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GESTATIONAL DIABETES: RISK FACTORS AND CLINICAL STUDY

Diabetology

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ABSTRACT

Introduction: The prevalence of gestational diabetes mellitus is increased sharply,it consists of a pathology that constitutes a real public health problem. A rigorous tracking is necessary in order to watch out the possible maternal fœtal complications that might occur.consequently, a systematic screening for every pregnant women is needed.Although the numerous works that have been done, there is still no existing universal screening. The aim of this study was to identify the risk factors, screening methods ,aspects of clinical and paracinical factors of gestational diabetes , its impact on pregancy concernig 150 women .

Results : Gestational diabetes mellitus was diagnosed for 65,3% during the second trimester of pregancy between 24 and 29 weeks ' gestation.the principal risk factors that were found out consisted of the family history diabetes (59,3%), the maternal age(44,6%), overweight (42,3%)There was no maternal mortality but morbidities like hydramnions ($p<0.001$)), pre-eclampsia ($p<0.001$)), urinary tract infection ($p<0.05$), puerperial sepsis ($p<0.05$)) and surgical interventions ($p<0.001$) were more prevalent in GDM compared to non-GDM groups. The prevalence of antipartum haemorrhage, post partum haemorrhage, and eclampsia did not vary between the groups. There was one still birth, one perinatal mortality (due to respiratory distress syndrome) and one congenital anomaly observed in neonates of GDM mothers. More pre-term ($p<0.01$), post-term ($p<0.01$), low birth weight ($p<0.001$) and macrosomic ($p<0.001$) babies were found among the babies of GDM mothers than non-GDM mothers

Conclusion : A strict and targeted screening, in addition to multidisciplinary care and adequate management of gestational diabetes mellitus may help to avoid short and long term harmful maternal complications.

KEYWORDS

pregnancy, hyperemesis gravidarum, hyperthyroidism

INTRODUCTION:

Gestational Diabetes Mellitus (GDM) is defined by the World Health Organization (WHO) as "anabnormal glucose tolerance leading to hyperglycemia of variable severity, with onset or first recognition of this pathology during pregnancy, regardless of the term (1). This definition is rather unclear because the GDM includes a heterogeneous population that includes pre-existing, subclinical diabetes, whether it is type 1 diabetes or type 2 diabetes, and the actual GDM that appears during pregnancy.The GDM is frequently encounteredand several maternal, fetal, and neonatal adverse outcomes have been associated with it. These risks may be functional and vital, Its prevalence is estimated between 0.5% and 15% worldwide (2), which makes it a real problem to public health. A multidisciplinary team approach is critical to success in diabetes care and complications prevention for both the mother and her fetus.

WHO defines gestational diabetes as fasting glucose level greater than 126 mg/dL and blood glucose two hours after oral absorption of 75 g glucose greater than 140 mg/dL(1).

In 2010, the International Association of Diabetes and Pregnancy Study Group (IADPSG), an international consensus group with representatives from multiple obstetrical and diabetes organizations, recommended a change to the previously mentioned definition of gestational diabetes. In the proposed new system, diabetes diagnosed during pregnancy is classified as overt (pre-existing) or gestational. A diagnosis of overt diabetes can be made in women who meet any of the following criteria at their initial prenatal visit:

- Fasting plasma glucose ≥126 mg/dL [7.0 mmol/L], or
- A1C ≥6.5 percent using a standardized assay, or
- Random plasma glucose ≥200 mg/dL [11.1 mmol/] that is subsequently confirmed by elevated fasting plasma glucose or A1C, as described above

A diagnosis of gestational diabetes can be made in women who meet either of the following criteria:

- Fasting plasma glucose ≥92 mg/dL [5.1 mmol/L], but <126 mg/dL [7.0 mmol/L] at any gestational age (fasting plasma glucose ≥126 mg/dL[7.0 mmol/L] is consistent with overt diabetes)
- At 24 to 28 weeks of gestation: 75 gram two hour oral glucose tolerance test (GTT) with at least one abnormal result: fasting plasma glucose ≥92 mg/dL [5.1 mmol/L], but <126 mg/dL [7.0 mmol/L] or one hour ≥180 mg/dL (10.0 mmol/L) or two hour ≥153 mg/dL (8.5 mmol/L).

