Matern Child Health J (2009) 13:415–423
DOI 10.1007/s10995-008-0350-4

Fetal Exposure to Secondhand Tobacco Smoke Assessed by Maternal Self-reports and Cord Blood Cotinine: Prospective Cohort Study in Krakow

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Published online: 25 April 2008

Abstract *Objectives* While the validity of self-reported smoking habits is generally judged as satisfactory, objective markers of secondhand smoke (SHS) exposure may be more useful in validating the causal links between prenatal SHS and health effects. The cohort study in Krakow provided an opportunity for comparative assessment of fetal exposure to SHS based upon questionnaires and cord blood cotinine measurements. *Methods* The study sample included 467 newborns born to women recruited in the first and second trimester of pregnancy. To compare the validity of self-reported SHS and cord blood cotinine levels in assessing the association between fetal passive smoking and health effects of newborns, we separately examined the regression coefficients of birthweight on self-reported number of cigarettes smoked by other household members during the entire pregnancy and cord blood cotinine levels. *Results* In the non-exposed newborns the geometric mean of cord blood cotinine was 0.077 ng/ml and was significantly lower than in newborns with a maternal report of SHS. Cord cotinine levels were more highly correlated with a self-reported number of cigarettes smoked daily at home in the third trimester of pregnancy. The two measures of SHS (number of cigarettes and number of hours of daily exposure) were equally well correlated with cord blood cotinine levels. Using cotinine as the exposure variable, overall the association was not significant; but among the subgroup with cord cotinine levels above the median ($\geq$0.083 ng/ml), the association with birthweight was significant (beta coefficient = -113.65, $P = 0.041$). *Conclusion* The study provides evidence that the assessment of fetal SHS exposure based on cord blood cotinine produced better estimates of the association between exposure and birth outcomes.

Keywords Maternal tobacco exposure · Assessment of fetal exposure · Cord blood cotinine · Questionnaire data

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Introduction

There is solid epidemiologic evidence that fetal exposure to tobacco combustion products resulting from active cigarette smoking (mainstream smoke) by mothers during pregnancy exerts a negative impact not only on birth outcomes and neonatal health [1–3], but is also a critical risk factor for asthma and infections of the respiratory tract during the first years of life [4–7]. Tobacco smoke is a complex mixture of gases and particulates. Levels of respirable particulates, nicotine, polycyclic hydrocarbons, CO, NO_2, and other substances in indoor environments increase with the number of smokers and the intensity of their smoking and decrease with the air exchange rate [8].

Infants exposed prenatally to secondhand tobacco smoke (SHS) are subjected to the same constituents as those in mainstream smoke, however, the pattern and amounts of exposure differ to a large extent [9]. Although the strongest evidence to date links fetal SHS exposure to harmful effects on birthweight of newborns [10–15] and health of infants and very young children [16–22], prenatal SHS exposure may also have health consequences in later childhood and adult life [23].

Fetal exposure to SHS is usually assessed by a questionnaire administered to pregnant women before or after delivery. While the validity of self-reported smoking habits is judged generally to be satisfactory, objective markers of SHS exposure may be more useful in establishing the causal links between prenatal SHS and health effects. Cotinine, a metabolite of nicotine—with the half-time averaging 17 h—has long been found to be a useful biological marker of tobacco smoke exposure and has been in widespread use in epidemiologic studies [24–26]. The marker has been found particularly appropriate in assessing tobacco exposure in active smokers [27, 28]. Although cotinine levels in people exposed to SHS have been studied by many research groups dealing with health outcomes in adults and most of them have found increasing level of cotinine with increasing levels of self-reported exposure to tobacco smoke [29], few studies have assessed the validity of questionnaires to assess fetal SHS exposure.

The present ongoing prospective cohort study provided an opportunity to measure the extent of fetal exposure to SHS in Poland and to compare the prevalence of prenatal SHS exposure using questionnaires administered twice to non-smoking pregnant women in the second and the third trimesters of pregnancy with serum cotinine concentrations measured in cord blood. An additional objective of the analysis was to compare the validity of self-reports and cotinine measurement to assess the association between fetal exposure to maternal SHS and health of newborns in terms of birthweight reduction.

