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OBSTETRIC AND PERINATAL OUTCOMES IN WOMEN WITH TYPE 1 DIABETES MELLITUS

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Abstract

Background and aims*: Pregnancy in women with type 1 diabetes mellitus (T1DM) is associated with increased risk of maternal and fetal complications. The aim of this study was to examine and to compare pregnancy outcomes between women with T1DM and a control group of non diabetic women.* ***Material and method****: The present study included all pregnancies in T1DM women followed at Diabetes Clinic, Emergency County Clinical Hospital, Timişoara, from 1990 to 2010.* ***Results****: We found a relative risk of spontaneous abortions of 1.85 (95%CI 1.01-3.39; p=0.05) and a relative risk of major congenital malformations of 4.32 (95%CI 1.55-12; p=0.005) in T1DM pregnancies compared to the control group. We also observed that the rate of stillbirth was more frequent in type 1 diabetic pregnancies (p=0.02). The offspring of T1DM women were more likely to be delivered preterm (32%) compared with the control group (9.5%). The relative risk of preterm delivery was 3.38 higher (95%CI 2.93-5.6; p<0.0001) in T1DM pregnancies compared with non diabetic mothers. There was a statistically significant difference in the proportion of macrosomic offspring between T1DM (17.3%) and non diabetic mothers (6.5%)* ***Conclusions****: The present study demonstrated that pregnancy outcome and perinatal complications are still high in T1DM pregnancies.*

key words: *diabetes mellitus, pregnancy loss, congenital malformations, spontaneous abortions, macrosomia, cesarean.*

Background and aims

Pregnancy in women with type 1 diabetes mellitus (T1DM) is associated with increased risk of maternal and fetal complications. The St. Vincent declaration set in 1989 a 5 year target to improve outcomes for pregnant women with pregestational diabetes (type 1 and type 2 diabetes mellitus) to that of women without diabetes [1]. Nowadays, the maternal mortality is equal to that of patients with no diabetes, and the fetal mortality has lowered from 40% during the 40s to 5-8% during the 70s and to 1.2-2% in specialized centers, values which are similar to those of general perinatal mortality in economical developed

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countries (1-1.5%) [2,3]. The fetus of women with diabetes mellitus (DM) is at risk for a variety of neonatal morbidities: spontaneous abortion, congenital malformations, stillbirth, perinatal death, growth disorders, respiratory distress, diabetic cardiomiopathy, neonatal hypoglycemia, hyperbilirubinemia, disorders of calcium and magnesium metabolism, polycitemia etc. [4].

There is a correlation between raised maternal blood glucose levels and adverse perinatal outcomes. Key elements for improving outcomes included a good glycaemic control with intensive insulin therapy or insulin pumps starting before conception and maintained during the time of organogenesis and, ideally, throughout the pregnancy, home blood glucose monitoring, continuous blood glucose monitors and fetal ultrasonography [5,6]. Perinatal mortality and morbidity is also lower in T1DM women who attend prepregnancy counseling and who are planning their pregnancy [7].

The aim of this study was to examine and to compare pregnancy outcome between women with T1DM and a control group of non diabetic women.

Material and method

The present study included all pregnancies in T1DM women followed at the Diabetes Clinic, Emergency County Clinical Hospital, Timişoara, from 1990 to 2010. Fetal outcome was divided in two groups: A - pregnancies ending with healthy babies and B - all pregnancies ending with pregnancy loss including induced abortion due to the high risk of pregnancy. Obstetric and perinatal outcome data were recorded, including gestational age at birth, birth weight, macrosomia, appropriate (AGA), large (LGA) and small (SGA) for gestational age newborns, mode of delivery, preterm delivery, spontaneous or induced abortion, stillbirth, congenital malformations and perinatal mortality.

Spontaneous abortion was defined as a clinically non-induced pregnancy loss reported to occur before 24 weeks of gestation. Stillbirth is defined as death of fetus after 24 week of pregnancy. Perinatal death was defined as the combined rate of stillbirth and early mortality within 7 days of life or late mortality within 28 days. Major congenital malformations were defined as those who were responsible for the death of the fetus. LGA was defined as birthweight $\geq 90^{th}$ centile and SGA as birthweight $\leq 10^{th}$ centile. AGA was defined as birthweight between 11-89^{th} percentile. Definitions of perinatal outcome also included prematurity (delivery < 37 weeks of gestation) and macrosomia (newborn birth weight ≥4000 g).

