



Original Article

## Prenatal Secondhand Smoke Exposure: Correlation Between Nicotine in Umbilical Cord Blood and Neonatal Anthropometry



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### ABSTRACT

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**Objectives:** Nicotine narrows uterine blood vessels reducing the flow of oxygen and nutrients to the developing fetus. This study examined the effects of fetal exposure to secondhand smoke on neonatal anthropometry.

**Methods:** This cross sectional study recruited 128 pregnant women in the third trimester of single pregnancies who had no chronic illness, were not active or ex-smokers, and who were willing to participate in the study. Pregnant women who were exposed to secondhand smoke had umbilical cord blood nicotine concentrations of  $\geq 1$  ng/mL. Neonatal anthropometry was assessed according to the newborn birth weight and length. The independent t-test was used to determine the neonatal difference in mean birth weight and length between the women who were exposed to secondhand smoke, and those who were not exposed. A multiple linear regression analysis was employed to assess the effect of secondhand smoke exposure on birth weight and birth length, controlling for potential confounding variables (weight gain during pregnancy, body mass index, parity, maternal age, and maternal hemoglobin).

**Results:** There were 35 women exposed to secondhand smoke (nicotine  $\geq 1$  ng/mL). Neonate birth weight and birth length were lower among mothers who were exposed to secondhand smoke. However, only neonate birth weight was significantly reduced by exposure to secondhand smoke ( $p = 0.005$ ). The mean birth weight of these neonates was  $2,916.5 \text{ g} \pm 327.3 \text{ g}$  which was 205.6 g less than in unexposed fetuses.

**Conclusion:** Exposure of mothers to secondhand smoke during pregnancy reduces fetal development and neonatal weight.

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## Introduction

Tobacco smoking is a serious threat to the health of pregnant women and their fetuses. Cigarette smoke contains nicotine that stimulates the narrowing of blood vessels, thereby reducing the flow of oxygen and nutrients necessary for fetal growth [1]. Exposure to secondhand smoke in pregnant women increases the risk of placental disorders, premature

birth, respiratory infections, asthma, sudden death syndrome, and hyperkinetic disorder [2]. A previous study showed that exposure to secondhand smoke during pregnancy reduced the average birth weight by 33 g and the birth length by 1 cm [3]. The negative impact on the health of the fetus due to exposure to cigarette smoke in pregnancy continues as the infant grows and matures. The long-term impacts may be behavioral, including difficulty to concentrate, hyperactivity, learning

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disabilities, and increased risk of taking up smoking in the future [4]. Roger [5] concluded that smoking during pregnancy increases the risk of attention disorders and social behavior.

According to the National Basic Health Research in 2013, 85% of households in Indonesia were listed as having a member of the household that smoked [6], compared with 78.4% in 2011 as reported by the GATS survey [7]. The high proportion of active smokers in households increases the likelihood of pregnant women being exposed to secondhand smoke.

Efforts to prevent smoking are important considering the prevalence of active and passive smokers in the home. For pregnant women, it would be beneficial because the health implications in the fetus may be permanent and sustainable [8].

Studies on exposure to secondhand smoke in pregnant women and its impact on fetal growth disorders are expected to provide the evidence needed to improve maternal and child health in Indonesia, and prevent smoking, but there are few of these studies available.

The present study examined secondhand smoke exposure in pregnant women and the effects on neonatal anthropometry.

## Materials and Methodss

### 1. Participants

This study was a cross-sectional observational study design where 128 pregnant women visiting antenatal clinics were recruited across 30 sites (Independent Midwife Practices, 16 Community Health Centers, and 6 Hospitals in Bengkulu City). Study inclusion criteria were; the pregnancy was in the 3rd trimester, single pregnancy, no cardiovascular disease, no diabetes mellitus, never smoked, and willing to participate in the study.

The study began with 1-week training of enumerators followed by a mapping of sampling sites in early December 2017. Consecutive recruitment of antenatal care visiting pregnant women who met the inclusion criteria started in the last week of December 2017 and the sampling ceased in mid-February 2017.

### 2. Data collection

Data collection was carried out by trained enumerators who divided into 4 teams lead by 1 field coordinator. Each team consisted of 1 health analyst, 1 nutritionist and 2 midwives. Data on demographic characteristics, including age, parity and education, were collected through interviews using a structured form. Hemoglobin concentration was determined with the HemoCue system using the blood taken from a finger prick. Data on maternal weight and height were obtained using a standardized digital weighing scale, and a microtoise

height scale, respectively. The trial participants were contacted regularly to avoid or minimize the loss to follow up.