Material and Methods

This study uses data from an earlier established birth cohort of children in Krakow taking part in a collaborative study between the Medical College of Jagiellonian University in Krakow and Columbia University in New York. The design of the study and the detailed selection of the population have been described previously [30]. Enrollment between November 2000 and July 2003 included a total of 582 pregnant women who were recruited from ambulatory prenatal clinics in the first and second trimester of pregnancy. Only women 18–35 years of age, who claimed to be non-smokers, with singleton pregnancies, without illicit drug use and HIV infection, free from chronic diseases such as diabetes or hypertension, and residents of Krakow for at least 1 year prior to pregnancy were eligible for the study. Prior to participation, women read and signed an informed consent. The Ethical Committee of the Jagiellonian University approved the research. Upon enrollment, a detailed questionnaire was administered to each woman to solicit information on demographic data, household characteristics, medical and reproductive history, occupational hazards, and smoking practices of others present in the home.

SHS exposure in pregnancy was recorded by standardized questionnaires administered twice by trained interviewers during the pregnancy. The first interview taken in the second trimester dealt with SHS exposure over the first two trimesters. The second interview occurred after delivery and was concerned with SHS exposure in the third trimester of pregnancy. We used the data to define exposure variables based on the number of cigarettes smoked daily at home or at work in the woman's presence during the first two trimesters and the third trimester of pregnancy and the average daily duration of SHS exposure at home and at work. In addition, we calculated a combined index of average number of cigarettes smoked by others in the presence of the mother at any site (home and/or work) weighted by the duration of exposure over the pregnancy (in months).

Cord blood specimens were collected at delivery and were stored at −70°C prior to analysis. The serum cotinine concentrations were measured at the U.S. Centers for Disease Control and Prevention using a sensitive isotope-dilution high-performance liquid chromatographic/atmospheric pressure ionization tandem mass spectrometric (LC/MS/MS) procedure [31, 32]. The limit of detection (LOD) was 0.050 ng/ml. About 20% of the specimens had cotinine levels below the LOD. A cord blood cotinine above 15.0 ng/ml was considered incompatible with a non-smoking status of the mother [33, 34]. Cord blood cotinine measurements were obtained for 484 newborns; but in the final multivariate statistical analysis, 467 babies were included, due to the exclusion of 17 newborns with blood cotinine levels $\geq$15 above ng/ml, which could indicate active smoking by the mothers during pregnancy. For statistical analysis, samples with non-detectable levels were assigned a value of 0.025, midway between the LOD of 0.05 and 0.

Since the cord blood cotinine distribution was markedly skewed, the geometric means with 95% confidence intervals were used for comparative statistical analysis across the SHS-exposure groups. Differences in characteristics between groups were tested by Chi-square statistics (categorical variables) or by *t*-test (numerical variables). Spearman rank correlation was used to assess the relationship between self-reported SHS and cord cotinine

levels. Multiple linear regression was used to examine the relationship between log transformed cord blood cotinine as a dependent variable and SHS exposure variables (number of cigarettes smoked daily in the household or number of hours of SHS exposure in the household in the last trimester of pregnancy and average weighted number of cigarettes smoked daily by others at any site over the whole pregnancy period). These SHS self-reported measures have been chosen since they demonstrated the highest correlation with cord cotinine. In multivariate linear analysis of the association between SHS exposure (cotinine) and birthweight, a set of potential confounders (maternal age and education, marital status) were included. Statistical analyses were performed with STATA 10 software for Windows.

Results

Cord blood cotinine levels were above the LOD (>0.05 ng/ml) in about 80% of the newborns. Mothers of newborns with detectable cord blood cotinine had a lower educational level, were younger, and more often were unmarried and reported being ex-smokers than mothers of newborns with non-detectable cotinine levels. They also reported a significantly greater number of cigarettes smoked daily by others in their households and declared more hours of SHS exposure in all three trimesters of pregnancy than those with cotinine below detectable levels (Table 1). Since there was a stronger correlation between cord cotinine and self-reported SHS exposure in the third trimester than in the first two trimesters of pregnancy, the main focus of the statistical analysis was on the relationship between cord cotinine and SHS self-reports in the last trimester.

Mothers of 351 babies (75.2%) indicated no SHS exposure at any site over the third trimester of pregnancy. About one fifth of mothers (18.9%) reported SHS exposure only at home, 4.9% only at work and 0.9% at both home and work.

