DETERMINATION OF RISK FACTORS FOR OBESITY AND ARTERIAL HYPERTENSION OF CHILDREN ACCORDING TO PERINATAL PROGRAMMING OF METABOLISM

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ABSTRACT

Aim of the study: to identify risk factors for obesity of children with exogenous-constitutional obesity and hypertension according to theories of early programming of metabolism.

Material and methods: 55 children with exogenous-constitutional obesity and arterial hypertension were examined, the anthropometric study method was applied, BP was determined, children and their parents were surveyed, medical outpatient records were studied. Relative risk factor calculated.

Results: The results of the study suggest that severe maternal anemia, fetoplacental insufficiency, maternal obesity were of equal importance in the development of obesity. The highest risk factors for visceral obesity of children with abdominal obesity were: birth weight less than 2500 gr, type 2 diabetes mellitus or impaired glucose tolerance in mothers, breastfeeding duration less than 6 months and excess protein nutrition based on cow's milk in the first year of life. In the development of arterial hypertension in background of abdominal obesity, the most significant risk factors were birth weight of more than 4000 gr and birth in a state of prematurity.

Keywords: risk factors, obesity, arterial hypertension, children

1. INTRODUCTION.

Obesity, according to the World Health Organization, is one of the actual problems of modern medicine. Therefore, over the past 30 years, the number of people with obesity and overweight has doubled [1]. At the same time, this also directly affected children and adolescents, it is interesting that according to the RAMS Institute of Nutrition, 21% children aged two years have a risk of developing obesity (Z-speed > 1 and < 2) and 27% children of this age already suffer from overweight (Z-speed > 2) [2].

Along with obesity, there is a clear trend of a steady increase in the conditions associated with it, in particular, arterial hypertension (AH). The prevalence of AH among children and adolescents when applying different diagnostic criteria ranges from 0.4 to 8%. [3,4]. It is proved that in children primary exogenous-constitutional obesity in 80% of cases is combined with AH [5].

The first 1000 days from conception to about 2 years of age is the period of most active growth, accompanied by the most important processes of differentiation and development of cells, tissues and organs. During this pre- and postnatal stage of development, the human body remains flexible and able to adapt, but at the same time fragile [6].

Recent studies show that the risk of non-infectious diseases, such as obesity, diabetes, hypertension, cardiovascular disease and impaired cerebral circulation, is determined by not only genetic risk factors and lifestyle in adulthood, but also to a large extent by perinatal metabolism programming [7,8].

Modern scientific research of early programming of excess weight metabolism and related metabolic disorders focuses on three hypotheses: the hypothesis of excess intrauterine nutrition, the hypothesis of inconsistency and
the hypothesis of accelerated postnatal growth [9,10,11]. Despite the numerous studies of risk factors for the development of obesity, the problem of the causes of disorders in the metabolic status of the child from the position of perinatal metabolism remains not sufficiently studied.

**Aim of the study:** to identify risk factors for obesity of children with exogenous-constitutional obesity and hypertension according to theories of early programming of metabolism.

### II. MATERIALS AND METHODS.

**Design and object of study**

A retrospective, cohort study of 55 children aged 12 to 18 years (average 14.60 ± 0.24 years) with exogenous-constitutional obesity was conducted, 24 girls (43.6%) and 31 (56.4%) boys observed. Children were identified during dispensary examinations in family clinics in Samarkand in the period 2018-2019. All the children examined belonged to the Uzbek population.

The criterion for including children was the SDS (standard deviation score) of body mass index (BMI) study between +2.0 and ≥+3.0.

Exclusion criteria were: secondary obesity and overweight genetic syndromes, refusal of the child and/or parents to be examined.

Children with exogenous-constitutional obesity were divided by the presence of abdominal (visceral) obesity (AO) and the presence of AH. I group 17 people (16.83%) with a uniform type of obesity. Group II included 38 children with AO, while 20 of them had a normal BP - IIA group and 18 children were diagnosed with arterial hypertension (AH) - II B group.

BMI in the I group of patients was within the range of 30.53 ± 0.34 kg/m² (from 29 to 33 kg/m²); in the IIA group 33.45 ± 0.34 kg/m² (from 30 to 36 kg/m²); in IIB group 33.90 ± 0.27 kg/m² (from 33 to 36 kg/m²; \( P < 0.0000 \) as compared to the first group).

