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ORIGINAL PAPER

Pregnancy outcomes in women with diabetes mellitus – the impact of diabetes type and treatment

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Abstract

Introduction: It has been estimated that approximately 16% of pregnancies worldwide are affected by pre-existing or gestational insulin-dependent (type 1) or independent (type 2) diabetes mellitus (DM). Diabetes mellitus in pregnancy remains a high-risk condition for both mother and child. This study aimed to investigate pregnancy outcomes regarding DM types.

Material and methods: The study included 323 DM patients delivered for 6 years (2012–2017). General and obstetric history data and all complications throughout the pregnancy and the early neonatal period were noted. Based on DM type, women were divided into 4 groups: pre-pregnancy/pre-existing DM, insulin-dependent or independent, and gestational diabetes mellitus with or without insulin therapy.

Results: The majority of women had pre-existing insulin-independent DM (type II 62%). Some types of pregnancy/maternal complications were registered in almost 85% of examined pregnancies. However, all babies were live born and mostly with good outcome (36.85% with early neonatal complications). Diabetes mellitus type could not predict the occurrence of neonatal complications (p = 0.342). Pre-existing insulin-dependent DM increased the risk for pregnancy complications (p = 0.031; OR = 1.656).

Conclusions: Diabetes mellitus type has a limited impact on pregnancy outcomes and the occurrence of maternal and neonatal complications. With adequate therapy the pregnancy outcome can be good regardless of DM type.

Key words: diabetes mellitus type, pregnancy outcome, maternal complications.

Introduction

The prevalence of obesity and metabolic diseases (such as type 2 diabetes mellitus [DM], dyslipidaemia, and cardiovascular diseases) has increased in recent years in both industrialized and developing countries [1, 2].

In particular, a rise in the number of reproductive-aged women diagnosed with DM (mostly insulin-independent type II) has been reported, especially among women with polycystic ovary syndrome [3–5]. Consequently, approximately 16% of pregnancies worldwide are thought to be affected by pre-existing or gestational insulin-dependent (type 1) or independent (type 2) DM [6–8].

Regardless of all the current diagnostic and therapeutic options for hyperglycaemia management as well as improved obstetric surveillance, DM in pregnancy remains a high-risk condition for both mother and child [9]. The most significant pregnancy complications associated with DM are congenital malformations, foetal macrosomia, shoulder dystocia/birth injury, preterm delivery with all its consequences, admission to newborn intensive care unit, and even higher perinatal mortality [7, 10–13].

The outcomes of women with type 1 and type 2 DM, according to literature data, seem to be equally poor, although results from different investigations are conflicting. Some authors have found that type 2 DM in pregnancy can lead to even worse outcomes than type 1 DM. Perinatal mortality rates are significantly higher in the case of type 2 DM, while the type of DM was

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not confirmed to influence the incidence of foetal malformations. Consequently, more studies on this matter are needed [14, 15]. Therefore, our study's aim was to investigate pregnancy outcomes regarding 4 DM types.

Material and methods

The study included all pregnant women with DM who were followed-up and delivered in our clinic throughout a period of 6 years (from 1 January 2012 to 31 December 2017). We excluded all first-trimester miscarriages from the study. The main inclusion criterion for our study was having a diagnosis of DM. The diagnosis of DM was based on World Health Organization diabetes diagnostic criteria (fasting plasma glucose level ≥ 7.0 mmol/l and/or plasma glucose ≥ 10 mmol/l 1 hour after a 75 g oral glucose load and/or glycated haemoglobin HbA_{1c} ≥ 48 mmol/mol) [16, 17].

According to protocols of obstetric surveillance in our institution, all pregnant women are screened for gestational diabetes mellitus (GDM) at 24–28 weeks of pregnancy. Moreover, in the case of patients with high risk for developing GDM, even more close monitoring is performed with laboratory testing. In the case of significant disturbance of serum glycaemic levels, DM is diagnosed as early as before the 24th gestational week (GW). Oral glucose tolerance test performed with 75 g anhydrous glucose dissolved in 200 ml of water was administered over 5 minutes after a minimum of 8 hours fasting. The glucose serum concentration was estimated immediately after testing as well as 60 and 120 minutes after glucose administration. Those diagnosed with GDM were first treated with life-style modifications (diabetic diet with reduced carbohydrates and calories and physical activity). They were followed up with monitoring of blood glucose in 2 weeks. If no corrections in glucose concentrations were noticed or if during the further pregnancy course glucose levels increased again, insulin therapy was administered.

