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Full length Research paper

Erectile dysfunction as a marker of impaired fasting blood glucose (IFG)

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Diabetes mellitus (DM) type II is one of the systemic disorders most frequently associated with erectile dysfunction (ED). It has been estimated that as many as 75% of men with DM will be confronted with the problem in about 5 – 10 years earlier than control. Equally, the incidence of impaired glucose tolerance (IGT) is high and it has been shown that greater than 20% of the population has IGT, while only 10% of the population develops frank DM in their life time. The aim of this study was to determine the prevalence of ED in both impaired fasting blood glucose (IFG) and early diabetes mellitus (DM) in a Nigerian tertiary diabetes treatment centre. This was a descriptive cross-sectional study. A total of 420 subjects were recruited for the study by systematic random sampling method. Erectile function domain (ED) was assessed by a respondent self–rated 'one through five questions' of the international index of erectile function (IIEF) . Analysis was done using the glucose oxidase method. IFG was significantly associated with ED ($p < 0.05$) as many (56.5%) of the subjects with IFG also had ED. Also, diabetes mellitus was significantly associated with ($p < 0.05$) ED. IFG like IGT are not clinical entities, but rather risk categories for future diabetes with much earlier medical presentation such as ED. This finding has important clinical implications for primary care physicians asking questions about sexual health with a dysglycemic screening of ED group for a modification to prevent the disease progression.

Key words: Erectile dysfunction, impaired fasting glucose, diabetes mellitus.

INTRODUCTION

According to the National Institutes of Health Consensus Development Panel on Impotence (1993), erectile dysfunction (ED) is defined as the persistent inability to attain or maintain an erection sufficient for satisfactory sexual performance. ED a very common disorder, IS reported to affect as many as 152 million men worldwide (National Institutes of Health Consensus Development Panel on Impotence, 1993; Feldman et al., 1994; Aytac et al., 1999). Recent global projection suggest that as many as 322 million men will experience ED by 2025 (Aytac et al., 1999). The largest increases in prevalence rate are expected to be in developing countries that have expanding populations and increased life expectances (Burnett, 1998). Apart from the psychosocial effect of ED on the quality of life, perhaps even more worrisome is the link between ED and a number of serious and in some cases, potentially life-threatening diseases. ED is commonly associated with some medical conditions that are prevalent in older age group. Diabetes mellitus (DM) type II is one of the systemic disorders most frequently associated with ED (Berrada et al., 2003; Shaeer et al., 2003; Osegbe et al., 2003; Hecht et al., 2001; Fedele et al., 2001). It has been estimated that as many as 75% of men with DM will be confronted with the problem (Burnett, 1997) in about 5 – 10 years earlier than control (Romeo et al., 2000). The prevalence of ED is known to increase progressively with age and is commonest in the older age group (Feldiabetesan et al., 1994; Kaisier, 1999). Duration of diabetes has been shown to significantly correlate with the erectile function score and patient with a history of DM longer than 10 years were three times more likely to develop ED as those with a history of less than 5 years (El- Sakka and Tayeb, 2003). The prevalence of ED among those whose duration of

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Table 1. Age group of subjects.

Age group (years)	No = 420	Percentage (%)
30–40	133	31.7
41–50	139	33.1
51–60	108	25.7
61–70	40	9.5
Total	420	100.0

diabetes is less than a year was 50%, while the rate increased to 96.8% among those with the disease lasting longer than 5 years (Burnett, 1997).

There is also increasing evidence that ED correlates significantly with the level of glycaemic control (El- Sakka and Tayeb, 2003; Thethi et al., 2005; Roth et al., 2003; Moulik and Hardy, 2003) . A retrospective analysis of a cohort of men with type II diabetes demonstrated that haemoglobin A_{1c} (HbA_{1c}) was an independent predictor of erectile function score (Romeo et al., 2000). An inverse relationship between the severities of ED assessed by the international index of erectile function (IIEF) score and HbA_{1c} has also been demonstrated (Fonseca et al., 2004). American diabetes association (ADA) has not previously recommended the use of HbA_{1C} for diagnosis of DM but rather as a control monitoring tool now recommend a threshold of >6.5% as diagnosis of DM and value between 5.7 - 6.4% as high risk future DM (Rosen et al., 1997).

Erectile dysfunction has been found to be better predictive of a dynamic and reversible state called impaired glucose tolerance (IGT) (Larsson et al., 1998). American diabetes association (ADA) criteria established that fasting blood glucose level of 5.6 - 6.9 mmol/L known as the impaired fasting glucose (IFG) correspond with IGT and HbA_1c (Rosen et al., 1997). HbA_1c is preferred to both IFG and IGT by the ADA after its standardization because of its convenience but its use is limited by cost. IFG and IGT are regarded as equivalent though some studies believe that IGT is more sensitive in detecting early glucose dysregulation (Larsson et al., 1998). However, the prevalence of IGT is higher in men with DM than in the general population (Robinson et al., 2003) and could be a marker for DM. The incidence of impaired glucose tolerance is high and it has been shown that more than 20% of the population has IGT, while only 10% of the population develops frank DM in their life time (Sairam et al., 2001). IGT serve as a marker for the state of insulin resistance (IR) and predicts both large and small vessel vascular complications independent of patient's progression to DM (Sairam et al., 2001). Neuropathy found in IFG and early DM is phenotypically similar. Neuropathy in IFG is found in 30 - 50% of patients with IGT and similarly in about 40% of early diabetics suggesting an early involvement of neuropathy (Robinson et al., 2003).

