

Universal Screening of Gestational Diabetes Mellitus In Upper Egypt: Prospective Cohort Study of The Prevalence, Risk Factors, and Short-Term Outcomes

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Abstract

Background: Despite the high prevalence of diabetes mellitus in Egypt, the real prevalence and epidemiology of gestational diabetes mellitus (GDM) in Upper Egypt is still lacking.

Objective: This study aims to determine the prevalence and risk factors of GDM among pregnant women in Upper Egypt and to evaluate the foetal and maternal outcomes of this disease.

Methods: This prospective cohort study was conducted between July 2014 and July 2018. Universal screening for GDM among all pregnant women attending primary health care clinics was done using Diabetes in Pregnancy Study Group of India (DIPSI) criteria. Those with GDM were followed up until the end of pregnancy. Maternal and foetal outcomes were recorded.

Results: GDM was diagnosed in 956 out of 7141 pregnant women (13.4%). Previous history of GDM, macrosomic babies, and family history of diabetes were all significantly higher in GDM women ($P < 0.001$ each). However, no definite risk factors were observed in about half of the GDM women. 29% of GDM women responded to medical nutrition therapy (MNT) alone. When the oral glucose tolerance test (OGTT) was repeated Postpartum, diagnosis of DM was established in 14.3% of the cohort, while 25.7% had impaired glucose tolerance.

Conclusions: The prevalence of GDM is relatively high in Upper Egypt. Half of GDM cases lack risk factors. Universal screening using OGTT should be routinely performed to all attendant pregnant ladies. Discrete MNT is not an enough management in most of GDM cases.

Keywords: GDM; Postpartum OGTT; diabetes; MNT; foetal outcome; maternal outcome.

Highlights

- This study is the first multi-center survey carried out in the Upper Egypt region.
- The study disclosed a high prevalence of GDM (13.4%) dictating the necessity of the universal screening and early detection of GDM using OGTT.
- This screening test should be applied to all pregnant women even those lacking any of the risk factor known.
- The rising trend of GDM among the Egyptian pregnant women should be checked by increased awareness of the community and encouragement of married women to maintain average weight.
- Further large-scale studies are needed to have a clear perception of the prevalence of GDM in Egypt.

Introduction

GDM is defined as any degree of dysglycemia occurring or first recognized during pregnancy [1]. GDM is one of the leading causes of morbidity and mortality for both the mother and the infant worldwide [2]. According to the 9th atlas of the International Diabetes Federation (IDF), Egypt is one of the top ten countries as regards diabetes prevalence worldwide [3]. As a consequence, the rate of GDM diagnosis is steadily rising [4]. Despite the medical and scientific progress in the field of diabetes, data about basic knowledge of GDM and its prevention still lack, especially in Egypt [5].

The prevalence of GDM is enhanced by many habits in the community. Urbanization and overconsumption of junk food, even among the low socioeconomic population, often lead to obesity. Unfortunately, overweight is erroneously considered a sign of beauty and good health among Egyptian ladies. Furthermore, the huge work burden posed on low socioeconomic Egyptian women either indoor or outdoor hinders them from suitably prioritizing their health.

GDM documented prevalence varies substantially worldwide, ranging from 1% to >14% [6]. Complexity and controversy have shadowed the diagnosis of GDM among health care providers owing to the lack of consensus and uniformity in the screening standards and diagnostic criteria of GDM [7]. Furthermore, it is challenging to compare the prevalence across countries and regions. The diagnosis of GDM offers a unique opportunity to identify individuals who are susceptible to develop type 2 diabetes mellitus (T2DM). These cases will get the benefit of early lifestyle modification and therapeutic intervention that would delay or even prevent the onset T2DM.

So far, the actual prevalence rate of GDM in Egypt is unknown. The universal screening for GDM was selected in the current study thanks to its high sensitivity. We chose the Diabetes in Pregnancy Study Group of India (DIPSI) criteria for diagnosis of GDM thanks to its simplicity; only one sample of blood is taken, besides the non-necessity for fasting [8-10].

Treatment of GDM aims at minimizing the risk of perinatal outcomes such as macrosomia, birth trauma, neonatal metabolic abnormalities, and the need for caesarean section [2,11]. Lifestyle modification is the first-line treatment and includes medical nutrition therapy (MNT), exercise, and glucose monitoring. Pharmacological treatment generally consists of insulin, glyburide, or metformin [4,11-13]. Insulin is the preferred pharmacological treatment for the management of GDM if lifestyle modification is insufficient in achieving euglycemia [11-13].

