

Maternal Smoking and Its Association With Birth Weight

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OBJECTIVE: Maternal smoking has been associated with a reduction in newborn birth weight. We sought to estimate how the pattern of maternal smoking throughout pregnancy influences newborn size.

METHODS: One hundred sixty pregnant smoking women were enrolled in a prospective study. We collected data on maternal age, education, prepregnancy body mass index, and parity, as well as alcohol and illicit drug use. Cigarette use was defined as self-reported consumption before pregnancy, at the time of study enrollment, and in the third trimester. Statistical analyses were performed based on bivariate correlations and multiple linear regression.

RESULTS: Of the smoking parameters examined, maternal third-trimester cigarette consumption was the strongest predictor of birth weight percentile (partial $r = -0.23$, $P < .001$). For each additional cigarette per day that a participant smoked in the third trimester, there was an estimated 27 g reduction in birth weight. Prepregnancy smoking volume was not significantly associated with birth weight percentile in bivariate ($r = -0.06$, $P = .47$) or multivariable analyses. Additional factors contributing to birth weight include gestational age (partial $r = 0.69$, $P < .001$), maternal body mass index (partial $r = 0.23$, $P < .001$), and parity (partial $r = 0.16$, $P < .004$). In total, these 4 variables explain 61% of the variance in newborn birth weight.

CONCLUSION: Maternal third-trimester cigarette consumption is a strong and independent predictor of birth weight percentile. This supports the hypothesis that reductions in maternal cigarette consumption during preg-

nancy will result in improved birth weight, regardless of the prepregnancy consumption levels.

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LEVEL OF EVIDENCE: III

Maternal smoking in pregnancy is associated with adverse pregnancy outcomes, including an increased risk for preterm birth, placental abruption, placenta previa, and low birth weight.^{1–4} The reductions in neonatal weight observed with maternal smoking may have life-long consequences because evidence points to significant pediatric and adult morbidity associated with reduced birth weights.^{5,6} Intervention trials aimed at reducing maternal smoking in pregnancy and retrospective analyses examining the relationship of maternal smoking to birth weight suggest that reductions or complete cessation of maternal smoking during the course of gestation is associated with improved birth weights, although these improvements have generally been modest in magnitude, in large part because of the marginal efficacy of the smoking cessation programs.^{7,8} Further limiting the interpretation of these apparent improvements in birth weight is the potential impact of maternal smoking cessation on prolonging gestation. The importance of accurate gestational age assignment and the potential relative impact of advancing gestational age on birth weight in those who have reduced smoking have not routinely been clearly delineated and segregated from an increase in fetal growth velocity as a source of the increased birth weights associated with maternal smoking reduction.^{8,9}

Additionally, when the timing of a reduction in maternal cigarette consumption during pregnancy has been specifically evaluated relative to its association with birth weight, the results are mixed. Some studies have suggested that early pregnancy cessation of smoking has the greatest impact on birth weight, pointing to a relatively small impact of third-trimester

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smoking level on birth weight, whereas others have suggested that third-trimester maternal cigarette consumption has the strongest association with birth weight.^{8,10,11} In this study our primary objective was to define smoking consumption at 3 distinct time points important to the evaluation of the effect of smoking on birth weight: before pregnancy, in early pregnancy at the time of study enrollment, and in late pregnancy. We also examined the change in amount of maternal smoking over time. Our overall goal was to examine the relative strength of the association of these indicators of maternal smoking volume to birth weight corrected for important confounding variables in well-dated pregnancies. Our secondary goal was to specifically quantify the effects of individual cigarette consumption on newborn birth weight, controlling for established contributors to newborn size.

MATERIALS AND METHODS

Data were obtained from 160 women enrolled in a university-based outpatient research clinic for smoking cessation and relapse prevention during pregnancy and postpartum. Participants were recruited from 1 of 3 large group obstetric practices or 1 single-practitioner obstetric practice in the greater Burlington, Vermont, area. Enrollment occurred between June 2001 and February 2003. All women receiving prenatal care at these clinics completed a brief questionnaire regarding basic sociodemographics and cigarette smoking. Those who acknowledged smoking any time during the current pregnancy were subsequently contacted by study staff in person or by phone regarding study participation. Women enrolled in the study had to have been enrolled in the program before 26 menstrual weeks of pregnancy. All participants had ultrasound confirmation of gestational age assignment, with ultrasound examinations performed at less than 20 weeks of gestational age. All women had data collected near the time of their first pregnancy visits. Women selected for inclusion in the present study provided an estimate of their prepregnancy cigarette consumption per day and a self-report of any cigarette smoking during the prior 7 days at the time of enrollment, along with a urine specimen for determining cotinine levels (the primary metabolite of nicotine) and an expired air specimen for determining breath carbon monoxide levels. These women were followed prospectively through the third trimester when self-reports of cigarette smoking, urine specimens for determining cotinine levels, and expired air for determining breath carbon monoxide levels were collected. Only women with complete data across all measures and assessments were included in the study.

