DOI: https://doi.org/10.17816/humeco678348 EDN: SYKSRD

Влияние курения матери на массу плаценты и соотношение массы плаценты к массе тела при рождении у доношенных новорождённых из одноплодных беременностей: исследование, основанное на регистре родов

О.А. Харькова, В.А. Постоев, А.А. Усынина

Северный государственный медицинский университет, Архангельск, Россия

АННОТАЦИЯ

Обоснование. Курение матери во время беременности является важным фактором риска неблагоприятных исходов беременности, в то же время исследования связи между курением и морфологией плаценты ограничены.

Цель исследования. Изучение взаимосвязи между курением матери во время беременности и массой плаценты, а также соотношением массы плаценты к массе новорождённого.

Методы. Проведено ретроспективное когортное исследование с использованием данных регистра родов Мурманской области. В анализ включили случаи одноплодной беременности на сроке родов более 37 полных недель гестации. Мультиномиальную логистическую регрессию использовали для оценки взаимосвязи между стандартной оценкой массы плаценты (низкой, средней, высокой) и отношением массы плаценты к массе тела при рождении, а также курением до и во время беременности, включая ежедневное количество выкуриваемых сигарет.

Результаты. Средняя масса плаценты у мальчиков составила 534,1 г, а у девочек — 523,7 г. У женщин, куривших во время беременности и до её наступления, вероятность низкой стандартной оценки массы плаценты была значимо ниже по сравнению с никогда не курившими. Скорректированное отношение относительных рисков (ООР) для курящих — 0,75 [95% доверительный интервал (ДИ) 0,70–0,81], для куривших до беременности — 0,86 (95% ДИ 0,76–0,97) соответственно. Вероятность более высокой стандартной оценки массы плаценты у курящих во время беременности и тех беременных, которые бросили курить до первой антенатальной явки, была значимо выше: скорректированный ООР для курящих — 1,35 (95% ДИ 1,25–1,45), скорректированное ООР для куривших до беременности — 1,21 (95% ДИ 1,09–1,36) по сравнению с некурящими соответственно.

У женщин, куривших до и во время беременности, вероятность низкого соотношения массы плаценты к массе тела при рождении была ниже по сравнению с женщинами, никогда не курившими [скорректированное ООР для курящих — 0,76 (95% ДИ 0,70–0,83); для бросивших курить — 0,87 (95% ДИ 0,77–0,97)]. Кроме того, у них отмечали более высокие показатели стандартной оценки этого отношения [скорректированное ООР для курящих —1,52 (95% ДИ 1,43–1,63); для бросивших курить — 1,18 (95% ДИ 1,06–1,31)]. Выявлена обратная зависимость между количеством выкуриваемых сигарет во время беременности и вероятностью получения более высокой стандартной оценки как массы плаценты, так и соотношения массы плаценты к массе тела при рождении.

Заключение. Исследование выявило, что у женщин, куривших во время беременности или прекративших курение до первой антенатальной явки, масса плаценты и её соотношение с массой тела новорождённого была выше. При этом у продолжающих курить наблюдали дозозависимый эффект. Полученные данные свидетельствуют о том, что не только отказ от курения, но и уменьшение количества выкуриваемых сигарет в день может снизить риски неблагоприятных событий для плода. Это подчёркивает потенциал использования данного подхода как мотивационного инструмента для продвижения стратегий первичной профилактики осложнений беременности среди курящих женщин.

Ключевые слова: плацента; масса при рождении; соотношение массы плаценты и массы при рождении; курение во время беременности; регистрация рождений.

Как цитировать:
Харькова О.А., Постоев В.А., Усынина А.А. Влияние курения матери на массу плаценты и соотношение массы плаценты к массе тела при рождении у доношенных новорождённых из одноплодных беременностей: исследование, основанное на регистре родов // Экология человека. 2025. Т. 32, № 6. С. 413–421. DOI: 10.17816/humeco678348 EDN: SYKSRD

Рукопись поступила: 10.04.2025 **Рукопись одобрена:** 08.07.2025 **Опубликована online:** 05.08.2025

DOI: https://doi.org/10.17816/humeco678348 EDN: SYKSRD

Effect of Maternal Smoking on Placental Weight and Placental-to-Birth Weight Ratio in Full-Term Singleton Births: A Birth Registry-Based Study

Olga A. Kharkova, Vitaly A. Postoev, Anna A. Usynina

Northern State Medical University, Arkhangelsk, Russia

ABSTRACT

BACKGROUND: Maternal smoking during pregnancy is a significant risk factor for adverse pregnancy outcomes. However, studies investigating the association between smoking and placental morphology are limited.

AIM: The study aimed to examine the association between maternal smoking during pregnancy and placental weight, as well as the placental-to-birth weight ratio.

METHODS: A retrospective cohort study was conducted using the data from the Murmansk County Birth Registry. The analysis included singleton births at ⩾37 completed weeks of gestation. Multinomial logistic regression was applied to assess the associations between standardized placental weight categories (low, medium, high) and the placental-to-birth weight ratio, and smoking before and during pregnancy, including the number of cigarettes smoked daily.

RESULTS: The mean placental weight was 534.1 grams for male newborns and 523.7 grams for females. Compared with women who never smoked, those who smoked during pregnancy and those who smoked before pregnancy had significantly lower odds of low standardized placental weight. The adjusted relative risk ratio (RRR)=0.75 (95% CI: 0.70–0.81) for smokers, and 0.86 (95% CI: 0.76–0.97) for those who smoked before pregnancy. The likelihood of a higher standardized placental weight was significantly greater among those who smoked during pregnancy and those who had quit smoking before the first antenatal visit: adjusted RRR=1.35 (95% CI: 1.25–1.45) for smokers and 1.21 (95% CI: 1.09–1.36) for those who quit before pregnancy, compared with non-smokers.

