

# Risk Factors and Management of Type 2 Diabetes Mellitus and Gestational Diabetes Mellitus

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## ABSTRACT

**Background:** To determine the risk factor and treatment of type 2 DM for women with a history of GDM.

GDM is associated with morbidity and mortality for mother and fetus and risk of medical diseases later in life for the mother and child like type 2 diabetes mellitus. There is relation between this type of diabetes and glucose tolerance post-partum and association with adverse perinatal outcome.

**Methods;** This study was conducted in Tripoli medical center at the Clinic of Gynecology and Obstetrics from 2018 to 2021, the study included 55 pregnant women who had gestational diabetes mellitus (GDM) and follow them after 6 weeks after delivery for 3 years. Diagnosis of type 2 diabetes is according to ADA 2021, the data collected by a doctor according to the questionnaire some of the women by face to face interview and some of them by telephone, the collected answers were analyzed and the results were presented using tables and figures.

**Result:** The result of the study showed that according to HbA1c, 31% of GDM become diabetic. The result also showed 50% of diabetic women her age was between 18-26 year, and about BMI the diabetic women was 36% of them are overweight. with regard the treatment the study reported 40% of diabetic women receive oral and insulin as treatment, the study showed the women how was poor controlled FBS in last trimester 34.1% become diabetic, about complication during the pregnancy 31% of diabetic women have no complication during the pregnancy.

**Conclusion:** women with a history of GDM need follow up for several years after delivery because the women with a history of GDM at risk of type 2 diabetes or GTD post-partum and the age and BMI and glycemetic control in last trimester is considered a risk factor for diabetes in our study.

## INTRODUCTION

Gestational diabetes mellitus (GDM) was defined as glucose intolerance in pregnant women at any time in pregnancy but recently American Diabetes Association change the definition to diabetes that is diagnosed in the second and third trimester of pregnancy (1,2). It affects 14% of all pregnancies about 135,000 women diagnosed with GDM in the year in the united states (3).

GDM causes maternal and fetal mortality and morbidity so early screening and diagnosis minimize and prevent the complication (4). women with GDM have a risk to develop hypertensive disorders increasing the risk of cesarean section and longtime risk of metabolic disorders as type 2 diabetes and cardiovascular disorder. neonatal of diabetic mothers have a risk of macrosomia, shoulder dystocia, respiratory distress syndrome, and risk of metabolic and cardiovascular disease about 60% of women with GDM have a risk to develop type 2 diabetes later in life (7).

There are several risk factors of GDM as overweight, obesity, excessive gestational weight gain, unhealthy

diet, genetic polymorphisms, advanced maternal age, In recent study in Libya, Bin Ramadan et al., (30) recorded that gestational diabetes in pregnant women were in the age  $\geq 35$  years, and concluded that increased maternal age is an important risk factor for the development of GDM. Family and personal history of GDM and other diseases of insulin resistance as polycystic ovary syndrome (PCOS) (6). These factors are directly or indirectly associated with impaired beta-cell function and or insulin sensitivity (7). Previous pregnancy complication as congenital heart disease, macrosomia, and intrauterine fetal death (IUFD) are a risk factor for GDM.

According to American Diabetes Association (ADA), the diagnosis of GDM depends on two strategies the test done at 24-28 weeks of gestation in women not previously diagnosed with diabetes. The one-step strategy derived from the IADPSG criteria by a 75g Oral glucose tolerance test (OGTT) with measurement of blood glucose at fasting after 8 hours of overnight fast at one hour then at two hours the diagnosis made if any of the following values are met or exceeded:

Fasting 92mg \ dl(5.1mmol\l)

1-hour 180mg \ dl(10.0mmol\l)

2-hour 153mg \ dl(8.5mmol\l) (2)

According to new NICE guidance published on 28 July, 2021 testing women with a risk factor for developing GDM and women with previous history of GDM offer early self-monitoring of blood glucose or 75g two-hour OGTT as soon as possible after the first antenatal visit (in the first or second trimester) and another one (75g 2hour OGTT) at 24-28week if the result of the first OGTT are normal the diagnosis of GDM made if women has result met or excess either a fasting blood glucose level of 5.6 mmol \ liter or a 2-hour blood glucose 7.8 mmol \ 7liter (8).