Women were participants in one of several clinical trials examining the efficacy of voucher-based incentives for promoting smoking cessation and preventing relapse. Those who reported smoking in the 7 days before the study intake assessment participated in a cessation trial ($n = 114$), while those who reported smoking at the time they learned of the pregnancy but not in the 7 days before the intake assessment participated in a relapse-prevention trial ($n = 46$). In each trial, women were randomized to receive vouchers exchangeable for retail items contingent on biochemically verified abstinence or, non-contingently, that is, independently of smoking status. Incentives were available throughout the antepartum period. Self-reported smoking status had no influence on earning incentives, which was determined exclusively based on urine-cotinine levels. Cotinine testing was conducted onsite using an enzyme immunoassay with a Roche Cobas Mira analyzer (Roche Diagnostics, F. Hoffmann-La Roche Ltd, Basel, Switzerland). The lowest concentration that can be differentiated from the negative urine calibrator at 95% confidence with the enzyme immunoassay system is 34 ng/mL. Specimens were frozen and shipped at approximately monthly intervals for confirmation testing by Labstat International Inc (Kitchener, Ontario, Canada) using a highly sensitive gas chromatography technique. Additional details of the treatment intervention have been described elsewhere.¹² Self-reports of cigarette usage during pregnancy were highly correlated with urinary cotinine levels determined by enzyme immunoassay both at the time of study enrollment ($r = 0.69$) and at the end of pregnancy ($r = 0.74$). Self-reported cigarette usage was then used to quantify consumption at the 3 time points assessed in the study: before pregnancy, at the time of study enrollment, and in late pregnancy.

Gestational age-specific birth weight percentiles were computed for each infant based on locally derived Vermont hybrid growth curves, which had been validated against normal intrauterine growth patterns.¹³⁻¹⁵ This growth standard combines ultrasound estimates of fetal weight for gestational ages below 35 weeks and birth weights at or above 35 weeks to characterize normal neonatal size over the course of gestation. The study was reviewed and approved by the University of Vermont institutional review board for human subjects.

Bivariate correlation analyses, based on Pearson correlation coefficients, were initially employed to examine factors associated with newborn size at birth. These bivariate analyses were performed on both gestational age-specific birth weight percentiles and



their corresponding standardized scores (z score). The standardized score represents the z score corresponding to a standard normal distribution (mean = 0, standard deviation = 1) computed from the gestational age-specific percentile rank. Results were consistent for the 2 outcome variables; thus, only bivariate correlation analyses relating to birth weight percentile are presented. To estimate the magnitude of the effect of smoking levels on birth weight, stepwise multiple regression was performed, with raw birth weight as the outcome measure and gestational age as one of the explanatory variables. Additional explanatory variables examined included maternal parity, age, prepregnancy body mass index, level of education, the presence of maternal hypertension, diabetes, narcotic or marijuana use in pregnancy, and neonatal gender. The smoking indices examined included the number of cigarettes consumed per day before pregnancy, at the time of registration into the study, and in the third trimester. Partial correlation coefficients represent the strength of the linear relationship between each independent variable and birth weight, after controlling for other predictors in the regression model.

Subjects were queried about alcohol consumption, and no subjects admitted to regular alcohol consumption. Data were evaluated to determine any impact of study group assignment on outcome parameters. None was observed.

RESULTS

Maternal and neonatal characteristics are displayed in Table 1. Participants reported smoking an average of 18.2 ± 10.4 (mean \pm standard deviation) cigarettes per day before pregnancy, 6.7 ± 7.3 cigarettes per

day in early pregnancy at an average of 12.0 ± 5.1 menstrual weeks of gestation, and 4.8 ± 6.7 cigarettes per day in the third trimester at a mean gestational age of 28.4 ± 2.5 weeks. A small percentage of participants had pregnancy complications that might have independently contributed to alterations of newborn size. Eighteen participants (11%) had hypertension identified during the pregnancy, 7 (4%) had diabetes, and 9 (6%) reported marijuana usage during the pregnancy. The mean birth weight percentile was 43.1 ± 29.8 , with a corresponding mean standardized score (z score) of -0.25 ± 1.0 .

