

Self-reported tobacco use and correlation with umbilical cord blood cotinine levels at delivery among Appalachian gravidas

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Statement of Purpose: To compare and correlate maternally reported rates of tobacco use to fetal cord blood levels of cotinine at the time of delivery. The rationale is to promote awareness of tobacco use during pregnancy in the tri-state region as discontinuation of smoking is a modifiable source of prenatal and perinatal morbidity and mortality

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Abstract

The detrimental effects of cigarette use during pregnancy are well documented. Studies have shown that cigarette smoking while pregnant is associated with multiple adverse outcomes including pre-term birth, placental abruption, placenta previa, fetal growth restriction, stillbirth, increased rate of birth defects, and increased risk of sudden infant death syndrome. Cotinine is the primary metabolite of nicotine and allows for measurement of active as well as passive exposure. Cotinine freely crosses the placental barrier and maternal concentrations are closely correlated with newborn plasma levels. The aim of this study was to compare maternally reported rates of tobacco use to fetal umbilical cord blood cotinine levels at the time of delivery. A cross-sectional study was conducted on 172 patients. Patients were asked a single yes or no question in regards to their cigarette use during pregnancy. Cord blood was collected at the time of delivery and analyzed for serum concentrations of cotinine. Cotinine levels greater than 3.0 ng/mL were considered consistent with the use of tobacco or tobacco cessation products. Maternal self-reporting of tobacco use indicates a reported tobacco use rate of 27.3% and an actual use rate of 30.2%. The reported tobacco non-use rate was 72.7% and the actual non-use rate was 66.3%. The prevalence of tobacco use during pregnancy in our study was 30.2%, while the overall rate in the United States is reported to be 12.3%. Our findings indicate that self-reported smoking prevalence and verified umbilical cord blood cotinine levels at the time of delivery have excellent correlation ($\kappa=0.76$). Compared to the national average our study group also had nearly double the rate of tobacco use. Due to the deleterious effects of cigarette use during pregnancy continued efforts to educate patients regarding cigarette cessation is of utmost importance as cessation of tobacco products will improve and promote maternal and fetal well-being.

Keywords

cigarette, Appalachia, gravida, fetus, smoking, nicotine, cotinine

Introduction

The detrimental effects of cigarette use during pregnancy are well documented. Studies have shown that cigarette smoking is associated with multiple adverse outcomes during pregnancy including pre-term birth, placental abruption, placenta previa, fetal growth restriction, stillbirth, increased rate of birth defects, and increased risk of sudden infant death syndrome.¹

The adverse effects of cigarette use extend beyond prenatal exposure. Nicotine is associated with adverse postnatal neurobehavioral, metabolic, cardiovascular, and respiratory outcomes, sudden infant death syndrome (SIDS) and childhood cancers.²⁻⁴ Nicotine is a neurological stimulant and considered a major contributor to the addictive effect of tobacco products. Cotinine is the primary metabolite of nicotine and allows for measurement of active as well as passive exposure. Cotinine freely crosses the placental barrier and maternal concentrations are strongly correlated with newborn plasma levels.^{5,6}

Overall the rate of reported smoking during pregnancy in the United States has decreased from 18.4% in 1990 to 12.3% in 2010.^{7,8} However, in the Pregnancy Risk Assessment Monitoring System, Tong et al reported that West Virginia was one of three states where smoking prevalence

increased between 1990-2010.⁸ The smoking prevalence in the state of West Virginia is 67% among adolescents between the age of 13-19 during the last 3 months of pregnancy.⁹

The aim of this study was to compare and correlate maternally reported rates of tobacco use to fetal cord blood levels of cotinine at the time of delivery among Appalachian gravidas. An additional objective was to examine the accuracy of self-reporting for smoking status in pregnant women. There is a lack of studies examining the frequency of tobacco use in Appalachia. The health effects of smoking are well recognized but discontinuation of smoking is a modifiable source of prenatal and perinatal morbidity and mortality. Identifying a higher than the national average frequency of tobacco usage supports the need to further educate the public regarding the adverse effects of smoking during pregnancy.

Methods

A cross-sectional study was conducted on 172 patients from April 2013 to February 2014. Inclusion criteria were consenting patients presenting to the labor and delivery unit at Cabell Huntington Hospital in active labor or admitted for induction of labor. Exclusion criteria were patients who delivered precipitously prior to being consented for the study. The study participants were asked a single yes or no question in regard to cigarette use during pregnancy. Cord blood was collected at the time of delivery and analyzed for serum concentrations of cotinine in ng/mL by the Cabell Huntington Hospital laboratory.

For the purpose of this study cotinine levels greater than 3.0 ng/mL were considered consistent with the use of tobacco or tobacco cessation products.¹⁰ A serum cord blood cotinine level of <3.0 ng/mL would classify a patient as a “non-tobacco user” and cotinine level of >3.0 ng/mL would classify a patient as a “tobacco user”. Self-reported maternal smoking data was collected at the time of admission and results were corroborated with cord blood analysis for cotinine. Demographic information was extracted from the subjects’ electronic medical records.

