What Is the Cost of Reducing Adverse Pregnancy Outcomes in Patients With GDM: A Retrospective Cohort Study

Luiza Oleszczuk-Modzelewska
2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, 2 Karowa St
Aneta Malinowska-Polubiec (anetapolubiec@interia.eu)
2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, 2 Karowa St
Ewa Romejko-Wolniewicz
2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, 2 Karowa St
Agnieszka Zawiejska
Department of Medical Simulation, Chair of Medical Education, Poznan University of Medical Sciences, 60-512 Poznan, 41 Jackowskiego St
Krzysztof Czajkowski
2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, 2 Karowa St

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Research Article

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Abstract

Background

Gestational diabetes mellitus is a frequent complication of pregnancy, affecting the health of mothers and their offspring. The new diagnostic strategy for GDM, proposed by IADPSG in 2010 and WHO in 2013, raised hope for a reduction in perinatal complications. The purpose of the study was to evaluate factors influencing obstetric results in a group of women diagnosed with diabetes, regardless of the adopted diagnostic criteria, compared to a group of pregnant women in whom GDM was excluded.

Methods

It was a retrospective study based on the analysis of births given after 37 weeks of pregnancy at the 2nd Department of Obstetrics and Gynaecology, Warsaw Medical University during the period from 2013 to 2015. All pregnant women had a 75g OGTT between the 24th and 28th weeks of pregnancy. The study compared risk factors for obstetric complications for patients with gestational diabetes to a group of women without GDM. The impact was analysed of the aforementioned factors on maternal and paediatric obstetric outcomes.

Results

The parameters significantly influencing the risk of composite adverse maternal outcomes were the circumference of the pregnant woman's abdomen [OR: 1.08 (1.04; 1.11)] and multiparity, which reduced the risk of this complication by almost half [OR: 0.47 (0.30; 0.75). The size of the maternal abdominal circumference before delivery was a strong factor correlating with the occurrence of perinatal complications in both the mother and the foetus in the entire examined cohort. A circumference over 100 cm increased the risk of at least one pregnancy complication (increased blood loss, soft tissue injuries, pre-eclampsia) by almost 40% (OR 1.38, $p < 0.001$).

Conclusions

Apart from normalization of glycaemia, stabilization of the percentage of adipose tissue and non-glycaemic obstetric risk factors may be necessary to obtain further improvement in obstetric outcomes in this pregnant population.

Background

Gestational diabetes mellitus (GDM) includes all types of impaired glucose tolerance that are first experienced or diagnosed during pregnancy. Maternal complications of GDM include pregnancy-induced hypertension, pre-eclampsia, the need to induce labour and the necessity to deliver the baby by caesarean section. It has been proven that in the future, these women are more likely to develop diabetes, cardiovascular diseases and metabolic syndrome [1, 2]. Foetuses of patients with gestational diabetes are more frequently diagnosed with large for gestational age (LGA), macrosomia and a higher percentage of perinatal injuries. New-borns of mothers with GDM are at risk of developing respiratory disorders, hypoglycaemia and hyperbilirubinaemia. It is believed that in the future, these children will more often suffer from diabetes, obesity, hypertension and metabolic syndrome [3, 4].

For several years, a progressive increase in the percentage of diabetes diagnoses in the world, including in pregnant women, has been observed. The International Diabetes Federation (IDF) reported that in 2015, diabetes was diagnosed in 16.2% (20.9 million) of all pregnant women. In this group, 85.1% (17.8 million) of diagnoses concerned gestational diabetes [5]. It is estimated that in Europe, the proportion of women with GDM ranges from 2 to 6% [5]. According to the database of the National Health Fund, in Poland, it amounted to 4.7% in 2010 and increased to 7.5% in 2012 [6]. Getahun et al. found that in a period of over 15 years (1989–2004), the number of patients with GDM in the American population increased by 122% [7]. Despite the growing trend of diabetes in pregnancy, there is still no consensus among leading diabetes societies regarding screening for GDM. In 2010, International Association of Diabetes and Pregnancy Study Groups (IADPSG), and in 2013 the World Health Organization (WHO) proposed changing the existing criteria for the diagnosis of GDM [8, 9]. In the new diagnostic strategy for gestational diabetes, based on results of the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study from 2008, the diagnostic criteria for this disease were associated with the risk of neonatal complications and not with the long-term risk of developing type 2 diabetes in the mother, as was the case so far [10]. In Poland, they came into force in 2014.