From 1990 to 2010 a total number of 99 T1DM pregnancies were registered. Their obstetric and pregnancy outcomes were compared with a group of 267 pregnancies of women without diabetes.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 5. Differences between median of the groups were studied using the Mann-Whitney test or the Student's t-test for differences between means. Pearson's correlation coefficient (r) was used to measure the strength of the association between two variables and its significance with t-distribution test. Fisher's exact test was used in the analysis of contingency tables. For the statistical tests α=0.05 significance levels was

accepted and for means and risk estimates a 95% confidence interval was computed.

Results

In the study group there were sixty-seven pregnancies ending with healthy babies (group A) and thirty-two pregnancies terminated with fetal loss (group B): 5 induced abortions, 15 spontaneous abortions, 8 major congenital malformations and 4 stillbirths. The major congenital malformations were: complete transposition of great arteries (2 cases), tetralogy of Fallot (1 case), hypoplastic left ventricle syndrome (1 case), anencephaly (2 cases), caudal regression syndrome (1 case) and association of ventricular septal defect and anorectal agenesis (1 case) We found a relative risk (RR) of spontaneous abortions of 1.85 (95%CI 1.01-3.39; p=0.05) and a RR of major congenital malformations of 4.32 (95%CI 1.55-12; p=0.005) in T1DM compared to the control group. We also observed that the rate of stillbirth was more frequent in T1DM pregnancies (p=0.02). The main characteristics of pregnancy loss are described in Table 1.

Table 1. Causes of pregnancy loss.

Results	Type 1 DM (n=99)		No diabetes (n=267)		p
	No.	%	No.	%	
Group A	67	67.7	237	88.8	<0.0001
Group B	32	32.3	30	11.2	
Causes of pregnancy loss					
Induced abortions	5	5	-	-	-
Spontaneous abortions	15	15.2	23	8.6	0.05
Major congenital malformations	8	8,1	6	2.25	0.005
Stillbirth	4	4	1	0.37	0.02

Table 2. Obstetric and perinatal outcomes.

		Type 1 DM (n=75)		No diabetes (n=243)		p
		No.	%	No.	%	
Term delivery	Deceased	5	6.6	2	0.8	0.003
	Alive	46	61.4	218	89.7	
Premterm delivery	Deceased	3	4	4	1.7	0.7
	Alive	21	28	19	7.8	
Macrosomia	Yes	13	17.3	16	6.5	0.009
	No	62	82.7	227	93.5	
Mode of delivery	Cesarean delivery	51	68	123	50.6	0.011
	Vaginal delivery	24	32	120	49.4	
Birth percentiles	SGA (C)	3	4	14	5.7	C + E vs. D 0.0002
	AGA (D)	48	64	206	84.8	
	LGA (E)	24	32	23	9.5	

Obstetric and perinatal outcomes were obtained in 75 cases of T1DM pregnancies and 243 pregnancies without diabetes by excluding the cases ending with induced abortions, spontaneous abortions and stillbirth. The main characteristics are described in Table 2.

The offspring of T1DM women were more likely to be delivered preterm (32%) compared with the control group (9.5%) (Figure 1). We found a RR of preterm delivery of 3.38 (95%CI 2.93-5.6; p<0.0001) in T1DM pregnancies compared with non diabetic mothers. Deceased infants whose mothers had T1DM (6.6%) compared with infants of mothers without diabetes (0.8%) were more likely to be born after 37 weeks of gestation.

There was a statistically significant difference in the proportion of macrosomic offspring between T1DM mothers (17.3%) and those without diabetes (6.5%) as shown in details in Figure 2. By comparing all pregnancies with and without DM we obtained a RR of macrosomia of 2.6 (95%CI 1.3-5.2; p=0.009) in T1DM mothers compared to the control group.