Approval from the Institutional Review Board at Marshall University was obtained prior to beginning the study. Statistical analysis for continuous variables was by independent sample t-test using SAS Enterprise Guide 7.1. The project was supported by the Robert C. Byrd Center for Rural Health, Marshall University, and funding was obtained through the Rural Health Initiative grant from the West Virginia Higher Education Policy Commission and the Marshall University School of Medicine Translational Research Pilot Grant program.

Results

The overall prevalence of tobacco products in our study using a cotinine cutoff of >3.0 ng/mL was 30.2% (Table 1). There were 41 patients who reported tobacco use whose cord cotinine levels were positive at >3.0 ng/mL and 6 patients who reported tobacco use and cord cotinine levels were measured <3.0 ng/mL. There were 114 patients who denied tobacco use whose cord cotinine levels were negative and 11 patients who denied tobacco use while cord cotinine was >3.0 ng/mL. Comparing maternal reports of tobacco use indicates a reported tobacco use rate of 27.3% and an actual use rate as measured by cotinine in cord blood of 30.2%. The reported tobacco non-use rate was 72.7% and the actual non-use rate was 66.3%.

Self-reported tobacco use showed excellent agreement with the cotinine levels measured in umbilical cord blood with a Cohen's kappa coefficient of 0.76 (0.61-0.80 is excellent agreement).¹¹ In our study a single yes or no question in regard to maternal tobacco use has a sensitivity of 79%, specificity of 95%, positive predictive value of 87% and negative predictive value of 91%.

Table 1: Correlation of maternal self-report and umbilical cord blood cotinine levels

Maternal Self-Report	Cord Cotinine >3.0 ng/mL	Cord Cotinine <3.0 ng/mL	Total
Yes	41	6	47
No	11	114	125
Total	52	120	172

Prevalence of tobacco use: 30.2%

Sensitivity 79%

Specificity 95%

Positive Predictive Value 87%

Negative Predictive Value 91%

Kappa = 0.76 (0.61-0.80 is excellent agreement)¹¹

Baseline characteristics were similar among our tobacco non-users and users for maternal age, BMI, race, urbanization, hemoglobin and hematocrit levels on admission, mode of delivery, estimated blood loss at the time of delivery, gestational age, hypertension, diabetes, and length of hospital stay (Table 2). Among the two groups there were no significant differences when comparing total pregnancies or pregnancy outcomes (term, preterm, abortions, living children). Maternal tobacco users were noted to be less likely to be married (17.3% vs. 57.5%), more likely to admit to substance abuse or dependence (26.92% vs. 2.50%), more likely to have Medicaid for insurance (86.54% vs. 49.17%), and more likely to be unemployed (73.08% vs. 54.17%).

Table 2: Maternal Information. Reported mean \pm SD for continuous variables or n (%) for categorical variables. 95% Confidence Interval.

	Tobacco Non-User (cotinine <3 ng/mL)	Tobacco User (cotinine >3 ng/mL)	p-value
Age	25.92+5.53	25.13+4.15	0.31
BMI	32.46+6.53	30.46+7.77	0.08
Cotinine Level (ng/mL)	0.09+.34	69.65+59.46	<.0001
Race			
White	113 (94.17)	51 (98.08)	
Other	7 (5.83)	1 (1.92)	
Marital Status			
Married	69 (57.5)	9 (17.31)	
Other	51 (42.5)	43 (82.69)	

Self-Reported Substance Abuse/Dependence	3 (2.50)	14 (26.92)	
Urbanization			
Urban	63 (52.5)	30 (57.69)	
Rural	57 (47.5)	22 (42.31)	
Insurance Type			
Private	57 (47.5)	5 (9.62)	
Medicaid	59 (49.17)	45 (86.54)	
None	4 (3.33)	2 (3.85)	
Employment			
Employed	55 (45.83)	14 (26.92)	
Not-Employed	65 (54.17)	38 (73.08)	
Mother Length of Hospital Stay (days)	3.76+3.84	3.40+2.08	0.44
Maternal Hypertension	25 (20.83)	11 (21.15)	
Maternal Diabetes	12 (10)	4 (7.69)	
Maternal Hemoglobin (g/dL)	11.74+1.22	11.87+1.23	0.53
Maternal Hematocrit (%)	35.31+3.85	35.84+3.46	0.39
Mode of Delivery			
Cesarean Delivery	31 (25.83)	18 (34.62)	
Vaginal Delivery	89 (74.17)	34 (65.38)	
Gestational Age at Delivery (weeks)	38.32+2.08	38.48+1.91	0.62
Estimated Blood Loss at Time of Delivery (mL)	395.4+195.4	423.8+229.2	0.41

Fetal outcomes were significantly different in regard to fetal weight, length of neonatal hospital stay, and neonatal intensive care unit admission (Table 3). Mean weight was 3311 \pm 65g in the non-tobacco users and 3057 \pm 60 in the tobacco users (mean \pm SD), with a p-value of 0.02. This finding is consistent with previously published literature.¹ Hospital length of stay for the infants was noted to be significantly different, with infants of tobacco non-users staying 5.08 \pm 9.62 days and infants of tobacco users staying 10.65 \pm 13.40 (mean \pm SD), p-value of 0.009. Infants born to tobacco users were also twice as likely to go to the NICU with 32.69% (n=17) of tobacco users and only 15.83% (n=19) of non-tobacco users infants being admitted to the unit.

