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Original Article

PROSPECTIVE STUDY ON THE EFFECT OF PHARMACEUTICAL CARE ON MATERNAL AND FETAL OUTCOMES IN GESTATIONAL AND PREGESTATIONAL DIABETIC PATIENTS

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ABSTRACT

Objective: The prevalence of diabetes in pregnancy has increased in the U. S. The majority is gestational diabetes mellitus (GDM), with the remainder primarily preexisting type 1 diabetes and type 2 diabetes (pregestational diabetes, PGDM). The present study investigates the demographics and clinical differences between both types.

Methods: This prospective study was conducted on ninety pregnant females with normal menstrual cycles before pregnancy. Demographics, oral glucose tolerance test (OGTT), and HbA1c were assessed.

Results: There was a significant difference in the term of Oral glucose tolerance test Week 24 during fasting, Oral glucose tolerance test Week 24 after one hour, Oral glucose tolerance test Week 24 after two hours, Oral glucose tolerance test Week 24 after three hours, Oral glucose tolerance test Week 28 during fasting, Oral glucose tolerance test Week 28 after one hour, Oral glucose tolerance test Week 28 after two hours, Oral glucose tolerance test Week 28 after three hours, HbA1c week 24 and HbA1c week 28; p-value<0.05.

Conclusion: pregnant women in this study who needed insulin were educated to self-monitoring of blood glucose, diet control, medication adherence, and exercise, and we adjusted the needed insulin dose for them with restrictive follow-up.

Keywords: Pregestational diabetic-prospective study-maternal and fetal outcomes

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INTRODUCTION

The prevalence of diabetes in pregnancy has been increasing in the U. S. The majority is gestational diabetes mellitus (GDM), primarily pre-existing type 1 diabetes and type 2 diabetes. The rise in GDM and type 2 diabetes in parallel with obesity in the U. S. and worldwide is particularly concerned. Type 1 diabetes and type 2 diabetes in pregnancy confer significantly greater maternal and fetal risk than GDM, with some differences according to the type of diabetes as outlined below. In general, specific risks of uncontrolled diabetes in pregnancy include spontaneous abortion, fetal anomalies, Preeclampsia, fetal demise, Macrosomia, neonatal hypoglycemia, and neonatal hyperbilirubinemia, among others. In addition, diabetes in pregnancy may increase the risk of obesity and type 2 diabetes in offspring later in life [1].

There are opportunities to educate all women and adolescents of reproductive age with diabetes about the risks of unplanned pregnancies and improved maternal and fetal outcomes with pregnancy planning [2]. Effective preconception counseling could avert substantial health and associated cost burdens in offspring [3]. Family planning should be discussed, and effective contraception should be prescribed and used until a woman is prepared and ready to become pregnant. To minimize the occurrence of complications, beginning at the onset of puberty or diagnosis, all women with diabetes of childbearing potential should receive education about: the risks of malformations associated with unplanned pregnancies and poor metabolic control and the use of effective contraception at all times when preventing pregnancy. Preconception counseling using developmentally appropriate educational tools enables adolescent girls to make well-informed decisions [4]. Preconception counseling resources tailored for adolescents are available at no cost through the American Diabetes Association (ADA) [5]. Pregnancy in women with normal glucose metabolism is characterized by fasting levels of blood glucose that are lower than in the non-pregnant state due to insulin-independent glucose uptake by the fetus and placenta and by postprandial hyperglycemia and carbohydrate intolerance as a result of diabetogenic placental hormones. In patients with preexisting diabetes, glycemic targets are usually achieved through a combination of insulin administration and medical nutrition therapy [2].

Because glycemic targets in pregnancy are stricter than in non-pregnant individuals, women with diabetes must eat consistent amounts of carbohydrates to match with insulin dosage and to avoid hyperglycemia or hypoglycemia. Referral to a registered dietitian is important to establish a food plan and insulin-to carbohydrate ratio and to determine weight gain goals. Early pregnancy is a time of insulin sensitivity, lower glucose levels, and lower insulin requirements in women with type 1 diabetes. 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 trimester. In women with normal pancreatic function, insulin production is sufficient to meet the challenge of this physiological insulin resistance and to maintain normal glucose [6].

In the current study, the aim of the present work is to assess and study the differences between pregestational and gestational diabetes.

MATERIALS AND METHODS

This prospective study was conducted on 90 pregnant females with normal menstrual cycles before pregnancy. The current study was conducted after ethics approval from the ethics committee at Misr University for Science and Technology with a number (FWA00025577) and college approval with a number (CP3).

At the time of initial recruitment, the purpose of the study was explained to the participants, and they were informed of the need for follow-up contact,

and all the patients were asked to sign a written consent of their approval. The 90 patients were collected from the obstetrics and gynecology outpatient clinic in the memorial Souad Kafafi University hospital as well as Al-Kasr Al-Einy Teaching hospital with comparable demographic data. Subjects were divided into three groups, Group I is non-diabetic pregnant with a normal glycemic profile (control), Group II is pregnant patients with proven diabetes during pregnancy (Gestational Diabetes), and Group III are pregnant women who became pregnant while Diabetic (Pregestational Diabetes). A normal result for a 1 h glucose screening test using 50 g glucose which is blood sugar that is equal to or less than 140 mg/dl (7.8 mmol/l) 1 h after drinking the glucose solution. A normal result means the absence of gestational diabetes [20].

Pregestational diabetes is defined as Type I or Type II DM that existed before conception.

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy [18].

