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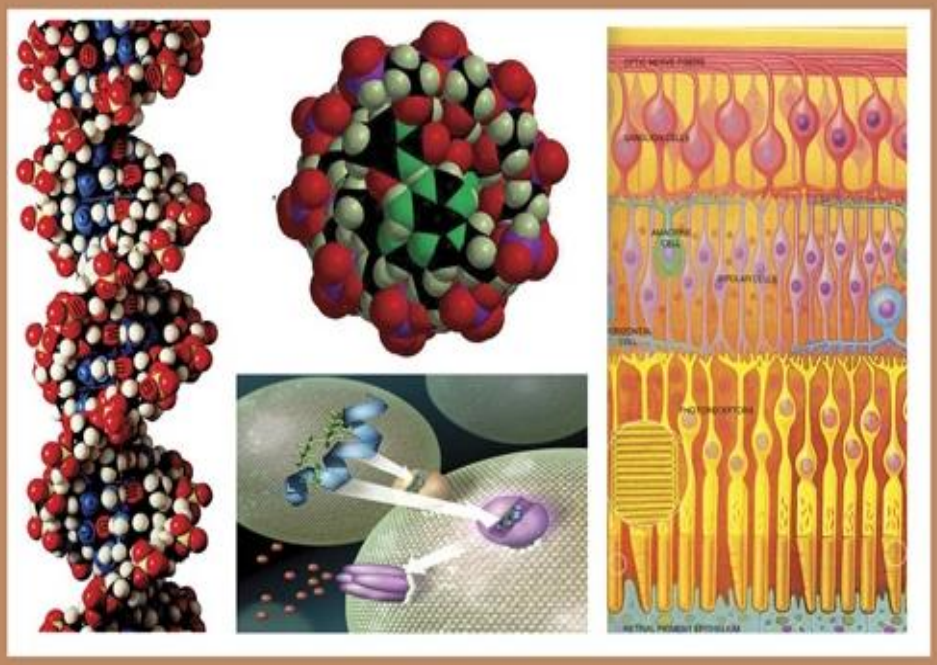

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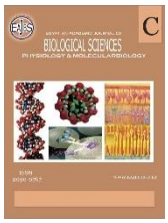

Follow Up of Maternal and Fetal Complications in Gestational Diabetes Women in Western Algeria

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ABSTRACT

Gestational diabetes (GDM) is one of the major problems experienced in pregnancy and contributes to complications of varying degrees. Our study tries to evaluate the maternal and fetal complications in GDM women in the western region of Algeria. Methods: We carried out a prospective study on 472 pregnant women whom 236 have gestational diabetes trouble, and 236 women non-diabetic. These patients were screened and followed up from November 2019 to July 2021 in the maternity department of the University Hospital Establishment of Oran city. Results: The rate of Body Mass Index (BMI)>25Kg/m2, maternal age>30 years, parity rate ≥2 in DGM women was higher than that of controls. The frequency of pregnancy-induced hypertension and obstetric pathologies of vascular origin HELLP Syndrome were significantly higher in GDM than non-GDM groups, respectively 10.4% vs 4.4% (p<0.001) and 2.3% vs 0.6 % (p=0.030). Moreover, the rate of Hypercholesterolemia, proteinuria, urea and creatinine levels were also higher in GDM group. Concerning the delivery induction, cesarean sections performed or scheduled and premature delivery, the rate was higher in GDM patients than in controls, respectively (24.2% vs 21.6%, p=0.268), (30.3% vs 24.8%, p=0.016), (1.9% vs 0.4%, p=0.033). The frequency of macrosomia in neonates, congenital malformations and glycemic imbalance,was significantly higher in GDM compared to Non-GDM groups, respectively (7.2 vs 3.4 %, p= 0.007), (3.8 vs 0.4%, p< 0.001), (6.4 vs 0.8%,p< 0.001). Conclusions: The real challenge will be to carry out regular monitoring, intensive care for pregnant women to prevent the risks of gestational diabetes.

