Original Article

Assessment of the Effect of Pre-Gestational Diabetes and Risk of Adverse Maternal, Perinatal and Neonatal Outcomes in Egypt

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ABSTRACT

Introduction: Most women with pre-gestational diabetes (PGD) characterized by disturbance in glucose metabolism may be due to variable degrees of insulin resistance (type 2), or a consequence of autoimmune destruction of the pancreatic β-cells (type 1). With increasing numbers type 1 diabetes diagnosed among youth and high prevalence of obesity among women of child-bearing age , the demographic pattern of PGD is changing.

Objective: The aim of this work was to assess the effect of pre-gestational diabetes and risk of adverse maternal, prenatal & neonatal outcomes in Alexandria-Egypt.

Subjective: This study conducted on 75 patients pregnant with pre-gestational diabetes mellitus in El-Shatby University Hospital. The aim of this work is to assess the effect of pre-gestational diabetes and risk of adverse maternal, prenatal & neonatal outcomes in Alexandria-Egypt.

Results: Regarding maternal complications, it was found that 14 patients (18.7%) have pre eclampsia, 8 patients (10.6%) have diabetic ketoacidosis , 5 patients (6.7%) have ICU admission.Regarding the mode of delivery it was found that 63 patients (94%) have caesarian section delivery while 4 patients (6%) have normal vaginal delivery. It was found that 4 patients (6.0%) have postpartum hemorrhage and 10 patients (7.5%) have wound complications after delivery. fetal complications was found that 7 patients (9.3%) have cardiac anomalies and 1 patients (1.4%) has Neural tube defect. 19 patients (33.9%) have Polyhydramnios, And 13 patients (17.3%) have intra uterine fetal Finally 3 patients (4%) have intra uterine growth restriction. Natal complications was found that 2 cases (3.7%) have Prolonged labour, 2 cases (3.7%) have Shoulder dystocia,5 cases (9.3%) have still birth, only 1 case (1.9%) has Erb's palsy while 9 neonates (16.7%) have neonatal intensive care unit admission. Neonatal complications was found that 16 patients (29.7%) have respiratory distress, 11 neonates (20.4%) have jaundice. 22 neonates (40.7%) have neonatal hypoglycemia.

Conclusion: Elevated HbA1C value of the increased risk of congenital fetal malformation especially neural tube defect & cardiac defects. Diabetes plays an increasing role in the number of children born with congenital anomalies**.**

Key Words: Maternal outcomes, neonatal outcomes, perinatal outcomes, pregestational diabetes.

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INTRODUCTION

Diabetes mellitus is one of the most common pre-existing maternal disorders and complicated approximately 1.3% of all pregnancies[1,2]. Most women with pre-gestational diabetes (PGD) characterized by disturbance in glucose metabolism may be due to variable degrees of insulin resistance (type 2), or a consequence of autoimmune destruction of the pancreatic β-cells (type 1). With increasing numbers type 1 diabetes diagnosed among youth and high prevalence of obesity among women of child-bearing age[3], the demographic pattern of PGD is changing. Besides, the sex ratio of newly diagnosed type 2 diabetes among youth was remarkably skewed to female[4] Therefore, continuous increase in diabetes rates in the global population will translate into higher prevalence of PGD eventually[5] Women with PGD are associated with adverse pregnancy outcomes[6] Pregnancies complicated by pre-gestational diabetes (PGD) are associated with a higher rate of adverse outcomes, including an increased range of preterm delivery, caesarean section, perinatal mortality, stillbirth, small for gestational age, large for gestational age, low birth weight, neonatal hypoglycemia, neonatal death, low Apgar score, NICU admission, jaundice and respiratory distress[7].

