group of negative pregnancy outcomes should be of public interest. Furthermore, risk estimates (if calculated with enough precision) could be used to estimate the overall impact of maternal smoking on infant health at birth.

MATERIAL AND METHODS

The present study was based on all births in Sweden during 1983–1996. Information was obtained from the Swedish Medical Birth Registry (MBR), which contains medical information on nearly all deliveries in Sweden (coverage approximately 99%).¹⁴ Nearly all pregnant women receive free antenatal care. At the first visit (usually during weeks 10–12) each woman is interviewed by a midwife and, among other things, the smoking habits of the woman (none, <10 cigarettes/day, or ≥ 10

cigarettes/day) are recorded. Standardised record forms are used in all antenatal clinics, delivery units, and paediatric examinations of newborn infants. Copies of these forms are sent to the National Board of Health where they are computerised.

In order to collect information on maternal educational level, the MBR is linked to the Registry of Education kept by Statistics Sweden. The latter registry contains information on the educational levels (the 9 years of compulsory school included) of each woman and their educational levels on 1 January 1996 were linked from it. Thus, the educational levels used in this study for estimating socioeconomic status do not necessarily refer to the actual educational levels of each woman at the time she is giving birth. This also makes it possible to estimate socioeconomic status for young women. No information on educational level could be obtained for women giving birth during 1996.

Gestational age according to ultrasound examination in early pregnancy is used for most infants. If this information is lacking or seems absurd, gestational duration is estimated with a hierarchic method using information on last menstrual period (LMP), the expected date of delivery (based on clinical examination and LMP) and the estimated length of pregnancy stated by the delivery hospital.

In order to estimate expected birth weights, a Swedish standard for birth weight according to gestational age was used.¹⁵ Infants weighing less than two standard deviations

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below their expected birth weight for gestational age (-2 SD) were considered small for gestational age (SGA). Expected head circumferences according to gestational age and limits for -2 SD, were calculated using reference intervals published by Royston and Wright.¹⁶

All odds ratios (ORs) in this report were calculated using Mantel and Haenszel's¹⁷ technique. Stratification was made for year of birth, maternal age (5 year classes), parity (previous births +1 and 1-4+) and (when specified) educational level (unknown, <10 years, 10-12 years, 13-14 years and ≥ 15 years). Ninety-five % confidence intervals (95% CIs) were estimated using Miettinen's¹⁸ method.

When comparing two stratified ORs, two-tailed z-tests were carried out using the same variance as used to estimate the 95% CIs.

RESULTS

Table 1 shows the numbers and adjusted ORs for maternal smoking by pregnancy outcome and dose level. As can be seen in the table, the current study confirms previous findings of a positive association between maternal

smoking with pre-term birth, low birth weight, SGA, stillbirths and neonatal deaths, a small head circumference and a low Apgar score at 5 min. When the case group was defined as infants belonging to any one of the selected outcome groups, a convincing association with maternal smoking was demonstrated. Furthermore, for all outcomes (except neonatal deaths), highly significant dose-response effects were shown (p-values for dose trends: for Apgar scores of <7 at 5 min $p=0.0135$, for neonatal deaths $p=0.37$ and for all other outcomes $p<0.001$).

The ORs shown in table 1 were used to estimate the attributable risk of maternal smoking on the various negative pregnancy outcomes (table 2). It is a trivial fact that the estimated number of smoking-related contributions to cases not only depends on the magnitude of the association between a certain outcome and maternal smoking but also on the absolute risk for the outcome. Consequently, the number of smoking-related cases for the different outcomes varied between 149 and 7,439. For all outcomes combined (no case was represented more than once), the attributable number of cases due to

Table 1 Numbers of miscellaneous pregnancy outcomes by maternal smoking habits in early pregnancy in Sweden 1983-1996: odds ratios (ORs) with 95% CI stratified for year of birth, maternal age, parity and educational level