The present study aims to determine the prevalence and risk factors of GDM among pregnant women in Upper Egypt governorates and to evaluate both maternal and foetal outcomes.

Methods

This prospective cohort intervention study was conducted in collaboration with the World Diabetes Foundation project (WDF 13-797) titled "Gestational Diabetes Care in Upper Egypt". The study had been conducted during the period starting by July 2014 through July 2018 including six milestones (6 months each), while the last year was for the post-partum maternal and foetal follow up. The study was conducted in all GDM centres in Upper Egypt. Multiple awareness campaigns for pregnant and non-pregnant women in their childbearing periods were additionally conducted throughout the period of this project.

We included all pregnant women attending primary health care clinics in Upper Egypt governorates at their 24-28 weeks of gestation. All Pregnant women with history of DM were excluded.

Intervention

Eligible participants signed a written consent after adequate counselling and reading the patient information sheet. Participants were given 75 g of glucose anhydrous dissolved in 200 ml of water. All participants were not fasting before the test. Blood samples for glucose estimation were collected after two hours using DIPSI criteria. Blood sugar level ≥ 140 mg/dl was diagnostic for GDM. Blood sugar values ≥ 200 mg/dl indicated the pre-existence of diabetes [4] and therefore were excluded from the study.

Medical nutrition therapy was advised to all GDM cases. If the blood glucose level didn't reach the target (FBG <92 mg/dl, one hour <140 mg/dl, and two hours <120 mg/dl) after two weeks, insulin was added. Metformin was the alternative in cases incapable to afford or refusing insulin.

Follow up

Women with GDM were followed by regular visits every two weeks until delivery and monthly for one year afterwards. The modes of delivery as well as any obstetric or medical complications were reported. At each visit, complete physical assessment, including weight and blood pressure monitoring was done. Check for the self-monitored blood glucose levels were also accomplished. Foetal assessment, including foetal movement, was assessed by an obstetrician and then by paediatrician post-partum.

Six to twenty-four weeks after delivery, OGTT was repeated for GDM women to detect cases that had frank T2DM.

Statistical analysis

Data were collected and analyzed using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). Continuous data were expressed in the form of mean $\pm$ standard deviation, while nominal data were represented in frequency (percentage). Student's t-test and Chi-square test were used to check the significance. Multivariate regression analysis was performed to evaluate the risk factors for GDM development. P-value was considered statistically significant if <0.05 .

Ethical considerations

The Assiut Faculty of Medicine Ethical Review Board had approved the study protocol and guaranteed that confidentiality would be maintained and ethical principles would be followed all through the study. Patients who met the eligibility criteria were informed, and their written consent was obtained before the start of the study.

Results

Results are summarized in tables 1-2 and figures 1-3. The study included 7141 pregnant women attending five GDM centres in the five major Upper Egypt cities. 956 out of the 7141 studied women were discovered to have GDM (prevalence rate = 13.4% according to DIPSI criteria).

719 (75.2%) of the GDM cases versus 3772 (61%) of the remaining cases were older than 25 years ($p<0.001$). 68% of the GDM were from urban areas, and 64.4% were not working. In addition, 40.2% of the GDM women were multiparous (have 3 or more conceptions) in comparison to 27.2% of those without GDM ($P<0.001$). Furthermore, most of the studied cohort had either increased body weight or were obese (42.8% and 44.6%, respectively), while normal pre-conception body mass index (BMI) was observed in only 12.7% of cases. BMI was significantly higher in GDM women (30.91 ± 5.95 vs. 29.40 ± 5.54 Kg/m², $p<0.001$) (Figure 1).

39.7% of GDM cases have a positive family history of diabetes, and 10.5% have a previous history of a macrosomic baby. Polycystic ovary syndrome (PCOS) and twin pregnancy were significantly higher in GDM cases (9% vs. 6%, $p<0.001$ and 6.5% vs. 3.5% respectively, $p<0.001$ in both). On the other hand, no definite risk factors were demonstrated in about half of the GDM women (49.4%). Both systolic (SBP) and diastolic blood pressure (DBP) were significantly higher in GDM women; (118.09 ± 12.55 vs. 115.39 ± 11.55 , and 74.97 ± 9.40 vs. 72.98 ± 8.71 for SBP and DBP respectively, $p<0.001$ in both).

