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VOIDING DYSFUNCTION AMONG FEMALE PATIENTS WITH DIABETES MELLITUS
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VOIDING DYSFUNCTION AMONG FEMALE PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

***Background*: Disordered bladder dysfunction is one of the complications of diabetes mellitus that occurs in the middle aged and elderly diabetic patients. Poor glycemic control leads to production of glycated end products that cause axonal degeneration and impairment of nerve conduction. This affects autonomic innervations to the bladder muscles and leads to disordered bladder function.**

***Objectives*: To highlight voiding dysfunction among female diabetic patients attending the diabetic clinic at MTRH.**

***Design*: This was a hospital based cross sectional study .**

***Setting*: Diabetic clinic at the Moi Teaching and Referral Hospital, Eldoret ,Kenya .**

***Subjects* /Participants: Involved 255 female patients .**

***Results*: Two hundred and fifty five female diabetic patients were interviewed with a mean age of 69±16.1 years. About 72(28.2%) had voiding dysfunction while 183(71.8%) had a normal bladder function.**

The mean age for patients with voiding dysfunction was 59.9 years compared with 49.3 years for those normal bladder function.

About 73.9% (187) out of 253 patients with recorded results had abnormal FBS of >5.6mmol/L), while 98% (197) out of 201 who had results had abnormal HB1C of >7mg/.

The association between age of the patients and voiding dysfunction was statistically significant, (Pearson Chi square (2)=17.267 Pr=0.001),and also between the duration a patient has suffered from DM and presence of Voiding dysfunction P=0.001.

There was no significant association between FSB (p=0.603) and HB1C(p=0.115) and voiding dysfunction.Patients with abnormal creatinine levels have odds of 1.2 of having voiding dysfunction compared to patients with normal creatinine (95.0% C.I 0.586 to 2.410). Similarly , patients with abnormal urea had 1.8 times odds higher of having voiding dysfunction (95.0% C.I 0.586 to 2.410) compared to those with normal urea levels.

***Conclusion*: Diabetic bladder dysfunction occurs among female DM patients and age of the patient and duration the patient has lived with the disease are important risk factors.**

INTRODUCTION

Disordered bladder function is a well recognised complication of diabetes mellitus. It manifests in a spectrum of clinical signs and symptoms ranging from overactive bladder in its early stages to overt detrusor dysfunction with urine retention. Diabetic cystopathy is one of the well-recognised complications of the disease that affects between 10% -55% middle aged or the elderly patients who have long standing and poorly controlled diabetes disease to varying degrees of severity (1-4). Reported incidence ranges between 25% and 87% in different studies among men and women with diabetes mellitus (DM) (2,5,6). DM is reaching epidemic proportions globally (7) with regional projection estimating prevalence at 3.3% in a third world country like Kenya. This figure is thought to be even higher since two thirds of diabetics are not aware that they have the disease (8).Diabetes mellitus, as part of the emerging epidemic, is expected to rise to 4.5% by the year 2025 if the trend is not checked (7). Most developing countries have a young population with Kenya having a mean age of 19.1 years, a life expectancy of 63.53 years and a prevalence rate of obesity of 4.2%. Diabetes and its complications are likely to be more common in future as part of an emerging epidemic of non-communicable diseases . Our health care system should therefore prepare for

it (9) based on information generated by research.

MATERIALS AND METHODS

This was a hospital based cross sectional study involving female patients attending the Moi Teaching and Referral Hospital (MTRH) diabetic clinic. The patients were recruited and interviewed on their clinic visiting day. Those recruited included female patients of all ages who have been diagnosed and are on follow-up with Diabetes mellitus. Excluded were female diabetic patients who has been diagnosed or suspected to have a pathology that causes bladder outlet obstruction or bladder dysfunction.

The researcher and the research assistants interviewed the patients during the clinic visits. A pre-designed data sheet was used to collect data that included the demographics of the patients, the type of diabetes and treatment, the control of diabetes using HB1C and FBS, clinical symptoms suggestive of bladder dysfunction which included lower urinary tract symptoms such as frequency,norcturia, presence of bladder sensation, straining to pass urine, the nature of the stream of urine and urgency of micturation. The last entry of laboratory information related to the blood sugar control including Fasting Blood Sugar (FBS) and glycosilated HB (HB1C), urea and creatinine were collected from the patient's record as a true reflection of the control of diabetes in the subjects.

Data was then entered into an excel spread sheet, cleaned then analysed. Descriptive statistics using mean for continuous data and proportion for categorical data was performed and presented. Comparative statistics was also performed using chi square for categorical data and multivariate analysis was performed and results presented.

RESULT

A total of 255 female diabetic patients were interviewed with a mean age of 69±16.1 years with a median of 68 years (Table 1).

Out of 253 who had FBS recorded, 73.9%(187) had a FBS of >5.6mmol/L (normal range 3.5-5.6mmol/L) ,while while out of 201 who has HB1C results 98% (197) had abnormal HB1C of >7mg/dl (normal range 5.0-7mg/dl). Up to (72) 28.2% patients had symptoms of urinary bladder voiding dysfunction while (183) 71.8% had a normal bladder function.

