

Original Scientific Article

## IDENTIFICATION OF FACTORS INFLUENCING BIRTH WEIGHT, LENGTH, AND HEAD CIRCUMFERENCE

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**Abstract.** *Newborn size at birth is an important indicator of fetal health, neonatal health, infant survival and childhood morbidity. The aim of our study was to assess and identify factors that significantly influence birth weight, length, and head circumference by performing a post hoc analysis of the data collected during the retrospective-prospective observational cohort study which was conducted at the Clinic for Gynecology and Obstetrics at the University Clinical Centre Kragujevac, Serbia. The influence of potential factors on birth weight, length, and head circumference was evaluated by multiple linear regression analysis. The study included 320 pregnant women and 332 newborns. Four factors had a significant negative effect on birth weight: smoking, twin pregnancy, use of methyl dopa and corticosteroids during pregnancy. Smoking, twin pregnancy and corticosteroid use also had a significant negative effect on birth length. Negative effect on fetal head circumference at birth had smoking, use of corticosteroids and antibiotics during pregnancy. Maternal height and gestational age at birth showed a positive influence on fetal anthropometric measurements. Clinicians should pay attention to pregnant women with lower body height, twin pregnancy, who smoke and use corticosteroids, methyl dopa and antibiotics.*

**Key words:** *birth weight, body length, head circumference, newborns, risk factors.*

### Introduction

Newborn size at birth (e.g. weight, length, and head circumference) is an important indicator of fetal health, neonatal health, infant survival and childhood morbidity [1]. Short babies, as well as long babies with low weight, were found to be at increased risk of hospitalization [2]. The measurement of head circumference is also an important screening procedure for detecting abnormalities in head growth [3]. In addition, studies have revealed inverse associations of birth size with development of diseases in adulthood (e.g. coronary heart disease, chronic kidney disease, metabolic syndrome, type 2 diabetes) [4]. Therefore, understanding the causes of variation in birth measurements is important in providing opportunities for timely prevention and intervention concerning related outcomes in both the perinatal period and later in life [4].

About 50% of the variation in birth weight, length, and head circumference may be explained by genetic factors [4]. In addition to genetics, maternal nutrient intake is also considered to be an important factor contributing to birth weight and length, but the direct association between diet quality of mother and its effect on birth length has not been clearly verified [5]. Environmental factors such as number of fetuses, parity, maternal anthropometric measurements, medication, and smoking, can also play a significant role in the attainment of a birth size [6]. The most frequent factors contributing to low birth weight in studies included in one systematic review included maternal age, maternal body mass index, preterm delivery, and maternal chronic diseases, respectively [7]. In addition, positive history of iron or multivitamin intake, folic acid, and vitamin C were seen to have positive effects on newborn's birth length [1]. On the other hand,

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Received August 30<sup>th</sup>, 2023 / Revised December 22<sup>th</sup>, 2023 / Accepted December 26<sup>th</sup>, 2023

results of the studies evaluating impact of exposure to certain medications during pregnancy on birth size are not consistent. For example, some studies found that newborns of methyl dopa-treated mothers had a higher rate of reduced birth weight after adjustment for sex and gestational age at birth and a smaller head circumference in male newborns [8], while other studies didn't observe this [9]. Also, a systematic review of association between in utero exposure to synthetic glucocorticoids and reduced birth size has found that 9 out of 17 studies reported a reduction in birth weight, 5 of 9 a reduction of head circumference and 2 of 4 a reduction in birth length [10].

Bearing in mind previously mentioned controversies and importance of understanding the causes of variation in birth measurements, the aim of our study was to assess and identify factors that significantly influence birth weight, length, and head circumference and to quantify the strength of their impact.

## Materials and Methods

This was a post hoc analysis of the data collected during the retrospective-prospective observational cohort study which was conducted at the Clinic for Gynecology and Obstetrics at the University Clinical Centre Kragujevac, Serbia [11]. The study is described in detail elsewhere and the Ethics Committee of the Clinical Centre Kragujevac had approved the study before its initiation (No. 01/20-661, approval date September 9, 2020), while participants were included after signing the informed consent form [11]. The study was conducted in accordance with the Declaration of Helsinki. Briefly, pregnant women matching inclusion criteria (pregnancy confirmed by a gynecology specialist by biochemical and/or ultrasound examination) and exclusion criteria (pregnant women under the age of 18, functionally illiterate pregnant women, confirmed high risk of genetic abnormalities of the fetus by a combination of ultrasound and biochemical examination during the 12th week of pregnancy, and subsequently pregnant women who gave birth to stillborn children) were consecutively recruited during their visits to the Clinic for pregnancy control and monitoring between September 29, 2020 and October 13, 2021 and data regarding pregnant women' age, place of living, educational level, height, lifestyle habits during pregnancy, presence of chronic and/or active diseases during pregnancy, data on medications used during pregnancy, number of previous births, number of previous miscarriages, number of fetuses, way of conception, presence of uterine or placental abnormalities, and quality and diversity of nutrition using Balkan Food Quality and Diversity in Pregnancy Questionnaire-18 (BFQDPQ-18) were collected [11]. The following data related to newborns during the birth were collected from medical documentation: gender, weight (g), length (cm), head circumference (cm), Apgar score at first minute and time of delivery [11]. The baseline characteristics of the included pregnant women and newborns are described in detail in previously published article [11].

