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# Fetal Macrosomia in Pregnant Women with Gestational Diabetes

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## ABSTRACT

*The aim of the study was to determine the frequency of fetal macrosomia in newborns from mothers with gestational diabetes mellitus (GDM) and healthy mothers, as well as determining the influence of fetal growth on pregnancy termination, on complications in pregnancy, during delivery and puerperium and on neonatal complications. In the study were included 351 pregnant women with GDM, as well as control group of 1502 healthy pregnant women. Newborns of mothers with GDM had significantly higher birth weight and length, ponderal index >2.85 was more frequent, they were macrosomic and hypertrophic (disproportional and proportional), had smaller Apgar score and more frequent neonatal complications ( $p < 0.05$ ). Fetal macrosomia and fetal hypertrophy alone or, particularly, connected with disproportional fetal growth, but disproportional hypotrophy as well, had significantly influence on greater frequency of delivery and puerperal complications, delivery completion with Cesarean section and neonatal complications in pregnant women with GDM.*

**Key words:** gestational diabetes mellitus, fetal macrosomia, disproportional growth

## Introduction

Gestational diabetes mellitus (GDM) is a carbohydrate intolerance that is manifested by hyperglycaemia. GDM is caused by insulin resistance and is firstly noted during pregnancy, wherein it shows adverse effects on the pregnancy itself, on the fetus and on future life of both the mother and the offspring. An incidence of GDM is 2–14%, which depends on population and ethnic factors, and also on different diagnostic parameters used<sup>1,2</sup>.

Although the exact mechanism of insulin resistance during pregnancy is not known, its known causes include: decrease of insulin receptors in target tissues, postreceptor blockage, an antireceptor activity of polyclonal antibodies, defects in the cellular mechanism of immune tolerance, defects of different genes, and finally the effects of hormone changes on homeostasis of glucose and lipids<sup>3,4</sup>.

Fetal growth is a complex process that involves interactions among mother, placenta and fetus. Newborn's birth weight is the result of genetic predisposition, available substrates (quantity of glucose, lipids, amino acids), and mother's and fetal endocrine statuses, all of which also determine a postnatal growth rate<sup>5</sup>.

The most important source of energy for a fetus is glucose, whereas insulin and insulin like growth factor I (IGF-I) are the most important growth hormones, which positively correlate to his growth<sup>6,7</sup>. Fetal macrosomy can be defined as a body weight above 4000 grams at term and large-for-gestational age baby above the 90th percentiles for a reliable gestational age or when it's weight is two standard deviations above the median of weight birth defined for defined population<sup>8–10</sup>. Chronic hyperinsulinemia in fetuses from diabetic pregnancies leads to

increase in total body mass with a moderate increase in body length accompanied with selective organomegalia, which is a result of hypertrophy of insulin-sensitive tissues. Newborn is not only large, but it has a disproportionately big trunk, wide shoulders in relation to the head measurements (there is lower ratio of head circumference in relation to shoulder width), a larger extremities diameter, higher values of skin folds and higher proportion of fat in the total weight<sup>11</sup>. Fetal growth is one of the criteria for determining clinical methods of treatment of pregnant women with diabetes<sup>12</sup>.

Significant problems in pregnant women with GDM are complications in pregnancy (urogenital infections, hypertension and pre-eclampsia) that correlate with poor metabolical control and perinatal outcome<sup>11,13</sup>. Pregnancy with GDM is characterized by an increase in the frequency of congenital malformation, neonatal complications (hypoglycemia, cardio-respiratory disorders, respiratory distress syndrome, anomalies, hyperbilirubinemia, macrosomy associated with injuries during delivery), as well as obesity and diabetes in childhood and later<sup>10,14</sup>. Frequency of neonatal complications is higher in the group of disproportional asymmetrical metabolic macrosomy in relation to proportional symmetric constitutional macrosomy<sup>15</sup>.

Due to the frequent complications in pregnant women with GDM, delivery should be completed earlier, and the rate of the Caesarean section in recent years reaches 60%<sup>11,16</sup>.