This study was designed to determine the prevalence of ED in IFG as a risk category for future diabetes mellitus (DM) rather than a clinical entity in a Nigerian tertiary diabetes treatment centre.

MATERIALS AND METHODS

This was a descriptive cross-sectional study carried out between January and April 2007 at the Department of Chemical Pathology and Family Medicine of the University of Ilorin Teaching Hospital (UITH) which serves as a 'National Health Insurance Scheme' for primary, secondary and tertiary healthcare centers.

The study population consisted of patients coming for treatment in the adult male outpatient clinics who satisfied the criteria for inclusion. These included men, who were in the age range of 34 – 70 years, that came for medical care at the adult male clinic and who gave their consent to participate in the study. The main exclusion were men who had not been sexually active in the 6 months preceding the study as a result of unavailability of sexual partners.

A total of 420 subjects were recruited for the study by systematic random sampling method after a clearance for the study was obtained from the ethical and research committee of the hospital. A semi structured questionnaire was used to collect data. ED was assessed by a respondent's self–rated one through five questions of the IIEF, which is the multidimensional questionnaire for assessing erectile dysfunction. The erectile function score represents the sum of questions, with a score of less than 21 indicating erectile dysfunction (Rosen et al., 1997).

Venous blood was collected from each respondent with a 5 ml vacutainer specimen bottle containing fluoride oxalate as anticoagulant and serially numbered. The samples were separated immediately and the plasma was stored at -8°C (freezer temperature) and analysed in batches. Analysis was done using the glucose oxidase method (Trinder, 1969). Normal plasma glucose (reference range of analysis centre): 2.5 to 5.0 mmol/L, Impaired fasting glucose (IFG): 5.1 to 7.7 mmol/L) and diagnostic diabetes mellitus value of 7.8 mmol/L. The subjects were divided into three groups of normoglycemic, impaired fasting glucose and diagnosed diabetic based on the result of the fasting blood glucose.

RESULTS

A total of 420 men aged between 34 and 70 years were recruited for the study. The mean age was 51.5 ± 17.1 years. (Table1) . 282 (67.1%) of the subjects were normoglycemic, while 138 (32.9%) were known to have dysglycemia or frank DM. Out of the 138 subjects, 85 (20.2%) were found to have impaired fasting glucose, while 53 (12.6%) were diagnosed to have DM using the ADA criteria (Table 2). The prevalence of ED was 56.5 and 81.1% in IFG and diabetes respectively. Only 2 (0.7%) had ED form the normoglycemic group (p-value 0.001). IFG was significantly associated with ED (p-value 0.05). Also, diabetes mellitus was significantly associated with (p-value 0.001) ED on Table 3.

DISCUSSION AND CONCLUSION

The high prevalence of ED in diabetics in this study is not

Table 2. Frequency of blood status among subjects.

Blood glucose status	Number (No)	Percentage (%)
Normoglycemia	282	67.1
Impaired fasting glucose (IFG)	85	20.2
Diabetes mellitus	53	12.6
Total	420	100.0

Table 3. Erectile dysfunction in normoglycemia and dysglycemia.

Variable	No ED	ED	p
Fasting plasma glucose	n_1 (%)	n_2 (%)	
Normoglycemia	280 (99.3)	2 (0.7)	0.001
Impaired fasting glucose	37 (43.5)	48 (56.5)	0.046
Diabetics	10 (18.9)	43 (81.1)	0.001
Total	327 (77.9)	93 (22.1)	

n_1 = Number of respondents with normal, impaired fasting glucose/diabetes without ED. n_2 = Number of respondents with normal, impaired fasting glucose/diabetes with ED. % = Percentage in row bracket. p = p value.

a usual finding because this is very similar to a figure of 57.4% reported in a recent study carried out in four Nigerian cities – Kano, Ibadan, Lagos and Enugu (Shaeer et al., 2003). Studies in other countries have also reported similar values of 53.6% in Morocco (Berrada et al., 2003), 51.3% in Singapore (Tan et al., 2003) and 52% in the United States (Feldman et al., 1994). DM is one of the systemic disorders most frequently associated with ED (Osegbe et al., 2003; Hecht et al., 2001; Romeo et al., 2000; Feldiabetesan et al., 1994) and it has been estimated that as many as 75% of men with DM will be confronted with the problem (Romeo et al., 2000). The commonest cause of ED currently among adult Nigerians is DM, unfortunately most of them are not ready to discuss it until when asked (Sam et al., 2009). Previous studies had shown that diabetics develop ED about 5 – 10 years earlier when compared to age-matched control subjects (Romeo et al., 2000). The prevalence of ED increased progressively with age and after about 60 years of age, it has been reported that 55 – 95% of men with diabetes were affected by ED (Feldiabetesan et al., 1994; Kaisier, 1999).