INTRODUCTION

Gestational diabetes (GDM) is characterized by an increase in blood sugar levels and generally discovered in the second half of pregnancy, which changes the maternal metabolism (Szymanska *et al.*, 2008), due to insulin resistance, caused by the gradual increase of the production of "anti-insulin" hormones (for example, placental hormones, cortisol and growth hormones) during pregnancy; which reduce the effects of insulin on the body (Shalayel *et al.*,2011), and also due to a high sugar diet (Shin *et al.*, 2015).

The prevalence of GDM varies according to the Continents: 13.61% in Africa (Muche *et al.,* 2019), 11.5% in Asia (Lee *et al.,* 2018), 7.6% in America (Casagrande *et al.,* 2018), 5.4% in Europe (Eades e*t al.,* 2017), and sometimes it varies even within the same country according to the ethnic origin of the inhabitants, the method of screening, the diagnostic criteria used and the prevalence of type 2 diabetes (T2DM) in each country (Choudhury & Devi Rajeswari, 2021).

Fetal and maternal complications can be caused by a poor control or untreated GDM (American Diabetes Association, 2019). Pregnant women with GDM tend to have a high-risk of abortion, hypertension, preeclampsia (Huang *et al.*, 2015), polyhydramnios, premature rupture of membranes and cesarean section (Choudhury & Devi Rajeswari, 2021; « Hyperglycemia and Adverse Pregnancy Outcomes », 2008; Najafi *et al.*, 2019). The newborn may also suffer from congenital deformities, birth defects as shoulder dystocia (Bartolo e*t al.,* 2016), hypoglycemia, respiratory distress syndrome, neonatal trauma, macrosomia, premature births or even infant mortality (Sunjaya & Sunjaya, 2018). Because of the high prevalence of GDM during these last decades, and its serious complications.

We aimed to conduct a prospective study on women with and without GDM, in order to assess and compare the follow up of maternal, fetal and neonatal complications during their pregnancy.

MATERIALS AND METHODS

Patients:

This prospective study was carried out at the level of maternity department of the University Hospital Establishment UHE 1st November of Oran, western Algeria, from November 2019 to July 2021. We recorded 236 patients with gestational diabetes diagnosed according to the World Health Organization (WHO) 2013 criteria, and 236 women without GDM as control (non-GDM group).

The diagnosis and the follow-up of the participants were carried out by a gynecologist or a diabetologist, from their 1st medical examination until the day they leave the establishment after childbirth.

Patients presenting GDM, had benefited a regular follow-up to control their pregnancies course and their glycemic balance.

Personal data (age, Body Mass Index (BMI), parity, weight gain), evaluation of maternal complications (hypertension (AHT), preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes and low platelets), hydramnios, hypercholesterolemia, hospitalization), delivery characteristics (induction of delivery, cesarean and premature delivery, birth defects), fetal and neonatal characteristics complications (macrosomia, respiratory distress, neonatal hypoglycemia, neonatal intensive care, neonatal death) during pregnancy were recorded from the medical file of each patient.

Patient hospitalization was necessary when the blood glucose values were abnormal or in the event of a premature delivery risk.

Each delivery that occurs before 37 weeks of amenorrhea (WA) was considered as premature delivery. Perinatal mortality included all spontaneous or medically interventional fetal deaths from 22 WA, stillbirths, as well as newborn deaths before the seventh day of life. Congenital malformations included all malformations seen in newborns or in fetuses that died after 22 weeks.

Monitoring of the child blood sugar was performed every 2 hours at least the first 24 hours after childbirth and the value of glucose was defined as hypoglycemia if it less than 0.40 g/L. Preeclampsia was defined by the occurrence of hypertension greater than or equal to 140 mmHg systolic

and 90 mmHg diastolic and proteinuria greater than 300 mg /24 hours. HELLP syndrome is often diagnosed during the

monitoring of preeclampsia, when the blood test showed an increase in liver enzymes, thrombocytopenia, intravascular hemolysis.

Macrosomia was defined as a fetal birth weight ≥ 4000 g.