The aim of the study was to determine the frequency of macrosomal fetal growth in newborns from healthy mothers and mothers with GDM, as well as determining the influence of fetal growth on pregnancy termination and on the frequency of complications in pregnancy, during delivery and puerperium and on neonatal complications. This paper describes the increased frequency of fetal macrosomy, especially the disproportionate macrosomy, as well as higher frequency of deliveries completed by Caesarean section, more frequent complications during pregnancy, delivery and newborn's period in pregnant women with GDM compared to healthy pregnant women. This study differs from earlier reports by its use of ponderal index (PI) in relation to percentile curve.

## Materials and Methods

This prospective study was made on patients from the Division of Diabetes and Fetal Growth of the Department of Gynecology and Obstetrics, University Hospital Center Zagreb, in the period 1995–2003. In the study, 351 pregnant women with GDM were monitored, as well as control group of randomly selected 1502 healthy pregnant women with singleton pregnancy of same gestational age, newborn's gender and similar mothers' parity.

All pregnancies ended between gestation weeks 28th and 44th by delivery of a live newborn. Gestational age was determined by the duration of amenorrhea, that was confirmed by the ultrasonic biometry during pregnancy; after delivery the gestational age was estimated by using

the method of Farr. Diagnosis of GDM is set according to the criteria of the World Health Organization<sup>17</sup>. Individual data on age and parity, complications in pregnancy, delivery and puerperium, mode of delivery and neonatal complications in pregnant women with GDM, as well as in the control group were analyzed.

Group of pregnant women with GDM consisted of 278 pregnant women with good regulation of glycaemia during pregnancy achieved only through diet with up to 1800 kcal per day. Other 73 pregnant women with GDM were on the same diet but, due to the elevated glycaemia, they were on insulin therapy, too.

Gestational age, birth weight (BW), length at delivery (BL), ponderal index ( $PI = \frac{BW}{BL^3} \times 100$ ) together with percentile values (CV), Apgar score at the end of first and fifth minute, blood pH values from umbilical cord and neonatal complications in newborns were analyzed.

The frequency of macrosomy and disproportional macrosomy in newborns were determined and its coherence with the way of completion of pregnancy and complications was analyzed. Ponderal index values lower than 2.32 and ponderal index higher than 2.85 were indicative for disproportional growth of newborns. Infants were classified, according to percentile values and corrected percentile values for the newborns weight of defined weeks of pregnancy by mother's parity and child's gender coherent to the year 1982 in Zagreb<sup>18</sup> into three groups: hypotrophic (<10 percentiles), eutrophic (10–90 percentiles) and hypertrophic (>90 percentiles).

To test the difference between the studied groups univariate analysis of variance (ANOVA) was performed, while to test quantitative variables student T-test for independent samples were implemented. The difference between the studied groups for qualitative data was tested by  $\chi^2$ -test for independent samples as well as by Fisher's test. P value <0.05 was considered as statistically significant. Statistical analysis was performed using SPSS software package (SPSS for Windows 11.5, SPSS Inc., Chicago, IL, USA).

## Results

All pregnant women (both healthy and those with GDM) analyzed in this study were of the same gestational age ( $39.63 \pm 1.98$  vs.  $39.33 \pm 2.14$  weeks,  $F = 1.567$ ,  $p = 0.211$ ), of the same newborn's gender ( $\chi^2 = 0.015$ ,  $p = 0.906$ ), and had the same parity ( $\chi^2 = 0.468$ ,  $p = 0.513$ ).

The women with GDM were significantly older than the healthy ones ( $31.56 \pm 5.73$  vs.  $28.19 \pm 5.19$  years,  $F = 9.735$ ,  $p = 0.002$ ), and thus more often  $\geq 30$  years old ( $217 - 62.8\%$  vs.  $574 - 38.2\%$ ,  $\chi^2 = 63.346$ ,  $p = 0.0001$ ). However, a relatively high frequency of GDM was noted in pregnant women of less than 30 years old (38.2%), and also in those younger than 25 (11.1%).

The GDM group, in previous pregnancies, had an increased rate of spontaneous abortions ( $90 - 25.6\%$  vs.  $235 - 15.6\%$ ,  $\chi^2 = 19.653$ ,  $p = 0.0001$ ), with more frequent intra-

uterine and subpartal deaths (17–4.8% vs. 23–1.5%,  $\chi^2=14.777$ ,  $p=0.0001$ ), and also neonatal deaths (15–4.3% vs. 18–1.2%,  $\chi^2=15.381$ ,  $p=0.0001$ ).