Based on DM type, all women were divided into 4 groups: pre-pregnancy/pre-existing DM, insulin-dependent or independent (types I and II; classes B, C, and D), and GDM with or without the need for insulin therapy (DM classes A1 and A2). In the case of GDM, the GW at the time of diagnosis was registered. We also noted if investigated women had an endocrinological or specialized gynaecological consultation before or during pregnancy regarding their DM and potential risks for pregnancy.

During the first pregnancy examination, general and obstetric medical history data such as maternal age, nationality, family history of DM, gravidity (number of previous term vaginal deliveries, Caesarean section – C/S, spontaneous miscarriages, intentional pregnancy abortions, and previous neonatal death), and the presence of comorbidities (chronic hypertension – HTA, i.e. blood pressure ≥ 140/90 mm Hg, other illnesses such as endocrinological, pulmonary, neurological, etc.) as well as all DM complications (retinopathy – DM class R, neuropathy, nephropathy – DM class F, etc.) were determined for all patients. Based on the patient's height and weight, the body mass index (BMI) was calculated according to the standard formula [16, 17].

Women were closely monitored throughout their pregnancy with regular monthly check-ups that included laboratory testing (blood count, biochemical analyses with glucose level determination both fasting and after meals, urine sampling, microbiological analyses, cardiotocography [CTG], gynaecological and ultrasound examination with measurement of foetal biometry and placental thickness, Doppler blood flow of umbilical and middle cerebral artery, and biophysical profile evaluation). We noted all pregnancy complications such as hypertension/pre-eclampsia, antepartum bleeding in the second or third trimesters, contractions, violation of uteroplacental and/or fetoplacental blood flow (VUPB, VFPB) on Doppler, amniotic fluid volume disturbances according to amniotic fluid index (AFI) (oligohydramnios or hydramnios), premature preterm rupture of membranes (PPROM), pathologic nonreactive CTG that was an indication for urgent C/S, foetal anomalies seen on ultrasound (US) exam, etc. In the case of impending preterm birth, women were treated with corticosteroids to enhance the maturation of foetal lungs.

At the end of pregnancy, we recorded the delivery type (spontaneous or induced vaginal delivery, planned or urgent C/S) and time (GW). As preterm delivery, we considered pregnancy termination before 37 GW. For every childbirth, weight was measured and the Apgar score in the first and fifth minutes was determined. We also noted the baby's sex (male/female).

In the early neonatal period, while still hospitalized (approximately for 3 days after birth in the case of no complications), all complications were registered, such as neonatal hypoglycaemia, i.e. blood glucose < 45 mg/dl, jaundice, congenital hypothyroidism, necrotizing enterocolitis, pulmonary HTA, pulmonary problems, neonatal strength problems, need for neonatal oxygenation, intubation, or resuscitation, convulsions, sepsis, and small or large anomalies. The baby's weight at discharge was also noted. Moreover, any sign of postpartum hypertension in mothers was recorded.

Finally, all data collected throughout pregnancy, as well as pregnancy outcomes, were analysed by methods of descriptive and analytical statistics using IBM SPSS 20 software for Windows. The main outcome measures in this study were having pregnancy complications, i.e. maternal and neonatal, assessed all together. The significance of differences between categories of assessed parameters of mothers and children before and after delivery, according to DM type, was examined by the Kruskal-Wallis χ^2 test. Correlations of investigat-

ed parameters with DM type were tested using Spearman correlation. Relative risks for the most common maternal and foetal complications regarding DM type were calculated using the standard formula: [a/(a + b)]/[c/(c + d)]. For the purpose of the study, the risk of having pre-existing and insulin-dependent DM was tested in comparison with gestational and insulin-independent DM, which was chosen as the control. Finally, binary logistic regression equations (adjusted for maternal age, BMI, and comorbidities) were used to investigate the impact of DM type on the occurrence of pregnancy and neonatal complications.