In the total study sample, the geometric mean of cotinine was 0.105 ng/ml (95% CI: 0.095–0.116). Newborns of mothers who declared to be ex-smokers ($N = 118$) had a significantly higher level of cord blood cotinine (geometric mean = 0.213, 95% CI: 0.165–0.274) than that of never-smoking mothers (mean = 0.083; 95% CI: 0.076–0.090). Ex-smokers were significantly more often exposed to SHS at home during pregnancy than never smokers.

Babies of unmarried women at the time of delivery had a significantly higher cord cotinine level (geometric mean = 0.219, 95% CI: 0.125–0.383) than those of married women (geometric mean = 0.100, 95% CI: 0.091–0.110). Both maternal education (number of schooling years) and maternal age were inversely correlated with cord blood cotinine levels; the corresponding Spearman rank correlation coefficients were $r = -0.322$, $P < 0.0001$ and $r = -0.172$, $P = 0.0003$.

Newborns of mothers who denied SHS exposure at home or work over the last trimester of pregnancy had mean concentration (geometric) of 0.077 ng/ml (95% CI: 0.071–0.083). Those newborns whose mothers reported SHS exposure at any site (home/work) in the third trimester had a higher cotinine level (geometric mean = 0.281 ng/ml; 95% CI: 0.218–0.362 ng/ml). Figure 1 presents geometric means of cord cotinine by sites of SHS exposure.

There was a significant association between cord cotinine levels and number of cigarettes smoked daily at home in the third trimester of pregnancy (Table 2). The strength of rank correlation between cord blood cotinine concentrations and either self-reported hours of SHS exposure at home or number of cigarettes smoked daily in the household in the third trimester was identical ($r = 0.52$). A slightly higher correlation was found for cotinine concentrations and the combined index of number of cigarettes smoked at home or work during the entire pregnancy ($r = 0.54$), but the difference was insignificant.

Cross-tabulation of cord blood cotinine levels (in quartiles) by self-reported SHS exposure (Table 3) showed that 37.4% of newborns whose mothers denied SHS exposure at any site in the third trimester had cord blood cotinine levels above the median (>0.083 ng/ml). On the other hand, 19.8% of newborns with reported SHS exposure in the last trimester of pregnancy had blood cord cotinine levels below the median concentration.

In the multivariate linear regression models, we examined the association between cord blood cotinine levels and self-reported number of cigarettes smoked daily by others in the third trimester of pregnancy after adjustment to potential confounders including maternal age, education (years of schooling), and marital status (Table 4). After adjusting for potential confounders, the percent of the explained variance of cord blood cotinine increased by 4–37.2%. The same statistical model, applied for hours of SHS exposure in the third trimester, explained a slightly lower (by 0.6%) proportion of cord cotinine variability. Therefore, we focused the subsequent multivariate statistical analysis on number of cigarettes smoked daily by others at any site in the third trimester as the main SHS self-reported exposure variable.

To compare two exposure measures of passive smoking (self-reports and cord blood cotinine levels) for assessing exposure impact on birth outcomes, we first examined the regression of birthweight in the total study sample on self-reported average weighted number of cigarettes smoked by others in the entire pregnancy period adjusted to potential confounders (maternal age, maternal height and prepregnancy weight, parity, gestational age and gender of child).

Table 1 Characteristics of the study sample by self-reported secondhand smoke exposure at home and cord blood cotinine level

