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PATTERN OF UTILISATION OF ORAL GLUCOSE TOLERANCE TEST: THE EXPERIENCE OF AMINU KANO TEACHING HOSPITAL, KANO

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ABSTRACT

Oral glucose tolerance test (OGTT) is the gold standard test for the diagnosis of type 2 diabetes mellitus (DM). It is considered as the oldest dynamic function test in clinical practice and has several advantages over other plasma-based tests for diagnosis of type 2 DM, notably random plasma glucose (RPG) and fasting plasma glucose (FPG). For instance, it is the only means through which diagnosis of impaired glucose tolerance can be made, and has a higher diagnostic yield compared to FPG. There is paucity of data on the utilization of OGTT particularly in northern Nigeria. This study therefore aimed to determine the utilization of OGTT in a tertiary Hospital in Kano, Northwestern Nigeria. This was a retrospective study carried out in Aminu Kano Teaching Hospital between January, 2013 and December, 2014. Following ethical approval, Hospital records of all clients who had OGTT in Chemical Pathology department of the Hospital were retrieved. The OGTTs were done using the 75g, 120 Minutes as recommended by WHO. Plasma Glucose were analyzed using quantitative glucose oxidase method described by Trinder. Data obtained were entered into Microsoft Excel and analyzed using statistical package for social sciences (SPSS) version 20. About 335 OGTTs were performed during the study period but 312 were selected. Majority of the clients were females, 290 (92.9%), aged between 20-39 years (74.0%). About 2/3rd of the clients 224 (78.5%) were pregnant women referred from antenatal clinic due to previous history of Gestational Diabetes Mellitus (GDM), previous macrosomic baby, and unexplained intra uterine foetal death. Non-obstetric indications for OGTT encountered were obesity, impaired fasting glycaemia and suspected acromegaly. Majority of clients who had OGTT were pregnant women who were referred for obstetric indications. Previous history of GDM was the commonest indication for OGTT. There was under-utilization of OGTT for non-obstetrics medical indications.

Keywords: OGTT, Diabetes mellitus, Gestational Diabetes, Nigeria

INTRODUCTION

Diabetes mellitus (DM) is an important modifiable risk factor of cardiovascular disease. It is one of the four priority non-communicable diseases (NCD)(WHO, 2016) As at 2010, the global prevalence of (DM) was estimated to be about 4.7% and is projected to increase to about 5.5% by the year 2030 (Shaw, 2010). According to the Global Burden of Disease Study, there was a 30.6% increase in the global burden of DM between 2005 to 2015 (333 million to 435 million) (UN, 2012). The global burden of this important non-communicable disease may probably rise to about 536 million by the year 2030(Shaw, 2010). In 2012, DM caused about 1.5 million deaths globally, while high blood glucose caused additional 2.2 million deaths by predisposing individuals to other non-communicable diseases, like cardiovascular diseases (WHO, 2016)

The United States of America, the World's most advanced economy shoulders a heavy burden of DM. The American Diabetes Association, (ADA) estimated

that about 20 million individuals are living with the disease and that more than a million and a half new cases are diagnosed annually (Lancet, 2016). Several studies have acknowledged that DM is the commonest cause of blindness and non-traumatic amputations in the US. Due to increasing urbanisation, sedentary life style and perhaps other factors yet to be fully ascertained, the prevalence of type 2 DM is rising at an alarming rate in most developing countries such as Brazil, China and India (Shaw, 2010)

On the African continent, Nigeria, which has the highest population, is not spared of the DM pandemic. The prevalence varies widely in different parts of the country with the highest prevalence in the more urbanized part of the Southwest and lowest in the rural communities of the North-central Nigeria (Olatunbosun, 1998). Though the prevalence of DM was less than 1% about three decades ago, studies conducted in the late 1990s estimated the prevalence of type 1 and 2 DM to be about 3.9%.

It has been estimated that about 8-10% of Nigerians have DM (Ogberra, 2014). DM is not a single disease; it is a spectrum of metabolic disorders characterized by chronic persistent hyperglycaemia secondary to a relative or absolute lack of insulin. Blood test to determine level of glucose in the plasma is one of the key components in the diagnosis of DM. The commonest type of diabetes is the type 2 diabetes which constitute more than 90% of all cases of the disease(Ogberra, 2014). It is mainly due to relative deficiency of insulin and is most commonly encountered in the obese subjects above the age of 30 years. Most patients with type 2 DM do not present with the classical osmotic features of polydipsia, polyuria and polyphagia(WHO, 2016). Patients may also present with other non-specific features such as unexplained weight loss and increased susceptibility to infections. It has been estimated that up to 25% of newly diagnosed type 2 DM patients may actually present with complications indicating that they might have been with the disease for at least four years prior to presentation.(Mary, 2009)