In the present study, all patients without a history of *diabetes mellitus* on their visit between the 24th and 28th weeks gestation were screened for Gestational Diabetes by a 1hour postprandial glucose test using 50 grams of glucose. Patients with abnormal high reading>140 mg/dl were directed to perform the 3 h modified OGTT (3 h test) using 100 grams glucose for further confirmation of gestational diabetes, in addition to Ultrasound screening for polyhydramnios and any congenital anomalies. After performing the above screening tests, we obtained the 30 patients with confirmed gestational diabetes, i.e., with at least two abnormal OGTT readings, and those with only one abnormal reading were classified as impaired glucose tolerance.

The standard criteria for the diagnosis of pregestational diabetes are as follows: HbA1c of 6.5% or higher, Fasting plasma glucose of 126 mg/dl or higher, or 2 h plasma glucose of 200 mg/dl or higher during a 100g OGTT or

Asymptomatic patient with random plasma glucose of 200 or higher (all plasma glucose values are recorded as mg/dl).

Pregnant women who meet the above criteria are considered to have type 2 diabetes mellitus [19].

Twenty patients diagnosed with gestational diabetes (group II) were advised to be on diet control, while the rest ten patients, as well as all the thirty patients with pre-gestational diabetes (Group III), received insulin on an individualized basis, and all their doses were accurately calculated concerning their trimester of pregnancy and the severity of their cases according to their glycemic profiles.

In the current study, the importance of self-monitoring of blood glucose, diet control, medication adherence if needed, and exercise was explained to the patient. On each visit, the patient was monitored for the blood glucose values and the results from both the ophthalmological and laboratory examinations (e. g., renal functions, hemoglobin A1c, thyroid function, etc.). The patient was asked to take good care of the quality and quantity of her food (diet control) which was very important to both the mother and her fetus. The patient was directed to record the blood glucose readings before the three meals and the postprandial 2 h in a copybook and was asked to bring these recorded readings with her each visit to check the efficacy of her insulin doses and if they needed further adjustment.

The target blood glucose values according to ACOG and the American Diabetes Association (ADA) 2021: Fasting ≤95 mg/Dl AND 2-hr postprandial ≤120 mg/dl

Insulin requirements during the first trimester are similar to those before pregnancy in women with type 1 DM. Dosing was adjusted based on self-monitoring of blood glucose (patient recorded readings in her copybook) and A1c values. Insulin dosing was calculated and adjusted as follows:

Table 1: Insulin dose for pregnant women

1–12 w gestation	0.7 U/kg
13-28 w	0.8 U/kg
29–34 w	0.9 U/kg
35 wks till term	1 U/kg

Approximately 2/3 of the total insulin dose was administered as rapid-acting insulin (e. g., Humalog or NovoRapid) before each meal and the other ⅓ was administered as long -acting insulin (Lantus or Levemir) once daily.

All the cases that participated in the present study were followed-up till their delivery, and their prenatal outcomes were observed as all the neonates were assessed for APGAR score at 1 and 5 min, respiratory Distress and cyanosis, glucose level, and insulin level.

Inclusion and exclusion criteria

Primigravida or Multipara, Age of the mother between 15-55 y, Single intrauterine pregnancy with ultrasound screening at the thirteenth and the twentieth weeks' gestation, No history of a medical disorder such as thyroid dysfunction or hypertension.

The exclusion criteria are

Unwilling to participate in the study, Twin pregnancy/abnormal lie or other known complications.

Interventions and follow-up

Demographic profiles like age, BMI, parity, family history of diabetes, and blood pressure will be evaluated. Full history taking, including current or past illness. Drug history, present or past, Full clinical examination including General examination and Abdominal examination, The following blood tests were performed: complete blood count, glycated hemoglobin, fasting blood glucose, and oral glucose tolerance test (OGTT) using Beckman Coulter AU 480 analyzer, Urine analysis performed using Beckman Coulter AU 480 analyzer was: urea, uric acid, and creatinine clearance, Ultrasound studies were carried out using Mindray dp20 to determine intrauterine gestational sac, gestational age, and viability of the fetus, as well as the presence of any congenital anomalies, Follow up of the patient until delivery was done, Pregnant diabetic women have been prescribed insulin therapy, and blood glucose (and other tests) were followed-up for the proper intervention. Sample size calculation was done about for a prospective study on the effect of pharmaceutical care on maternal and fetal outcomes in gestational and pregestational Diabetic patients by using Oral glucose tolerance test 24 w during fasting. The mean (SD) of PDV (cm/s) 101.4±12.7, which did according to [1], we calculated that the minimum proper sample size was 30 participants in each group to be able to reject the null hypothesis with 90% power at $\alpha = 0.05$ level using one-way analysis of variance and test ratio and with an accommodated 15 % dropout rate with Sample size calculation was done using G*Power software version 3.1.2 for MS Windows. The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013 and Microsoft Office Excel 2007. Descriptive statistics were done for quantitative data as minimum and maximum of the range as well as mean±SD (standard deviation) for quantitative normally distributed data, while it was done for qualitative data as number and percentage. Inferential analyses were done for quantitative variables using the Shapiro-Wilk test for normality testing, independent t-test in cases of two independent groups with normally distributed data, and ANOVA test with post hoc Bonferroni test for more than two independent groups with normally distributed data. In qualitative data, inferential analyses for independent variables were done using the Chi-square test for differences between proportions with the post hoc Bonferroni test. The level of significance was taken at P value<0.050 is significant. Otherwise, it is non-significant.