The new recommendations raised hope for a standardization of the system for diagnosing diabetes in pregnancy and thus a reduction in perinatal complications, the percentage of which is inconclusive [11–15].

The purpose of the study was to evaluate factors influencing obstetric results in a group of women diagnosed with diabetes, regardless of the adopted diagnostic criteria, compared to a group of pregnant women for whom diabetes was excluded, both according to the 2011 and 2014 criteria.

Methods

This study was retrospective and was based on the analysis of births that occurred at the 2nd Department of Obstetrics and Gynaecology, Warsaw Medical University during the period from 1 January 2013 to 31 December 2015. The analysis included patients who gave birth after 37 weeks of pregnancy. All pregnant women had an oral glucose tolerance test (OGTT) of 75 g between the 24th and 28th weeks of pregnancy. The following patients were excluded from the study: patients with multiple pregnancy, with pre-gestational diabetes and with gestational diabetes diagnosed based on the basis of abnormal fasting glucose results during early pregnancy, with random glycaemia, based on OGTT of 75 g performed before the 24th or after the 28th week of pregnancy, or with incomplete results of the three-point OGTT.

In Poland, the 2011 criteria for diagnosing diabetes considered an abnormal result to be at least one of the following glucose values in the 75-g OGTT: fasting ≥ 100 mg/dL, 1 hr ≥ 180 mg/dL, or 2 hr ≥ 140 mg/dL. Meanwhile, the criteria adopted in 2014, according to IADPSG and WHO, considered at least one of the following results of the 75-g OGTT to be abnormal: fasting ≥ 92 mg/dL, 1 hr ≥ 180 mg/dL, or 2 hr ≥ 153 mg/dL.

This study compared patients with gestational diabetes to a group of women in whom GDM was excluded. The risk factors for obstetric complications were the age of the pregnant woman, the value of the maternal body mass index (BMI) before pregnancy, gestational weight gain (GWG), the circumference of the mother's abdomen measured at the level of the navel before delivery, women who had had at least one child in the past (multiparity), birth body weights of older children over 4000 g, fasting blood glucose, blood glucose in the second hour of the 75-g OGTT, diagnosis of diabetes in the current pregnancy, the need to implement insulin therapy to maintain normoglycaemia and female sex of the foetus.

The impact was analysed of the aforementioned factors on the following maternal and paediatric obstetric outcomes: weight gain of pregnant women with respect to Institute of Medicine (IOM) recommendations, incidence of pregnancy-induced hypertension or pre-eclampsia, incidence of composite adverse perinatal outcomes, including haemorrhage or perinatal trauma, the necessity to terminate pregnancy by caesarean section due to foetal indications, the birth weight of new-borns, including the percentage of children with macrosomia, the incidence of hypoglycaemia or hyperbilirubinemia (treated with phototherapy) in the first three days of the new-borns' life, and the percentage of children with congenital anomalies or rare neonatal complications.

We used SPSS 14.0 for Windows (SPSS Inc. Chicago, USA) and MedCalc 19.0 (MedCalc Software, Mariakerke, Belgium) to perform statistical analysis.

Descriptive results are expressed as the mean ± standard deviation or median (interquartile range). Categorical variables are expressed as percentages.

Multivariate logistic regression (forward method) was used to identify predictors for dichotomous adverse maternal and foetal outcomes in the pooled analysis of the entire group (patients with GDM and normoglycaemic controls). Variables that correlated with the outcomes with a $p < 0.1$ in the bivariate analysis were included in the models. The results are presented as adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs). Predictors for continuous variables were identified using multiple linear regression models (forward method), with gestational weight gain or birth weight as dependent variables. All variables that showed a bivariate correlation with a $p < 0.1$ with these outcomes were entered in the models as independent variables. A $p < 0.05$ was considered statistically significant in the multivariate analysis.

A ROC analysis was used to calculate the diagnostic power of maternal abdominal circumference measured before delivery as a predictor of adverse neonatal outcomes. Two-sided $p < 0.05$ was considered statistically significant.

Ethics approval for this study was obtained from the Warsaw Medical University institutional review board (AKBE13/15).