The comparison group was 20 non-obese children aged 12 to 18 years (14.9 ± 0.38 years), girls were 9 (45%), and boys 11 (55%). This contingent was selected in the city family clinics of Samarkand. All children were assigned to health group I and belonged to the Uzbek population. The average BMI value in the comparison group was within the range of SDS -1.0 to 1.0 and was 20.50 ± 0.46 kg/m², with a spread of values from 18 to 24 kg/m². The difference in BMI value with the main observation group is reliable (\( P < 0.0000 \)).

**Ethical Consideration**

The study was approved by the Medical Ethics Committee of the Ministry of Health of the Republic of Uzbekistan in accordance with the Declaration of Helsinki. Both informed and written consents were obtained from the parents or from appropriate relatives or guardians of the patients and healthy individuals of the control group. The trial is registered at the US National Institutes of Health (ClinicalTrials.gov ID NCT04611412. 31.10.2020).

**Researches:**

BMI of children and adolescents was compared with percentile diagrams developed by WHO for children from 5 to 19 years old (WHO Growth Reference, 2007). The body weight index was defined as the ratio of body weight (in kg) to body length in the lying position or height in the standing position (m²).

The abdominal (visceral) type of obesity was determined by measurement the waist volume (WV), which was compared with percentile tables for a certain age and sex according to the recommendations of the Russian Scientific Society of Cardiology (RSSC-2009) [12]. The study included children with a centile interval of WV≥90%. The orienteer of the correct measurement of WV were: middle of distance between iliac crest and 12 chest rib along the most protruding points of anterior abdominal wall circumference. Measurement of waist circumference is a simple and highly informative method for assessing visceral fat volume in the body. With the help of computed tomography correlation between degree of development of visceral adipose tissue and value of waist circumference in children is proved [13]. According to IDF recommendations, abdominal obesity can be diagnosed from the age of 6 years, if the waist circumference is equal to or more than 90 percentiles for the studied age [12].
Arterial hypertension was diagnosed in accordance with the recommendations of the Russian Scientific Society of Cardiology and the Association of Pediatric Cardiologists of Russia to diagnosis, treatment and prevention of AH of children and adolescents, when diagnosing mean levels of SBP and/or DBP at 3 visits equal to or exceeding 95th percentile for a given height, sex and age.

Detection of AH in children and adolescents began by measuring the patient's growth and determining his percentile of growth according to a special table [14]. After that, three-fold measurement of BP with interval of 2-3 min was carried out, and the average values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined based on the results of 3 measurements. The obtained SBP and DBP results were compared with the child's growth percentile, age and sex using tables of BP values [14].

Parents were surveyed and medical documentation (Forms 003/y and 112) of children with exogenous-constitutional obesity was analyzed. In addition, based on a specially developed questionnaire, children with exogenous-constitutional obesity were surveyed. When conducting a survey of children and their parents, they had special importance: heredity, pregnancy course, weight and length of birth, diet in the first two years of life, eating habits, physical activity. Patients were examined in accordance with the principles of biomedical ethics on the basis of informed voluntary consent of children and their parents, in accordance with the rules of the Helsinki Declaration of the World Medical Association (2000).

Statistical processing:

Statistical processing of the results was carried out using the methods of variation statistics using the Stat plus for Windows and Microsoft Excel 9.0 applications. Distribution of each indicator was assessed for statistical analysis. The statistical significance of the difference in quantitative indicators between the two groups was estimated by the Mann-Whitney criterion at a significance level of p < 0.05. To compare the percentages, the fraction error was calculated by determining statistical significance using the Yeats-adjusted z-test for continuity. To assess the differences between the shares that do not have a normal distribution, the χ² and Fischer's exact test were applied at a given p < 0.05 (5%) level. A relative risk factor (RR) was calculated with 95% confidence interval calculation.

III. RESULTS:

Firstly, we were interested in studying the birth weight. In 21 (38.0%) obese children, the birth weight was within the limits of 3324.50 ± 78.21 gr, one third of children -17 (31.0%; p < 0.05 compared to the control group) had a weight of 2500 gr and lower, which averaged 2170.58 ± 43.93 gr. It should be noted that this contingent of children was born in the normal gestation period (38-40 weeks). 1/3 obese children (17 (31,0%; p < 0.05 compared to the control group) had an excess birth weight of more than 4000 gr, which averaged 4065.29 ± 55.13 gr. In the control group, almost the entire sample of children had a normal birth weight, which amounted to 17 cases (85%; p < 0.05 compared to the main group), with 2 cases of excess (10%) and one case (5%) of low birth weight.