Statistical Analysis:

Regarding to the statistical analysis, the results of qualitative data were presented as frequencies, and quantitative data were presented as mean with standard deviation (SD). For comparison test, continuous variables were tested using the independent sample *t* test, Pearson chi-square test ($\chi 2$) was used for categorical variables. The level of significance was at p-value <5%. All data were processed and analyzed using SPSS 22.0 (Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2013).

RESULTS

Totally 472 pregnant women were involved in this prospective study, with the mean age of GDM and Non-GDM patients respectively of 32.86 ± 5.608 and 31.08 ± 4.748 years ($p< 0.001$). The most interval age affected by GDM was comprised between 30 and 34 years (15.04%) (**Fig. 1**), and almost a quarter of these GDM patients gave birth at least twice (24.2%) and were more frequently overweight (BMI> 25 kg/m^2) (33.2%) compared to non-diabetic women (20.3%) ($p< 0.001$).

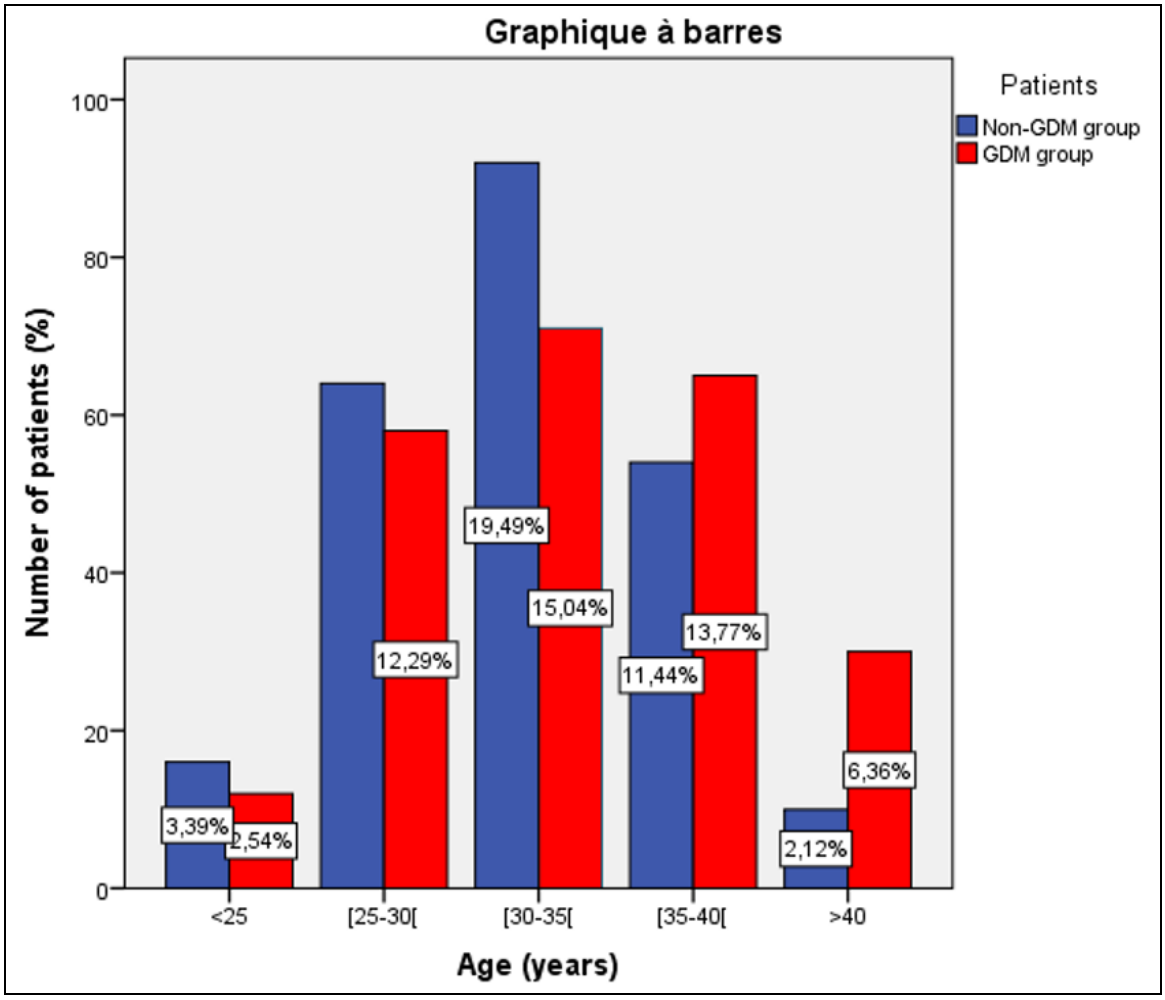

Fig. 1. Distribution of patients according to their interval age.

The analysis of personal characteristics of both pregnant women groups such as age, parity, BMI, and weight gain are shown in Table1, whereas, the results analysis of maternal complications during the pregnancy are shown in Table 2. Among the principal interesting data, the AHT was shown to be significantly higher in the GDM group (10.4%) compared to the non-GDM group (4.4%) ($p< 0.001$), and the rate of urine albumins greater than 300 mg /24 hours was four times higher in GDM group (6.4% vs 1.7%) (p <0.001). HELLP Syndrome was significantly noted in GDM group (2.3% vs 0.6%) ($p= 0.030$). Moreover, almost a third of our patients were suffering from anemia (28.9%). The delivery characteristics data for GDM and Non-GDM groups are listed in Table 3.