### **Management of GDM:**

According to the fifth international workshop conference on gestational diabetes mellitus the target of glycemic control is:

Fasting glucose less than 95mg \ dl {5.3mmol\l} and either

One-hour postprandial glucose less than 140mg\dl{7.8mmol\l} or

Two-hour postprandial glucose less than 120mg \ dl{6.7mmol\l} (1).

The first step in the treatment of GDM is lifestyle changes started with weight management physical activity such as walking for 30 minutes after a meal to enhance blood glucose control and medical nutrition therapy (5,10).

Nutrition therapy for GDM is a personal nutrition plan that should give adequate calorie intake to promote fetal and maternal health to rich glycemic goals and promote weight gain according to the institute of medicine recommendations 2009 (5). There are specific dietary advice for a patient with GDM as increased water intake, regular meal time, increase vegetable and fruit and reduce carbohydrate, salt, saturated fat, processed meat intake. Moderate sucrose, fructose, and artificial sweeteners intake (11). In UK the total daily energy intake of 1,940 kcal in pregnancy, increasing to 2,140 kcal in the third trimester as the royal college of obstetricians and gynecologists (RCOG) recommended (5).

Pharmacologic therapy is considered when lifestyle modification is failed to rich and maintain optimal glycemic target. However, Pharmacologic therapy is considered when lifestyle modification is failed to rich and maintain optimal glycemic target.

Oral hypoglycemic agent;

Oral hypoglycemic drugs as metformin or glyburide are widely used for gestational diabetes but it is not being approved by the food and drug administration for this indication (12). Metformin is acting to lower blood glucose by suppression of hepatic glucose output, increasing hepatic insulin sensitivity, and increasing peripheral glucose uptake due to changes in glucose metabolism in pregnancy the metformin is the best choice of oral antihyperglycemic agent for the management of GDM. Metformin was used if the blood glucose target is not achieved after 1-2 weeks of changes in diet and exercise (8).

Metformin can prevent fetal macrosomia ( $\geq 4000$  g) in women with GDM especially in lean and moderately overweight women (13). It is across the placenta the large dose of metformin was needed in pregnancy due to alteration in pharmacokinetics during pregnancy. It is unlikely that metformin leads to an increased vitamin B12 deficiency during pregnancy (5).

It is associated with a decreased risk of neonatal hypoglycemia and less maternal weight gain than insulin (13). However, the failure rate of metformin in GDM appeared to be higher than glyburide (24). Although the metformin was associated with a decreased risk of hypertension or preeclampsia in GDM women (9), There is no controlled data on the use of metformin during pregnancy, and long term safety is still unknown (14,24).

Glibenclamide crosses the placenta and has a high rate of neonatal hypoglycemia and macrosomia than metformin and insulin (14). Although it is used in women that do not achieve the glycemic target by changes in diet and exercise (12), long term safety data for offspring exposed to glyburide are not available (14,24).

Insulin is the only FDA approved medication for the treatment of gestational diabetes and it is standard therapy in women with GDM to target glycemic goal cannot be achieved with nutrition and exercise. Ageel and her colleagues 2021 reported that the neonatal complication such as, the macrosomia and with good neonatal condition were more in the insulin group (29).

The insulin does not cross the placenta according to American college of obstetricians and gynecologist, 2013 insulin is prescribed at a starting dose is 0.7-1.0 unit/kg/day in divided doses the dose adjustment depending on the daily glucose level, additional to the pattern of women's diet (12,15). Subsequently, the dose of insulin is divided into 50% neutral protamine Hagedorn insulin and 50% as three pre-prandial rapid-acting injections this regimen is more commonly used (15) and both long action with short-action analogs as aspart and lispro insulin are approved to be used in pregnancy (11). During pregnancy there is a risk of neonatal hypoglycemia with insulin use (16). Consider continuing self-monitoring blood glucose (SMBG) allows the woman to evaluate her response to the therapy and achieve the glycemic goal (17). The American College of obstetricians and gynecologist (2013) recommends four-time daily self-glucose monitoring done at fasting and either 1 or 2 hours after each meal (12).

