ORIGINAL ARTICLE

Neonatal Outcomes in Type 1 Diabetes Pregnant Women, A Single-Center Retrospective Study

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Abstract

Background: Pregnancy in women with type 1 diabetes mellitus (T1DM) is associated with an increased risk of congenital malformations, and obstetric complications including increased rates of cesarean section birth, prematurity, and neonatal adverse outcomes including large for gestational age (LAG), and hypoglycemia. Our aim of this study is to investigate and evaluate the prevalence and the different neonatal outcomes of T1DM pregnant women compared to nondiabetic healthy pregnant women in a single-center experience to improve the effectiveness of interventions for the treatment of pregnant women with T1DM.

Methods: This is a retrospective cohort study of 113 pregnant women (43 pregnant patients with T1DM and 70 non-diabetic healthy pregnant women) who underwent regular follow-in the antenatal period and delivered at King Fahad Military Medical Complex (KMMC) - Dhahran between 2018 and 2023.

Results: A total of 117 pregnant women (47 with Type-1 diabetes mellitus-T1DM and 70 healthy controls) were included in the study. The proportion of elective C-sections was significantly high in women with T1DM 21 (44.7%) and the proportion of neonatal hypoglycemia who need treatment was also significantly high in diabetic women 20 (42.6%). NICU / SCBU admission was significantly high in diabetic women 23 (48.9%).

Conclusion: The high prevalence of neonatal adverse outcomes especially hypoglycemia and intensive care admission of T1DM pregnant women compared to non-diabetic pregnant women indicates that this model of antenatal diabetes care must be improved to enhance maternal and fetal outcomes, especially in such high-risk groups and challenging problems.

Key Words: *Pregnancy; Type-1 diabetes; Hypoglycemia; Neonatal; Saudi Arabia*

Introduction

Type 1 diabetes mellitus (T1DM) is an autoimmune disease characterized by selective destruction of the insulin-secreting cells. Women with type 1 diabetes mellitus (T1DM) face specific and significant difficulties and challenges in maintaining optimal glycemic control during pregnancy. Type 1 diabetes pregnant women specifically are at risk of adverse maternal and neonatal outcomes. Maternal complications include pre-eclampsia, premature delivery, and cesarean section delivery. Also, adverse neonatal outcomes include congenital

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abnormalities and malformations, especially congenital heart diseases and anomalies of the nervous system, macrosomia, neonatal hypoglycemia, neonatal respiratory distress syndrome, and serious complications like IUFD [1-3]. Those unfavorable adverse outcomes are probably related to poor glycemic control, particularly in the periconceptional period and in the first trimester of pregnancy [4].

The management of type 1 diabetes mellitus (T1DM) in pregnancy is challenging due to several factors including pregnancy hormones, insulin sensitivity variations with different terms of pregnancy as early pregnancy is a time of insulin sensitivity, lower glucose levels, and lower insulin requirements in women with type 1 diabetes and the situation rapidly reverses as insulin resistance increases exponentially during the second and early third trimesters and levels off toward the end of the third [30] also, the increased risk of fetal and maternal complications. So, maintaining optimal glycemic control is essential and necessary in pregnancy to reduce the risk of adverse maternal and neonatal outcomes by achieving better glucose levels and good multidisciplinary care between endocrinologists or diabetologists, obstetricians, neonatologists and allied health professional specialists is required [5]. Also, Self-monitoring of blood glucose plays a significant role in the reduction of perinatal mortality and morbidity in pregnant women with type 1 diabetes mellitus (T1DM) [6,7]. Continuous monitoring and following T1DM and the control of blood glucose over the whole pregnancy has provided a vision of the effects of poor maternal glycemic control on various neonatal outcomes [8].

In this study, we aimed to evaluate the neonatal outcomes in T1DM pregnant women and analyzed the variables that affect maternal-fetal outcomes to improve the effectiveness of interventions for the treatment of pregnant women with T1DM. Also, to compare the neonatal outcomes of T1DM pregnant women with nondiabetic healthy pregnant women.

