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Influence of gestational diabetes in twin pregnancy on the condition of newborns and early neonatal complications

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ABSTRACT

Objectives: Diabetes mellitus is the most common metabolic complication in pregnancy and increasing worldwide. In Europe, it occurs in 3–5% of pregnant women. The rate of twin pregnancy has been increased similarly to gestational diabetes mellitus (GDM). Twin pregnancy is associated with a higher complication rate compared to singleton pregnancy. The growing prevalence of GDM and twin pregnancy has given rise to their increasing concurrent presentation.

Material and methods: The retrospective analysis included 212 twin-pregnant patients. The analysis excluded cases of miscarriage and early fetal death in the first trimester of pregnancy. The influence of GDM on the condition of newborns and mothers after delivery was analyzed. For statistical analysis R 3.6.2 software was used.

Results: No statistically significant relationship between GDM and Non-GDM group and periparturient complications was found. Birth weight was significantly higher in the GDM G2 group. Apgar Score was the lowest in the GDM G1 group. In the group of larger newborns of the GDMG1 group respiratory distress syndrome (RDS) , a higher incidence of second-degree intracranial bleeding and grade II of preterm retinopathy were observed. There was no statistically significant relationship between GDM G1, GDM G2 and other neonatal complications.

Conclusions: In summary, our results indicate that GDM in twin pregnancy does not increase the risk of cesarean section but increases some neonatal complications. In conclusion women with twin pregnancies complicated by GDM require specialist care during pregnancy and childbirth should take place in a third-level reference center.

Key words: twins; GDM; newborn; neonatal; complications

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INTRODUCTION

Diabetes mellitus is the most common metabolic complication in pregnancy and increasing worldwide. In Europe, it occurs in 3–5% of pregnant women. That increase is mainly due to older maternal age, rising rate of obesity and more stringent diagnostic criteria [1, 2]. There are two types of diabetes in pregnancy: gestational diabetes mellitus (GDM) when hyperglycemia is first diagnosed in pregnancy and pregestational diabetes mellitus (PGDM) when woman with any type of diabetes is pregnant. [3, 4] In Poland gestational diabetes mellitus is diagnosed according to recommendations of the Polish Diabetes Society of 2020. The gestational diabetes mellitus is divided into diabetes treated by lifestyle modification with diet therapy (GDM G1) and diabetes treated by insulin therapy (GDM G2).

Hyperglycemia has a great influence on the development of the fetus and the condition of the newborn. Adverse perinatal outcomes include macrosomia, birth

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injury, greater rate of surgical deliveries, risk of neonatal severe respiratory distress syndrome and neonatal metabolic disorders such as hypoglycemia, hyperbilirubinemia, hypocalcemia [3, 5, 6].

The rate of twin pregnancy has been increased similarly to GDM. It is mainly caused by greater use of assisted reproductive technology and shift toward an older maternal age [2].Unfortunately twin pregnancy is also associated with a higher complication rate compared to singleton pregnancy. Women with twin pregnancy are exposed to miscarriage, gestational diabetes mellitus (GDM), hypertension, anemia, placenta previa, placental abruption, preterm labour, premature rupture of membranes [2, 7, 8]. The growing prevalence of GDM and twin pregnancy has given rise to their increasing concurrent presentation [3].

Some studies have shown an increased risk for gestational hypertension, preeclampsia, cesarean section in women with twin pregnancy and GDM compared to women with twin pregnancy without GDM [8]. The aim of our study is to assess whether the increased risk associated with twin pregnancy is exacerbated in the presence of GDM. One of the most frequent complication of newborns is respiratory distress syndrome (RDS) which remains a significant health problem. Does gestational diabetes mellitus significantly increase the risk of its occurrence? In addition, we want to show whether the type of GDM (GDM G1 or GDM G2) has an influence on the type of pregnancy complications and condition of the newborns.

MATERIAL AND METHODS

A retrospective analysis of computer documentation was performed on patients with multiple twin pregnancies, who gave birth in the Department of Maternal and Fetal Medicine, Gynecology and Neonatology in Bydgoszcz over the period 2014–2018, as well as of computer neonatal documentation of newborns — a total of 212 patients.