The women who smoked before or during pregnancy were less likely to have a low placental-to-birth weight ratio compared with never-smokers (adjusted RRR=0.76 [95% CI: 0.70–0.83] for smokers; adjusted RRR=0.87 [95% CI: 0.77–0.97] for those who quit), and were more likely to have a high standardized ratio (adjusted RRR=1.52 [95% CI: 1.43–1.63] for smokers; adjusted RRR=1.18 [95% CI: 1.06–1.31] for those who quit). An inverse relationship was identified between the number of cigarettes smoked during pregnancy and the likelihood of obtaining higher standardized values for both placental weight and placental-to-birth weight ratio.

CONCLUSION: The study revealed that smoking during pregnancy and quitting prior to the first antenatal visit were associated with higher placental weight and placental-to-birth weight ratio, with a dose-dependent effect observed among smokers. These findings suggest that not only smoking cessation but also reduction in daily cigarette consumption may lower the risk of adverse fetal outcomes, which may serve as a potential motivational tool for promoting primary prevention strategies aimed at reducing adverse pregnancy outcomes among women who smoke.

Keywords: placenta; birth weight; placental-to-birth weight ratio; smoking pregnancy; birth registry.

To cite this article:
Kharkova OA, Postoev VA, Usynina AA. Effect of maternal smoking on placental weight and placental-to-birth weight ratio in full-term singleton births: a birth registry-based study. *Ekologiya cheloveka (Human Ecology).* 2025;32(6):413–421. DOI: 10.17816/humeco678348 EDN: SYKSRD

Submitted: 10.04.2025 **Accepted:** 08.07.2025 **Published online:** 05.08.2025

DOI: https://doi.org/10.17816/humeco678348 EDN: SYKSRD

基于出生登记数据的研究：母亲吸烟对足月单胎新生儿胎盘重量及胎盘重量与出生体重比值的影响

Olga A. Kharkova, Vitaly A. Postoev, Anna A. Usynina

Northern State Medical University, Arkhangelsk, Russia

摘要

论证。孕期母亲吸烟是不良妊娠结局的重要危险因素，然而，关于吸烟与胎盘形态学特征之间关系的研究仍然有限。

目的。本研究旨在探讨母亲孕期吸烟与胎盘重量及胎盘重量与出生体重比值之间的相关性。

方法。本研究为回顾性队列研究，数据来源于Murmansk District Birth Registry。纳入对象为妊娠满37周的足月单胎分娩病例。采用多项logistic回归分析评估胎盘重量标准评分（低、中、高）及胎盘重量与出生体重比值与孕前及孕期吸烟的关联性，包括每日吸烟支数。

结果。男婴胎盘平均重量为534.1克，女婴为523.7克。在孕期吸烟者和孕前吸烟者中，胎盘重量标准评分较低的发生概率显著低于从未吸烟的女性。调整后的相对风险比（relative risk ratio, RRR）分别为：孕期吸烟者为0.75（95%置信区间：0.70–0.81），孕前吸烟者为0.86（95%置信区间：0.76–0.97）。与此同时，孕期吸烟者及在首次产前就诊前戒烟的孕妇胎盘重量标准评分较高的发生概率显著更高：调整后RRR为1.35（95%置信区间：1.25–1.45），孕前戒烟者为1.21（95%置信区间：1.09–1.36），与从未吸烟者相比。

在孕前和孕期吸烟的女性中，胎盘重量与出生体重比值标准评分较低的发生概率低于从不吸烟的女性（孕期吸烟者的调整后相对风险比为0.76（95%置信区间：0.70–0.83）；孕前吸烟者为0.87（95%置信区间：0.77–0.97）），而该比值标准评分较高的发生概率则更高（孕期吸烟者的调整后相对风险比为1.52（95%置信区间：1.43–1.63）；孕前吸烟者为1.18（95%置信区间：1.06–1.31））。此外，研究还发现，孕期每日吸烟支数与胎盘重量及胎盘重量与出生体重比值的标准评分之间呈现负向剂量–反应关系。

结论。本研究发现，孕期吸烟者及在首次产前就诊前戒烟的孕妇，其胎盘重量和胎盘重量与出生体重比值较高，其中孕期吸烟者的该关联呈剂量依赖性。这证实了，不仅完全戒烟，减少每日吸烟数量亦可降低胎儿不良结局的风险；该发现可作为促进吸烟孕妇实施妊娠不良结局一级预防策略的重要动机工具。

关键词：胎盘；出生体重；胎盘与出生体重比；吸烟怀孕；出生登记。

引用本文：

Kharkova OA, Postoev VA, Usynina AA. 基于出生登记数据的研究：母亲吸烟对足月单胎新生儿胎盘重量及胎盘重量与出生体重比值的影响. *Ekologiya cheloveka (Human Ecology).* 2025;32(6):413–421. DOI: 10.17816/humeco678348 EDN: SYKSRD

收到: 10.04.2025 **接受:** 08.07.2025 **发布日期:** 05.08.2025

BACKGROUND

Maternal smoking during pregnancy is one of the most common modifiable risk factors of adverse short- and long-term pregnancy outcomes such as miscarriages [1], preterm deliveries [2, 3], low birthweight (BW) [3], and some birth defects [2–4]. Some complications are related to placenta development and can be partially explained by disfunction of trophoblasts and hormonal disbalance in early pregnancy caused by smoking [1] and vascular effects of nicotine [5]. All women are advised to quit smoking before conception or during the first trimester of pregnancy. It was found that the most benefits were observed in case of smoking cessation before week 15 of pregnancy [6]. It can improve the prognosis and reduce the risk of adverse pregnancy outcomes. However, the prevalence of smoking in pregnant women in many countries, including Russia, is still relatively high. For example, our previous study in the North-West of Russia revealed up to 25% and 18% smoking mothers before and during pregnancy, respectively [7].

