Effect of age, parity, and smoking on pregnancy outcome: A population-based study

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OBJECTIVES: The purpose of our study was to investigate the combined interactive effects of maternal age, parity, and smoking on pregnancy outcome.

STUDY DESIGN: This was a population-based Swedish study (n = 538,829).

RESULTS: Multiple logistic regression analysis showed that the smoking-related effect on the relative increase in the odds ratio of low birth weight and preterm delivery was significantly greater among multiparous patients than nulliparous; among multiparas, smoking increased the odds ratios for low birth weight and preterm delivery by 2.4 and 1.6; the corresponding relative increases in the odds ratios among nulliparas were 1.7 and 1.1, respectively. With advancing maternal age there was a smoking-related relative increase in the odds ratios for small-for-gestational-age births. Moreover, the age effect on the relative increase of low birth weight, preterm delivery, and small-for-gestational-age births was greater among nulliparas than multiparas.

CONCLUSIONS: Older smokers are at an especially high risk for small-for-gestational-age births, and parous smokers are at an especially high risk for low birth weight and preterm delivery. (Am J Obstet Gynecol 1993;168:16-21.)

Key words: Maternal age, parity, smoking, low birth weight, small-for-gestational-age, preterm delivery

Maternal age, parity, and smoking are well-documented risk factors for adverse pregnancy outcomes.[1-3] Their influence on perinatal mortality is primarily mediated through an increase in late fetal death.[4-5] These factors reduce fetal growth and gestational age.[6-7]

Although maternal age, parity, and smoking have similar adverse effects on pregnancy outcome measures, interactions of these variables on risk modifications have not been well-studied. The age effect on perinatal mortality is more pronounced among nulliparas than among multiparas.[1] The effect of smoking on fetal growth increases with maternal age.[7, 8] In one study the interaction between maternal age and smoking was reported to have similar effects on birth weight and gestational age.[7]

In 1973 a medical birth registry was set up by the National Board of Health and Welfare in Sweden.[9] This data set provided an excellent opportunity to investigate and assess the public health importance of different interactions of maternal age, parity, and smoking habits on various pregnancy outcome measures in a large, population-based cohort.

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Material and methods

Description of sample. Our study is based on births from 1983 to 1988 from the Swedish birth register (n = 597,000). Our analysis was restricted to single births of women with Nordic citizenship aged ≥20 years (n = 538,829).

The Swedish medical birth register held by the National Board of Health and Welfare receives information on births from all hospitals. The information is prospectively collected from each woman starting with the first antenatal visit. All births and deaths are validated each year against a population register based on information from the parishes. This cross-checking was done by using the mother's unique identification number. The medical birth register covers more than 99% of all births in Sweden.[10]

Data analyses. Late fetal death was defined as a stillbirth occurring at ≥28 weeks' gestation. Early neonatal death was defined as a death occurring during the first 6 completed days of life. Low birth weight (LBW) was defined as birth weight <2500 gm. Preterm delivery was defined as a delivery at ≤36 completed weeks. Small-for-gestational-age (SGA) was defined as <2 SDs below the mean birth weight for the gestational age

Table I. Number of births and deaths to Nordic women by maternal age, parity, and maternal smoking habits (single births in Sweden 1983 to 1988)

		Late fetal death		*Early neonatal death*	
	No. of births	*No.*	*Rate per 1000*	*No.*	*Rate per 1000*
Age					
20-24	132,641	431	3.2	360	2.7
25-29	204,152	652	3.2	478	2.3
30-34	138,722	477	3.4	393	2.8
≥35	63,314	314	5.0	212	3.4
Parity					
0	214,327	824	3.8	598	2.8
≥1	324,502	1,050	3.2	845	2.6
Smoking					
Nonsmokers	355,656	1,084	3.0	867	2.4
Daily smokers					
All	147,181	625	4.2	399	2.7
1-9 Cigarettes	89,742	339	3.8	238	2.7
≥10 Cigarettes	57,439	286	5.0	161	2.8
Missing data	35,992	165	4.6	177	4.9
TOTAL	538,829	1,874	3.5	1,443	2.7

according to the Swedish birth-weight curve.[11] Gestational age was estimated by ultrasonographic measurements in 29%; in 71% the date of the last menstrual period was used. In Sweden >95% of pregnant women attend antenatal care before the fifteenth gestational week.[12]

Maternal age, parity, and maternal smoking habits were used as independent variables. Parity was classified into nulliparous (no previous births) and multiparous (≥1 previous birth). Information regarding smoking habits was collected at each woman's first antenatal visit. Smoking habits were classified as nonsmoker (i.e., nondaily smoker), smoking between 1 and 9 cigarettes per day, and smoking ≥10 cigarettes per day.