### **Post-partum follows up:**

Based on the 50% percent risk of developing type 2 diabetes in women with GDM within 20 years was evaluated them as an International work shop conference on gestational diabetes recommend (12) that the evaluation is done by 75-g OGTT at 4-12 weeks after the delivery. HbA1c is not reliable as indicator for glycemic control as result of increase red cell turnover in pregnancy therefore, OGTT is more sensitive for detecting glucose intolerance if the result is normal to perform annual HbA1c or fasting blood sugar or 75g OGTT using non-pregnant thresholds every 1-3 year (1). The changes in diet, exercise and weight management with or without metformin can prevent type 2 diabetes as some data suggest (10). In previous studies found that the longer duration of lactation is decrease the risk of type 2 diabetes among women with a history of GDM (18).

The Predictors of postpartum diabetes type 2 in women with GDM is a family history of diabetes, history of pregnancy-induced hypertension, pre-pregnancy BMI, FSB level in last trimester, and 2-hour glucose level at 26-30 weeks of gestation (19). The aim of the present study was to determine the risk factor and management of type 2 diabetes mellitus for women with a history of GDM.

## METHODS AND SUBJECTS

### Sample Collection

This study was a prospective cross-sectional study, it was conducted in Tripoli medical center at the Clinic of Gynecology and Obstetrics from 2018 to 2021, the study included 55 pregnant women who had gestational diabetes mellitus (GDM) and follow them after 6 weeks post delivery for 3 years. Diagnosis of type 2 diabetes is according to ADA 2021, the data collected by a doctor according to questionnaire some of the women by face to face interview and some of them by telephone, the collected answers were analyzed and the results were presented using tables and figures. patients were asked about their age, BMI kg/m, the highest level of education she completed, parity, fetal outcome, treatment of GDM and blood sugar state after puerperium.

### Ethical clearance

The study was ethically cleared and approved by the ethical review committee of the Tripoli medical center with a supporting letter from the Medical Technology Research Team at the University of Tripoli/ Faculty of Medical Technology. Data were collected after getting approval from the hospital medical director and head of Gynecology and Obstetrics department. Written informed consent from each study participant. Data confidentiality was kept through avoiding personal identifiers and anonymity of personal data records.

### Statistical analysis

Statistical analysis was performed using the statistical package SPSS version 21. For each continuous variable, normality was checked by Shapiro-Wilk tests and by histograms (Shapiro  $p > 0.05$ ). Comparisons between the values of the continuous variables were applied using both the Kruskal-Wallis test and Mann-Whitney test were used for the data not normally distributed. Values of  $P < 0.05$  were considered as statistically significant.

Data are presented tabular and graphically by descriptive statistics methods. Nominal and categorical values are shown through frequencies and proportions, while quantitative values are shown through arithmetic means and standard deviations.

## RESULTS

Fifty-five of hyperglycemic pregnant women who had gestational diabetes mellitus (GDM) and met the inclusion criteria were included in the study. Accordingly, 73% of women who had fasting glucose level equal to or below than 126 mg/dL, whereas only 27% of women who had fasting glucose level higher 126 mg/dL after child' birth. Considering about HbA1C, 69% of women who had HbA1C level equal to or below than 6.5% after child'birth, whereas 31% of women who had HbA1C level higher 6.5% after child' birth the statistically significant was ( $p= 0.00$ ) (Tab.1).

Table 1: shows the FBS and HbA1C after childbirth

	Category	n	Ob served Prop.	Test Prop.	Exact Sig. (2-tailed)
FBS after the child's birth	$\leq 126$	40	73%	50%	0.00
	$> 126$	15	27%		
HbA1c after the child's birth	$\leq 6.5$	38	69%	50%	0.00
	$> 6.5$	17	31%		

Table 2: Age distribution of women diagnosed with type 2 diabetes

	GDM	Type 2 diabetes			
	n	n	%	Mean	P-value
18- 26 y	6	3	50.0	273.33	0.05
27-35 y	35	9	25.7	186.33	
36- 44 y	14	3	21.4	156.67	
Total	55	15	27.3	197.80	