Examination of bivariate correlations demonstrated significant associations between multiple independent variables and birth weight percentile. Maternal characteristics, including education ($r = 0.16$, $P = .048$) and body mass index ($r = 0.28$, $P < .001$), were positively correlated with newborn birth weight percentile. Self-reported narcotic use ($r = -0.18$, $P = .022$) was inversely associated with birth weight percentile. Maternal age did not demonstrate a significant independent relationship with weight percentile ($r = 0.15$, $P = .057$). Of the smoking indices examined, cigarette consumption at the time of enrollment ($r = -0.18$, $P = .028$) and in the third trimester ($r = -0.27$, $P < .001$) were significantly and negatively correlated with birth weight percentile. Urine cotinine at time of enrollment and during the third trimester were also significantly and negatively correlated with birth weight percentile ($r = -0.18$, $P = .024$ and $r = -0.24$, $P = .002$, respectively). We found no significant association between self-reported prepregnancy smoking volume and newborn size ($r = -0.06$, $P = .47$). The observed changes in smoking level from prepregnancy estimates to either enrollment or the third trimester were not significantly associated with birth weight percentile. As expected, smoking levels across assessment times within individuals were highly correlated. Prepregnancy smoking level was strongly associated with both smoking level at enrollment ($r = 0.50$, $P < .001$) and in the third trimester ($r = 0.51$, $P < .001$). Cigarette consumption at the time of study enrollment and in the third trimester was also highly correlated ($r = 0.67$, $P < .001$).

Results of the multiple regression analysis (Table 2) indicated that, of the smoking variables examined, maternal third-trimester cigarette consumption was the strongest predictor of birth weight after adjusting for gestational age (partial $r = -0.23$, $P < .001$). For each additional cigarette per day smoked in the third trimester, there was an estimated 27-g reduction in birth weight (Fig. 1). Smoking level at study enrollment was not a significant predictor after accounting

Table 1. Maternal and Neonatal Features (n = 160)

Maternal age (y)	23.4 \pm 5.2
Maternal race (% white)	98
Maternal education (y)	12.2 \pm 2.1
Marital status [n (%)]	
Married	40 (25)
Separated/divorced/widowed	7 (4)
Single/never married	86 (54)
Other	27 (17)
Maternal prepregnancy BMI (kg/m ²)	25.9 \pm 6.7
Parity (% nulliparous)	56
Gestational age at delivery (wk)	38.6 \pm 2.7
Preterm deliveries [n (%)]	17 (11)
Newborn gender (% female)	49
Newborn birth weight (g)	3,266 \pm 684

BMI, body mass index.

Data are expressed as mean \pm standard deviation unless otherwise indicated.



Table 2. Multivariate Linear Regression Analysis Predicting Birth Weight

Independent Variable	Coefficient	Partial <i>r</i>	Partial <i>r</i> ²	<i>P</i>
Gestational age (wk)	183.7	0.69	0.48	< .001
3rd trimester cigarettes/d	-26.9	-0.23	0.05	< .001
Maternal BMI	21.4	0.23	0.05	< .001
First birth	-203.6	-0.16	0.03	.004

BMI, body mass index.

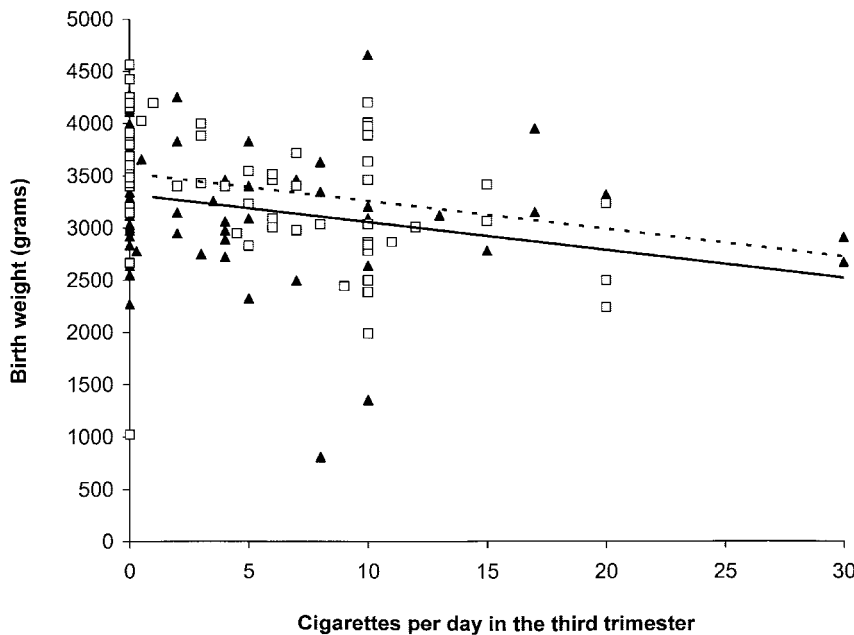


Fig. 1. The relationship between third-trimester cigarette consumption and newborn birth weight is illustrated for both primiparous (*filled triangles, solid regression line*) and multiparous women (*open boxes, dotted regression line*) at the sample means for gestational age and body mass index. The effect of each added cigarette consumed in the third trimester on newborn birth weight (≈ -27 grams) is independent of parity.