Umbilical cord blood specimens were taken after delivery of the placenta to measure the nicotine levels the neonates were exposed to by secondhand smoke exposure of the mother. The concentration of nicotine in the cord blood was measured using Gas Chromatography-Mass Spectrometry performed at Jakarta Regional Health Laboratories. The study outcomes were birth weight and length which were measured immediately after birth by trained personnel.

### 3. Measurement and statistical analysis

Secondhand smoke exposure was determined based on blood nicotine and its major metabolite, cotinine, at a lower limit of 1 ng/mL [9]. The computation and categorization of body mass index (BMI), maternal weight gain, and maternal age, were recorded according to the Indonesian Ministry of Health standardized methods of measurements. BMI was categorized as normal weight (18.5-24.9 kg/m<sup>2</sup>), underweight (< 18.5 kg/m<sup>2</sup>), and overweight (25.0-29.9 kg/m<sup>2</sup>). Maternal weight gain was grouped based on the increase in maternal weight during pregnancy adjusted for pre-pregnancy BMI. Parity was grouped based on the National Population and Family Planning Board recommended parity grouping. Maternal anemia was recorded when blood hemoglobin levels were < 11g/dL. Bivariable analyses (*t*-test and ANOVA) were undertaken to assess differences in birth weight and birth length according to the level of secondhand smoke exposure. Multiple linear regression was used to control for factors that could potentially confound the relationship between secondhand smoke exposure and fetal size. Values were deemed to be statistically significant when  $p < 0.05$ .

## Results

Study participants were typically aged 20-35 years (82%) and were housewives (79.9%; Table 1). More than half of the participants (55%) had an income equal to or greater than the regional minimum wage of Bengkulu Province ( $\geq$  IDR 1,730,000). The mean nicotine concentration in umbilical cord blood was 1.3 ng/mL, while the mean birth weight was 3,045 g, and the mean birth length was 48.6 cm (Table 2).

Table 3 shows the neonatal anthropometry classified by risk factors. Mean birth weight differed according to nicotine concentration group, pre-pregnancy BMI, and maternal weight gain. Mothers who were exposed to secondhand smoke gave birth to neonates that weighed less than those born to mothers who were not exposed to secondhand smoke ( $p = 0.014$ ). The mean neonatal birth weight was significantly higher

Table 1. Demographic characteristics of pregnant women (N = 128).

Characteristic	n	%
Maternal age (y)		
< 20	9	7.1
20-35	105	82.0
> 35	14	10.9
Maternal work status		
Housewife	102	79.7
Employed	26	20.3
Maternal education level		
Elementary school	17	13.3
Junior middle school	25	19.5
Senior middle school	51	39.8
University or higher	35	27.4
Paternal education level		
Elementary school	19	14.8
Junior middle school	25	19.6
Senior middle school	56	43.8
University or higher	28	21.8
Family monthly income (Rp)		
< 1,730,000	57	44.5
≥ 1,730,000	71	55.5
Household size		
2 people	30	23.4
3-4 people	62	48.4
≥ 5 people	36	28.2

Table 2. Descriptive statistics for nicotine, birth weight, and birth length.

Variable	n (%)	Mean (SD)	Min-Max
Nicotine (ng/mL)			
≥ 1	35 (27.3)	1.3 (2.5)	0.01 – 11.5
< 1	93 (72.7)		
Birth weight (g)			
< 2,500	10 (7.8)	3,045.5 (367.7)	2,200 – 3,960
≥ 2,500	118 (92.2)		
Birth length (cm)			
< 48	46 (35.9)	48.6 (1.9)	44.5 – 54
≥ 48	82 (64.1)		

between overweight and normal weight mothers ( $p = 0.003$ ), and between mothers who gained the most weight during pregnancy and those that gained a normal amount of weight ( $p = 0.036$ ). However, there was no significant association between neonatal size (weight and length) and anemia status, age, or maternal parity.

Table 4 summarizes the results of multiple linear regression. The results indicate that neonate birth weight differed by the level of secondhand smoke exposure after the effects of maternal weight gain and Pre-pregnancy BMI included in the regression were controlled for statistically. Exposure to secondhand smoke significantly reduced birth weight by 205.6 g ( $p = 0.005$ ).