In the analysis of birth weight depending on the type of obesity and the presence of AH, it was revealed that in the group of children with a uniform type of obesity, the average birth weight was (3266.3 ± 145.4) g, while in children with abdominal obesity and with normal BP, the average body weight vary(2426.70 ± 48.15 g). In the group of children with AO and AH, there were unambiguous parameters, since in this group there were cases of births of children with both body weight above 4000 gr and body weight below 2500 gr, no normal birth weight indicators were found. In this regard, the average birth weight was 3199.44 ± 216.39.

According to the latest theories, the dynamics of body weight growth and growing in the first 2 years of a child's life are of great importance in the development of obesity. In this regard, an analysis of outpatient medical records of obese children revealed that 28 (50.9%) obese children showed a significant trend towards rapid growth and accumulation of excess body weight. So the average body weight in them was 11845.28 ± 230, 20gr (p < 0.0000 in relation to control), with a height of 81.0 ± 0.58 cm, while in the control group the average mass of children was in the range of 10062.0 ± 156.88 gr and the growth was 80.15 ± 0.40 cm. These facts were confirmed by the BMI indicator which was in the range of 20.33 ± 0.20 kg/m²,(p < 0.0000 with respect to control) in children aged 1 year, which characterized body weight as excessive within the SDS range of -1 to ≥+2. Children of the control group, BMI was 16.02 ± 0.17 kg/m², which characterized body weight within the median (SDS -1 to +1).
When comparing the indicators in groups, it was found that the largest indicators for body weight gain were observed in the group of children with AO. Average body weight in children in the II B group at the age of 1 year was 13216.67 ± 237.53 gr, with an increase of 81.0 ± 0.32 cm and a BMI of 21.12 ± 0.14 kg/m². This was significantly larger by relation to children with a uniform type of obesity (11021.88 ± 389.00 gr, p < 0.0000 with an increase of 80.4 ± 2.1 cm and a BMI of 19.5 ± 0.2 kg/m²; p < 0.0000), and with a group of children who had AO and normal BP (11227.50 ± 343.54 gr, p < 0.0000,80.5 ± 0.62 cm and BMI 20.18 ± 0.21 kg/m²; p<0.0000).

In turn, children of group 1 also showed an excess of body weight and height compared to children of the control group (11021.88 ± 389.00 gr, p < 0.0000, with an increase of 80.4 ± 2.1 cm and a BMI of 19.5 ± 0.2 kg/m²; p<0.0000)

A retrospective analysis of body weight and height at 2 years was not performed, as outpatient medical records of children in more observation measures of body weight and growth of children at 2 years of age were lacked.

When studying the perinatal history, it was found that a violation of fetoplacental circulation or premature aging of the placenta in mothers of children of the studied groups was observed in 10 (18.1%) cases of the main group, and the absence of this condition in the control group (p > 0.05). It should be noted that in the group of children with uniform fat deposition, fetoplacental insufficiency was observed in 3 (17.6%) cases, in IIA group 3 (15%) and in IIB group 4 (22.2%) cases (p < 0.05 in relation to the control).

A condition such as pregnant anemia in mothers of children of the study groups, which leads to fetal hypoxia, was observed in almost the same percentage ratio of 94.5% (52 cases) in the main and 90% (18 cases) in the control group. However, when detecting cases of severe anemia, the predominance of this anemia in mothers in the group with AO was revealed. So cases of severe anemia in group 1 were observed in 6 (35.2%), in IIA group in 8 (40%) and in IIB 9 (50%, p < 0.0000 in relation to control) mothers of children with obesity, while in control only 1 mother there was a case of severe anemia of pregnant women (5%).

Gestosis of pregnancy were also observed, including gestosis of 2 and 3 trimesters of pregnancy. Severe gestosis of pregnancy, including preeclampsia, occurred in 2 (11.7%) mothers of children with a uniform type of obesity, in 3 (15%) mothers with AO, and in 3 mothers (16.6%, p < 0.05 in relation to control) children with AO and AH. No cases of severe gestosis were observed in the control group.

The intranatal period was complicated in 16 (29%, p < 0.05 in relation to the control) children of the main group, while 28 (50.9%) children were born with an Apgar score of 7-8 points and 9 (16.3%) with a score of 4-6 points. In children of the control group, intranatal complications were observed in only 2 cases (10%).