Multiple logistic regression analyses were performed to estimate the odds ratio (OR) for each pregnancy outcome with respect to combinations of the independent variables such as maternal age, parity, and smoking.[13] The ORs were used as an approximation of the relative risk, and nonsmoking, multiparas aged 20 to 24 years were the reference group. The number of deaths in certain age-parity groups were not large enough to permit a detailed exploration of the possible impact of the amount of cigarettes smoked per day. In the multivariate analyses maternal smoking was therefore treated as a dichotomous variable. Women on whom information about smoking habits was missing were excluded from the regression analyses. A backward-stepping procedure was used in the multiple logistic regression analysis to eliminate the interaction terms between the independent variables that were not statistically significant at or above the p value of 0.05. The statistical analyses were done with SAS and the BMDP LR computer packages.[14, 15]

Results

Among the 538,829 births there were 1,874 late fetal deaths and 1,443 early neonatal deaths (Table I). High maternal age, nulliparity, and maternal smoking were associated with increased rates of late fetal death. With respect to LBW, preterm, and small-for-gestational-age (SGA) infants, rates were highest among mothers aged ≥35 years and lowest among mothers aged 25 through 29 years (Table II). Compared with multiparas, nulliparas experienced higher rates of LBW, preterm, and SGA infants. Compared with nonsmokers, the rates of LBW infants, preterm deliveries, and SGA infants increased with the amount smoked per day and among those with missing smoking data.

In the multiple logistic regression analyses of late fetal death, the OR increased with maternal age across parity groups (Table III). Smoking increased the OR for late fetal death by 40% within each age-parity group. The absolute risks of smoking, however, differed between the age-parity groups: among 20- to 24-year-old multiparas, smoking increased a low basic risk of late fetal death from OR = 1.0 to OR = 1.4; among nulliparous women aged ≥35 years, a high basic risk of OR = 2.4 was increased to OR = 3.5. The interaction terms (between smoking and maternal age, smoking-parity and age-parity) did not have a significant effect on the risk of late fetal death.

The odds ratios of early neonatal mortality showed a modest U-shaped relationship by age and parity (data not shown). Within each age-parity group smokers had higher ORs than nonsmokers. Once again, the highest OR appeared among the nulliparas aged 35+ who smoked (OR 1.6, 95% confidence interval (CI) = 1.2, 2.1).

Table II. Number of LBW infants, preterm deliveries, and small-for-gestational-age infants by maternal age, parity, and maternal smoking habits (live single births in Sweden 1983 to 1988)

	LBW (<2500 gm)		*Preterm birth (≤36 wk)*		*SGA (<−2 SD)*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Age						
20-24	5,033	3.8	8,004	6.1	3,030	2.3
25-29	6,335	3.1	10,320	5.1	3,778	1.9
30-34	4,637	3.4	7,230	5.2	2,703	2.0
≥35	2,840	4.5	4,383	7.0	1,449	2.3
Parity						
0	9,467	4.4	13,936	6.5	5,959	2.8
≥1	9,378	2.9	16,001	4.9	5,001	1.5
Smoking						
Nonsmokers	9,407	2.7	17,505	4.9	4,886	1.4
Daily smokers						
All	7,601	5.2	9,701	6.6	5,206	3.6
1-9 Cigarettes	4,245	4.7	5,583	6.2	2,890	3.2
≥10 Cigarettes	3,356	5.9	4,118	7.2	2,316	4.1
Missing data	1,837	5.1	2,731	7.6	868	2.4
TOTAL	18,845	3.5*	29,937	5.6†	10,960	2.0‡

*Total of 3133 live infants where birth weight was missing were included in the denominator. The population with birth weight missing does not differ within age-parity-smoking groups.

†Total of 1809 live infants where gestational age was unknown were included in the denominator. The population with gestational age missing does not differ within age-parity-smoking groups.

‡Total of 4907 live infants where birth weight or gestational age was unknown were included in the denominator.