29% of GDM women were controlled with MNT only, while 31% of them needed the addition of metformin to MNT, and 40% were controlled after the addition of insulin to MNT (Figure 2).

As regards the maternal outcome of GDM cases, 39.3% developed preeclampsia, 81.5% delivered by cesarean section (CS), and 17 % had preterm labour. As regards the foetal outcome of GDM babies, 74.3% had persistent physiologic jaundice, 52.1% needed neonatal intensive care unit (NICU) admission, 20.9% developed hypoglycaemia, 14.3% were macrosomic, 3.6% had congenital cardiac problems, and 7.1% died (Table 1).

After delivery, only 560 out of 956 (58.6%) continued regular follow up. Oral glucose tolerance test (OGTT) performed four to twenty-four weeks postpartum disclosed normal test in 60%, impaired glucose tolerance in 25.7%, and frank T2DM in 14.3% (Fig. 3)

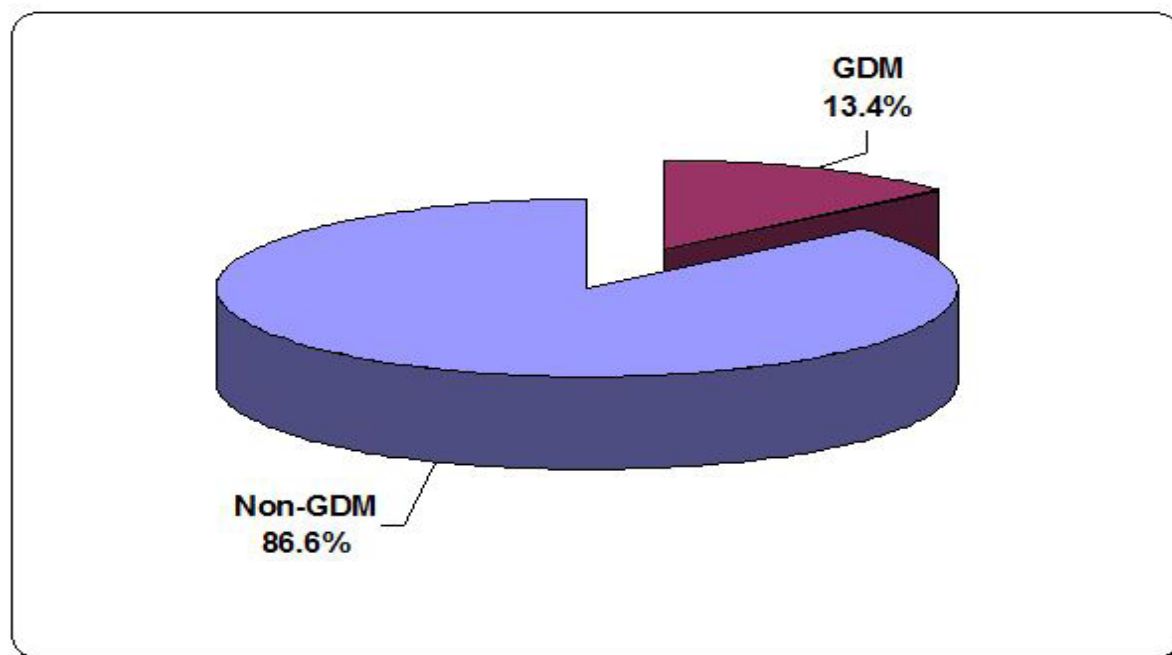


Figure 1 : Incidence rate of GDM according to DIPSI criteria; GDM= gestational diabetes mellitus