Another important class of diabetes is the gestational diabetes mellitus (GDM). It is defined as a disorder affecting carbohydrate metabolism of variable severity of onset or first recognition during the index pregnancy (WHO, 2016). It has been estimated that about 10-25% of all pregnant women have either previously undiagnosed diabetes or gestational diabetes.(Jiwani, 2012). Majority (75-90%) of these women have gestational diabetes. In Nigeria, it was documented that GDM complicates between 3-5% of all pregnancies (Mwari, 2014). Early diagnosis and commencement of appropriate treatment of all patients with GDM has been shown to be associated with reduced foetal as well as maternal morbidity and mortality (Mwari, 2004)

The foregoing greatly underscores the importance of having an accurate diagnostic tool that can be used for screening asymptomatic patients as well as for monitoring the adequacy or otherwise of various treatment modalities.

Biochemical investigations used to screen or actually diagnose DM may be broadly classified into two main categories. There are tests that are exclusively based on plasma glucose and those solely based on glycated proteins such as fructosamine and glycated haemoglobin.

Plasma glucose-based tests are the random or casual plasma glucose (RPG), fasting plasma glucose (FPG) and glucose challenge tests such as the oral glucose tolerance tests (OGTT). Both RPG and FPG are simple, cheap and may be offered to the client during routine clinic visit as they do not require elaborate preparation on the side of the client, the practitioner and the laboratory. However, OGTT requires elaborate preparations on the side of the client and the clinical laboratory.

OGTT is considered to be the oldest dynamic function test (DFT) in routine clinical practice. The procedure has been in routine clinical use since the 1920s(Mary, 2009). It is actually considered to be the gold standard for the diagnosis of type 2 DM. The

procedure also has additional advantages over the use of FPG. It is the only means through which the diagnosis of impaired glucose tolerance (IGT), an independent risk factor for cardiovascular disease, can be made. OGTT also has a slightly higher diagnostic yield compared to FPG. The procedure is recommended by both the World Health Organisation (WHO) and National Diabetes Data Group (NDDG), albeit by means of slight modifications in both the procedure and diagnostic cut-off points(Barr, 2010). The WHO recommends using 75g, 120 minutes OGTT for both pregnant and non-pregnant adult subjects. Similarly, NDDG, maintains the 75g for non-pregnant adults but recommended the use of 2 step procedure incorporating 'O' Sullivan's screening and subsequent 100 g, 180 minutes OGTT for screening and definitive diagnosis of GDM(Mary, 2009).

Apart from clients with obvious biochemical diagnosis of DM, other disorders of carbohydrate metabolism that may be diagnosed using OGTT include impaired fasting glycaemia (IFG), impaired glucose tolerance (IGT), lag storage curve and flat curve; although the exact terminology may differ from one facility to another. These individuals have increased tendency of developing overt diabetes. IGT is also an independent cardiovascular risk factor.

Several international and local bodies including the WHO, American Diabetes Association (ADA) and International Diabetes Federation(IDF) continue to advocate the use of glycated haemoglobin (HbA1c) in both screening asymptomatic but at risk subjects, diagnosis of symptomatic patients as well as monitoring the effectiveness of various life style modifications and therapeutic interventions in patients with DM (Barr, 2002). HbA1c is relatively cheap, can be offered to patients during routine clinic visits, it assesses the glycaemic control over the previous 6-8 weeks(Barr, 2002). However, several studies have demonstrated some important shortcomings in the use of HbA1c especially in screening of symptomatic patients in whom derangement of glucose metabolism is strongly suspected. Due to the relatively non-linear contributions of FPG and IGT to the overall glycation of Haemoglobin, it was amply demonstrated that FPG is responsible for the elevated HbA1c above the diagnostic cut off values of $\geq 6.5\%$. Values slightly above the upper reference limit and within the non-diagnostic ranges have been found to be contributed mainly by the high post prandial plasma glucose, which can be aptly demonstrated by OGTT(Barr, 2002)

There is paucity of published literature on this important and most commonly used dynamic function test in this region. Famuyiwa and colleagues conducted three (3) OGTTs during the first, second and the third trimester in about twenty (20) apparently healthy pregnant women and inferred that there are slightly lower plasma glucose levels for each upper limit of normal compared to what was found in their Caucasian counterparts (Famuyiwa, 1988). Similarly, Omololu and Olufemi conducted the two step, and 3- hour OGTT in about 200 healthy pregnant subjects in Lagos, South West Nigeria (Omololu, 2014).