Results

In the analysed material, based on the OGTT, in the group of 285 (58.5%) pregnant women, at least one of the glycaemic values met the criteria for a diagnosis of diabetes, either according to the 2011 or 2014 criteria, while the other group of 202 (41.5%) women did not meet any of the criteria for diagnosing diabetes.

Women with at least one abnormal glycaemic result, regardless of the adopted criteria for the diagnosis of diabetes, were compared to the group in which the OGTT result was normal, regardless of the criteria and had the following characteristics: significantly older mean age (32.4 ± 4.7 vs 31.1 ± 4.1, $p < 0.001$) with significantly higher BMI before pregnancy (24.6 ± 4.6 vs 22.7 ± 3.6, $p < 0.01$), the vast majority of patients were obese (13.5% vs 3%, $p < 0.001$), less likely to give birth for the first time (38.2 vs 50.2%, $p < 0.03$), more often had relatives with diabetes (48.1% vs 23.8%, $p < 0.01$) and had a history of GDM-complicated pregnancy (18.8% vs 0%, $p < 0.001$). These results are shown in Table 1.

Table 1
Potential risk factors for obstetric complications

	Pregnant women with GDM *N = 285 (58.5%)*	**Control group pregnant women *N = 202 (41.5%)***	***P***
Age	32.4 ± 4.7	31.1 ± 4.1	< 0.001
Prepregnancy BMI [kg/m2]	24.6 ± 4.6	22.7 ± 3.6	< 0.001
Prepregnancy BMI ≥ 25.0 kg/m2 [%]	37.7%	25.7%	0.006
Prepregnancy BMI ≥ 30.0 kg/m2 [%]	13.5%	3.0%	< 0.001
Nulliparity [%]	38.2%	50.5%	0.024
History of GDM [% of these with the history of at least one delivery]	18.8%	0.0%	< 0.001
History of BW > 4000g [% of these with the history of at least one delivery]	16.3%	10.6%	0.249
Gestational age at diagnosis/ at testing [weeks]	25.4 ± 1.5	25.2 ± 1.5	0.055
75gOGTT fasting [mg/dl]	87.1 ± 11.7	77.5 ± 6.5	< 0.001
75gOGTT 1 hr [mg/dl]	166.5 ± 28.2	117.3 ± 25.5	< 0.001
75gOGTT 2 hrs [mg/dl]	144.2 ± 23.3	100.0 ± 19.1	< 0.001
GDM according to both 2011 and 2014 criteria [%]	61.6%	–	
Gestational weight gain [kg]	10.7 ± 5.8	14.5 ± 5.1	< 0.001
Maternal abdominal circumference measured prior the delivery	103.3 ± 8.7	103.0 ± 6.9	0.969
Insulin therapy necessity [%]	15.4%	–	
Female foetus [%]	48.4%	54.0%	0.223

BMI: Body Mass index; GDM: Gestational Diabetes Mellitus; BW: Birth Weight; OGTT: Oral Glucose Tolerance Test

Pregnant women diagnosed with diabetes, irrespective of the criteria, gained significantly less weight during pregnancy (10.7 kg ± 5.8 vs 14.5 kg ± 5.1, $p < 0.001$) [Table 1], and they had less frequent excess weight gain according to IOM criteria (24.2% vs 47.5%); instead, weight gain below the recommended IOM guidelines was more frequently observed in this subgroup [Table 2].

If we compared patients with GDM to the normoglycaemic control group, no statistically significant differences were observed with respect to the incidence of maternal complications, the condition of new-borns or in the incidence of neonatal complications between the groups. There was only a trend for borderline statistical significance of more frequent urgent caesarean section due to foetal indications in the group with gestational diabetes (26.4% vs 16.2%, $p = 0.06$). These results are shown in Table 2.