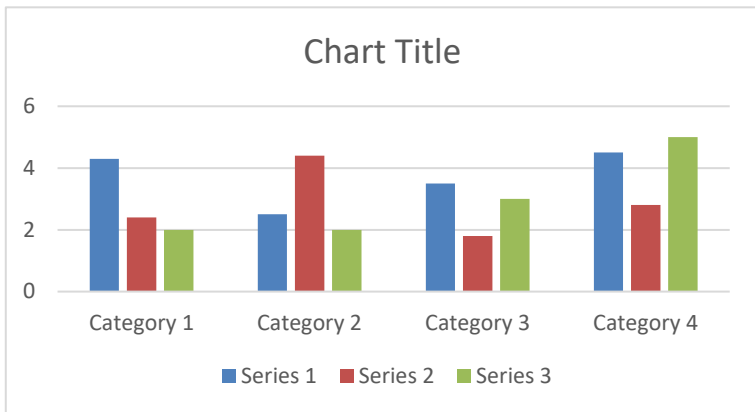


Table 2 and Figure 1. show the incidence of GDM how diagnosed with type 2 DM by age in this study the incidence was highest in the 18–26 years old group with 50% with man 273.33 moreover, in the two age groups was 27-35 years, 36-44 years, respectively 25.7%, and 21.4%. There was a significant interaction between GDM how diagnosed with type 2 DM and age ( $P \leq 0.05$ ).

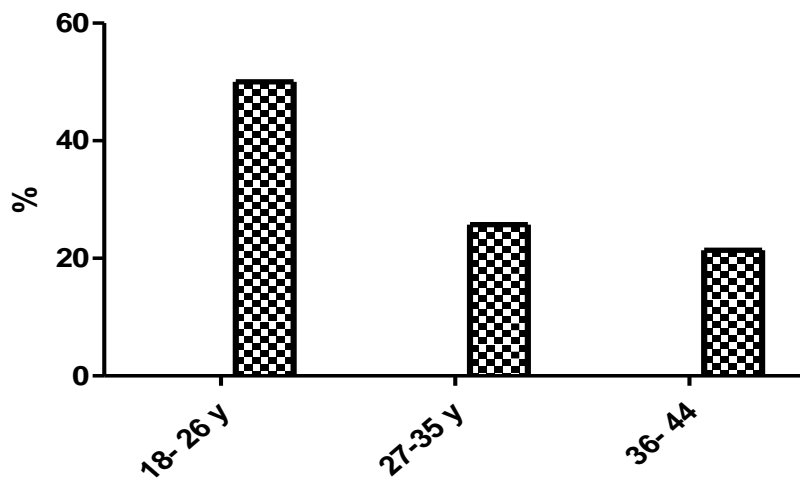


Fig.1: Age distribution of women diagnosed with type 2

Table 3: BMI distribution of women diagnosed with type 2

	GDM	Type 2 diabetes		
	n	n	%	P-value
normal weight	11	4	36.4	0.02

overweight	25	9	36.0	
Obesity	19	2	10.5	
Total	55	15	27.3	

Figure (2) shows the outcome-based comparison between BMI for pregnant women with GDM and how diagnosed with type 2 diabetes; the results showed that 36,4% of women who have normal weight diagnosed with type 2 diabetes post-partum, as for results about women which have overweight, this study showed that 36% from them diagnosed with type 2 diabetes. As for women which have obesity were the least incidence of type 2 diabetes from all BMI groups, they just represent 10.5%, which indicates having statistically significant means difference between the BMI groups, the BMI effects in the incidence of type 2 diabetes postpartum.

