A BRIEF ORIGINAL CONTRIBUTION

Maternal Age Modifies the Effect of Maternal Smoking on Intrauterine Growth Retardation but Not on Late Fetal Death and Placental Abruption

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To investigate whether the effect modification of smoking by maternal age previously reported for small for gestational age births was also obtained for late fetal death and placental abruption, the author analyzed single births in Sweden (n = 1,057,711) from 1983 to 1992. An effect modification of smoking by maternal age was obtained only with regard to fetal growth: Compared with nonsmokers aged 40-44 years, the risk of small for gestational age births among women smoking at least 10 cigarettes per day in the same age group was 4.5, whereas the corresponding risk increase among teenagers was only 2.0. The present results support the hypothesis that smoking actually influences fetal growth more among older smokers. Am J Epidemiol 1997; 145:319-23.

abruptio placentae; fetal death; fetal growth retardation; maternal age; smoking

Increasing maternal age and smoking are reportedly associated with increased risks of late fetal death, placental abruption, and fetal growth retardation (1-4). The negative effects of smoking on fetal growth are also reported to increase with maternal age (5-7). Whether there is a similar effect modification of smoking on late fetal death and placental abruption has not been studied.

The Swedish Medical Birth Register includes prospectively collected information about maternal characteristics, pregnancy complications, and pregnancy outcome of births in Sweden (8). With this data set, it was possible to study the effect modification of smoking by maternal age on late fetal death, placental abruption, and fetal growth in one large population-based cohort.

MATERIALS AND METHODS

This study was based on infants born in Sweden from 1983 through 1992 and whose births were registered in the Swedish Medical Birth Register. The analyses were restricted to single births to mothers aged 15-44 years at delivery.

From 1983 on, the Birth Register has received prospectively collected comprehensive information on births from all hospitals. Starting with the first antenatal visit, antenatal, obstetric, and pediatric data are recorded on standardized records that are forwarded to the Birth Register. All births and deaths are validated each year against another population register, using the mother’s unique personal identification number. The Birth Register covers more than 99 percent of all births in Sweden (8).

Maternal age at delivery was categorized into 5-year groups. Parity was defined as the number of previous births including stillbirths. Information regarding family situation and smoking was collected at the first prenatal visit. Family situation was classified as cohabiting with infant’s father or not, and smoking habits were classified as nonsmokers (i.e., nondaily smokers), moderate smokers (one to nine cigarettes per day), and heavy smokers (at least 10 cigarettes per day).

Pregnancy complications were coded according to the Swedish version of the International Classification of Diseases, Eighth Revision, through 1986 and thereafter, the Ninth Revision. The following codes were used for placental abruption: Eighth Revision, 632.1 and 651.4; Ninth Revision, 641C.

Late fetal death was defined as stillbirth occurring at 28 weeks of gestation or later. Small for gestational age (SGA) was defined as <2 standard deviations below the mean birth weight for the gestational age according to the currently used Swedish birth weight
curve (9). Gestational age was assessed by ultrasonic measurements in 45 percent of the women or estimated from the date of the last menstrual period in 55 percent. In Sweden, more than 95 percent of the pregnant population attend antenatal care classes before the 15th gestational week (10).

Multiple logistic regression analyses were performed to estimate the effect of maternal age and smoking on late fetal death, placental abruption, and SGA birth. Odds ratios were calculated to approximate the relative risk, using the PROC LOGIST in the SAS software program package (11, 12). The reference group included nonsmoking women aged 25-29 years. Parity and family situation were used as covariates, as these variables influenced pregnancy outcomes and were associated with maternal age and smoking habits. Information about smoking habits and family situation was missing in 7 percent, respectively; and these groups were also included in the regression analyses. Information on place of residence (urban/rural) and mother's citizenship (Nordic/non-Nordic) was also available; however, as these variables had no effect on pregnancy outcomes, they were eventually not included.

To evaluate effect modification of smoking by maternal age on risk of late fetal death, placental abruption, and SGA birth, separate regression analyses were performed for each of the six age groups. The presence of effect modification was evaluated by examining the patterns of the estimated odds ratios rather than single coefficients and confidence intervals, which are sensitive to differences in the sizes of the subgroups on which they are based. An effect modification was judged to be present if the set of estimated odds ratios showed a monotone change of the dose-response relation between smoking and the outcome across the age groups.

RESULTS

Of 1,057,711 single births, there were 3,675 late fetal deaths (3.5 per 1,000 births), 5,712 placental abruptions (5.4 per 1,000), and 32,288 SGA infants (3.1 percent). Rates of late fetal death and SGA increased with maternal age from 35 years and older, and the rate of placental abruption increased from 30 years and older. Cigarette smoking clearly influenced the rates of late fetal death, placental abruption, and SGA birth in a dose-dependent manner. Parity and family situation also influenced these rates. When information about smoking habits and family situation was missing, rates of late fetal death and placental abruption were increased (table 1).

| TABLE 1. Single births in Sweden by number, rates of late fetal death, placental abruption, and small for gestational age (SGA), by maternal age, smoking habits, parity, and family situation, 1983–1992 |
|---|---|---|---|---|---|---|
| Age (years) | Births | No. | % | Late fetal death | No. | Rate/1,000 | Placental abruption | No. | Rate/1,000 | SGA* | No. | % |
| 15–19 | 32,427 | 3 | 122 | 3.8 | 172 | 5.3 | 1,314 | 4.1 |
| 20–24 | 249,205 | 23 | 807 | 3.2 | 1,243 | 5.0 | 8,254 | 3.3 |
| 25-29 | 390,908 | 37 | 1,249 | 3.2 | 1,947 | 5.0 | 11,011 | 2.8 |
| 30–34 | 264,261 | 25 | 888 | 3.4 | 1,554 | 5.9 | 7,611 | 2.9 |
| 35–39 | 102,659 | 10 | 497 | 4.8 | 655 | 6.4 | 3,381 | 3.3 |
| 40–44 | 18,251 | 2 | 112 | 6.1 | 141 | 7.7 | 717 | 4.0 |

