



SJMLS-3(3)-010

Evaluation of Proteinuria in Normotensive Diabetics Attending Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria*Bunza F.U*¹ and Wasagu, I.Z.¹**Chemical Pathology Department, School of Medical Laboratory Science,
Usmanu Danfodiyo University Sokoto, Nigeria¹**Author for correspondence*: fbunza@gmail.com/+234-803-830-1842***Abstract**

Proteinuria has been generally regarded as an indicator for the degree of glomerular damage in diabetes. The levels of proteinuria correlate well with the extent of renal dysfunction and interventions that retard the progression of diabetes-related renal disease also reduce proteinuria. The aim of this study was to collate information on the incidence of proteinuria among normotensive diabetics attending Usmanu Danfodiyo University Teaching Hospital, Sokoto (UDUTH). The study involved 100 diabetics and 50 health controls. Proteinuria was estimated using Biuret method and fasting blood glucose was done using glucose oxidase method. The study shows that an overall 22% of the patients had diabetes-related proteinuria (17% males and 5% females). The duration of the disease < 5 years (42.0%) and > 5 years (58.0%) had 14.5% and 31.1% diabetes related proteinuria respectively. An average age of <30 years (30%) and >30 years (70%) had diabetes related proteinuria of (17.1%) and (24.6%) respectively. FBG differed significantly ($p < 0.05$) between patients ($11.01 \pm 1.03 \text{ mmol/L}$) and controls ($4.38 \pm 0.07 \text{ mol/L}$). Urinary protein excretion was significantly higher in diabetes (143.7 ± 5.78) than in controls (90.43 ± 5.78). Increased urinary protein excretion was observed ($p < 0.05$) with duration of diagnosis < 5 years ($228 \pm 5.4 \text{ mg/24hrs}$) and < 5 years ($264 \pm 9.1 \text{ mg/24hrs}$). Statistically significant increase in proteinuria ($p < 0.05$) was also observed in males ($254 \pm 10.0 \text{ mg/24hrs}$) when compared to females ($194 \pm 29 \text{ mg/24hrs}$). Given that the large number of individuals with diabetes is increasing; the number of diabetic

nephropathies is undoubtedly enormous. This could produce major constraints on health care budgets in the future. This urgently calls for not only good control of diabetes to prevent nephropathy but also to address the larger issue of primary prevention of diabetes, that is, reduction in the prevalence of diabetes itself by aggressive life style modifications.

Keywords: proteinuria, diabetes mellitus, normotensive, fasting blood glucose.

Introduction

Proteinuria has been generally regarded as a marked for the degree of glomerular damage in diabetes (Remuzzi and Bertani, 1990). The levels of proteinuria correlate well with the progression for renal dysfunctions and interventions that retard the progression of diabetes-related renal disease also reduce proteinuria. However, it has not yet been known whether the flux of proteins across the glomerular basement membrane is causally implicated in the evolution of diabetes renal disease or simply reflects glomerular damage (Remuzzi and Bertani, 1990).

The association of proteinuria with diabetes mellitus was first recognized in the eighteenth century and later Kimmelstied and Wilson (1936) who defined the condition by describing the lesions of nodular glomerulosclerosis and the association with proteinuria and hypertension in type 2 diabetes (Kimmelstiel and Wilson, 1936). These features represent a late stage in the progression of the condition (Kimmelstiel and Wilson, 1936). Complications associated with

proteinuria in diabetes includes: increased risk of cardiovascular disease (CVD), arterial and venous thrombosis, including renal vein thrombosis, pulmonary oedema due to fluid overload, acute renal failure due intravascular depletion and increase risk of bacterial infection including spontaneous bacteria peritonitis (Kittell, 2012).

According to the Centre for Disease Control and Prevention in 2008, approximately 44% of new cases of kidney disease were caused by diabetes. About 48,374 diabetics already began treatment progressed to end stage renal disease (ESRD), and about 202,290 diabetics with ESRD have been on long-term dialysis or had a renal transplant (CDCP, 2012). In 2010 United State Renal Data System reported 29.1% of individuals with self-reported diabetes had stage 2 or 3 chronic kidney disease (CDCP, 2012). Diabetes renal disease typically manifests after 10 years' duration in type 1, whereas approximately 3% of newly diagnosed type 2 have overt nephropathy (Mogensen, 1999).