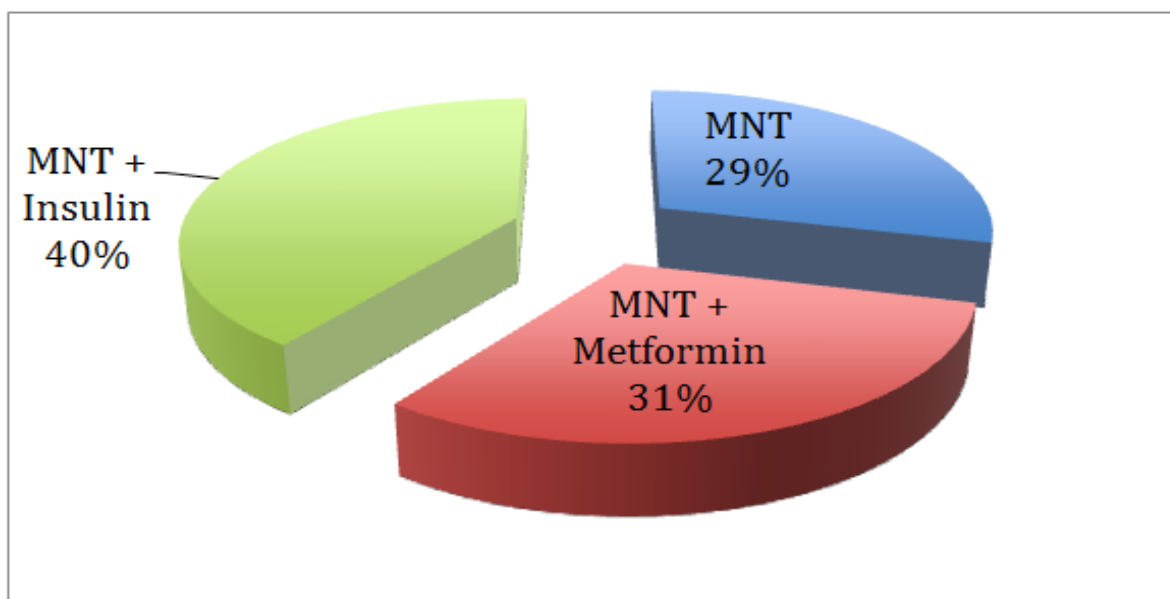


Figure 2 : Response to treatment among gestational diabetes cases.
MNT= medical nutrition treatment

Table 1: Multivariate analysis for GDM risk factors

Parameter	P value	Odd ratio	95% confidence interval	
			Lower	Upper
Age: (years)				
25 - < 30 years	0.011*	1.292	1.062	1.573
≥ 30 years	0.000*	1.604	1.293	1.989
Parity:	0.033			
Para 1 – 3	0.400	1.310	0.698	2.460
Para > 3	0.138	1.635	0.854	3.127
Working	0.000*	1.624	1.401	1.884
Age at marriage (≥ 20 years)	0.002*	1.295	1.104	1.519
History of GDM	0.000*	2.558	1.828	3.580
History of Macrosomic baby	0.000*	1.604	1.238	2.078
Polycystic ovary	0.148	1.210	0.934	1.567
Twin pregnancy	0.007*	1.524	1.125	2.065
Family history of diabetes	0.000*	1.576	1.360	1.827

GDM=gestational diabetes mellitus

Table (2) shows the results of multivariate regression analysis for the risk factors of GDM. Women's age <30 years, working women, age at marriage ≥ 20 years, previous history of GDM, previous macrosomic baby, twin pregnancy, and family history of diabetes were all significant predictors for development of GDM.

Discussion

Gestational DM is a growing pandemic with a prevalence rate worldwide between 1 and 14% of pregnancies [6-8]. In the current study, the prevalence rate of GDM using DIPSI criteria was 13.4% of pregnancies in Upper Egypt. This figure approaches the top of the range and is almost the double of the recently reported average prevalence of 7% [14]. A recent study in El-Minia, one of Upper Egypt Governorates, discovered a prevalence rate of 8.86% by DIPSI criteria versus 7.43% by International Association of the Diabetes and Pregnancy Study Groups (IADPSG) [15]. A more recent study in Assiut, another Upper Egypt governorate, found a higher prevalence