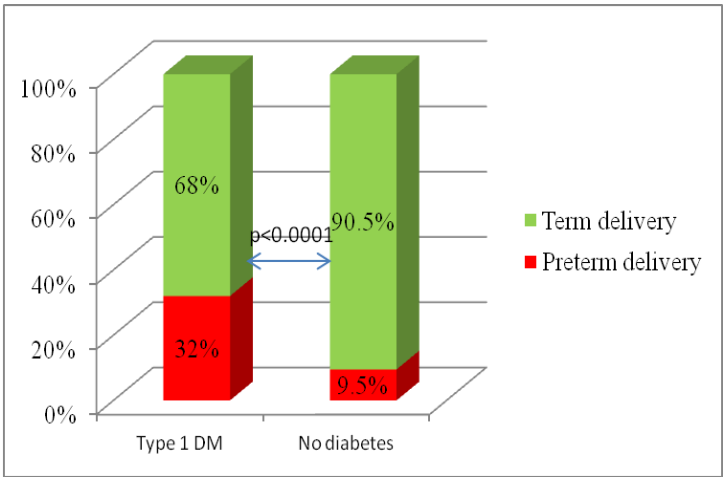

Figure 1. Prevalence of preterm delivery in the study groups.

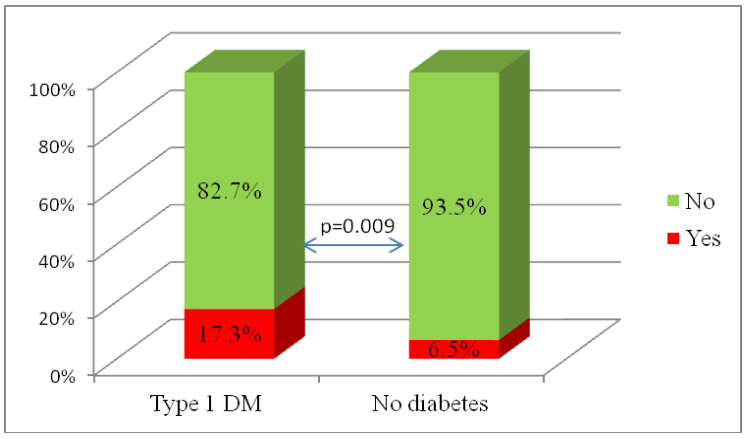

Figure 2. Prevalence of macrosomia in the study groups.

Women with T1DM had a significantly higher rate of cesarean delivery (68%) compared with those without DM (50.6%) (Figure 3).

We found that 4% of the infants born from T1DM mothers were SGA, 32% of them were LGA and 64% were AGA (Figure 4). We obtained a RR of SGA/LGA in T1DM mothers of 2.36 (95%CI 1.5-3.6; p=0.0002) compared with the control group.

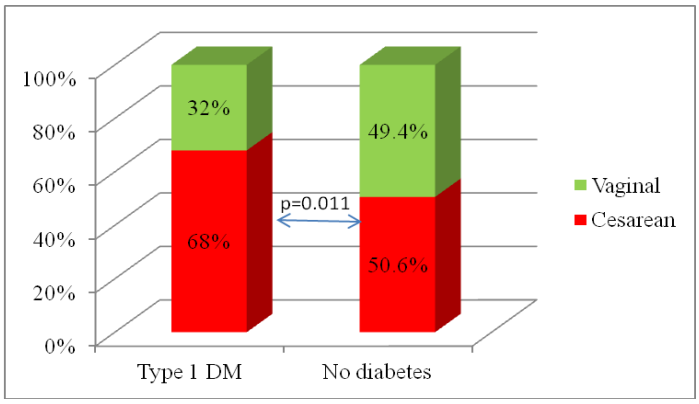

Figure 3. Delivery mode in the study groups.