Cigarette smoking

No | 717,250 | 68 | 2,167 | 3.0 | 2,899 | 4.0 | 16,115 | 2.3 |
1–9/day | 164,270 | 15 | 610 | 3.7 | 1,282 | 7.8 | 7,581 | 4.6 |
≥10/day | 103,481 | 10 | 515 | 5.0 | 1,021 | 9.9 | 5,881 | 5.7 |
Missing | 72,710 | 7 | 383 | 5.3 | 510 | 7.0 | 2,711 | 3.7 |

Parity

0 | 444,860 | 42 | 1,724 | 3.9 | 2,388 | 5.4 | 18,509 | 4.2 |
1–2 | 542,403 | 51 | 1,646 | 3.0 | 2,756 | 5.1 | 12,062 | 2.2 |
≥3 | 70,448 | 7 | 305 | 4.3 | 568 | 8.1 | 1,717 | 2.4 |

Cohabitation with infant's father

Yes | 933,587 | 88 | 3,051 | 3.3 | 4,824 | 5.2 | 27,142 | 2.9 |
No | 55,129 | 5 | 230 | 4.2 | 362 | 6.6 | 2,669 | 4.9 |
Missing | 68,995 | 7 | 394 | 5.7 | 526 | 7.6 | 2,477 | 3.6 |

Total | 1,057,711 | 100 | 3,675 | 3.5 | 5,712 | 5.4 | 32,288 | 3.1 |

*Rates are based on live births.
In table 2, an analysis of the risks of late fetal death, placental abruption, and SGA birth are presented using logistic regression. Compared with women aged 25–29 years, the odds ratio of late fetal death was 1.6 among women aged 35–39 years and 1.9 among women aged 40–44 years. The risks of placental abruption and SGA also increased with age. Compared with nonsmokers, moderate smokers faced a 30 percent increased risk of late fetal death, whereas the corresponding increase in risk among heavy smokers was 70 percent. Compared with nonsmokers, the odds ratios of placental abruption among moderate smokers and heavy smokers were 2.0 and 2.5, respectively; and the odds ratios of SGA births related to smoking were of similar magnitude.

The effect modification of smoking by maternal age on pregnancy outcome is illustrated in table 3, where logistic regression models for separate maternal age groups are presented. In all age groups, the risks of late fetal death, placental abruption, and SGA births increased with amount smoked. In the analyses of late fetal death and placental abruption, there is no apparent effect modification of the smoking-related risks by maternal age. In the analyses of SGA birth, the odds ratios related to heavy smoking consistently increased with maternal age. Compared with nonsmokers aged 40–44 years, the risk of SGA births among heavy smokers in the same age group was 4.5, whereas the corresponding increase among teenagers was only 2.0. Moreover, the ratio of odds ratios between heavy and moderate smokers increased with age and was always highest among the oldest smokers.

**DISCUSSION**

These data confirmed the results from previous studies that the smoking-related risk of SGA birth increases with maternal age (5–7). However, in the same data set, there were no effect modifications of smoking by maternal age on late fetal death and placental abruption. Since more than one million births were included, the study also had power enough to investigate possible effect modification of smoking by...
maternal age on rare outcomes, such as late fetal death and placental abruption.

Differences in smoking habits between young and older pregnant women have been put forward as one explanation for the observed effect modification of smoking by maternal age on fetal growth (6). In accordance with previous investigations, smoking increased the risks of late fetal death, placental abruption, and SGA birth in a dose-dependent manner (1-5). If older smokers smoked more during pregnancy than younger smokers, one would expect that older smokers faced higher risks not only of SGA birth but also of late fetal death and placental abruption. The lack of effect modification of smoking by maternal age on late fetal death and placental abruption does not support the hypothesis that the increased risk of SGA births among older smokers is mediated through differences in smoking habits between age groups.

Smoking itself may influence fetal growth more among older smokers. Smoking during pregnancy probably has a direct toxic effect on fetal growth (13, 14). Smoking during pregnancy increases fetal carboxyhemoglobin concentration and increases the vascular resistance due to the vasoconstrictive effects of nicotine and the reduced prostacyclin synthesis (15-17). These toxic effects of tobacco smoke or the biologic response to these changes may be more pronounced among older smokers. Evidently, this possible change by age for intrauterine exposure of tobacco metabolites is not associated with increased risks of late fetal death or placental abruption.

A tendency to delay childbearing has been observed in many developed countries, such as Sweden and the United States (18, 19). The age of 35 years or more has traditionally been used to characterize the “older mother,” and this cutoff has also been used often in research. However, the age-related risks of adverse pregnancy outcomes also increase with maternal age after 35 years (20, 21). In the present investigation, mothers in their early forties faced an almost twofold risk of late fetal death, which is an accordance with a recently published Canadian study (21).

The present study confirms previous studies that the smoking-related risk of fetal growth retardation may be especially pronounced among older smokers (5, 7). The public health implications of this finding are, however, not obvious. It is questionable whether special efforts of smoking cessation focusing on older pregnant women would be effective. Not many women stop smoking during pregnancy; and compared with young smokers, older smokers are even less likely to quit (22). Moreover, infants born to older women may benefit less in birth weight by smoking intervention than younger women (23). From a clinical point of view, however, it is clear that older smokers should be monitored especially closely with regard to signs of fetal growth retardation.

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REFERENCES