



PREVALENCE OF MICROALBUMINURIA AMONG DIABETIC PATIENTS IN USMANU DANFODIYO UNIVERSITY TEACHING HOSPITAL, SOKOTO

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ABSTRACT

Diabetic nephropathy is a common phenomenon in patients with diabetes. Its prevalence risk factors have not been fully described in black African patients. This study determined the prevalence of microalbuminuria (mal) among diabetic patients in Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto. It involved 100 diabetics and 50 healthy controls. Mal was estimated by BCG-dye binding method, while fasting blood glucose (FBG) by glucose oxidation method. The prevalence of mal varied between males (24.3%) and females (16.6%). The duration of the disease ranged from < 5 years (42.0%) with 8(14.5%) having abnormal mal, (58%) >5 years with (31%) having abnormal mal, (30%) < 30 years having (17.1%) having abnormal mal and (70%) >30 years having (24%) with abnormal mal. The prevalence of mal was 22% (17% males and 5% females). FBG differed significantly ($p < 0.05$) between patients (11.01 ± 1.03 mmol/l) and control subjects (4.38 ± 0.07 mmol/l). Urinary albumin excretion was significantly higher in diabetics than in control (57.65 ± 18.92 versus 24.16 ± 1.48 mg/24hrs respectively). Mal significantly ($p < 0.05$) increased with duration of diagnosis of diabetes (108.6 ± 14 versus 214.6 ± 9.1 mg/24hrs in <5 years and >5 years group respectively). Poor glycaemic control was the only modifiable predictor for the development of mal. Other non-modifiable risk factors related to progression of mal are sex and duration of disease. Early diagnosis of mal and aggressive glycaemic control is hereby recommended.

Keywords: Microalbuminuria, Diabetic nephropathy, Fasting blood glucose

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders of predominantly carbohydrate metabolism in which glucose is underutilized, producing hyperglycaemia (David, 2001). Some individuals may experience acute life-threatening hyperglycaemic episodes, such as ketoacidosis, or hyperosmolar coma (David, 2001). As the disease progresses, individuals are at increased risk for development of specific complications including retinopathy- leading to blindness, nephropathy- leading to renal failure, neuropathy (nerve damage), etc. (David, 2001).

Among the aforementioned complications, diabetic nephropathy is the leading cause of death and disability in diabetes (Foster, 1991). Diabetic nephropathy encompasses all the lesions occurring in the kidney of diabetic patients. It may be functionally silent for long period of time (about 10-15 years) (Foster, 1991). Diabetes has become the most common single cause of end-stage renal disease (ESRD) in the U.S and Europe (ADA, 2004). This is due to the fact that: 1) diabetes, particularly types 2, is increasing in prevalence; 2) diabetes patients now live longer; and 3) patients with diabetic ESRD are now being accepted for treatment in ESRD programme where formerly they had been excluded (ADA, 2004). In the U.S, diabetic nephropathy accounts for about 40% of new cases of ESRD, and in 1997, the cost for treatment of diabetic patients with ESRD was in excess of \$ 15.6 million (Robert, 2000). About 20-30% of patients with Type 1 or Type 2

diabetes develop nephropathy, but in type 2 diabetes a considerably smaller fraction of this progresses to ESRD (ADA, 2004). The hallmark for the diagnosis of diabetic nephropathy is microalbuminuria (Robert, 2000).

Microalbuminuria (mal) is defined by a urinary albumin between 30 and 300mg/24hrs or 20-200µg/min for timed urine collection (Ruggent, 1998; Ritz, 1999 Stehouwer, 1996). Diabetic nephropathy is defined by a raised urinary albumin excretion of > 300mg/24hrs, indicating clinical mal (Parving, *et al*, 1988). Mal is more prevalent in salt-sensitive hypertensives (Ivandic *et al*; 1996). Diabetic nephropathy is a syndrome of albuminuria, declining glomerular filtration rate (GFR), arterial hypertension and increased cardiovascular risk that affects 20-40% of type 1 and type 2 diabetic patients (WHO, 1999). Diabetic patients (mostly type 2) accounts for about one third of all patients requiring renal replacement therapy in Western countries (Parving *et al*; 1988).

Among the earliest changes demonstrable in diabetic nephropathy is glomerular hyper-perfusion. This is accompanied by mal which serves as a sensitive early indicator of adverse effects of diabetes on the kidney and is a powerful predictor of the subsequent course (Timothy *et al*, 2000). Mal is the best documented predictor of high risk for development of diabetic nephropathy in both type 1 and type 2 diabetes, and numerous trials in both type have documented and demonstrated the usefulness of mal in intervention studies (Parving *et al.*, 2001).

