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IMPACT OF DIFFERENT *DIABETES MELLITUS* TYPES ON PREGNANCY OUTCOMES OF PREGNANT WOMEN

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ABSTRACT

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both. It is the most common metabolic disorder that occurs during pregnancy. It has two clinical patterns; either gestational or pregestational diabetes. Pregnancy in women with diabetes mellitus is associated with an increased risk of congenital malformations, obstetric complications and neonatal morbidity. This study aimed to evaluate the impact of different types of diabetes mellitus without vascular changes on maternal and fetal outcomes. The study was done at Mosul General hospital - Department of Obstetrics and Gynecology- Mosul /Iraq during the period from September 2018 to September 2019 and included 100 cases of gestational and pregestational diabetic pregnant women. The results showed that mean age of the studied group was (28.7±6.45) ranging from (18 to 41) years and the mean BMI of the studied group was (25.9±3.9) ranging from (18 to 32) and 44% of PGDM and 32% of GDM patients were obese. There was no statistically significant difference in positive family history of diabetes and previous history of congenital fetal malformation, Intra Uterine Fetal Death and gestational diabetes mellitus between the two groups. There was no statistically significant difference in gestational age at delivery and mode of delivery in current pregnancy between the two groups. Both gestational or pregestational showed no statistical difference between maternal and fetal outcomes. It can be concluded from our study that in either diabetes, gestational or pregestational, there was no statistical difference between maternal and fetal outcomes. Optimal control of blood glucose resulted in lower neonatal and maternal complications. Further studies on large geographical scale and larger sample size are required to support our conclusion.

KEYWORDS: Pregestational diabetes; Gestational diabetes; Maternal; Fetal outcomes.

INTRODUCTION

Diabetes is disorder in which the body doesn't produce insulin or there is resistance to it. In Type 1 diabetes, the body produces little or doesn't produce insulin at all due to auto destruction of B cells of the pancreas also called (juvenile onset diabetes). In Type 2 diabetes the body doesn't respond to insulin due to insulin resistance also called (adult-onset diabetes).[1]

Overt Diabetes Mellitus is defined as women with a random plasma glucose level greater than 200mg/dl plus classic signs and symptoms such as polydipsia, polyuria and unexplained weight loss or a fasting glucose exceeding 125mg/dl are considered by the ADA (American Diabetes Assoctiation-2004) to have overt diabetes.[2]

Gestational diabetes mellitus (GDM) is operationally defined as impaired glucose tolerance with onset or first recognition during pregnancy. Its diagnosis is based on single step procedure. In accordance to World Health Organization recommendations, the guideline endorses 2h 75g oral glucose tolerance test, irrespective of last meal timings with a cutoff value of ≥140 mg/dL using a plasma standardized glucometer.[3] The pre-existing diabetes in pregnancy refers to diabetes diagnosed before pregnancy. The prevalence of pre-existing diabetes has increased in the past decade primarily as a result of the increase in type 2 diabetes. Studies of women with preexisting diabetes show higher rates of complications compared to the general population.[4]

Maternal complications of diabetes mellitus include increase in asymptomatic bacteriuria, urinary tract infections, preeclampsia, polyhydramnios which may lead to preterm labor, abruption placenta, postpartum hemorrhage which in turn increases operational delivery. Fetal outcomes include intra uterine fetal death, respiratory distress syndrome, hypoglycemia, congenital malformations and hyperbilirubinaemia.[5]

All women of childbearing age with diabetes should be counseled about the importance of tight glycemic control prior to conception. Observational studies show an increased risk of diabetic embryopathy, especially anencephaly, microcephaly, congenital heart disease, and caudal regression, directly proportional to elevations in HbA1C during the first 10 weeks of pregnancy.[6]

Glycemic Targets: (Fasting < 95mg/dL, 1-hour PP (post prandial < 140mg/dL, 2 hr PP <120mg/dL). Fasting and postprandial self-monitoring of blood glucose are recommended in both GDM and preexisting diabetes in pregnancy to achieve glycemic control. Due to increased red blood cell turnover, HbA1C is slightly lower in normal pregnancy than in normal nonpregnant women. The HbA1C target in pregnancy is 6-6.5%; <6% may be optimal if this can be achieved without significant hypoglycemia, but the target may be relaxed to <7% if necessary, to prevent hypoglycemia.[7]

PATIENTS AND METHODS

This cross-sectional study of pregnant diabetic women who attended to Mosul General hospital - Department of Obstetrics and Gynecology- Mosul /Iraq during the period from September 2018 to September 2019. Of the 135 diabetic women, 35 cases were excluded from the study due to missing during follow up (17 cases), and 18 cases refused participation. One hundred diabetic pregnant women were included in the study and were eligible for the final analysis.