Table 3. Interval estimated mean of birth weight and length by risk factors and covariates.

Determinant	Birth weight (g)		Birth length (cm)	
	Mean ± SD	p	Mean ± SD	p
Exposed to secondhand smoke (ng/mL)				
Nicotine ≥ 1 (n = 35)	2,916.5 ± 327.3	0.014*	48.3 ± 1.8	0.387
Nicotine < 1 (n = 93)	3,094.1 ± 371.9		48.7 ± 1.9	
Pre-pregnancy BMI				
Underweight (n = 14)	2,910.7 ± 340.5	1.000	47.9 ± 1.9	0.100
Overweight (n = 32)	3,241.7 ± 345.9	0.003*	49.3 ± 2.0	0.051
Normal (n = 82)	2,991.9 ± 355.4		48.4 ± 1.9	
Maternal weight gain				
Low (n = 46)	2,905.5 ± 294.2	0.036*	47.9 ± 1.9	0.058
Over (n = 26)	3,210.9 ± 317.6	0.390	49.1 ± 1.5	1.000
Normal (n = 56)	3,083.7 ± 405.7		48.8 ± 2.1	
Hemoglobin				
Anemia (n = 65)	3,013.3 ± 383.3	0.316	48.6 ± 1.9	0.966
Non-anemia (n = 63)	3,078.7 ± 350.8		48.6 ± 1.9	
Maternal age				
< 20 years (n = 9)	2,965.6 ± 185.7	1.000	47.8 ± 0.8	0.749
> 35 years (n = 14)	3,051.1 ± 373.1	1.000	48.6 ± 2.0	1.000
20-35 years (n = 105)	3,055.0 ± 425.5		48.9 ± 1.9	
Parity				
≥ 2 (n = 43)	3,059.5 ± 358.1	0.760	48.8 ± 2.1	0.418
< 2 (n = 85)	3,038.4 ± 364.1		48.5 ± 1.9	

Independent t test for comparing 2 groups and Anova for comparing more than 2 groups.

\*Statistically significant mean ± SD.

BMI = body mass index.

Table 4. Regression model of birth weight and birth length.

	Birth weight			Birth length		
	Adjusted difference	95% CI	<i>p</i>	Adjusted difference	95% CI	<i>p</i>
Exposed to secondhand smoke	-205.6	-348.6- -62.6	0.005	-0.34	-1.1-0.5	0.400
Maternal weight gain	30.7	14.3-47.2	≤ 0.001	0.07	-0.1-0.2	0.136
Pre-pregnancy BMI	27.9	10.2-45.7	0.002	0.11	0.1-0.2	0.021

BMI = body mass index; CI = confidence interval.

## Discussion

Several studies have shown that being exposed to secondhand smoke during pregnancy is associated with an increased risk of fetal growth restriction observed as reduced neonate birth weight and length [2,3]. However, there are inconsistencies in the effects due to exposure of secondhand smoke during pregnancy with birth outcomes because self-reporting is used [10]. Reporting on the use of cigarettes and exposure to secondhand smoke can be inaccurate due to recall bias, and lack of detailed information on smoking patterns, and exposure factors such as proximity to smokers and the air flow. In this study a concentration of nicotine in cord blood above 1 ng/mL was used to more accurately define exposure to secondhand smoke, and below 1 ng/mL of nicotine was considered as not exposed to secondhand smoke.

In this current study, in women exposed to secondhand smoke, the mean concentration of nicotine in umbilical cord blood was 1.3 ng/mL. The secondhand smoker group had significantly lower mean neonatal weight compared to those not exposed to smoke (2,916.5 ± 327.3 versus 3,094.1 ± 371.9). This was in line with a cross-sectional comparative study in a Malaysian tertiary obstetric hospital involving 200 non-smoking pregnant women [11]. In pregnant women, nicotine and its major metabolite cotinine, is a vasoconstrictor that reduces uterine blood flow by 30%-40%, resulting in a decreased supply of oxygen and nutrients requirements for fetal growth. Cotinine also suppresses the production of amino acids and reduces the activation of enzymes related to fetal growth [9].