Studies have shown a strong correlation between the degree of mal and the rate of progression of renal disease. This correlation has led to the hypothesis that mal itself may contribute to the progression of renal disease and not simply a consequence of it (David, 2001). The appropriate urine sample to use for investigation of albumin excretion still is being debated (Newman and Christopher, 2001). For example a 24 hour- sample, an over night sample, a first morning void, a second morning void, or just a random sample all have been recommended (Newman and Christopher, 2001). Regarding the technical aspect of this strategy, morning urine sample provides the same result as 24 hour collection, making the 24hour collection unnecessary (Walter and Hoffer, 2003).

The knowledge of prevalence of mal in diabetic population in any community is undoubtedly important since the degree of nephropathies occurring in diabetes can be assessed satisfactorily from such information (Mogensen,1984). In 1997 reports from several renal units in Nigeria began to place diabetic nephropathy as the third most common cause of ESRF (Sanusi and Umar, 2007). Mal and events such as glomerular hyperfiltration and hypertension can serve as markers for renal events in diabetics and their presence predict development of clinical diabetic nephropathy (Mogensen *et al*, 2003). Consequently, there are calls for preventive nephrology in the case of diabetics which involves the search for markers of kidney disease (Umugbe *et al*; 2005). Where such markers are found, intervention strategies can be put in place to retard or slow down the eventual development of ESRD (Umugbe *et al*; 2005). Therefore, the aim of this study was to collate information on the prevalence of microalbuminuria as an index of renal damage in diabetic patients in Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

MATERIALS AND METHODS

All chemicals and reagents for this study were purchased from Johnson Solomon (Export) Ltd, London, U.K and Randox Ltd. These include: Kits for albuminuria and blood glucose estimation.

Ethical Consideration and Clearance:

An ethical clearance certification for the purpose of this study was also obtained from the relevant ethical committee prior to the commencement of this investigation.

Sample Size:

Using the formula:

$$n = Z^2 pq / d^2 \text{ (Aroaye, 2003).}$$

Where,

n= Minimum sample size

z= Standard normal deviation, that is 1.96 or 2, standard deviation at 95% confidence level.

P= Prevalence rate of microalbuminuria in diabetic patients=10% or 0.10.

q= 1-p = 1-0.10 = 0.9.

d= Precision (or tolerable error margin) = 5% or 0.05.

$$n = \frac{1.96^2 \times 1.0 \times 0.9}{0.05^2} = 138$$

Sample Collection:

For the purpose of this study two urine samples were collected from each subject and analysed. These include: 24hrs urine sample and first morning void using boric acid as preservative.

Experimental Design:

One hundred (100) diabetic patients and fifty (50) apparently healthy individuals were recruited for this study. Bromocresol Green (DCG) Dye-binding method was employed for urine albumin estimation and blood glucose using glucose oxidase method.

Statistical Analysis:The analysis of the data obtained was treated accordingly using Graph pad Instat 3 © (2008) statistical package. The data obtained for microalbuminuria were compared against age group, sex, duration of disease of the subjects. Means were compared using Student t-test. A p-value less than 0.05 (p<0.05) was considered as statistically significant.

RESULTS

The demographic and clinical characteristics of the study subjects are presented in Table 1. Thirty percent (30%) (15/50) of the control subjects, 33.3% (10/30) of IDDM (type 1), 28.5% (20//70) of NIDDM (type 2) and 30% (45/150) of the total subjects were females. There was no significant (p>0.05) difference between males and females, within the group with regard to age, duration of diabetic state and glycaemic status. The mean ages of the male, female and pooled IDDM (Type 1) patients were significantly lower than the corresponding ones for the NIDDM (type 2). However, patients with IDDM and control have similar mean ages (36.10±3.67 to 37.50±2.29). For type 2 diabetic, males (47.54±2.28 yrs) were younger than female (52.25±2.43yrs).

The mean duration of diabetes was found to be shorter in type 1 patients (2.98±0.53yrs) than in type 2 patients (7.68±0.91 yrs). There was no significant difference in mean duration of diabetes between males and females with type 1 diabetes but males have slightly shorter duration. In type 2 diabetes mean duration was higher in females (8.15±0.93yrs) than in males (6.98±0.84yrs). Similarly, mean fasting blood glucose (FBG) was not significantly different between males (4.25±0.07) and females (4.67±0.16mmol/l) in the control group. In patients with IDDM, there is no significant difference (p>0.05) in the level of FBG between males (11.37±0.69 mmol/l) and females (11.56±1.03). In NIDDM patients there was also no significant difference (p>0.05) between the sexes in the levels of FBG but females have slightly higher levels. Overall, mean FBG was slightly higher in patients with IDDM (11.44±0.35 mmol/l) compared to NIDDM patients (10.69±1.01mmol/l).