Material and Method

This is a retrospective analysis study included 113 pregnant women (43 pregnant patients with T1DM and only 70 non-diabetic healthy pregnant women who were selected randomly) who underwent regular follow-in the antenatal period and were delivered at King Fahad Military Medical Complex (KMMC) - Dhahran between 2018 and 2023. The required data were obtained from KFMMC delivery room registry records and the electronic database of our institution. Approval was obtained from the Ethics Committee of King Fahad Military Medical Complex (KMMC) – Dhahran. Exclusion criteria for both T1DM and non-diabetic pregnant women were ages below 18 years old and patients without regular follow-up or delivery in our institution. Exclusion criteria for non-diabetic pregnant women (control group) also, was including any pre-gestational diabetes or pre-gestational co-existing diseases (chronic hypertension, renal disease, systemic autoimmune disease, etc.). Exclusion criteria for the T1DM pregnant women group also included no glycated hemoglobin (HbA1c) at the time of pregnancy. All T1DM pregnant women were on an MDI regimen (basal-bolus insulin therapy consisted of a minimum of four daily subcutaneous insulin doses, three short-acting insulin analogues before the main meals, and one long-acting insulin analogue).

History was extracted from the electronic database for each patient, with particular attention to the obstetric history including age at pregnancy, number of pregnancies, gestational age at delivery, history of previous abortion and mode of delivery, the glycated hemoglobin (HbA1c) for T1DM, and neonatal history. The obstetrician and endocrinology divisions of our institution performed patient

follow-ups. Usually, target HbA1c is less than 6.5%, worsening of blood sugar regulation was defined as increasing HbA1c. Cesarean section and preterm birth (birth at less than 37 weeks gestation) ratios are presented as gestational outcomes. Perinatal mortality is also defined as neonatal deaths before the 28th postpartum day.

Neonatal hypoglycemia is defined as blood glucose levels below 40 mg/dL (9). Fetal macrosomia is defined by a newborn weight of 4kg or above. Large for gestational age (LGA) is defined as infants with a birth weight above the 90th percentile. Shoulder dystocia is defined by the failure to deliver the fetal shoulders using solely gentle downward traction, the need for additional delivery maneuvers to deliver the baby successfully, and/or a documented head-to-body interval of greater than 1 minute. It can lead to obstetric brachial plexopathies (31).

IUGR is defined as a rate of fetal growth that is less than normal considering the growth potential of that specific infant. Small for gestational age (SGA) has been defined as having a birth weight less than two standard deviations below the mean or less than the 10th percentile of a population-specific birth weight for a specific gestational age.

Respiratory problems are defined as any problem necessitating invasive respiratory support at any duration. Admissions to the neonatal intensive care unit (NICU) right after the delivery and major congenital anomalies are also recorded. The obtained data was used for descriptive analysis of the whole cohort. Further analyses were performed to compare neonatal outcomes in T1DM pregnant women compared to non-diabetic healthy pregnant women.

Statistical and data analysis

The estimated sample size for T1DM was 31 and for non-diabetes was 62. The number of T1DM pregnant women group and control group which are the non-diabetic healthy pregnant women, we compare the two groups in terms of the neonatal outcomes and regarding the level of HbA1c between the two groups if less than 7% or more than 7%. Data was analyzed by IBM SPSS.22. All categorical variables were presented as frequencies and percentages while all continuous data was presented as mean (± SD). The chi-square test was used to check the differences between categorical variables; the t-test was used to compare the mean age and gestational age between the two groups. Binary logistic regression was used to calculate the odds ratios. Statistical significance was set at $P<0.05$.

Results

A total of 117 pregnant women (47 with Type-1 diabetes mellitus-T1DM and 70 healthy controls) were included in the study. The baseline characteristics of both groups are presented in (Table 1). The mean (SD) age of diabetic women was 29.38 ± 5.27 years and non-diabetic women was 31.23 ± 5.28 years. Age distribution was statistically similar in both groups (p=0.067). Preterm delivery was significantly higher in diabetic women at 36.91 ± 1.94 weeks (p=0.025) as compared to non-diabetic women at 38.94 ± 1.81 weeks. The distribution of gravidity and parity was statistically similar in both groups as p-values were greater than 0.05.

The proportion of elective C-sections was significantly high in women with T1DM 21 (44.7%) as compared to controls 13 (18.6%) (p=0.0024) while the proportion of Normal vaginal delivery-NVD was significantly high in controls 45 (64.3%) (p=0.021) and proportions of emergency C-section were similar in both groups. (Table-2).