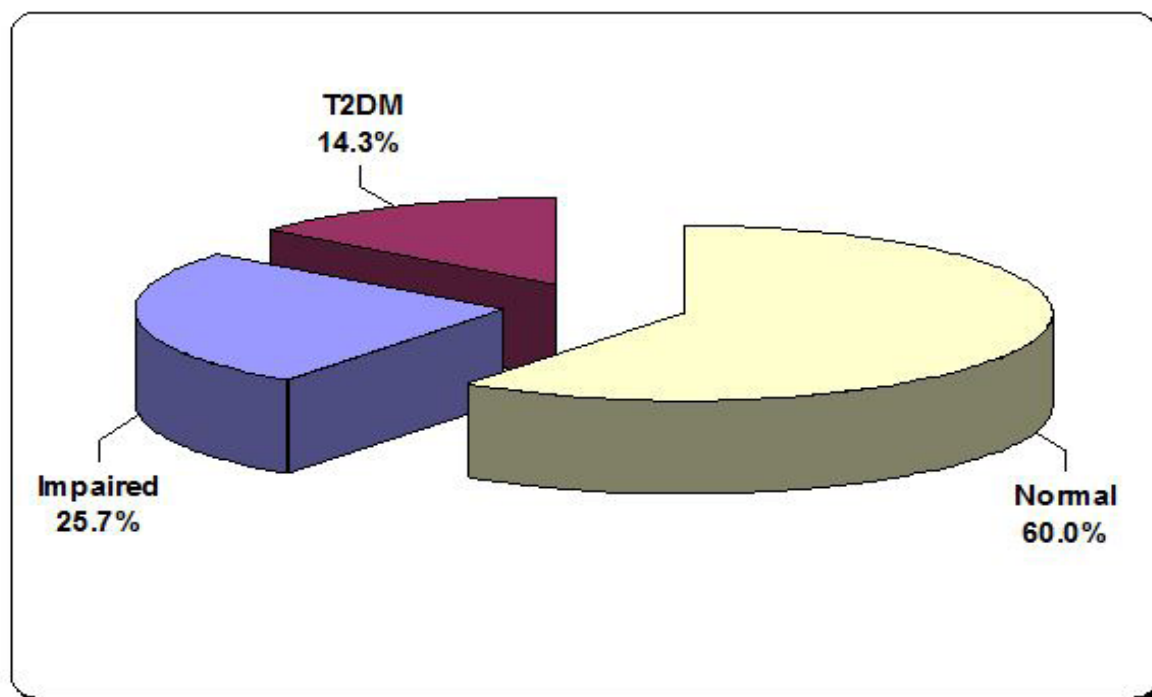


Figure 3 : Postpartum oral glucose tolerance test in the gestational diabetes mellitus cases

rate using IADPSG criteria (12.4%) [t6]. On the other hand, two studies performed in North Egypt demonstrated a relatively lower prevalence rate of 8% and 6% [17,18]. In these four studies, the number of the studied cases was relatively small (700, 355, 250, and 150 respectively). In addition to the small sample size, there were variations in the applied diagnostic criteria and the socio-demographic characteristics of the studied populations. The discrepancy in the prevalence rate dictates the need for the international professional organizations' input to unify a reliable methodology of diagnosis and establish new cut-off values.

Among women that developed GDM, maternal age >25 years, multiparity (>3), and obesity were significantly higher than in non GDM women. A recent meta-analysis has supported the impact of maternal age on the incidence of GDM. The risk of GDM progressively increases within the successive age groups [19]. In their recent study, Abu-Heija et al., observed a steady increase in the incidences of GDM with increasing parity, however, this increase was not statistically significant. On the other hand, GDM increased significantly with increasing pre-pregnancy BMI [20]. These findings were also observed in earlier studies [9, 16, 18, 21-23]. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study Cooperative Research Group has demonstrated that higher maternal BMI was associated with an increased likelihood of pregnancy complications, including complications related to foetal growth, adiposity, and preeclampsia [24].

Regarding the risk factors for developing GDM, the present study found that women with a past history of GDM had a four-fold increased risk of GDM (OR 4.03 2.94-5.52). Furthermore, having

a previous history of macrocosmic baby or a family history of DM doubled the risk for GDM (OR 2.33: 1.84-2.96), (OR 1.84:1.60-2.12); respectively. These data emphasize the role of genetic susceptibility toward this disease [16, 25]. Polycystic ovarian syndrome (PCOS) is a common cause of insulin resistance. Women with PCOS had a higher risk of developing GDM [16, 26, 27]. However; in the current study, the history of PCOS was not a significant predictor for developing GDM.

About half of our cohort had no risk factors of GDM. The same was true in a previous study of a nearby geographic area in Assiut (31.8%) [16]. This finding was similar to a Malaysian study where 23.8% of women diagnosed to have GDM were without any Known risk factor [28]. This finding would encourage the universal screening for GDM among all pregnant women. However, there is uncertainty as to whether or not to use universal screening versus selective ones. WHO (2006) recommended universal screening while the American Diabetes Association (ADA, 2019) and the American College of Obstetricians and Gynecologists (ACOG, 2018) recommend screening for GDM in high-risk women [29-31].

