BIRTH WEIGHT AND METABOLIC RISK IN WOMEN OF DIFFERENT NUTRITION LEVELS

TELESNA MASA NA ROĐENJU I METABOLIČKI RIZIK KOD ŽENA RAZLIČITIH KATEGORIJA UHRANJENOSTI

Mirjana MILOŠEVIĆ¹, Biljana SRĐIĆ¹, Edita STOKIĆ², Marina RASTOVIĆ³, Tatjana PAVLICA⁴ and Radenko MATIĆ⁵

Summary
Introduction: Nowadays, obesity is one of the most important health problems in both developed and developing countries. Recent studies have shown a significant association of obesity and its complications with birth weight. The aim of our study was to analyze the effect of birth weight on the occurrence of metabolic disorders in normal weight and obese women.

Material and Methods: The study group included 134 females of average age 41.71±11.56 years. In these women the relationship between birth weight and anthropometric and biochemical parameters, as well as with blood pressure values was analyzed.

Results: Our results show that women with higher birth weight had higher values of the anthropometric indicators of fat mass and distribution (such as body mass index, total fat mass, waist circumference and hip circumference), as well as higher values of high density lipoprotein-cholesterol. In contrast, the values of systolic and diastolic blood pressure and low density lipoprotein-cholesterol were lower in women with higher birth weight. The analysis of metabolic profile in women of different nutritional status indicates that normal weight women with metabolic syndrome had a lower birth weight when compared with normal weight women without metabolic risk (3.15 vs. 3.40 kg, p<0.05).

Conclusion: Higher birth weight is related with higher fat mass, while lower birth weight is related with metabolic disturbances. Birth weight seemed to be determinant of metabolic risk in normal weight women

Key words: Birth Weigh; Obesity; Risk Factors; Metabolic Syndrome X; Nutritional Status; Adult; Middle Aged; Female

Sažetak
Uvod: Gojaznost je jedan od najznačajnijih zdravstvenih problema današnjice sa kojim se suočavaju kako razvijene, tako i zemlje u razvoju. Dosadašnja ispitivanja su pokazala značajnu povezanost gojaznosti i njenih komplikacija sa telesnom masom na rođenju. Cilj našeg istraživanja bio je da se analizira uticaj telesne mase na rođenju na pojavu metaboličkih poremećaja kako kod normalno uhranjenih, tako i kod gojaznih žena.

Materijal i metode: Ispitivačku grupu činile su 134 osobe ženskog pola prosečne starosti 41,71±11,56 godina. U ove žene je analiziran odnos telesne mase na rođenju sa antropometrijskim i biohemijskim parametrima, kao i sa vrednostima krvnog pritiska.

Rezultati: Naši rezultati ukazuju na veće vrednosti parametara masa i distribucije masnog tkiva (indeks telesne mase, ukupna masna masa, obim struka i obim kukova) kod žena sa većom mase na rođenju. Suprotno, vrednosti sistolnog i dijastolnog krvnog pritiska, kao i vrednosti hladnog krvnog pritiska, su veće kod žena sa većom mase na rođenju. Analizom metaboličkog rizika kod žena različitog stepena uhranjenosti uočava se da su normalno uhranjene žene sa rizičnim metaboličkim profilom imale niže vrednosti telesne mase na rođenju u poređenju sa normalno uhranjenim ženama bez metaboličkog rizika (3.15 vs. 3.40 kg, p<0.05).

Zaključak: Osobe koje su imale veću telesnu masu na rođenju imale su veće vrednosti ukupne masne mase tela, dok je mala telesna masa na rođenju povezana sa metaboličkim poremećajima. Telesna masa na rođenju pokazala je mogućim determinantom metaboličkog rizika kod normalno uhranjenih osoba.

Ključne reči: Težina na rođenju; Gojaznost; Faktori rizika; Metabolički sindrom X; Nutritivni status; Odrasli; Srednje godine; Ženski

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Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>BMI</td>
<td>body mass index</td>
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<tr>
<td>HDL</td>
<td>high density lipoprotein</td>
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<tr>
<td>LDL</td>
<td>low density lipoprotein</td>
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<tr>
<td>HOMA-IR</td>
<td>insulin resistant index</td>
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Introduction

Nowadays, obesity is one of the major health problems in both developed and developing countries. The incidence of obesity reaches epidemic proportions - according to current data of the World Health Organization, more than one billion people are considered to be overweight, while 400 million people are considered to be obese [1-3]. The available data show that 54% of Serbian population are overweight, while in Vojvodina 35.5% of its population are overweight and 23% are obese [4]. Obesity is one of the most important risk factor not only for diseases such as type 2 diabetes and cardiovascular diseases, but also for some malignant diseases - breast, endometrial, prostate or colon cancer.