The study was based on the diagnosis from the Hospital Treatment Information Card and diabetes consultations during hospitalization.

In order to identify fetuses based on medical records and to facilitate statistical calculations, a division into a larger and smaller newborn was introduced in the analyses of the condition of the newborn, neonatal complications and congenital abnormalities.

In the analysis cases of miscarriage, early fetal death in the first trimester of pregnancy and patients who were treated during pregnancy in the Department of Maternal and Fetal Medicine, Gynecology and Neonatology but delivered in other units were excluded.

The analysis of quantitative variables (*i.e.*, expressed in number) was performed by calculating the mean, standard deviation, median, quartiles, minimum and maximum.

The analysis of qualitative (*i.e.*, non-numeric) variables was performed by calculating the number and percentage of occurrences of each value.

The comparison of the values of qualitative variables in the groups was performed using the chi-square test (with Yates's correction for 2×2 tables) or the Fisher's exact test where low expected frequencies appeared in the tables.

The comparison of the values of quantitative variables in two groups was performed using the Mann-Whitney test.

The comparison of the values of quantitative variables in three or more groups was performed using the Kruskal-Wallis test. After detecting statistically significant differences, post-hoc analysis with Dunn's test was performed to identify the statistically significantly different groups.

The comparison of the values of quantitative variables in two repeated measurements was performed with the Wilcoxon test for bonded pairs.

A significance level of 0.05 was adopted in the analysis, so all p values below 0.05 were interpreted as showing significant relationships.

RESULTS

In twin pregnancies complicated by gestational diabetes, increased pregnancy supervision is obligatory, both on the part of obstetrics and diabetes. The distribution of twin pregnancies in terms of the time of labour is similar in the group with gestational diabetes and in the group without diabetes.

In the group with gestational diabetes there was no case of preterm labour before the 28th week of pregnancy. Four pregnancies were finished before 32 weeks of gestation, but no statistically significant correlation was found between GDM and delivery before 32 weeks of gestation.

Vast majority of patient, both with and without GDM, gave birth in the period 33–37 t.c. In both groups, more than one third of patients gave birth after 37 weeks of pregnancy. There was no statistically significant relationship between GDM and intrauterine death. There was no association between GDM in twin pregnancies and the type of delivery. In both cases, caesarean section was by far the most popular choice (Tab. 1).

There was no statistically significant relationship between GDM and complications of early puerperium such as: puerperal anemia, blood loss requiring blood transfusion, perinatal hysterectomy, pre-eclampsia, eclampsia, post-dural syndrome, endometritis, postpartum depression.

Birth weight was significantly higher in the group of patients treated with insulin than in the group without insulin in the case of the smaller children of the couple (Fig. 1). In larger children, the birth weight was significantly higher in the group with insulin than in the group treated with diet, where it was significantly higher than in the

Table 1. The gestational age at the end of pregnancy and the type of delivery depending on the occurrence of gestational diabetes mellitus (GDM)

Parameter		GDM		p
		No (n = 177)	Yes (n = 33)	
Gestational age at birth	Extremely premature delivery	6 (3.4%)	0 (0.0%)	p = 0.489
	Very premature delivery	11 (6.2%)	4 (12.1%)	
	Moderately premature delivery	96 (54.2%)	16 (48.5%)	
	Delivery at the right time	64 (36.2%)	13 (39.4%)	
Type of delivery	Natural delivery	22 (12.4%)	1 (3.0%)	p = 0.138
	Caesarean section	155 (87.6%)	32 (97.0%)	

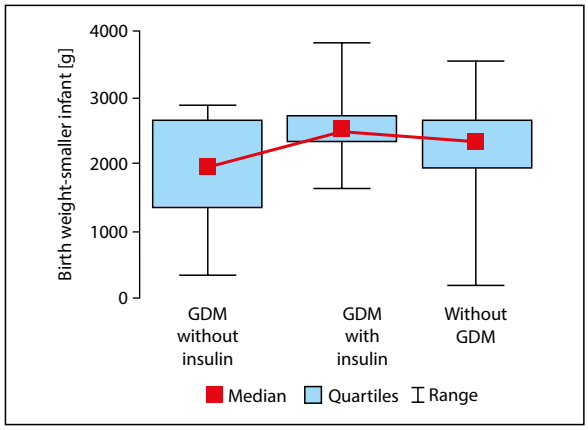

Figure 1. Weight of the smaller infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