Those straining while passing urine were 8.2%(n=21),poor stream of urine 3.9%(n=10), a sensation of incomplete bladder emptying 10.2%(n=26),norcturia 5.5%(14) and urgency of 9.0%(23).

The mean age of patients with voiding dysfunction was 59.9 years compared with 49.3 years for those with normal bladder function.

There was a strong association between age of the patients and voiding dysfunction (Pearson Chi-square (2) =17.267 Pr=0.001).

There was also a significant correlation between the age of the patient and duration of DM, r=.237 $p<0.05$.

Those with voiding dysfunction had mean of 10.8 years of living with DM compared to a mean of 7.9 years without voiding dysfunction. There was a significant correlation between the difference in the mean duration, $p<0.05$.

There was also a significant correlation between the duration a patient had suffered from DM and the development of Voiding dysfunction P=0.001.

The chi-square test showed no significance association between FSB (p=0.603) and HB1C (0.115) and voiding dysfunction.

The odds of a patients with abnormal FBS developing voiding dysfunction was 1.2 (95% C.I 0.380to 3.980), while the odds of a patient with abnormal HBA1C was 2.1 (95% C.I 0.842 to 5.495). There was a weak association between FBS and voiding dysfunction.

Patients with abnormal creatinine levels have odds of 1.2 of having voiding dysfunction compared to patients with normal creatinine (95.0% C.I 0.586 to 2.410).

Similarly, patients with abnormal urea had 1.8 times odds higher of having voiding dysfunction (95.0% C.I 0.586 to 2.410) compared to those with normal urea levels.

Figure 1
Comparing age of the patient, duration of DM , blood sugar control and voiding dysfunction

	Voiding dysfunction	Normal voiding	p-value
N=255	72(28.2%)	183(71.8%)	0.001
Age(Years)	59.9	49.3	0.001
Duration of DM(years)	10.8	7.9	<0.05
FB S(3.9-7.2mmol/L)			
abnormal	138(54.6%)	49(19.4%)	0.19
normal	54(21.3%)	12(4.7%)	
HB1C (4-5.6mg%)			
normal	4(2%)	0(0%)	0.580
abnormal	154(76.6%)	43(21.4%)	

DISCUSSION

The process of micturation begins with sensing bladder filling then relaying nervous impulse to the central nervous system. Processed information is sent through efferent pathways back to the bladder wall which result in voiding. It is the increasing urinary bladder volume that provokes afferent signal to the central nervous system. The molecular basis for the distension sensing response of the urothelium is thought not just to be a physical barrier, but also response to physical and chemical stimuli by releasing various substances including adenosine tri-phosphate (ATP), nitric oxide (NO), substance P, acetylcholine, adenosine, antiproliferative factor, cytokines, atrophic factors, and prostanoids (10). The areas of the brain involved in bladder control include the anterior and medial frontal lobes, limbic regions basal ganglia,thalamus and brainstem (11,12). Hyperglycemia leads to formation of advanced glycated end products (13) which cause axonal degeneration and impairment of nerve conduction which latter manifest as bladder hyposensitisation. Bladder biopsies in diabetes patients show decreased acetyl cholinesterase activity perhaps due to axonal degenerative and Schwann cell proliferation which is an attempt to regeneration after demyelisation or axonal degeneration (14). Patients with poorly controlled diabetes mellitus have glycosuria and osmotic diuresis.This leads to increased urine volume which enhances bladder stretch and hence increased intravesical pressure. The result is detrusor muscle hypertrophy which leads to increased residual volume upon decompensation (15). This is considered to represent end-stage bladder failure (16).

The prevalence of DM in a third world countries is estimated at 3.3% and it is expected to rise to 4.5% by the year 2025 if the trend is not checked (9). This picture is replicated in most developing countries (17) DM is reported to be reaching epidemic proportions worldwide (12).

The mean age of patients in this study was 69±16.065 years with a median age of 68 years. In this study , 28.2% of female diabetic patients had symptoms of bladder dysfunction . A prevalence range of between 25% and 87% has been found in other studies [18]. This study corroborates what has been found in other studies in developed countries . DM patients in third world countries are hardly evaluated for Voiding dysfunction. This is likely due to lack of awareness among health workers that this is a known complication of DM. The diagnosis in most cases is only made when a diabetic patient presents with urine retention as a results of detrusor underfunction, which unfortunately, is the extreme end of the spectrum of diabetic cystopathy. Lack of awareness that voiding dysfunction is one of the complications of DM our set up could be a contributing factor. The onset of voiding dysfunction in DM is usually insidious process that leads to progressive reduction in desire to void (19). The symptoms however are varied with slightly over half of patients (55%) having detrusor hypereflexia, 23% reduced detrusor contractility and a further 10% demonstrating detrusor areflexia with the remaining 11% with indeterminate findings (2). These varied findings can therefore be missed out by a clinician who is not deliberately looking for them. Though only female patients were recruited in this study, the prevalence rate has been estimated to be the similar in both sexes (20,21).The mean age of patients voiding dysfunction was 59.9 years compared with 49.3 years for those with normal bladder function (Table 1). In this study, there was a strong statistically significant association between age of the patients and voiding dysfunction (Pearson Chi square (2)=17.267 Pr=0.001). This implies that Older DM patients are more likely to develop voiding dysfunction and therefore an effort has to be made during their follow-up to pick out the symptoms. Clinicians need to bear this in mind much more so when evaluating male patient who may have similar symptoms related to Bladder outlet obstruction occasioned by prostatic enlargement because LUTS

overlap in the two conditions. The decision on the modality of treatment ,especially if it is surgical, should not overlook the likelihood of existence of voiding dysfunction due to DM because the outcome of surgery will not be satisfactory.

