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ORIGINAL ARTICLE

Effect of Different Types of Diabetes Mellitus without Vascular Changes on Maternal and Fetal Outcomes

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ABSTRACT

Background: Pregnancy in women with diabetes mellitus is associated with an increased risk of congenital malformations, obstetric complications and neonatal morbidity. The current study was aimed to assess the effect of different types of diabetes mellitus without vascular changes on maternal and fetal outcome**s.**

Methods: This was a cross sectional study done at Zagazig university hospital and included 50 cases of gestational and pregestational diabetic pregnant women in third trimester of pregnancy (28wks to 40wks) attending at Zagazig University hospitals in the period from March until September 2019. Patients divided into 2 groups: Group I: included 25 pregnant women with pregestational diabetes mellitus (Type 1and Type 2 DM) without vascular changes, Group II: included 25 pregnant women with gestational diabetes mellitus. Fasting &2 h postprandial blood glucose level, HbA1c, Complete general and abdominal examination, Obstetric Ultrasonography was done for all patients.

Results: There was no statistical 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 studied groups. There was no statistical significant difference in gestational age at delivery and mode of delivery between the two groups.

Conclusion: We concluded that either diabetes was 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 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 patient do not respond to insulin according to insulin resistance also called (adult onset diabetes) [1].

Overt Diabetes Mellitus was defined when the random plasma glucose level > 200 mg/dl in addition to symptoms such as polyuria, polydipsia, and unexplained weight loss or when fasting glucose > 125 mg/dl due to the ADA (American Diabetes Assoctiation-2004) due to overt diabetes [2]. The pre-existing diabetes in pregnancy refers to diabetes diagnosis before pregnancy. The prevalence of pre-existing diabetes was increased

in the past decade primarily due to of the increase in type-2 diabetes. Studies of preexisting diabetes in women showed high rates of complications compared to normal women [3].

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 [4].

The diabetic women of childbearing age must inform about the importance of tight glycemic control before conception. Many studies reported a high risk of diabetic embryopathy, especially microcephaly, congenital heart disease, anencephaly, and caudal regression,

due to elevations in HbA1C during the first 10 weeks of pregnancy [5].

The current study was aimed to assess the effect of different types of diabetes mellitus without vascular changes on maternal and fetal outcomes.

METHODS

The cross sectional observational study was done at Zagazig University Hospitals and included 50 cases of gestational and pregestational diabetic pregnant women in third trimester of pregnancy (28weeks to 40weeks) attending at Zagazig University Hospitals during the period from March until September 2019.

Sample size: Assuming that the percentage of preterm labor patients with Type 2 diabetes versus patients with gestational diabetes was 35% versus 37% the sample was calculated using open Epi with power test 80% and confidence interval 95% to be 50 patients.

Written informed consent was taken from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Ethical Code of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Pregnant women with pregestational diabetes mellitus (type 1 or type 2 diabetes) without vasculopathy. Pregnant women diagnosed with gestational diabetes mellitus (GDM) due to the 75 gm 2 hour oral glucose tolerance test (OGTT) in the second half of pregnancy. Single tone pregnancy

Exclusion criteria: pregnant diabetic women with Chronic disorder as thyroid, renal and cardiac disease. Pregnant diabetic women with vascular changes as retinopathy, nephropathy, and neuropathy. Multifetal gestations. Gestational age less than 28 weeks.

Patients divided to 2 groups: Group I: included 25 pregnant women with pregestational diabetes mellitus (Type 1and Type 2 DM) without vascular changes, Group II: included 25 pregnant women with gestational diabetes mellitus.

All participants were subjected to the following: Personal history: Name, age, positive consanguinity, date of marriage, special habits, residence, work. Any complain. Any medical disorder (DM: type of diabetes, time of diagnosis, type of treatment).

Menstrual history: Date of Last menstrual period for calculation of gestational age.

Past history: Previous of history macrosomic infant, unexplained IUFD, neonatal death and any medical illness were reported.

Family history: Of DM, any other medical disorder.

General examination: for detection of any systemic disease and measuring vital signs, height and weight of patient for calculate BMI.

Maternal BMI was measured by dividing the weight (kilograms) by square of the height (meters).

