Diagnosis of gestational diabetes mellitus in Nigerian pregnant women - comparison between 75G and 100G oral glucose tolerance tests

***J. K. Olarinoye[1], A. E. Ohwovoriole[2] and G. O. Ajayi[3]**

[1]Department of Medicine, University of Ilorin, Ilorin Kwara State, Nigeria.

[2]Department of Medicine, University of Lagos, Lagos, Nigeria

[3]Department of Obstetrics and Gynaecology, University of Lagos, Lagos Nigeria.

Summary

***Study Objective*: To compare the diagnostic performances of 75g and 100g oral glucose tolerance tests in detecting Gestational Diabetes Mellitus in Nigerian pregnant women.**

***Materials and Methods:* 248 women in 3rd trimester attending antenatal clinic of the Lagos University Teaching Hospital, Lagos, between November 1997 and July 1999 were randomly subjected to standard oral glucose tolerance tests (OGTT). 110 had 100g OGTT while138 had 75g OGTT.**

The plasma glucose response (PGR) was assessed and glucose tolerance status of each patient was determined using WHO (1985) criteria to interpret 75g OGTT and National Diabetes Data Group (NDDG) (1979) criteria for 100g OGTT. The PGR in the two study groups were compared. The prevalence rates of GDM using either of the two criteria were evaluated and compared. Incidences of foetal macrosomia in GDM cases diagnosed by either set of criteria were also compared.

***Results:* The mean age of the study subjects was 30.7(±4.2) years while the BMI was 25.4(±4.9) kg/m^2. The mean parity was 1.33. Traditional risk factors for GDM were found in 47.5% of them.**

The plasma glucose response (PGR) to 100g OGTT was found to be higher than that of 75g OGTT at 1 hour, 2hour and 3 hour sampling times but the difference was only significant at 3rd hour (p values = 0.68, 0.137, 0.007 respectively). The total area under the glucose response curve (AUC) for 75g OGTT was 345.1 (±49.5) AAU while for 100g OGTT, it was 363.4(±61.4) AAU. The difference was not statistically significant (p value >0.05). The prevalence rate of GDM diagnosed by 75g OGTT was 11.6% while that of 100g OGTT was 4.5%. The difference was significant (p value = 0.04). The incidence rate of foetal macrosomia among GDM cases diagnosed by 100g OGTT was 66.7% as against 23.1% among those diagnosed by 75g OGTT. Statistical difference could not be determined because of the small number.

***Conclusion:* Plasma glucose response to OGTT among Nigerian pregnant women has little or no respect for the load of the glucose administered. 100g OGTT- based NDDG criteria was more stringent than 75g OGTT-based WHO criteria in identifying GDM. However it appears to be more specific for detecting the complications associated with the condition though it will require a larger study to validate this claim.**

Key words: ***Gestational diabetes mellitus, Plasma glucose response, Fetal macrosomia***

Résumé

Objectif d'étude:- Comparer des performances diagnostiques de 75g et 100g test de la tolérance du glucose oral dans la détection du diabète pancréatiques gestational chez des femmes enceintes nigerianes.

Matériels et méthodes:- 248 femmes dans le 3ème trimestre qui frequentaient la clinique antenatale du centre hospitalier Universitaire de Lagos entre novembre 1997 et juillet 1999 ont été subi au hazard au test de la tolérance du glucose oral (OGTT). 110 avaient 100GTT tandis que 138 avaient 75g ogtt.

La reponse du plasma glucose (PGR) était évalué et le statut de la tolérance du glucose de chaque patient était étudié à travers le critère d'OMS (1985) afin d'interpreter 75g d'OGTT et Groupes des Données des Diabètes Nationals (NDDG) (1979) critère pour 100 OGTT. Les PGR dans les deux groupes ont été comparés. Le taux de prévalence de GDM avec utilization de l'un soit l'autre de critere étaient évalué et comparé.

L'incidences de la macrosomie du foetus dans les cas de GDM diagnostiques a travers soit l'un soit l'autre série de critére ont été également comparés.