A comparison of neonatal outcomes between both groups is presented in (Table-3). APGAR score at 1 min and APGAR score at 5 min<7

were significantly associated with diabetic women 9 (19.1%) as compared to controls 3 (4.3%) (p=0.009) & 5 (10.6%) as compared to controls 1 (1.4%) (p=0.027) respectively. The proportion of NICU / SCBU admission was significantly high in diabetic women 23 (48.9%) as compared to controls 10 (14.3%) (p<0.0001) and the proportion of hypoglycemia was also significantly high in diabetic women 20 (42.6%) (p<0.0001). All other outcomes were statistically similar in both groups.

TABLE 1

Baseline Characteristics of Pregnant Women in Both Groups (n = 117)

A	B	Groups Type-1 DM n = 47	Non-Diabetic n = 70	p-values
Age years	Mean	29.38 ±5.27	31.23 ±5.28	0.067
	Min - Max	20 - 41	20 - 40	
Gestational Age Weeks	Mean	36.91 ±1.94	38.94 ±1.81	0.025
	Min - Max	28 - 40	31 - 41	
Gravida	PG	10 (21.3%)	13 (18.6%)	0.72
	Multigravida	37 (78.7%)	57 (81.4%)	
Parity	Nulliparous	10 (21.3%)	13 (18.6%)	
	Primiparous	2 (4.3%)	1 (1.4%)	0.58
	Multiparous	35 (74.5%)	56 (80%)	

TABLE 2

Comparison of Modes of Delivery between Both Groups (n = 117)

MOD	Groups Type-1 DM n = 47	Non-Diabetic n = 70	P-values
Elective CS	21 (44.7%)	13 (18.6%)	0.0024
Emergency CS	6 (12.8%)	12 (17.1%)	0.53
NVD	20 (42.6%)	45 (64.3%)	0.021

TABLE 3

Comparison of Neonatal Outcomes in Both Groups (n = 117)

A		Groups		Total
Type-1 DM **n = 47**		**Non-Diabetic** **n = 70**		
APGAR 1	< 7	9 (19.1%)	3 (4.3%)	0.009
	≥ 7	38 (80.9%)	67 (95.7%)	
APGAR 5	< 7	5 (10.6%)	1 (1.4%)	0.027
	≥ 7	42 (89.4%)	69 (98.6%)	
Macrosomia	Yes	7 (14.9%)	4 (5.7%)	0.087
	No	40 (85.1%)	66 (94.3%)	
IUFD	Yes	2 (4.3%)	0 (0%)	0.082
	No	45 (95.7%)	70 (100%)	
IUGR	Yes	2 (4.3%)	1 (1.4%)	0.322
	No	43 (91.5%)	69 (98.6%)	
RDS	Yes	8 (17%)	7 (10%)	0.23
	No	39 (83%)	63 (90%)	
NICU/SCBU Admission	Yes	23 (48.9%)	10 (14.3%)	<0.0001
	No	24 (51.1%)	60 (85.7%)	
Hypoglycemia	Yes	20 (42.6%)	1 (1.4%)	<0.0001
	No	27 (57.4%)	69 (98.6%)	

TABLE 4

Odds Ratios (n = 117)

A	OR T1DM	95% CI for OR	p-values
Mod of Delivery Cesarean section	2.4	1.1 – 5.2	0.02
APGAR Score 1 < 7	5.3	1.4 – 20.7	0.017
APGAR Score 5 < 7	8.2	0.9 – 72.7	0.058
NICU/SCBU Yes	5.7	2.4 – 13.9	<0.001
Hypoglycemia Yes	53.1	5.96 - 473.17	<0.0001

TABLE 5

Sample Size for Unmatched Case-Control Study

Two-sided confidence level(1-alpha)			95
Power (% chance of detecting)			90
Ratio of Controls to Cases			2
Hypothetical proportion of controls with exposure			27
Hypothetical proportion of cases with exposure:			63.82
Least extreme Odds Ratio to be detected:			4.77

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Sample Size - Cases	28	27	31
Sample Size - Controls	56	54	62
Total sample size:	84	81	93

Odds ratios were also calculated to compare the outcomes between T1DM and controls. T1DM pregnant women have a significantly high rate of C-section (OR=2.4, 95% CI 1.1 – 5.2; p=0.02), APGAR Score<7 at 1 (Or=5.3, 95% CI 1.4–20.7; p=0.017), T1DM pregnant women group have also a significantly high rate of NICU/SCBU admission of their newborns (OR=5.7, 95% CI 2.4–13.9; p<0.001) and also neonatal hypoglycemia (OR=53.1, 95% CI 5.96 - 473.17; p<0.0001).

