

# Screening of type 2 diabetes mellitus after gestational diabetes in Assiut University Hospital

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## Objective

To determine the percentage of development of type 2 diabetes after gestational diabetes mellitus (GDM) and to evaluate risk factors associated with increased susceptibility to developing type 2 diabetes mellitus (T2DM) after GDM.

## Patients and methods

A prospective study included 1150 pregnant women not known to have DM before gestation, who presented to GDM outpatient clinic of Assiut University Hospital between the period of May 2016 and May 2017, where 150 women were found to have GDM according Diabetes in Pregnancy Study Group India criteria.

## Results

Based on the result of 75 g oral glucose tolerance test 6–24 weeks after delivery, the study found that 12.7% of women with GDM had T2DM, 21.3% of GDM women had impaired fasting glucose, 13.3% of women with GDM had impaired glucose tolerance, and 52.7% of women with GDM had normal glucose tolerance. The study showed that predictors of the development of T2DM in women with GDM were family history of DM ( $P = 0.001$ ), insulin therapy during pregnancy ( $P = 0.001$ ), high glucose level at the time of diagnosis ( $P = 0.03$ ), previous history of GDM ( $P = 0.002$ ), and high BMI ( $P = 0.04$ ).

## Conclusion

Postpartum follow-up of patient with GDM is very important for early diagnosis of T2DM and early detection of prediabetic patients to prevent their progression to being diabetic.

## Keywords:

gestational diabetes, risk factors, type 2 diabetes

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## Introduction

Nearly half a billion people live with diabetes. Low-income and middle-income countries carry almost 80% of the diabetes burden. Rapid urbanization, unhealthy diets, and increasingly sedentary lifestyles have resulted in previously unheard higher rates of obesity and diabetes, and many countries do not have adequate resources to provide preventive or medical care for their populations [1].

In 2017, ~38.7 million people, or 9.6% of adults aged 20–79 years, were living with diabetes in Middle East and North Africa region. Approximately 49.1% of these are undiagnosed. Although 55.5% of all adults in the region live in urban areas, 67.3% of people with diabetes live in urban environments. The vast majority of people with diabetes in the region are living in low-income or middle-income countries (83.8%) [1].

The rates of diabetes in Egypt have significantly increased, exceeding international rates. Egypt is now ranked eighth highest in the world in terms of the disease [1].

The American Diabetes Association (ADA) [2] redefined gestational diabetes mellitus (GDM) as

follows: ‘diabetes diagnosed in the second and third trimesters of pregnancy’.

Screening for GDM is usually done at 24–28 weeks of gestation because insulin resistance increases during the second trimester and glucose levels rise in women who do not have the ability to produce enough insulin to adapt to this resistance [3].

Well-documented risk factors for GDM include advanced maternal age, family history of diabetes, previous GDM, having a macrosomic baby, non-white race/ethnicity, being overweight or obese, and cigarette smoking [4].

Pregnant women with GDM have an increased incidence of preeclampsia, preterm labor, pyelonephritis, polyhydramnios, and cesarean delivery. The long-term complications include a higher risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease [5].

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In addition, there are many potential effects of GDM on the fetus. Short-term effects include a much larger birth weight (fetal macrosomia), shoulder dystocia, difficult or operative delivery, stillbirth, and increased perinatal morbidity and mortality. Long-term effects include an increased incidence of childhood obesity and early adulthood T2DM [6].

### Patients and methods

A prospective study included 1150 pregnant women not known to have DM before gestation, presented to GDM outpatient clinic of Assiut University Hospital between the period of May 2016 and May 2017. This study was in collaboration with World Diabetes Foundation (WDF 13–797) project about Gestational Diabetes Care in Upper Egypt that was performed in Assiut University Hospital where pregnant women were screened for GDM. Diagnosed women and their off-spring received GDM-related health education and postpartum follow-up.

### Inclusion criteria

All women diagnosed with GDM in their pregnancy between 24 and 28 weeks of gestation in GDM outpatient clinic of Assiut University Hospital were included.