Variables	Total $N = 467$	Cord blood cotinine (ng/ml)		
		≤0.05 $N = 106$	>0.05 $N = 361$	P*
Maternal age				
Mean	27.64	28.39	27.42	0.0138
SD	3.55	3.09	3.65	
Maternal education				
Elementary	44 (9.4%)	3 (2.8%)	41 (11.4%)	0.0002
Intermediate	110 (23.6%)	15 (14.2%)	95 (26.3%)	
High/university	313 (67.0%)	88 (83.0%)	225 (62.3%)	
Marital status				
Married	439 (94.0%)	103 (97.2%)	336 (93.1%)	0.1839
Unmarried	28 (6.0%)	3 (2.8%)	25 (6.9%)	
Ex-smoking status				
No	349 (74.7%)	95 (89.6%)	254 (70.4%)	0.0001
Yes	118 (25.3%)	11 (10.4%)	107 (29.6%)	
Third trimester of pregnancy				
Number of cigarettes smoked daily at home by household members				
0 cigarette/day	374 (80.1%)	104 (98.1%)	270 (74.8%)	0.0000
≤5 cigarettes/day	55 (11.8%)	2 (1.9%)	53 (14.7%)	
6–10 cigarettes/day	26 (5.6%)	0 (0.0%)	26 (7.2%)	
>10 cigarettes/day	12 (2.6%)	0 (0.0%)	12 (3.3%)	
Third trimester of pregnancy				
Average hours of SHS exposure at home				
0 h	374 (80.1%)	104 (98.1%)	270 (74.8%)	0.0000
≤1 h	51 (10.9%)	2 (1.9%)	49 (13.6%)	
2–5 h	33 (7.1%)	0 (0.0%)	33 (9.1%)	
>5 h	9 (1.9%)	0 (0.0%)	9 (2.5%)	
First two trimester of pregnancy				
Number of cigarettes smoked daily at home by household members				
0 cigarette/day	379 (81.2%)	104 (98.1%)	275 (76.2%)	0.0000
≤5 cigarettes/day	56 (12.0%)	2 (1.9%)	54 (15.0%)	
6–10 cigarettes/day	19 (4.1%)	0 (0.0%)	19 (5.3%)	
>10 cigarettes/day	13 (2.8%)	0 (0.0%)	13 (3.6%)	
First two trimesters of pregnancy				
Average hours of SHS exposure at home				
0 h	379 (81.2%)	104 (98.1%)	275 (76.2%)	0.0000
≤1 h	60 (12.8%)	2 (1.9%)	58 (16.1%)	
2–5 h	24 (5.1%)	0 (0.0%)	24 (6.6%)	
>5 h	4 (0.9%)	0 (0.0%)	4 (1.1%)	
Weighted SHS exposure (number of cigarettes) over all three trimesters				
0 cigarette/day	352 (75.4%)	103 (97.2%)	249 (69.0%)	0.0000
≤5 cigarettes/day	77 (16.5%)	3 (2.8%)	74 (20.5%)	
6–10 cigarettes/day	23 (4.9%)	0 (0.0%)	23 (6.4%)	
>10 cigarettes/day	15 (3.2%)	0 (0.0%)	15 (4.2%)	

* P-level given for the differences between the group below 0.05 ng/ml and above 0.05 ng/ml in cord blood cotinine level

The weighted average number of cigarettes smoked by others at any site over pregnancy in two different periods was assumed to be a better estimate of self-reported SHS exposure over the whole pregnancy period in the context of birthweight reduction than self-reported SHS recorded at delivery. The results of the analysis showed that, in the total sample, the effects of self-reported number of cigarettes smoked or cord cotinine level on birthweight

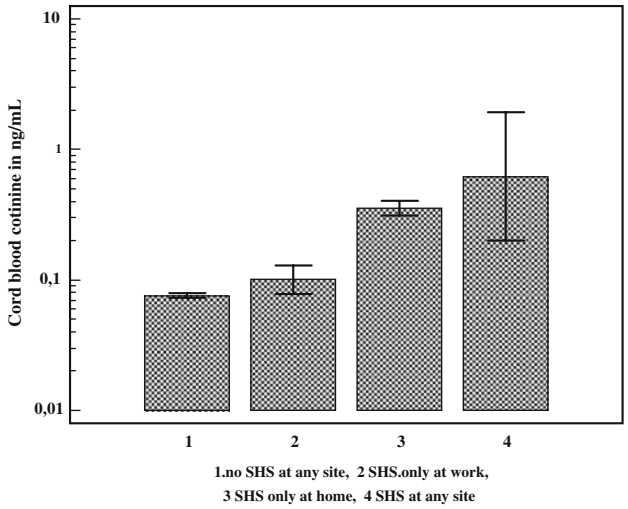

Fig. 1 Geometric means (error bars: 1 SEM) of cord blood cotinine by the self-reported SHS exposure site in the last trimester of pregnancy. Analysis of variance for the trend in cord cotinine levels across the groups: $F = 76.12$ (df: 3, 463) $P < 0.0001$. Difference of cord cotinine levels between the groups: group 1 (SHS−) versus group 4 (SHS both at and work) $P < 0.001$. Group 1 (SHS−) versus group 3 (SHS only at home) $P < 0.001$. Group 1 (SHS−) versus group 2 (SHS only at work) $P > 0.05$. Group 2 (SHS only at work) versus group 4 (SHS both at home and work) $P < 0.001$. Group 2 (SHS only at work) versus group 3 (SHS only at home) $P < 0.001$. Group 3 (SHS only at home) versus group 4 (SHS both at home and work) $P > 0.05$