Epidemiological studies have shown a significant correlation between obesity and its complications and birth weight [5-8]. Research has shown that heart diseases cause death two to three times more often in people born with low birth weight than in those whose birth weight was higher than 4 kg [9]. It is believed that predisposition for the development of cardiometabolic disorders in adults is the result of adaptation of neuroendocrine mechanisms to poor energy supply during fetal development. Inadequate conditions and stress during prenatal period cause hypersensitivity of immune system, structural and functional changes of some organs and tissues - inadequate ratio between collagen and elastin increases tendency towards inflammation and vascular damage increases, that being the base for acceleration of atherosclerosis [10,11].

On the other hand, higher birth weight is associated with the risk of developing obesity in later life [12,13]. However, it is still unknown which component of body composition is affected by birth weight and whether it is a consequence of genetic predisposition or exclusively prenatal factors that caused higher birth weight.

Recent studies have shown that among normal-weight persons are those who are metabolically obese and that some overweight people are actually metabolically healthy [14,15]. The question is wheather these profiles are programmed during fetal life. Regarding this matter, the aim of our research was to analyze the effect of birth weight on the occurrence of metabolic disorders in normal-weight and obese women.

Material and Methods

The study group included 134 females of average age 41.71 ±11.56 years and different nutritional status. The participants underwent anthropometrical measurements, their blood pressure was measured and the blood sample was taken for biochemical analyses. In addition, these women were asked about their birth weight.

The following anthropometric parameters were measured: body height, weight, waist circumference and hip circumference.

Body height was measured by Harpenden anthropometer (Holtain Ltd, Crosswell, UK) with accuracy of 0.1 cm. Body weight was measured within-in the process of bioelectrical impedance measuring. Body mass index (BMI), calculated as the person’s body mass in kilograms divided by the square of her height in meters, was used to estimate nutritional status. According to the recommendations of the World Health Organization, the participants having BMI of 18.5 to 24.9 kg/m² were considered to be normal-weight, those whose BMI was between 25 and 29.9 kg/m² were overweight and those whose BMI was higher than 30 kg/m² were obese [1]. Waist and hip circumference were measured by Holtain measurement tape (Holtain Ltd, Crosswell UK) with an accuracy of 0.1 cm.

The standard equipment, Riva-Rocci sphygmomanometer, was used to measure systolic (SBP) and diastolic (DBP) blood pressure.

Glycaemia and parameters of lipid status were also analyzed and the values of insulinemia and insulin resistance index (HOMA-IR) were determined in 104 participants. Total cholesterol (HOL) and tryglycerides (TG) were determined by enzymatic procedures; whereas, HDL-cholesterol was determined by precipitation with sodium phosphotungstate and LDL-cholesterol by Friedwald’s formula [16]. The values of fasting glucose were measured by Diab glucosa GOD-PAP’s method. Enzyme immunoassays was used to determine serum insulin and insulin resistance, while insulin resistance was assessed by insulin resistance index: (glycaemia (mmol/L) x insulinemia (µU/mL))/22.5 [16].

Criteria of Karelis et al. were used to determine metabolic risk [17]. These criteria take into account the value of tryglycerides (<1.7 mmol/L), total cholesterol (<5.2 mmol/L), LDL-cholesterol (<2.6 mmol/L), HDL-cholesterol (>1.1 mmol/L) and HOMA-IR (<1.95). Those participants who met four of five criteria were labeled as metabolically healthy regardless of their nutritional status. Based on the assessment of metabolic risk the participants were divided into four groups: normal weight metabolically healthy, normal weight metabolically obese, obese but metabolically healthy and overweight with metabolic risk.

Software package SPSS Statistics 17.0 was used for statistical analyses.

Results

Table 1 shows the descriptive characteristics of the study group. The participants were of different nutritional status (BMI values ranged from 17.86 to 59.30 kg/m²) and of different type of fat distribu-
tion, and with different metabolic profiles (waist circumference was between 59 and 151 cm).