The study data were analyzed by descriptive statistics and presented in tables. Means  $\pm$  standard deviations were used for presenting continuous data, and frequencies (percentages) for presenting categorical variables. The influence of potential factors on birth weight, length, and head circumference was evaluated by multiple linear regression analysis. The statistical validity of the regression was checked by analysis of variance (F value) and percentage of outcomes variability explained ( $R^2$ ). Influence of potential factors was assessed by their B coefficients within the regression equation, including confidence intervals (CIs). All calculations were performed by the Statistical Program for Social Sciences (SPSS version 18).

## Results

The study included 320 pregnant women with an average age of  $30.35 \pm 5.50$  years and a total of 332 newborns (12 pairs of twins): 181 (54.5%) male and 151 (45.5%) female. Mean  $\pm$  standard deviation (range) of the anthropometric measurements at birth were as follows: weight (in g)  $3222.32 \pm 679.32$  (990–4790), length (in cm)  $48.67 \pm 3.46$  (35–59) and head circumference (in cm)  $34.23 \pm 2.04$  (25–39).

Results of the last step of the backward multiple linear regression analysis are presented in the Table 1. Variables entered at the beginning of the analysis for birth weight, length, and head circumference were: age of pregnant women, gestational age at birth, body height of pregnant women, quality and diversity of pregnant women's nutrition, smoking, obesity, diabetes mellitus, hypertension, thrombophilia, hypothyroidism, anemia, colpitis, cystitis, number of previous miscarriages, number of previous births, uterine or placental abnormalities, twin pregnancy, anticoagulant drugs, progesterone, corticosteroids, calcium channel blockers, methyl dopa, antibiotics, number of drugs excluding vitamins and minerals, the use of drugs from FDA A, B, C and D category.

Four factors had a significant negative effect on birth weight: smoking, twin pregnancy, use of methyl dopa and corticosteroids during pregnancy. On the other hand, two factors, including body height of pregnant women and gestational age at birth, had a significant positive effect on birth weight.

Smoking, twin pregnancy and corticosteroid use during pregnancy also had a significant negative effect on birth length, while body height of pregnant women and gestational age at birth had a significant positive effect on birth length.

We observed a significant negative effect of smoking, use of corticosteroids and antibiotics during pregnancy on head circumference at birth. On the other hand, age and body height of pregnant women, as well as gestational age at birth had a significant positive effect on head circumference at birth.

**Table 1** Results of the last step of the backward multiple linear regression analysis evaluating factors affecting birth weight, length and head circumference

Variables	B	p	95% CI	
<b>Birth weight</b>				
Constant	-6142.735	0.000*	-7632.359 to -4653.111	
Body height	17.037	0.000*	9.946 to 24.128	
Smoking	-196.647	0.002*	-317.718 to -75.575	
Diabetes mellitus	146.116	0.060	-6.070 to 298.303	
Methyldopa	-145.561	0.033*	-278.987 to -12.136	
Corticosteroids	-287.921	0.001*	-455.263 to -120.578	
Twin pregnancy	-434.109	0.000*	-632.035 to -236.182	
Gestational age at birth	172.327	0.000*	148.929 to 195.726	
R <sup>2</sup> , F(p)	0.623; 71.426 (0.000*)			
<b>Birth length</b>				
Constant	11.667	0.010*	2.758 to 20.576	
Body height	0.047	0.027*	0.005 to 0.089	
Smoking	-0.813	0.028*	-1.539 to -0.086	
Corticosteroids	-1.818	0.000*	-2.814 to -0.821	
Twin pregnancy	-1.719	0.005*	-2.905 to -0.533	
Gestational age at birth	0.769	0.000*	0.630 to 0.908	
R <sup>2</sup> , F(p)	0.480; 56.274 (0.000*)			
<b>Head circumference at birth</b>				
Constant	11.474	0.000*	5.886 to 17.062	
Age	0.048	0.005*	0.015 to 0.081	
Body height	0.033	0.013*	0.007 to 0.059	
Smoking	-0.585	0.011*	-1.032 to -0.137	
Antibiotics	-0.547	0.009*	-0.957 to -0.137	
Corticosteroids	-0.961	0.003*	-1.600 to -0.322	
Gestational age at birth	0.421	0.000*	0.337 to 0.506	
R <sup>2</sup> , F(p)	0.428; 37.853 (0.000*)			

B – unstandardized coefficient; CI – confidence interval; p – statistical significance; \* – Statistically significant

## Discussion

Our study showed that maternal smoking and use of corticosteroids during pregnancy are significant risk factors for lower body weight, body length and head circumference at birth. Twin pregnancy was associated with lower birth weight and length of newborns, but it did not affect the head circumference of the newborns. The use of methyldopa during pregnancy significantly reduced the birth weight, while the use of antibiotics during pregnancy was accompanied by a lower head circumference of the newborns. Maternal height and gestational age at birth showed a positive influence on the weight, length and head circumference of newborns, while age of pregnant women was another factor in positive correlation with head circumference at birth.