Currently, the prognosis of these high-risk pregnancies has been significantly improved thanks to the better knowledge of the pathophysiology of the GDM and the progress made during the last decades.Moreover, fetal and perinatal mortality has dropped dramaticallyfrom about 65% before Insulin discovery to 2-5% nowadays (4)Through this study, we identified the clinical aspect and the management of women with GDM.

MATERIALS AND METHODS:

This is a descriptive longitudinal retrospective study of patients followed for gestational diabetes in the department of obstetrics& gynecology A in liaison with the endocrinology department in Charles Nicole university-basedhospital. The medical records of these patients were collected over a period of five years, from January the 1st 2010 to December 31, 2014. It involved 150 pregnant women with gestational diabetes. The inclusion criteria were as follows: only women diagnosed according to the WHO recommendations and the recommendations of the IADPSG 2010 were included. Patients with pre-existing diabetes were excluded from the study. The screening of the GDM used in Charles Nicole Hospital was based on two different screening methods. Initially, the WHO recommendations had been followed and day by daythe 2010 recommendations of the IADPSG were being followed. Once the diagnosis was confirmed, a close

liaison between diabetologists and obstetricians was established. The patients were hospitalized on a monthly basis for a short period of time. The number of admissions changed variably depending upon the patient's education level, whether a good glycemic control was maintained or not, and whether metabolic and/ or gynecological-obstetrical complications occurred or not.

RESULTS:

44.6% of patients were over 35 years old. The mean age of our patients was 33.2 years (± 5,372), ranging from 20 to 44 years old. More than half of our patients (59.3%) had a diabetic person in the family, although the relationship was not specified. 47.3% of whom were non-insulin dependent diabetics. The majority of our patients (64%) did not have a pathologic medical history. Only 14 patients were followed for subfertility and 7 for high blood pressure. Obstetrical history of patients was dominated by a history of gestational diabetes, followed by history of recurrent miscarriages, preeclampsia, and macrosomia of 16%; 11.3%; 9.3% and 6% respectively. The intrauterine fetal death and the polyhydramnios represented 2.7% and 0.7% respectively. The risk factors demonstrated in this chart are: patient age, weight estimate, GDM history, various obstetrical history, and history of diabetes in the family. Patients with no risk factors for the GDMconstituted 24% of the population. Those with one and two risk factorsmade up the majority of patients with 28.7% and 25.3% respectively.

On the other hand, the patients who had had up to five risk factorsconstituted a minor part with1.3% to 8.7%. In our study, we found a positive and statistically significant correlation between the number of risk factors in a patient and the different diagnostic methods of the GDM with p value = 0.002. In the majority of cases, GDM screening was performed during the second trimester of pregnancy in 65.3%, during the period of 13^{th} to 24^{th} gestational week in 38%, and during the period of 24^{th} to 28^{th} gestational week in 27.3%. Only 5.3% of patients were diagnosed during the first trimester of pregnancy. On the other hand, 15.4% of our patients were diagnosed as early as 29 weeks of age, of whom 2.7% were diagnosed after the 35^{th}weeks. More than half of our patients (63.3%) were diagnosed according to WHO screening program against only 18% that werescreened according to the recommendations of the IADPSG 2010. However, 10% of our patients were screened twice using both methods.

Screening according to WHO recommendations:

The mean gestational agewas 25 weeks ± 5.82 weeks. The meanfasting plasma glucose value was 97.22 mg/d l ± 2.47. The meantwo-hour plasma glucose values after the 75 gram two hour oral glucose tolerance testwas 177 mg/ dl ± 38.7 mg/ dl.

Screening according to the recommendations of the IADPSG 2010:

The mean gestational age was comparable to the other group of 24 weeks ± 6.6 weeks. The mean value of the fasting glucose was 96.79 mg/ dl ±.30 mg/ dl. The mean one-hour plasma glucose values after the 75 gram two hour oral glucose tolerance test was 194.07 mg/ dl ±.54 mg/ dl. The mean two-hour plasma glucose values after the 75 gram two hour oral glucose tolerance test was 178.43 mg/ dl ±70 mg/ dl.