### Exclusion criteria

Pre-GDM and diabetes in the first trimester were the exclusion criteria.

### Ethical approval

- 1 Confidentiality was maintained during all stages of the assessment
- 2 Informed consent was taken from patients participate in the study
- 3 Approval of the ethical committee of assiut medical school was obtained

All pregnant women were subjected to the following: detailed history and clinical examination, including name, age, residence, marriage age, age of the patient at diagnosis of GDM, hypertension history, history of preeclampsia, gestational age at the beginning of GDM care, oral glucose tolerance test (OGTT), glucose values during pregnancy, method used for managing GDM (lifestyle modification or the need for insulin treatment or metformin during pregnancy), family history of diabetes, and lifestyle; anthropometric characteristics by measuring their weight, height, and calculating BMI; maternal outcomes, including vaginal candidiasis, polyhydramnios, preterm labor, abortion, premature rupture of membranes, and

cesarean section; and fetal outcomes, including normal babies, macrosomia, stillbirth, shoulder dystocia, hypoglycemia, trauma/injury, congenital abnormality, respiratory distress syndrome, and NICU admission.

### Laboratory investigations

- (1) OGTT was done at 24–28 weeks of gestation using 75-g glucose anhydrous.

Pregnant women were given 75-g anhydrous glucose in 250–300 ml of water, and plasma glucose was estimated after 2 h. A 2-h plasma glucose more than or equal to 140 mg/dl is taken as GDM according to Diabetes in Pregnancy Study Group India.

- (2) OGTT was done at 6–24-week postpartum for women with GDM using 75-g glucose anhydrous.
  - (a) T2DM was diagnosed when fasting plasma glucose was  $\geq 126$  mg/dl and/or 2 h after 75-g glucose administration, the value was  $\geq 200$  mg/dl.
  - (b) Impaired fasting glucose was when fasting plasma glucose was more than 100 mg/dl and less than 126 mg/dl and 2-h after 75-g normal glucose administration, the value was less than 140 mg/dl.
  - (c) Impaired glucose tolerance was when glucose values 2 h after 75-g glucose administration were 140 mg/dl and less than 200 mg/dl and fasting plasma glucose was less than 100 mg/dl.
  - (d) Normal glucose tolerance was when fasting plasma glucose less than 100 mg/dl and 2-h after 75-g glucose administration the value was less than 140 mg/dl.

### Statistical analysis

Data were collected and analyzed using SPSS (Statistical Package for the Social Science, version 20; IBM, Armonk, New York, USA). Continuous data were expressed in the form of mean  $\pm$  SD or median (range), whereas nominal data were expressed in the form of frequency (percentage).

Nominal data were compared by  $\chi^2$  test, whereas continuous data were compared using Student's *t* test. Multivariate regression analysis was used to determine the independent risk factors for prediction of T2DM in those women with GDM. *P* value was significant if less than 0.05.

### Results

Table 1 shows that 150 (13%) among 1150 pregnant women had GDM. Family history of DM was the most frequent risk factor for GDM (56.7%) in our study, with *P* value of 0.01. In addition, the study found that obesity was a significant risk factor for GDM, with BMI more than 30, with *P* value of 0.03, as obesity is one of major risk factor for DM in our population. The

**Table 1 Demographic data of the studied pregnant women**

Variables	GDM (n=150)	No GDM (n=1000)	
Age (years)	29.07±5.35	27.11±4.09	0.87
Range	17-43	17-40	
Age of marriage (years)	21.33±3.57	23.03±2.22	0.11
Range	12-30	14-32	
Residence			
Rural	104 (69.3)	700 (70)	0.22
Urban	46 (30.7)	300 (30)	
Socioeconomic class			
Low	33 (22)	321 (32)	0.06
Middle	117 (78)	679 (68)	
Occupation			
Housewife	129 (86)	830 (83)	0.08
Employee	21 (14)	170 (17)	
Hypertension	12 (8)	100 (10)	0.33
Family history of diabetes mellitus	85 (56.7)	200 (20)	<b>0.01</b>
Previous history of GDM	25 (16.7)	20 (0.2)	<b>0.03</b>
Parity	4 (1-9)	2 (1-3)	<b>0.03</b>
Anthropometric measurements			
BMI (kg/m <sup>2</sup> )	31.39±5.49	26.11±2.98	<b>0.03</b>
Normal weight	13 (8.7)	670 (67)	<b>0.02</b>
Overweight	137 (91.3)	330 (33)	
Waist circumference (cm)	91.53±15.67	87.01±12.98	