Previous studies have also shown that smoking leads to reduced birth weight, length, and head circumference [12]. Tobacco smoke consists of several thousand chemicals, including numerous toxic substances that exacerbate oxidative stress and inflammation, which can harm placental development and/or be passed through the placenta to the fetus [13]. The negative impact of smoking on the body weight of the fetus is dose-dependent and present throughout the pregnancy, with the most pronounced negative effect during the third trimester [14].

It is known that the use of corticosteroids during pregnancy reduces the risk of respiratory distress syndrome, intraventricular hemorrhage, necrotizing enterocolitis and neonatal death in preterm newborns [15]. However, some studies indicated that antenatal administration of corticosteroids causes dose-dependent reduction in birth weight, length and head circumference, which was confirmed by the results of our study which could possibly be explained by the fact that these drugs may shift metabolism from cellular growth to precocious differentiation of cellular proteins in more than 15 different tissues [15,16].

Twins have the same genetic growth potential as singletons, but it is limited by the functional capacity of the placenta and uterus [17]. Growth slows from the beginning of the third trimester of twin pregnancy so the difference in the weight of twins in relation to singletons progressively increases with gestational age [17]. The results of a prospective cohort study conducted on 171 women with twin gestations in the United States showed that dichorionic twins had a smaller estimated body weight and abdominal circumference, but similar head circumference and body length as singletons [18]. Our results partially coincide with the results of this study, since we showed that twin pregnancies were accompanied by smaller weight and length, but not smaller head circumference of newborns.

Methyldopa has been considered the drug of choice for the treatment of hypertension in pregnancy for decades [8]. However, similar to our results, some studies have shown that the use of methyldopa in pregnancy is accompanied by a reduction in fetal birth weight [8]. On the other hand, it is known that chronic hypertension is an independent and significant risk factor for fetal growth restriction and small for gestational age newborns [19]. Therefore, it may be difficult to separate the effects of the disease itself on the development and body weight of the fetuses from the side effect of methyldopa used for its treatment.

There is a lot of controversy about the effect of antenatal antibiotics use on the birth weight. Some studies indicated that antibiotic use in pregnancy may affect birth weight, while others showed that it does not affect the risk of small or large for gestational age newborns [20]. The potential effect of antenatal antibiotics on anthropometric measurements in newborns has not been the subject of a large number of studies.

Previous studies indicated a positive correlation between maternal height and the fetal body length, head circumference and birth weight of the newborns [21,22], which is in line with our results. The influence of maternal body height on weight and anthropometric measures of fetal growth can be explained by a mechanical assumption that mothers with shorter height have smaller uterine size and thus limited potential for fetal growth [23]. In addition, gestational age of newborns had significant positive effects on birth weight, length and head circumference in previous studies [24], which is in line with our results. We also found that maternal age is in significant positive correlations with head circumference at birth. Results of a randomized controlled trial conducted in India confirm our findings, showing that fetuses of

younger pregnant women are smaller in all anthropometric measurements from the first trimester to birth in comparison with fetuses of older mothers [25].

It should be emphasized that our study has certain limitations. First, we must point out that our study was an epidemiological study. Epidemiological studies can only show statistically significant associations, but they cannot prove that a link is causative. Second, it was a unicentric study, which may limit the generalizability of the results. Third, part of the data related to the period of pregnancy before recruiting pregnant women was collected retrospectively, which may have affected the quality of the data and precluded us from gathering data on some potential factors that may affect anthropometric measures at birth (e.g., information about all relevant antenatal infections, such as TORCH infections), as well as information about indications for the use of corticosteroids (we were unable to assess in how many women they were indicated for acceleration of fetal lung maturation). A prospective study involving a larger number of participants is needed to provide more valid conclusions.

## Conclusion

In conclusion, clinicians should pay special attention to pregnant women with lower body height, twin pregnancy, who smoke and use corticosteroids, methyldopa and antibiotics during pregnancy in order to prevent low weight, body length and head circumference of newborns at birth.

**ACKNOWLEDGMENTS:** *This study was partially supported by Ministry of Science, Technological Development and Innovations of Republic of Serbia, grant no. 175007, contract no. 451-03-47/2023-01/200111.*

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