Worldwide, there are many guidelines with recommendations for appropriate management strategies for GDM once lifestyle modifications have been instituted and failed to achieve control. Pharmacologic treatment of GDM remains controversial; while ACOG (2018) is firmly recommending insulin as the preferred first-line, ADA (2019) dictated that most women with GDM could achieve normoglycemia with nutritional therapy alone [30,31]. In the current study, we found that onl 29% of the GDM women

responded to MNT, while 31% needed the addition of metformin to MNT, and 40% needed insulin addition. These data match the observations of other investigators [16, 32], while others found that insulin was needed in only 20 and 8% of GDM women, respectively [33,34].

Women with GDM are more likely to develop T2DM and require lifelong diabetes screening [35]. Within 5–16 years after pregnancy, up to 65% of women with previous GDM present with T2DM [36]. Unfortunately, Loss of health coverage after pregnancy limits access to follow-up care. For this reason, there are no large registries for tracking postpartum T2DM among women in under-resourced communities. These women face challenges with access to care after pregnancy [35]. In the present study, only 560 women attended the scheduled postpartum OGTT. 60% of the women tested (n=336) had normal OGTT and 40% (n=224) had abnormal test as either impaired glucose tolerance in 25.7% (n=144) or frank diabetes in 14.3% (n= 80). These results were slightly inconsistent with a previous study from Upper Egypt, which demonstrated that 52.7% of GDM women postpartum returned to normal, 12.7% had overt diabetes, 21.3% had impaired fasting glucose, and 13.3% had impaired glucose tolerance [37]. Also, another earlier studies done in Brazil and Iran demonstrated that overt postpartum diabetes mellitus and IGT were 8.1% and 21.4%, respectively, while 70.5% restored normoglycemic state [38,39]. However, some other studies reported a lower prevalence rate of diabetes that ranged from 2-8% [40-42].

Study limitations

Lack of structured dietitians explaining the role of MNT in the management of GDM and the noncompliance of pregnant women to MNT may explain the decreased response to MNT. Another limitation was that considerable number of GDM women missed the post-partum follow-up. This miss is likely due to the lack of motivation.

Recommendations

Increased awareness about the importance of universal screening for GDM in every pregnant woman in her perinatal care should be encouraged. MNT is very important during pregnancy and after delivery to avoid undesirable weight gain, particularly in high areas of obesity and type2 diabetes. Electronically generated telephone and SMS reminder messages to patients may improve the rates of postpartum testing for the persistence of glucose intolerance in GDM.

Conclusions

The prevalence of GDM is relatively high in Upper Egypt, probably related to poverty and the unhealthy dietary habits. Half of these cases are without risk factors. Universal screening by OGTT is thus recommended. MNT alone was not adequate for control of many cases. GDM women should be motivated not to miss the post-partum follow-up

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Lobna Eltoony suggested this work, supervised the study in all included centers, shared in writing the manuscript, made the last revision and approved it for submission. Walaa Khalifa supervised data collection in Assiut governorate, and shared in writing the manuscript. Hani Mobarkout was responsible for data collection from Aswan and Luxor governorates and filled data for statistical analysis. Nagla Ahmad shared in planning, collected data from Kena and Sohag governorates, made the statistical analysis and coordinated with obstetricians and paediatricians. Khaled Elhadidy collected data from Menia and Beny Sweef governorates. Mohammad Mashahet collected data from Fyoum governorate. Ehab Salem was responsible for Guiza governorate. Ahmed M. Abbas Monitored the maternal and foetal outcome of GDM cases in Aswan, Luxor, Kena, Sohag and Assiut governorates. Omar Shaaban Monitored the maternal and foetal outcome of GDM cases in Menia, Beny Sweef, Fyoum, and Guza governorates. Hend Yousef planned and supervised the implementation of life style modification program to all overweight and obese pregnant ladies, designed and supervised the implementation of MNT for GDM women, and supervised metformin or insulin treatment to GDM cases that failed to respond to MNT. Usama Sharaf El Din was responsible for collection of references, shared in writing the draft of the manuscript and was responsible for finalizing and excusion of the manuscript in its final shape, he is the corresponding author.

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