Furthermore, PGD has also been associated with increased risk of maternal complications including shoulder dystocia, gestational hypertension, and pre-eclampsia[8-10], making pre-pregnancy care particularly glycaemic control and obstetrical interventions of great importance. The patients with a markedly elevated A1C

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value of the increased risk of CFMF especially NTD & cardiac defects[11]. More recent studies on PGD have reported various results: preterm delivery and stillbirth were still significantly increased in some studies[2,12,13] despite good metabolic control, while other studies[14-16] reported that PGD was no longer a significant factor. These conflicting results may be partly due to ethnic diversity, insufficient power, phenotypic heterogeneity, and even publication biases[17].

AIM OF THE WORK

The aim of this work was to assess the effect of pre-gestational diabetes and risk of adverse maternal, prenatal & neonatal outcomes in Alexandria-Egypt.

PATIENTS AND METHOD

This is a descriptive study which conducted on 75 patients pregnant with pre-gestational diabetes mellitus in El-Shatby University Hospital.

Inclusion criteria

- Primigravida and multigravida with pregestational diabetes.
- Age: 20 years to 35 years old, Body mass index (BMI) less than 30.

Exclusion criteria

- Pregnant women with gestational diabetes. Any other medical illness

METHODS

This study carried out on cases fulfilling the inclusion criteria, admitted to El-Shatby University Hospital each of them will be subjected to the following:

1. FIRST TRIMESTER:

- Detailed history.
- Classification of diabetes: type 1 or 2.
- If the patient take Insulin or oral hypoglycemic.
- If there were complications associated in the pregnancies before.
- Idea about glycemic control: if she has self-monitoring paper.

Routine investigations: CBC, ABO group & Rh, serology (HBV, Rubella, syphilis) & urine (asymptomatic bacteriuria, pus cells).

Glycated hemoglobin (Hb A1C): it reflects the glycemic control over the prior 8-12 weeks & thus assists in counseling her regarding the risks of miscarriage, CFMF & preeclampsia. The American Diabetes Association (ADA) recommends aiming for an HBA1c < 6.5%.

Assessment of comorbidities

Ultrasound: booking visit at (6-8 weeks) to document viability, as the rate of miscarriage is high in women with diabetes especially those with poor glycemic control, recurrent pregnancy loss & neural tube defect.

2. SECOND TRIMESTER:

- Visits every 4-6 wk, but more frequently if complications arise or glycemic control is suboptimal.

Screening for Congenital Fetal Malformation: full anomaly scan (U/S) is done at 18-20 wk & focus on Neural Tube Defect & cardiac anatomy.

3. THIRD TRIMESTER:

- Visits every 1-2 wk until 36 wk, then weekly until delivery.
- Close monitoring of maternal blood glucose levels (Hb A1C) .
- Monitoring FWB to minimize the risk of IUFD.
- Evaluation for macrosomia or IUGR: U/S at 28-32 wk. to assess fetal growth & repeat at 3-4 wk intervals.
- Evaluation for obstetrical or medical complications necessitating premature delivery.

Antepartum Monitoring: the ACOG recommend using fetal movement counting, biophysical profile &/ or NST weekly starting at 32-34 wk then increase the frequency of testing to twice weekly from 36 wk until delivery.

Umbilical artery Doppler may be required to assess for IUGR fetuses

If non-reassuring fetal testing due to. a reversible problem such as hyperglycemia or DKA, it is advisable

to resuscitate the fetus in utero by treating the medical disorder (pathological FHR patterns will often revert to normal when the mother's metabolic status is corrected).

DELIVERY

- When emergency early delivery is indicated, it is important to remember that RDS is more likely to develop than in infants of women without diabetes delivered early.
- Woman with good glycemic control & no vascular disease (as nephropathy or retinopathy), delivery at 39 wk is indicated if favorable cervix.
- Woman with good glycemic control, no vascular disease, normal fetal growth, reassuring fetal surveillance & no history of IUFD, but unfavorable cervix, induction of labor can be safely delayed until 40 wk.
- In cases with repeated unexplained IUFD, terminate 1-2 wk earlier.
- According to ACOG, prophylactic CS can be done to prevent brachial plexus injury due to Shoulder dystocia if macrosomia.