In our pregnant patients, the mean term of delivery recorded was 39.2 weeks (27-42 weeks), and the rate of preterm birth in the GDM group was significantly higher than in non-GDM group (1.9% vs 0.4%) (p = 0.033).

More than half of patients gave birth by cesarean section (55.1%), while only 19.7% of cases had a vaginal route birth. Fetal and neonatal characteristics are indicated in Table 4. Regarding to childbirth complications, the shoulder dystocia as well macrosomia was significantly increased in GDM group ($p < 0.05$), however, no significant differences were found between two groups regarding to the intensive care as well as the neonatal death ($p > 0.05$).

Table 1. Personal characteristics of studied patients.

	GDM group n=236 [n (%)]	**Non- GDM group n=236 [n (%)]**	***p* value**
Mean maternal age	32.86 ± 5.608	31.08 ± 4.748	**< 0.001[1*]**
Maternal age > 30 years	148 (31.4)	112 (27.3)	**0,001***
Mean parity	2.49± 1.161	1.63 ± 0.843	**< 0.001[1*]**
Parity ≥ 2	114 (24.2)	38 (8.1)	**< 0.001[1*]**
Mean BMI (Kg / m²)	26.962± 4.509	24.546± 1,945	**< 0.001[1*]**
BMI ≥25 Kg/m²	157 (33.3)	96 (20.3)	**< 0.001[2*]**
Weight gain > 16Kg	178 (37.7)	157 (33.3)	**0.033[2*]**

(1) means were compared with independent sample t-test, (2) Pearson chi-square test ($\chi 2$), (*) p< 0.05 was considered as significant.

Table 2. Maternal complications of GDM and Non-GDM groups.

	GDM group n=236 [n (%)]	**Non- GDM group n=236 [n (%)]**	***p* value**
AHT	10.4%	4.4%	**<0,001[1*]**
Proteinuria> 300mg/24h	6.4%	1.7%	**<0.001[1*]**
Preeclampsia	2.8%	1.5%	0.081[1]
HELLP Syndrome	2.3%	0.6%	**0.030[1*]**
Anemia	13.1%	15.7%	0.223[1]
Urea (g / l)	0.49 ± 0.95	0.37 ± 1.1	0.191[2]
Creatinine	9.01 ± 5.39	7.74 ± 3.31	**0.002[2*]**
Hydramnios	20.3%	16.1%	0.056[1]
Hypercholesterolemia	30.1%	25.8%	0.064[1]

(1) Pearson chi-square test ($\chi 2$), (2) means were compared with independent sample t-test, (*) p< 0.05 was considered as significant.

