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Original Article

Outcomes of type 1 diabetes mellitus in pregnancy; effect of excessive gestational weight gain and hyperglycaemia on fetal growth

Mohammed Bashir [a,*], Emad Naem [a], Faten Taha [b], Justin C. Konje [c], Abdul-Badie Abou-Samra [a]

[a] Qatar Metabolic Institute, Hamad Medical Corporation, Doha, Qatar
[b] Department of Obstetrics and Gynaecology, Women's Wellness and Research Centre, Hamad Medical Corporation, Doha, Qatar
[c] Women's Clinical Services Management Group (WCMG), Sidra Medicine, Doha, Qatar

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ABSTRACT

Aims: To study pregnancy outcomes in patients with type 1 diabetes mellitus (T1DM) and the factors associated with poor outcomes.
Methods: A retrospective study of 110 patients with T2DM who attended our diabetes in pregnancy clinic at the Women's Wellness and Research centre, Doha, between March 2015 and December 2016 and 1419 normoglycaemic controls.
Results: There was no difference in age, weight, and BMI between the two groups. The incidence of macrosomia, shoulder dystocia and stillbirth were similar in the two groups while that of pre-term labour, pre-eclampsia, Caesarean section (CS), large for gestational age (LGA), neonatal ICU (NICU) admission and neonatal hypoglycaemia were significantly higher in the T1DM than in the control group. From a multivariate regression analysis, excessive gestational weight gain was associated with increased risk of LGA (OR 4.53; 95% CI [1.42–14.25]). Last trimester HBA1c was associated with increased risk for macrosomia [OR 2.46, 95% CI [1.03–5.86)]; LGA [OR 3.25, 95% CI [1.65–6.40)]; increased risk for C-section (OR 1.96, 95% CI [1.12–3.45]), and increased risk of NICU admission (OR 2.46, 95% CI [1.04–5.86]). The changes in HBA1C between the first and last trimester HBA1c was associated with a reduction in the risk of LGA [OR 0.46, 95% CI [(0.28–0.75)]
Conclusion: T1DM in pregnancy is associated with adverse pregnancy outcomes compared to the general population. Reducing gestational weight gain and improving glycaemic control might improve pregnancy outcomes.

1. Introduction

Type 1 diabetes mellitus (T1DM) is associated with an undisputed increased risk of maternal and fetal morbidity and mortality [1]. One of the five years targets of the St. Vincent's declaration was to "achieve pregnancy outcome in the diabetic woman that approximates that of the non-diabetic woman" [2]. It has been 29 years since this declaration was signed and this target has not been achieved by many countries [3]. Achieving normal or near normal glucose levels in patients with type 1 diabetes is challenging. The continuous change in food intake and insulin sensitivity during pregnancy result in unpredictable fluctuation in glucose levels needing frequent adjustment of insulin doses. As a result the risk of moderate and severe hypoglycaemia is increased substantially in patients with T1DM [4]. Most of the guidelines recommend to adjust the glucose targets during pregnancy in patients with T1DM to avoid undue hypoglycaemia [5,6]. In addition to poor glycaemic control, pre-pregnancy BMI, excessive gestational weight gain and smoking are recognised risk factors for poor pregnancy outcomes in patients with T1DM [7].

There is evidence that pregnancy outcomes in T1DM have improved over time in some countries [8]. There are not too many studies that have reported on pregnancy outcomes in T1DM patients from the Middle-East and North Africa (MENA) region. This study aims to describe the outcomes of pregnancies complicated with T1DM and to examine the effects of maternal weight and glycaemic control on pregnancy outcomes.

* Corresponding author. Qatar Metabolic Institute, Hamad Medical Corporation, P.O Box 3050, Doha, Qatar.
E-mail addresses: mbashir@hamad.qa, mohdbashir80@gmail.com (M. Bashir).

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2. Methods

This was a retrospective cross-sectional study undertaken at the Women's Wellness and Research Centre (WWRC) formely known as the Women's Hospital of Hamad Medical Corporation, Doha, Qatar. The WWRC is the largest maternity hospital in the state of Qatar delivering between 16-18,000 women per year. The diabetes clinic in the WWRC is the largest provider of diabetes care during pregnancy in the state of Qatar.

We reviewed the outcomes of pregnancies in women with T1DM that were managed in our institution between March 2014 and December 2017. For controls, we identified women without diabetes based on normal oral glucose tolerance (OGTT) test screening result. Pre-pregnancy weight is recorded in the first visit based on patient self-report and is found on the electronic medical records as '' pre-pregnancy weight''. If this was not recorded, we used the last recorded weight before conception (provided this was within the last 6 months) as pre-pregnancy weight otherwise weight was considered as a"missing" variable. We took the last height measured before conception or the height recorded in the first trimester as a variable for calculating the BMI. Maternal age was taken as the age of the mother at conception. Macrosomia was defined as birth weight >4000 g; large for gestational age (LGA) was birth weight >90th percentile; small for gestational age (SGA) as birth weight <10th percentile, and pre-term delivery as delivery <37 weeks of gestation. We calculated the average weekly gestational weight gain (wGWG) ((weight at delivery (kg)-weight at conception (kg))/(Gestational age at delivery (weeks)). Gestational weight gain (GWG) was also classified as excessive or adequate if it exceeds the institute of medicine (IOM) recommendations [9]. The differece between the first trimeseter and last (third) trimeseter HBA1c was calculated as (first trimeter HBA1C-last trimeseter HBA1C). The study was approved by the Institutional Review Board (IRB) of Hamad Medical Corporation. Only pregnancies that continued after 24 weeks gestation were included in the outcome analysis.