Table 2
Obstetric results

	Pregnant women with GDM *N = 285 (58.5%)*	**Control group pregnant women *N = 202 (41.5%)***	***P***
GWG above IOM recommendations [%]	24.2%	47.5%	< 0.001
GWG below IOM recommendations [%]	45.6%	20.3%	
Pregnancy induced hypertension/ preeclampsia [%]	6.0%	4.5%	0.543
Composite adverse maternal outcome – at least one of the following: intrapartum injury/ intrapartum haemorrhage	37.9%	35.1%	0.568
Intrapartum maternal injury	6.1%	8.0%	0.468
Intrapartum haemorrhage – blood loss more than 500 mL	32.0%	27.2%	0.271
Emergency CS due to foetal conditions *	26.4%	16.2%	0.06
Mode of delivery cc/forceps/VE/ spontaneous	31.9%/3.5%/64.6%	33.7%/5.0%/60.4%	0.599
BW [grams]	3412 ± 438	3420 ± 428	0.677
BW > 4000g	9.1	8.9	1.00
Neonatal hypoglycaemia	4.9%	–	–
Neonatal hyperbilirubienia/fototherapy	21.1%	17.3%	0.413
Foetal congenital malformation	7.7%	5.9%	0.477
Rare adverse neonatal outcome (occurrence below 5%) – at least one of the following: prematurity/ intrapartum injury/ hypoglycaemia	8.1%	5.4%	0.285
Intrapartum neonatal injury	3.2%	5.4%	0.250

GWG:Gestational Weight Gain; IOM: The Institute of Medicine; emergency CS due to foetal conditions*: percentage of cases out of all caesarean sections; BW: Birth Weight; VE: Vacuum Extraction

Table 3 shows the predictive factors for individual obstetric complications in the study group. The results of the multivariate analysis indicate that both the result of the 75-g glucose load curve and the diagnosis of GDM, as well as maternal BMI, significantly modified the risk of excessive and insufficient weight gain in pregnancy. Of note, the importance of the female sex of the foetus as a factor significantly increased the probability of insufficient weight gain during pregnancy [OR: 1.65 (1.10; 2.47)]. On the other hand, the only parameters significantly influencing the risk of composite adverse maternal outcome were the circumference of the pregnant woman's abdomen [OR: 1.08 (1.04; 1.11)] and multiparity, which reduced the risk of this complication by almost half [OR: 0.47 (0.30; 0.75). Multivariate analysis of predictors of neonatal complications indicated that the abdominal circumference of the pregnant woman significantly increased the risk of all examined endpoints.

Table 3
Predictors of maternal and foetal outcomes in the study group – analysis of multivariate regression models

The outcome	Variables in the model (multiple linear for continuous variables, or logistic regression for dichotomous variables)	Unstandardized B/ exp(B) (95%CI)	*P*	R^2 for the model
Gestational weight gain	2-hours glycaemia in 75g OGTT	-0.04 (-0.060; 0.016)	0.001	0.183
	Prepregnancy BMI	-0.23 (-0.35; -0.12)	< 0.001	
	GDM yes/no	-2.43 (-3.88; -0.98)	0.001	
	Female neonate yes/no	-1.23 (-2.18; -0.28)	0.011	
	Fasting glycemia in 75g OGTT	0.07 (0.02; 0.12)	0.005	
	Multiparity yes/no	-1.15 (-2.11; -0.19)	0.015	
GWG above recommendations (logistic)	Fasting glycaemia in 75g OGTT	1.03 (1.00; 1.05)	0.023	0.190
	2-hours glycaemia in 75g OGTT	0.99 (0.98; 0.99)	0.022	
	Prepregnancy BMI	1.12 (1.06; 1.18)	< 0.001	
	GDM yes/no	0.31 (0.16; 0.57)	< 0.001	
	Female neonate yes/ no	0.56 (0.37; 0.85)	0.006	
GWG below recommendations (logistic)	Prepregnancy BMI	0.90 (0.85; 0.95)	< 0.001	0.162
	GDM yes/no	4.44 (2.85; 6.92)	< 0.001	
	Female neonate yes/no	1.65 (1.10; 2.47)	0.015	
Birth weight – *for the whole cohort*	Maternal abdominal circumference measured prior the delivery	12.1 (6.9; 17.3)	< 0.001	0.217

CI: confidence interval; OGTT: Oral Glucose Tolerance Test; BMI: Body Mass Index; GWG: Gestational Weight Gain; GDM: Gestational Diabetes Mellitus; eCS: elective Caesarean Section