The average hospitalization period of pregnant women with GDM was significantly longer compared to the healthy ones (2.49±1.54 vs. 0.22±0.57 days,  $F=2074.396$ ,  $p=0.0001$ ), due to increased incidence of complications ( $p<0.05$ ): polyhydramnion, Rh immunization, cerclage cervicis, hypertension, urinary infections, congenital malformations. Hypertension was several fold more frequent in women with GDM than in healthy ones (34–9.7% vs. 21–1.4%,  $\chi^2=67.866$ ,  $p=0.0001$ ), as well as pre-eclampsia (27–7.7% vs. 40–2.7%,  $\chi^2=20.649$ ,  $p=0.0001$ ), chronic hypertension (14–4.0% vs. 18–1.2%,  $\chi^2=13.036$ ,  $p=0.0003$ ), and asymptomatic bacteriuria (47–13.4% vs. 93–6.2%,  $\chi^2=21.109$ ,  $p=0.0001$ ). The frequency of premature deliveries was increased in pregnant women with GDM (11.4%) too, in relation to the control group (9.2%).

The frequency of prepathological (23–6.6% vs. 55–3.7%,  $\chi^2=5.602$ ,  $p=0.018$ ) and pathological (13–3.7% vs. 19–1.3%,  $\chi^2=9.679$ ,  $p=0.002$ ) cardiotocograms was significantly higher in pregnant women with GDM, as compared to the healthy ones. They also had increased rate of delivery and puerperal complications (28–8.0% vs. 32–2.1%,  $\chi^2=31.042$ ,  $p=0.0001$ ).

The average weight and length of newborn babies from mothers with GDM was significantly higher than of those from healthy mothers ( $p<0.05$ ), except the ponderal index for which the difference was not significant (Table 1).

Newborns are divided into three groups based on ponderal index: disproportional small (<2.32), proportional (2.32–2.85), and disproportional large (>2.85).

The newborns of mothers with GDM were significantly more disproportional large than those of healthy mothers, which were dominantly of proportional size (Table 2).

Table 3 presents the frequency of macrosomic newborns that weighted  $\geq 4000$  grams and  $\geq 4500$  grams, and also the rate of ponderal index dependant macrosomic proportional and disproportional growth. Significantly higher incidence of macrosomic growth was observed in the group of newborns from mothers with GDM ( $p<0.05$ ). As with macrosomic newborns, the frequency of hypertrophic newborns ( $CV>90$ ) was much higher in the group of mothers with GDM, than in the control group (120–34.2% vs. 230–15.3%,  $\chi^2=66.161$ ,  $p=0.0001$ ).

The viability of newborns was estimated by an Apgar score, determined at the end of the first and fifth minute after birth. The average Apgar score values were significantly lower in neonates from mothers with GDM both in the first (9.37±1.37 vs. 9.71±1.02,  $F=28.221$ ,  $p=0.0001$ ), and in the second (9.74±0.70 vs. 9.90±0.58,  $F=19.767$ ,  $p=0.0001$ ) measurement. The frequency of neonates with Apgar score 4–7, according to the first measurement, was considerably higher in a group of mothers with GDM (28–8.0% vs. 56–3.7%,  $\chi^2=11.868$ ,  $p=0.001$ ). There were no statistical differences of the rate of Apgar score below 7 (6–1.7% vs. 20–1.3%) and Apgar score below 4 (0–0.0% vs. 3–0.2%) at the fifth minute among both groups ( $p>0.05$ ).

Newborns from mothers with GDM showed an increased rate of both congenital malformations (18–5.1% vs. 29–1.9%,  $\chi^2=11.766$ ,  $p=0.001$ ) and neonatal complications (133–37.9% vs. 300–20.0%,  $\chi^2=51.012$ ,  $p=0.0001$ ): hyperbilirubinemia, perinatal infections, kefalhaemathoma, clavicular fracture, brachial plexus injuries. During early neonatal period two newborns died in a group of

**TABLE 1**  
THE MEAN VALUE OF BIRTH WEIGHT, BIRTH LENGTH AND PONDERAL INDEX OF NEWBORNS FROM WOMEN WITH GESTATIONAL DIABETES AND HEALTHY ONES