Bold means: Statistically significant ( $P$  value <0.05). Data were expressed in the form of  $n$  (%) and mean±SD. GDM, gestational diabetes mellitus.  $P$  value was significant if less than 0.05.

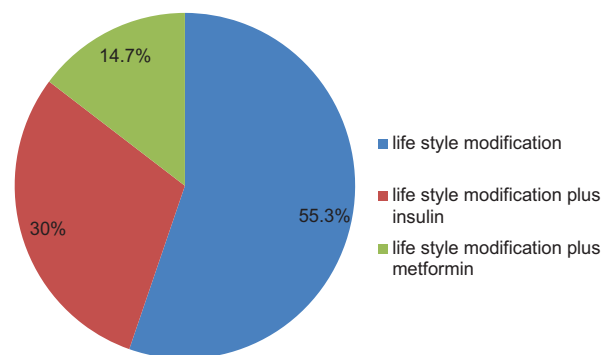
study also found that increasing parity was significantly higher in those with GDM in comparison with those without GDM, with  $P$  value of 0.03. Furthermore, the study showed that previous history of GDM increased risk for GDM with  $P$  value of 0.03.

GDM was controlled with education and lifestyle modification, whereas insulin therapy in addition to lifestyle modification was required in 45 (30%) of enrolled women, and 22 (14.7%) women required metformin (Fig. 1).

#### Maternal outcome in the current study

Table 2 shows the maternal outcome in the current study. The majority (86%) of women needed cesarean section. Preterm labor occurred in 18 (12%) women, whereas four (2.7%) women experienced premature rupture of membranes. Polyhydramnios, vaginal candidiasis, and abortion occurred in nine (6%), three (2%), and nine (6%) women, respectively.

Regarding maternal outcome, there were no significant differences between different types of management with exception of preterm labor, which was frequently higher in those women with GDM and managed with lifestyle modification.

**Figure 1**

Management of GDM in the enrolled women. GDM, gestational diabetes mellitus.

#### Fetal outcomes in the women with gestational diabetes mellitus

Table 3 shows the fetal outcome in the current study. There was only one neonate who was stillbirth, and only one neonate had shoulder dystocia. Neonatal jaundice occurred in the majority (78.7%) of neonates, whereas macrosomia presented in 66 (44%) neonates. Twelve (8%) neonates experienced respiratory distress syndrome, whereas six (4%) neonates were hypoglycemic. Trauma and injury occurred in three (2%) neonates, whereas six (4%) neonates had different forms of congenital anomalies. Eighty-nine (59.3%) neonates needed neonatal ICU. Majority (99.3%) of neonates were alive.

Regarding fetal outcomes, there were no significant differences between different types of management with exception of hypoglycemia, which was frequently higher in those women with GDM and managed with lifestyle modification plus insulin. Macrosomia was the least in those managed with lifestyle plus metformin and higher frequency of ICU in those women with GDM and managed with lifestyle modification.

Based on the result of 75-g OGTT 6–24 weeks after delivery, our study found that 12.7% of women had T2DM, 21.3% of women had impaired fasting glucose, 13.3% of women had impaired glucose tolerance, and 52.7% of women had normal glucose tolerance (Fig. 2).