Bernstein. *Third-Trimester Smoking and Birth Weight. Obstet Gynecol* 2005.

for third-trimester smoking. Additional direct independent contributors to birth weight, after adjusting for gestational age, included maternal body mass index (partial $r = 0.23$, $P < .001$) and parity (partial $r = 0.16$, $P < .004$). The total model included 4 variables and explained 61% of the variability in newborn birth weight.

DISCUSSION

Maternal cigarette consumption has been clearly associated with an increased incidence of low birth weight neonates. The greatest source of this effect appears to be a reduction in fetal growth velocity rather than an increase in the frequency of preterm birth. Randomized intervention trials aimed at increasing smoking cessation, where gestational age at delivery is matched, demonstrate that birth weight can be improved independently of an effect on mean gestational age at delivery.¹⁶ The current observations, performed in a population with accurate gestational age assignment and controlling for important covariates of fetal growth, support these observations.

Although smoking is clearly associated with re-

duced birth weight, the specific relationship of smoking level and the timing of smoking reductions in pregnancy to birth weight appears to be complex. Our data suggest that, after accounting for established factors known to influence birth weight, a linear relationship persists between the self-reported consumption of cigarettes in the third trimester and newborn birth weight. This stands in contrast to evidence suggesting that there is a greater impact of the first few cigarettes consumed and that the reduction in birth weight is smaller per cigarette as baseline smoking volume increases.⁸ The relationship identified in the current study suggests that, for every additional cigarette consumed per day in the third trimester, there is a reduction of approximately 27 g in newborn birth weight. This per-cigarette effect appears to be greater than that observed by Mathai et al¹⁷ who noted a 12-g reduction in birth weight for every additional cigarette consumed. Our findings also represent a greater impact per cigarette on birth weight than the values identified by England et al,⁸ who noted approximately 12–13 g of birth weight lost per day for each additional self-reported cigarette



consumed in the third trimester, when overall consumption was between 2 and 10 cigarettes per day. The greater per-cigarette influence on birth weight in our data can be accounted for, in part, by the continuous linear relationship we observed. Rather than a large effect of the first cigarettes and a smaller per-cigarette effect thereafter, we have observed a continuous effect that results in a similar overall effect of cigarette consumption on birth weight. This may have resulted from an improved accounting of confounding variables in the current study. Other investigators, identifying a poor correlation of self-reported maternal cigarette consumption with urinary cotinine, have reported on the relationship of urinary cotinine to birth weight. These data have generally supported the idea that there is a linear relationship between cigarette consumption and birth weight.^{18,19}

The correlations of urinary cotinine with prospectively evaluated self-reporting of cigarette consumption in this study were good, with correlation coefficients of 0.69 and 0.74 for observations performed at the time of study enrollment and in late pregnancy, respectively. These correlations are significantly stronger than some of those previously reported, and several explanations for the discrepancy are possible.^{18,20–23} The high correlation noted in the current study may have resulted from the fact that all of the participants were enrolled in a longitudinal prospective evaluation of a smoking cessation/relapse prevention program in pregnancy where it was clear that biochemical confirmation of smoking status would be evaluated at routine and regular intervals. In addition, the high correlation between self-reported smoking amount and urinary cotinine observed in this study may have resulted in part from the racial homogeneity apparent in our study group, where the vast majority of the participants were white women. Previous studies have outlined important racial differences in the body's handling of nicotine and in the relationship of urinary cotinine to self-reported cigarette consumption.^{22,23} Examining a homogeneous population may eliminate some of the variation in this relationship contributed by genetic factors, which may serve to influence a more consistent relationship between urinary cotinine and maternal smoking volume. Estimates of passive cigarette exposure were not specifically quantified, but the high correlation between self-reported consumption and urine cotinine suggests the potential of only a small confounding influence.

The current study does not specifically report the results of an intervention trial. Although all enrolled participants were examined under study conditions

and were randomized to different interventions to either preventing smoking relapse (for those who stopped smoking in early pregnancy) or promote smoking cessation (for those who were smoking in early pregnancy), the current study was collapsed across condition to examine the association of cigarette consumption at the different time points on birth weight. The resulting data are encouraging in that they suggest that continued efforts aimed at reducing cigarette consumption in pregnant smokers are warranted throughout pregnancy and can lead to improvements in birth weight, even when these reductions occur in the last half of pregnancy.

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