RESULTS

There was no statistically significant difference between the three studied groups regarding the demographic characteristics in terms of age, socio-economic class, education, and work; p-value<0.05) table 1.

There was no statistically significant difference between the three studied groups in terms of age and gestational age; (p-value 0.204, 0.128 respectively. There was a significant difference in terms of BMI; (p-value 0.001). According to parity, there was no significant

difference between the three groups p=0.766. There was a significant difference in terms of Mode of delivery, presence of Family history, Pregnancy-induced hypertension (PIH), Incidence of Preeclampsia, Proteinuria, Pyuria, Preterm delivery, Birth weight, Macrosomia, Neonatal hypoglycemia, APGAR-5 score<7.0, and NICU admission p-value<0.05) table 2.

Table 2: Baseline of included studies N= number

Variables	Measures	Control (N=30)	Gestational (N=30)	Pregestational (N=30)	p-value
Age (years) (N	20.0–	17 (56.7%)	12 (40.0%)	13 (43.3%)	P=0.392
and Percentage)	30.0–40.0	13 (43.3%)	18 (60.0%)	17 (56.7%)	
Socio-economic	Low	9 (30.0%)	14 (46.7%)	8 (26.7%)	
class(N and	Middle	17 (56.7%)	12 (40.0%)	14 (46.7%)	P=0.299
Percentage)	High	4 (13.3%)	4 (13.3%)	8 (26.7%)	
Education(N	Below uni.	9 (30.0%)	12 (40.0%)	6 (20.0%)	
and Percentage)	University	17 (56.7%)	14 (46.7%)	17 (56.7%)	P=0.467
	Postgraduate	4 (13.3%)	4 (13.3%)	7 (23.3%)	
Work(N and	Nor working	11 (36.7%)	10 (33.3%)	11 (36.7%)	
Percentage)	Desk work	15 (50.0%)	15 (50.0%)	13 (43.3%)	P=0.958
	Active work	4 (13.3%)	5 (16.7%)	6 (20.0%)	

Table 3: Baseline characteristics of the included studies, data was given in mean±SD, and number and total

Measures	Control (N=30)	Gestational (N=30)	Pregestational (N=30)	p-value
Age (mean±SD)	28.3±5.7	30.7±6.2	30.2±4.4	0.204
Gestational age (mean±SD)	37.9±0.9	37.8±0.9	37.4±1.2	0.128
BMI (mean±SD)	24.3±3.8	27.0±3.6	29.8±4.3	0.001
Parity Primiparous (N and Percentage)	10 (33.3%)	8 (26.7%)	7 (23.3%)	0.766
Mode of delivery (N and Percentage)	4 (13.3%)	11 (36.7%)	16 (53.3%)	0.005
Family history present (N and Percentage)	3 (10.0%)	5 (16.7%)	13 (43.3%)	0.005
Pregnancy induced hypertension (PIH) (N and Percentage)	1 (3.3%)	8 (26.7%)	13 (43.3%)	0.001
Incidence of Preeclampsia (N and Percentage)	0 (0.0%)	3 (10.0%)	6 (20.0%)	0.037
Polyhydramnios (N and Percentage)	0 (0.0%)	1 (3.3%)	3 (10.0%)	0.160
Oligohydramnios (N and Percentage)	0 (0.0%)	0 (0.0%)	1 (3.3%)	0.364
Proteinuria (N and Percentage)	1 (3.3%)	6 (20.0%)	12 (40.0%)	0.002
Pyuria (N and Percentage)	2 (6.7%)	7 (23.2%)	13 (43.3%)	0.004
Preterm delivery(N and Percentage)	1 (3.3%)	3 (10.0%)	10 (33.3%)	0.003
Birth weight (kg) (N and Percentage)	3.1±0.3	3.3±0.4	3.6±0.5	0.001
Macrosomia (N and Percentage)	0 (0.0%)	2 (6.7%)	6 (20.0%)	0.021
Low birth weight(N and Percentage)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0.364
Fetal anomalies(N and Percentage)	0 (0.0%)	1 (3.3%)	2 (6.7%)	0.355
Neonatal hypoglycemia(N and Percentage)	0 (0.0%)	1 (3.3%)	6 (20.0%)	0.008
APGAR-5 score<7.0(N and Percentage)	1 (3.3%)	5 (16.7%)	12 (40.0%)	0.002
Incidence of Neonatal respiratory distress (N and Percentage)	0 (0.0%)	1 (3.3%)	4 (13.3%)	0.064
Neonatal jaundice(N and Percentage)	0 (0.0%)	1 (3.3%)	3 (10.0%)	0.160
NICU admission(N and Percentage)	1 (3.3%)	4 (13.3%)	9 (30.0%)	0.016
Fetal and neonatal death(N and Percentage)	0	0	0	-

On the other hand, we did not find any significant difference in terms of Polyhydramnios, Oligohydramnios, Low birth weight, fetal anomalies, and Incidence of Neonatal Respiratory Distress Neonatal jaundice p-value>0.05). In terms of fetal and neonatal death, no event was reported in table 2.

There was a significant difference in the term of Oral glucose tolerance test Week 24 during fasting, Oral glucose tolerance test Week 24 after one hour, Oral glucose tolerance test Week 24 after two hours, Oral glucose tolerance test Week 24 after three hours, Oral glucose tolerance test Week 28 during fasting, Oral glucose tolerance test Week 28 after one hour, Oral glucose tolerance test Week 28 after two hours, Oral glucose tolerance test Week 28 after three hours, Hba1c week 24 and Hba1c week 28; p-value<0.05 table 3 [fig. 1,2,3,4,5].