#### Multivariate regression analysis for prediction of type 2 diabetes mellitus and prediabetic in women with gestational diabetes mellitus

The current study showed that predictors to development of T2DM in women with GDM were family history of DM [odds ratio (OR), 5.99;  $P$  = 0.001], insulin therapy (OR, 10.98;  $P$  = 0.001), high glucose level at time of diagnosis (OR, 4.98;  $P$  = 0.03), previous history of GDM (OR, 8.66;  $P$  = 0.002), and high BMI (OR, 1.29;  $P$  = 0.04) (Table 4).

**Table 2 Maternal outcome in those with gestational diabetes mellitus based on type of management**

Variables	Total (n=150)	Lifestyle (n=83)	Lifestyle+insulin (n=45)	Lifestyle+metformin (n=22)	P1	P2	P3
Vaginal candidiasis	3 (2)	2 (0.2)	1 (2.2)	0	0.06	0.87	0.11
Polyhydramnios	9 (6)	7 (8.4)	2 (2.2)	0	0.07	0.11	0.34
Preterm labor	18 (12)	18 (19.3)	2 (4.4)	0	<b>0.01</b>	<b>0.03</b>	0.78
Abortion	9 (6)	6 (7.2)	1 (2.2)	2 (9)	0.34	0.14	0.38
PROM	4 (2.7)	2 (0.2)	0	2 (9)	0.57	0.08	0.06
Cesarean section	129 (86)	72 (83)	39 (87)	18 (82)	0.21	0.27	0.71

Bold means: Statistically significant ( $P$  value <0.05). Data were expressed in the form of  $n$  (%). PROM, premature rupture of membrane. P1, compared lifestyle with lifestyle+insulin. P2, compared lifestyle with lifestyle+metformin. P3, compared lifestyle+insulin with lifestyle+metformin.

**Table 3 Fetal outcomes in those with gestational diabetes mellitus based on type of management**

Variables	Total (n=150)	Lifestyle (n=83)	Lifestyle+insulin (n=45)	Lifestyle+metformin (n=22)	P1	P2	P3
Jaundice	118 (78.7)	64 (77.1)	36 (80)	18 (81.6)	0.06	0.17	0.14
Macrosomia (>4000 g)	66 (44)	38 (45.7)	20 (44.4)	8 (36.4)	0.76	0.41	0.14
Stillbirth	1 (0.7)	1 (0.1)	0	0	0.63	0.63	0.08
Shoulder dystocia	1 (0.7)	0	0	1 (4.5)	0.32	0.64	0.28
Hypoglycemia	6 (4)	4 (0.5)	2 (3.6)	0	<b>0.03</b>	0.26	<b>0.04</b>
Trauma/injury	3 (2)	3 (0.3)	0	0	0.09	0.17	0.71
Anomalies	6 (4)	4 (0.5)	1 (2.2)	1 (4.5)	0.24	0.43	0.56
ARDS	12 (8)	9 (2.71)	2 (3.6)	1 (4.5)	0.07	0.06	0.09
Need to ICU	89 (59.3)	62 (74)	20 (44)	7 (32)	<b>0.02</b>	<b>0.01</b>	<b>0.03</b>

Bold means: Statistically significant ( $P$  value <0.05). Data were expressed in the form of  $n$  (%). ARDS, respiratory distress syndrome.  $P$  value was significant if less than 0.05. P1, compared lifestyle with lifestyle+insulin. P2, compared lifestyle with lifestyle+metformin. P3, compared lifestyle+insulin with lifestyle+metformin

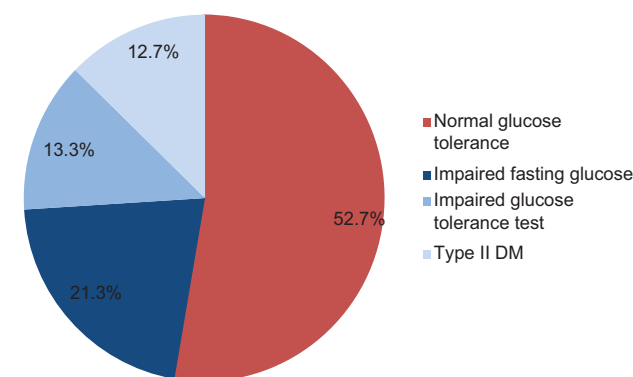
**Table 4 Multivariate regression analysis for prediction of type 2 diabetes mellitus in women with gestational diabetes mellitus**