The outcome	Variables in the model (multiple linear for continuous variables, or logistic regression for dichotomous variables)	Unstandardized B/ exp(B) (95%CI)	*P*	R^2 for the model
	Maternal height	17.4 (10.6; 24.1)	< 0.001	
	Female neonate yes/no	-137.8 (-215.1; -60.5)	0.001	
	Gestational weight gain	10.4 (3.4; 17.4)	0.004	
	Fasting glycaemia in 75g OGTT	4.8 (1.1; 8.6)	0.011	
Birth weight – *for a subgroup with a history of at least one delivery*	Birth weight of the largest child from previous pregnancy/ pregnancies	0.26 (0.17; 0.35)	< 0.001	0.358
	Gestational weight gain	13.9 (3.9; 24.0)	0.007	
	Female neonate yes/no	-202.9 (-318.0; -87.8)	0.001	
	Maternal abdominal circumference measured prior the delivery	11.6 (4.0; 19.2)	0.003	
	Maternal height	10.4 (0.4; 20.4)	0.041	
Ponderal Index	Birth weight	0.001 (0.001; 0.002)	< 0.001	0.039
Macrosomia (logistic)	Maternal abdominal circumference measured prior the delivery	1.07 (1.03; 1.11)	0.001	0.183
	Maternal height	1.07 (1.00; 1.14)	0.036	
	Multiparity yes/no	2.20 (1.03; 4.70)	0.042	
	Female neonate yes/no	0.21 (0.09; 0.53)	0.001	
eCS for fetal condition (logistic)	Multiparity yes/no	0.30 (0.13; 0.70)	0.005	0.133
	Maternal height	0.91 (0.85; 0.98)	0.007	

CI: confidence interval; OGTT: Oral Glucose Tolerance Test; BMI: Body Mass Index; GWG: Gestational Weight Gain; GDM: Gestational Diabetes Mellitus; eCS: elective Caesarean Section

The outcome	Variables in the model (multiple linear for continuous variables, or logistic regression for dichotomous variables)	Unstandardized B/ exp(B) (95%CI)	P	R^2 for the model
	Maternal abdominal circumference measured prior the delivery	1.08 (1.03; 1.12)	< 0.001	
Rare adverse neonatal outcome (logistic)	Maternal age	0.89 (0.82; 0.98)	0.013	0.124
	Maternal abdominal circumference measured prior the delivery	1.08 (1.03; 1.13)	< 0.001	
	Maternal height	0.90 (0.84; 0.97)	0.004	
Phototherapy (logistic)	Insulin therapy yes/no	2.84 (1.27; 6.35)	0.011	0.128
	Maternal abdominal circumference measured prior the delivery	1.07 (1.02; 1.1)	0.002	
Neonatal hypoglycaemia (logistic) – *data available only for women with GDM*	Maternal abdominal circumference measured prior the delivery	1.12 (1.06; 1.19)	< 0.001	0.193
Composite adverse maternal outcome – postpartum haemorrhage and/or intrapartum injury (logistic)	Maternal abdominal circumference measured prior the delivery	1.08 (1.04; 1.11)	< 0.001	0.123
	Multiparity yes/no	0.47 (0.30; 0.75)	0.001	
Preeclampsia and/or gestational hypertension (logistic)	Prepregnancy BMI	1.15 (1.06; 1.3)	0.001	0.123
	Multiparity yes/no	0.24 (0.08; 0.73)	0.012	

CI: confidence interval; OGTT: Oral Glucose Tolerance Test; BMI: Body Mass Index; GWG: Gestational Weight Gain; GDM: Gestational Diabetes Mellitus; eCS: elective Caesarean Section

Table 4 shows data on maternal abdominal circumference measured before delivery as a predictor of obstetric complications in the entire cohort (GDM patients and the control group). The size of the maternal abdominal circumference before delivery was a strong factor correlating with the occurrence of perinatal complications in both the mother and the foetus in the entire examined cohort. A circumference over 100 cm increased the risk of at least one pregnancy complication (increased blood loss, soft tissue injuries, pre-eclampsia) by almost 40% (OR 1.38, $p < 0.001$). A circumference over 98 cm increased the risk of foetal macrosomia by 20% (OR 1.24, $p < 0.005$), and a circumference over 104 cm increased the risk of one of the complications during the neonatal period by 50% (OR 1.54, $p < 0.005$). Furthermore, in the group with gestational diabetes, a circumference over 103 cm doubled the risk of neonatal hypoglycaemia during the first days after delivery (OR 2.01, p < 0.0001).