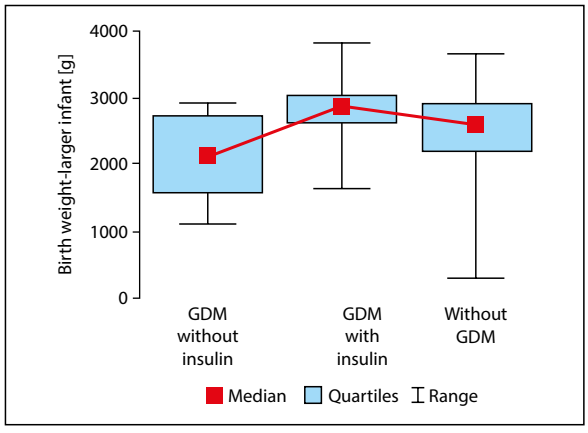

Figure 2. Weight of the larger infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

group without GDM (Fig. 2). The birth weight of smaller newborns was on average: 1,847.8 g (median 1930 g) in the GDM G1 group, 2513.3 g (median 2475 g) in the GDM

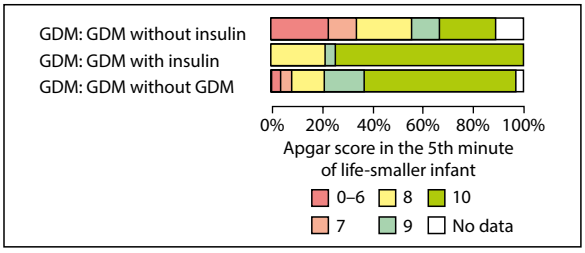

Figure 3. Apgar score in the 5th minute of life of the smaller infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

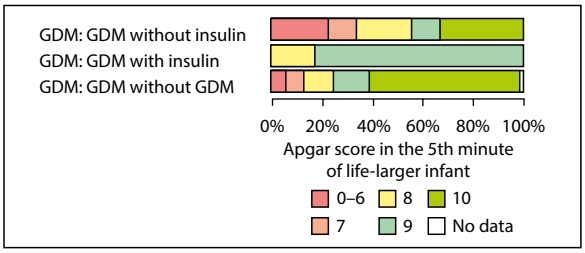

Figure 4. Apgar score in the 5th minute of life of the larger infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

G2 group and 2236.0 g (median 2320 g) in the group without GDM. The birth weight of larger newborns was on average: 2,085.6 g (median 2,130 g) in the GDM G1 group, 2,791.3 g (median 2,860 g) in the GDM G2 group and 2502.2 g (median 2,640 g) in the group without GDM.

The Apgar score in the 5th minute was the best in the group without GDM, slightly worse in the group with insulin, and the worst in the group without insulin in both smaller and larger children. In addition, larger children with GDM G1 pregnancies presented lower Apgar scores in the 1st minute (Fig. 3 and 4).

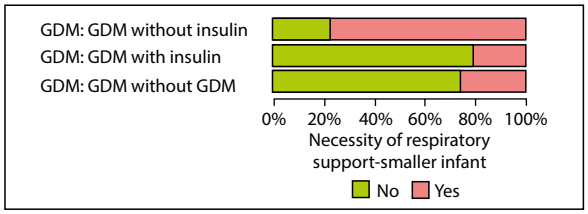

Figure 5. Necessity of respiratory support in the smaller infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

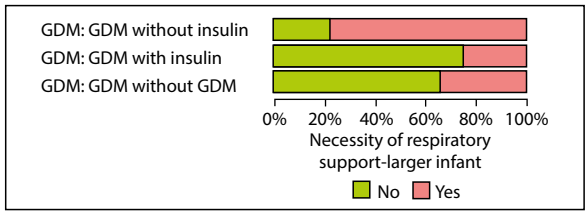

Figure 6. Necessity of respiratory support in the larger infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

The need for respiratory support was the rarest in the GDM G2 group: 20.8% in the smaller children and 25% in the larger children, slightly more frequent in the group without GDM: 26% in the smaller children and 33.9% in the larger children, and the most frequent in the GDM group G1: 77.8% in both smaller and larger children (Fig. 5 and 6).