Hypertension is strongly associated with insulin resistance, even in the absence of diabetes (HDS, 1993). About 40-70% and only about 25% of type 2 diabetes and type 1 diabetes respectively have been described to be hypertensive (Hasslacher *et al.*, 1985). Hypertension has been considered to be an independent risk factor for development of proteinuria (Rossing *et al.*, 1993). Diabetes renal disease characterized by nephrotic syndrome and diffuse scarring of the glomeruli is due to long-standing diabetes and a prime reason of dialysis in many developed countries. It is also identified as a small blood vessel complication of diabetes. During its early course, diabetes neuropathy often has no symptoms and can take 5-10 years after kidney damage begins (Medical Encyclopedia). These late symptoms include severe tiredness, headache, a general feeling of illness, nausea, vomiting, frequent voiding, lack of appetite, itching skin and leg swelling (Medical Encyclopedia). The aim of this study is to investigate the incidence of proteinuria among normotensive diabetics attending Usman Danfodiyo University Teaching Hospital Sokoto, Nigeria.

Material and Methods

Chemicals and Equipment

All chemicals and reagents for this study are of analytical grade. Kits for proteinuria and blood glucose estimation were purchased from Randox Company Ltd.

Ethical Consideration and Clearance

Ethical clearance for this study was sought and obtained from the relevant Ethical and Research Committee of the hospital prior to the commencement of the study.

Analytical Design

One hundred (100) diabetics and fifty (50) apparently healthy individuals (normoglycaemic) as control were recruited for this study. Biuret method was employed for urinary protein estimation and blood glucose was done using glucose oxidase method.

Inclusion and Exclusion Criteria

The diastolic and systolic blood pressure of more than 90/140 mmHg for both controls and the patients were excluded for this study.

Sample Collection

First morning void and 24 house urine samples, and venous blood sample from both controls and patients were collected into their appropriate containers. Boric acid was used as preservative for urine samples and EDTA as anticoagulant in blood samples.

Statistical/Data Analysis

The data obtained was presented as mean \pm SEM (standard error of mean) and analyzed using Graph Pad Instat 3© (2008) statistical package. The values obtained were compared using students' t-test. For all statistical analysis, a p-values less than or equal to 0.05 (≥ 0.05) were considered statistically significant.

Results

A total of one hundred and fifty (150) subjects of both genders were recruited for this study. They consisted of seventy (70) type 2 diabetics, thirty (30) type 1 diabetics and fifty (50) controls (Table 1). 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 type 1 diabetes, 28.5% (20/70) of type 2 subjects were females. There were no significant differences ($p>0.05$) between males and females within the group as regards to age, duration of disease and glycaemic status.

The mean \pm SEM of 24 hours proteinuria and first morning void in type 1 diabetics and controls is shown in Table 2. The means proteinuria (both 24 hours and first morning void) in the type 1 diabetes were significantly higher ($p<0.05$) than the corresponding values in controls. Table 3 shows the Mean \pm SEM for proteinuria in type 2 diabetes and controls. Both 24 hours proteinuria and first morning void was shown to be significantly higher ($p<0.05$) in type 2 diabetics than in control.

The incidence of proteinuria according to gender, age and duration of disease is shown in Table 4. Males, age and duration of disease greater than five years have greater influence on the incidence of proteinuria. The predictors of proteinuria are presented in Table 5. Statistically significant difference ($p<0.05$) was observed between the duration of diagnosis <5 years (228 ± 5.4) and <5 years of diagnosis (264 ± 9.1). There is also statistically significant difference ($p<0.05$) between males (254 ± 10.0) and females (194 ± 29.0). However, there is no statistically significant difference ($p>0.05$) between patients with <30 years of age (273 ± 7.4) and >30 years of age (271 ± 10.0).

Table 1: Demographic and clinical characteristics of the study subjects

Subject	N	Mean age	Mean DOD/Yrs	Mean FBG/mmol/L
Control	50	47.9 \pm 1.68		4.38 \pm 0.07
Male	35	49.31 \pm 2.0		4.25 \pm 0.07
Female	15	46.73 \pm 1.85		4.67 \pm 0.16
IDDM (type 1)	30	37.03 \pm 2.84	3.28 \pm 0.58	11.44 \pm 0.35*
Male	20	37.50 \pm 2.29	3.01 \pm 0.46	11.37 \pm 0.59*
Female	10	36.10 \pm 3.67	3.54 \pm 0.65	11.56 \pm 1.03*
NIDDM (type 2)	70	50.23 \pm 3.12	7.18 \pm 0.91	10.69 \pm 1.01*
Male	50	47.54 \pm 2.28	6.98 \pm 0.84	10.59 \pm 0.81*
Female	20	52.25 \pm 2.43	8.15 \pm 0.93	10.95 \pm 0.73*
<i>p-value</i>		>0.05	>0.05	<0.05

*N=number of population group, SEM=standard error of mean, *= values differs significantly from control, P-value ≤ 0.05 , DOD = duration of disease, FBG=fasting blood glucose, Mmol/L = millimole per liter, Yrs=years, p-value is within the group.*