Table III. OR and 95% CI for late fetal death after adjustments for effects of parity, maternal age, and maternal smoking habits (Sweden 1983 to 1988, n = 502,837)

	Maternal age (yr)							
	20-24		*25-29*		*30-34*		*≥35*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
Multiparas								
Nonsmokers	1.0*		1.1	0.96-1.2	1.3	1.1-1.5	1.8	1.5-2.1
Daily smokers	1.4	1.3-1.6	1.6	1.3-1.8	1.8	1.5-2.2	2.6	2.1-3.2
Nulliparas								
Nonsmokers	1.3	1.2-1.5	1.5	1.2-1.8	1.7	1.4-2.1	2.4	1.9-3.0
Daily smokers	1.9	1.7-2.2	2.1	1.7-2.6	2.4	1.9-3.1	3.5	2.7-4.5

*Reference group.

The OR for LBW increased with maternal age across parity groups except among 25- to 29-year-old multiparas. Within each age group the OR was higher among nulliparas compared with multiparas; within each age-parity group the OR was higher among smokers compared with nonsmokers (Table IV). When interaction terms were introduced the age-related increase of LBW was more marked among nulliparas than multiparas ($p < 0.0001$). More importantly, however, the smoking-related risk for LBW was higher among multiparas than nulliparas ($p < 0.0001$). As illustrated in Table IV, among multiparas aged 20 to 24 years, smoking increased the OR from 1.0 to 2.4; the corresponding increase in ORs among nulliparas aged 20 to 24 years was from 1.8 to 3.1 (relative increase in OR = 1.7).

Although maternal age, nulliparity, and smoking statistically significantly influenced preterm delivery ($p < 0.0001$ for all), the size of the effect was less for preterm delivery than for LBW (Table V). Once again, the age-parity and smoking-parity interaction terms were significant ($p < 0.0001$, respectively); the age effect on the relative increase in the ORs was greater among nulliparas, and the smoking effect was greater among the multiparas.

In addition, to study the effect of maternal age, parity, and smoking on mean birth weight and mean

Table IV. OR and 95% CI for LBW (<2500 gm) after adjustments for effects of parity, maternal age, and maternal smoking habits (Sweden 1983 to 1988, n = 498,242)

	Maternal age (yr)							
	20-24		*25-29*		*30-34*		*≥35*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
Multiparas								
Nonsmokers	1.0*		0.9	0.8-0.96	1.1	1.01-1.2	1.6	1.4-1.7
Daily smokers	2.4	2.3-2.5	2.1	2.0-2.3	2.6	2.4-2.8	3.7	3.4-4.1
Nulliparas								
Nonsmokers	1.8	1.6-1.9	1.8	1.7-1.9	2.3	2.1-2.5	3.1	2.8-3.5
Daily smokers	3.1	2.8-3.3	3.1	2.9-3.4	4.0	3.6-4.3	5.5	4.9-6.1

*Reference group.

Table V. OR and 95% CI for preterm delivery (≤36 weeks) after adjustments for effects of parity, maternal age, and maternal smoking habits (Sweden 1983 to 1988, n = 499,947)

	Maternal age (yr)							
	20-24		*25-29*		*30-34*		*≥35*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
Multiparas								
Nonsmokers	1.0*		0.9	0.8-0.9	1.0	0.9-1.04	1.4	1.3-1.5
Daily smokers	1.6	1.6-1.7	1.4	1.3-1.5	1.6	1.5-1.7	2.3	2.1-2.4
Nulliparas								
Nonsmokers	1.5	1.4-1.6	1.5	1.4-1.5	1.6	1.5-1.7	2.1	1.9-2.2
Daily smokers	1.7	1.6-1.8	1.6	1.5-1.7	1.8	1.6-1.9	2.3	2.1-2.5

*Reference group.

Table VI. OR and 95% CI for small-for-gestational-age (<−2 SD) after adjustments for effects of parity, maternal age, and maternal smoking habits (Sweden 1983 to 1988, n = 497,063)

	Maternal age (yr)							
	20-24		*25-29*		*30-34*		*≥35*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
Multiparas								
Nonsmokers	1.0*		0.9	0.8-1.04	1.1	0.97-1.2	1.2	1.1-1.4
Daily smokers	2.5	2.3-2.7	2.4	2.2-2.7	2.9	2.6-3.3	4.4	3.9-5.0
Nulliparas								
Nonsmokers	1.8	1.7-2.0	1.9	1.7-2.1	2.5	2.2-2.8	2.5	2.2-3.0
Daily smokers	4.5	4.0-5.1	4.9	4.4-5.4	6.6	5.9-7.5	9.0	7.7-10.4

*Reference group.

gestational age, an analysis of covariance was done for each outcome. The results of these analyses were consistent with the multiple logistic regression analyses of LBW and preterm delivery.