	Smoking		Non-smoking n	OR for smoking	
	<10 cigs/day n	≥ 10 cigs/day n		<10 cigs/day OR (95% CI)	≥ 10 cigs/day OR (95% CI)
Gestational age					
<32 weeks ^a	1,709	1,259	5,790	1.41 (1.33-1.49)	1.69 (1.58-1.80)
32-36 weeks ^a	10,880	7,892	43,627	1.18 (1.16-1.21)	1.42 (1.38-1.45)
≥ 37 weeks ^b	196,847	119,157	987,628		
Birth weight					
<2500 g ^a	9,723	7,540	28,129	1.60 (1.62-1.70)	2.15 (2.09-2.21)
≥ 2500 g ^b	199,333	120,436	1,007,465		
Birth weight for gestational age					
< -2 SD ^a	7,667	6,049	17,847	2.08 (2.02-2.13)	2.68 (2.60-2.76)
≥ -2 SD ^b	201,389	121,927	1,017,747		
Apgar score at 5 minutes					
<7 ^a	2,295	1,570	9,796	1.13 (1.07-1.18)	1.24 (1.18-1.32)
≥ 7 ^b	209,931	128,315	1,042,267		
Head circumference					
<32 cm ^a	8,494	6,240	26,724	1.48 (1.44-1.52)	1.79 (1.74-1.85)
≥ 32 cm ^b	199,029	120,864	1,000,818		
Head circumference for gestational age					
< -2 SD ^a	12,198	8,468	38,795	1.45 (1.42-1.48)	1.70 (1.65-1.73)
≥ -2 SD ^b	194,730	118,219	986,499		
Stillbirths and neonatal deaths					
Stillbirths ^a	808	688	3,324	1.16 (1.08-1.26)	1.61 (1.48-1.75)
Deaths 0-28 days ^a	733	479	2,921	1.14 (1.05-1.24)	1.18 (1.06-1.30)
Alive at 28 days ^b	213,894	130,911	1,060,053		
Any of these outcomes					
Yes ^a	31,390	22,503	110,932	1.39 (1.37-1.41)	1.65 (1.62-1.68)
No ^b	184,045	109,575	955,366		

a: Case group

b: Reference group

maternal smoking could be estimated at 15,036, which represents approximately 1% of all births.

The percentage of smokers among Swedish women declined during the study period. In 1983, 31.4% of all pregnant women smoked in early pregnancy, whereas in 1996 the corresponding percentage was 16.1%. The proportion of heavy smokers among smoking women showed a tendency to decline, but was relatively constant during the study period (1983 39.4% and 1996 36.9%). Figure 1 shows the estimated percentage of smoking-related cases (all outcomes combined) for each year of birth.

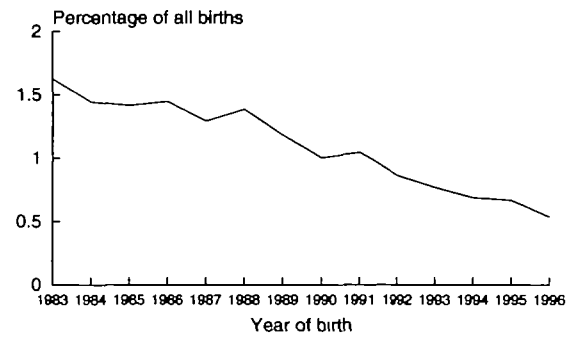


Figure 1 Estimate of the percentage of attributable cases caused by maternal smoking among all births during a certain year as specified. Cases were defined as infants in any one of the outcome groups: gestational age <37 weeks, birth weight <2500 g, SGA, head circumference <32 cm, head circumference < -2 SD of expected according to gestational age, stillbirths and neonatal deaths and Apgar score <7 at 5 min

DISCUSSION

The associations between maternal smoking and the miscellaneous outcomes which were investigated in the present study are all well known. However, these associations have never been calculated with greater precision as they are based on 1.4 million births with prospectively collected smoking information. Various confounders were adjusted for but this affected the risk estimates only marginally. The consonance between the present and previous studies and the convincing dose-response effect are further evidence that the associations between maternal smoking and those negative pregnancy outcomes are causal. However, it must be stressed that the biological mechanisms for the smoking-related risk presumably substantially differ between the outcomes considered in the present study. However, if estimating the overall impact of maternal smoking during pregnancy on infant health at birth, all the well-known, smoking-related, negative pregnancy outcomes must be considered simultaneously as a great proportion of infants are likely to appear in several outcome groups.