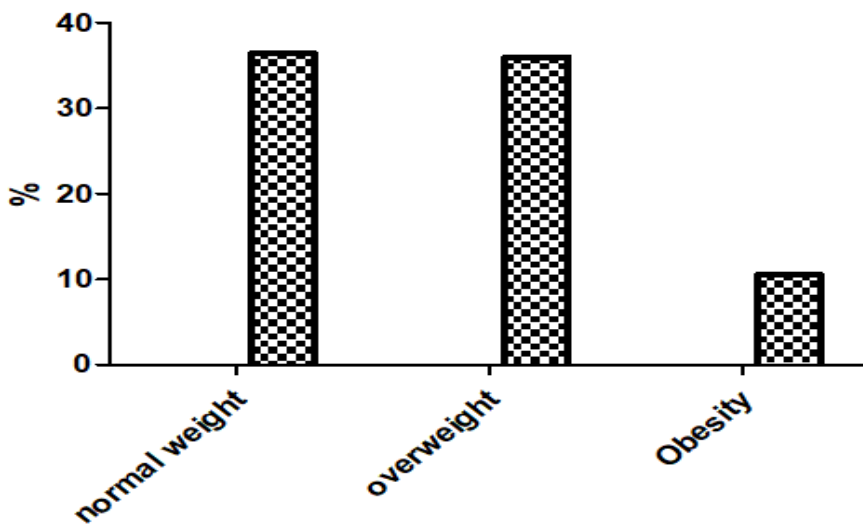


Fig. 2. BMI distribution of women diagnosed with type 2.

Table 4. Educational level of women diagnosed with type 2.

	GDM	Type 2 diabetes		
	n	n	%	P-value
intermediate	15	3	20.0	0.49
high school	9	3	33.3	
primary school	11	6	54.5	
college	20	3	15.0	
Total	55	15	27.3	

Table (4) shows the outcome-based comparison between education for pregnant women with GDM and how diagnosed with type 2 diabetes; the table showed that 54.5% of women who had primary school diagnosed with type 2, as for results about women had high school, this study showed that 33.3% from them diagnosed with type 2. About women who had intermediate-level education, the results showed that 20% of them were diagnosed with type 2. Although, for women had colleges educational were the least percent from all educational level groups (15%), the result was not statistically significant (p value=0.49), which indicates haven't statistically significant means difference between the educational level groups about FBS value.

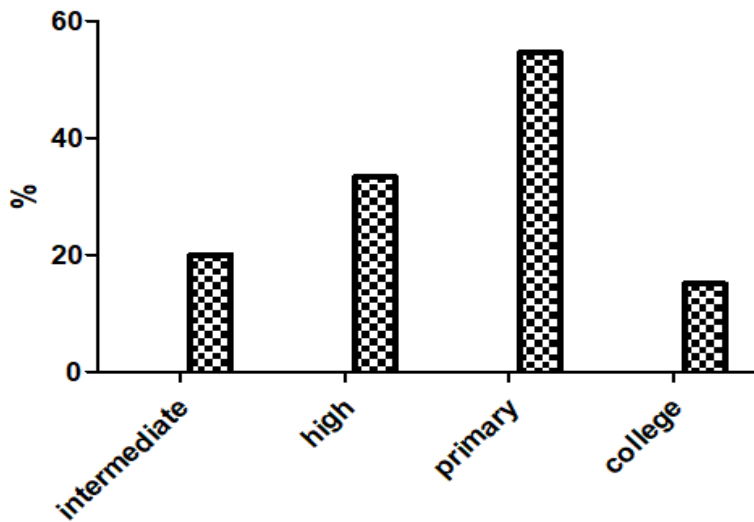


Fig. 3. Educational level of women diagnosed with type 2 diabetes.

Table 5. parity distribution of women diagnosed with type 2 diabetes.

	GDM	Type 2		
	n	n	%	P-value
1-3	28	8	28.6	0.53
4-6	10	2	20.0	
7-9	17	5	29.4	
Total	55	15	27.3	

Regarding the Parity for pregnant women with GDM that how diagnosed with type 2 diabetes; the table (5) showed that 29.4% of women which had between 7 to 9 kids diagnosed with type 2 diabetes, as for results about women which had between 1 to 3 kids, the results showed that 28.6% of them diagnosed with type 2 diabetes. Although the women which had between 4-6 were the least percent from all groups, 20%. In addition, the result wasn't statistically significant (p value=0.53).