RESULTS

The mean age of the studied group was 29.95±2.99. Regarding the BMI the majority of the patient (64.0%) was overweight the mean BMI was 25.28±2.22. The majority of the patients was multigravida (62.7%). The uncontrolled HbA1c was 34 cases (45.3%) , while the controlled HbA1c was 41 cases (54.7%), the mean value of Hb A1c was 8.5 ± 0.72 as shown in (Table 1). The outcome parameters was shown in (Table 2, Figure 1),

The results shows that there was a significant relation between the uncontrolled HbA1c and abortion, preeclampsia, IUFD, Late or early preterm and respiratory distress as shown in (Table 3).

The HbA1C show a significant prediction of variables natal complication, and respiratory distress the cut off value of HbA1c for the two variables was 6.8, and the p value less than 0.001, the sensitivity, specificity and accuracy for the two variables was more than 80.0% . The time of delivery and congenital malformation show insignificant prediction value.

Table 1: Distribution of the studied group regarding demographic and maternal data and HbA1c category to Patient's urine analysis

		Number	%	Range	Mean	S.D.
Age (years)	< 30	31	41.3	23.0-34.0	29.95	2.99
	> 30	44	58.7			
BMI (kg/m^2)	Normal weight	27	36.0	21.0-29.0	25.28	2.22
	Over weight	48	64.0			
Parity	Primigravida	28	37.3			
	Multigravida	47	62.7			
Hb A1c	Controlled	41	54.7	5.0-12	8.5	0.72
	Uncontrolled	34	45.3			

Table 2: Distribution of the studied patients group regarding outcome

Outcome	Number	%
Abortion		
No	67	89.3
Yes	8	10.7
Time of delivery "n=67"		
early preterm < 28w	6	9.0
Late Preterm < 37w	39	58.2
Full term	22	32.8
Polyhydramnios "n=67"	19	28.4
Antepatum He	0	0.0
Preeclampsia	14	20.9
DKA	8	11.9
ICU admission	5	7.4
Postpartum He	4	6.0
Wound complications	10	14.9
Congenital malformation"n=67"		
No	59	88.1
Cardiac	7	10.4
Neuraltubedefect	1	1.5
IUFD	13	19.5
IUGR	3	4.5

Table 3: Relation between HbA1c level and out come parameters

	HbA1c category				X^2 P
	Controlled		Uncontrolled		
	No.	%	No.	%	
Abortion	0	0.0	8	23.5	7.829 0.005*
Congenital malformation					
No	38	92.7	21	80.8	2.323 0.312 N.S.
Cardiac	3	7.3	4	15.4	
Neuraltube defect	0	0.0	1	3.8	
Preeclampsia	0	0.0	14	53.8	24.1983 0.000017*
IUFD	4	9.8	9	34.6	6.2874 0.01216*
IUGR	0	0.0	3	11.5	
Time of delivery					
Full term	18	43.9	4	15.4	9.326 0.009438*
Late Preterm	22	53.7	17	65.4	
Early preterm	1	2.4	5	19.2	
DKA	2	4.9	6	23.1	5.0116 0.025178
Respiratory distress	3	7.3	13	50.0	15.9459 0.000065*
Mode of delivery					
NVD	2	4.9	2	7.7	0.2245 0.635
CS	39	95.1	24	92.3	

Table 4: Sensitivity, specificity and accuracy of HbA1c in predict the natal complication

	Area Under the curve	Cut off value	*P value*	Asymptotic 95% C.I.		Sensitivity Specificity Accuracy
				Lower Bound	Upper Bound	
Variables Natal complication	0.840	> 6.8	0.0001*	0.741	0.940	85.0 81.0 83.0
Respiratory distress	0.858	> 6.8	0.0001*	0.756	0.961	86.0 82.0 83.0
Time of delivery	0.593	>7.0	0.167	0.462	0.725	62.0 56.0 60.0
Congenital malformation	0.664	> 6.9	0.089	0.490	0.838	69.0 61.0 64.0