In 13 (23.6%) cases, pregnancy was unresolved: 2 (11.76%), 3 (15%) and 4 (22.2%) cases respectively in I, IIA and IIB groups. Prematurity was prevailing in abdominal obesity and normal BP group and absence in control group.

16 (30.7%) mothers of obese children suffered from extragenital pathology (chronic kidney disease, cardiovascular system, etc.). At the same time, a uniform distribution by observation groups was observed, so in-group I 5 (29.4%) was observed, in IIA group 6 (30%), in IIB group 5 (27.7%), at a low observation frequency in the control group (3 cases, 15%; p> 0.05).

In contrast to previous data, there was a predominance of mothers with 1-2 degrees of obesity in children with AO and AH (IIB group) - 10 (55.5%) cases, which was significantly more compared to both control indicators (2 cases, 10%, p < 0.05) and children with a uniform distribution of fat fiber (1 group, 3 cases, 17.6%, p < 0.05). In children of the IIA group with AO but no BP elevation, the number of obese mothers also accounted for half of the observations as in the IIB group (10 cases, 50%).

Feature of health state of children's mothers with abdominal type of obesity was that, it was followed by existence of cases of diabetes 2 types at 2 mothers (11.1%) in IIB to group and violation of tolerance to glucose at 2 (10%) mothers of IIA and at 1 mother in IIB to group. No cases were observed in the control group and I group.

In addition, 19 (34.5%) mothers of obese children noted a significant increase of body weight during pregnancy, with a uniform distribution across all groups 4 (23.5%), 5 (25%) and 5 (27.7%), respectively, in I, IIA and IIB. groups.
Over the years, the focus of the infant nutrition study has been the study of the consumption of individual nutrients, the adequacy of feeding for growth and development. In recent years, there has been a noticeable change in the interest of infant nutrition research in studying its health status in subsequent years of life. So, to our data, in the obese group exclusively breastfeeding up to 6 months there were 20 (36.3%) children, and 35 (63.6%; p < 0.05 with respect to control) - on a mixed and artificial. In the control group, natural feeding for up to 6 months was given 15 (75%; p < 0.05 in relation to the main group) of children and 5 (25%) - mixed and artificial.

During analysis of child feeding by groups, it was found that in 1 group with a uniform type of obesity, the incidence of children exclusively breastfeeding to 6 months of life was 8 (47%), while in the group of children with AO, the incidence of breastfeeding was 7 (35%) and the smallest number of children was observed in the group of children with AO and AH - 5 (27.7%, p < 0.05 with respect to the control).

When comparing the quality of nutrition of children's ambulatory documentation and a survey of parents, the following was found: in the group of obese children with mixed and artificial feeding, there were indications of the use of adapted mixtures, as well as the use of whole milk and milk porridge. Partially adapted mixtures or industrial porridge was also used.

In groups with exogenous-constitutional obesity, it was found that children on artificial or natural feeding, who received adapted milk mixtures up to 3 months, were observed in 5 (29.4%), 6 (30%) and 5 (27.7%) cases (in I, IIA, IIB groups); up to 6 months in 4 (23.5%), 5 (25%), and 4 (22.2%) of cases (in I, IIA, IIB groups, respectively). Soon, they almost completely switched to porridge prepared on diluted or whole cow's milk (rice porridge, etc.). The average age of the beginning of production of cow's milk and milk porridge in the form of fodder and the main food source was in this group 3.32 ± 0.11 months.

In analyzing the anamnestic data of control group’s children, it was revealed that 5 children out of 20 (25%) had indications of using adapted mixtures as the main type of nutrition. Basins were introduced according to age limits, respectively, porridge was used as food once a day. In this group, mainly the first basement was cereal porridge. Whole or diluted cow's milk, as well as porridge prepared on cow's milk, children of the control group began to receive at the age of 7.28 ± 0, 18 months, which was reliably later compared to children with obesity (p < 0,0000).

Particular attention should be paid to the fact that 20 (36.5%) respondents of a group of obese children used kefir (a fermented milk product) or yogurt as their first feed. The average age for obtaining kefir or yogurt was 4.20 ± 0.16 month, while in the control group kefir was assigned on average at the age of 6.25 ± 0.18 month (p < 0,0000).