We postulate that, compared to older patient ,younger patients have tissues which retain the ability to regenerate after injury which delays the appearance of voiding dysfunction.

Patients with voiding dysfunction had suffering from DM for a longer mean duration of 10.8 years compared to the 7.9 year duration of those without voiding dysfunction. This difference in the mean duration was statistically significant $p<0.05$ (Table 1). Delay the development of type 2 DM, by encouraging healthy lifestyles such as physical exercise and proper diet would be one of the ways of preventing voiding dysfunction attributed to DM.

Age of the patients and duration of suffering was significantly correlated, $r=.237$ $p<0.05$.

This closely matches a duration of 7.41 ±3.8 years by Uday B Nayak *et al* (22) and 8.2 ± 2.6 years by Noronha J L *et al* (23). However, a study by Hong-Jeng Yu et al puts this duration at a much higher age of > 20 year than what was found in this study (24). It is apparent that patients in this study develop voiding dysfunction much earlier than patients in the latter study. This could be attributed to poor glycemic control in majority of these patients. Out of 253 who has FBS recorded, 73.9%(187) had a FBS of >5.6mmol/L (normal range 3.5-5.6mmol/L) ,while while out of 201 who has HB1C results 98%% (197) had abnormal HB1C of >7mg/dl (normal range 5.0-7mg/dl) (Table 1).

There was however no significance association between FSB ($p=0.603$) and HB1C (0.115) and voiding dysfunction. We recognise that this could be because we only relied on a single entry of the latest test result done rather than an average of the tests done for the duration that the patients has been on follow up.

Poor glycemic control causes oxidative stress that leads to cell damage (25). Hyperglycemia leads to formation of advanced gyrated end products (8) which cause axonal degeneration and impairment of nerve conduction which latter manifest as bladder hyposensitisation.

Diabetes has been identified as an important risk factor in development of urinary incontinence in women (26).

Polyuria as a result of glycosuria causes bladder hypertrophy and this is responsible for the initial symptoms of bladder dysfunction.

Voiding dysfunction could therefore be used as a marker of good glycemic control in diabetic patients (27, 28). The odds of a patients with abnormal FBS developing voiding dysfunction was 1.2 with a 95% C.I 0.380- 3.980, while the odds of a patient with abnormal HBA1C was 2.1 with a95% C.I 0.842- 5.495. In this study, there was a weak association of FBS and bladder voiding dysfunction. This corroborates a different study that has shown that the measures of DM type 2 control, that is HBA1C and FBS have not been independently associated with voiding dysfunction in one study (29).

Poor glycemic control contributes to production of free radicals which lead to production of glycated end products that cause axonal degeneration and impairment of nerve conduction (8). This requires exposure of the neurons to glycated end products over a longer duration of time. Good daily glycemic control from the onset should therefore be the goal by clinicians in prevention or delaying bladder dysfunction in diabetic patients.

Prolonged retention leads to vesicoureteric reflux and hydroureteronephrosis and uremia which may set in as a sequel to continuing kidney damage due to diabetic glomerulosclerosis. Besides diabetic nephropathy, this is a likely an additional cause of renal damage in diabetic patients (30).

Focusing only on diabetic nephropathy as the pathophysiology of renal failure may lead to graft loss in those patients who undergo renal transplant if their bladder function is not adequately evaluated. New kidney transplant centers in developing countries should be well equipped to perform adequate urodynamic studies in diabetic patients who are scheduled for transplant.

Patients with abnormal creatinine levels were found to have 1.2 times odds higher of suffering from voiding dysfunction compared to patients with normal creatinine levels. Similarly, patients with abnormal levels of Urea had 1.8 times odds higher of having voiding dysfunction compared to patients with normal urea levels. These results mean that diabetic patients registering abnormal urea and creatine levels are more likely to have voiding dysfunction. This therefore emphasizes the importance of evaluation diabetic patients for bladder dysfunction because it may affect the outcome when they are treated either conservatively or definitively for renal failure.

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In conclusion, diabetic bladder dysfunction in diabetic women and by extension men occurs among our diabetic patients and needs to be identified and managed. Poor glycemic control is the most important risk factor in causing early appearance of symptoms. We recommend a larger study should be undertaken to show if strict glycemic control mitigates against development of voiding dysfunction among diabetic, and to determine the role of bladder dysfunctions in development of renal failure in diabetic patients.

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