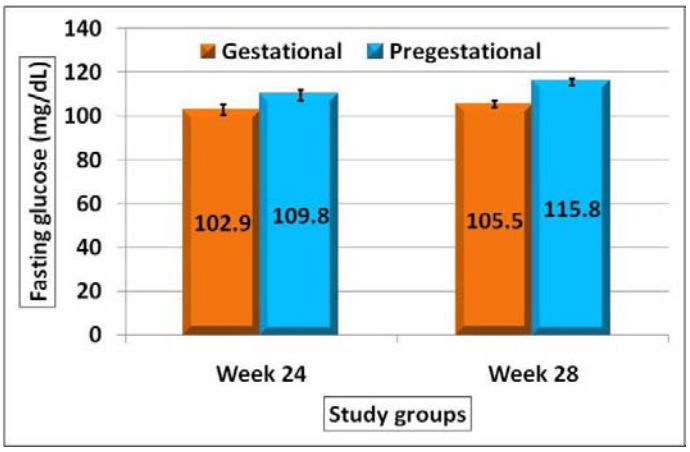

Fig. 1: Oral glucose tolerance test (fasting) among the diabetic groups

Table 4: Outcome results in the included studies, data was givin in mean±SD, and number and total

Measures	Gestational (N=30)	Pregestational (N=30)	p-value
Oral glucose tolerance test Week 24 during fasting (mean±SD)	102.9±13.4	109.8±9.3	0.024
Oral glucose tolerance test Week 24 after one hour (mean±SD)	188.4±9.2	193.1±6.3	0.024
Oral glucose tolerance test Week 24 after two hours (mean±SD)	159.3±5.1	166.8±9.0	0.001
Oral glucose tolerance test Week 24 after three hours (mean±SD)	142.6±6.6	158.2±8.8	0.001
Oral glucose tolerance test Week 28 during fasting (mean±SD)	105.5±13.3	115.8±9.3	0.001
Oral glucose tolerance test Week 28 after one hour (mean±SD)	191.5±9.4	199.3±6.3	0.001
Oral glucose tolerance test Week 28 after two hours (mean±SD)	162.6±5.1	172.5±9.1	0.001
Oral glucose tolerance test Week 28 after three hours (mean±SD)	146.2±6.6	163.9±9.0	0.001
Hba1c week 24(mean±SD)	6.5±0.3	6.9±0.3	0.001
Hba1c week 28(mean±SD)	6.5±0.3	6.9±0.3	0.001