The prevalence of ED higher is in men with IFG than in the general population (El-Sakka and Tayeb, 2003; Thethi et al., 2005) because neuropathy is a complication occurring over time in more than 50% of the IGT patients and in 10-18% of diabetics (Robinson et al., 2003). Erectile dysfunction has also been found to be predictive of IGT (Shaeer et al., 2003) because of the direct metabolic injury role observed in IGT patients (Robinson et al., 2003). Direct metabolic tissue injury caused by hyperglycaemia is more important to microvascular complications especially neuropathy. It can be concluded that ED is a marker symptom for IFG, and as such, IFG should be actively sought in men presented with ED (Moulik and Hardy, 2003; Larsson et al., 1998). A similar observation was found that ED is not only independently associated with undiagnosed DM (Grover et al., 2006), but also with impaired fasting glucose in a clinical survey of 3921 Canadian men seen by primary care physicians. (Grover et al., 2006; Spollet, 1999).

The overall pathogenesis picture of ED in dysglycemia may be linked to a combination accelerated atherosclerosis, alteration in the corporal erectile tissue and neuropathy (Veves et al., 1998). These changes may include smooth muscle degeneration, endothelial cell dysfunction and abnormal collagen deposition. Advanced glycosylated end products have been shown to be elevated in the penile tissue of diabetic patients and to reduce nitrogen (II) oxide (NO) at the site (Veves et al., 1998). *In vivo* studies of isolated corpus cavernosum tissue in diabetic men have shown functional impairment in neurogenic and endothelium-dependent relaxation of corpus cavernosum smooth muscle (Veves et al., 1998).

Erectile dysfunction in diabetes is thus multifactorial with both vasculopathy and neuropathy playing significant roles (Hecht et al., 2001; Thethi et al., 2005) . The ability to increase blood flow depends on an intact neurogenic vascular response (Hecht et al., 2001). Since acetylcholine is important in the production of NO, a decrease in the amount of acetylcholine leads to decreased production of NO. Diabetic autonomic neuropathy leads to impaired endothelium-dependent and independent vasodilatation even in the absence of clinical macro-vascular disease (Veves et al., 1998). The presence of peripheral neuropathy also increases the risk of ED, probably because of undiagnosed autonomic neuropathy. Almost 100% of patients with diabetic

autonomic neuropathy will have ED (Hecht et al., 2001). The interaction between endothelial dysfunction and autonomic neuropathy results in inability to increase blood flow under conditions of stress or increased demands, such as during an erection (Hecht et al., 2001). This interaction may also explain the relationship between ED and silent myocardial ischemia in diabetic patients as there is a strong and independent association between ED and silent coronary artery disease (CAD) in apparently uncomplicated type II diabetic patients (Veves et al., 1998). It was concluded that ED may become a potential marker to identify those diabetic patients that would benefit from screening for silent CAD and suggest the need to perform an exercise electrocardiogram (ECG) for all diabetics before starting treatment for ED; especially in patients with additional cardiovascular risk factors (Jensen et al., 1999).

IFG is a clinical presumptive diagnosis rather than a clinical entity. Fasting plasma glucose must be monitored over time to confirm the diagnosis of DM. A significant number of respondents had impaired fasting glucose (IFG) and this category of impaired glucose homeostasis that has been recommended by ADA as corresponding to the impaired glucose tolerance (IGT) (Larsson et al., 1998). People with IFG like those with IGT have increased risks of progressing to diabetes and macrovascular disease, although prospective data are sparse and early data suggest a lower risk of progression than IGT (Robinson et al., 2003).

ADA has defined FPG levels of 5.6 - 6.9 mmol/l or IGT values of 7.8 - 11.0 mmol/l as an intermediate group referred to as pre-diabetics, indicating the relatively high risk for the future development of diabetes. (SMCD, 2010). The diagnostic cut point of ADA from analyses is 7.0 mmol/l for FPG and confirmed the long-standing diagnostic 2-h PG value of 11.1 mmol/l (SMCD, 2010) rather than the World Health Organization (WHO) diagnostic value of 7.8 mmol/L (Larsson et al., 1998). It is expected that these diagnostic changes will result in about a 10% increase in diagnosis of diabetes, but it is hoped that in treating more people for type II diabetes, the complications may be reduced. (Medicine digest, 1998) . The reference value for the analysis centre of this study was FPG of 7.8 mmol/L for diagnosis of DM (reference range of 2.5 mmol/L to 5.0 mmol/L for normal glycaemia and between 5.1 mmol/L and 7.7 mmol/L interpreted as IFG.

From this study IFG was statistically associated with ED (almost 60% of this group of people had ED). This observation has also been reported by other workers (Grover et al., 2006). IFG like IGT are not clinical entities, but rather risk categories for future diabetes and or CVD with much earlier medical presentation such as ED (Fuller et al., 1980; Alberti, 1996). This finding has important clinical implications for primary care physicians asking questions about sexual health leading to screening for these risk groups of people and a chance for modification to prevent disease progression.

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