The subjects were afterwards divided into five categories based on their birth weight: <2.50 kg, 2.50-2.99 kg, 3.00-3.49 kg, 3.50-3.99 kg and ≥4.00 kg. The values of measured parameters in each category are shown in Graphs 1, 2 and 3 (the values were first logarithmically transformed in order to improve the linearity). It is noticeable that the higher the birth weight, the higher the anthropometric indicators of fat mass and distribution as well as the values of HDL-cholesterol are. Thus, the average values of BMI and fat mass in women born with birth weight less than 2.5 kg were 22.56±3.14 kg/m² and 25.60±8.19%, respectively, while in those whose birth weight was over 4 kg they were 25.19±5.06 kg/m² and 31.38±8.34%. In contrast, the values of systolic and diastolic blood pressure and LDL-cholesterol were lower in women with higher birth weight. The average value of LDL-cholesterol in women with the lowest birth weight was 4.16±1.21 mmol/l, while in those whose birth weight was over 4 kg it was 3.55±0.99 mmol/l. However, the differences between the values of mentioned parameters in different categories of birth weight were not statistically significant.

The metabolic risk was estimated in 104 subjects whose value of HOMA-IR had been determined; they were then divided into four categories depending on the degree of their nutritional status and metabolic profile. The subjects with the metabolic risk profile had lower values of birth weight compared with those without the metabolic risk, but of the same nutritional status (Table 2); whereby, a slightly larger difference was noticed among normal weight women (3.40±0.50 kg vs. ≥4.00 kg).

### Table 1. Characteristics of the study group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>X ± SD</th>
<th>Min - Max</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>41.71 ± 11.56</td>
<td>20.00 – 76.00</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>3.34 ± 0.56</td>
<td>1.35 – 4.95</td>
</tr>
<tr>
<td>Body height (cm)</td>
<td>165.11 ± 6.26</td>
<td>148.70 – 180.00</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>70.26 ± 18.77</td>
<td>45.00 – 170.00</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.85 ± 7.09</td>
<td>17.86 – 59.30</td>
</tr>
<tr>
<td>Fat mass (%)</td>
<td>30.44 ± 8.28</td>
<td>9.10 – 55.40</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>114.54 ± 17.26</td>
<td>90.00 – 180.00</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>73.72 ± 9.91</td>
<td>50.00 – 100.00</td>
</tr>
<tr>
<td>Glycaemia (mmol/l)</td>
<td>4.87 ± 1.59</td>
<td>3.30 – 19.70</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.24 ± 1.41</td>
<td>0.46 – 12.53</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.58 ± 1.10</td>
<td>2.72 – 8.18</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/l)</td>
<td>1.53 ± 0.80</td>
<td>0.63 – 9.95</td>
</tr>
<tr>
<td>LDL-cholesterol (mmol/l)</td>
<td>3.59 ± 0.98</td>
<td>1.34 – 6.92</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>81.17 ± 16.64</td>
<td>59.50 – 151.00</td>
</tr>
<tr>
<td>WSR</td>
<td>0.49 ± 0.10</td>
<td>0.35 – 0.90</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>102.73 ± 10.25</td>
<td>83.50 – 150.00</td>
</tr>
<tr>
<td>WHR</td>
<td>0.79 ± 0.10</td>
<td>0.66 – 1.21</td>
</tr>
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</table>

Graph 1. Values of anthropometric parameters in different categories of birth weight

Grafikon 1. Vrednosti antropometrijskih parametara u različitim kategorijama telesne mase na rođenju

Graph 2. Values of biochemical parameters in different categories of birth weight

Grafikon 2. Vrednosti biohemijskih parametara u različitim kategorijama telesne mase na rođenju
Table 2. Birth weight versus nutritional status and metabolic risk

<table>
<thead>
<tr>
<th>Birth weight (kg)</th>
<th>Telesna masa na rođenju (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight/Normalno uhranjenje</td>
<td></td>
</tr>
<tr>
<td>Without metabolic risk/Bez metaboličkog rizika</td>
<td>3.40 ± 0.50</td>
</tr>
<tr>
<td>At metabolic risk/Sa metaboličkim rizikom</td>
<td>3.15 ± 0.66</td>
</tr>
<tr>
<td>Obese/Gojazne</td>
<td></td>
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<tr>
<td>Without metabolic risk/Bez metaboličkog rizika</td>
<td>3.47 ± 0.20</td>
</tr>
<tr>
<td>At metabolic risk/Sa metaboličkim rizikom</td>
<td>3.42 ± 0.54</td>
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Graph 3. Values of blood pressure in different categories of birth weight

Grafikon 3. Vrednosti krvnog pritiska u različitim kategorijama telesne mase na rođenju

Discussion

Numerous literature data suggest an association between low birth weight and risk for development of metabolic disorders, cardiovascular diseases, and even central deposition of adipose tissue in later life [18,19]. Conversely, higher birth weight is brought into connection with late onset of adiposity and lower risk of cardiovascular diseases and type 2 diabetes [18]. The aim of our research was to analyze the effect of birth weight on the occurrence of metabolic disorders in normal and obese women. The results indicate an association between higher birth weight and overweight in adulthood, as well as the probable impact of low birth weight on the development of metabolic risk profile in normal weight subjects.