Table 4
ROC curve analysis for maternal abdominal circumference measured prior the delivery as a predictor of selected fetomaternal outcomes in the study group

The outcome	AUC (95% CI)	*P*	Cut-off value	Sensitivity	Specificity	OR (95% CI) for the outcome at the cut-off
Macrosomia	0.63 (0.58; 0.68)	0.0041	98 cm	91.4%	32.4%	1.24 (1.12; 1.37)
Composite adverse maternal outcome	0.65 (0.61; 0.70)	< 0.001	100 cm	74.4%	49.6%	1.38 (1.22; 1.57)
Neonatal hyperbilirubinemia	0.58 (0.53; 0.63)	0.033	108 cm	35.5%	79.0%	1.46 (1.02; 2.09)
Neonatal hypoglycaemia in the subgroup with GDM	0.80 (0.74; 0.85)	< 0.0001	103 cm	88.9%	60.3%	2.01 (1.52; 2.64)
Rare adverse neonatal outcomes	0.64	0.004	104 cm	60.0%	63.5%	1.53 (1.14; 2.06)

ROC: Receiver Operating Characteristic; AUC: Area Under the Curve; CI: Confidence Interval; OR: Odds Risk

Discussion

The number of patients with gestational diabetes in the world is continuously increasing. According to various estimates, over the last twenty years, the percentage of women with GDM has increased by 10–100%, especially in highly developed countries, and in 2019, hyperglycaemia was diagnosed in approximately 16% of pregnancies worldwide, of which GDM accounted for 84% of all cases [16–21]. This fact allows us to predict a significant increase in the number of obstetric complications and forces researchers to identify factors that may affect their development.

In our study, we demonstrated that the diagnosis of diabetes in pregnancy increases the risk of having a child with macrosomia by 10-fold (OR 10.4, p < 0.005) and 13-fold in multiparous women (OR 13.9, p < 0.005). These results are identical to other available publications [22–25]. To date, the individual influence of blood glucose values at individual measurement points in the 75-g OGTT on obstetric complications is not fully understood. The HAPO study, which was the basis for changing the existing criteria for the diagnosis of GDM, demonstrated a linear relationship between maternal glucose levels and the child’s birth weight [10]. Zhu et al. and Zawiejska et al. found that macrosomia was diagnosed significantly more often in children of patients with fasting hyperglycaemia [19, 26]. On the other hand, Kerenyi et al. [25] found that the curve illustrating the relationship between fasting glucose measured during the 75-g OGTT and the birth weight of the foetus and the risk of LGA was U-shaped ($p = 0.004$), indicating that both in patients with low and high fasting blood glucose levels, the risk of foetal hypertrophy was increased. In a publication by Black et al. [27], attention was also drawn to the significant influence of hyperglycaemia in the 2nd hour of the 75-g OGTT on the increased risk of pregnancy induced hypertension (PIH), preterm labour and hyperbilirubinaemia in new-borns.

In our study, we did not identify any correlation between the glycaemic status of patients from particular groups and the percentage of maternal (here: pre-eclampsia) or foetal complications (Table 2). On the other hand, significant predictors of obstetric complications, independent of the severity of hyperglycaemia at the time of diagnosis of GDM, included patients’ anthropometric markers indirectly related to the amount of adipose tissue, i.e., BMI before pregnancy and abdominal circumference measured before delivery. Many studies have confirmed that overweight and obesity before pregnancy are independent risk factors for the development of perinatal complications [28–34]. In the multicentre LifeCycle Project-Maternal Obesity and Childhood Outcomes Study group, maternal and foetal complications were observed in as many as 61% of pregnancies in women with a BMI ≥ 40 kg/m² [34]. Ouzounian et al. determined that the risk of macrosomia was doubled in patients with BMI ≥ 30 kg/m² compared to pregnant women with normal BMI before pregnancy and was threefold higher in patients with excessive vs normal weight gain in pregnancy according to the IOM recommendation of 2009 [28]. Similar relationships were demonstrated in the work of Bodnar et al. [35].