Statistical analysis was performed using STATA 15 software (College Station, TX: Stata Corp LP). Variables are expressed as a percentage (%) for frequencies and mean ± standard deviation for normally distributed continuous variables. Student *t*-test was used to compare continuous variables between the two groups. Univariate Chi-square test and multivariate analysis were used to compare categorical data. Multivariate logistic regression analysis was performed to examine the independent effects of first trimester HBA1C, pre-conception BMI, GWG and last trimester HBA1c on macrosomia, LGA, Caesarean section (C-section), neonatal intensive care Unit (NICU) admission and neonatal hypoglycaemia. $P < 0.05$ was considered significant.

3. Results

A total of 110 women with T1DM (index group) and 1419 non-diabetics (control group) were included in this study. Five pregnancies (4.6%) in the index group were excluded from our analysis of outcomes because they ended as miscarriage prior to 24 weeks gestation (i.e. ended before viability).

Table 1 shows the baseline characteristics in the two groups. There was no difference between the two groups in age, pre-pregnancy weight, pre-pregnancy BMI, and the prevalence of overweight and obesity. T1DM patients were more likely to be Qatari nationals compared to the normal group.

As shown in Table 2, the average duration of diabetes mellitus at the time of booking was 13.7 ± 4.8 years. The mean first trimester HBA1C was 7.9 ± 1.5% (63 mmol/mol), and the mean third trimester HBA1C was 6.70 ± 1.4% (50 mmo/mol). The target pre-pregnancy HBA1C of ≤7.0% (53 mmol/mol) was met by 38 patients (34.6%) and the target last trimester HBA1C of ≤6.5% (48 mmol/mol) was met by 46 patients (41.8%).

Table 1
Baseline characteristics. Data are expressed as means ±SD or actual number of subjects and percentages.

	DM-1 (110)	Control (1419)	P value
Age (Years)	29.5 ± 5.0	29.6 ± 5.5	0.8189
Pre-pregnancy weight (kg)[a]	69.7 ± 14.3	72.8 ± 16.9	0.0588
Pre-pregnancy BMI*(kg/m^2)[a]	27.7 ± 5.5	28.8 ± 6.1	0.0794
BMI Categories			0.109
Normal (18–24.9)	37 (35.2%)	379 (27.7%)	
Overweight (25–29.9)	48 (36.2%)	467 (34.2%)	
Obese (≥30)	39 (28.6%)	521 (38.1%)	
Ethnicity			<0.001
Qatari	59 (53.6%)	535 (37.7%)	
Arab	41 (37.3%)	512 (36.1%)	
Asian	7 (6.4%)	305 (21.5%)	
Other	3 (2.7%)	67 (4.7%)	

[a] 3.7% are missing.

Table 2
Summary of T1DM characteristics, glycaemic control, and medications. Data are expressed as means ±SD or actual number of subjects and percentages.

	T1DM (110)
Mean Duration of diabetes (years)[a]	13.7 ± 7.8
Mean First trimester HBA1C (%)	7.9 ± 1.5
≤7.0% (53 mmol/mol)	38 (34.6%)
>7.0% (53 mmol/mol)	72 (65.4%)
Mean Last Trimester HBA1C (%)	6.7 ± 1.4
≤6.5% (48 mmol/mol)	46 (41.8%)
>6.5% (48 mmol/mol)	64 (58.2%)

[a] <1% missing.

Table 3 summarises pregnancy outcomes in the two groups. T1DM patients gained significantly more weight during pregnancy compared to the control group (wGWG 0.28 ± 0.17 kg/week vs 0.19 ± 0.17 kg/week; $p < 0.001$). T1DM group delivered earlier than the control group with a mean GA at delivery of 36.5 ± 2.22 weeks vs 38.8 ± 2.06 weeks ($p < 0.001$) respectively. There was no difference between the two groups in the incidence of pregnancy induced hypertension (PIH), macrosomia, shoulder dystocia and stillbirth. The incidence of small for gestational age was lower in the T1DM group compared to the control group (6.7% vs 14.2% $p < 0.001$). Apart from the above all other outcomes were worse in the T1DM group compared to the control group.

Multivariate regression analysis showed excessive GWG were associated with (OR4.53; 95% CI [1.42–14.45]) after correction for age, pre-pregnancy BMI, first trimester HBA1c and last trimester HBA1C (Table 4). Last trimester HBA1c was associated increased risk for macrosomia [OR 2.46, 95% CI [1.03–5.86)]; LGA [OR 3.25, 95% CI [1.65–6.40)]; an increased risk for C-section (OR 1.96, 95% CI [1.12–3.45]), and an increased risk of NICU admission (OR 2.46, 95% CI [1.04–5.86]) after correction for age, BMI, GWG and first trimester HBA1C. Furthermore, after correcting for age, BMI and gestational weight, the difference between the first and last trimester HBA1c was associated with a reduction in LGA [OR 0.46, 95% CI [(0.28–0.75)].

4. Discussion

This study showed that pregnancies in women with T1DM are at higher risk of maternal and neonatal complications compared to the background population. T1DM was associated with an increased risk of pre-eclampsia, induction of labour, pre-term