Table 3: Fetal Information. Reported as mean \pm SD for continuous variables or n (%) for categorical variables. 95% Confidence Interval.

Gender	Tobacco Non-User (cotinine <3 ng/mL)	Tobacco User (cotinine >3 ng/mL)	p-value
Male	65 (54.17)	28 (53.85)	
Female	55 (45.83)	24 (46.15)	
1 Minute Apgar	8.28 \pm 1.20	8.31 \pm 0.88	0.88
5 Minute Apgar	8.97 \pm 0.29	8.85 \pm 0.46	0.08
Birth Weight (grams)	3311 \pm 65	3057 \pm 60	0.02

Baby Length of Hospital Stay (days)	5.08±9.62	10.65±13.40	0.009
Head Circumference (cm)	33.99±3.62	33.81±1.87	0.67
Fetal Height (cm)	165.3±7.17	165.6±7.01	0.80
Immediate Post-Partum Location			
Well-Born Nursery	101 (84.17)	35 (67.31)	
NICU	19 (15.83)	17 (32.69)	

Discussion

West Virginia currently ranks first in United States with 27 of every 100 adults being tobacco users.^{12,13} A recent report indicated that 67% of West Virginia pregnant adolescents 19 years of age or younger smoked during the last 3 months of pregnancy.⁹ Overall the rate of reported smoking during pregnancy in the United States is 12.3%.^{7,8} Our study indicates that smoking prevalence (based on a cotinine level of >3.0 ng/mL) at the time of delivery among Appalachian gravidas was 30.2%. These findings indicate that self-reported smoking prevalence and verified umbilical cord blood cotinine levels at the time of delivery were much higher than the national average in the United States. Our study is the first to correlate umbilical cord cotinine levels in babies born in West Virginia with self reported smoking habit of the mothers during pregnancy.

The results of our study are consistent with previous inquires examining self-reported tobacco use among pregnant women and the correlation with serum concentrations of cotinine. A study of 448 women using a maternal serum cotinine concentration of >10.0 ng/mL to define tobacco users determined that 94.9% of women who denied smoking and 87.0% of women who stated they smoked reported their status accurately ($\kappa=0.83$).¹⁴ Kvalvik et al studied a subsample of 2,997 women in the Norwegian Mother and Child Cohort Study (MoBa) to assess self-reported tobacco use and plasma cotinine concentrations at 18 weeks gestational age using a cutoff of 12ng/mL.¹⁵ The sensitivity and specificity for self-reported smoking was 82% and 99% respectively. In our study a cotinine level of 3.0 ng/ml or higher was considered positive for exposure to tobacco usage and this value was based on a previous report by another laboratory.¹⁰ This cutoff was adopted for our study as our mothers were of different races and the lower level will include individuals that occasionally smoke. Cotinine levels resulting from exposure to second-hand smoke has declined over the past 30 years due to increased smoke free public areas. Cotinine levels in nonsmokers exposed to second-hand smoke are less than 1 ng/ml;¹⁰ it is unlikely that second-hand smoke exposure was identified as a smoker in our study as our cutoff level was 3.0 ng/ml.

Intervention strategies to promote cessation of tobacco use, prevent relapse, and avoid secondhand smoke exposure are essential and should be incorporated during routine prenatal visits.¹⁶ Techniques for intervention range from counseling, cognitive and behavioral therapy, hypnosis, acupuncture to pharmacologic therapy.^{17,18} Each method may have a different effect and outcome, so it is important to individualize the approach for each patient and provide the risks and benefits that are associated with each option. Smoking cessation prior to 15 weeks gestation has been shown to provide the greatest benefits for both the fetus and the mother, however, cessation of smoking at anytime during the pregnancy has shown to be beneficial.^{19,20}

In fact, cessation prior to the third trimester can offer a significant reduction in the low birth weight that is caused by maternal smoking.²⁰

This study does have limitations. The self-reported daily amount of cigarettes smoked was obtained however it was not ascertained when the study participants last had a cigarette prior to presenting to the labor and delivery unit. Perhaps this could be a contributing factor to our patients who reported using tobacco products but the resultant umbilical cord blood for cotinine was negative. Another contributing factor could be innate differences in regard to the fetal metabolism of nicotine and its metabolite cotinine that was measured for this study. Further studies are needed in the area of fetal metabolism of tobacco products. There was also the potential for selection bias as all patients who presented to the labor and delivery unit were not enrolled in the study.

In our study of Appalachian gravidas self-reported smoking prevalence and verified umbilical cord blood cotinine levels at the time of delivery have excellent correlation. Compared to the national average our study group also had nearly double the rate of tobacco use. Due to the deleterious effects of cigarette use during pregnancy continued efforts to educate patients regarding cigarette cessation is of utmost importance as cessation of tobacco products will improve and promote maternal and fetal well-being.

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