Patient follow-up:

More than half of our patients (56.7%) were hospitalized in our department once a month for a fulland comprehensive assessment of their diabetes. 8.7% of the patientswere closely monitored and hospitalized fortnightly. Unfortunately, 34.7% of our patients were hospitalized only once during the period of the study. The majority of our patients (86%) had controlled diabetes. Accomplishing a good glycemic control required medical nutritional therapy and initiating insulin therapy in 14% of those patients. The majority of our cohort (84.7%) has a well-controlled diabetes with medical nutritional treatment against (15.3%)in whom insulin use was required. The mean gestational age at which the insulin therapy was initiated in poorly-controlled diabetes patients was 26 weeks ± 6.15 weeks, ranging from12 weeksto 37 weeks and 3 days. The mean dose of insulin, representing intermediate insulin and regular insulin is 19 ± 12 IU, with a minimum dose of only 4 IU and a maximum dose of 48 IU.

The main maternal complications:

A significant percentage of women (29.3%) with GDMs developed at least one complication during their follow-up. Preeclampsia complicated or not with eclampsia accounted for 27.3% of the overall complications. Pyelonephritis came second with 25%. Threatened miscarriage, preterm labor or preterm delivery occurred in 18.3% of the patients who had already had complications and in 5.3% of all patients.

- Fetal Complications:

12.7% of the detailed fetal anatomic ultrasound examinationsdetected congenital malformations. Polyhydramnios and fetal macrosomia were the most common complications encountered with an incidence of 20% for each. Fetal heart anomalies (15%) followed by fetal growth restriction (FGR)(10%) and pyelectasis (10%)were other fetal anomaliesillustrated in our study. 20.8% of the ultrasound examinations performed during the third trimester were pathological. Many anomalies were found. Of which, fetal macrosomia seemedto be the common anomaly with 34.4%. Polyhydramnios was ranked second with 25%. Particularly, both of those anomalies were encountered concomitantly in 18.8% during the last trimester of pregnancy. Fetal cardiac abnormalities: septal hypertrophy dominated all fetal heart defects with 66.7%. The various other anomalies were reported with percentages of 11.1% equally.

- Corticotherapy:

If there is a risk of preterm birth between 22 and 36 weeks, patients benefit from corticosteroid therapy with intramuscular injection of dexamethasone, repeated if necessary. Approximately 1/3 of patients followed for GDM (34.7%) received corticosteroid therapy. The mean gestational age at which the first injection of dexamethasone was administered was 31 weeks± 2, 68 weeks ranging from 26 weeks to 37 weeks.

- Delivery:

More than half of the patients(58.7%) had caesarean section. 17.3% of the patients had a spontaneous onset of labor, while labor was augmented in 6.7% of the patients.

- Complications during childbirth:

Preeclampsia followed by postpartum hemorrhage was at top of complications with an incidence of 36.4% and 27.3% respectively.

Neonatal complications:

The mean length of hospital stay in neonatal intensive care unit (NICU) was 3.89 ± 2.447 days[2-10] days.26.7% of the 75 mothers who were contacted mentioned that their child had been hospitalized for more than a day in NICU, 27.8% of them reported that neonatal respiratory distress had been the cause. However, suspicion of Fetomaternal infectionsconstituted 33.3% of total neonatal hospitalizations. The occurrence of neonatal jaundice was not insignificant that the incidence rate reached 16.7% in our series. 4% of the patients had Down syndrome and one of them had a bilateral hydrocele. 3 cases of stillbirth were reported. Fetomaternal infections was involved in 2 of the newborns who died, and cerebral hemorrhage at 4 months of age was the cause responsible in the third case.