In the group of larger newborns, the average duration of stay in the Neonatology Department turned out to be significantly longer in the case of GDM G1 compared to the GDM G2 group and the non-diabetic group and amounted to 26,1 days (median 20), 9 days (median 5) and 11,4 days (median 7) respectively. In smaller infants, a similar relationship was not confirmed ($p > 0.05$ in the Kruskal-Wallis test) (Fig. 7 and 8).

There was no statistically significant relationship between GDM G1, GDM G2, and birth body length, discharge weight, and NICU admission in the case of the smaller child of the twin pair.

In the group of smaller infants of twin pregnancies complicated by GDM G1, anemia was more frequent (Tab. 2). Statistical significance was not demonstrated in the group of larger infants.

In the group of larger newborns from twin pregnancies complicated by GDM G1, respiratory distress syndrome (RDS) was diagnosed more often. In the group of smaller children, there is no significant relationship between GDM G1 and RDS. However, it is necessary to consider the more frequent incidence of more serious degrees of RDS requiring mechanical support in both groups of newborns with GDM G1.

Grade II preterm retinopathy occurred more frequently in the group of larger infants with GDM G1, but with no significant association in the group of smaller infants.

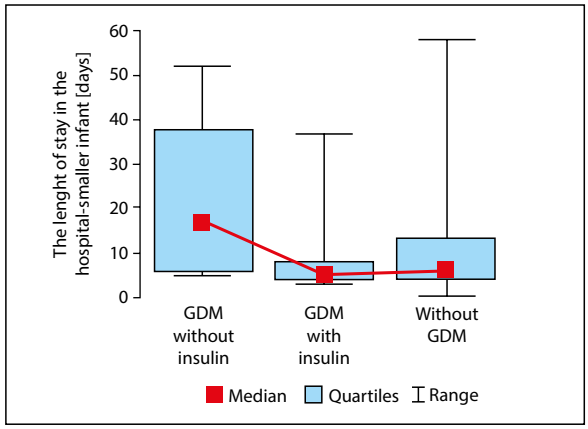

Figure 7. The length of stay in the hospital of the smaller infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

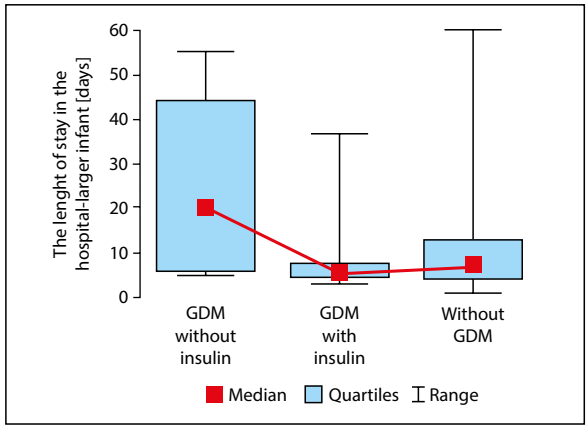

Figure 8. The length of stay in the hospital of the larger infant from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

Table 2. The incidence of anemia of the smaller newborn from a twin pregnancy depending on the onset and type of gestational diabetes mellitus (GDM)

Complications – smaller infant	GDM			p
	GDM G1 (n = 9)	GDM G2 (n = 24)	No GDM (n = 177)	
Anemia	3 (33.3%)	1 (4.2%)	14 (7.9%)	p = 0.044

Table 3. The incidence of complications in the larger infant: II-degree intracranial bleeding, respiratory distress syndrome, II-degree premature retinopathy depending on the onset and type of gestational diabetes mellitus (GDM)

Complications – larger infant	GDM			p
	GDM G1 (n = 9)	GDM G2 (n = 24)	No GDM (n = 177)	
II-degree intracranial bleeding	2 (22.2%)	0 (0.0%)	4 (2.3%)	p = 0.027
respiratory distress syndrome	6 (66.7%)	5 (20.8%)	57 (32.2%)	p = 0.041
II-degree premature retinopathy	2 (22.2%)	0 (0.0%)	2 (1.1%)	p = 0.02

Gestational diabetes G1 and G2 are not associated with grade I premature retinopathy.