Résultats:- L'âge moyens des sujets d'étude était 30,7 (± 4,2) ans tandis que le BMI était 25,4(± 4,9) Kg/m2. La parité moyenne était 1,33. Des facteurs de risqué traditionnel pour GDM était notés chez 47,5% des cas. La réponse de plasma glucose (PGR) par rapport au 100g OGTT était notée d'étre plus élevée plus que celle de 75g OGTT pendant une heure, 2 heures et 3 heures temps d'echantillonnage mais la différence était seulement importante à la troisieme heure (P valeurs = 0, 68, 0, 137, 0, 007 respectivement). La superficie totale de la courbe de réponse du glucose (AUC) pour 75g OGTT était 345,1 (± 49,5) AAU tandis que pour le 100g OGTT, c'était 363, 4 (+-61,4) AAU, La différence n'était pas statistiquement importante (P valeur > 0,05). Le taux de fréquence de GDM diagnostiqué par 75g OGTT était 11.6% tandis que celui de 100g OGTT était 4,5%. La différence était importante (valeur) = 0,4).

Le taux de l'incidence de la macrosomie du foetus parmis des cas de GDM diagnostiqué par 100g OGTT était 66,7% par rapport à 23,1% parmi les cas diagnostiques par 75Gogtt. On n'arrive pas à decider la difference des données statistiques à cause du peu de nombre.

Conclusion:- Réponse du plasma glucose au OGTT chez des femmes enceintes nigerianes a un peu ou bien aucun respect pour le fardeau du glucose administré. De la base de 100Gogtt. Du critère de la base 100 OGTT - NDDG était plus rigoureux que du critère de la base 75g OGTT OMS dans l'indentification de GDM. Toutefois, il parait qu'il est plus spécifique dans la détection des complications associées avec cette maladie même s'il sera nécessaire d'effectuer une étude approfondie afin d'accepter cette décision.

Introduction

Gestational Diabetes Mellitus (GDM) is defined as

* *Correspondence*

carbohydrate intolerance of various severity first diagnosed in pregnancy, regardless of whether or not the glucose tolerance returns to normal after the delivery[1].

Its prevalence ranges from 1 to 14% of pregnant women depending on the population group as well as the diagnostic criteria used[1]. GDM is associated with increased morbidity and mortality in both the mother and the child. The degree of perinatal morbidity and mortality seen in GDM patients is almost the same as in those with pre-gestational DM[2]. Since it is such a common condition and associated with significant morbidity and mortality, its early detection is very important as treatment greatly affects pregnancy outcome[3].

However, the diagnosis of GDM is very controversial. This is because of different diagnostic criteria that have been used over the years[4]. The oral glucose tolerance test (OGTT) is the standard test for diagnosing GDM but there is no consensus regarding the glucose load to use and the criteria for interpreting the plasma glucose response in pregnancy[5].

There are two standard criteria being used worldwide. The National Diabetes Data Group (NDDG) [6] adopted a modification of the O'Sullivan criteria[7] based on 100G OGTT while the other set of criteria are those by the World Health Organization (WHO) based on 75G OGTT[8]. The controversy is further compounded by the fact that these criteria were defined using Caucasian populations and African women are known to have definite glucose homeostasis different from their Caucasian counterparts[9]. It is therefore expedient to carry out a prospective comparative study in a Nigerian population to determine if there is a significant difference in the diagnostic performances of these two methods of detecting glucose intolerance in pregnancy.

Subjects, materials and methodology

Design: The research was a prospective comparative study.

Setting: All consecutive consenting pregnant women attending the Antenatal Clinic (ANC) of the Lagos University Teaching Hospital, Lagos, Nigeria between the period of November 1997 and July 1999 whose Gestational Ages (GA) were 28 weeks and above were recruited into the study.

Sample size: 293 subjects were recruited into the study, however only 248 completed it. The remaining 45 women were lost to follow- up.

Exclusion criteria: Women with pre-gestational DM and those who were on drugs that could affect glucose tolerance in pregnancy were excluded. Two women who could not tolerate glucose drink because of vomiting and severe uterine contractions had to discontinue their participation in the study.

Methodology: A brief clinical history was taken and physical examination was carried out on each woman to determine the clinical characteristics like age, Body Mass Index (BMI), Blood Pressure (BP) etc.