Placental weight (PW) and placental-to-birth weight ratio (PW/BW) are well-known indicators of adverse pregnancy outcomes as they reflect prenatal functioning [8]. An unbalanced PW/BW may indicate abnormal placental functioning or placental adaptation to an adverse intrauterine environment. Previous research showed that low PW z-scores were associated with a two-fold increase in fetal death, whereas high z-scores were associated with higher odds of neonatal morbidity [9]. Salavati *et al.* (2017) determined BW/PW in 3311 deliveries and found that low BW/PW was associated with higher risk of neonatal morbidity [10]. Shehata *et al.* (2010) [11] found that low BW/PW was associated with higher risks of intensive care unit admission, low Apgar scores, and fetal death. These findings indicate that PW/BW, when interpreted based on defined thresholds and in relation to other clinical parameters, is a useful diagnostic tool for identifying potential intrauterine growth restrictions and placental insufficiency in newborns. Research on the relationship between smoking and placental morphology, especially PW/BW, is scarce. In addition, smoking cessation effects on placenta are still unclear. Some studies showed significant difference in the placental structure and weight between smoking and non-smoking mothers [12] and higher PW/BW in smoking mothers [9, 10]. However, other authors consider that despite lower first-trimester placental vascularization flow indices, a negative smoking effect on PW is not evident yet [15]. Another important issue is how smoking cessation during pregnancy affects placental development. Some studies revealed a positive effect of smoking cessation on anthropometric measurements in newborns compared with offspring of smoking mothers due to improved placental transfer [3, 16].

Currently, most studies in Russia investigate relationships between smoking and placental insufficiency [17, 18], premature maturation of placenta, and histological changes in pregnant smokers [18, 19]. The relationship between smoking before and during pregnancy and high PW and PW/BW have, to our knowledge, not been studied yet.

Two population-based birth registries established in the Murmansk County (MC) in the North-West of Russia two decades ago contain data on maternal smoking behavior before and during pregnancy and morphological examinations of placenta in all deliveries in this region, allowing to investigate changes in placental morphology in pregnancy.

Aim

The study was aimed to explore potential associations between maternal smoking status during pregnancy (including the effect of smoking cessation and daily number of smoked cigarettes) and PW, including PW/BW. Thus, our primary objectives were to: (i) determine PW and BW for gestational age and sex; and (ii) examine a potential association between smoking status during pregnancy (including daily number of smoked cigarettes) and z-scores of PW and PW/BW.

METHODS

Study Setting, Design, and Sample Size

The Murmansk County Birth Registry (MCBR) has registered all births from 22 weeks of gestation in MC from January 1, 2006 to December 31, 2011. The detailed information on its design, implementation, and data collection was presented in our previous study [20].

In this study, we used all cases with singleton pregnancy delivered at > 37 completed weeks of gestation from the registry. Our study focused on two main tobacco-smoking issues related to pregnancy: (i) smoking status before pregnancy and during the first antenatal visit, and (ii) the number of cigarettes smoked daily. Sampling details are summarized in Fig. 1.

Data Collection

The MCBR contains anonymized maternal data, such as age, parity, weight and height measured at the first antenatal visit, marital status, residence, ethnic origin, education, and self-reported smoking status at the first antenatal visit (including the number of cigarettes per day before and during pregnancy), collected from medical records and personal interviews with pregnant women. Data on the mode of delivery, gestational diabetes, preeclampsia/eclampsia, gestational age, year of delivery, and anemia to be included in the MCBR were taken from individual obstetric records. In addition, the MCBR contains data on the sex of newborns, PW, and BW.

Dependent Variables

PW and BW were measured in grams. PW/BW was calculated by dividing PW by BW in grams. We calculated z-scores in the sample using means and standard deviation of PW and PW/BW for each gestational age. Moreover, z-scores were calculated separately for male and female

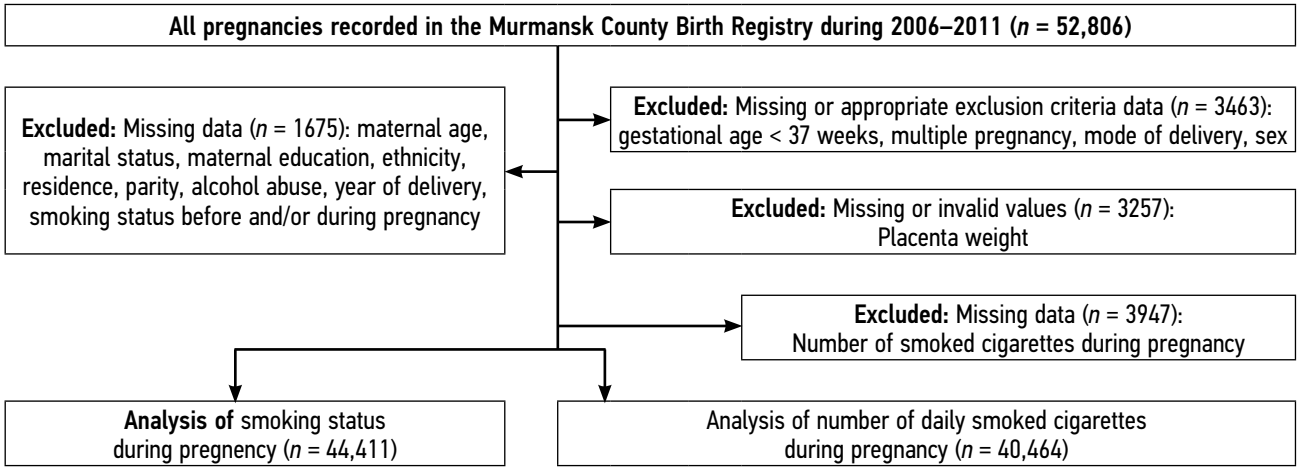

Fig. 1. Study population selection flow chart.

newborns. PW and PW/BW z-scores were classified as < –1; – 1 to + 1; and > +1.

