Mohamed Sultan*1 and Ebtisam Dribika2

1Associate Professor, OBS & GYN Department Tripoli University, Tripoli – Libya.
2Academy of Graduate Studies, Department of Biological Sciences, Tripoli- Libya.

*Corresponding Author: Dr. Mohamed Sultan
Associate Professor, OBS & GYN Department Tripoli University, Tripoli – Libya.

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is one of the more common disorders of pregnancy and its incidence increased progressively, its importance lies in its association with adverse pregnancy outcomes, and increased maternal risk of future diabetes but the exact incidence is widely variable globally, and the associated risk factors are not fully investigated. Objective: To estimate the proportion of mothers who transform from having GDM to type 2. DM within the puerperium and to determine the risk factors associated with increased chance to become frankly diabetic following pregnancy complicated by GDM. Patients & Methods: A longitudinal descriptive prospective study. 64 pregnant women diagnosed with GDM in the current pregnancy presented to diabetic pregnancy outpatient department (dpopd), Aljalaa Maternity Hospital, Tripoli-Libya in the period from April 2014 to April 2015. After delivery, discontinue treatment of DM and assess the level of blood sugar weekly via serial blood sugar (SBS), fasting and two hours post prandial until six weeks post-delivery where DM confirmed or excluded via 75g oral glucose tolerance test (OGTT), Pregnant women with preexisting diabetes or discovered diabetic early in pregnancy with high HbA1c (which indicates unrecognized preexisting diabetes) were excluded from the study. Results: After 6 weeks of delivery, out of 64 patients diagnosed with GDM 22 (34.4%) converted to T2DM. Out of 37 patients whose age was ≥ 35 years 14(37.8%) became diabetic (mean age 34.7±5.3 y). From patients who had (B+) blood group 4 (44.4%) out of 9 patients were converted to T2DM. Out of 7 patients who were on insulin and metformin 3 (42.8%) became diabetic. Patients who had a positive family history of diabetes 8 (44.4%) out of 18 patients converted to T2DM. From patients whose BMI was ≥ 30 kg/m² out of 55 patients 19 (34.5%) converted to T2DM. From patients whose HbA1c was more than 6%, we found that 13 (46.4%) out of 28 patients were converted to T2DM. From patients who had hypothyroidism out of 9 patients 4(44.4%) converted to T2DM. From patients who had ≥ 4 previous children, 9 (60%) became diabetic. Number of patients with history of polycystic ovary syndrome (PCOS) and converted to (T2DM) was 2 (50%) out of 4 patients. Mothers who had large birth weight (≥ 4 kg) and converted to T2DM were 5 (50%) out of 10. Mothers who fed their babies from bottle were 29 patients, 12 (41.4%) converted to T2DM. Conclusion: About a third of pregnant women with GDM will become diabetic as early as 6 weeks post-delivery and may be more later on. The risk is increased with the advanced maternal age, having (B+) blood group, using of insulin during pregnancy, positive first degree relatives history of diabetes, BMI ≥ 30, HbA1c > 6% at the time of GDM diagnosis, patients with hypothyroidism, giving birth to a macrosomic baby, high parity, positive history of polycystic ovary syndrome (PCOS) and bottle feeding.

KEYWORDS: Diabetes Mellitus, Gestational Diabetes Mellitus (GDM), Pregnancy.

INTRODUCTION

Pregnancy induces progressive changes in maternal carbohydrate metabolic process. As pregnancy advances, insulin resistance and diabetogenic stress due to placental contra-insulin hormones necessitate compensatory increase in insulin secretion. When this compensatory mechanism fails due to pancreatic β cells inadequacy, gestational diabetes develops[1] However, 50% of women with GDM will develop type 2 diabetes mellitus (T2DM) later in their life[2]. Due to many adverse effects of GDM on mother and fetus early diagnosis and appropriate management is essential for improvement of pregnancy.[3] Prevalence of GDM varies between 1-16% depending on the geographical variation and ethnicity and from one region to another in the same country.[4]

There is increased risk of development of type 2 DM in patients of GDM[5] and incidence of type 2 DM is about 44% in patients who required insulin or oral hypoglycemic agents or onset of GDM before 24 weeks.[6] GDM may also recur in a future pregnancy and approximately 55% of patients who were obese or with macrosomic
infants will have GDM in subsequent pregnancy[5] Patients should be informed that about 40-60% of them will have overt diabetes when they are in their 5th decade.