Table 3. Delivery characteristic and Childbirth complications of GDM and Non-GDM groups.

	GDM group n=236 [n (%)]	Non- GDM group n=236 [n (%)]	*p* Value
Hospitalization (days)	7.01 ± 6.44	5.51 ± 4.852	**0.004**[2*]
Mean term of delivery	39.15 ± 1.93	39.44 ± 1.56	0.073[2]
Premature	1.9%	0.4%	**0.033**[1*]
Induction of childbirth	24.2%	21.6%	0.268[1]
Cesarean delivery	30.3%	24.8%	**0.016**[1*]
Childbirth complication, %			
Childbirth complication	6.8%	2.1%	**<0.001**[1*]
Shoulder dystocia	1.3%	0.2%	0.057[1]
Closed neck	0.0%	1.5%	
Postpartum hemorrhage	0.2%	0.0%	
Umbilical cord coiling	0.6%	0.0%	
Perineal tear	2.8%	0.2%	
Inhalation of amniotic fluid	1.1%	0.2%	
Episiotomy	0.8%	0.0%	

(1) Pearson chi-square test ($\chi 2$), (2) means were compared with independent sample t-test, (*) $p < 0.05$ was considered as significant.

Table 4. Fetal and neonatal complications of GDM and Non-GDM groups

	GDM group n= 236 [n (%)]	Non- GDM group n= 236 [n (%)]	*p* Value
Congenital malformations	3.8%	0.4%	**<0.001**[2*]
Mean weight	3220.76 ± 613.564	3074 ± 477.794	**0.004**[1*]
Macrosomia	7.2%	3.4%	**0.007**[2*]
Respiratory distress	5.7%	0.8%	**<0.001**[2*]
intensive care	1.3%	0.8%	0.523[2]
Hypoglycemia	6.4%	0.8%	**<0.001**[2*]
Neonatal death	0.6%	0.0%	0.082[2]

(1) means were compared with independent sample t-test, (2) Pearson chi-square test ($\chi 2$), (*) $p < 0.05$ was considered as significant.

DISCUSSION

In the present study, the clinical data of 472 patients from Oran city, western Algeria region, were prospectively analyzed and the results indicated that the average age of pregnancy at the first medical examination at diabetology department was 10.31 ± 6.349 WA. Concerning the analysis of the maternal complications during the pregnancy, the results showed a high rate of hypertension and HELLP syndrome in the GDM group.

Some factors existed in GDM women such as an increase in insulin, endothelial dysfunction caused by hyperinsulinemia, amplified by lipid abnormalities and activation of adrenal nervous were hypothesized to be involved in pathogenesis of hypertension during pregnancy (Szymanska *et al.*, 2008).

Several studies have reported an increased risk of gestational hypertension and preeclampsia in pregnancies complicated by diabetes, and GDM is often considered as a risk factor of developing preeclampsia (Carpenter,

2007; Ottanelli *et al.,* 2020). A study conducted in 2018 by Cao *et al.*, suggested that high blood glucose levels detected during pregnancy affects other tissues, especially small blood vessels. Consequently, hypertrophy and proliferation of smooth vascular tissues may contribute to the association between GDM and the subsequent development of preeclampsia (Cao *et al.*, 2018). Although, the mechanisms remain to be elucidated, many studies have suggested that hyperglycemia has a role in the etiology of this disease (Cao *et al.*, 2018; Warrington *et al.*, 2013). In the literature, the data about association between GDM and preeclampsia are contradictory. Östlund *et al.* had found that there is a significant association (Östlund *et al.*, 2004) while, no association was observed in Vivet-Lefébure *et al.* study (Vivet-Lefébure *et al.*, 2007). Similarly, no statistical significant association between GDM and preeclampsia was detected in our patients, despite the increased proteinuria levels and the highest rate of THA in GDM group.

In our series, 2.3% of GDM women were affected by HELLP syndrome, this result is in agreement with a recent study of Lisonkova et al. in which had reported that a high association between HELLP Syndrome and GDM exists (Lisonkova et al., 2020), but to specify the real relationship between the GDM and the appearance of vascular systems pathologies, further studies with better control of many confounding factors were required.