Table 2 presents microalbuminuria levels in the control subjects. The mean microalbuminuria (Mal) in males (22.28±1.77mg/24hrs and 6.14±10.75mg/dl) was discovered to be slightly lower than the females (28.87±2.49mg/24hrs and 7.08±1.41mg/dl). Table 3 shows mean values of mal in males (56.90±16.05mg/24hrs and 6.36±2.22mg/dl) is significantly higher than in females (40.2±20.0mg/24hrs and 4.78±2.13mg/dl).

Table 4 presents mal in type 2 diabetics. There is significantly higher mean value of mal in males

(71.25±18.25mg/24hrs and 7.57±0.5mg/dl) than in females (57.65±18.25mg/24hrs and 7.29±2.61mg/dl).

Predictors of mal are presented in Table 5. There is statistically significant difference (p<0.05) between duration of diagnosis < 5 years (178.6±5.4) and > 5 years of diagnosis (214.6±9.1). There is also statistically significant difference (p<0.05) between males (204.6±10) and females (144.0±29). However, there is no statistically significant difference (p>0.05) between patients with <30 years of age (223.8±7.4) and > 30 years of age (221.7±7.0).

Table 1: Demographic and clinical characteristics of the study subjects

Subject	n	Mean age ± SEM (yrs)	Mean DOD ± SEM (yrs)	Mean FBG ± SEM (mmol/l)
Control	50	40.6 ± 1.68	—	4.38 ± 0.07
Male	35	49.31 ± 2.0	—	4.25 ± 0.07
Female	15	46.73 ± 1.85	—	4.67 ± 0.16
IDDM (type 1)	30	37.03 ± 2.84	2.98 ± 0.53	11.44 ± 0.35
Male	20	37.50 ± 2.29	3.01 ± 0.46	11.37 ± 0.69
Female	10	36.10 ± 3.67	3.54 ± 0.65	11.56 ± 1.03
NIDDM (type 2)	70	51.23 ± 3.12	7.18 ± 0.91	10.69 ± 1.01
Male	50	47.54 ± 2.28	6.98 ± 0.84	10.59 ± 0.81
Female	20	52.25 ± 2.43	8.15 ± 0.93	10.95 ± 0.73
p-value	—	>0.05	>0.05	>0.05

n= number of population group, SEM= standard error of mean, DOD= duration of disease, FBG= fasting blood glucose, mmol/l= milli mole per litre, Yrs= years, P-value is within the group.

Table 2: Microalbuminuria in the Control Subjects

Parameters	male (n=35)		female (n=15)		Pooled	
	Range	mean ± SEM	Range	mean ± SEM	Range	mean ± SEM
Mal (mg/24hrs)	10-40	22.28 ± 1.77	10-40	28.87 ± 2.49	10-40	24.16 ± 1.48
Mal (mg/dl) (1 st mv)	0.00-15.0	6.14±0.91	0.029-14.20	7.08±1.41	0.00-15.0	5.58±0.78
p- value	<0.05		<0.05		<0.05	

n= number of the control subjects SEM= standard error of mean, mg/dl= milligram per deciliter, mg/24hrs = milligramme per 24 hours, 1st mv= first morning void, Mal= microalbuminuria, p-value is within the group.

Table 3: Microalbuminuria in type 1 diabetes in the Study Subjects

Parameters	male (n=20)		female (n=10)		Pooled (n=30)	
	Range	mean ± SEM	Range	mean ± SEM	Range	mean ± SEM
Mal (mg/24hrs)	12-259	56.90±16.05	12-220	40.2±20.0	12-259	40.20±11.02
Mal(mg/dl) (1 st mv)	0.006-29.83	6.36±2.22	0.006-19.8	4.78±2.13	0.006-29.83	5.94±2.12
p- value	<0.05		<0.05		<0.05	

n= number of the population group SEM= standard error of mean, mg/dl= milligram per deciliter, mg/24hrs = milligramme per 24 hours, 1st mv= first morning void, Mal= microalbuminuria, p-value is within the group.

Table 4: Microalbuminuria in type 2 diabetes in the Study subjects

Parameters	male (n=50)		female (n=20)		Pooled (n=70)	
	Range	mean ± SEM	Range	mean ± SEM	Range	mean ± SEM
Mal (mg/24hrs)	10-270	71.25±18.25	10-265	57.65±18.92	10-270	67.56±19.21
Mal (mg/dl) (1 st mv)	0.028-45.9	7.57±0.59	0.008-43.2	7.29±2.61	0.006-45.9	7.49±1.82
p- value	<0.05		<0.05		<0.05	

SEM= standard error of mean, 1st mv= first morning void, mg/dl= milligram per deciliter, mg/24hrs= milligramme per 24 hours, Mal= microalbuminuria, p-value is within the group.