Normal (18.5 – 25) kg/m2, over weight (25-30) kg/m2, obese> 30 kg/m2 [6]

Abdominal examination: Inspection: Abdominal size was given an idea to fetal size. Palpation: fundal level, presentation, position and engagement of the presenting part.

Investigations: Maternal screening for diabetes for group II using 1 hour postprandial blood glucose level is done during period of hospital admission from (24-28weeks), if the patient had the high risk criteria so, screening at once, if the level is >140 mg/dl, so the screening is positive and 75gm 2 hour oral glucose tolerance test (OGTT) was performed as follow:

A fasting blood glucose sample was being obtained to compare other glucose values; each patient has drink a sweet liquid containing a certain amount of glucose. For the glucose tolerance test, has drink 75 grams.

Blood samples were collected at interval time of 1, 2, and 3 hours after drinking the glucose.

Values that indicate gestational diabetes:

Fasting: ≥ 92 mg/dL or 5.1 mmol/L.

1-hour: ≥ 180 mg/dL or 10.0 mmol/L.

2-hour: ≥ 153 mg/dL or 8.5 mmol/L.

3-hour: ≥ 140 mg/dL or 7.8 mmol/L. [7]

Pregnant diabetics were diagnosed with at least two values of plasma glucose levels exceeding the carpenter and constant criteria dosed by the American Diabetes Association [5].

Follow up of our patients in antenatal outpatient clinic: Every 2 weeks till 36 weeks, then every

week till delivery for uncomplicated patients, in each visit:

Maternal investigations: (HB, AST, ALT, Urea, Creatinine, Urine analysis &coagulation profile, FBS, HbA1C, PPBS).

Fetal investigations: (ultrasound, CTG). Trans-abdominal ultrasound examination for fetal viability, gestational age confirmation, measurement of fetal abdominal circumference (AC), and calculation of expected fetal birth weight (EFBW) before delivery.Doppler US to assess placental vascularization and calculate flow indices (was done to preeclamptic patients).Neonatal birth weight was measured in grams upon delivery.

Large for gestational age was defined as those with birth weight above 90th centile for age, and whose birth weight falling below 10th centile are defined as small for gestational age.

Statistical analysis

The collected data was entered to and analyzed by computer using Statistical Package of Social Services, version 25 (SPSS). Results were presented by tables and graphs. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequencies and proportions. Pearson Chi square test ($\chi 2$) and fisher's exact were used to analyze qualitative independent data. P value of ≤0.05 was taken as significant.

RESULTS

Table (1), showed that the age of studied groups was (27.5±7.1) years in PGDM and (30.5±5.40) years in GDM with no statistical significant difference in maternal age between studied groups and regarding the BMI, 44% of PGDM was obese. Table (2) showed that there was no statistically significant difference in gravidity, parity and abortion between studied groups. Table (3); showed that there was no statistical significant difference in the gestational age at delivery and mode of delivery in current pregnancy between two groups. Table (4) showed that there was no statistically significant difference in maternal complications between studied groups. Table (5), showed that there was a statistical significant difference in fasting blood glucose and HbA1C between two groups, but regarding postprandial blood glucose, there was no statistically significant difference. Table (6), showed that there was no statistical significant difference between GDM and pre-GDM groups regarding neonatal weight, Apgar score at 1 &5 minutes and neonatal RBS

Table 1: Comparison between pregestational and gestational diabetic groups as regards maternal age and BMI.

Variable	pre-GDM N=25		GDM N=25		P
Maternal age (years) Mean ± SD Range	27.5±7.1 (19-43)		30.5±5.4 (19-40)		0.9
BMI(kg/m2) Mean ± SD Range	26.5±4.7 (18.5-35)		26±3.8 (18.5+33)		0.6
	No	**%**	**No**	**%**	
Underweight <18.5	0	0%	0	0%	
Normal 18.5-24.9	9	36%	11	44%	
Overweight 25-29.9	5	20%	6	24%	
Obese > 30	11	44%	8	32%	

Table 2: Comparison between pregestational and gestational diabetic groups as regard gravidity, parity and abortion.

Variable	Pre-GDM n=25	%	GDM n=25	%	P
Gravidity: Primigravida Multigravida	4 21	16% 84%	6 19	24% 76%	0.2
Parity: Nulliparous Multiparous	2 19	10% 90%	1 18	5% 95%	0.4
Abortion *	5	22%	7	31%	0.5

Patient with previous history of abortion was 22 patients. p -value > 0.05 is non-significant

Table 3: Comparison between pregestational and gestational diabetic groups as regards gestational age at delivery and mode of delivery in current pregnancy.