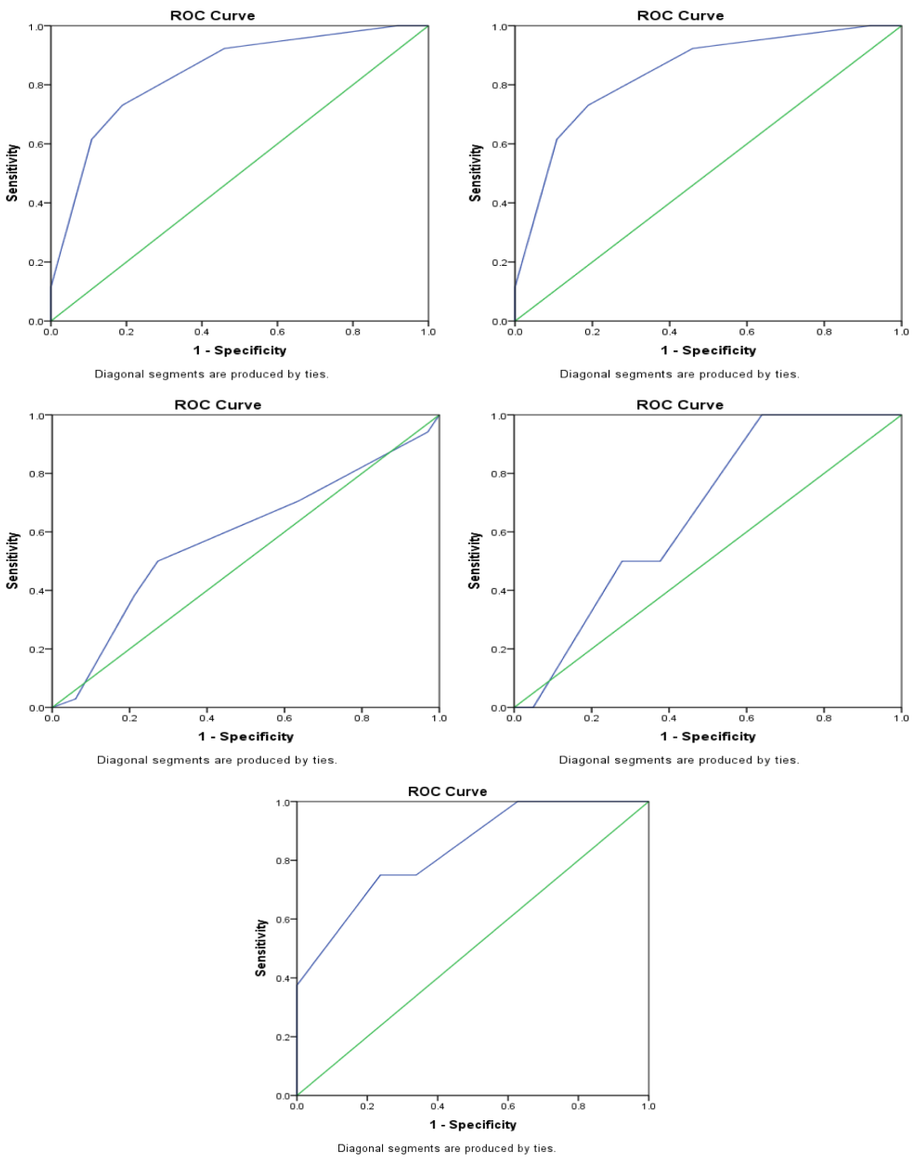

Fig. 1: ROC curve to predict the Sensitivity, specificity and accuracy of HbA1c in predict the natal complication

DISCUSSION

Regarding medical conditions our study showed that 13 patients (17.3%) have abnormal renal function test, patient's neuroexamination show that 100 % have a normal examination, patient's fundus examination show that 2 % have diabetic retinopathy.

There was a study done by H. R. Murphy *et al*[12], Prospective cohort study of 682 consecutive diabetic pregnancies in East Angliaon 408 (59.8%) were Type1 diabetes and 274 (40.2%) were Type2 diabetes, this study reported that 16 patients (2.3 %) showed nephropathy, 13 patients (1.9 %) showed neuropathy while 133 patients (19.5 %) have diabetic retinopathy.