Table 5: Predictors of Microalbuminuria in the Study Subjects

Subject Variables	MAL (Mg/24hrs)	P-value
DOD <5yrs	178.6±5.4	<0.05
DOD>5yrs	214.6±9.1	
<30yrs of age	223.8±7.4	>0.05
>30yrs of age	221.7±7.0	
Male	204.6±10	<0.05
Female	144.0±29	

DOD= duration of disease, Mal= microalbuminuria, yrs= years, p-value is between the variables.

DISCUSSION

In this study, the prevalence of microalbuminuria (mal) in diabetic patients in UDUTH, Sokoto, is 22% (22/100), 17 male and 5 female. This is lower than prevalence of 25% (6 male and 4 female) in 40 type II diabetic patients reported from Illorin, Nigeria, (Adebisi, *et al*, 2001). This is also lower than the prevalence of 38% reported by Orluwene and Momoh, (2008) in Port Harcourt, 37.6% in Lagos (Iwalokun *et al*, 2006), 50% reported in Benin by Umugbe *et al*, (2005) and 52% reported by Erasmus *et al*, (1992) in a study conducted in Ilorin. Most of the studies quoted above used 'MICRAL test,' a strip for urinary albumin assessment. This might have resulted in higher rate of 52% than the 22% of the present study.

Studies in the white UK population revealed a prevalence of mal of 7%-9% (Gatling *et al*, 1988), while in Mexican Americans it was 31%, Pima Indians 26% (Nelson *et al*; 1989), Naurans 42% and Hispanic Americans 35% (Hamman, *et al*, 1991). Prevalence of 19.7% from a tertiary hospital in Velilore, South India was reported by John, *et al*, (1991), Vijay *et al*, reported a prevalence of 15.7% MAL among 600 Type 2 diabetic patients at a diabetic center in Chennai (Schmitz and Vaeth, 1995).

This variation in prevalence can be attributed to factors such as difference in populations, definitions of mal, method of urine collection etc. However, this could also reflect true differences in the ethnic susceptibility to nephropathy. Earlier studies by Vijay *et al*, (1991), from Chennai, have demonstrated a familial clustering of diabetic nephropathy among south Indian type 2 diabetics. Genetic susceptibility linked to angiotensin gene as shown in Oji- Kree Indians could also be an important determinant for development of diabetic renal disease (Hegele, 1999). Some studies related duration of diabetes, male sex, preexisting retinopathy and poor glycaemic control as major risk factors for mal (Marshall and Alberti, 1981; Haffner *et al*, 1993). Age was reported as one of the risk factors in the Wisconsin study of a Darnish population (Olivarius, *et al*; 1993) and in the Pima

Indians (Olivarius *et al*;1993). The association of glycaemic control with mal has been well established by various studies (Allawi, *et al*, 1988, Hamman, *et al*, 1991). Other factors which are reported to be associated with mal are alcohol intake (Allawi *et al*, 1988), foot ulcers and smoking (Hamman *et al*, 1991).

In this study the prevalence of mal across genders was statistically significant (p>0.05). Mal was shown to be higher among male subjects (24.3%), compared with female (16.6%), patients. This agrees with previous studies (Mattock *et al*; 1988, Thoklid *et al*, 1994) , and it is in support of the documented higher prevalence of nephropathy among male patients with diabetes (Torffirrit *et al*, 1991, Andersen *et al*, 1983). This is probably because women have a lower creatinine excretion than men (Andersen *et al*, 1983).

Therefore, the present study, shows that detection of mal as early as possible in the course of the disease is very important in the management of diabetic nephropathy in our environment. In developing countries like Nigeria, this is even more important because of the financial constraints and kidney replacement therapy is seldom an option. It is therefore imperative that those who care for patients with diabetes mellitus to be knowledgeable about diabetic nephropathy and attentive to its prevention, onset, progression and treatment in their patients. Measurement of mal is a useful adjunct in this direction. Measurement of microalbuminuria should be included in the routine investigation for better management of diabetic patients. Early detection will help to reduce the incidence of diabetic nephropathy and rate of mortality and morbidity among these patients.

CONCLUSION

In this study the prevalence of mal in diabetic patients was found to be: 22%, 17% male and 5% female. The reference values of 10-40mg/24h and 0.00-15mg/dl for mal in UDUTH Sokoto was established.

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