DISCUSION

GDM represents an abnormal glucose tolerance leading to hyperglycemia of variable severity, with onset or first recognition of this pathology during pregnancy, regardless of the term (1). Our clinical research is a retrospectivestudy with many difficulties encountered and several shortcomings to be acknowledged. We wanted to provide a full assessment of our patients. Moreover, of the 150 patients recruited in our five-year study, only 77 of them stayed in contact with us. Thus, completing the missing data and postnatal follow-up were not obvious for all women. On average, 30± 1 patients per year were followed. This may mean that the prevalence of GDM in our study has remained stable throughoutthe period of the study. The GDMprevalence is estimated to be at between 1 and 4% of pregnancies (5) and it seems to vary from 1 to 14% in other study (6). Recent studies concerning the epidemiology of gestational diabetes appear to be all consistent with each other since they point out to a tendency to increase in prevalence over the past twenty years (7). Thus, the prevalence of GD has significantly increased, due to the fact that the glycemic thresholds for diagnosing GD have become slightly lower andonly one elevated glucose value is needed with the cut-offs are slightly lower contrary to the old criteria that were based on two pathological values. This higher prevalence could be explained by the increase in obesity rate, older maternal age, and the increased likelihood in leading sedentary lifestyle (8).

Maternal age is a risk factor for gestational diabetes. The mean age of our patients was 33.2 years (± 5,372). The age of most of our patients ranged between 25 and 34 years old. More specifically, 44.6% of that population was over the age of 35. Linear correlation between age and the risk of GDM was observed. The age that defines women at risk varies in the literature between 25 and 45 years. According to a study conducted in the United States in 2006, the prevalence of gestational diabetes increased with the age of patients regardless of their origins (9). Furthermore, a study undertaken in 2010 by Galtier illustrated an increase in the prevalence of GDM with age (10). Patients with no risk factor for the GDMmade up 24% of the sample, those with one or two risk factorsconstituted the majority of the patients, 28.7% and 25.3% respectively. There were also 16% of women who had a minimum of three risk factors. These results are consistent with the literature. According to the "Summary Report on the Screening and Diagnosis of Gestational Diabetes" issued in July 2005 by the High Authority for Health “HAS” (11): "The percentage of the gestational diabetes risk in the population is very high.In some population groups, depending on the factors and thresholds set to diagnose, only 10% of women would have no risk factor.

The meangravidity number in our study was 2.72 ± 1.651 and the parity number was 1.03 ± 1.049, of which 40% of the women were nulliparous. However, some authors consider multiparity as a risk factor for GDM. There are confounding factors such as maternalage and body mass index (BMI). Indeed, multiparous women seem to be older and obese. However, itmay be difficult to evaluate those factors separately and their association to GDMappears to be inconsistent in the literature (10). GDM recurred in 16% of our patients, whereas a study conducted in 2007 by Kim et al. (12) illustrated that the recurrence rate varied between 30 and 84% after a complicated pregnancy of a GDM and that rate seemed to be higher in specific ethnic groups.

The purpose of all the commonly used screening and diagnostic tests with different glucose loads, assay methods and threshold valuesis that identifying pregnant women with diabetes followed by appropriate therapy can decrease fetal and maternal morbidity (13).

We suggest universal screening, rather than.
All French societies and associations (IADPSG, CNGOF, SFD) recommend a first-trimester selective screening based upon risk factorsby measuring fasting plasma glucose.GDM risk factors are(22):

- maternal age greater than or equal to 35 years
- a BMI greater than or equal to 25 kg / m2
- a history of macrosomia
- a history of gestational diabetes
- a history of diabetes in at least one first-degree relative Between 24 and 28 weeks, screening is provided for patients with fasting plasma glucose level in the first trimester of less than 92mg /dl. This is followed by the 75- gram two houroral glucose tolerance test (OGTT). One elevated value is sufficient to establish the diagnosis.