Ethical and methodological standards

Each patient was informed about the procedures and signed an informed consent form to allow data collection for research purposes. The design, analysis, interpretation of data, drafting, and revisions conformed to the Helsinki Declaration, the Committee on Publication Ethics guidelines (https://publicationethics.org/), the Reporting of Studies Conducted Using Observational Routinely Collected Data (RECORD) statement, available through the Enhancing the Quality and Transparency of Health Research (EQUATOR) network (www.equator-network.org). Considering it as an observational study without an experimental arm or intervention in an anonymized dataset, a formal Institutional Review Board was not mandatory. The study was not advertised, and no remuneration was offered to the patients to enter or continue the study. An independent data safety and monitoring committee evaluated the ad interim and final results of this study. Over the study period, there were no significant differences in the facilities available for patient care and in the referral patterns of our service.

Results

The study included 323 pregnant women with diagnosed DM, who had a mean age of 34.26 ±6.56 years. Women who had GDM, who required insulin therapy, were the oldest (mean ±SD = 36.46 ±6.51 years). Our patients were generally obese, with an average BMI of 34.01 ±7.85 in the overall sample. Body mass index was the highest in the group of women who had pre-existing DM without insulin therapy (mean ±SD = 39.3 3 ±7.77). The investigated women mostly had 1 term delivery before the investigated pregnancy. Only 32 cases of previous neonatal deaths in our sample of women with DM were reported.

The most common type of DM in our sample was GDM that was not treated with insulin (61.92%), while only 8.67% of women had pre-existing insulin-dependent DM. Most women did not have DM-related complications, but more than 75% had some other comorbidity. Diabetes mellitus-related complications were the most frequent in women with pre-existing insulin-dependent DM, while HTA was mostly registered in women who had GDM without insulin therapy. Insulin therapy was mostly administered in pregnancy if DM was diagnosed in earlier GW.

Pregnancy complications were registered in 84.83% of cases, but there were few significant differences in complication occurrence regarding DM type. Also, complications were multiple in 50.78% of pregnancies. Multiple complications were most common in patients with pre-existing insulin-dependent DM (7.43%). Premature preterm rupture of membranes occurred in significantly fewer women with pre-existing DM and in more women with GDM. Furthermore, women with pre-existing DM were mostly delivered by C/S.

However, most children had a good pregnancy outcome, with a mean Apgar score higher than 7. Moreover, all investigated children were live born and had no problem with infections (sepsis). Foetal anomalies, although rare, were most common in women with pre-existing DM who did not require insulin therapy. Moreover, significantly fewer children had early neonatal complications (in total 36.85%). Neonatal convulsions were registered just in 1 child, whose mother had pre-existing insulin-dependent DM.

The investigated parameters of women and children, as well as pregnancy complications and outcomes according to DM type, are presented in Tables 1 and 2.

Insulin-dependent DM was associated with younger patient age (rho = –0.332; p = 0.001), lower weight and BMI (rho = –0.295; p = 0.001), lower gravidity (rho = –0.165; p = 0.003), earlier GW at DM diagnosis (rho = –0.539; p = 0.001), having DM-related complications (retinopathy rho = 0.594; p = 0.001; nephropathy rho = 0.558; p = 0.001; neuropathy rho = 0.391; p = 0.001), pathologic CTG findings (rho = 0.152; p = 0.006), and need for foetal maturation (rho = 0.215; p = 0.001), but less common occurrence of PPROM (rho = –0.129; p = 0.021), delivery by C/S (rho = 0.121; p = 0.031), mostly preterm (rho = –0.203; p = 0.001), and with smaller birth weight of the newborn (rho = –0.114; p = 0.041). Children of these mothers had lower Apgar score in the fifth minute (rho = –0.124; p = 0.026) and more frequent early neonatal convulsions (rho = 0.161; p = 0.004) causing the need for resuscitation (rho = 0.123; p = 0.027).