In the group of larger children with GDM G1 pregnancies, a higher incidence of second-degree intracranial bleeding was observed, but with no apparent correlation in smaller infants. There was no relationship between more severe degrees of IVH and GDM G1, GDM G2, both in the group of smaller and larger newborns (Tab. 3).

There was no statistically significant relationship between GDM G1, GDM G2 and other neonatal complications, such as: polycythemia, neonatal haemorrhagic disease, neonatal hypotrophy, persistent fetal circulation, NEC, pneumonia, 1st degree preterm retinopathy, perinatal hypoxia, death of a live born newborn , jaundice.

There was no statistically significant relationship between GDM G1, GDM G2 and birth defects. However, it should be considered that patients with diagnosed hemodynamically significant fetal heart defects were transferred to highly specialized units with the option of cardiac surgery.

DISCUSSION

Gestational diabetes is a condition of impaired glucose tolerance that was first diagnosed during pregnancy. In Poland, all pregnant women are covered by diabetes prevention in line with the Recommendations of the Polish Society of Gynecologists and Obstetricians. The panel of tests in the first trimester of pregnancy includes fasting glycaemia, among others. In case of abnormalities, further diagnosis is implemented depending on the fasting glycaemia.

Additionally, an oral glucose loading test is performed at 24–28 weeks of gestation. If gestational diabetes is diagnosed, the patient is provided with diabetes care, and childbirth should take place in a third-level reference center [9].

Studies on the impact of diabetes in pregnancy on the fetus have shown that maternal diabetes is significantly related to neonatal RDS, even if the gestational age at delivery exceeded 34 + 0 [5, 6].

Perhaps the more frequent preterm infant retinopathy in newborns of mothers with GDM results from more frequent respiratory support as the studies of extreme premature infants show that significant risk factors for retinopathy are mechanical ventilation, low gestational age, low birth weight, and blood transfusion [10, 11].

Sheehan A. et al. [7] compared the course of single and twin pregnancies with and without GDM. It has been shown that twin pregnancy, compared to the effects of GDM, is the most important risk factor for an adverse perinatological outcome, including very premature delivery, cesarean section and neonatal complications. GDM in twin pregnancies did not increase the risk of neonatal complications, except for hypoglycemia. The study of Guillen-Sacoto et al. [12] has shown the higher risk for the newborns of severe SGA, hypoglycemia, and polycythemia in twin pregnancies.

The meta-analysis carried out by McGrath et al. [1] did not show a relationship between gestational diabetes in twin pregnancy and respiratory complications, hypotrophy, or disturbed carbohydrate metabolism in the newborn. Nevertheless, newborns from a twin pregnancy complicated with GDM showed a slightly lower birth weight and more frequent admission to the ICU.

Worse birth status in newborns with GDM G1 twin pregnancies compared to GDM G2 and in patients without glucose tolerance impairment may result from insufficient compliance with dietary recommendations and, consequently, lack of glycemic control. Insulin therapy in pregnancy is associated with greater discipline of pregnant patients in relation to a diet with limited easily digestible carbohydrates. There is a known relationship between mechanical ventilation of the newborn and preterm retinopathy requiring laser therapy [13]. Moderate and late prematurity and its complications may be related to inadequate glycemic control and dietary adherence in pregnant women. Observational studies by Antoniou et al. showed a relationship between the increased value of HBA1c at the end of pregnancy and prematurity [14].

CONCLUSIONS

In summary, our results indicate that GDM in twin pregnancy does not increase the risk of cesarean section. Caesarean section was the most popular choice in both groups. A higher percentage of newborns were born in a severe or moderate condition in the group of twin pregnancies complicated by GDM. Newborns from twin pregnancies complicated by GDM G1 presented respiratory distress syndrome (RDS) more often. In conclusion, women with twin pregnancies complicated by GDM require specialist care during pregnancy and childbirth should take place in a third-level reference center.

Conflict of interest

All authors declare no potential conflicts of interest.

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