Independent Variables

Smoking status during pregnancy was defined as *smoker* (women who smoked before and during pregnancy), *quitter* (women who quit smoking during pregnancy), and *non-smoker* (women who smoked neither before nor during pregnancy). For pregnant smokers, the number of cigarettes smoked daily was treated as a categorical variable, i.e. 0; 1–5; 6–10; and ⩾ 11.

Data Analysis

Distribution of continuous variables were checked for normality using the Shapiro–Wilk test and presented as a mean and standard deviation. Two-sample t-test was used to compare the mean values (PW and BW) in two groups of data. Simple linear regression was used to determine the relationship between PW, BW, and gestational age for male and female newborns separately. An analysis of covariance (ANCOVA) was conducted with gestational age as a covariate to determine the difference in PW between maternal smoking categories. We used a multinomial logistic regression to assess the correlations between z-scores (low, medium, and high) of PW and PW/BW and smoking status during pregnancy, including the daily number of smoked cigarettes. Medium z-scores were chosen as the base outcome; therefore, it was used as the reference to build the regression models. Unadjusted and adjusted relative risk ratios (RRR) derived from multinominal logistic regression models were calculated with 95% confidence intervals (CI). Maternal age (⩽ 19 years, 20–24 years, 25–29 years, 30–34 years, and ⩾ 35 years), parity (0, 1, and ⩾ 2 deliveries), marital status (married, cohabitation, or single [including divorced or widowed women]), place of residence (urban and rural), ethnic origin (Russian or other), education (university, etc.), year of delivery, body mass index (⩽ 18.4, 18.5–24.9, 25.0–29.9, ⩾ 30, or unspecified), mode of delivery (vaginal or caesarean section), gestational diabetes, preeclampsia/eclampsia, anemia, and BW were used for mutual adjustment as potential confounders in multinominal logistic regression models. Statistical processing was performed using STATA v. 14 (StataCorp LLC).

Ethical Approval

The MCBR establishment and data collection was approved by the Regional Healthcare Office of the Murmansk County. A special law was adopted by the regional government on mandatory registration of births in the MCBR for all delivering women. The registry database does not contain any personal identifiers.

This study was approved by the Ethical Committee of the Northern State Medical University (Arkhangelsk, Russia) (No. 08/12-14 dated December 10, 2014).

RESULTS

Placental Weight and Birth Weight by Gestational Age and Sex

The mean PW for male newborns was 534.1 g (SD:117.9 g) and 523.7 g (SD: 116.6 g) for female newborns. The mean BW for male newborns was 3500 g (SD: 457.1 g) and 3366 g (SD: 439.0 g) for female newborns (see Table 1).

Moreover, mean PW and BW increased with gestational age. Linear regression: PW_{males}, B=6.25 (95% CI 5.0–7.5) and $PW_{females}$, B=7.05 (95% CI 5.8–8.3); BW_{males}, B=97.5 (95% CI 92.9–102.1) and $BW_{females}$, B=94.3 (95% CI 89.8–98.9). Difference in PW in the groups by smoking status stratified by gestational age and sex is shown in Table 2.

Association Relationship between Smoking Status During Pregnancy and Z-Scores of Placental Weight and Placental-to-Birth Weight Ratio

The relationships between smoking status during pregnancy and z-scores of PW and PW/BW are shown

Table 1. Mean placental weight and birth weight by gestational age and sex (g)

Gestational age	Male newborns, Mean (SD)			Female newborns, Mean (SD)			*p* value[1]	
	n	PW	BW	*n*	PW	BW	PW	BW
37 weeks	1555	508.9 (123.2)	3148 (467)	1275	498.9 (117.8)	3023 (423)	0.029	< 0.001
38 weeks	3788	524.2 (119.1)	3352 (433)	3236	511.8 (117.9)	3205 (430)	< 0.001	< 0.001
39 weeks	6765	534.9 (118.2)	3493 (432)	6133	523.1 (115.8)	3354 (418)	< 0.001	< 0.001
40 weeks	6854	540.6 (117.2)	3594 (428)	6458	528.8 (115.4)	3440 (408)	< 0.001	< 0.001
41 weeks	2794	541.8 (112.3)	3633 (448)	3024	532.3 (116.2)	3500 (425)	0.002	< 0.001
⩾ 42 weeks	1244	539.2 (116.6)	3612 (474)	1285	536.0 (116.7)	3483 (455)	0.497	< 0.001
Total	23,000	534.1 (117.9)	3500 (457)	21,411	523.7 (116.6)	3366 (439)	< 0.001	< 0.001

Note: PW, placental weight; BW, birth weight; [1] calculated using the two-sample t-test.

in Table 3. Smokers and those who quit smoking during pregnancy were less likely to have low PW z-score only after adjustment for potential confounders compared to non-smokers: adjusted RRR_{smoker}=0.75 (95% CI 0.70–0.81) and adjusted $RRR_{quitter}$=0.86 (95% CI 0.76–0.97). Moreover, smokers and quitters were less likely to have low PW/BW z-score both before and after adjustment for socio-demographic and medical parameters of pregnant women compared to non-smokers. Smokers and quitters were more likely to have high z-scores of PW and PW/BW compared to non-smokers as shown by the unadjusted and adjusted values summarized in Table 3.