Variables	Odds ratio	$P$
Family history of DM	<b>5.99</b>	<b>0.001</b>
Insulin therapy	<b>10.98</b>	<b>0.001</b>
High glucose level at time of diagnosis	<b>4.98</b>	<b>0.03</b>
Previous history of GDM	<b>8.66</b>	<b>0.002</b>
BMI ( $\geq 30$ kg/m <sup>2</sup> )	<b>1.29</b>	<b>0.04</b>
Early onset of GDM	1.22	0.11
Age (>35 years)	2.12	0.09

DM, diabetes mellitus; GDM, gestational diabetes mellitus.  $P$  value was significant if less than 0.05.

## Discussion

The current study included 1150 pregnant women screened for GDM. The Diabetes in Pregnancy Study Group India guidelines had been used for screening of the pregnant women; of them 150 (13%) women were diagnosed with GDM in their pregnancy between 24 and 28 weeks of gestation in gestation diabetes outpatient clinic of Assiut University Hospital. All pregnant women included in the study were evaluated clinically about any risk factor for GDM where a woman was considered to have GDM if 2-h postprandial blood glucose was equal or exceeded 140 mg/dl. It was demonstrated that family history of DM was the most frequent risk factor for GDM (56.7%) followed by previous history of GDM (16.7%) and multigravida ( $P = 0.03$ ). In addition, our study found that obesity was a significant risk factor for GDM with BMI more

**Figure 2**

Overall, 75-g OGTT 6–24 weeks after delivery in the studied women. OGTT, oral glucose tolerance test.

than 30 ( $P = 0.03$ ) as obesity is one of major risk factor for DM in our population. Our study also found that increasing parity was significantly higher in those with GDM in comparison with those without GDM ( $P = 0.03$ ). Furthermore, our study showed that previous history of GDM increased risk for GDM ( $P = 0.03$ ). According to the study done in Hamad Qatar by Bener *et al.* [7], the prevalence of GDM in Qatar was 16.3% as those women with GDM in Bener *et al.* [7], were significantly higher in the age group of 35–45 years. Advanced maternal age, low monthly income, family history of diabetes, and obesity were the main significant risk factors for GDM in their study, which was in agreement with our study. Another study was done in Nigeria

by Wokoma *et al.* [8] where the prevalence of GDM was 2.98 per 1000 pregnancies. This prevalence is lower than that of our study as they did not assess family history or other associated risk factors to GDM.

According to the study done in Kingdom of Saudi Arabia by Farooq *et al.* [9], polyhydramnios was a common complication with a reported incidence in nine (18%), premature labor occurred in seven (14%), premature rupture of membranes five (10%), vaginal candidiasis three (6%), and abortion occurred in one (2%). This study was in agreement with our study in the incidence of premature labor but shows increased incidence of polyhydramnios and vaginal candidiasis. A study done in Hamad Qatar by Bener *et al.* [7] showed preterm labor in 19.8%, premature rupture of membrane in 15.3%, and cesarean section in 27.9%, which was in disagreement with our study. Another study done in Kingdom of Saudi Arabia by Gasim [10] showed 24.1% needed cesarean section. The high and unprecedented increase in cesarean section rates reported in this study may be partly owing to cesarean sections that are not medically indicated, physician practice patterns, financial incentives, and patient preferences. As regarding maternal outcome in relation to different types of management, our study showed that there were no significant differences between different types of management with exception of preterm labor which was frequently higher in those women with GDM and managed with lifestyle modification.

Another study done in Brazil by Silva *et al.* [11] demonstrated that preterm labor was higher in GDM women treated with diet only, which agreed with our study.

In addition, a study done in Macedonia by Simeonova-Krstevska *et al.* [12] showed that gestational age at delivery was significantly lower in the insulin group, and consequently, the percent of preterm labor was higher in the insulin group, which was in contrary with our study.