In our study, we found that higher pre-pregnancy BMI values correlated with a higher risk of pre-eclampsia during pregnancy (OR 1.15, $p < 0.001$). On the other hand, the increased abdominal circumference measured in patients before delivery had a significant impact on increasing risk of perinatal complications in women (increased blood loss, injury of soft tissues of the birth canal) [OR 1.08, $p < 001$], caesarean section due to urgent indications connected to the risk to the foetus (8% increase) and high birth weight of new-borns (12-fold increase in the risk; OR 12.1, $p < 0.001$). Moreover, among other complications during the early neonatal period, we observed influence of high maternal abdominal circumference on increasing risk of hypoglycaemia in the first days of life (by 12%; OR 1.12, $p < 0.001$), the need for phototherapy due to hyperbilirubinaemia (increase by 7%) and the risk of at least one complication during the neonatal period, i.e., hyperbilirubinaemia, hypoglycaemia or respiratory disorders (by 8%; OR 1.08, $p < 0.001$). Additionally, Gao et al. showed that both overweight or obesity before pregnancy and increased abdominal circumference in a patient significantly increased the risk of developing GDM, caesarean section delivery and macrosomia [36]. It is worth emphasizing that in the population of non-pregnant women, waist circumference is considered an indicator of insulin resistance, and its increased value has been included in the criteria for diagnosing metabolic syndrome [37–41]. Some sources report waist-to-hip ratio (WHR) to be superior to BMI for predicting the risk of developing type 2 diabetes, hypertension and cardiovascular disease in adults [42–46]. Obviously, the measurement of abdominal circumference in pregnancy is a specific measurement that is technically difficult and related to a non-standard population, but the relationships observed in our study between neonatal complications and increased abdominal circumference in term pregnancy confirm that this parameter also informs the “metabolic condition” of the mother and should be taken into account in the context of expected perinatal complications. Our observation of the influence of maternal parameters related to insulin resistance and an excessive percentage of adipose tissue on the risk of obstetric complications may also explain the persistence of a high percentage of obstetric complications in the population of pregnant women with hyperglycaemia in pregnancy, despite optimization of metabolic control. This was also confirmed by data from our multivariate regression models, which indicate that weight gain in pregnancy or the circumference of the pregnant woman’s abdomen measured before delivery, and not the severity of carbohydrate tolerance disorders, remain risk factors for significant obstetric complications. This means that the parameters describing the “maternal metabolic status” remain a significant risk factor for adverse maternal-foetal outcomes when effective treatment eliminates the risk associated with hyperglycaemia in pregnancy.

Another risk factor for obstetric complications includes excessive weight gain during pregnancy [28–30, 47]. Kominiarek et al. found that GWG above that recommended by the IOM in 2009 was associated with an increased risk of shoulder dystocia (OR 1.74, 95% CI 1.41–2.14), macrosomia (OR 2.66, 95% CI 2.03–3.48) and neonatal hypoglycaemia (OR 1.60, 95% CI 1.16–2.22) [48]. In a systematic review and meta-analysis by Goldstein et al., excessive weight gain during pregnancy correlated with a significantly higher rate of caesarean sections (OR 1.30, 95% CI 1.25–1.35), macrosomia (OR 1.95, 95% CI 1.79–2.11) and LGA (OR 1.85, 95% CI 1.76–1.95). In the same study, it was noted that if the weight gain in pregnancy was too low, it significantly increased the risk of small for gestational age (SGA) baby (OR 1.53, 95% CI 1.44–1.64) and preterm labour (OR 1.70, 95% CI 1.32–2.20) and decreased the risk of LGA and macrosomia [49]. Similar results were found in the work of Papazian et al. [50]. In our study, we did not identify any significant relationships between weight gain in pregnant women and the risk of obstetric complications. We did notice, however, that patients with GDM, compared to healthy pregnant women, had a significantly higher pre-pregnancy BMI (24.6 ± 4.6 vs 22.7 ± 3.6, $p < 0.01$) and were mostly obese (13.5% vs 3%, $p < 0.001$). It is also worth emphasizing that the diagnosis of diabetes in pregnancy was associated with a twice lower risk of excessive weight gain in pregnancy (OR 2.43, $p = 0.001$), although the increased risk of excessive weight gain in pregnancy was significantly associated with a higher BMI before pregnancy (OR 1.12, $p < 0.001$), higher fasting glucose in the OGTT (1.03, $p < 0.05$) and lower blood glucose in the 2nd hour of OGTT (OR 0.99, $p < 0.05$). Fasting hyperglycaemia is a marker of hepatic insulin resistance and one of the components of metabolic syndrome [51]. Therefore, in the context of our research, the positive relationship between excessive weight gain in pregnancy and fasting hyperglycaemia should be interpreted as a clinical manifestation of the relationship between pregnancy weight gain and insulin resistance.