Having insulin-independent DM correlated with having HTA (rho = 0.141; p = 0.011), higher glucose serum levels (rho = 0.121; p = 0.029) as well as higher BMI (rho = 0.241; p = 0.001), earlier GW at DM diagnosis (rho = –0.126; p = 0.024), more previous neonatal deaths (rho = 0.138; p = 0.013), more foetal anomalies seen on ultrasound (US) scan (rho = 0.145; p = 0.009), and more deliveries by CS (rho = 0.173; p = 0.002).

Table 1. Descriptive parameters of investigated women and children according to diabetes mellitus type

Parameters	DM insulin		DM no insulin		GDM insulin		GDM no insulin		Between groups	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	*p*
Age [years]	27.10	3.83	35.90	5.59	36.46	6.51	34.31	6.34	16.162	0.001
BMI [kg/m^2]	28.11	3.15	39.33	7.77	36.67	9.19	33.15	7.08	14.853	0.001
Gravidity	1.14	1.55	2.36	2.20	2.38	1.98	2.21	2.18	2.562	0.055
GW at DG	1.01	0.01	23.46	5.09	25.69	8.19	27.66	8.77	91.812	0.001
Max gluco	6.68	2.91	6.55	1.66	6.52	2.31	6.31	4.28	0.138	0.937
Plac thick [mm]	38.41	8.37	40.82	11.46	38.50	8.17	37.29	6.87	1.664	0.175
AFI	25.58	47.04	57.21	62.73	57.96	82.73	48.32	65.83	1.306	0.273
GW birth [week]	36.91	2.18	37.58	1.53	37.58	2.82	37.53	2.65	0.543	0.653
Wei birth [g]	3562.32	838.05	3870.20	811.05	3750.16	893.94	3568.05	884.34	1.548	0.202
Ap 1 min	7.35	1.16	7.56	1.04	7.46	1.16	7.56	1.13	0.348	0.790
Ap 5 min	8.39	0.95	8.56	0.81	8.61	0.87	8.63	0.95	0.575	0.632

AFI – amniotic fluid volume index, BMI – body mass index, DG – diagnosis, DM – diabetes mellitus, GDM – gestational diabetes mellitus, GW – gestational week, Max gluco – maximal serum glucose level in pregnancy, Plac thick – placental thickness, Wei – weight

Insulin as a therapy for GDM was administered more often for older women (rho = 0.151; p = 0.006), with higher BMI (rho = 0.122; p = 0.008) and glucose serum levels (rho = 0.112; p = 0.043). In this group of patients, AFI was often increased (rho = 0.133; p = 0.017). However, GDM with insulin therapy correlated positively with having more and multiple neonatal complications (rho = 0.115; p = 0.039) as well as having pre-eclampsia (rho = 0.138; p = 0.013).

Gestational diabetes mellitus without insulin therapy was associated with higher GW at diagnosis (rho = 0.442; p = 0.001), lower glucose serum levels (rho = –0.195; p = 0.001), fewer DM-related complications (retinopathy rho = –0.248; p = 0.001; nephropathy rho = –0.154; p = 0.006; neuropathy rho = –0.132; p = 0.017), smaller AFI and oligohydramnios (rho = 0.125; p = 0.024), delivery more often as spontaneous vaginal (rho = 0.125; p = 0.025), higher GW at delivery (rho = 0.119; p = 0.032), less frequent neonatal resuscitation (rho = –0.124; p = 0.026), as well as fewer neonatal complications overall (rho = –0.125; p = 0.024).

Calculated relative risks for the most common maternal and foetal complications regarding DM type are presented in Table 3. It can be seen that having pre-existing in comparison to GDM increases the risk of development or advancement of DM-related maternal complications, the occurrence of pregnancy and neonatal complications, foetal anomalies, and delivery by C/S. Conversely, it decreases the risk of pre-eclampsia, baby weight abnormalities, and preterm birth. Having insulin-dependent compared to independent DM increases the risk of development or advancement of DM-related maternal complications, the occurrence of pregnancy and neonatal complications, foetal anomalies, and baby weight abnormalities. On the other hand, it reduces the risk of delivery by C/S, pre-eclampsia, and preterm birth.