Discussion

The management of type 1 diabetes mellitus (T1DM) in pregnancy is challenging because of the increased risk of fetal and maternal complications. Prenatal counseling including glucose level control and a "special antenatal care program" is required to achieve better perinatal and pregnancy outcomes [5]. Even the Prolonged duration of T1DM disease can negatively affect the neonatal outcome if not controlled [10]. Potential adverse effects of diabetes on pregnancy outcomes, the presence of diabetes-related complications, medication-related risks, effect of physiological changes of pregnancy on glycemic control, all of this should be discussed with the patients. However, many pregnancies are unplanned, and many women do not receive appropriate counseling before conceiving [11].

The main goal of treatment by achieving better glycemic control is to reduce maternal complications and neonatal adverse outcomes (congenital anomalies, preeclampsia, macrosomia, and Hypoglycemia.) [5, 12, 13]. A multidisciplinary team that consists of an endocrinologist, obstetrician, educators, and nutritionist should be established to achieve optimal patient care and it is the key to better outcomes. Although a potentially modifiable factor, suboptimal glycemic control is not entirely responsible for adverse outcomes of infants born to mothers with T1DM [14]. The Diabetes Control and Complications Trial has shown that it is possible to reduce morbidity owing to T1DM before, during, and after pregnancy, but not to eliminate it [15, 16]. The ADA guidelines 2023 also strongly advise women with diabetes who are planning to become pregnant to maintain HbA1c<6.5 and to achieve glucose levels as close to normal as is

safely possible, to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications [30]. In our study, we have shown that 70.2% of T1DM pregnant women get pregnant on high-level HbA1c above target which is HbA1c more than 7%, which is the opposite of the recommended target HbA1c less than 6.5%.

The risk of macrosomia and having an LGA neonate was found to be higher in pregnancies with diabetes, especially in women with excess gestational weight gain [17]. In our study, we found that the proportion of elective C-sections was significantly higher in women with T1DM was 57.5% compared to the control group 35.7% (including elective and emergency C-sections in both tow groups) due to either medical concerns (previous C-section, emergency C-section… etc.), patient's desire or medicolegal concerns. Neonatal macrosomia proportion was 14.9% with only 3 cases ended up by shoulder dystocia. Low rates of such complications may be explained by the slightly higher cesarean section rates in patients with T1DM, as in our study [18].
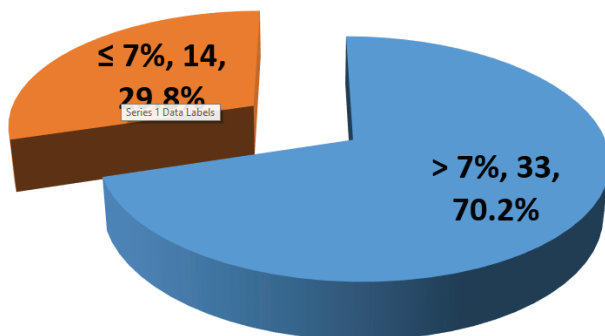

Figure 1) *Hemoglobin A1C levels in T1DM Pregnant Women at conception (n=47).*

In addition, Intra-uterine fetal growth restriction, preterm labor, and IUFD are other obstetric complications associated with diabetes in pregnancy [12, 13, 19]. In our study, the mean gestational age in T1DM pregnant women group was 36.91 ± 1.94 weeks (p=0.025). The IUGR rate was 4.3% and in non-diabetic pregnant women was only 1.4%. IUFD in T1DM pregnant women group was 36.91 ± 1.94

weeks (p=0.025). IUGR rate was also 4.3% and in non-diabetic pregnant women was 0%, no IUFD case was demonstrated in this group.