OBJECTIVES
The aim of the study is to estimate the proportion of mothers who transform from having GDM to T2DM, after puerperium and also to determine the risk factors associated with increased chance to become frankly diabetic following pregnancy complicated by GDM.

PATIENTS AND METHODS
A longitudinal descriptive, prospective study. Pregnant women diagnosed with GDM according to WHO criteria[6] at 20 or more weeks of gestation in the current pregnancy presented to diabetic pregnancy out- patient department (dpopd), Aljala Maternity Hospital, Tripoli – Libya, in the period from April 2014 to April 2015, After delivery, discontinue treatment of DM and assess the level of blood sugar weekly via serial blood sugar (SBS), fasting and two hours post prandial until six weeks post-delivery when DM confirmed or excluded via 75g oral glucose tolerance test (OGTT).

Type of treatment during pregnancy: Out of the 64 patients, 6(9.4%) were on diet control only, 51(79.7%) were on metformin and 7 (10.9%) on insulin plus metformin. Family history of diabetes: Patients who had positive first-degree family history of diabetes were 18 (28.1%), while 46 (71.9%) were not.

Glycated hemoglobin (HbA1c) of the patients: The patients were divided into 2 groups according to their (HbA1c) values at the time of GDM diagnosis. One group their (HbA1c) was 6 or less. The number of patients from this group was 36 (56.2%). The other group of patients with (HbA1c) values more than 6. The number of patients from this group was 28 (43.8%).

Other medical problems: Out of 64 patients, 10 (15.6 %) had hypertension, 9 (14.1%) had hypothyroidism. The rest of the patients 45 (70.3%) were free from other diseases rather than (GDM).

Parity of Patients: Number of previous children was between 0 and 7, patients with 0 parity were 17 (26.6%), with (1-3) parity were 32(50%), and with (≥ 4) parity were 15 (23.4%).

Previous history of gestational diabetes mellitus: Patients with previous history of gestational diabetes mellitus (GDM) were 10 (15.6%), while 54 (84.4%) had no history of previous GDM. History of polycystic ovary syndrome (PCOS): Out of 64 patients diagnosed with gestational diabetes mellitus 4(6.2%) had history polycystic ovary syndrome, 60 (93.8%) were free of (PCOS). History of previous large for gestation baby: Out of 64 patients, 3(4.7%) had babies with birthweight is 4 kilograms (kg) or more, the other 61(95.3%) were not.

Outcome of the babies: All babies were born alive and no cases of stillbirth. Out of 64 deliveries only 1 (1.6%) had congenital anomalies (esophageal atresia).

Weight of the babies at time of delivery: The number of mothers who gave birth to babies who had low birth weight (1.5-2.4 kg) were 3 (4.7%), average birth weight (2.5-3.9 kg) were 51 (79.7%) and large birth weight (≥ 4 kg) were 10 (15.6%).

Feeding of the babies: The number of babies who were on bottle-feeding was 29 (45.3%) and babies who were on breast-feeding were 35 (54.7%).