Table 2 Geometric means of cord blood serum cotinine concentrations in newborns by the number of cigarettes smoked at home in the third trimester of pregnancy

Self-reported SHS category (number of cigarettes)	*N*	Geometric mean cotinine (ng/ml)	95% Confidence interval	
No exposure	374	0.077	0.071	0.083
1–5 cigarettes	55	0.257	0.188	0.351
6–10 cigarettes	26	0.466	0.282	0.770
>10 cigarettes	12	1.013	0.431	2.488
Total	467	0.105	0.095	0.116

Analysis of variance for trend $F = 87.94$ (df: 3, 463) $P < 0.0001$

Comparison between groups: SHS (−) versus SHS (1–5 cigarettes) $P < 0.001$; SHS (−) versus SHS (6–10 cigarettes) $P < 0.001$; SHS (−) versus SHS (>10 cigarettes) $P < 0.001$; SHS (1–5 cigarettes) versus SHS (>10 cigarettes) $P < 0.001$; SHS (1–5 cigarettes) versus SHS (6–10 cigarettes) $P < 0.05$; SHS (6–10 cigarettes) versus SHS (>10 cigarettes) $P > 0.05$ (insignificant)

reduction were not significant (Table 5a, b). However, in the subsample of newborns with cord cotinine levels above the median of (>0.083 ng/ml), while the effect of self-reported SHS remained insignificant (Table 6a), cord blood cotinine level was inversely and significantly associated with birthweight (Table 6b).

Table 3 Cord blood cotinine levels (in quartiles) by self-reported SHS exposure at any site in the third trimester of pregnancy

Cord blood cotinine levels (ng/ml)	Self-reported SHS status		Total
	SHS (−)	SHS (+)	
≤0.05	98 (27.9%)	8 (6.9%)	106 (22.7%)
0.054–0.083	122 (34.8%)	15 (12.9%)	137 (29.3%)
0.084–0.177	96 (27.4%)	25 (21.6%)	121 (25.9%)
>0.178	35 (10.0%)	68 (58.6%)	103 (22.1%)
Total	351 (100%)	116 (100%)	467 (100%)

Pearson $\chi^2(3) = 125.8254$; $P < 0.0001$

Discussion

The study results showed that the main contributor to the total burden of fetal SHS was exposure of mothers to SHS at home. Of several self-reported SHS variables used in the course of our study, the average number of cigarettes smoked in the home or the duration (in hours) of SHS exposure in the third trimester at home correlated best. The study has shown that about one-third of the variability in cord cotinine level was explained by self-reported SHS exposure (number of cigarettes smoked at home). We found that 37.4% of newborns whose mothers denied SHS exposure at home or work in the third trimester had cord blood cotinine levels above the median (>0.083 ng/ml). In addition, 19.8% of newborns with reported SHS exposure in the last trimester of pregnancy showed blood cord cotinine levels below the median concentration. This may result from the fact that they have been exposed only early in the last pregnancy trimester and not shortly before birth or it may be an expression of the misclassification of SHS exposure status based solely on self-report, which may dilute the association and bias risk estimates toward the null. Although both SHS exposure measures (self-report and cotinine measurements) were not significantly associated with birthweight in the overall sample, after restricting to cord cotinine levels above the median values, cotinine was inversely and significantly correlated with birthweight.

Our data on SHS exposure and birthweight, which suggest that the linear statistical models are not optimal for establishing the true dose–response relationship, are consistent with the results of the study performed by Haddow et al. [35], which showed that no significant birthweight differences occurred between the low and middle cotinine exposure groups. The inverse relationship between cotinine and birthweight was inverse and significant only among 34.4% of women who had serum cotinine levels between 1.0 and 9.9 ng/ml. These results do not necessarily demonstrate a threshold for the effects of cotinine, but may reflect the small number of subjects studied.