Cases of frequent snacks of children in the form of cookies, bread and sweet tea were also observed in 26 (47.2%) children under 1 year of age in the main group, while in the control group, similar high-carbohydrate snacks were observed in only 3 (15%) children.

When calculating relative risk scores (RRs) according to theories of perinatal metabolism programming, it was found that in children with abdominal obesity and arterial hypertension, RR scores had the highest confidence margins. You can see the data obtained in Table 1.

The findings showed that all risk factors, consistent with theories of perinatal metabolism programming, were relevant in the development of obesity in children. At the same time, severe anemia of the mother, fetoplacental insufficiency, maternal obesity was of equal importance in the development of obesity. Children with AO, the highest risk factors for visceral obesity had a birth weight of less than 2500 grams, type 2 diabetes mellitus or impaired glucose tolerance in mothers, breastfeeding duration less than 6 months and excess protein nutrition in the first year of life. In the development of AH in background of AO, the most significant risk factors were birth weight of more than 4000 gr and birth in a state of prematurity.

IV. DISCUSSION.

One important risk factor for childhood obesity and hypertension is birth weight. According to Barker D. 1993 [15], it was found that in the group of patients born of low body weight, there were more frequent cases of hypertension and insulin-independent diabetes mellitus, the so-called insulin-resistant or metabolic syndrome. These data also had confirmation in our studies, which revealed that only 1/3 of obese children had normal birth
weight, and 1/3 of the cases, children were born with a body weight below 2500 gr at normal gestation time (38-40 weeks). The relative risk score (RR) in children also showed the statistical significance of low birth weight in the development of abdominal obesity.

According to the theories of perinatal metabolism programming, body weight more than 4000 grams is also important in the development of obesity, in our studies this fact also took place, and statistically significant in the development of AH against the background of AO [9,10].

The role of early postnatal nutrition, weight gain in first life year and subsequent blood pressure was studied by Cheung YBc et al. (2000), which for 30 years observed the growth, development and nature of blood pressure in 122 subjects born with a body weight of less than 2500 g. The researchers proved that higher blood pressure levels and body weight accompanied higher weight-growth rates in children aged 6-18 months at the age of 30 years [16].

These facts were also confirmed in our studies, where the group of children with AO and AH experienced the largest spike in body weight and growth in first life year. Children of this group showed the largest difference in birth weight and 1 life year, which was accompanied by a significant difference in body weight and BMI compared to the control group (p < 0.0000), as well as the group with a uniform type of obesity (p < 0.0000), which can be regarded as a valuable diagnostic sign of the development of AH on background of AO in children.

Despite the well-known claim that the main cause of obesity is the imbalance between distribution and consumption energy, in recent years many new scientific facts have appeared, indicating the early origins of obesity (antenatal and early postnatal periods) [16,17].

A number of scientific papers attribute the risk of obesity to the nature of the mother's diet during pregnancy (both excessive and insufficient), as well as the short duration of breastfeeding. A similar hypothesis was first put forward more than 30 years ago by a German researcher (G. Dorner, 1973), who noted that "the concentration of hormones and metabolites in critical periods of early development programs the risk of developing some adult diseases" [19]. Numerous studies in this direction support the hypothesis that nutrition in the period of antenatal development and in breast age program the risk of obesity in subsequent years of life [20].

The period of intrauterine development is characterized by high plasticity of metabolism, the ability to adapt all metabolic systems of the body to environmental factors. Impaired nutrition of the mother, utero-placental circulation, as well as hypoxia, stress, anemia lead to delayed development of the fetus and, possibly, form an "economical phenotype," which contributes to the accumulation of adipose tissue, impaired lipid metabolism and the formation of cardiovascular pathology.

It is believed that insufficient nutrition of the mother during pregnancy, prematurity, birth of a child with low body weight or symptoms of delayed intrauterine development are risk factors that often lead to obesity, arterial hypertension and insulin-resistant diabetes [21].

The data we obtained also reflected these hypotheses, so the detected cases of fetoplacental insufficiency in mothers of the study groups, cases of severe anemia as risk factors, were equally high in the development of a uniform type of obesity and abdominal type of obesity. Such a risk factor as prematurity was a risk factor for the development of AO and AH.