There are other outcomes which were not considered in the present study but for which the evidence of positive associations with maternal smoking are strong. For example, several investigators have reported a positive association between maternal smoking and infertility/subfertility,^{19,20} late spontaneous abortion,^{2,21} sudden

infant death syndrome,²²⁻²⁴ intellectual impairment in children,^{25,26} and childhood death.²⁷ Thus, the overall impact of maternal smoking on reproduction may be even more alarming than the results of the present study suggest.

There is probably no overall teratogenic effect of maternal smoking.²⁸ However, for certain malformations a positive association with maternal smoking has been reported by independent investigators (oral clefts,²⁹⁻³² limb reduction defects,³³⁻³⁵ kidney malformations,^{36,37} and craniosynostosis^{38,39}). As the absolute risk for each specific malformation is small, the number of smoking-related cases of these malformations is negligible compared to the number of cases with the outcomes considered in the present study.

The smoking information used in the present study is valid for the first trimester. In those cases where women

Table 2 The impact of maternal smoking on miscellaneous negative pregnancy outcomes in Sweden 1983-1996: risk estimates calculated after application of the stratified ORs for any smoking shown in table 1

	Risk estimates (%)			Smoking-related contribution of cases ^a		
	Smokers	Non-smokers	Total	Estimated numbers ^b	% of all cases	% of all infants
Gestational age <32 weeks	0.23	0.15	0.21	2,436	27.8	0.06
Gestational age 32-36 weeks	5.40	4.30	4.60	3,625	5.8	0.27
Birth weight <2500 g	5.00	2.80	3.30	7,439	16.4	0.54
SGA	4.00	1.80	2.30	7,406	23.5	0.54
Apgar scores (5 min) <7	1.10	0.90	1.00	541	4.0	0.04
Head circumference <32 cm	4.20	2.70	3.00	5,130	12.4	0.38
Head circumference for gestational age < -2 SD	5.90	3.90	4.40	6,597	11.1	0.49
Stillbirths	0.42	0.32	0.34	361	7.5	0.03
Neonatal deaths	0.33	0.28	0.33	149	3.6	0.01
Any of these outcomes	14.90	10.60	11.70	15,036	9.1	1.06

a: Smoking rate in population 24.6%

b: Based on records with valid information (see table 1) Population size approximately 1.4 million births

have stopped (or begun) smoking during pregnancy, the smoking information may not refer to the most relevant period for the outcomes considered in the present study. Misclassification of this type will bias the results towards unity.

A significant association between such a common exposure as smoking and a certain negative outcome is of great general interest. However, for each individual an association between a certain exposure and a certain outcome is, irrespective of the magnitude of the association, of marginal interest as long as the absolute risk for the disease is negligible. However, when all the most well-known, smoking-related, negative pregnancy outcomes are considered, the risk for each individual is not negligible. The absolute risk for any of these outcomes is approximately 15% among infants of smoking mothers. Adequate information about the level of this risk and the fact that this risk could be reduced by one-third would be a persuasive argument when encouraging women who are planning a pregnancy to give up smoking.

The impact of decreasing smoking rates on the overall risk for the negative delivery outcomes considered in the present study was persuasively demonstrated.

The clinical significance of an outcome which occurs in 12% of all births could of course be questioned. Many infants who are defined as SGA are, for instance, not growth retarded, but belong to the first percentiles of the normal distribution of weights at birth. Furthermore, compared to smoking-related cases of growth retardation, cases with unknown aetiology may be more severe as those infants may be affected not only by growth retardation, but also by the specific condition (e.g. disease) which negatively influenced their growth. However, even if the case group is diluted with some normal but small infants, the group is likely to identify infants who are at an increased risk of future poor physical and psychological health.

The evidence that maternal smoking has a negative effect on pregnancy outcome is by now overwhelming. In the present study, the risk estimates for maternal smoking were calculated with great precision which made them suitable for application to population counts in order to estimate the attributable effect of maternal smoking on various negative pregnancy outcomes. Together with the growing knowledge about the influence of infant health on future physical and psychological development,⁴⁰⁻⁴⁹ it could certainly be speculated whether any society can afford maternal smoking during pregnancy. In a population in which 25% of pregnant women smoke, approximately 1% of all children are given a suboptimal introduction to life because of their mother's smoking habits. In the Swedish population investigated in the present study, this represented 15,000 children.

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