The increased creatinine levels detected in GDM plasma of our patients might be due to the alteration of kidneys function or to the increased blood flow and glomerular filtration during pregnancy.

An American multicenter, randomized trial study conducted on 958 pregnant women by Landon et al. have found that the rate of prematurity was similar in GDM and Non-GDM groups. They suggested that the increased risk of preeclampsia in GDM patients could partly explain the increased rate of prematurity (Landon *et al.*, 2009), however, in our study the rate of prematurity was higher in GDM group but no significant difference of preeclampsia rate was found. Our result corroborates with those found by HAPO study carried out on 25,505 pregnant women at 15 centers in nine countries which showed that there is a significant and continuous relationship between the risk of premature birth and the elevation glycemia (« Hyperglycemia and Adverse Pregnancy Outcomes », 2008),

As in other series (Olerich *et al.*, 2021; Sudasinghe et al., 2018), we observe a wider practice of delivery induction in the GDM group with more frequent recourse to cesarean section, in both scheduled delivery or during labor. The practice of delivery induction, usually performed in the high-risk pregnancy department around 38 or 39 WA, is justified by the desire to attempt a vaginal birth when the risks associated to macrosomia were reduced.

The rate of cesarean sections in our study was about 30 % in GDM group, these results were consistent with those found in previous studies which showed that the emergency cesarean section rate was increased significantly among GDM women (Boriboonhirunsarn & Waiyanikorn, 2016; Goldman *et al.*, 1991; Naylor, 1996).The most likely reason for the increased cesarean section in GDM patients is the elevated fetal weight (Xiong *et al.*, 2001), the reduction of the risk of instrumental delivery use and shoulder dystocia(Ovesen *et al.*, 2015)which can be caused by fetal macrosomia. This neonatal complication remains the main consequence of this obstetric pathology and, at the same time, the first objective of the management of the GDM. Excessive fetal weight is the

consequence of fetal hyperinsulinemia which results from increased maternal-fetal transfer of glucose and other nutrients (Xiong *et al.,* 2001). Our result agreed several studies that have found that the incidence of macrosomia was significantly higher in GDM women (Gasim, 2012; Jensen *et al.,* 2000; Ovesen *et al.,* 2015).

Moreover, it's known that GDM was associated with a significant number of adverse neonatal outcomes. Newborns were more likely to be admitted to neonatal intensive care unit because of their respiratory distress and hypoglycemia. Also, a high rate of malformation and neonatal death were more observed in GDM group, these results are consistent with previous studies which found an association between these neonatal complications and gestational diabetes (Bener, 2011; Karasneh *et al.,* 2021; Kc *et al.,* 2015).

Limitations of Our Study:

Our study was conducted on a population of 472 pregnant women in which medical data are collected from one center, and a multicentric study would be preferable to follow up a larger number of patients affected by GDM.

Conclusions

The obtained results allowed us to clearly identified the most important maternal and fetal complications linked to GDM. Among them AHT, HELLP syndrome, cesarean section, prematurity, congenital deformities, respiratory distress, hypoglycemia and macrosomia. An active management of GDM is recommended to avoid or reduce maternal and neonatal complications, the real challenge for health professionals will be to carry out a regular monitoring, an intensive care, and to sensitize and improving the lifestyle of these pregnant women.

Ethics Approval: The experiments were approved by the Institutional Board Review and Ethics Committee of the University Department of Biology, Djillali Liabes University of Sidi Bel Abbes.

List of Abbreviations:

GDM: Gestational diabetes mellitus; T2DM: Type 2 diabetes mellitus; UHE: University Hospital Establishment; WHO: the world health organization; BMI: body mass index; WA: weeks of amenorrhea; AHT: arterial hypertension, HELLP syndrome: hemolysis, elevated liver enzymes and low platelets syndrome;

Consent for Publication: Not applicable.

Availability of Data and Materials: Not applicable.

Competing Interests: The authors declare that they have no competing interests

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