Finally, based on performed logistic regression, a significant equation of relationship between DM type and pregnancy complications was obtained (B = 1.721; Wald = 123.158; R^2 Nagelkerke = 0.069; classification = 84.8%; χ^2 = 19.113; p = 0.038). It was proven that pre-existing insulin-dependent DM increases the risk of pregnancy complications (p = 0.031; OR = 1.656). Conversely, the DM type could not predict the occurrence of neonatal complications (χ^2 = 0.902; p = 0.342).

Discussion

Diabetes mellitus is one of the most common medical complications of pregnancy at present. According to literature data, GDM is most prevalent (87.5%) in patients with DM [18, 19]. On the other hand, pre-existing insulin-dependent DM accounts for 7.5% while insulin-independent accounts for 5% of pregnancies complicated with DM [20, 21]. In our study, the most common DM type was pre-existing insulin-independent DM (almost 62%). The investigated women were on average in their 30s and obese, while more than 75% had some other comorbidity. Women with insulin-dependent GDM were the oldest. We found that DM-related complications were the most frequent in pre-existing insulin-dependent DM patients.

It is well known that pregnancy is considered to be a diabetogenic state. The changes in the maternal organism that occur during pregnancy have the goal of ensuring adequate nutrients for the developing foetus. Therefore, it is considered that the maternal metabolism is in an anabolic state [10, 14]. During pregnancy, metabolic changes include a more significant fall in plasma glucose and amino acids and a rise in free lipids after fasting than in the non-pregnant state. These metabolic changes during pregnancy resemble type II DM

Table 2. Differences in frequency of examined maternal and neonatal parameters according to diabetes mellitus type

Maternal parameters		DM type				Between groups	
		DM insulin	DM no insulin	GDM insulin	GDM no insulin	χ^2	*p*
Diabetes mellitus type	With insulin	28	–	–	–	279.311	0.001
	No insulin	–	30	–	–		
	GDM insulin	–	–	65	–		
	GDM no insulin	–	–	–	200		
DM in family	No	23	24	56	176	1.908	0.592
	Yes	5	6	9	24		
History of neonatal death	No	25	23	59	184	6.906	0.075
	Yes	3	7	6	16		
Consulted for risk	No	25	26	59	168	2.155	0.541
	Yes	3	4	6	32		
Having retinopathy	No	7	25	63	178	86.290	0.001
	Yes	21	5	2	22		
Having nephropathy	No	7	26	65	170	80.566	0.001
	Yes	21	4	0	30		
Having neuropathy	No	15	24	65	176	37.933	0.001
	Yes	13	6	0	24		
Having chronic hypertension	No	26	17	50	154	10.723	0.013
	Yes	2	13	15	46		
HTA after pregnancy	No	24	18	45	134	5.051	0.168
	Yes	4	12	20	66		
Preeclampsia	No	25	28	61	164	7.579	0.056
	Yes	3	2	4	36		
Antepartum bleeding	No	28	29	63	193	1.006	0.801
	Yes	0	1	2	7		
Preterm rupture of membranes	No	28	29	54	173	7.802	0.049
	Yes	0	1	11	27		
Oligohydramnios	No	23	29	62	172	7.335	0.062
	Yes	5	1	3	28		
Hydramnion	No	21	21	44	155	2.854	0.415
	Yes	7	9	21	45		
Other maternal comorbidities	No	9	8	15	46	1.262	0.738
	Yes	19	22	50	154		
Number of pregnancy complications	No	1	3	13	32	16.291	0.001
	One	3	10	25	72		
	Multiple	24	17	27	96		
Has pregnancy complications	No	1	3	13	32	4.821	0.185
	Yes	27	27	52	168		
Neonatal parameters		**DM type**				**Between groups**	
		DM insulin	**DM no insulin**	**GDM insulin**	**GDM no insulin**	χ^2	*p*
Anomalies seen on ultrasound	No	20	19	55	170	10.553	0.014
	Yes	8	11	10	30		
Uteroplacental flow violation	No	23	21	46	148	1.515	0.679
	Yes	5	9	19	52		

Table 2. Cont.