Regarding timing of delivery our study showed that 8 patients (10.7 %) have abortion, 6 patients (9%) have early preterm delivery(> 28 w), 39 patients (39 %) have late preterm delivery (> 37 w) and 22 patients have full term delivery.

In agreement with our results H. Wahabi *et al*[13] study subcohort, compared the maternal and the neonatal outcomes of diabetic women with pre-GDM and GDM to the outcomes of nondiabetic mothers who delivered among the Saudi pregnant population . From the total cohort, 9723 women participated in this study. Of the participants, 2354 (24.2%) had GDM,418 (4.3%) had pre-GDM, and 6951 were nondiabetic .

This study reported that 11 patients (2.7 %) of pregestational diabetic mothers have early preterm delivery, 48 (11.9 %) have late preterm delivery, 341 (84.4 %) have full term delivery while 4 patient have postdate delivery (more than 41 w)

Another study done by Lisa A Owens *et al*[14], retrospective case–control study was to examine pregnancy outcomes in women with type 1 diabetes and type 2 diabetes directly and compare pregnancy outcome of each group with matched normal-glucose tolerant controls. it include 323 women with diabetes and 660 glucose-tolerant controls .

This study reported that 188 patients (85.2 %) have miscarriage 84 patients (26 %) have late preterm delivery

Regarding fetal complications our study showed that 7 patients (9.3 %) have a cardiac anomalies and 1 patient (1.4 %) has neural tube defect, 19 pateints (33.9 %) have polyhydramnios, 13 patients (17.3 %) have intrauterine fetal death while 3 patients (4 %) have IUGR

According to congenital malformation there was a study done by Sally K Abell *et al*[43], cohort study in a specialist diabetes and maternity network in Victoria. To compare contemporary pregnancy outcomes in women with and without type 1 diabetes, and to examine the effects of obesity and glycaemic control on these outcomes. It included 107 pregnancies to women with type 1 diabetes and 27075 pregnancies to women without diabetes. Women with type 2 diabetes or gestational diabetes were excluded. This study reported that 4 patients (4 %) have congenital malformation. Another study done by Lisa A Owens *et al*[15],reported that 12 patients (3.7 %) have congenital malformation. In this study they reported that 29 patients (8.98 %) have polyhydramnios

Keenan E. Yanit *et al*[16], carried out a retrospective cohort study of 532088 women undergoing singleton births in California . Women were categorized into chronic hypertension, pregestational diabetes, both, or neither. Pregnancy outcomes were compared to examine the impact of chronic hypertension and pregestational diabetes on pregnancy outcomes. Number of diabetic mothers is 3718 This study reported that 30 patients (0.8 %) have IUFD

Another study done by Peter W. G. Tennant *et al*[16], This study includes 1548 in women with pre-existing diabetes singleton live births delivered at or after 20 completed weeks of gestation. This study reported that 46 patients (2.97 %) have IUFD

Regarding fetal weight our study showed that 5 patients (9.3 %) have small for gestational age (< 2 kg), 10 patients (18.5 %) have macrosomia (> 4 kg) while 39 patients (72.2 %) have a weight between 2 – 4 kg

Lisa A Owens *et al*[15], reported that 87 patients (26.9 %) have a weight > 4 kg, 22 patients (6.8 %) have a weight > 4.5 kg while 24 patients (7.4 %) have small for gestational age. Another study done by Sally K Abell *et al*[18], reported that 7 patients (7 %) have small for gestational age while 47 patients (44 %) have large for gestational age. While H. Wahabi *et al*[14] reported that 16 patients (7.5 %) have macrosomia

Regarding natal complications our study showed that 2 patients (3.7 %) have Prolonged labour, 2 patients (3.7 %) have Shoulder dystocia,5 patients (9.3 %) have still birth, only 1 patients (1.9 %) has Erb's palsy while 9 neonates (16.7 %) have neonatal intensive care unit admission.