One factor in the development of obesity in children is the presence of cases of obesity in the mother, with impaired carbohydrate metabolism, as well as a significant increase in body weight during pregnancy. These facts contribute to the breakdown of metabolic processes and their laying and design at the antenatal period. When interviewing mothers of children of the study groups, we obtained data characterizing the high incidence of obesity in mothers, with the presence of cases of type 2 diabetes mellitus and impaired glucose tolerance. At the same time, obesity as a risk factor was of high equivalent importance in all study groups, and impaired carbohydrate metabolism as a risk factor was important in the development of abdominal obesity and AH. Population studies of recent years show the real impact of excess postnatal nutrition on the risk of obesity, with the use of excess protein being of greatest importance. It should be assumed that the level of real protein consumption by children of the first months of life of breastfeeding is very low. Adapted industrial mixtures, despite high technology, cannot bring the level of protein closer to its content in breast milk (8-10 g/l). At the
same time, the delivery of cow's milk is widespread in developing countries, which also contribute to excessive protein consumption [6,9,10,22,23].

Our studies have also shown the significant impact of exclusive breastfeeding duration as a factor in the development of obesity in children, and excess protein nutrition. A feature of local nutrition is the early introduction of mixtures and porridge based on whole milk, which was a contribution to the development of obesity in children of the Uzbek population.

V. CONCLUSION

Summarizing the presented data, it should be assumed that the main risk factors for developing obesity in children are low or high birth weight, prematurity, breastfeeding duration less than 6 months, excess protein nutrition.

Obese children, especially those with abdominal obesity and hypertension, had an aggravated perinatal history, with severe anemia of pregnant women, the presence of obesity in the mother with concomitant carbohydrate metabolism disorders, and a significant increase in body weight during pregnancy being a significant risk factor.

LITERATURE

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Table 1.

Risk scores (RRs) in children of compared groups from the position of perinatal metabolic programming

<table>
<thead>
<tr>
<th>Risk Indicators</th>
<th>RR</th>
<th>Lower limit 95% CI</th>
<th>Upper limit 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight less than 2500 gr</td>
<td>I group n=17</td>
<td>1,511</td>
<td>1,889*</td>
</tr>
<tr>
<td></td>
<td>IIA group n=20</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IIB group n=18</td>
<td>3,068*</td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Group A</td>
<td>Group B</td>
<td>Group C</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
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<tr>
<td>Birth weight above 4000 gr.</td>
<td>1,373</td>
<td>1,571</td>
<td>2,240*</td>
</tr>
<tr>
<td></td>
<td>0,709</td>
<td>0,863</td>
<td>1,247</td>
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<tr>
<td></td>
<td>2,657</td>
<td>2,861</td>
<td>4,023</td>
</tr>
<tr>
<td>Severe Mother Anaemia</td>
<td>2,338*</td>
<td>2,296*</td>
<td>2,800*</td>
</tr>
<tr>
<td></td>
<td>1,336</td>
<td>1,393</td>
<td>1,573</td>
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<tr>
<td></td>
<td>4,089</td>
<td>3,784</td>
<td>4,983</td>
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<tr>
<td>Feto-placental insufficiency in mothers</td>
<td>2,153*</td>
<td>2,020*</td>
<td>2,578*</td>
</tr>
<tr>
<td></td>
<td>1,218</td>
<td>1,226</td>
<td>1,484</td>
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<tr>
<td></td>
<td>3,805</td>
<td>3,329</td>
<td>4,478</td>
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<tr>
<td>Prematurity</td>
<td>1,511</td>
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<td></td>
<td>0,624</td>
<td>0,819</td>
<td>1,044</td>
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<tr>
<td></td>
<td>3,662</td>
<td>3,082</td>
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<tr>
<td>Extragenital pathology in mothers</td>
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<td></td>
<td>0,940</td>
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<td></td>
<td>3,392</td>
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<td>Grade 1-2 obesity in the mother</td>
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<td>2,020*</td>
<td>3,068*</td>
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<td></td>
<td>1,218</td>
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<td></td>
<td>3,805</td>
<td>3,329</td>
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<td>Impaired glucose tolerance or type 2 diabetes mellitus in mothers</td>
<td>-</td>
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<td></td>
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<td>Significant body weight gain in maternal pregnancy</td>
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<td></td>
<td>3,205</td>
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<tr>
<td>Breastfeeding duration less than 6 months</td>
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<td></td>
<td>3,657</td>
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<td>Excess protein nutrition in the first year of life</td>
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<td>3,500*</td>
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<td>3,213</td>
<td>5,339</td>
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Note: * P < 0.05 with respect to the control group.