All pregnant women diagnosed with gestational diabetes mellitus (GDM) have been followed up for 6 weeks after delivery (puerperium), 22 (34.4%) converted to T2DM, and the others their blood sugar return to normal.
Proportion of patients converted to type 2 diabetes mellitus (T2DM)

- Converted to T2DM: 34.4%
- Normal blood sugar: 65.6%

Fig. (1)

Percentage of converters to T2DM after puerperium according to the age group

- < 35 Years: 29.6%
- ≥ 35 Years: 70.4%

Fig. (2)

Blood groups and conversion to type 2 diabetes mellitus after puerperium

- Yes
- No

Fig. (3)
**Type of treatment and conversion to type 2 diabetes mellitus after puerperium**

- **Diet**: 33.3% Yes, 66.7% No
- **Metformin**: 33.3% Yes, 66.7% No
- **Insulin + metformin**: 42.8% Yes, 57.2% No

**Fig. (4)**

**Family history and conversion to type 2 diabetes mellitus after puerperium**

- **Positive family history**: 44.4% Yes, 55.6% No
- **Negative family history**: 30.4% Yes, 69.6% No

**Fig. (5)**

**Gestational weeks at GDM diagnosis and conversion to type 2 diabetes mellitus after puerperium**

- **20 - 24 wks**: 66.7% Yes, 14.3% No
- **25 - 29 wks**: 85.7% Yes, 14.3% No
- **30 - 34 wks**: 52.3% Yes, 47.7% No
- **35 - 40 wks**: 70.6% Yes, 29.4% No

**Fig. (6)**
Body mass index and the conversion to type 2 diabetes mellitus after puerperium

Fig. (7)

Glycated haemoglobin values (HbA1c) and conversion to type 2 diabetes mellitus after puerperium

Fig. (8)

Patient's other medical problems and conversion to type 2 diabetes mellitus after puerperium

Fig. (9)
DISCUSSION

Out of 64 pregnant women diagnosed with GDM, 22 patients (34.4%) had developed T2DM (Fig.1) according to WHO criteria of diabetes 2006 on average of 6 weeks postpartum which was slightly lower than a Korean study performed on 311 participants, 119 (38.3%) women were found to have persistent glucose intolerance. Another cross-sectional study conducted at University Malaya Medical Centre by Chew et al, 2012, to determine the prevalence of type 2 DM (T2DM) where 448 women enrolled in the study. The prevalence of T2DM was 35.5%.[7] When the age correlated with the result of serial blood sugar after six weeks of delivery, the average age of patients converted to T2DM was older than who did not convert to T2DM Fig.(2). Oldfield et al, 2007 indicated the older maternal age at follow up, enhancing the hyperglycemia, and high amount of insulin needed during pregnancy as the risk factors of developing T2DM. [9] Henry et al 1991, Women with GDM have a greater risk of developing diabetes in the future compared with those women who have normal glucose tolerance during pregnancy. The incidence of diabetes was higher among women who were older.[10] The highest percentage of converters to T2DM after 6 weeks of delivery were from patients with B+ blood group 4 (44.4%) out of 9 patients (Fig.3). A result from a study “to evaluate the relationship of ABO blood type and Rhesus factor with type 2 diabetes mellitus risk” by Fagherazzi et al, 2015, the greatest increase in risk was seen for those with the B (+) blood group.[11] One of the risk factors for developing T2DM after 6 weeks of delivery of the current study was using of insulin in addition to metformin for controlling of blood glucose during the pregnancy (Fig.4). Eades et al, 2015 show that women who were at highest risk of developing T2DM after GDM those who used insulin during their pregnancy and those with FBG of 126 mg/dl and over,[12] Konarzewska et al, 2004 reported that postpartum glucose tolerance disorders appeared in 63.3% of insulin treated subjects compared with 30.1% of women treated with diet only.[13] Another risk factor for conversion to T2DM after puerperium in this study was the positive family history of diabetes (first degree relatives) Fig.(5), where after six weeks of delivery, patients who had positive family history of diabetes 8 (44.4%) out of 18 patients converted to T2DM, while in patients with no family history of diabetes mellitus 14 (30.4%) out of 46 patients became diabetic after at least six weeks of delivery. In this study the highest percentage of converters to T2DM after puerperium were from mothers who were diagnosed with GDM at (30-34) weeks of gestation, where out of the 22 patients 11 (52.4%) became diabetic after puerperium Fig.(6). While other studies showed that gestational age of less than 24 weeks at diagnosis of GDM was an additional risk factor for postpartum glucose intolerance.[14] The highest percentage of converters to T2DM after puerperium were from patients with BMI (30-≥40) Fig.(7), where out of 55 patients 19 (34.5.5%) converted to T2DM, comparing to the patients with BMI (25-29.9) out of 7 patients 2 (28.6%) converted to T2DM, where the two patients who had normal BMI (18.5-24.9) were excluded due to their small number, Steinhart et al, (1997) reported that patients who developed T2DM had greater BMIs.[15] In this study the percentage of the converters to T2DM after puerperium was higher in patients with HbA1c more than 6 (46.4%) Fig.(8), comparing to the patients with HbA1c ≤ 6, the percentage of converters to T2DM was (25%), these were largely in agreement with previously published studies of HbA1c measured at GDM diagnosis and postpartum abnormal glucose, Both Oldfield, 2007[16] and Ogonowski, 2009[17] found that higher HbA1c at GDM diagnosis was associated with increased risk of postpartum hyperglycemia.
This study also showed that the highest percentage of converters to T2DM after puerperium was from patients with hypothyroidism (44.4%) [9]. Vitacolonna et al., 2012 reported that a significant increase in thyroid autoimmunity was seen in women previously affected by gestational diabetes, this increased prevalence of thyroid autoimmunity was not associated with the development of impaired glucose metabolism after pregnancy. [18]