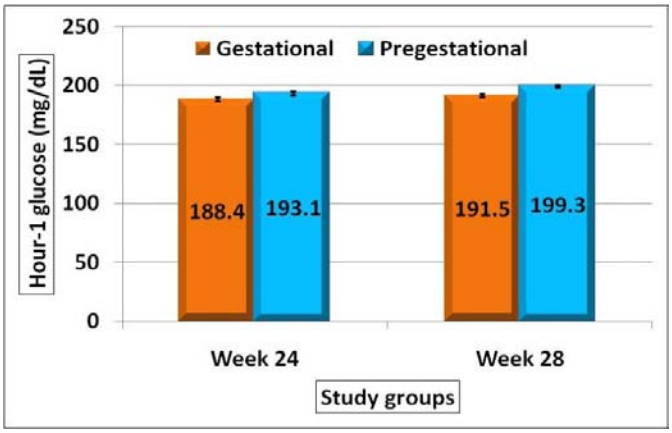

Fig. 2: Oral glucose tolerance test (hour-1) among the diabetic groups

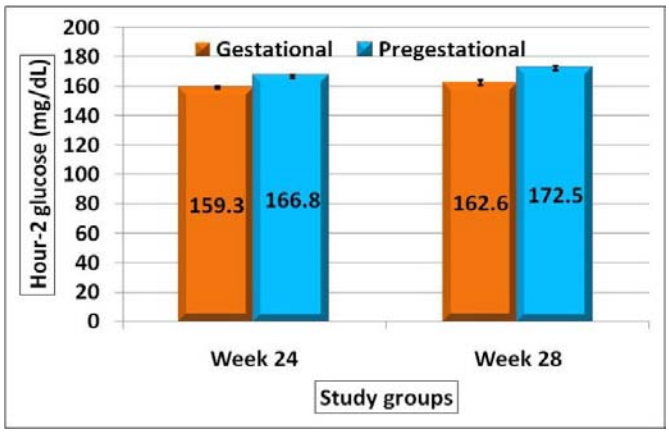

Fig. 3: Oral glucose tolerance test (hour-2) among the diabetic groups

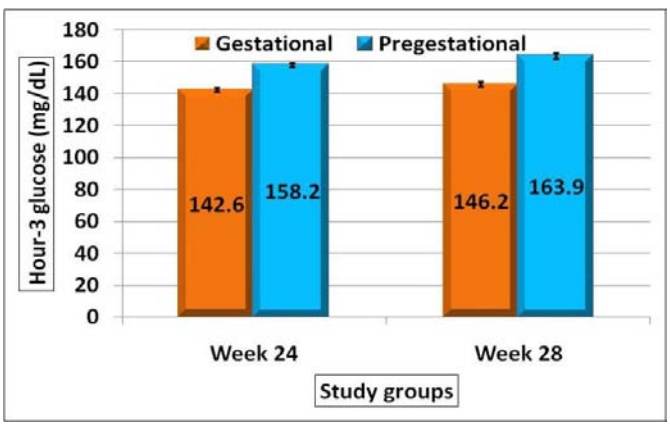

Fig. 4: Oral glucose tolerance test (hour-3) among the diabetic groups

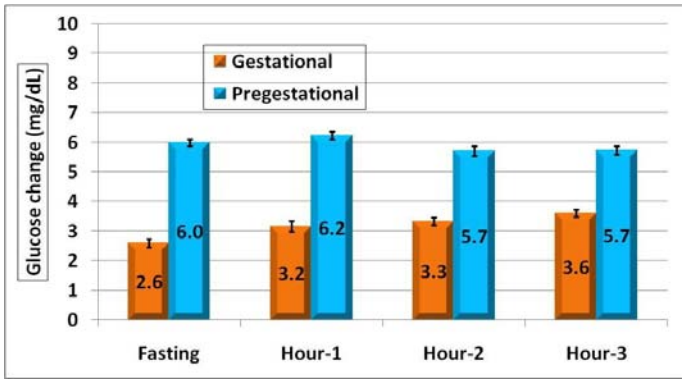

Fig. 5: Oral glucose tolerance test change among the diabetic groups

DISCUSSION

The rate of Diabetes in Egypt has significantly increased, exceeding international rates. The International Diabetes Federation (IDF) listed Egypt among the world's top 10 countries in the number of patients with diabetes [7-10]. GDM affects approximately 14% of pregnancies worldwide, representing approximately 18 million births annually.

There was a significant difference in the term of Oral glucose tolerance test Week 24 during fasting, Oral glucose tolerance test Week 24 after one hour, Oral glucose tolerance test 24 w after two hours, Oral glucose tolerance test 24 w after three hours, Oral glucose tolerance test Week 28 during fasting, Oral glucose tolerance test Week 28 after one hour, Oral glucose tolerance test Week 28 after two hours, Oral glucose tolerance test Week 28 after three hours, HbA1c 24 w and HbA1c week 28. We also found that the gestational age was less than the pregestational age group in the mean, which put it in priority.

In the present study, the presence of a DM family history was more common in the PGDM group, followed by the GDM Group; however, the differences were only significant between the Control and GDM groups, and this agrees with Shefali *et al.*, 2006 [11-15] Also, with Eltoony *et al.*, 2021 [16-18] found that family history of Diabetes and GDM were the major risk factors for GDM in Recent study aimed at estimating the prevalence of GDM in Aswan Governorate in Egypt and determining the risk factors associated with GDM. In terms of maternal-related comorbidities, the current study found that pregnancy-induced hypertension and Preeclampsia, as well as proteinuria and pyuria, were most Prevalent in the PGDM group. This study also found that the PGDM group had a higher incidence of polyhydramnios and Oligohydramnios than the GDM group.

Our findings supported those of Fong *et al.*, 2014 [19, 20], as several clinical comorbidities were found to be significantly Higher in PGDM when compared to GDM after controlling for Covariates. Chronic disease conditions such as chronic hypertension were more common in subjects with PGDM, and Battarbee *et al.*, 2020 [21-24] study concluded that PGDM had more comorbidities than GDM. In the current study, the PGDM group performed significantly better on the oral glucose tolerance test at different Hours than the GDM group. Also, the PGDM group had significantly higher hba1c levels at 24 and 28 w than the GDM group. These findings agreed with those of Shefali *et al.*, 2006 [25] and Middleton *et al.*, 2016 [26], who investigated the Relationship between glycemic control and pregnancy outcomes and discovered higher HbA1c in type 1 and type 2 diabetes when compared to GDM. According to a systematic review and meta-analysis, Preconception diabetes care for T1DM and T2DM is effective in Reducing diabetes-related congenital malformations, preterm delivery, and maternal hyperglycemia in the first trimester of pregnancy [27]. This systematic review concluded that preconception Care is effective in reducing congenital malformations, preterm delivery, and perinatal mortality, as well as lowering HbA1c by an average of 2.43 percent in the first trimester of pregnancy [28].

The ADA 2016 standards of care recommend a target of HbA1c 6–6.5% (42–48 mmol/mol), but state that 6% (42 Mmol/mol) may be optimal as pregnancy progresses, and HbA1c Levels may need to be monitored more frequently than usual, i.e., Monthly [29]. In terms of delivery-related risks, the current study found that preterm delivery and cesarian delivery were most common in the PGDM, followed by the gestational Group. Only the difference was found between the control and PGDM groups were significant. According to Fong *et al.*, 2014 [30], subjects with PGDM were more likely to have a cesarean delivery, a failed induction, Or shoulder dystocia. They were less likely to have a post-term Birth. PGDM patients had a slightly longer mean length of hospital stay than GDM patients. These results also agree with the Findings of the Wahabi *et al.*, 2017 study [31]. In terms of neonatal problems in the current study, Macrosomia Macrosomia was most common in the PGDM group, followed by the GDM group, and did not occur in the control group. Only the differences between the control and PGDM groups were statistically significant.