They found the prevalence of GDM to be about 5.0%. In an apparent attempt to document the utilization of OGTT in some tertiary Hospitals in Nigeria, Oparinde and co-workers evaluated utilization of OGTT among patients of their metabolic clinic in Ilorin, North Central Nigeria (Oparinde, 2006). The commonest indication for conducting OGTT in their study was impaired glucose tolerance, followed by suspected GDM.

This work aimed to report the pattern of utilization of OGTT services at the Department of Chemical Pathology of Aminu Kano Teaching Hospital (AKTH), Kano, North-West Nigeria. The various indications for the procedure, the referring clinics and the patients' socio-demographic variables were retrieved. The various diagnoses made at the end of the procedure were also reviewed. The investigators hope that information obtained from the study may likely lead to improved utilisation of this important procedure and eventually early diagnosis and commencement of treatment which will result in reduction of both mortality and morbidity.

MATERIALS AND METHODS

This is a retrospective study that was carried out between January, 2013 and December, 2014. Before the commencement of this study, ethical approval was obtained from the Ethical Committee of Aminu Kano Teaching Hospital, Kano. The medical records of all clients that had OGTT at the Department of Chemical Pathology of Aminu Kano Teaching Hospital from 1st January, 2013 to 31stDecember, 2014, were retrieved and analysed. All patients with complete records of gender, referring clinic, indication and gestational age for obstetric patients were included. Those with incomplete records were excluded from the study. Patients whose samples were taken elsewhere and submitted to the laboratory for analysis were also excluded. All plasma glucose assays were performed using Quantitative Glucose Oxidase method described by Trinder (Randox, 2013). The Department of Chemical Pathology at AKTH uses the WHO recommended one step, 75g, 3 point or 2 Hour OGTT on all non-pregnant adults and the NDDG recommended, 100g 4 -point OGTT on all patients referred for suspected GDM. WHO and the NDDG criteria were used to interpret all documented results accordingly.

All data were entered into Microsoft Excel worksheet, it was checked for errors by triangulation and subsequently analysed using Statistical Package for the Social Sciences version 20.0.

AKTH is a Five Hundred bedded tertiary health centre located in Tarauni Local Government area of Kano state. The Hospital provides both in and out patients services for thousands of patients from Kano, Jigawa, Katsina and places as far as Zamfara state and some areas of Niger Republic. The Hospital has a well-developed multispecialty laboratory services in Chemical Pathology, Haematology, Microbiology and Morbid Anatomy. The Department of Chemical Pathology of the Hospital provides emergency, routine and specialized investigations for both outpatients and inpatients of the Hospital and those from other health facilities on referral basis (AKTH, 2014)

RESULTS

A total of 335 OGTT procedures were performed during the study period of which 312 were included in the study. The clients were made up of 290 (92.9%) females and 22(7.1%) males, aged between 7-65 years. Majority of these patients (74.0%) were aged between 20-39 years (Table 1). Most of our clients were referred from the antenatal clinic with the following indications: previous history of GDM, previous macrosomic baby, and unexplained intra uterine foetal death, IUFD (Figure 1). Most of the non-Obstetric indications include obesity of which one is a seven-year-old male child who was referred to our unit for biochemical evaluation of childhood obesity and was eventually found to have Cushing's syndrome. Five patients were referred from Family Medicine Department for IFG and 2 for suspected acromegaly who eventually had modified OGTT with Growth Hormone (GH) assay. The outcome of those patients showed that majority of our patients 210 (67.3%) had findings within reference limits, 29(9.3%) had GDM, 33(10.6%) had IGT, 8(2.6%) type 2 DM while about 10 patients had IFG and about 7.1% had values within non-diagnostic ranges. As illustrated in figure 2.

About 245 pregnant women had the NDDG recommended 100g, 3-Hour OGTT. These patients were referred from the antenatal clinic of AKTH for various indications. Our findings revealed the commonest indication for OGTT in these women to be previous history of GDM and followed closely by family history of DM. Other less common indications were those with unexplained furunculosis, florid vaginal warts or vulvovaginal candidiasis (Table 2). We did not encounter any patient sent for re-evaluation at 6 weeks postpartum.