A negative dose–response relationship was found between the number of cigarettes smoked daily during pregnancy and the odds of low z-scores of both PW and PW/BW. Adjustment for potential confounders did not change this relationship (see Table 4).

However, positive dose–response relationship was observed between the high z-scores of PW and PW/BW and the number of cigarettes smoked daily during pregnancy (see Table 4). Moreover, mothers who smoked ⩾ 11 cigarettes per day during pregnancy were 2.97 and 3.55 times more likely to have a high z-score of PW and PW/BW, respectively, compared to non-smokers.

DISCUSSION

In our singleton pregnancy study, mean PW at any week of gestation was lower compared with mean PW (SD) of 612 (138) g at term pregnancies (37–42 weeks) reported by Nascente *et al.* (2020) [21]. We found that mean BW increased with gestational age for both female and male newborns born at 37–41 weeks of pregnancy. Other studies also showed a trend toward a higher BW in infants born at 37–41 weeks, which is consistent with our findings [21–23].

In our study, smokers and quitters were more likely to have high z-scores of PW and PW/BW as opposed to non-smokers. These findings are consistent with previous studies, where it was confirmed that continued smoking during pregnancy caused higher PW [9, 10, 24]. For example, in a birth cohort study conducted in Japan involving 91,951 records, both PW and PW/BW were higher in smokers compared with non-smokers [24]. Heidari *et al.* (2018) also found higher mean PW in smokers (610 g) as compared with non-smokers (455 g) [8]. A recent meta-analysis showed a 182 g heavier placenta in smoking pregnant women compared with quitters [10]. In contrast to non-smokers, PW demonstrated a higher mean value in quitters [25].

Table 2. Mean placental weight by smoking status stratified by age and sex (g)

Gestational age	Placental weight (male newborns), Mean (SD)			Placental weight (female newborns), Mean (SD)		
	Non-smoker	Quitter	Smoker	Non-smoker	Quitter	Smoker
37 weeks	507 (122)	520 (134)	513 (122)	501 (121)	505 (122)	491 (106)
38 weeks	524 (120)	531 (110)	522 (118)	511 (115)	516 (128)	514 (125)
39 weeks	532 (117)	546 (117)	542 (124)	521 (116)	529 (115)	528 (116)
40 weeks	538 (115)	544 (124)	551 (122)	526 (114)	535 (111)	540 (121)
41 weeks	540 (112)	543 (112)	547 (113)	531 (114)	536 (125)	536 (120)
⩾ 42 weeks	540 (116)	511 (110)	542 (119)	537 (120)	553 (107)	527 (106)
Total	532 (117)	539 (118)	539 (120)	522 (116)	530 (117)	527 (119)
p[1]		< 0,001			0,002	

Note: [1] calculated using ANCOVA (gestational age as a covariate).

Table 3. Relationship between smoking status before and during pregnancy and z-scores of PW and PW/BW in the Murmansk Region (*n* = 44,411)

Z-score		Unadjusted RRR (95% CI)			Adjusted RRR (95% CI)		
		Smoking status during pregnancy			Smoking status during pregnancy		
		Non-smoker	Quitter	Smoker	Non-smoker	Quitter	Smoker
PW[1]	Low	1.00	0.91 (0.81–1.02)	0.98 (0.92–1.05)	1.00	0.86 (0.76–0.97)	0.75 (0.70–0.81)
	High	1.00	1.14 (1.03–1.27)	1.16 (1.08–1.24)	1.00	1.21 (1.09–1.36)	1.35 (1.25–1.45)
PW/BW[2]	Low	1.00	0.85 (0.76–0.96)	0.71 (0.65–0.77)	1.00	0.87 (0.77–0.97)	0.76 (0.70–0.83)
	High	1.00	1.21 (1.09–1.35)	1.73 (1.62–1.84)	1.00	1.18 (1.06–1.31)	1.52 (1.43–1.63)

Note: Z-score (– 1;1) was used as a reference; Z-score of less than – 1 was defined as low; Z-score higher than + 1 was defined as high; PW, placental weight; BW, birth weight; [1] Relative risk ratio adjusted for the variables (maternal age, parity, marital status, residence, ethnicity, education, year of delivery, body mass index, mode of delivery, gestational diabetes, preeclampsia/eclampsia, anemia, and birth weight); [2] Relative risk ratio adjusted for all variables, except birth weight.

Table 4. Relationship between the number of cigarettes smoked daily during pregnancy and z-scores of PW and PW/BW in the Murmansk Region (*n* = 40,464)

Z-score		Unadjusted RRR (95% CI)[1]			Adjusted RRR (95% CI)[2]		
		Cigarettes smoked daily during pregnancy (0 as a reference)			Cigarettes smoked daily during pregnancy (0 as a reference)		
		1–5	6–10	⩾ 11	1–5	6–10	⩾ 11
PW[1]	Low	0.62 (0.52–0.73)	0.56 (0.47–0.67)	0.52 (0.38–0.72)	0.47 (0.39–0.56)	0.36 (0.29–0.43)	0.30 (0.21–0.42)
	High	1.55 (1.38–1.74)	1.81 (1.62–2.03)	2.01 (1.66–2.42)	1.87 (1.65–2.13)	2.48 (2.19–2.82)	2.97 (2.41–3.64)
PW/BW[2]	Low	0.38 (0.31–0.46)	0.31 (0.24–0.39)	0.29 (0.19–0.46)	0.42 (0.34–0.52)	0.34 (0.27–0.43)	0.32 (0.21–0.51)
	High	2.16 (1.93–2.41)	3.10 (2.80–3.44)	4.14 (3.49–4.91)	1.87 (1.67–2.09)	2.69 (2.42–3.00)	3.55 (2.98–4.23)

Note: Z-score (– 1;1) was used as a reference; Z-score of less than – 1 was defined as low; Z-score higher than + 1 was defined as high; PW, placental weight; BW, birth weight; [1] Relative risk ratio adjusted for the variables (maternal age, parity, marital status, residence, ethnicity, education, year of delivery, body mass index, mode of delivery, gestational diabetes, preeclampsia/eclampsia, anemia, and birth weight); [2] Relative risk ratio adjusted for all variables, except birth weight.