Our findings supported those of Wahabi *et al.*, 2017 [32] and Battarbee *et al.*, 2020 [33], who found an increased risk of large for gestational age and preterm birth in PGDM compared to GDM, as well as [34, 35] studies that Discovered diabetic pregnant women, in general, had an Increased Risk for this complication. When screening for fetal anomalies in the current study, we revealed that it was most common in the pregestational Group, (6.7 %) showing fetal anomalies, compared to only (3.3%). In comparison, there were no fetal anomalies in the Control group. The differences between the three groups studied were not statistically significant (P>0.05). Unfortunately, it will be difficult to link congenital Anomalies detected in the postnatal period to any maternal Condition due to the lack of a national registry for congenital anomalies and the difficulty of following a cohort of children with the frequent change of address and healthcare provider [36]. Our findings illustrated that the PGDM group suffered from neonatal Respiratory Distress, followed by the gestational Group with only one woman, and were least frequent in the control group, which showed no occurrence of neonatal respiratory Distress. The differences between the three studied groups were Non-significant. (P>0.05), in agreement with [37].

The maternal PGDM has consistently been found to increase the risk of delayed pulmonary lung maturity [38, 38], but the association between gestational diabetes and respiratory morbidity has been inconsistent [39]. There is a biological explanation for why there is a link between maternal PGDM and severe neonatal morbidity, but not necessarily between GDM and respiratory morbidity. Maternal hyperglycemia during pregnancy causes transient fetal hyperglycemia via placental diffusion. Elevated fetal glucose levels stimulate the fetal pancreas to produce insulin, which inhibits type II pneumocyte maturation in the lung and acts as a potent growth hormone. The severity of these fetal consequences is influenced by the degree and duration of hyperglycemia in women with PGDM. [40] APGAR-5 score<7.0 and NICU admission in the present study were most frequent in the PGDM group than in the GDM group. The differences were significant only between the control and the PGDM groups. Also, Neonatal hypoglycemia and Neonatal jaundice were most frequent in the PGDM group.

Our findings supported [36, 37] findings that PGDM increases the risk of adverse pregnancy outcomes, including a nearly fourfold increase in the risk of stillbirth and fetal Distress and a more than twofold increase in the risk of preterm birth and admission to the NICU. This can be explained by the fetus being exposed to a more and severe hyperglycemic environment for a longer period of time than in the GDM. Similar studies established a linear relationship between the degree of hyperglycemia and the development of certain maternal and neonatal complications [41, 42].

The present study agreed with the findings of Battarbee *et al.*, 2020 [43]. PGDM was linked to an increased risk of both respiratory distress syndrome and mechanical ventilation; however, gestational diabetes was not linked to neonatal respiratory morbidity. Neither pregnancies nor gestations were linked to neonatal mortality.

Many factors could have influenced the differences in the outcomes between these two conditions, including the fetus's prolonged exposure to maternal hyperglycemia in the case of PGDM, resulting in prolonged fetal hyperinsulinemia and increased C peptide levels and thus more severe effects on fetal weight gain, Macrosomia Macrosomia, and related complications such as CS delivery [41]. Moreover, prolonged hyperglycemia in PGDM affects the placental vascular bed and can result in an increased risk of stillbirth, antenatal and intrapartum asphyxia, and hence the low APGAR scores at birth noted in this study. Such observation could have been supported further if enough data were available to investigate the effect of the duration of PGDM on the birth weight [44-47].

Limitation of the study: the small number of included studies, the study design was a prospective study not randomized controlled study, and we wanted to investigate it as a global study.

CONCLUSION

After follow-up on pregnant women, we did educate all women how to monitoring their blood glucose and alternative method to manage it such as food management as well as medication adherence, and exercise.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Study conception and design: Shireen Mohsen, Acquisition of data: Shireen Mohsen, Analysis and interpretation of data Shireen Mohsen, Drafting of manuscript: Shireen Mohsen, Dr. Ahmed El-Berry, Dr. Hoda Rabea and Critical revision: Shireen Mohsen, Dr. Ahmed El-Berry