TABLE 1: Age Distribution of Subjects that Had OGTT in AKTH

Age(yrs)	Number	%
<10.0	1	0.3
10.0-19.0	26	8.3
20.0-29.0	125	40.1
30.0-39.0	106	33.9
40.0-49.0	45	14.4
>50.0	9	3
Total	312	100

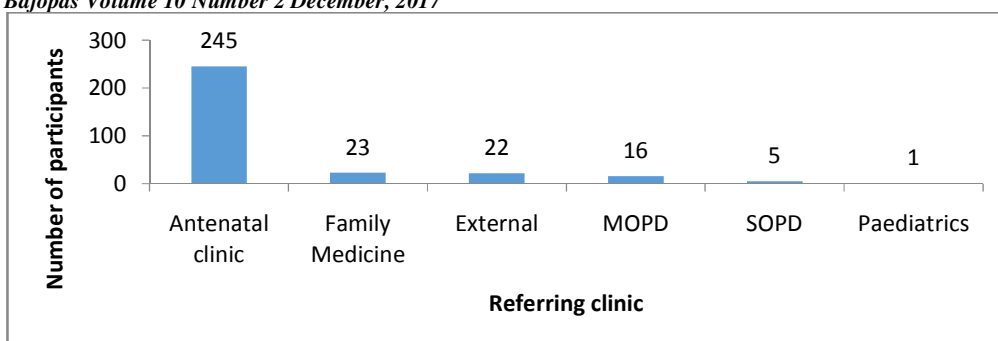


Figure I: A vertical Bar Chart Depicting the Number of OGTT referred from various clinics in AKTH. SOPD: Surgical outpatient Department, MOPD: Medical outpatient Department, External: External medical facility

Table 2: Indications for screening study subjects for GDM

Indication	Number	%
Overweight	38	15.5
Previous GDM	86	35.1
Previous IUF	14	5.7
Previous Macrosomia	27	11.1
Family History	71	28.9
Others	9	3.7
Total	245	100

Key: GDM: Gestational Diabetes Mellitus, IUF: Intrauterine Foetal Death

DISCUSSION

The use of OGTT for the diagnosis of disorders of carbohydrate metabolism is well documented as the procedure has been in continuous use for over 80 years (Jiwani, 2012). We presented the pattern of utilization of this important diagnostic procedure in our centre. The commonest indications of OGTT in AKTH was found to be mainly Obstetric, with more than 92% of our patients referred from the Antenatal clinic as suspected cases of GDM. This is at variance with the findings from Ilorin, North central Nigeria where the commonest indication was IFG. This may be due to low level of awareness among obstetricians practicing in that clime. It may however be due to possible over utilization of the procedure by the Obstetricians in Kano. Our study also observed that there were very few requests made from Internal Medicine Department of our centre. This may be because AKTH is a referral centre that attends mainly to patients who have had their diagnosis of DM elsewhere and are usually referred for management of chronic or acute complications of DM. This is further buttressed by the apparently higher number of requests received from the Family medicine department. This study also observed the poor utilisation of OGTT for the evaluation of patients with insulin resistance, reactive hypoglycaemia and acromegaly. This may be due to low index of suspicion, lack of awareness of the usefulness of OGTT in making these diagnoses or the relatively high cost of growth hormone (GH) assay, which must be included as part of the diagnostic work up for those with suspected acromegaly. Our study found the prevalence of GDM to be much higher than what was found at Lagos University Teaching hospital (LUTH). (Nwanri, 2014). This may be due to the fact that the LUTH study examined the use of OGTT in healthy pregnant women in contrast to our work where the

procedure was conducted only on patients referred from the antenatal clinic with various Obstetric risk factors. We have equally noted the lack of utilisation of OGTT services for reassessing patients with GDM at 6 weeks postpartum. This may be due to lack of adequate counselling by the care givers.

CONCLUSION

Oral glucose tolerance test remains an important biochemical investigation for the diagnosis of impaired glucose tolerance, diabetes mellitus and gestational diabetes mellitus. Obstetricians were the major users of the procedures in our centre with previous gestational diabetes and family history of diabetes being the commonest indications.

Recommendations

Based on our findings, the following recommendations are hereby suggested:

- 1 There is need for the stakeholders in the generation and utilization of Chemical Pathology investigative procedures especially OGTT to meet and develop protocol for the evaluation of suspected cases of carbohydrate and other metabolic disorders.
2. There is also the need for adequate public enlightenment on the need for adequate screening of pregnant women with risk factors for GDM. This may be done using both electronic and print media. Public Health Physicians, Obstetricians and Chemical Pathologists should play important roles.

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Conflict of Interest: There are no conflict of Interest

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