As we calculated, the diagnosis of diabetes during pregnancy reduced the risk of excessive weight gain in pregnancy by 30% (OR 0.31, $p < 0.001$) and increased the risk of weight gain under 12 kg (OR 4.44, $p < 0.01$) by four-fold. These results also suggest that treatment of hyperglycaemia with well-controlled diabetes in pregnancies that still experience complications result from non-glycaemic risk factors, including components of metabolic syndrome. One of the effects of multidisciplinary care for pregnant women with GDM may be low weight gain in pregnancy, which is difficult to interpret unequivocally due to the lack of guidelines for the group of patients with gestational diabetes. For others, it is possible to slow down intrauterine growth, which protects against macrosomia and intrauterine death of the foetus. In light of the data available to us, it seems that the price of these benefits may be an increased risk of accelerated weight gain in infants and obesity in early school age children [52, 53]. However, one should also take into account the latest data presented by the LifeCycle Project consortium, which showed, in a population of approximately 200,000 pregnant women, that in women with a BMI > 30, the optimal weight gain for reducing obstetric complications is lower (0–6 kg) than that recommended by the IOM for pregnant women with a similar BMI (5–9 kg) [34]. Additionally, authors of a retrospective observational study of 2,842 women with GDM published in 2020 confirmed the dominant pattern of weight gain in pregnancy below the level recommended by IOM in this population (50.3% of the examined patients) [54].

The results of our study indicate that the glycaemic status of patients may be a predictor of certain maternal complications, including abnormal weight gain in pregnancy, but neither gestational diabetes nor blood glucose levels at individual 75-g OGTT measurement points were predictors of neonatal complications in the study cohort. On the other hand, it is noteworthy that the anthropometric conditions of pregnant women and gestational weight gain, which are indicators of the "metabolic status" of women, may significantly correlate with the occurrence of obstetric complications, although their long-term effects on the mother and child require further study.

Conclusions

The results of our research indicate another area of medical intervention in pregnancy complicated by high metabolic risk. Apart from normalization of glycaemia, stabilization of the percentage of adipose tissue and non-glycaemic obstetric risk factors may also be necessary to obtain further improvement in obstetric outcomes in this pregnant population.

List Of Abbreviations

GDM: Gestational diabetes mellitus; IADPSG: The International Association of Diabetes and Pregnancy Study Groups; WHO: World Health Organization; OGTT: Oral glucose tolerance test; LGA: Large for gestational age; OR: Odds risk; IDF: International Diabetes Federation; HAPO: Hyperglycemia and Adverse Pregnancy Outcome; BMI: Body mass index; GWG: Gestational weight gain; aORs: adjusted odds risk, CIs: Confidence intervals; ROC: Receiver operating characteristic; IOM: The Institute of Medicine; PIH: Pregnancy induced hypertension; WHR: waist-to-hip ratio; SGA: small for gestational age.

Declarations

Ethics approval and consent to participate

Ethics approval for this study was obtained from the Warsaw Medical University institutional review board (AKBE13/15).

We confirm that all the experiment protocol for involving human data was in accordance with the Declaration of Helsinki in the manuscript.

We confirm that informed consent was obtained from all subjects or, if subjects are under 18, from a parent and/or legal guardian.

Consent for publication

No applicable.

Availability of data and materials

The datasets used or analysed during the current study are available from the corresponding author on reasonable request. Contact: anetapolubiec@interia.eu

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KC and AZ designed the study. LOM collected the data, searched the published works and extracted articles. LOM, AMP, AZ, ERW analysed and interpreted the data, drafted and edited the manuscript. All authors read and approved the final manuscript.

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Authors' information's

[1]2nd Department of Obstetrics and Gynecology, Medical University of Warsaw, 00-315 Warsaw, 2 Karowa St, Poland. [2]Department of Medical Simulation, Chair of Medical Education, Poznan University of Medical Sciences, 60-512 Poznan, 41 Jackowskiego St, Poland.

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