Variable	Pre-GDM n=25	%	GDM n=25	%	X2	P
GA at delivery:					0.35	0.551
<37weeks	2	8%	1	1		
≥37weeks	23	92%	4%	4%		
Mode of delivery in current pregnancy						
CS	17	68%	15	15	0.34	0.555
NVD	8	32%	60%	60%		

χ^2 : chi-square test. p -value > 0.05 is non-significant

Table 4: Comparing maternal complications between pregestational and gestational diabetic groups (n=50)

Maternal complications	Total N	%	Pre-GDM N=25	%	GDM N=25	%	P
No complication	23	46%	13	52%	10	40%	0.5
Gestational HTN	6	12%	4	16%	2	8%	
PET	9	18%	3	12%	6	24%	
PROM	1	2%	0	0%	1	4%	
Preterm labor	3	6%	2	8%	1	4%	
Polyhydramnios	9	18%	5	20%	4	16%	
oligohydramnios	4	8%	3	12%	1	4%	
Infection (UTI-candidiasis)	4	8%	3	12%	1	4%	

*Some patient has more than one complication. p -value > 0.05 is non-significant

Table 5: Comparison between pregetational and gestational diabetic groups as regards of mean **f**asting, Postprandial blood sugar and HbA1C (N=50)

Variable	Pre-GDM n=25	GDM n=25	P
FBS			
Mean ± SD	118±28.9	143±31.7	0.001**
Range	(80-172)	(90-235)	
PPBS	180.6±58.1 (95-300)	188.5±65.6 (98-300)	0.6
HbA1c	6.2±0.9 (5.1-8)	6.9±0.98 (5.3-9.5)	0.01*

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

Table 6: Comparison between pregestational and gestational diabetic groups as regards mean of (neonatal weight – Apgar scoring at 1 and 5 minutes- neonatal RBS).

Variable	Pre-GDM n=25	GDM n=25	P
Neonatal weight (Kg)	3.2±0.6	3.6±0.7	0.5
Apgar score at 1 min	8.9±1.6	9.1±1.3	0.8
Apgar score at 5 min	9.3±1.7	9.6±2.1	0.4
Neonatal RBS within 1st hour of delivery	58.4±10.1	54.7±12.8	0.7

Student t- test. p -value > 0.05 is non-significant

DISCUSSION

Gestational diabetes mellitus (GDM) is operationally defined as impaired glucose tolerance during pregnancy. Its diagnosis is based on single step procedure. In accordance to World Health Organization recommendations, the guideline endorses 2/h 75g oral glucose tolerance test, irrespective of last meal timings with a cutoff value of ≥140 mg/dL using a plasma standardized glucometer. [8]

The current study revealed that the age of studied groups was (27.5±7.1) years in PGDM and (30.5±5.40) years in GDM with no statistically difference in maternal age between two groups. Which in agreement with the present study, the study of *Sugiyamaa et al.,* [9] who found that there was no stat*i*stically significant difference in maternal age between studied groups.

Maternal overweight and obesity were associated with multiple congenital malformation and fetal loss (miscarriage, stillbirth, neonatal mortality, and perinatal morbidity). The presence of obesity and diabetes increase the risk of malformations, with different anomalies [10].

The present study revealed that the 84%, 76 % of PGDM and GDM in respectively were multigravida. There were a higher proportion of multigravida than secoundigravida and primigravida women 37.1%, 17.7%, and 14.5% respectively) among women with GDM, these results agreed with study of *Salge et al.,* [11], who reported that 16% of the studied group were primigravida, (82%) were multiparous.

The present study revealed that was 36%, 64% of PGDM and GDM had previous history of abortion. In the study of *Shefali et al.,* [12], they studied the pregnancy outcomes in mothers with PGDM and GDM. The abortions percent was 2.7% in the GDM group, while in the PGDM group it was 10.1% which mean that PGDM increase the risk for abortions. In current study that was, 96% of GDM group delivered at gestational age ≥37 weeks and 4% of them was preterm and as regard mode of delivery 68%, 60% of PGDM and GDM patients in respectively delivered by CS. The rate of CS was much higher due to high incidence of macrosomia and many patients had previous CS.