Smoking during pregnancy affects the development and function of placenta. However, the underlying mechanisms remain unclear. In contrast to non-smokers, heavy smokers had 1.5-times lower total volume of placenta blood vessels and 2-times lower volume density of blood vessels. These differences were statistically significant. In smokers, the total volume of intervillous space, syncytiotrophoblast, and fibrin was almost 1.5-times higher compared with the control (non-smoker) group [12]. Previously, it has been suggested that abnormal vascularisation of the placenta and subsequent placental insufficiency in smokers were the leading causes of adverse pregnancy outcomes [26]. In addition, previous studies observed a differential expression of angiogenic factors in placenta in pregnancy with complications [9, 27, 28]. Pfarrer *et al.* (1999) explained the higher PW in smokers by adaptive angiogenesis in placental villi [29]. Their findings suggested an adaptive response of the capillary bed in fetus within placental villi in smoking pregnant women. It increases the surface area used for gas and nutrients exchange by reducing the negative effect of hypoxia. Gloria-Bottini *et al.* (2015) [30] confirmed a discordant effect of smoking on BW and PW in Haptoglobin 2 phenotype mothers, but a concordant effect on BW and PW in mothers carrying the Haptoglobin 1 allele. These results further support the hypothesis of a possible relationship between BW and PW and maternal haptoglobin phenotype. In contrast, previous studies did not confirm the expected negative effect of smoking on PW. This inconsistency may be explained by methodological limitations of the study [11].

In this study, both the PW and PW/BW z-scores were related to the number of cigarettes smoked daily during pregnancy. The women who smoked eleven or more cigarettes per day had heavier placentas and higher PW/BW compared with light (1–5 cigarettes) smokers. Consistent with a Mendelian study [10], our study showed that continued smoking during pregnancy causes a higher PW. Furthermore, we found a higher PW/BW in smokers compared with quitters and in quitters compared with non-smokers. In contrast to non-smokers, quitters and smokers were approximately 1.2 and 1.5 times, respectively, more likely to have high PW/BW z-scores.

We observed a positive dose–response relationship between the high z-scores of PW and PW/BW and the number of cigarettes smoked daily. Our study is consistent with earlier findings, which showed that PW/BW in smokers increased with the number of cigarettes smoked, regardless of the smoking status in the third trimester [25].

Our study is the first in Russia to determine the relationship between smoking before and during pregnancy and PW using

a large population-based sample, which included all pregnant women in the region. This can mitigate the risk of sampling biases; however, a relatively high number of missing records in registered pregnancies may affect the results. We have not used any imputation technique to deal with the problem of missing data, leading to exclusion of approx. 17%–18% of observations. This may potentially decrease the power of the study, but it is still higher than 80%. Pregnancy cases with missing records can probably be systematically different from those without any omissions. We did not perform sensitivity analysis in this study. However, our previous study based on the MCBR did not show any difference between those with and without missing data on core maternal parameters.

Another limitation of the study affecting its results is a possible data bias as questions on smoking status can be sensitive for pregnant women and the relevant data on this behavior factor collected by doctors may be misclassified. However, consistent results of the previous study allow the self-assessment of smoking to be treated with confidence.

CONCLUSION

The mean PW for male newborns was 534.1 g (SD: 117.9 g) and 523.7 g (SD: 116.6 g) for female newborns and increased with gestational age. The study found a higher PW and PW/BW ratio in smokers and whose who quitted before the first antenatal visit and this relationship has dose–response relationship for smokers. Our findings confirm that both smoking cessation and decrease in the number of cigarettes smoked daily may reduce the risks of adverse pregnancy outcomes for the fetus. It can potentially be used as a motivation tool to promote primary prevention strategies aimed at reducing adverse pregnancy outcomes in smoking women.

ADDITIONAL INFORMATION

Author contribution: O.A. Kharkova: design of the study, statistical analysis, data interpretation, writing—original draft; V.A. Postoev, A.A. Usynina: published data search and analysis, writing—original draft, writing—review & editing. All the authors approved the version of the manuscript to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical approval: The study was approved by Ethical Committee of the Northern State Medical University (Arkhangelsk, Russia) (Protocol No. 08/12-14 dated December 10, 2014).

Disclosure of interests: The authors have no relationships, activities, or interests for the last three years related to for-profit or not-for-profit third parties whose interests may be affected by the content of the article.

Statement of originality: No previously published material (text, images, or data) was used in this work.

Data availability statement: The editorial policy regarding data sharing does not apply to this work.

Generative AI: No generative artificial intelligence technologies were used to prepare this article.

Provenance and peer review: This paper was submitted unsolicited and reviewed following the standard procedure. The peer review process involved two members of the editorial board and the in-house scientific editor.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. О.А. Харькова — дизайн исследования, статистический анализ, интерпретация результатов, написание текста рукописи; В.А. Постоев, А.А. Усынина — сбор и анализ литературных данных, написание и редактирование текста рукописи. Все авторы одобрили рукопись (версию для публикации), а также согласились нести ответственность за все аспекты работы, гарантируя надлежащее рассмотрение и решение вопросов, связанных с точностью и добросовестностью любой её части.