All study subjects were randomly selected for 75G or 100G Oral Glucose Tolerance Tests (OGTT). No special dietary precaution was taken since they were all on average African diet which is very rich in carbohydrate. They were asked to fast for at least 8 hours before the test. The tests were usually carried out by 8.00 a.m. in the clinic or at the departmental laboratory. They were allowed to rest for 5 - 10 minutes before the commencement of the test. The fasting plasma glucose sample was taken after which a solution of 75G or 100G anhydrous glucose in 250mls of water was given to each subject to ingest over 5 minutes. Venous blood samples were thereafter taken hourly for 3 hours after glucose consumption. During the test, subjects were discouraged from any physical activities or eating but water could be taken. Plasma glucose estimation was determined according to the method described by Trinder[10] using glucose oxidase enzyme solution.

The glucose tolerance status for each subject was determined based on the NDDG (1979) criteria[6] for 100G OGTT and WHO (1985) criteria[8] for 75G OGTT. The NDDG set of criteria are stated below:

Fasting.....105mg/dl
1 hour.....190mg/dl
2 hour.....165mg/dl
3 hour.....145mg/dl

Any individual whose plasma glucose value exceeded any two threshold-values was diagnosed as having GDM. For WHO criteria only the 2 hr glucose value was used. Since patients with Impaired Glucose Tolerance (IGT) in pregnancy are regarded as being diabetic, anybody with 2hr plasma glucose value $\geq$ 140 mg/dl was diagnosed as having GDM.

The area under the glucose tolerance curve was calculated in Arbitrary Area Unit (AAU) using the equation:

AAU = Sum of glucose concentration - 1/2 (Sum of first and last glucose concentration)[11].

The plasma glucose values at different sampling times for the two study groups as well as the area under the glucose tolerance curves were compared using Student's t - test. The women were followed up till delivery and the weights of their babies at birth were measured. Babies weighing $\geq$4.0kg were regarded as having fetal macrosomia.

Results were collated and analyzed using Epi - info 6 computer statistical program.

Results

248 pregnant women in their 3rd trimester were recruited for the study. They were all Nigerians. Their ages ranged from 18-41 years with a mean of 30.7(±4.2) years. The mean parity was 1.33 while their mean pre-pregnancy BMI was 25.4 (±4.9) kg/m^2.

One hundred and thirty-five (47.5%) of the respondents had at least one of the traditional risk factors for GDM. Of these, 25 (8.8%) had positive first-degree family history of DM, 48 (16.9%) had history of fetal macrosomia in their previous pregnancies while 62 (21.8%) had a previous history of pregnancy loss like still birth, neonatal death or spontaneous abortion. Glycosuria was detected in 29 (9.9%) of the subjects while 36 (12.2%) were obese. Only one woman had a previous history of GDM.

Plasma glucose response

Out of the 248 women, 110 were randomly selected to have 100g OGTT while 138 had 75g OGTT. The two groups

Table 1 Comparison of age, parity, BMI and presence of risk factors in women who had 75g versus 100g OGTT

Clinical characteristics	100gOGTT N	100gOGTT Mean (SD)	75gOGTT N	75gOGTT Mean(SD)	Pvalue
Age (years)	105	30.9 (4.5)	126	30.79 (4.1)	0.93
Parity (years)	110	1.2(1.2)	121	1.41(1.5)	0.27
BMI (kg/m2)	71	25.9 (5.6)	70	25.13(4.6)	0.33
Risk Factors(%)	108	46.2(0.5)	126	48.4(0.5)	0.75

Table 2 Plasma glucose response to 75g OGTT

	Plasma glucose response (mg/dl)		
Time (hr)	N	Range	Mean (SD)
0	138	47 - 231	93.9 (23.4)
1	138	87 - 300	133.0 (30.2)
2	138	53 - 313	118.4 (34.2)
3	25	63 - 260	94.0 (38.3)

Table 3 Plasma glucose response to 100g OGTT

	Plasma glucose response (mg/dl)		
Sampling time (hr)	N	Range	Mean (SD)
0	110	56 - 175	94.3 (16.0)
1	110	88 - 225	135.0 (25.8)
2	110	75 - 219	124.5 (23.1)
3	110	63 - 316	113.4 (29.1)