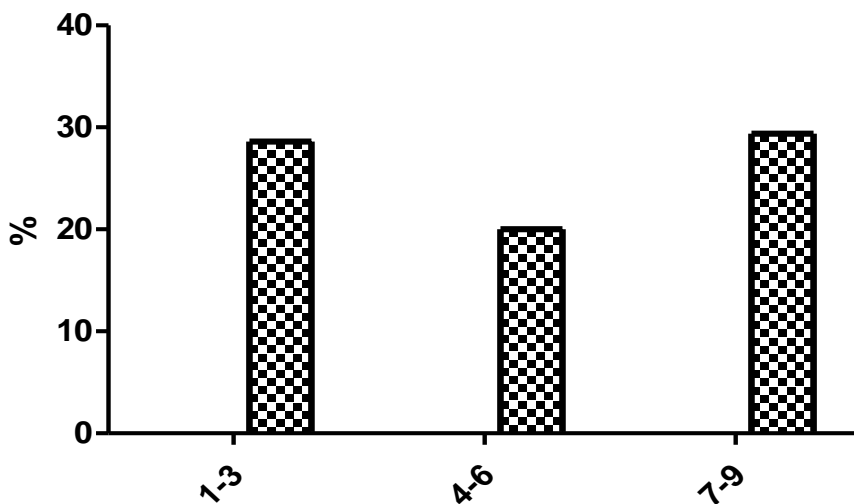


Fig.4. Parity distribution of women diagnosed with type 2.

Table 6. GDM distribution of women diagnosed with type 2 diabetes

	GDM	Type 2 diabetes		
	n	n	%	P-value
7-16 week	16	3	18.8	0.43
17-26 week	18	8	44.4	
27-36 week	21	4	19.0	
Total	55	15	27.3	

Table (6) the outcome-based comparison between pregnant women based Onset of GMD and how diagnosed with type 2 diabetes; although this study showed that women whose GMD started with them at 17 to 26 weeks had the highest percent of type 2 diabetes (44.4%), opposite women who GMD started with them at 27 to 36 weeks they had low percent of type 2 diabetes (19%), as for results about women which GMD started with them at 7 to 16 week, results showed that 18.8% from them diagnosed with type 2 diabetes. The result wasn't statistically significant (p-value =0.43).

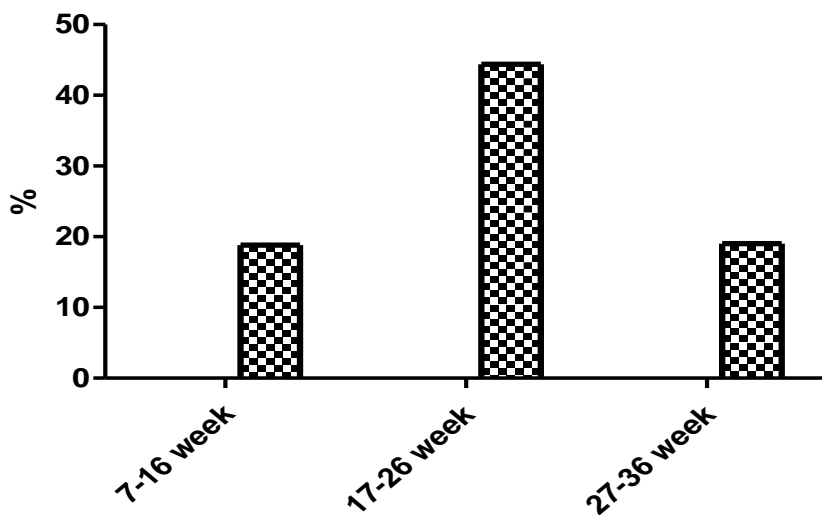


Fig. 5. Onset of GDM distribution of women diagnosed with type 2 diabetes.

Table 7. Treatment distribution of women diagnosed with type 2 diabetes.

	GDM	Type 2 diabetes		
	n	n	%	P-value
oral	22	5	22.7	0.70
insulin	16	4	25.0	
Oral+insulin	15	6	40.0	
diet	2	0	0.0	
Total	55	15	27.3	



Regarding the treatment types who pregnant women with GDM that diagnosed with type 2 diabetes post-partum used; table 7: shows that women who use oral+ insulin had a higher percent (40%), while almost equal percent for women which use oral only or insulin only, it was 25% about oral, and 22.7% about insulin, moreover. as for results about women that used diet, results didn't find any of them become diabetic post-partum for them. The result wasn't statistically significant (p-value =0.7).