It is shown that birth weight is positively correlated with body weight in later life. However, the data are heterogeneous with regard to influence of birth weight on body composition – a positive correlation is suggested both with fat and fat-mass [20]. Some authors assume that a higher cardiometabolic risk in subjects who had low birth weight resulted actually from their programmed lower fat-free mass [21], while others think that low birth weight predisposes central fat distribution [22]. Our findings suggest a closer relationship of birth weight to the size of fat component – persons with high birth weight had higher total fat mass than those with low or average birth weight.

Several studies indicate an association between low birth weight and high values of total cholesterol, fibrinogen and especially high values of blood pressure [23-27]. Huxley et al. [6] estimated that the reduction of birth weight by 1 kg led to an increase in systolic pressure by 2 to 5 mmHg. Eriksson et al. [9] found that people with lower birth weight were two to three times more likely to die from heart disease than those with higher birth weight. Our results also show that persons with low birth weight have higher values of systolic and diastolic pressure, total and LDL-cholesterol, and lower values of HDL-cholesterol in later life than people with higher birth weight. It is supposed that changes of adipose tissue play a key role in this and that after birth there is a sudden increase of adipose tissue with favoring its central deposition and modification of adipokine production (primarily, the reduction of adiponectin), thus contributing to the development of insulin resistance [18].

Recent studies have shown that the metabolic status is not directly dependent on the nutrition level and that obese people are not necessarily metabolically obese as well as that normal weight people could be metabolically obese. Data on the frequency of a healthy metabolic profile among obese people are heterogeneous – between 12.3% [17] and 51.3% [15], while the frequency of metabolic disorders among normal weight people, according to most studies, is less than 20% [28,29]. The data obtained for our population show that 14.35% of obese women have a healthy metabolic profile [30]. Boucharou-Nouet et al. [18] found that higher birth weight, followed by a rapid increase of body weight during the first two years of life, created the conditions for the development of protective mechanism for central obesity and insulin resistance, which could explain the occurrence of "metabolically healthy obesity", and that insulin resistance was related to the increase in body weight after the age of four. Salonen et al. [28] refer to the role of slow increase in body weight during the first seven years on the development of metabolic syndrome, while
Barker et al. [19] emphasize the effects of low birth weight on the development of insulin resistance only in people with high values of body mass index. Bearing in mind the association of low birth weight with metabolic risk profile, Ruderman et al. [14] included low birth weight in the screening system for detection of metabolic obesity in normal weight people. Conus et al. [29], however, found no significant differences in birth weight between normal weight women with and without metabolic obesity (3.13 vs. 3.15 kg). The difference in our study was slightly higher, although it was not statistically significant (3.15 vs. 3.40 kg) and shows a tendency to the development of a bit riskier metabolic profile in normal weight women with low birth weight. On the other hand, obese women at metabolic risk are insignificantly different in birth weight from those who are without the same risk.

A possible shortcoming of our study could be the fact that our sample was small, which may be the reason why there were no statistically significant differences. We were unable to obtain information about possible gestational diabetes in the participants’ mothers that could contribute to greater homogeneity of the group by excluding its effect on birth weight. It is also necessary to mention that criteria for defining normal metabolic profile are not completely harmonized. We used the criteria set by Karelis and associates that take into account the values of total, HDL- and LDL-cholesterol, triglycerides and insulin resistance index. However, when evaluating metabolically healthy and obese people some studies use other criteria that include values of other parameters such as blood pressure, glycaemia or C-reactive protein. Their use might reveal some more aspects of the influence of birth weight on the cardiometabolic profile.

**Conclusion**

Based on these results we can conclude that women with low birth weight had higher values of systolic and diastolic pressure, total and low density lipoprotein-cholesterol and lower values of high density lipoprotein-cholesterol compared to women with higher birth weight. Moreover, people with higher birth weight had higher values of body mass index, total body fat mass as well as waist and hip circumference. Birth weight seemed to be determinant of metabolic risk in normal weight women.

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