The mean gestational age at delivery was 37 weeks (38.7 in the control group). Fifty-six (56%) mothers delivered vaginally (7 need forceps assistance) and 58 (44%) need cesarean section, while 22% of controls underwent cesarean section, twenty-four women underwent emergency cesarean section, and unsatisfactory progress of labor was the most indication [13].

Soliman et al., [14] revealed that Preterm delivery was highly significant in women with DM and GDM (13.7% and 9%, respectively versus normal women (6.4%); p<0.001).

The study on the hand revealed that there was no statistical 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 studied groups.

In agreement with us, another study of *Macintosh et al.,* [15], who revealed that there was a statistically significant increases in 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 diabetic women with (48/1000 births for type 1 diabetes; 43/1000 for type 2 diabetes). The increase of anomalies of the nervous system, notably neural tube defects (4.2-fold), and congenital heart disease (3.4-fold).

The present study revealed that there was no statistical significant difference in maternal complications between the studied groups as gestational hypertension, PROM, preterm labor. Study of Soliman et al., [14], who revealed that Pregnant women with DM or GDM had high risk of hypertension compared normal controls (9.9%, 5.5% and 3.5%, respectively; p<0.001).

The current study revealed that there was no statistical significant difference in fetal complications between the studied groups. In agreement with our study, the study of *Sugiyamaa et al.,* [9] found that there were no significant differences between the GDM and ODM groups in neonatal outcomes. LGA infants are a significant complication of GDM. Also Stogianni et al., [16] assessed the prevalence of LGA in pregnant women, with and without diabetes; it was 21.6% (60/278) in diabetic and 17.0% (23/135) in women without diabetes. In Preexisting Diabetes Mellitus PDM group, a higher number of infants in the T1DM group was LGA, 60% (22/37) compared to 27% (3/11) in T2DM group, without statistical

significant difference (p = 0.15), while two children were macrosomic at birth 4.3% (2/48) in the PDM group. The current study revealed that there was no statistically significant difference between GDM and pre-GDM groups regarding neonatal weight, Apgar score at 1 & 5 minutes and neonatal RBS.

In the previous study of *Owens et al.,* [17] found no statistical significant difference in the mean birth weight (3.54 kg) between studied groups. There was increase in babies born >4 kg to women with T1DM. Neonatal hypoglycemia was prevalent in offspring of both T1 DM and T2 DM pregnancies but it was higher in offspring of T1DM than T2DM. Hypocalcemia, neonatal jaundice, shoulder dystocia and polycythemia were similar between studied groups but these were relatively rare outcomes and no significant differences in these outcomes. The stillbirth rate was higher in babies of T1DM mothers but no difference was observed in mothers with T2 DM.

The present study assessed Laboratory investigations of the studied group and found that the fasting blood glucose ranged from 80 to 235, HbA1C ranged from 5.3 to 9.5 and PPBS ranged from 95 to 300. In agreement with our study, the study of *Owens et al.,* [17] found that the mean HbA1C in pregnancy was lower in women with T2DM compared with T1 DM (5.8 vs. 6.6%, p = 0.001). In each trimester and prior to delivery the mean HbA1C was also significantly lower in women with T2DM compared with T1 DM and in both groups HbA1C improves as pregnancy progresses reaching a nadir of 6.4% and 5.7% in women with T1DM and T2 DM respectively.

The Improvement of pregnant women with dysglycemia in the diagnosis and management lead to a remarkable improvement in the neonatal outcome and reduction of macrosomia rate, hypoglycemia, NICU admission and congenital malformations. Obesity and overweight in women during the childbearing period contributed to the occurrence of high rates of dysglycemia during pregnancy. Reducing obesity during the childbearing period and control glucose during pregnancy are highly recommended to prevent any morbidity during pregnancy of women with DM and GDM [14].

CONCLUSION

We concluded that either diabetes was gestational or pregestational there was no statistical difference between maternal and fetal outcomes. Optimal control of blood glucose resulted in lower neonatal and

Conflict of Interest

The authors of this manuscript declare no relevant conflicts of interest, and no relationships with any companies, whose products or services may be related to the subject matter of the article.

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