In addition, another study done by Balani *et al.* [13] showed that there is no significant difference between the metformin and insulin groups, comparing need for cesarean section which agreed with our study.

Regarding fetal outcomes, our study showed one (0.7%) neonate was stillbirth and only one neonate had shoulder dystocia. Neonatal jaundice occurred in majority (78.7%) of neonates, whereas macrosomia presented in 66 (44%) neonates. Twelve (8%) neonates experienced respiratory distress syndrome, whereas

six (4%) neonates were hypoglycemic. Trauma and injury occurred in three (2%) neonates, whereas six (4%) neonates had different forms of congenital anomalies.

A study done in India by Dudhwadkar and Fonseca [14] demonstrated the incidence of macrosomia in GDM to be 40%; moreover, four (8%) babies had congenital malformations, and respiratory distress was seen in 12% ( $n = 6$ ) patients, whereas four (8%) babies had hypoglycemia, which corresponded with our study results.

Our study showed high incidence of neonatal jaundice occurred in majority (78.7%) of neonates, and this disagreed with Dudhwadkar and Fonseca [14] and Gasim [10] who showed hyperbilirubinemia was seen in 10 and 8%, respectively.

Regarding fetal outcomes, our study showed that there were no significant differences between different types of management with the exception of hypoglycemia which was frequently higher in those women with GDM and managed with lifestyle modification plus insulin. This agreed with a study done in Macedonia by Simeonova-Krstevska *et al.* [12].

In addition, we found fewer macrosomic neonates in the metformin group than in the diet and insulin groups.

Furthermore, our study found that there were no significant differences between different types of management with exception of high birth weight and higher frequency of ICU in those women with GDM and managed with lifestyle modification, which disagreed with a study done by Silva *et al.* [11] which showed higher rates of LGA births in women treated with insulin when compared with those treated with metformin or diet therapy, and the type of treatment did not affect the need for NICU admission.

Based on the result of 75-g OGTT 6–24 weeks after delivery, the studied women with GDM were divided into T2DM [19 (12.7%)], impaired fasting glucose [32 (21.3%)], impaired glucose tolerance [20 (13.3%)], and normal glucose tolerance [79 (52.7%)], which was consistent with a study done in Brazil by Alves *et al.* [15].

Another study done in Tehran, Iran, by Hossein-Nezhad *et al.* [16] demonstrated that the prevalence of overt postpartum diabetes mellitus and IGT was 8.1 and 21.4%, respectively, whereas 70.5% had restored normoglycemic state.

The current study showed that predictors to development of T2DM in women with GDM were

family history of DM (OR, 5.99;  $P = 0.001$ ), insulin therapy during pregnancy (OR, 10.98;  $P = 0.001$ ), high glucose level at time of diagnosis (OR, 4.98;  $P = 0.03$ ), previous history of GDM (OR, 8.66;  $P = 0.002$ ), and high BMI (OR, 1.29;  $P = 0.04$ ).

A study done in Brazil by Alves *et al.* [15] showed that women with a family history of T2DM, higher prepregnancy BMI, earlier diagnosis of GDM, higher levels of plasma glucose at the diagnosis of GDM, and the need of insulin are the ones with an increased risk of developing T2DM in the postpartum period; this was in agreement with the findings of our study.

### Recommendations

- (1) Universal screening for GDM should be done for all pregnant women
- (2) There are still various controversies regarding the ideal approach for screening gestational diabetes, so preventive measures should be suggested to improve insulin sensitivity. Further research should be done to develop efficient and cost-effective screening protocols
- (3) Further advanced studies among larger population are required to generate more reliable data to prevent false positives and increase the specificity of the test
- (4) Early diagnosis and management of GDM reduce the risks for both mother and fetus
- (5) Postpartum follow-up of patient with GDM is very important for early diagnosis of T2DM and early detection of prediabetic to prevent their progression to diabetic
- (6) Strategies to increase the return index for the glucose status reevaluation in the postpartum should be done.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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