Этическая экспертиза. Проведение исследования одобрено локальным этическим комитетом Северного государственного медицинского университета (Архангельск, Россия) (протокол № 08/12-14 от 10.12.2014).

Источники финансирования. Отсутствуют.

Раскрытие интересов. Авторы заявляют об отсутствии отношений, деятельности и интересов за последние три года, связанных с третьими лицами (коммерческими и некоммерческими), интересы которых могут быть затронуты содержанием статьи.

Оригинальность. При создании настоящей работы авторы не использовали ранее опубликованные сведения (текст, иллюстрации, данные).

Доступ к данным. Редакционная политика в отношении совместного использования данных к настоящей работе не применима.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

Рассмотрение и рецензирование. Настоящая работа подана в журнал в инициативном порядке и рассмотрена по обычной процедуре. В рецензировании участвовали два внешних рецензента, член редакционной коллегии и научный редактор издания.

REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. Shiverick KT, Salafia C. Cigarette Smoking and Pregnancy I: Ovarian, Uterine and Placental Effects. *Placenta.* 1999;20(4):265–272. doi: 10.1053/plac.1998.0377
2. Avşar TS, McLeod H, Jackson L. Health Outcomes of Smoking During Pregnancy and the Postpartum Period: An Umbrella Review. *BMC Pregnancy Childbirth.* 2021;21(1):254. doi: 10.1186/s12884-021-03729-1
3. Ratnasiri AWG, Lakshminrusimha S, Dieckmann RA, et al. Maternal and Infant Predictors of Infant Mortality in California, 2007–2015. *PLOS ONE.* 2020;15(8):e0236877. doi: 10.1371/journal.pone.0236877 EDN: LXJDIG
4. Olives JP, Elias-Billon I, Barnier-Ripet D, Hospital V. Negative Influence of Maternal Smoking During Pregnancy on Infant Outcomes. *Archives de Pédiatrie.* 2020;27(4):189–195. doi: 10.1016/j.arcped.2020.03.009 EDN: QWGGJT
5. Zdravkovic T, Genbacev O, McMaster MT, Fisher SJ. The Adverse Effects of Maternal Smoking on the Human Placenta: A Review. *Placenta.* 2005;26:S81–S86. doi: 10.1016/j.placenta.2005.02.003
6. ACOG Committee Opinion, Number 807. Tobacco and Nicotine Cessation During Pregnancy. *Obstetrics & Gynecology*. 2020;135(5):e221–e229. doi: 10.1097/aog.0000000000003822 EDN: CQWQAK
7. Kharkova OA, Krettek A, Grjibovski AM, et al. Prevalence of Smoking Before and During Pregnancy and Changes in This Habit During Pregnancy in Northwest Russia: a Murmansk County Birth Registry Study. *Reproductive Health.* 2016;13(1):18. doi: 10.1186/s12978-016-0144-x EDN: XNSNOD
8. Hayward CE, Lean S, Sibley CP, et al. Placental Adaptation: What Can We Learn from Birthweight:Placental Weight Ratio? *Frontiers in Physiology.* 2016;7:28. doi: 10.3389/fphys.2016.00028

9. Hutcheon JA, McNamara H, Platt RW, et al. Placental Weight for Gestational Age and Adverse Perinatal Outcomes. *Obstetrics & Gynecology.* 2012;119(6):1251–1258. doi: 10.1097/AOG.0b013e318253d3df

10. Salavati N, Gordijn SJ, Sovio U, et al. Birth Weight to Placenta Weight Ratio and its Relationship to Ultrasonic Measurements, Maternal and Neonatal Morbidity: A Prospective Cohort Study of Nulliparous Women. *Placenta.* 2018;63:45–52. doi: 10.1016/j.placenta.2017.11.008

11. Shehata F, Levin I, Shrim A, et al. Placenta/Birthweight Ratio and Perinatal Outcome: A Retrospective Cohort Analysis. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2011;118(6):741–747. doi: 10.1111/j.1471-0528.2011.02892.x

12. Heidari Z, Mahmoudzadeh-Sagheb H, Sheibak N. Placenta Structural Changes in Heavy Smoking Mothers: A Stereological Aspect. *Current Medical Research and Opinion.* 2018;34(11):1893–1897. doi: 10.1080/03007995.2018.1444590

13. Wang N, Tikellis G, Sun C, et al. The Effect of Maternal Prenatal Smoking and Alcohol Consumption on the Placenta-To-Birth Weight Ratio. *Placenta.* 2014;35(7):437–441. doi: 10.1016/j.placenta.2014.04.006

14. Jaitner A, Vaudel M, Tsaneva-Atanasova K, et al. Smoking During Pregnancy and its Effect on Placental Weight: A Mendelian Randomization Study. *BMC Pregnancy and Childbirth.* 2024;24(1):238. doi: 10.1186/s12884-024-06431-0 EDN: RUTKYV

15. Reijnders IF, Mulders AGMGJ, van der Windt M, et al. The impact of Periconceptional Maternal Lifestyle on Clinical Features and Biomarkers of Placental Development and Function: A Systematic Review. *Human Reproduction Update.* 2018;25(1):72–94. doi: 10.1093/humupd/dmy037 EDN: YLUCPZ

16. Kharkova O, Grjibovski A, Krettek A, et al. Effect of Smoking Behavior before and during Pregnancy on Selected Birth Outcomes among Singleton Full-Term Pregnancy: A Murmansk County Birth Registry Study. *International Journal of Environmental Research and Public Health.* 2017;14(8):867. doi: 10.3390/ijerph14080867EDN: XPIHYX