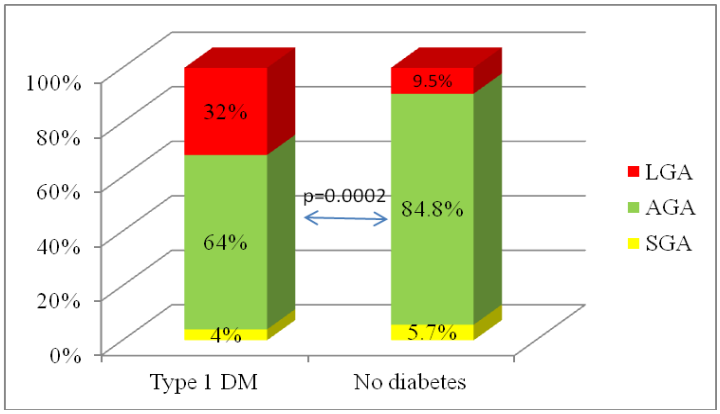

Figure 4. Prevalence of the birth percentiles in the study groups.

Discussions

In the last two decades there has been a great medical progress in improving pregnancy outcomes in women with T1DM. Although maternal mortality has been reduced, the morbidity and perinatal mortality of the fetus are still increased in diabetic pregnancies which make these to be considered further on as pregnancies with increased fetus risk. Successful outcomes in diabetic pregnancy depend on the experience of the diabetic and obstetric teams and the contribution of the pregnant woman herself, especially to maintain euglycemia, during the time of organogenesis and, ideally, throughout the pregnancy, and her compliance to periodic monitoring rhythm [5,6].

Our data clearly demonstrated that the rate of pregnancy loss in T1DM is still high. In our study this rate was 3 times higher than in the non diabetic group. We observed a rate of pregnancy loss of 32.3% in T1DM mothers. For comparison, Nielsen et al. identified 573 pregnancies in 301 women with T1DM. The rate of pregnancy loss reported by them was 29%, the RR observed being 3.3 higher than in the non diabetic population [8].

The causes of pregnancy loss in the present study were induced abortion, spontaneous abortion, congenital malformations and stillbirth. The prevalence of induced abortion was 5% and the rate of spontaneous abortions was 1.85 fold higher than that of the non diabetic group. This finding is consistent with that of other studies.

A study performed by Pearson et al. on 423 T1DM mothers found that the prevalence of spontaneous abortion was 12.7% and that of the induced abortion of 1.7% [9].

Major congenital malformations occurred 4.32 times more often in the diabetic group. Higher rates (2 to 8 times higher in diabetic women) have been reported in literature [10,11].

The prevalence of stillbirth in the present study was 4%, higher than in the non diabetic group. Similarly, the Diabetes and Pregnancy Group from France reported a prevalence of stillbirth of 4.2% in type 1 diabetic mothers [12].

Preterm delivery was 3.38 times higher in diabetic pregnancies than that in the control group. Similar findings were found by Kries at al. who reported a 2.67 fold higher rate than that of the control group [13].

Macrosomia represents the most frequent fetopathy in the offspring of diabetic mothers. It is associated with an increased risk of Erb palsy, respiratory distress, neonatal hypoglycemia, hyperbilirubinemia, polycitemia etc. [14]. In our study, the prevalence of macrosomia in the offspring of T1DM mothers was 32%. It occurred 3.38 times often then in the control group. Similar data were found by Gonzalez et al. who reported a prevalence of 20.6% in T1DM pregnancies [1].

In this study, the rate of cesarean section was high in both groups (68% in T1DM mothers and 50.6% in the control group). The high rates of cesarean deliveries could be explained by a less expectative policy where spontaneous initiation of delivery is not encouraged. This finding is in agreement with other studies. Thus, in Finland and Denmark the reported prevalence of cesarean delivery in type 1 diabetic pregnancies was 63.5% and 55.9%, respectively [15,16].

An unexpected observation was the high prevalence of LGA (32%) in the diabetic pregnancies, 3 times higher than in the control group. Also the RR of SGA/LGA in T1DM mothers was 2.36 fold higher compared to the control group. Similar data were reported in different studies [17,18].

Conclusion

In conclusion, the present study demonstrated that pregnancy outcome and perinatal complications are still high in T1DM pregnancies. An adequate maternal self-care (maintaining normal glycemia during the period of organogenesis and, ideally, during the entire pregnancy period, as well as for her compliance to the rhythm of periodic monitoring) and professional care can improve the outcomes of the offspring of T1DM mothers.

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