Counseling of participating women, clear caption of the intervention, and an informed written consent was then taken from all of them. Medical, past, surgical and obstetric histories were reviewed, general and abdominal examinations were carried out, and findings were recorded.

Estimation of gestational age (GA) was done from the date of LMP in women with prior regular periods or estimated from early ultrasound scan (USS) at 7 weeks' gestation. GA was verified by the 13th week USS. Fetal anomaly scan was arranged at around 20 weeks' gestation. Then women were followed up as per the standard pregnancy care for diabetes where they attended every 2 weeks until 28 weeks' gestation, every 1 weeks until 36 weeks' gestation then twice weekly thereafter until delivery. Targeting a fasting glucose level of 60-100mg/dl, 1-hour postprandial glucose below 120mg/dl, and glycosylated hemoglobin (HbA1c) below 6.1%.[8] All women were on insulin therapy.

Pregnant women with pregestational diabetes mellitus (type 1 or type 2 diabetes) without vasculopathy, pregnant women diagnosed with gestational diabetes mellitus (GDM) by using the 75gm 2-hour oral glucose tolerance test (OGTT), and singleton pregnancy were included in the study.

Women with hypertension, thyroid or connective tissue disorders, women with multifetal gestations, uncontrolled diabetics, and abnormal glycosylated hemoglobin (HbA1c) level, above 6.1% were excluded. The study groups were divided into two main groups:

a) Group I included 50 pregnant women with pregestational diabetes mellitus (Type 1 and Type 2 DM) without vascular changes.
b) Group II included 50 pregnant women with gestational diabetes. GDM was generally diagnosed by OGTT in the second half of pregnancy.

The OGTT was performed in the morning after a nightlong fasting from 8 to 12h. The criteria for diagnosing GDM were at least one abnormally high out of three plasma glucose value measurements during the 75gm OGTT (normal values: a fasting level <92mg/dl, 1-hour level <180mg/dl, 2-hour level <153mg/dl). The venous blood glucose levels were measured using the glucose oxidase method (Glucose Analyzer; Beckman, Brea, CA). The glucose tolerance was classified by the latest criteria of the International Association of Diabetes in Pregnancy Study Group (IADPSG)[9] by using the 75gm 2-hour oral glucose tolerance test (OGTT) at 24-28week gestation.

Fetal investigations included **a**) CTG **b**) Trans-abdominal ultrasound examination for fetal viability, gestational age confirmation, measurement of the fetal abdominal circumference (AC), and estimation of expected fetal birth weight (EFBW) Hospital admission of the patients will be at the time of delivery or if developed any complication of diabetes. **c)** Neonatal birth weight is measured in grams upon delivery. **d)** Large-for-gestational-age fetuses are defined as those with birth weight above the 90th centile for age, and whose birth weight falling below 10th centile is defined as small-for- gestational-age. **e)** Mode of delivery will be according to hospital protocol.

Statistical analysis

Data were analyzed by Statistical Package for the Social Sciences software for analysis (SPSS version 20). Qualitative represented as number and percentage and quantitative represented by mean±SD. The difference and association of qualitative variable was estimated by Chi-square test (X^2) and quantitative parametric groups by t-test, non-parametric by Mann Whitney, correlation by Pearson's correlation and regression. P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS

Table (1): Socio-demographic data of the studied groups.