	GDM (n=351) $\bar{X}\pm SD$	Healthy (n=1502) $\bar{X}\pm SD$	F	P
Birth weight (g)	3506.6±732.7	3350.2±585.1	18.372	0.0001
Birth length (cm)	50.4±3.1	49.9±2.7	9.884	0.002
Ponderal index	2.69±0.27	2.67±0.24	3.300	0.069

GDM – gestational diabetes

**TABLE 2**  
PONDERAL INDEX OF NEWBORNS FROM MOTHERS WITH GESTATIONAL DIABETES AND HEALTHY ONES

Ponderal index	GDM (n=351) n (%)	Healthy (n=1502) n (%)	$\chi^2$	p
<2.32	21 (6.0)	97 (6.5)	0.108	0.743
2.32–2.85	234 (66.6)	1086 (72.3)	4.412	0.036
>2.85	96 (27.4)	319 (21.2)	6.115	0.013

GDM – gestational diabetes

**TABLE 3**  
FREQUENCY OF MACROSOMIC NEWBORNS FROM MOTHERS WITH GESTATIONAL DIABETES AND HEALTHY ONES

Macrosomy (g)	GDM (n=351) n (%)	Healthy (n=1502) n (%)	$\chi^2$	p
<4000	267 (76.0)	1317 (87.7)	30.929	0.0001
≥4000	84 (24.0)	185 (12.3)	31.797	0.0001
≥4500	23 (6.6)	29 (1.9)	22.284	0.0001
≥4000 proportional	37 (10.5)	90 (6.0)	9.224	0.002
≥4000 disproportional	47 (13.5)	95 (6.3)	20.436	0.0001
≥4500 proportional	6 (1.7)	9 (0.6)	4.367	0.037
≥4500 disproportional	17 (4.8)	20 (1.3)	17.930	0.0001

GDM – gestational diabetes

mothers with GDM, while in the other group died four (0.6% vs. 0.7%,  $\chi^2=0.812$ ,  $p=0.368$ ). These differences are not statistically relevant.

The mothers with GDM had increased frequency of Caesarean section (132–37.6% vs. 134–8.9%,  $\chi^2=190.421$ ,  $p=0.022$ ). No difference was observed concerning fetal presentation nor did it influenced the delivery methods ( $p>0.05$ ).

In mothers with GDM that delivered their newborns by Caesarean section, it was correlated with macrosomic, disproportional macrosomic and disproportional hypertrophic newborns ( $p<0.05$ ). The greatest frequency of Caesarean section occurred in mothers with GDM that carried disproportional hypotrophic newborns (90.0%), while it was lower in cases where newborns were eutrophic (32.8%), or proportional eutrophic (30.1%), or proportional hypotrophic (17.6%). Healthy mothers deliv-

ered hypertrophic and hypotrophic newborns (11.7%) by Caesarean section mostly than eutrophic (8.0%) (Table 4).

No difference was noted among mothers with GDM concerning frequency of delivery and puerperal complications in relation to the size of a neonate, while in the group of healthy mothers much more complications occurred when disproportional hypertrophic (5–4.9% vs. 26–1.9%,  $\chi^2=4.260$ ,  $p=0.039$ ) and disproportional eutrophic (5–9.6% vs. 26–1.8%,  $\chi^2=15.196$ ,  $p=0.0001$ ) newborns were delivered.

As neonatal complications are concerned, children delivered by mothers with GDM had the most frequent complications when macrosomic proportional (≥4000 g, PI 2.32–2.85) (20–54.1% vs. 121–36.9%,  $\chi^2=4.591$ ,  $p=0.032$ ), macrosomic proportional (≥4500 g, PI 2.32–2.85) (5–83.3% vs. 128–37.1%,  $\chi^2=5.356$ ,  $p=0.021$ ), hypertro-