Table 4 Multivariate regression estimate of mean (log) cotinine as a function of the reported numbers of cigarettes smoked daily at home by others during the third trimester of pregnancy adjusted for confounders ($N = 467$)

Predictor variables	Coefficient	Standard error	t	$P > t$	95% confidence interval	
Maternal age (years)	−0.004	0.005	−0.85	0.396	−0.015	0.006
Maternal education (years of schooling)	−0.020	0.007	−2.93	0.004	−0.033	−0.007
Marital status	0.031	0.015	2.06	0.040	0.001	0.060
Number of cigarettes smoked daily by others						
<5 cigarettes	0.479	0.054	8.82	0.000	0.373	0.587
<10 cigarettes	0.683	0.078	8.74	0.000	0.529	0.836
>10 cigarettes	0.942	0.115	8.22	0.000	0.717	1.167
Constance	−0.712	0.164	−4.35	0.000	−1.034	−0.391

Adj. $R^2 = 0.372$

Table 5 Linear multivariate regression of birth weight (g) as a function of the self-reported number of cigarettes smoked daily at home or work by others during the entire pregnancy adjusted for confounders

Predictor variables	Coefficient	Standard error	t	$P > t$	95% confidence interval	
(a) Self-report						
Maternal age	2.42	5.15	0.47	0.639	−7.71	12.55
Parity	70.14	32.09	2.19	0.029	7.068	133.20
Maternal prepregnancy weight	11.84	2.07	5.72	0.000	7.77	15.91
Maternal height	9.35	3.43	2.72	0.007	2.61	16.08
Gender of child	−192.76	34.87	−5.53	0.000	−261.29	−124.23
Gestational age	164.11	13.41	12.24	0.000	137.76	190.46
Number of cigarettes smoked[a]	−1.47	4.46	−0.33	0.742	−10.23	7.30
Constance	−5,347.22	806.83	−6.63	0.000	−6,932.76	−3,761.68
(b) Cotinine						
Maternal age (years)	2.47	5.09	0.49	0.628	−7.53	12.46
Parity	69.93	31.66	2.21	0.028	7.72	132.14
Maternal prepregnancy weight (kg)	11.85	2.08	5.70	0.000	7.77	15.94
Maternal height (cm)	9.34	3.45	2.71	0.007	2.56	16.12
Gender of child	−193.02	34.81	−5.54	0.000	−261.43	−124.61
Gestational age (weeks)	163.81	13.53	12.11	0.000	137.22	190.39
Cotinine level (log transformed)	−12.30	39.89	−0.31	0.758	−90.69	66.10
Constance	−5,349.43	806.62	−6.63	0.000	−6,934.56	−3,764.29

Estimated in the total study sample ($N = 467$, $R^2 = 0.356$)

[a] Average number of cigarettes smoked daily by others at any site over pregnancy period: 0, no cigarettes; 1, <5 cigarettes; 2, 6–10 cigarettes; 3, >10 cigarettes

The cord blood cotinine levels measured in our study were much lower than levels observed in other cotinine-based studies involving newborns. For example, mean (arithmetic) cord blood cotinine levels were 0.71 ng/ml in the study by Haddow et al. [35], 0.20 ng/ml in the De-Lorenze et al. study [36] and 1.26 ng/ml in the Rebagliato et al. study [21]; these studies did not present geometric mean cotinine levels. Data published recently by Picchini et al. [37] showed even higher average concentrations of cotinine in cord blood. In the latter study, the median concentrations of cotinine in cord blood of newborns without SHS exposure was 1.62 ng/ml compared to 2.40 ng/ml in SHS-exposed newborns. It is important to note that these studies used different lab techniques from ours.