There was a study done by K. Hildén *et al*[19], the study cohort included 1294006 women with data on early pregnancy .number of women have pregestational diabetes was 14833. The study population consisted of all women with a singleton birth in Sweden between 1998 and 2012.

This study reported that 58 patients (0.4 %) have still birth, 85 patients (0.6 %) has Erb's palsy, 94 patients (0.6 %) have low APGAR score (< 4 at 5 minutes)

H. Wahabi *et al*[14] reported that 7 patients (3.3 %) have still birth, only one patient (0.47 %) has shoulder dystocia, 23 neonates (10.7 %) have neonatal intensive care unit admission. While 7 patients (3.3 %) have low APGAR score (< 7 at 5 minutes)

Lisa A Owens *et al*[15], reported that 6 patients (1.9 %) have Shoulder dystocia,8 patients (2.5 %) have still birth, while 160 neonates (49.5 %) have neonatal intensive care unit admission. Sally K Abell *et al*[18], reported that 11 neonates (11 %) have neonatal intensive care unit admission. 7 patients of 41 (17 %) have Shoulder dystocia, 7 patients of 40 (17 %) have low APGAR score (< 7 at 5 minutes)

Regarding neonatal complications our study showed that 16 patients (29.7 %) have respiratory distress, 11 neonates (20.4 %) have jaundice. 22 neonates (40.7 %) have neonatal hypoglycemia, in agreement with out results, Lisa A Owens *et al*[15], reported that 22 neonates (6.8 %) have jaundice while 50 neonates (15.5 %) have neonatal hypoglycemia. Also, Sally K Abell *et al*[18], reported that 16 patients (15 %) have respiratory distress, 40 neonates (37 %) have jaundice. 41 neonates (38 %) have neonatal hypoglycemia while 7 neonates (7 %) have perinatal death

Regarding maternal complications our study showed that 14 patients (18.7 %) have pre eclampsia, 8 patients (10.6 %) have diabetic ketoacidosis, 5 patients (6.7 %) have ICU admission.

Regarding the mode of delivery it was found that 63 patients (94 %) have caesarian section delivery while 4 patients (6 %) have normal vaginal delivery.

It was found that 4 patients (6.0%) have postpartum hemorrhage and 10 patients (7.5 %) have wound complications after delivery

According to DKA there was a study done by Bryant, S.N. *et al*[20] a retrospective cohort study of pregnancies complicated by DKA between October 1999 and June 2015.

This study reported that during this period, we identified 33 women with 40 admissions (incidence: 0.2%). The majority of women had type 1 diabetes (67%), and almost all presented with nausea and vomiting (97%).

H. Wahabi *et al*[14] reported that 9 patients (2.2 %) have pre eclampsia . 166 patients (39.9 %) have caesarian section delivery, 239 patients (57.5%) have normal vaginal delivery, While 11 patients (2.6%) have instrumental delivery

Lisa A Owens *et al*[15], reported that 21 patients (6.5 %) have pre eclampsia . 214 patients (66.3 %) have caesarian section delivery, 10 patients (3.0%) have postpartum hemorrhage and 2 patients (0.6%) have antepartum hemorrhage

Sally K Abell *et al*[18], reported that 66 patients (62 %) have caesarian section delivery. 5 patients (5 %) have pre eclampsia

Keenan E. Yanit *et al*[17], reprted that 353 patients (9.5%) have pre eclampsia and 52 patients (1.4 %) have placental abruption

CONCLUSIONS

From the results of this study we concluded that elevated HbA1C value of the increased risk of congenital fetal malformation especially neural tube defect & cardiac defects. Diabetes plays an increasing role in the number of children born with congenital anomalies.

There is association between poor periconceptional control of diabetes and increased rates of fetal anomalies.

Preconception care improves maternal and fetal outcomes in women with pre-existing diabetes. This involves educating women about the importance of optimal glycemic control prior to pregnancy.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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