**TABLE 4**  
IMPACT OF FETAL GROWTH ON THE COMPLETION OF DELIVERY

Fetal growth (n=GDM/Healthy)	Caesarean section – n (%)		
	GDM (n=132)	Healthy (n=134)	p
Macrosomic ≥4000 g (84/185)	33 (39.3)	16 (8.6)	0.0001
Macrosomic ≥4500 g (23/29)	14 (60.9)	3 (10.3)	0.0002
Proportional macrosomic (37/90)	9 (24.3)	4 (4.4)	0.002
Disproportional macrosomic (47/95)	24 (51.1)	12 (12.6)	0.0001
Hypotrophic (27/137)	2 (11.8)	24 (17.5)	0.739
Eutrophic (204/1135)	66 (32.4)	91 (8.0)	0.0001
Hypertrophic (120/230)	54 (45.0)	19 (8.3)	0.0001
Disproportional hypertrophic (60/103)	32 (53.3)	12 (11.7)	0.0001
Proportional hypertrophic (60/127)	21 (35.0)	7 (5.5)	0.0001
Disproportional large eutrophic (36/220)	16 (44.4)	13 (5.9)	0.0001
Proportional eutrophic (156/863)	47 (30.1)	69 (8.0)	0.0001
Disproportional small eutrophic (12/52)	4 (33.3)	9 (17.3)	0.243
Proportional hypotrophic (17/87)	3 (17.6)	8 (9.0)	0.378
Disproportional hypotrophic (10/48)	9 (90.0)	16 (33.3)	0.001

GDM – gestational diabetes

phic (55–45.8% vs. 78–32.4%,  $\chi^2=4.887$ ,  $p=0.027$ ), and less so if they were eutrophic (67–32.8% vs. 66–44.9%,  $\chi^2=5.276$ ,  $p=0.022$ ) and eutrophic disproportional (PI > 2.85) (8–22.2% vs. 125–39.7%,  $\chi^2=4.185$ ,  $p=0.041$ ). On the other hand, in the group of healthy mothers the incidence of neonatal complications was much higher in disproportional hypotrophic (PI < 2.32) (17–35.4% vs. 283–19.5%,  $\chi^2=7.395$ ,  $p=0.007$ ), and disproportional eutrophic (PI < 2.32) (19–36.5% vs. 281–19.4%,  $\chi^2=9.247$ ,  $p=0.002$ ) newborns.

## Discussion

This study has presented the increased frequency of fetal macrosomy, especially the disproportional macrosomy, higher frequency of deliveries completed by Caesarean section, complications in pregnancy, during delivery, puerperium and neonatal complications in pregnant women with GDM compared to the healthy pregnant women.

Maternal age and increase of the age is considered to be the highest relative risk for the emergence of GDM. The risk increases after the age of 25<sup>19</sup>. The results of this research confirm the influence of age on the frequency of GDM, as well as the legitimacy of the screening on GDM in the age groups younger than 30 years.

Increased frequency of hypertension in pregnancy and preeclampsia among pregnant women with GDM can be associated with poor metabolic control of the disease and with the mother's constitutional factor of increased sensitivity of endothelial activity, while poor placentation plays a minor role<sup>20</sup>. Cartagena<sup>21</sup> has established less perinatal complications in pregnant women with GDM who had better perinatal care. Significantly higher frequency of pre-term birth in pregnant women with GDM in comparison with the control group was not found. Similar results were found by Yogev and Langer in 1526 pregnant women with GDM with the frequency of pre-term birth of 10.7%, which was not different from the control group of healthy pregnant women. Better metabolic control of glycaemia reduced the frequency of premature delivery<sup>22</sup>. Significantly higher frequency in prepathologic and pathologic cardiotocogram records in pregnant women with GDM refers to chronic hypoxia in fetuses of mothers with GDM<sup>23</sup>.

Djelmiš et al. in the earlier works found significantly higher birth weight values (3558.2±817.6 g vs. 3132.4±534.4 g), ponderal index (2.82±0.28 vs. 2.63±0.24), macrosomy (53.4% vs. 8.3%) and disproportional macrosomy (35.2% vs. 5.8%) in pregnant women with diabetes compared to healthy ones<sup>24</sup>. Results of this survey are in accordance with their results. This work shows in detail the prevalence of macrosomal newborns (PT ≥4000 g and PT ≥4500 g), as well as the frequency of the same macrosomy groups (that with proportional and disproportional growth specified by ponderal index and percentile values). Frequency of all subgroups of macrosomal newborns in women with GDM, disproportional macrosomy as well as proportional and disproportional hyper-

trophic newborns, was statistically significantly higher compared to the control group. Authors from Slavonki Brod have found an increased frequency of GDM from 1.0 to 6.7%, decrease of frequency of macrosomy from 13.3 to 12.2% and decreased frequency of perinatal mortality, preterm birth, fetal and maternal complications in pregnancy and on child birth, as a result of an appropriate estimation of glucose tolerance during pregnancy<sup>25</sup>. Authors from Bosnia and Herzegovina have found that the frequency of macrosomy (≥4000 g) in 13.1% of pregnant women was associated with the prolonged pregnancy, mother's obesity, GDM, hypertension and male gender of the newborns, as well as bad perinatal outcome<sup>26</sup>. Diabetic pregnancy is associated with higher frequency of macrosomy, accelerated and larger fetal growth that are matched with a higher frequency of disproportional growth.