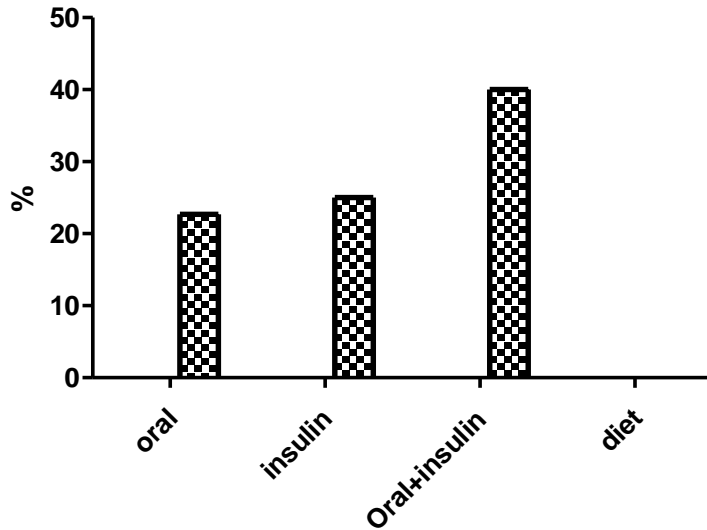


Fig. 6. Treatment distribution of women diagnosed with type 2 diabetes.

Table 8. FBS in last trimester of women who diagnosed with type 2 diabetes

	GDM	Type 2 diabetes		
	n	n	%	P-value
Well controlled $\leq 95$	11	0	0.0	0.00
poor controlled $> 95$	44	15	34.1	
Total	55	15	27.3	

The following table (8) shows that 34% how were poorly controlled in the last trimester become diabetic, and about the women how was well controlled FBS in the last trimester we found 0% no one become diabetic post-partum, we found statistically significant (p= 0.00).

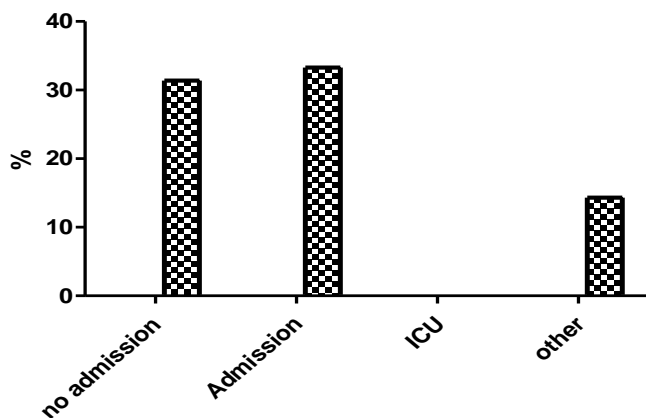


Fig.7. FOC of women how diagnosed with type 2 diabetes

Table 10. Complication during the pregnancy (CDP) of women diagnosed with type 2 diabetes

	GDM	Type 2 diabetes		
	n	n	%	P-value
No Complication	28	9	32.1	0.37
With Complication	27	6	22.2	
Total	55	15	27.3	

Table (10) shows the outcome-based comparison between CDP for pregnant women with GDM that how diagnosed with type 2 diabetes; the results showed that 32.1% of women who haven't complications become diabetic post-partum, moreover, their mean was (202.7), as for results about women which have a complication, this study showed that 22.2% from them become diabetic post-partum, where their mean was (190.3). The results weren't statistically significant (p value=0.37).

Table 8. Fetal out Come (FOC) of women diagnosed with type 2 diabetes

	GDM	Type 2 diabetes		
	n	n	%	P-value
no admission	35	11	31.4	0.23
Admission	9	3	33.3	
ICU	4	0	0.0	
other problems	7	1	14.3	
Total	55	15	27.3	

Table (8) shows the outcome-based Fetal out Come (FOC) for pregnant women with GDM and how diagnosed with type 2 diabetes; the results showed that 33.3% of women that their baby admitted to nursery, moreover, in contrast, the results from women which haven't admission showed that 31.4% of them become diabetic post-partum, as for results about women which have other problems, results found that 14.3%. The results didn't find any women who their baby admitted to ICU. The results weren't statistically significant (p value=0.23), which indicates the FOC hasn't effect in the incidence of type 2 diabetes.