17. Chursina OA, Konstantinova OD, Kshnyaseva SK, Mazurovskaya OP. Influence of Tobacco Smoking During Pregnancy on the Fetoplaceltal System and Health of Newborns. 2019;18(5):66–72. doi: 10.20953/1726-1678-2019-5-66-72 EDN: VDFESC

18. Shchegolev AI, Tumanova UN, Mishnev OD. Effect of Smoking on the Development of Placental Lesions. *Gynecology.* 2018;20(2):34–40. doi: 10.26442/2079-5696_2018.2.34-40 EDN: XTGRTV

19. Gabitova NKh, Cherezova IN, Vasina AI. Toxic Effects of Chronic Nicotine and Alcohol Intoxication on a Newborn Child. *Practical medicine.* 2023;21(5):86–90. doi: 10.32000/2072-1757-2023-5-86-90 EDN: ISOEKG

20. Anda EE, Nieboer E, Voitov AV, et al. Implementation, Quality Control and Selected Pregnancy Outcomes of the Murmansk County Birth Registry in Russia. *International Journal of Circumpolar Health.* 2008;67(4): 318–334. doi: 10.3402/ijch.v67i4.18339 EDN: LLMFJB

21. Nascente LMP, Grandi C, Aragon DC, Cardoso VC. Placental Measurements and their Association With Birth Weight in a Brazilian Cohort. *Revista Brasileira de Epidemiologia.* 2020;23:e200004. doi: 10.1590/1980-549720200004 EDN: TYJJTO

22. Villar J, Ismail LC, Victora CG, et al. International Standards for Newborn Weight, Length, and Head Circumference by Gestational Age and Sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *The Lancet.* 2014;384(9946):857–868. doi: 10.1016/S0140-6736(14)60932-6

23. Cole TJ, Freeman JV, Preece MA. British 1990 Growth Reference Centiles for Weight, Height, Body Mass Index and Head Circumference Fitted by Maximum Penalized Likelihood. Statistics in Medicine. 1998;17(4): 407–429. doi: 10.1002/(SICI)1097-0258(19980228)17:4<407::AID-SIM742>3.0.CO;2-L

24. Mitsuda N, N Awn JP, Eitoku M, et al. Association Between Maternal Active Smoking During Pregnancy and Placental Weight: The Japan environment and Children's study. *Placenta.* 2020;94:48–53. doi: 10.1016/j.placenta.2020.04.001 EDN: UDQTUK

25. Larsen S, Haavaldsen C, Bjelland EK, et al. Placental Weight and Birthweight: the Relations With Number of Daily Cigarettes and Smoking Cessation in Pregnancy. A Population Study. *International Journal of Epidemiology.* 2018;47(4):1141–1150. doi: 10.1093/ije/dyy110

26. Pintican D, Poienar AA, Strilciuc S, Mihu D. Effects of Maternal Smoking on Human Placental Vascularization: A Systematic Review. *Taiwanese Journal of Obstetrics and Gynecology.* 2019;58(4):454–459. doi: 10.1016/j.tjog.2019.05.004

27. Åsvold BO, Vatten LJ, Romundstad PR, et al. Angiogenic Factors in Maternal Circulation and the Risk of Severe Fetal Growth Restriction. *Am J Epidemiol.* 2011;173(6):630–639. doi: 10.1093/aje/kwq373

28. Kawashima A, Koide K, Ventura W, et al. Effects of Maternal Smoking on the Placental Expression of Genes Related to Angiogenesis and Apoptosis during the First Trimester. *PLoS ONE.* 2014;9(8):e106140. doi: 10.1371/journal.pone.0106140

29. Pfarrer C, Macara L, Leiser R, Kingdom J. Adaptive Angiogenesis in Placentas of Heavy Smokers. *The Lancet.* 1999;354(9175):303. doi: 10.1016/S0140-6736(99)01676-1 EDN: DCLYMH

30. Gloria-Bottini F, Bottini E. Smoking and the Correlation Between Birth Weight and Placental Weight. Evidence of Interaction With Maternal Haptoglobin Phenotype. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2015;185:136–139. doi: 10.1016/j.ejogrb.2014.12.019 EDN: YBRYAP

ОБ АВТОРАХ

*** Olga A. Kharkova,** Cand. Sci. (Psychology), Associate Professor;
address: 51 Troicki ave, Arkhangelsk, Russia, 163069;
ORCID: 0000-0002-3130-2920;
eLibrary SPIN: 2167-7550;
e-mail: harkovaolga@yandex.ru

Vitaly A. Postoev, MD, Cand. Sci. (Medicine), Associate Professor;
ORCID: 0000-0003-4982-4169;
eLibrary SPIN: 6070-2486;
e-mail: v.postoev@nsmu.ru

Anna A. Usynina, MD, Dr. Sci. (Medicine), Associate Professor;
ORCID: 0000-0002-5346-3047;
eLibrary SPIN: 3735-1100;
e-mail: perinat@mail.ru

AUTHORS' INFO

*** Харькова Ольга Александровна,** канд. психол. наук, доцент;
адрес: Россия, 163069, Архангельск, Троицкий пр-кт, д. 51;
ORCID: 0000-0002-3130-2920;
eLibrary SPIN: 2167-7550;
e-mail: harkovaolga@yandex.ru

Постоев Виталий Александрович, канд. мед. наук, доцент;
ORCID: 0000-0003-4982-4169;
eLibrary SPIN: 6070-2486;
e-mail: v.postoev@nsmu.ru

Усынина Анна Александровна, д-р мед. наук, доцент;
ORCID: 0000-0002-5346-3047;
eLibrary SPIN: 3735-1100;
e-mail: perinat@mail.ru

* Автор, ответственный за переписку / Corresponding author