Mother's hyperglycaemia leads to fetal hyperglycaemia and hyperinsulinemia, which causes hyperplasia and hypertrophy of the Langerhans' islets and, consequently, increased growth of fetal tissues and organs. Whereas placenta does not allow transfer of fetal insulin to mother, a large quantity of mother's glucose is metabolized in the fetus leading to increased lipogenesis, visceromegalia and excessive growth of the fetus. Research has proven that macrosomal newborns from mothers with diabetes have a significantly higher level of insulin in umbilical vein than eutrophic and hypotrophic newborns, that confirms the importance of insulin as the most important tissue growth hormone. Positive correlation between glucose and insulin in the fetal circulation and amniotic fluid shows their strong influence on fetal growth. Significantly higher were the value of IGF-I from umbilical vein's blood, and they were in positive correlation with fetal growth and duration of pregnancy, while the value of growth hormone were lower in comparison to eutrophic and hypotrophic newborns<sup>7</sup>.

Due to the chronic intrauterine hypoxia, fetuses of pregnant women with GDM have lower Apgar score and lower umbilical vein pH in comparison to the control group<sup>23</sup>. A low Apgar score at first minute is often caused by a temporary depression, whereas low fifth-minute score usually is associated with several obstetric risk factors and implies complications of clinical importance<sup>27</sup>.

Congenital malformations and neonatal complications were significantly more often in the group of pregnant women with GDM in comparison to the control group, while significant differences in early neonatal mortality rate among the investigated groups were not present.

This work shows significantly higher frequency of completion of birth through Caesarean section, as well as a significant influence of fetal macrosomy and fetal hypertrophy alone, especially when associated with disproportional fetal growth, as well as a significant influence of disproportional eutrophy and hypotrophy on the increased frequency of birth completion by Caesarean section in pregnant women with GDM compared to healthy pregnant women. Navti et al.<sup>28</sup> found fetal macrosomy

( $\geq 4500$  g) in 1.4% of pregnant patients, where 61.6% of the deliveries began spontaneously, they were induced in 31.6%, while in 6.8% elective Caesarean section was performed. The delivery was in 65.8% completed spontaneously vaginal, in 17.5% operative vaginal and in 16.7% by emergency Caesarean section. Frequency of shoulder dystocia and of Caesarean section was significantly higher. Macrosomy in newborns is the indirect cause of increased frequency of Caesarean section in women with borderline and untreated GDM. Despite the regulation of GDM and normalization of birth weight, the frequency of births completed by Caesarean section remains high<sup>29</sup>. Miller and Gillmer believe that diabetes in pregnant women is not indication for Caesarean section. If the estimation of fetal weight is exceeding 4250 grams or if there is a significant difference in the proportion of the value of the circumference of the abdomen and head of the fetus, elective Caesarean section should be considered. Completion of the delivery by Caesarean section is neither routine indication, nor contraindication. Increased incidence of fetal macrosomy and risk of injury during delivery, due to cephalopelvic disproportion and shoulder dystocia, call for an evaluation of fetal weight before completion of the delivery by vacuum extraction or forceps<sup>16</sup>. Many studies emphasize the completion of pregnancy with fetal macrosomy by Caesarean section, while others do not confirm that<sup>30</sup>. Active, rather than expectant management of labor at term for women with GDM, may reduce rates of macrosomia and related complications<sup>31</sup>. Women diagnosed with GDM by the Carpenter and Coustan criteria, but not by the National Diabetes Data Group criteria, had higher risk of operative deliveries, macrosomia and shoulder dystocia<sup>32</sup>.