Variable	pre-GDM N=50		GDM N=50		P
Maternal age (years)					
Mean ± SD	27.9±5.8		29.5±7.1		0.22
Range	(18-42)		(19-41)		
BMI (kg/m^2)					
Mean ± SD	25.9±3.9		26.2±4.2		0.71
Range	(18.2-32)		(18.9+34)		
	No	**%**	**No**	**%**	
Underweight <18.5	0	0%	0	0%	0.46
Normal 18.5-24.9	18	36%	22	44%	
Overweight 25-29.9	10	20%	12	24%	
Obese > 30	22	44%	16	32%	
Gravidity:					
Primigravida	7 14%		10	20%	0.59
Multigravida	43 86%		40	80%	
Parity:					
Nulliparous	8	16%	4	8%	0.17
Multiparous	42	84%	46	92%	
Abortion	17	34%	25	50%	0.054
Positive Family history of DM	12	24%	6	12%	0.069
Previous history					
GDM	0	0%	2	4%	0.082
CFMF*	1	2%	0	0%	0.082
IUFD**	2	4%	1	2%	0.274
Neonatal death***	3	6%	3	6%	1

CFMF: cardiac abnormality.
**IUFD: unexplained IUFD.
***Neonatal death=due to cardiac abnormality and complication of prematurity
P -value is non-significant.

Table (2): Comparison between studied groups regarding mean Fasting, Postprandial blood sugar and HbA1C (N=100).

Variable	Pre-GDM N=50	GDM N=50	P Value
FBS			
Mean ± SD	120±20.4	111± 21.5	0.034*
Range	(80-170)	(90-230)	
PPBS	163.1 ±68.4	155.9± 61.2	0.580
	(95-300)	(98-300)	
HbA1c	6.0±0.6	5.7± 0.7	0.023*
	(5.1-8)	(5.3-9.5)	

*Statistically significant difference (P ≤ 0.05).
**Statistically highly significant difference (P ≤ 0.001).

Table (3): Comparing maternal complications between studied groups.

Maternal Complications	Total N =100%		Pre-GDM N=50 %		GDM N=50 %	
No complication	42	42%	24	48%	18	36%
Gestational HTN	14	14%	9	18%	5	10%
PET	15	15%	5	10%	10	22%
PROM	1	1%	0	0%	1	2%
Preterm labor	9	9%	5	10%	4	8%
Polyhydramnios	17	17%	10	20%	7	14%
Oligohydramnios	9	9%	7	14%	2	4%
ction (UTI candidiasis)	9	9%	6	12%	3	6%

Table (4): Comparison between the studied groups regarding fetal outcomes.

Fetal Complications	Pre-GDM N=50 %	GDM N=50 %	P
Macrosomia≥4kg	13 26%	7 14%	0.067
IUFD*	2 4%	1 2%	0.274
Hypoglycemia	1 2%	0 0%	0.158
Preterm baby	5 10%	4 8%	0.382
CFMF**	1 2%	0 0%	0.158
NICU admission	5 10%	4 8%	0.382
Birth injuries	0 0%	0 0%	---
Variables	**Pre-GDM (n=50)**	**GDM (n=50)**	**P value**
Neonatal weight (Kg)	3.4 ± 0.5	3.6 ± 0.8	0.137
Apgar score at 1min	8.7 ± 1.1	9.0 ± 1.2	0.195
Apgar score at 5min	9.1 ± 1.5	9.5 ± 1.8	0.230
al RDS within 1st hour of delivery	57.5 ± 11.2	55.2 ± 13.2	0.355
GA at delivery:			
<37weeks	5 10%	4 8%	0.696
≥37weeks	45 90%	46 92%	
Mode of delivery			
CS	32 64%	29 58%	0.340
NVD	18 36%	21 42%	

Table 5: Ultrasound findings among the studied group (N=200).

Variables	Total n=100 %	Pre-GDM n=50 %	GDM n=50 %
Normal	65 65%	27 54%	38 76%
IUFD	3 3%	2 4%	1 2%
Polyhydramnios*	17 17%	10 20%	7 14%
Oligohydramnios**	9 9%	7 14%	2 4%
Placenta previa	3 3%	3 6%	0 0%

One woman might have more than one finding.
*polyhydraminous AFI more than 25cm.
**oligohydraminous AFI less than 5cm.

This table shows that (65%) of the studied group had normal U/S, and (17%) of them had Polyhydramnios, Oligohydramnios was found in (9%) of them.