In the analyses of SGA births the OR increased with age across parity groups except among 25- to 29-year-old multiparas (Table VI). Once again, the OR was higher among nulliparas compared with multiparas within each age group and was also consistently higher among smokers compared with nonsmokers. Compared with the other outcomes the range of OR was greater in the analyses of SGA births (ranging from 0.9 to 9.0). This greater range can partly be explained by the two interactions obtained: the nulliparity-related risk for SGA increased with age ($p < 0.001$), and the smoking-related risk increased with age ($p < 0.0001$). Among nulliparas aged 20 to 24 years, smoking increased the OR from 1.8 to 4.5 (relative increase in

OR = 2.5); among nulliparas aged ≥35 years, the corresponding increase in OR was from 2.5 to 9.0 (relative increase in OR = 3.6). Similar relative differences in ORs were also observed among multiparas.

Comment

The main objective of our study was to investigate possible interactions between maternal age, parity, and smoking with respect to pregnancy outcome. Because this study was based on an analysis of >500,000 births, we had the statistical power to estimate the effects of such interactions on LBW, preterm delivery, and SGA. The age-related increase in ORs of LBW, preterm delivery, and SGA was greater among nulliparas than multiparas (Tables IV through VI). Although the increased risk of adverse pregnancy outcomes associated with the older nulliparas has been known for some time,[2] we are aware of no reports of statistically significant interaction between age and parity on LBW, preterm delivery, and SGA. Similar to earlier studies, the smoking-related increase in OR for SGA was greatest among older mothers[7, 8] (Table VI). The smoking-related effects on the increase in odds ratios of LBW and preterm delivery were more pronounced among multiparas than among nulliparas (Tables IV and V). These findings differ with the results of Wen et al.,[7] in which the smoking-related risk for preterm delivery increased with advancing maternal age. Because there is a strong relationship between maternal age and parity it can be speculated that Wen et al. would have had the same results if their analyses had included the interaction between smoking and parity.

The results of the interaction analyses raise more questions than they provide answers, and any speculation about the causes of these interactions must by necessity be regarded as strictly hypothetical. The effect of the age-smoking interaction on SGA has previously been reported.[7, 8] Among smokers increasing maternal age usually means longer lifetime exposure to cigarettes that may interact with the direct toxic effects of tobacco smoke.

Parity and maternal age may both affect utero-placental perfusion. The negative interaction between advancing maternal age and parity may be the result of a further decrease in utero-placental perfusion; this may be one of the mechanisms for the increased risks of an unsuccessful pregnancy outcome observed among delayed childbearers.[16]

The interaction effect of parity and smoking on LBW and preterm delivery was unexpected. The information on smoking habits was self-reported data obtained in the first trimester. Although relatively few smokers quit smoking during pregnancy,[17] compared with multiparous women nulliparous women are more likely to quit.[18] If parity differences in smoking cessation rates during pregnancy or amount smoked daily contributed to the differences in the smoking-related increased risk for LBW, the same should hold true for SGA.[3, 19] Conceivably maternal age, parity, and smoking influence fetal growth and gestational age by different mechanisms.

We intentionally restricted our analysis to three independent variables: maternal age, parity, and smoking habits. The definitions of these variables are relatively uniform between countries, and similar risk estimates for outcomes like late fetal death, LBW, and SGA have been reported from different populations.[4, 5, 20] The variables also have an independent effect on pregnancy outcome measures after controlling for possible confounders.[21] The importance of other potential risk factors, such as socioeconomic and psychologic variables, differ markedly between populations.[21, 22] Swedish pregnant women are relatively homogenous and receive the same antenatal and obstetric care; the influence of socioeconomic factors on pregnancy outcome is limited.[10] These factors make this population ideally suited for studying the effects of maternal age, parity, and maternal smoking on pregnancy outcome.

Today smoking is prevalent among young women in Sweden and also in the United States; 30% to 40% of women <25 years of age are reported to be daily smokers.[23, 24] As the rate of births among women aged ≥30 continues to increase in both countries,[25, 26] the public health significance of smoking among childbearers in the older reproductive ages may become increasingly important.

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