Neonatal parameters		DM type				Between groups	
		DM insulin	DM no insulin	GDM insulin	GDM no insulin	χ^2	*p*
Fetoplacental flow violation	No	20	24	56	164	2.903	0.407
	Yes	8	6	9	36		
Pathologic cardiotocography	No	15	20	52	158	10.630	0.014
	Yes	13	10	13	42		
Foetal maturation	No	21	26	60	173	5.084	0.166
	Yes	7	4	5	27		
Delivery type	Vaginal	24	23	61	177	9.230	0.026
	CS	4	7	4	23		
Birth time	Term	9	5	12	38	3.024	0.388
	Preterm	19	25	53	162		
Weight abnormal < 10 or > 10%	No	17	15	30	109	2.180	0.536
	Yes	11	15	35	91		
Neonatal resuscitation	No	23	24	55	177	2.394	0.495
	Yes	5	6	10	23		
Intubation and oxygenation	No	26	26	57	179	0.756	0.860
	Yes	2	4	8	21		
Neonatal convulsions	No	27	30	65	200	10.536	0.015
	Yes	1	0	0	0		
Neonatal hypoglycaemia	No	27	29	61	191	0.531	0.912
	Yes	1	1	4	9		
Postpartum foetal anomalies	No	27	28	62	193	0.756	0.860
	Yes	1	2	3	7		
Pulmonary problems	No	27	27	60	190	1.849	0.604
	Yes	1	3	5	10		
Neonatal jaundice	No	26	30	61	196	5.297	0.151
	Yes	2	0	4	4		
Neonatal strength problems	No	26	29	61	192	1.030	0.794
	Yes	2	1	4	8		
Other neonatal complications	No	22	27	52	171	2.535	0.469
	Yes	6	3	13	29		
Number of neonatal complications	No	18	17	36	133	2.222	0.528
	One	2	7	15	28		
	Multiple	8	6	14	39		
Has neonatal complications	No	18	17	36	133	3.197	0.362
	Yes	10	13	29	67		

DM – diabetes mellitus, GDM – gestational diabetes mellitus, HTA – hypertension

with progressive insulin resistance of up to 50% in late pregnancy. The leading cause of these metabolic changes is an accumulation of pregnancy hormones that act against insulin, causing insulin resistance. Therefore, the requirements of insulin to maintain standard glycaemic control are higher during advanced pregnancy [22, 23]. In order to compensate for insulin resistance, an increase in postprandial insulin production occurs in healthy organisms. Conversely, this compensatory mechanism is dysfunctional in DM patients due to deficient b-cell insulin reserves (absolutely as in type 1, or relatively in type 2 diabetes or GDM). Therefore, in diabetic pregnancy, progressive increases up to 3-fold of insulin are required throughout the later stages of pregnancy. Even higher insulin doses are required in the case of obesity and physical inactivity [14, 17, 24].

Current data suggest that the risk of serious adverse outcomes, including congenital malformations and

Table 3. The relative risk for the most common maternal and foetal complications regarding diabetes mellitus type

Parameters		DM type					
		Pre-existing DM	Gestational DM	Relative risk	Insulin-dependent	Insulin-independent	Relative risk
Has pregnancy complications	Yes	54	220	2.41	79	195	1.01
	No	4	45		14	35	
Has neonatal complications	Yes	23	96	1.12	39	80	1.24
	No	35	169		54	150	
DM related to mother complications	Yes	35	52	4.14	27	60	1.11
	No	23	213		66	170	
Preeclampsia	Yes	5	40	0.58	7	38	0.51
	No	53	225		86	192	
Foetal anomalies	Yes	19	40	2.18	18	41	1.07
	No	39	225		75	189	
C/S	Yes	11	27	1.76	8	30	0.71
	No	47	238		85	200	
Baby weight abnormalities	Yes	26	126	0.91	46	106	1.11
	No	32	139		47	124	
Preterm birth	Yes	44	215	0.78	72	187	0.85
	No	14	50		21	43	