The results in the current study showed that 50% of studied group had pregestational DM and 50% had gestational DM, and revealed that the mean age of studied groups was (27.9±5.8) years in PGDM and (29.5±7.1) years in GDM with no statistically difference in maternal age between two groups. The mean BMI of studied groups was (25.9±3.9) ranging from (18.2-32) and 44% of PGDM and 32% of GDM patients were obese. The study revealed that there was no statistically significant difference in positive family history of diabetes and previous history of congenital fetal malformation, Intra Uterine Fetal Death and gestational diabetes mellitus between the two groups showed that the 86%, 80 % of PGDM and GDM groups was multigravida respectively. The present study revealed that 34% of PGDM and 50% of GDM has previous history of abortion (Table 1).

In the current study, 92% of GDM group was delivered at gestational age >37 weeks and 8% of them were preterm and in regard to mode of delivery, 64%, 58% of PGDM and GDM patients respectively delivered by CS.

The present study evaluated US findings among participants mothers and found that (65%) of the studied group had normal U/S, and 17% of them had Polyhydramnios, and Oligohydramnios was found in only (9%) of them (Table 5). The present study revealed that there was no statistically significant difference in maternal complications between the two groups as gestational hypertension was (18%VS 10%) respectively, PROM was (0 VS 2%) respectively, preterm labor (10% VS 8%) respectively, infection was (12% VS 6%) respectively, polyhydramnios (20% vs 14%) respectively, and oligohydramnios (14% VS 4%) respectively (Table 3).

The current study revealed that there was no statistically significant difference in fetal complications between the two groups. Also there was no statistically significant difference between GDM and pre-GDM groups regarding neonatal weight (3.4±0.5) and (3.6±0.8) respectively, Apgar score at 1&5 minutes (8.7±1.1 and 9.1±1.5) and (9.0±1.2 and 9.5±1.8) respectively and neonatal RDS (57.5±11.2 and 55.2±13.2) respectively (Tables 4&5).

DISCUSSION

In as study by Salge et al.[11], it was found that the mean

age of the studied women was (28.5±5.71) years. In agreement with the present study, the study of Sugiyamaa et al.[12] found that there was no significant difference in maternal age between the 2 groups.

The study of Soliman et al.[13] assessed BMI and found that 55% of DM, 38% of GDM and 25.6% of controls were obese (p<0.001). Pregestational BMI was higher in ODM (Overt diabetes) than in GDM, but gestational weight gain was not significantly different between these groups.[12] Maternal overweight and obesity are associated with multiple congenital malformation and fetal loss (miscarriage, stillbirth, neonatal mortality, and perinatal morbidity). When obesity and diabetes coexist, the risk of malformations is further increased, with different contribution of obesity and hyperglycemia to different anomalies.[14]

There was a higher proportion of multigravida than secundigravida and primigravida women 37.1%, 17.7%, and 14.5% respectively) among women with GDM that was in accordance with our study in which 14% of the studied group were primigravida, (82%) were multiparous.[15] In the study of Shefali et al., 2006, compared to the pregnancy outcomes in mothers with PGDM and GDM. The prevalence of abortions in the GDM group in his study was 2.7% compared to 10.1% in the PGDM group showing that PGDM are at increased risk for abortions.[16]

In contrast to us, the study of Stogianni et al.[17] among pregnant women with any diabetes type more delivered preterm (21% vs. 6%, p=0.0001) and by CS (30% vs. 19%, P=0.05) compared to those not complicated by diabetes. The mean gestational age at delivery was 37 weeks (38.7 in the control group). Seventy-four (56%) mothers delivered vaginally (7 required forceps assistance) and 58 (44%) required cesarean section. In comparison, 22% of controls underwent cesarean section, twenty-four women underwent emergency cesarean section, and the most common indication was unsatisfactory progress of labor.[18] Soliman et al.[13] revealed that Preterm delivery was significantly higher in women with DM and GDM (13.7% and 9%, respectively versus normal women (6.4%); p<0.001). In another study of Shefali et al.[16] found that preterm delivery was 6 (7.6%) in PGDM and 12 (8.2%) in GDM.

In agreement with us, another study of Macintosh et al.[19] revealed that statistically significant increases were confined to anomalies of the nervous system (prevalence ratio 2.7, 1.5 to 4.4; P<0.001) and congenital heart disease (prevalence ratio 3.4, 2.5 to 4.6; P < 0.001). The prevalence of major congenital anomaly was 46/1000 births in women with diabetes (48/1000 births for type 1 diabetes; 43/1000 for type 2 diabetes), more than double that expected. This increase was driven by anomalies of the nervous system, notably neural tube defects (4.2-fold), and congenital heart disease (3.4-fold). Anomalies in 71/109 (65%) offspring were diagnosed antenatally.