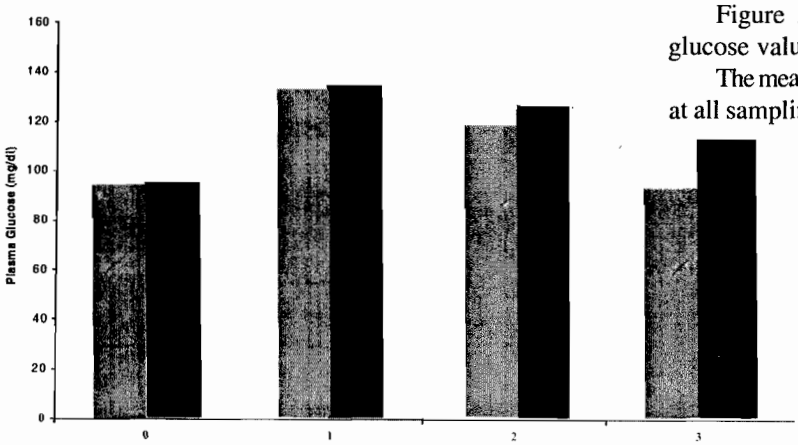

Fig. 1 ***Plasma glucose response to 75g and 100g OGTT***

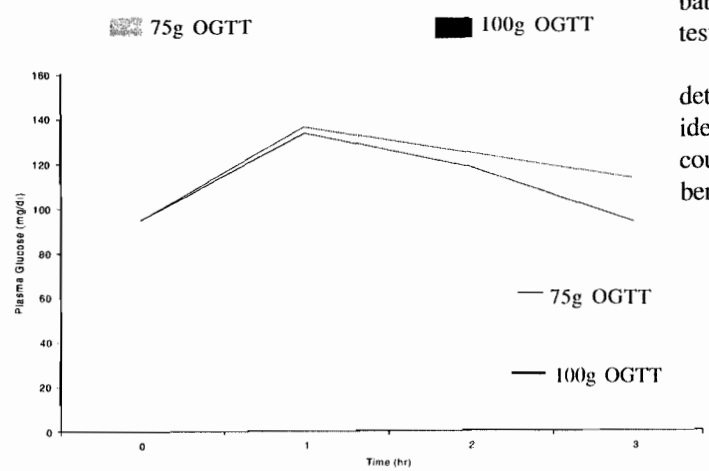

Fig. 2 ***Glucose response curve of 75g and 100g OGTT***

were matched for age, parity, BMI and presence of risk factors for GDM as shown in Table 1. There were no significant differences between the two groups.

Table 2 shows the descriptive statistics of the plasma glucose response to 75g OGTT. It can be seen that the mean plasma glucose reached the peak value at 1hour after glucose intake and had dropped to the fasting level by the 3rd hour sampling time.

According to the WHO criteria[8] for the interpretation of OGTT in pregnancy, 16 (11.6%) of the women were diagnosed as having GDM. Four (2.9%) had 2hr plasma glucose value ≥ 200 mg/dl (11.1 mmol/l) while the remaining 12 (8.7%) had values in the Impaired Glucose Tolerance (IGT) range. The remaining 122 (88.4%) were normal.

Table 3 shows the plasma glucose response values to 100g OGTT in 110 women. The PGR peaked at 1hr sampling time, then the level dropped gradually but did not return to the fasting level three hours after the glucose load. According to the NDDG (modified O'Sullivan) criteria[6], 5 (4.5%) women had GDM while the remaining 105 (95.5%) were normal.

The prevalence rate of GDM in Nigerian women according to 75G OGTT- based criteria was 11.6% while according to 100G OGTT- based NDDG criteria it was 4.6%. The difference was statistically significant (p value = 0.04). Amongst the 248 women screened by either set of criteria, 21 tested positive bringing the overall prevalence of GDM among Nigerians to 8.5%.

Figure 1 demonstrates the comparison of the plasma glucose values between the two groups.

The mean PGR to 100G OGTT was greater than 75G OGTT at all sampling times but the difference was only significant at 3hr (p= 0.007).