Nicotine in maternal blood disrupts fetal growth in 2 ways. Directly, nicotine disrupts absorption of calcium, vitamin C and other vitamins and minerals needed for fetal growth [12]. Nicotine binds acetylcholine, which is a placental signal molecule that plays an important role in controlling nutrient absorption, blood flow and fluid volume in the placental vessels, as well as vascularization during placental development [5]. This condition results in an imbalance of

receptor activation and function that leads to pathological conditions in the form of placental insufficiency [5,12]. In a second pathway, nicotine causes vasoconstriction in blood vessels, resulting in reduced blood flow to the fetus through the umbilical cord to reduce the distribution of food substances needed by the fetus. The presence of nicotine in the blood may also be a secondary marker of oxidative stress experienced by the mother and fetus, i.e. the higher the level of nicotine, the greater the exposure to harmful smoke which causes oxidative stress in the vascular system, and also reduces blood flow in the umbilical cord. As a result, there is a cell imbalance and a decrease in the number of cells. Furthermore, there is a decrease in organ growth and a slower accumulation of fat muscle, which can cause lower birth weight [12,13].

Fetal growth restriction is not only due to exposure to cigarettes. There are other factors that also affect fetal growth including nutritional status, nutritional intake, alcohol consumption, maternal disease, and environmental health of residence [14,15]. These factors are thought to compound the effect of secondhand smoke on fetal growth restriction.

Maternal weight gain during pregnancy, and pre-pregnancy BMI are confounding variables for the association of secondhand smoke with birth weight. Maternal BMI before pregnancy is often associated with birth weight because it describes the environmental aspects of the fetus and the availability of resources from the mother. Maternal BMI has a direct physiological effect on fetal growth through nutrient supply and hormonal profiles. Maternal weight gain during pregnancy is also known to have a positive correlation with neonate birth weight. Adequacy of maternal weight gain is 1 of the best predictors for birth outcomes. Pregnant women with inadequate weight gain have an increased risk of perinatal morbidity and mortality [16].

After controlling for confounding variables, multivariate analyses indicated that exposure to secondhand smoke by pregnant women reduced mean neonate birth weight by 205.6 g. This finding is in line with previous studies, which reported lower birth weights due to secondhand smoke that ranged from 15-

200 g less than unexposed neonates [12,17,18]. A retrospective cohort study by Norsa'adah et al found a low reduction in the mean birth weight (12.9 g) [19]. The variation in lower birth weights because of exposure to secondhand smoke compared with no exposure, is wide-ranging. It may be caused by differences in study design, sample size, and the variables controlled in each study. However, the negative effects of secondhand smoke on birth weight have been consistently demonstrated.

In this current study fetuses exposed to secondhand smoke weighed 205.6 g less than unexposed fetuses and 30% of these mothers had a husband with a low level of education and only 7.9% of pregnant women had a high level of education. This would create concerns especially among the lower socio-economic families.

In our studies, the pregnant women with poorly-educated husbands had greater exposure to cigarette smoke (31.8%), than pregnant women with highly-educated husbands (25%).

A lower mean birth length for mothers who were exposed to secondhand smoke was observed in this study, although it was not statistically significant. It has been reported that secondhand smoke can reduce the birth length by 0.3 cm [16]. Low birth length, is an indication of a skeletal system growth failure and long-term nutritional deficiencies that can occur during pregnancy, and is a determinant of future stunting. This condition is closely related to higher morbidity and mortality, delays in cognitive development and increased risk of chronic disease later in life [20,21]. The incidence of low birth length (< 48 cm; 20.2%) and stunting (32.9%) was very high in Indonesia in 2013.

Efforts to prevent smoking are very important considering that smoking is the most influential contributor to fetal growth disorder that can be controlled. Interventions during pregnancy to reduce exposure to cigarette smoking in the home should be a priority for health programs.

There are limitations to this study including the assessment of exposure to cigarette smoke was based only on the concentration of nicotine without considering other chemicals in cigarette smoke that may also be involved in interfering with fetal growth. In addition, the loss to follow-up was 15% due to study withdrawal, late arrival at delivery, or the cord blood specimen taken was spoiled.

## Conclusion

Exposure to secondhand smoke during pregnancy, as indicated by the nicotine concentration in umbilical cord blood, was associated with low neonatal birth weight. A comparable association with birth length was not observed. Efforts to protect pregnant women from exposure to secondhand smoke

are imperative, not only in public areas, but importantly in the home.

## Conflicts of Interest

The authors declare that they have no competing interest.

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