Women with history of GDM are at an increased risk of adverse maternal and perinatal outcome and at increased risk of future diabetes predominantly Type II including their children and therefore there are two generations at risk.[20] The present study evaluated US findings among participants mothers and found that (76%) of the studied group had normal U/S, and 14% of them had Polyhydramnios, Oligohydramnios was found in only (4%) of them.

Poorly managed gestational diabetes is associated with fetal macrosomia and polyhydramnios, but the pathogenesis has not been elucidated yet.[21] Any degree of glucose intolerance during pregnancy is associated with adverse maternal and fetal outcome. The adverse maternal complications include hypertension, preeclampsia, urinary tract infection, hydramnios, increased operative intervention and future DM.[22]

Another study of Soliman et al.[13] revealed that Pregnant women with DM or GDM had higher prevalence of hypertension versus normal controls (9.9%, 5.5% and 3.5%, respectively; p<0.001). GDM is associated with an increased risk of complications for both the mother and the child. The rate of preeclampsia and cesarean section is increased in the mother and the risk of macrosomia is increased in the newborn.[18]

In agreement with our study, the study of Sugiyamaa et al.[12] found that no significant differences in neonatal outcomes were observed between the GDM and ODM groups. LGA infants are a well-recognized and significant complication of GDM. Other studies have also demonstrated higher rates of abnormalities in pregnancy outcomes in PGDM compared to GDM.[23] Also, Stogianni et al.[17] assessed Frequency of LGA among all mothers, with and without diabetes, was 21.6% (60/278) and among those without diabetes 17.0% (23/135).

Studies of women with preexisting diabetes show higher rates of complications compared to the general population, including perinatal mortality, congenital malformations, hypertension, preterm delivery, large-for-gestational age infants, Caesarean delivery and other neonatal morbidities.[19] In the previous study of Owens et al. found that there was no difference in mean birth weight between groups (3.54kg) and controls. There was an increase in babies born >4kg to women with T1DM compared to matched controls. Neonatal hypoglycemia was more prevalent in offspring of both T1 DM and T2 DM pregnancies when compared to matched-controls and higher in offspring of T1DM than T2DM. The stillbirth rate was higher in babies of T1DM mothers compared to controls, but no difference was seen in mothers with T2 DM.[24]

Babies born to women with diabetes have significantly higher rates of being large for gestational age (LGA) (birth weight >90th percentile for gestational age and

sex), macrosomia (birth weight >4,000g or 8lb 13 oz), and neonatal hypoglycemia.[23] In the study of Prakash et al., 2017, the deaths occurred in neonates with birth weight which was less than average for gestational age.[18] Similarly, in the study by Sreelakshmi et al.[25], Respiratory distress was more common in neonates with above average birth weight. It was less in neonates born to mothers with optimal BS control. However, this was not an expected finding.

Respiratory distress was noted more commonly in the intervention arm of the trial done by Crowther et al.[26]

Serious perinatal complications specifically attributable to gestational diabetes are in general rare.[27] Women with PGDM had significantly higher fasting plasma glucose [p<0.034] levels compared to GDM.[16]

In agreement with our study, the study of Owens et al.[24] found that overall, the mean HbA1C in pregnancy is lower in women with T2 compared to T1 DM (5.8 vs. 6.6%, p=0.001). In each trimester and prior to delivery, mean HbA1C is also significantly lower in women with T2 compared to T1 DM and in both groups HbA1C improves as pregnancy progresses reaching a nadir of 6.4% and 5.7% in women with T1 and T2 DM respectively at term.

In contrast to us, the study of Macintosh et al.[19] found that most women (1606; 68%) recorded measurement of glycaemic control by 13 weeks of pregnancy. Diabetes during pregnancy is an increasingly common metabolic disorder, associated with significantly increased risks for both mother and child, Pregnancies complicated by diabetes are associated with significantly increased risks for both mother and child.[17]

Obesity and overweight in women during the childbearing period appear to contribute to the occurrence of high rates of dysglycemia during pregnancy. Measurements to reduce obesity during the childbearing period and accurate glucose control during pregnancy are highly required to prevent any morbidity during pregnancy of women with DM and GDM.[13]

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