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Holmes VA, Young IS, Patterson CC, Pearson DWM, Walker JD, Maresh MJA, McCance DR. Optimal glycemic control, pre-eclampsia, and gestational hypertension in women with type 1 diabetes in diabetes and pre-eclampsia intervention trial. Diabetes Care. 2011;34(8):1683-8. doi: 10.2337/dc11-0244.
2. Jensen DM, Korsholm L, Ovesen P, Beck-Nielsen H, Moelsted-Pedersen L, Westergaard JG, Moeller M, Damm P. Peri-conceptional A1C and risk of serious adverse pregnancy outcome in 933 women with type 1 diabetes. Diabetes Care. 2009;32(6):1046-8. doi: 10.2337/dc08-2061.
3. Charron Prochownik D, Sereika SM, Becker D. Long-term effects of the booster-enhanced ready-girls preconception counseling program on intentions and behaviors for family planning in teens with diabetes. Diabetes Care. 2013;36(12):3870-4. doi: 10.2337/dc13-0355.
4. Peterson C, Grosse SD, Li R, Sharma AJ, Razzaghi H, Herman WH, Gilboa SM. Preventable health and cost burden of adverse birth outcomes associated with pregestational diabetes in the United States. Am J Obstet Gynecol. 2015;212(1):74.e1-9. doi: 10.1016/j.ajog.2014.09.009, PMID 25439811.
5. Charron Prochownik D, Downs J. Diabetes and reproductive health for girls. Alexandria, VA: American Diabetes Association; 2016.
6. Manderson JG, Patterson CC, Hadden DR, Traub AI, Ennis C, McCance DR. Preprandial versus postprandial blood glucose monitoring in type 1 diabetic pregnancy: a randomized controlled clinical trial. Am J Obstet Gynecol. 2003;189(2):507-12. doi: 10.1067/s0002-9378(03)00497-6, PMID 14520226.
7. Committee on Practice Bulletins–obstetrics. Practice Bulletin No. 137. Gestational diabetes mellitus. Obstet Gynecol; 2013.
8. Chew EY, Mills JL, Metzger BE. Metabolic control and progression of retinopathy: the S142 Management of Diabetes in Pregnancy Diabetes Care. Jan 2018;41 Suppl 1.
9. Institute of Medicine, National Research Council. Weight gain during pregnancy: reexamining the guidelines. Washington, DC: National Academies Press; 2009.
10. Cundy T, Gamble G, Neale L, Elder R, McPherson P, Henley P, Rowan J. Differing causes of pregnancy loss in type 1 and type 2 diabetes. Diabetes Care. 2007;30(10):2603-7. doi: 10.2337/dc07-0555, PMID 17586739.
11. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care. 2002;25(10):1862-8. doi: 10.2337/diacare.25.10.1862, PMID 12351492.
12. Sutherland HW, Stowers JM, Pearson DWM (Eds.). Carbohydrate metabolism in pregnancy and the newborn IV. Edinburgh: Churchill Livingstone; 1984.
13. Tobias DK, Hu FB, Chavarro J, Rosner B, Mozaffarian D, Zhang C. Healthful dietary patterns and type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Arch Intern Med. 2012;172(20):1566-72. doi: 10.1001/archinternmed.2012.3747, PMID 22987062.
14. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet. 2006;368(9542):1164-70. doi: 10.1016/S0140-6736(06)69473-7, PMID 17011943.
15. Ratner RE, Christophi CA, Metzger BE. Diabetes prevention program research group. Prevention of Diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. J Clin Endocrinol Metab. 2008.
16. Aroda VR, Christophi CA, Edelstein SL. Diabetes prevention program Research Group. The effect of lifestyle intervention and metformin on preventing or delaying diabetes among women with and without gestational diabetes: the diabetes prevention program outcomes study 10 y followup. J Clin Endocrinol Metab. 2015.
17. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: a systematic review of controlled studies. BMJ. 2005;330(7491):565. doi: 10.1136/ bmj.38380. 674340.E0, PMID 15743856.
18. Henderson JT, Whitlock EP, O'Conner E, Senger CA, Thompson JH, Rowland MG. Low dose aspirin for the prevention of morbidity and mortality from preeclampsia: a systematic evidence review for the U.S. Preventive Services Task Force, 2017.
19. Werner EF, Hauspurg AK, Rouse DJ. A cost-benefit analysis of low-dose aspirin prophylaxis for the prevention of preeclampsia in the United States. Obstet Gynecol. 2015;126(6):1242-50. doi: 10.1097/AOG.0000000000001115, PMID 26551178.
20. American Diabetes Association. 13. Management of Diabetes in Pregnancy. Diabetes Care. 2017;40(Suppl 1):S114-9. doi: 10.2337/dc17-S016, PMID 27979900.
21. Yasuhi I, Soda T, Yamashita H, Urakawa A, Izumi M, Kugishima Y, Umezaki Y. The effect of high-intensity breastfeeding on postpartum glucose tolerance in women with recent gestational diabetes. Int Breastfeed J. 2017;12:32. doi: 10.1186/s13006-017-0123-z, PMID 28725256.
22. American Diabetes Association. 12. Management of Diabetes in Pregnancy. Diabetes Care. 2016;39 Suppl 1:S94-8. doi: 10.2337/dc16-S015, PMID 26696688.
23. Battarbee AN, Venkatesh KK, Aliaga S, Boggess KA. The association of pregestational and gestational diabetes with severe neonatal morbidity and mortality. J Perinatol. 2020;40(2):232-9. doi: 10.1038/s41372-019-0516-5, PMID 31591489.
24. Bental Y, Reichman B, Shiff Y, Weisbrod M, Boyko V, Lerner Geva L, Mimouni FB, Collaboration With the Israel Neonatal Network. Impact of maternal diabetes mellitus on mortality and morbidity of preterm infants (24-33 weeks' gestation).

Pediatrics. 2011;128(4):e848-55. doi: 10.1542/peds.2010-3443. PMID 21930550.