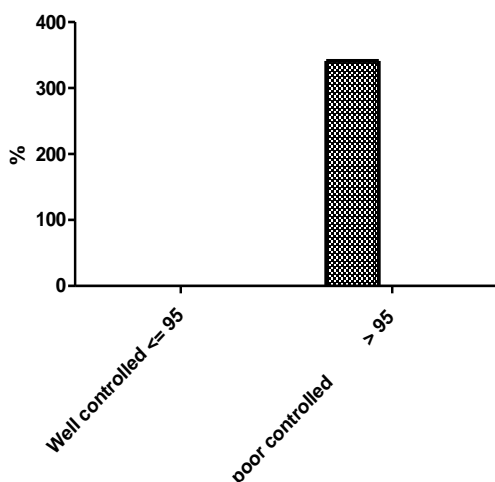


Fig. 8. The FBS in the last trimester

## DISCUSSION

The incidence of GDM increasing and the rate of development of diabetes type 2 among the women who had gestational diabetes mellitus increasing rapidly during the first year's post-partum. The result of this study reported that the rate of development of type 2 diabetes or glucose tolerance diseases is 27%. There is relationship between fasting blood sugar and HBA1c post-partum and type 2 diabetes mellitus. Previously, some studies of women with GDM reported that higher HBA1c is associated with postpartum type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance (25–26). However, The study by Dalfra and his colloquies, 2001 was in disagreement with the current study in which did not find such an association (28).

Our finding indicates that the risk of GDM becomes significantly and progressively increased from 18 years onwards 26 years. This finding conflict with American Diabetes Association recommendation on the use of age  $\geq 25$  years as the cutoff for screening and the observation that maternal age  $\geq 25$  years is the factor most predictive of GDM (25).

The associations of BMI and weight change with risk of type 2 diabetes among women with a history of GDM (27). Our results were consistent with those of previous reports among women with a history of GDM that examined the associations of risk of type 2 diabetes. As well as women with GDM that has poor control in the last trimester was more incidence of type 2 diabetes (31).

Furthermore, women who require treatment, special insulin and oral hypoglycemic drugs, to control hyperglycemia in pregnancy, are at the higher rate of type 2 diabetes progression but this result was no significant difference in the risk factor for type 2 diabetes mellitus. However, treatment with insulin indicates the inability of beta cell mass to increase insulin secretion in the cause of increasing insulin resistance as a consequence of pregnancy-induced metabolic changes. Regarding, women treated with insulin in pregnancy have a 3-fold increased possibility of type 2 diabetes progression, compared with women with GDM who did not need insulin treatment (14). in 2002, Kim et did a meta-analysis include 28 studies with a follow-up period was from 6 weeks to 28-year post-partum from 1965 to 2001, and the risk of developing of type 2 diabetes mellitus was 2.6% to 70% (20), in 2004, konarzewska, study show that more than 50% of women with GDM developed diabetes or other GTD during first 6 year post-partum (21), in 2009, Bellamy and his colleagues reported that meta-analysis 20 studies from 1969 to 2009 and the study with the largest number of GDM reported the incidence of type 2 diabetes as 3.7% at 9- month post-partum and 18.9% at 9 year post-partum (22), in 2020, A, Shafiq show that the incidence of type 2 diabetes was 6.6% at medium 2.3 years' post-partum, in 2020, Zhuyu li et al., studied meta-analysis including twenty-eight studies from 1966 to 2019, the estimated risk of type 2 diabetes in this study was 19.72% at 10 years, 29.36% at 20 years, 39% at 30 years, 48.64% at 40 years and 58.27% at 50 years, respectively (23).

The high incidence rate of diabetes in an old study is due to old criteria of diagnosis of GDM and the other reason was that most women how had GDM did not take special measures as healthy life style, controlling body weight, monitoring blood glucose, to decrease the risk of post-partum diabetes (19).

## CONCLUSION

GDM is a medical condition that should be screened, diagnosed early in women at high risk and treated well, as uncontrolled GDM can be effect on the mother and the fetal growth. Fortunately, pregnant women with uncontrolled GDM at highly risk with type 2DM. Therefore, women with a history of GDM need follow up for several years after delivery. As well the age and BMI and glycemic control in last trimester is considered a risk factor for diabetes in our study.

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