DM – diabetes mellitus, C/S – Caesarean section
DM related to mother complications – retinopathy, nephropathy, neuropathy, etc.

perinatal mortality, are similar in type 1 and 2 diabetes. Moreover, it seems that type 2 DM patients might have even more complications during pregnancy than type 1 DM patients [7]. One potential reason is the fact that, compared with type 1 DM, women with type 2 DM are less likely to receive pre-pregnancy counselling and less often plan their pregnancies [25]. Conversely, they are more often hypertensive, overweight, and of lower socioeconomic status. Women with type 1 DM, due to the severity of their condition, seem to have more regular medical check-ups, enabling better glycaemic control both preconceptionally and during pregnancy [15, 26]. On the other hand, it was found that maternal complications and C/S rates were higher in the case of early (developed before 24 GW) than late GDM patients [27].

The influence of hyperglycaemia on adverse pregnancy outcomes was demonstrated in numerous investigations. Also, long-term metabolic and cardiovascular consequences of hyperglycaemia during pregnancy are now recognized for both mother and child. In some investigations, 50% of followed infants of mothers with type 1 DM had complications related to glucose control, while 10% required admission to an intensive care unit after birth [7, 28]. Risks of DM in pregnancy for both mothers and children are well established, and they could be influenced by the type and duration of DM, glycaemic control, and DM-related complications. Foetal risk includes miscarriage, preterm delivery, stillbirth, perinatal mortality, congenital anomalies, small/large for gestational age (SGA/LGA), shoulder dystocia and birth injury, neonatal hypoglycaemia, polycythaemia, hypocalcaemia, and respiratory distress syndrome. Maternal risk incorporates accelerated DM complications such as retinopathy and nephropathy, hypoglycaemia, diabetic ketoacidosis, preeclampsia, hydramnios, operative delivery, and infection [7, 10]. Factors involved in diabetes-related complications are very complex and have been investigated systematically. In the middle of pregnancy placental growth hormone progressively replaces pituitary growth hormone in the maternal circulation. According to a recently published study, this factor can be used as a laboratory marker to predict which patients will have abnormal glucose challenge test results [29].

Multidisciplinary obstetric surveillance is needed for women with advanced diabetic complications, to prevent risks for both mother and child. Diabetic ketoacidosis is a serious problem to the health and even viability of the foetus, and every mother should be instructed in monitoring urinary ketones and seek urgent advice if needed. The advanced microvascular disease can cause intrauterine growth retardation. Pregnancy is a risk factor for the progression of diabetic retinopathy. Perinatal survival rates, although mostly high, are found to vary with the stage of DM nephropathy and are accompanied by very high rates of pre-eclampsia, preterm delivery, and foetal growth restriction [14, 30].

Pre-eclampsia is a leading cause of maternal and foetal morbidity and mortality. In developed countries, this syndrome affects 2–7% of pregnancies in women

without DM [31, 32]. All DM types, as well as obesity, further increase pre-eclampsia occurrence by up to 10–20% [33]. Insulin resistance at 22–26 weeks' gestation is confirmed as a significant independent predictor of pre-eclampsia. Recent studies examining the pathophysiology of pre-eclampsia in DM patients have focused on the potential roles of endothelial dysfunction with angiogenic imbalance, increased oxidative stress, haptoglobin phenotype, total antioxidant status, and dyslipidaemia [34, 35].

Literature data indicate that mothers with DM have a 2-fold greater risk of having a child with congenital malformations than healthy women. Authors found that 4% of foetuses of women with DM had at least one major congenital anomaly, out of which the most common were anomalies of the heart (1.7%) and musculoskeletal system (0.7%) [7]. Numerous studies have confirmed that the incidence of congenital malformations is linearly associated with HbA_{1c} serum levels. Adequate glycaemic control before pregnancy and during the first trimester reduces the rates of congenital anomalies as well as spontaneous abortions and other adverse outcomes [15, 20].