The percentage of converters to T2DM after puerperium was 60% from patients of greater parity (≥4 children), while 37.5% of patients with less parity (1-3 children) converted to T2DM after puerperium. Fig. (10), the percentage of patients who became diabetic after puerperium was higher in patients with history of PCOS (50%) than in patients who had no history of PCOS (33.3%), Fig. (11), Kim C et al., 2002 reported that, PCOS patients have a higher risk of conversion from normal glycaemia to IGT or DM, irrespective of pregnant state. [19]

The mothers who had babies with low birth weight, all of them had a normal blood sugar after puerperium, the percentage of mothers converted to T2DM after puerperium was 33.3% in mothers who had babies with an average weight (2.5-3.9 kg) and in mothers who had babies with large birth weight (≥4 kg) was 50% Fig. (12), Steinhart et al., 1997 reported that Patients who developed T2DM had greater BMIs, parity, and infant weights. [23] The percentage of mothers converted to T2DM after puerperium was 44.1% in mothers who fed their babies from bottle and 28.6% in mothers whose babies were on breast-feeding Fig. (13). Kajos et al., 1993 concluded that, lactation, even for a short duration, has a beneficial effect on glucose and lipid metabolism in women with gestational diabetes. Breast-feeding is associated with reduced blood glucose levels and a reduced incidence of T2DM among women with a history of GDM. [20]

CONCLUSION
We conclude that
1. About a third of pregnant women with GDM will become T2DM as early as 6 weeks post-delivery and may be more later on.
2. The risk is increased with the advanced maternal age, having (B+) blood group, use of insulin during pregnancy, positive first degree relatives history of diabetes, BMI (30–40), HbA1c (>6%) at the time of GDM diagnosis, patients with hypothyroidism, high parity, positive history of polycystic ovary syndrome (PCOS), giving birth to a macrosomic baby and bottle feeding.

ACKNOWLEDGMENT
We are very grateful to Dr. Laila Sabei, Dr. Taher El Mhales and Dr. Fathi Eshreef from Community & Family Medicine department, Tripoli University, for their helping, co-operation and guiding through the statistical part of this thesis.

REFERENCES
16. Oldfield MD, Donley P, Walwyn L, Scudamore I, Gregory R. Long term prognosis of women with