Infants of patients with diabetes are also at higher risk of hypoglycemia, respiratory distress, and intensive care admission [20-21]. Neonatal hypoglycemia screening in all newborns from diabetic mothers is mandatory from the first hour of life, due to the consequences of these episodes, independent of the initial good and balanced presentation at birth [22]. Most studies describe hypoglycemia as levels under 30-50mg/dl (1.6-2.8 mmol/l) in the first 24 hours of post-natal life and 45-50mg/dl (2.5-2.8 mmol/L) after 24 hours [22, 23, 26]. The threshold levels of different studies for the definition of neonatal hypoglycemia are under 45mg/d (2.5mmol/l) or 40 mg/dl (2.2mmo/l) or 36mg/dl (2 mmol/l) (22, 23, 24-28). In a recent study Neonatal hypoglycemia is defined as blood glucose levels below 40 mg/dL [29]. We found in our study that pregnant women with T1DM have a higher frequency of perinatal complications, especially neonatal hypoglycemia (blood glucose levels below 40 mg/dL) was 42.6% compared to only 1.4% in the control group and newborn intensive care admission to SCBU or NICU 48.9% versus 14.3% in the control group, even rate of neonatal respiratory distress was higher in T1DM pregnant women group 17% (Figure-2). APGAR scores in one and five-minute below 7 are also used for evaluating neonatal outcomes and we found in our study to be 10.6% compared to 1.4% in to control group.
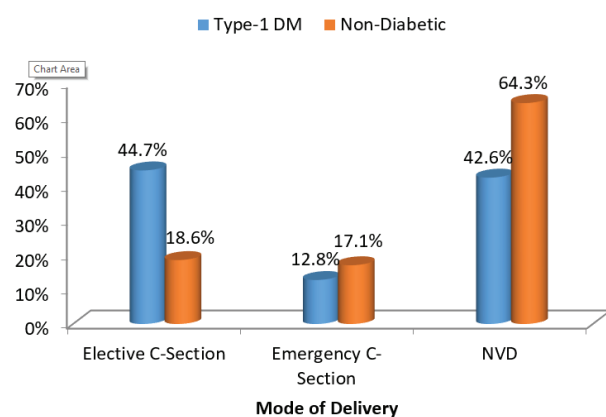
Figure 2) *Comparison of Modes of Delivery between Both Groups (n = 117).*
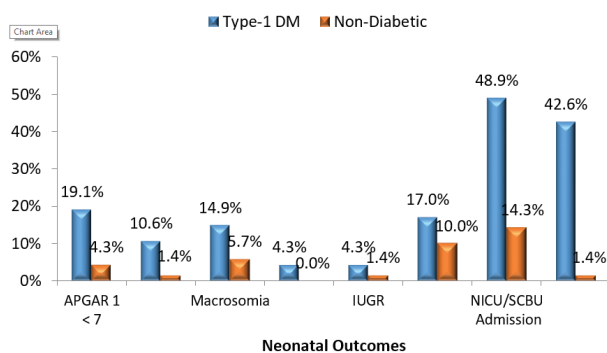
Figure 3) *Comparison of Neonatal Outcomes in Both Groups (n = 117).*

The ADA 2023 guidelines also strongly advise preconception counseling and discussion regarding family planning and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until an individual's treatment plan and A1C are optimized for pregnancy [30].

Conclusions

Type 1DM is a challenging problem during pregnancy in terms of having better maternal and neonatal outcomes. The high prevalence of unplanned pregnancy in T1DM women without optimal control of HbA1c and poor pre-pregnancy care, preconception counseling for all T1DM women who wish for pregnancy must be improved to improve outcomes whether maternal or fetal for this high-risk group. In this retrospective analysis, we demonstrate significant some unfavorable neonatal outcomes of T1DM pregnant women. To address this and to improve the effectiveness of interventions for the treatment of pregnant women with T1DM, future quality improvement measures will need to be implemented to reinforce strict follow-up of the patients by the endocrinology, high-risk pregnancy obstetrician, and perinatology divisions for better pregnancy outcomes.

Authors contribution

AM and OM concepted the study and design and are the main contributors to the writing of the manuscript. AM was responsible for data collection. AM and OM wrote the manuscript. AM, OM, JR, and HA all edited and reviewed the manuscript, and approved the final version for publication. OM is the project leader and general instructor.

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