Our data concerning fetal SHS exposure are consistent with the results of a study in pregnant women in California by Kaufman et al. [38]. In the latter study the serum cotinine was assessed in pregnant women at gestation age of 15–18 weeks and used the same laboratory technique for determining serum cotinine. The authors found a significant correlation between serum cotinine in women and the reported number of smokers in the household ($r = 0.35$). The geometric mean blood cotinine was 0.06 ng/ml in

Table 6 Linear multivariate regression of birth weight (g) as a function of the self-reported number of cigarettes smoked daily at any site by others during the pregnancy adjusted for confounders (a), or as a function of cord cotinine concentration (b)

Predictor variables	Coefficient	Standard error	t	$P > t$	95% confidence interval	
(a) Self-report						
Maternal age	−7.99	7.79	−1.02	0.307	−23.35	7.38
Party	98.87	42.99	2.30	0.022	14.11	183.62
Maternal height	12.71	4.96	2.56	0.011	2.93	22.49
Maternal prepregnancy weight	12.22	3.00	4.07	0.000	6.30	18.14
Gender of child	−145.27	52.81	−2.75	0.006	−249.39	−41.15
Gestational age	150.69	19.73	7.64	0.000	111.79	189.58
Number of cigarettes smoked daily[a]	−42.02	30.23	−1.39	0.166	−101.62	17.57
Constance	−5,130.90	1,158.09	−4.43	0.000	−7,414.26	−2,847.55
$N = 220$, $R^2 = 0.323$						
(b) Cord cotinine						
Maternal age	−9.17	6.34	−1.45	0.150	−21.67	3.33
Parity	102.29	48.00	2.13	0.034	7.66	196.91
Gender of child	−157.87	51.32	−3.08	0.002	−259.03	−56.71
Gestational age	149.12	22.24	6.70	0.000	105.27	192.96
Maternal height	12.10	4.83	2.51	0.013	2.59	21.62
Prepregnancy maternal weight	11.83	2.48	4.76	0.000	6.93	16.72
Cord blood cotinine (log transformed)	−113.65	55.22	−2.06	0.041	−222.50	−4.80
Constance	−5,014.1	1,130.54	−4.44	0.000	−7,242.69	−2,785.6
$N = 220$, $R^2 = 0.338$						

Estimated in the subsample of the newborns with cord blood cotinine above the median (>0.083 ng/ml)

[a] Average number of cigarettes smoked daily by others at any site over pregnancy period: 0, no cigarettes; 1, <5 cigarettes; 2, 6–10 cigarettes; 3, >10 cigarettes

those who denied the presence of smokers in the household, 0.18 ng/ml in those who reported one smoker, and 0.29 ng/ml for two or more smokers. The concentrations of cord cotinine (geometric mean 0.077 ng/ml) that were found in our study among newborns without self-reported SHS were similar to these results.

Eighty percent of newborns in our study had cord blood cotinine levels above the detection limits, but the prevalence of self-reported SHS fetal exposure was only 25.2%. Prospective epidemiologic studies have provided varying prevalence rates of SHS exposure in pregnancy. In population based studies from 51 to 80% of non-smoking women reported being exposed to SHS during pregnancy [21, 39].

The inconsistencies between studies regarding serum cotinine as a biomarker of SHS exposure may be explained by several factors, with differences in laboratory techniques being the most important one. In the past, many SHS studies used insensitive laboratory methods for determining cotinine. In our study we used advanced laboratory methods that enabled detection of very small amounts of cotinine in the blood [31]. In addition, cotinine in body fluids as a biomarker of self-reported SHS exposure has some limitations including the inability to provide a measure of long-term SHS exposure and the variation in cotinine metabolism and clearance rates in the mothers of newborns. It is also important to note that cotinine is not the active mediator in causing adverse neonatal health effects. The level of cotinine in body fluids may not be a good marker of other constituents of SHS because the ratio of nicotine to other SHS components is highly variable and depends on ventilation rate, size of space, sampling duration, time since smoking, and air distribution patterns [40].

Conclusion

Despite these limitations our study provides evidence that the assessment of fetal SHS exposure based on cord blood cotinine produced better estimates of the association between exposure and birth outcomes.

Acknowledgments This is part of an ongoing comparative longitudinal investigation on the health impact of prenatal exposure to outdoor/indoor air pollution in infants and children being conducted in New York City and Krakow. The study received funding from an RO1 grant entitled, "Vulnerability of the Fetus/Infant to PAH, $PM_{2.5}$ and ETS" (5 RO1 ES10165 NIEHS; 02/01/00–01/31/04) and from the NIEHS (RO1 ES010165-0451) the Lundin Foundation and the Gladys T. and Roland Harriman Foundation. Principal investigator: Prof. FP Perera.

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