25. Billionnet C, Mitanchez D, Weill A, Nizard J, Alla F, Hartemann A, Jacqueminet S. Gestational diabetes and adverse perinatal outcomes from 716,152 births in france in 2012. Diabetologia. 2017;60(4):636-44. doi: 10.1007/s00125-017-4206-6, PMID 28197657.
26. Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, Dietz PM. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care. 2007;30(8):2070-6. doi: 10.2337/dc06-2559a, PMID 17416786.
27. Cacho Diaz B, Garcia Botello DR, Wegman Ostrosky T, Reyes Soto G, Ortiz Sanchez E, Herrera Montalvo LA. Tumor microenvironment differences between primary tumor and brain metastases. J Transl Med. 2020;18(1):1. doi: 10.1186/s12967-019-02189-8. PMID 31900168.
28. Eltoony LF, Ibrahem SA, Hafez MZE-D, Ali OM, Elsewify WAE. Prevalence and risk factors for gestational diabetes in Aswan, Egypt according to international Association of the Diabetes and Pregnancy study groups (IADPSG). Egypt J Hosp Med. 2021;82(4):701-7. doi: 10.21608/ejhm.2021.150445.
29. Farrar D, Simmonds M, Bryant M, Sheldon TA, Tuffnell D, Golder S, Dunne F, Lawlor DA. Hyperglycaemia and risk of adverse perinatal outcomes: systematic review and meta-analysis. BMJ. 2016;354:i4694. doi: 10.1136/bmj.i4694. PMID 27624087.
30. Fong A, Serra A, Herrero T, Pan D, Ogunyemi D. Pre-gestational versus gestational diabetes: a population-based study on clinical and demographic differences. J Diabetes Complications. 2014;28(1):29-34. doi: 10.1016/j.jdiacomp.2013.08.009, PMID 24094665.
31. Kawakita T, Bowers K, Hazrati S, Zhang C, Grewal J, Chen Z, Sun L, Grantz KL. Increased neonatal respiratory morbidity associated with gestational and pregestational diabetes: a retrospective study. Am J Perinatol. 2017;34(11):1160-8. doi: 10.1055/s-0037-1604414, PMID 28738436.
32. Knowler WC, Drews K, Redman L, Joshipura KJ, Arteaga SS, Pi-Sunyer X, Van Horn L, Wing RR, Klein S, Group L-MR 2018. Changing glucose tolerance during pregnancy-implications for diagnosis of gestational diabetes mellitus (GDM). Am Diabetes Assoc. 2018;67 Suppl 1:119-OR. doi: 10.2337/db18-119-OR
33. Kong L, Nilsson IAK, Gissler M, Lavebratt C. Associations of maternal diabetes and body mass index with offspring birth weight and prematurity. JAMA Pediatr. 2019;173(4):371-8. doi: 10.1001/jamapediatrics.2018.5541, PMID 30801637.
34. Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. Diabetes Res Clin Pract. 2020;162:108044. doi: 10.1016/j.diabres.2020.108044.
35. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS, Sacks DA. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358(19):1991-2002. doi: 10.1056/NEJMoa0707943, PMID 18463375.
36. Middleton P, Crowther CA, Simmonds L. Different intensities of glycaemic control for pregnant women with pre-existing diabetes. Cochrane Database Syst Rev. 2016(5). doi: 10.1002/14651858.CD008540.pub4.
37. Persson M, Shah PS, Rusconi F, Reichman B, Modi N, Kusuda S, Lehtonen L, Hakansson S, Yang J, Isayama T, Beltempo M, Lee S, Norman M, International Network for Evaluating Outcomes of Neonates. Association of maternal diabetes with neonatal outcomes of very preterm and very-low-birth-weight infants: an international cohort study. JAMA Pediatr. 2018;172(9):867-75. doi: 10.1001/jamapediatrics.2018.1811, PMID 29971428.
38. Shefali AK, Kavitha M, Deepa R, Mohan, V. Pregnancy outcomes in pre-gestational and gestational diabetic women in comparison to a non-diabetic women-A prospective study in Asian Indian mothers (CURES-35). The Journal of the Association of Physicians of India. 2006;54:613-8. PMID 16941791.
39. Stacey T, Tennant PW, Mccowan LM, Mitchell EA, Budd J, Li M, Thompson JM, Martin B, Roberts D, Heazell AE. Gestational diabetes and the risk of late stillbirth: a case-control study from England, UK. BJOG: An International Journal of Obstetrics and Gynaecology. 2019;126(8):973-82. doi: 10.1111/1471-0528.15659, PMID 30891907.
40. Wahabi H, Fayed A, Esmaeil S, Mamdouh H, Kotb R. Prevalence and complications of pregestational and gestational Diabetes in Saudi women: analysis from Riyadh Mother and Baby cohort study (RAHMA). BioMed Research International. 2017;2017:6878263. doi: 10.1155/2017/6878263, PMID 28386562.
41. Wahabi HA, Alzeidan RA, Bawazeer GA, Alansari LA, Esmaeil SA. Preconception care for diabetic women for improving maternal and fetal outcomes: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2010;10:63. doi: 10.1186/1471-2393-10-63, PMID 20946676.
42. Wahabi HA, Esmaeil SA, Fayed A, Al-Shaikh G, Alzeidan RA. Pre-existing diabetes mellitus and adverse pregnancy outcomes. BMC Res Notes. 2012;5:496. doi: 10.1186/1756-0500-5-496, PMID 22963905.
43. Wahabi HA, Fayed A, Esmaeil SA. Maternal and perinatal outcomes of pregnancies complicated with pre-gestational and gestational diabetes mellitus in Saudi Arabia. J Diabetes Metab. 2014;5:2.
44. Wojtyla C, Stanirowski P, Gutaj P, Ciebiera M, Wojtyla A. Perinatal outcomes in a population of diabetic and obese pregnant women-the results of the national polish survey. International Journal of Environmental Research and Public Health. 2021;18(2):560. doi: 10.3390/ijerph18020560, PMID 33440848.
45. AM, KK. Pharmacoeconomic evaluation of antidiabetic therapy at a tertiary health care institution. Asian J Pharm Clin Res. July 2021;14(6):115-20.
46. Mussttaf GS, Habib A, Mahtook M. Drug prescribing pattern and cost-effectiveness analysis of oral antidiabetic drugs in patients with type-2 diabetes mellitus: real-world data from indian publication. Asian J Pharm Clin Res. May 2021;14(7):45-9. doi: 10.22159/ajpcr.2021.v14i7.41677.
47. Mahmood A, Ball P, Morrissey H. Exploring pharmacy students Knowledge and understanding of eating disorders and their impact on mental health and quality of life. Int J Curr Pharm Sci. Sep 2021;13(5):63-9.