This investigation presented a significantly higher frequency of neonatal complications in proportional and hypertrophic macrosomic newborns from pregnant women with GDM. In the group of healthy pregnant women significantly higher frequency of neonatal complications was observed in hypotrophic and eutrophic disproportionate newborns. Ballard et al.<sup>15</sup> found 45% macrosomal and 19% of disproportionate macrosomic newborns in mothers with GDM, as compared to 8% and 1%, respectively, in the control group, indicating a significantly higher frequency of complications in neonatal disproportionate macrosomic newborns from mothers with GDM. Boulet et al.<sup>33</sup> found an increased risk of delivery as well as neonatal complications involving macrosomic children. Number of complications increases with the weight above 4500 grams; the infant's weight over 5000 grams was a significant indicator of risk for unfavorable neonatal outcome. A frequency of fetal death increases with the fetal weight  $\geq 4250$  grams in nondiabetic pregnancies and  $\geq 4000$  grams in diabetic ones<sup>34</sup>. Anoon et al.<sup>35</sup> found 0.24% of newborns with delivery weight  $\geq 5000$  grams

(68% of male newborns among them), with their mothers being significantly older, excessively heavy weighted, multiparas, with GDM, with prolonged pregnancy, or having earlier macrosomic children. These deliveries were accompanied with a significantly greater frequency of Caesarean section, postpartal haemorrhage, fetal hypoxia, shoulder injury and neonatal traumas after vaginal delivery, which occurred with a frequency of 59.5%. In that study fetal macrosomy and fetal hypertrophy alone or combined with disproportionate fetal growth had the strongest impact on the increased frequency of neonatal complications among pregnant women with GDM.

Intrauterine changes of the fetus in pregnant women with diabetes in later life have long-term consequences for the regulation of glucose homeostasis and insulin sensitivity. Consequence of early damage of the development of pancreatic  $\beta$ -cells is occurrence of impaired glucose or diabetes in adult age<sup>36</sup>. Women with GDM in early pregnancy have a high risk of developing diabetes (especially diabetes mellitus type 2) in later life. They show characteristics of insulin resistance, such as the central type of obesity, dislipidemia and hypertension associated with increased morbidity as well as significantly higher frequency of glucose intolerance and metabolic syndrome. Young women with GDM are the group with high risk, but by changing the way of life possible cardiovascular complications and progression to diabetes would be reduced<sup>37</sup>.

The main problems of diabetic pregnancies are congenital anomalies, spontaneous miscarriages, misregulation of fetal growth, occurrence of hypertension, fetal hypoxia, also the methods of birth completion, and neonatal complications.

## Conclusion

As a conclusion, an optimal regulation of glycaemia (by diet or insulin) in pregnant women is of fundamental importance for the prevention of diabetic complications during pregnancy. There is a need for good preconception metabolic regulation of the disease, also a self-control during pregnancy, ultrasonic monitoring of the fetus, good cooperation of obstetricians and diabetologists and, finally, the care of diabetic pregnancy in a regional center. An elimination of congenital anomalies, the reducing of complications of pregnancy and birth, a lower of frequency macrosomy and neonatal complications, even very low perinatal mortality, similar to the one in the general population, would be achieved by an early detection and treatment of hypertension and bacteriuria, along with fetal monitoring at the end of pregnancy, programmed birth induction or elective Caesarean section just before the term with verified intrauterine fetal maturity.

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## FETALNA MAKROSOMIJA U TRUDNICA S GESTACIJSKIM DIJABETESOM

## SAŽETAK

Cilj rada je bio utvrditi učestalost fetalne makrosomije u novorođenčadi rođenih od majki koje boluju od gestacijskog dijabetesa melitusa (GDM) i zdravih majki, kao i utjecaj fetalnog rasta na način dovršenja trudnoće i učestalost komplikacija u trudnoći, porodu i puerperiju, te neonatalnih komplikacija. U istraživanje je uključeno 351 trudnica s GDM i 1502 zdrave trudnice kao kontrolna skupina. Novorođenčad trudnica s GDM su značajno veće porodne težine i duljine, učestalijeg  $PI > 2,85$ , makrosomna su i hipertrofična (disproporcionalno i proporcionalno), imaju manje vrijednosti Apgar indeksa i veću učestalost neonatalnih komplikacija. ( $p < 0,05$ ). Fetalna makrosomija i fetalna hipertrofija same, posebice udružene s disproporcionalnim fetalnim rastom, ali i disproporcionalna hipotrofija, imaju značajan utjecaj na povećanu učestalost komplikacija u porodu i puerperiju, dovršenja poroda SC i neonatalnih komplikacija u trudnica s GDM.