Foetal exposure to DM can alter foetal growth and increase the risk of macrosomia due to the accumulation of more fatty tissue. The hypothesis that maternal hyperglycaemia accelerates foetal growth through foetal hyperinsulinaemia has provided a basis for the concept of foetal programming. Diabetes mellitus-exposed children are at increased risk of obesity and type 2 DM later in life [24, 36].

Neonatal hypoglycaemia reflects foetal hyperinsulinaemia. The monitoring of neonatal blood glucose should start after birth and continue for a few days until levels are persistently above 2 mmol/l. Low blood glucose associated with abnormal clinical signs of reduced consciousness is an indication for transfer to an intensive care unit where intravenous glucose should be rapidly administered [7, 14, 29].

Neonatal jaundice or hyperbilirubinaemia in DM-affected neonates is also not very frequent. Studies reported jaundice in about 5–20% of infants of women with GDM. A higher rate (37.0%) is found only in the preterm birth of infants of women with type 1 DM [37].

In some investigations, the risk of respiratory distress syndrome (RDS) as a result of delayed foetal lung maturation in neonates of mothers with different types of diabetes was significantly higher than in those born to mothers without diabetes. However, some other studies, after adjusting for confounders, found no association of DM with poor neonatal respiratory outcomes [38].

The timing and mode of delivery in DM pregnancies are crucial. All women should have a plan for delivery in order to avoid perinatal morbidity (intrauterine foetal death) and mortality (injury during delivery) [39]. Major complications of vaginal delivery are associated with foetal macrosomia and include obstructed labour, shoulder dystocia with brachial plexus injury, postpartum haemorrhage, and third- and fourth-degree tears. Therefore, C/S rates for women with pregestational DM in most parts of the world are higher than 50% [7, 28, 40].

Although planned C/S does prevent birth injury of the foetus, iatrogenic prematurity has resulted in increased admission to neonatal intensive care among DM-affected children. Preterm labour can be particularly hazardous for the infants of mothers with DM. Therapy for uterine contraction suppression and corticosteroids for the acceleration of foetal lung maturation was found to increase and extend maternal hyperglycaemia requiring additional insulin therapy [7, 20].

Perinatal mortality, as well as preterm delivery, were found almost 4 times more often in DM pregnancies than in the general population. Perinatal mortality rates in cases of DM-affected children in Europe are 3–5 times higher than the healthy population and range from 27.8 to 48 per 1000 births. The main reasons are preterm delivery and all its complications, RDS, hypocalcaemia, and polycythaemia [14, 40–43].

We found that in almost 85% of examined pregnancies, some types of complications were registered. However, all children were live born and mostly with good pregnancy outcome. We registered in total a rate of 36.85% of early neonatal complications. A potential cause for such findings is the fact that we managed to have timely diagnosis and optimal management of all investigated women according to current protocols.

In our study, insulin-dependent DM was associated with having DM-related complications, but less often the occurrence of PPROM. Most of these patients were delivered by Caesarean section and preterm. Their children had lower Apgar score, lower birth weight, and more frequent early neonatal complications requiring resuscitation. Having insulin-independent DM correlated with having HTA, more previous neonatal deaths, more foetal anomalies, and more deliveries by C/S. Insulin-dependent GDM patients more often had pre-eclampsia, polyhydramnios, as well as more and multiple neonatal complications. Insulin-independent GDM was associated with having fewer DM-related complications, oligohydramnios, spontaneous vaginal delivery at term, less frequent neonatal resuscitation, and less neonatal complications overall.

Nevertheless, in our sample, the majority of tested complications occurred at a similar frequency regardless of DM type. Multiple complications were most prevalent in women with pre-existing insulin-dependent DM. It was proven that pre-existing insulin-dependent DM increases the risk of pregnancy complications. On the other hand, the DM type could not predict the occurrence of neonatal complications.

Conclusions

The results of our study indicate that DM type has a limited impact on pregnancy outcomes and the occurrence of maternal and neonatal complications. Pre-existing insulin-dependent DM increases the risk of pregnancy complications, but neither DM type could predict neonatal complications. With adequate current and timely therapy, pregnancy outcomes for both mothers and children could be good regardless of having DM.

Disclosure

The authors report no conflict of interest.

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