Treatment:
An effective treatment regimen consists of dietary therapy, self-blood glucose monitoring, and the administration of insulin if target blood glucose concentrations are not met with diet alone (14).Identifying women with GDM is important because meta-analysis of randomized trials by Horvath et al. (14) has shown that appropriate therapy can decrease maternal and fetal morbidity, particularly macrosomia and preeclampsia. The randomized, multi-center National Institute of Child Health and Human Development (NICHD) study conducted by Landon et al, in America, included 958 women with moderate GDM. This study compared between a "treated" group and a "control" group. It well illustrated the appropriate management of the GDM allowed to reduce the caesarean section rate (26.9% versus 33.8%, p = 0.02) and the macrosomia rate (5.9% versus 14.5%). %, p <0.001). In our series, 100% of women admitted to our department received nutritional counseling by a registered dietitian upon diagnosis (at least once) and were placed on an appropriate diet. Recently, insulin therapy is the approach of choice for GDM treatment if normoglycemia cannot be maintained by medical nutritional therapy(15). Of the women who were followed for GDM, 15.3% had to be placed on insulin therapy as target glucose levels had been exceeded despite dietary therapy. Insulin initiation seemed essential if the glucose targets were not reached after two weeks of diet. Some authors illustrate that in about 30% of cases, insulin treatment will be eventually used (16).

Maternal complications:
GDM exposes both of the mother and fetus to potentially severe complications.

1- Preeclampsia:
Most of our patients (87.3%) maintained a normal blood pressure. Only 11.3% developed pregnancy-induced hypertension. This association "GDM-preeclampsia" was described by most cohort studies including the HAPO study (18) where glucose levels were linearly correlated with preeclampsia. A large Swedish study (17) showed that the rate of preeclampsia in the GDMgroup was 6.1% compared with 2.8% in the control group.

2-Infectious complications:
The main infectious complications are predominantly demonstrated by urinary tract infection. 2.7% of our patients had at least one episode of urinary tract infection during pregnancy.

3- Caesarean section risk:
This rate is much higher in our study compared to other ones, reaching 58.7%. This could be explained by poor glucose control, increased macrosomia rate, or late diagnosis of GDM and its fetal consequences. The large population study (n = 23,316) HAPO (18) showed a strong and direct correlation between maternal plasma glucose and caesarean section rate. d. Preterm labor and premature delivery: Digianni et al. (23) conducted a trialthat showed the GDM increased the risk of the occurrence of preterm labor and prematurity. The result isapplicableto the HAPO study as well (18).

Fetal& neonatal complications:
Macrosomia is the leading fetal complications in our series. One-third of fetal complications during the third trimester appear to be related to macrosomia.Macrosomia, in turn, is associated with an increased risk of operative delivery (cesarean or instrumental vaginal) and adverse neonatal outcomes, such as shoulder dystocia, brachial plexus injury, and clavicular fracture (8). During the neonatal period and as far as the hospitalized neonates in the (NICU) were concerned, neonatal respiratory distress was ranked second after fetomaternal infections in our study. In the literature, the risk of neonatal respiratory distress is estimated at 5.6% in neonates of mothers with GDM compared to 2.2% in the general population (13). Children born to mothers with GDM have a very high risk of hypoglycemia, hyperbilirubinemia and hypocalcemia compared to other children born to non-diabetic mothers (8).

The incidence of fetal hypoglycemia varies from 25 to 40% according to various studies (20). According to the HAPO study (11), there appears to be a weak association between hyperbilirubinemia and maternal plasma glucose. Historically, O'Sullivan (21) illustrated in his study an increase in perinatal mortality in the group of newborns of GDMmothers compared to the control group (6.5% versus 1.5%). However, recent studies do not find this association any more. It is controversial. Higher neonatal mortality rate seems to be encountered among those who have pregestational diabetes rather than GDM. In our series, 4% of the patients had Down syndrome and one of them had a bilateral hydrocele. 3 cases of stillbirth were reported. Fetomaternal infections was involved in 2 of the newborns who died, and cerebral hemorrhage at 4 months of age was the cause responsible in the third case. Aneuploidy and congenital malformations are generally more demonstrated in pregestational diabetes compared to GDM. Data from multiple studies have consistently shown a higher risk of major congenital malformations and miscarriage associated with increasing first trimester glycated hemoglobin values.

CONCLUSION:
The DG is a fairly frequent gestational situation that constitutes a maternal, fetal and neonatal risk, both functional and vital, which makes it a real public health problem. A strict and targeted screening, in addition to multidisciplinary care and adequate management of gestational diabetes mellitus may help to avoid short and long term harmful maternal complications.

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