Figure 2 shows the glucose tolerance curves to both 75g and 100g loads. The mean area under the glucose response curves in the 75g OGTT group (AAU_{75}) was 345.1 (±49.5)AAU, while the one for 100g OGTT group (AAU_{100}) was 363.4 (±61.4)AAU. There was no significant difference between the two values (p > 0.05).

Of the women diagnosed positive for GDM by either criteria, 31.3% had fetal macrosomia i.e. babies weighing ≥ 4.0kg while in the remaining women who tested negative, 11.3% had fetal macrosomia (p=0.01).

Incidence of fetal macrosomia among the GDM cases detected by 75g OGTT was 23.1% while among the DM cases identified by 100g OGTT it was 66.7%. However the figures could not be compared statistically because of the small number.

Discussion

The diagnosis of GDM is very controversial. This study attempted to resolve some of these controversies by comparing two common standard methods of diagnosing GDM among the Nigerian women.

Comparison of the plasma glucose response in the two study groups showed that the blood glucose values at 1hr, 2hr and 3hr were higher for 100g glucose load although the difference was only significant in

the third hour sampling (Fig 1). This is quite contrary to an earlier study in Nigeria where it was observed that glycaemic response was higher for 75g glucose load than for 100g glucose load, the difference being significant only in the fasting and 2hr samplings[12].

The mean areas under the glucose response curve in the two OGTT groups were also found not to be significantly different from each other. This shows that among Nigerian pregnant women studied in their third trimester, interpretation of OGTT may have little or no regard for the amount of glucose load administered. However, though there is no significant difference in the maximum glycaemic response as well as total area under the glucose tolerance curves in the two OGTT groups, the descending slope of the curve is higher in the 75g group (Fig 2). By the third hour, the plasma glucose in the 75g OGTT had returned to the fasting level whereas for 100g OGTT it did not return to the fasting level. 75g OGTT in Nigerian pregnant women therefore gives a glucose response curve that is closer to normal than 100g OGTT.

The overall GDM prevalence of 8.5% was far higher than an earlier study in Nigeria which found the prevalence of GDM to be 1.5% using NDDG criteria[13]. In this study, the prevalence rate using NDDG criteria was 4.5% while the prevalence using WHO criteria was 11.6%. This agrees with the assertion in earlier studies that the incidence of GDM in a particular population group can be influenced by the diagnostic criteria used[4]. A similar study comparing these two diagnostic methods found the prevalence of GDM to be 1.4% using NDDG criteria and 15.7% by the WHO criteria[14].

The higher prevalence rate in the WHO group was because of the lower cut - off values used for diagnosis. The NDDG appears to be more stringent and may tend to underdiagnose GDM in Nigerian women. This will result in some patients being left out who would have benefited from treatment. On the other hand, the WHO criteria may lead to over diagnosis thereby leading to treatment of some women who do not need treatment.

It would be desirable to compare the diagnostic performances of these two tests using a gold standard but no such gold standard exists in GDM diagnosis. The value of any diagnostic test is its ability to detect the clinical implications and complications attached to that condition. Of all the feto-maternal implications of GDM, fetal macrosomia is the most consistent and most easily measurable and that is why it was used as the clinical endpoint in this study.

Although several variables like maternal BMI, maternal age and social status can affect the fetal birth weight, this study has demonstrated that the incidence of fetal macrosomia was higher among women diagnosed positive for GDM than those who tested negative. However, the incidence rate of 66.7% in the NDDG group was far higher than 23.1% in the WHO group. The 100g OGTT-based NDDG criteria is therefore more specific at identifying pregnant women at risk of having fetal macrosomia than 75g-based WHO criteria. This claim will however require a larger study to validate.

Conclusion

The prevalence of Gestational Diabetes Mellitus among the Nigerian pregnant women is rising hence should be routinely screened for in all the antenatal clinics. Increasing the glucose load used in diagnostic OGTT does not significantly affect the glycaemic response but the criteria used in interpreting it matters. 100g OGTT- based NDDG criteria seems to be less sensitive at picking cases of Gestational Diabetes Mellitus but more specific at identifying fetal macrosomia than 75g OGTT- based WHO criteria.

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