Table 2: Proteinuria (Means \pm SEM) in type 1 diabetic and control subjects

Parameters	Males	Females	Pooled
Prot (mg/24hrs) (control)	90.43 \pm 5.78	104 \pm 6.06	96.24 \pm 4.48
Prot (mg/24hrs) (type 1 DM)	140.75 \pm 25.18*	112.5 \pm 29*	131.33 \pm 23.81*
Prot (mg/dl) (1 st mv) (control)	5.9 \pm 1.16	11.93 \pm 10.75	6.91 \pm 0.98
Prot (mg/dl) (1 st mv) (type I diabetes)	8.84 \pm 2.86*	5.47 \pm 2.03*	8.28 \pm 2.46*
<i>p-values</i>	<0.05	<0.05	<0.05

SEM = Standard error of mean, *= values differ significantly from control, p-value ≤ 0.05, prot = proteinuria, 1st mv= first morning void, Mg/24hrs = milligram/24hrs, p-value is between the groups.

Table 3: Proteinuria (Mean±SEM) in type 2 diabetic and control subjects

Parameters	Males	Females	Pooled
Prot (mg/24hrs) (control)	90.43±5.78	104±6.06	96.24±4.48
Prot (mg/24hrs) (type 2 diabetes)	143.7±26.20*	127.5±22.6*	136.86±7.24*
Prot (mg/dl) (1 st mv) (control)	7.9±1.16	11.93±10.75	8.91±0.98
Prot (mg/dl) (1 st mv) (type I diabetes)	10.94±0.73*	9.94±3.1*	10.15±2.02*
p-values	<0.05	<0.05	<0.05

SEM= standard error of mean, *= values differs significantly from control, p-value ≤ 0.05, Prot= proteinuria, 1st mv= first morning void, mg/24hrs= milligram/24hours, p-value is between the groups.

Table 4: Prevalence of proteinuria according to demographic, incidence of variables and duration disease

Subject	N	With proteinuria	Percentage (%)
Males	70	17	24.3
Females	30	5	16.6
<30 years of age	30	6	17.1
<30years of age	70	16	24.6
<5years DOD	42	8	14.5
<5yrs DOD	58	14	31.1

DOD = duration of diagnosis, Yrs = years, % = percentage, N=number of population group.

Tables 5: predictors of proteinuria (Mean±SEM) in the diabetes subject

Subjects variables	Prot (mg/24hrs)	p-value
DOD < 5years	228±5.4*	<0.05
DOD > 5years	264±9.1*	
<30year of age	273±7.4	>0.05
>30years of age	271±7.0	
Males	254±100*	<0.05
Females	194±29*	

Prot = proteinuria, DOD= duration of diagnosis, mg/24hrs = milligram/24hrs, *= values differ significantly between the variables, p -value ≤ 0.05 .

Discussion

The present study shows that overall, 22% of the patients had diabetes-related proteinuria with 17% in males and 5% in females. After 5 years duration of disease, the frequency of diabetes-related proteinuria increased to 31%. Our finding is consistent with previous report by Stephenson *et al.* (1995) who reported that type 1 and type 2 diabetics had similar prevalence rates of proteinuria. In Type 1 diabetes, proteinuria is associated with nephropathy and renal failure (Krolewski *et al.*, 1985), while in type 2 diabetics, proteinuria is widely associated with cardiovascular rather than renal disease (Mogensen, 1984). Among Europeans, diabetic nephropathy is reported to develop in 35% of type 2 diabetics (Tung and Levin, 1988). Prevalence rates would of course vary widely depending on methodology and definitions used for proteinuria. Fabre *et al.* (1982) reported a prevalence of 48% with abnormal protein excretion ($>150\text{mg}/24\text{hours}$) among 510 type 2 diabetics.

Studies from the UK have shown that among migrant Asian Indians, the prevalence of both diabetes and non-diabetes renal disease is higher compared with Europeans (Burden *et al.*, 1992). Similarly, John *et al.* (1991) in a report from Vellore in Southern Indian found that 8.4% of patients had persistent proteinuria (over 5000mg in 24hours).

Vijay *et al.* (1994), working at another diabetes central at Chennai, found a much high prevalence of proteinuria (18.7%) (Vijay *et al.*, 1994). However, the later study was confined to inpatients, that is, patients admitted to hospitals. This would undoubtedly introduce an additional bias of more severely ill patients being included in the study and this could explain the difference between the two studies.

The result of this study suggests that duration of diabetes is associated with proteinuria. The duration of diabetes has been shown to be a risk factor for nephropathy by almost all earlier studies (DCCTRG, 1993). The Diabetes Control

and Complications Trial Research Group and Prospective Diabetes Group studies have shown the impact of blood glucose control on reducing risk of retinopathy and nephropathy (UKPDS, 1998).

Conclusion

In conclusion, given that the large number of individuals with diabetes is increasing, the number of diabetic nephropathies is undoubtedly enormous. This could produce major constraints on health care budgets in the future. This urgently calls for not only good control of diabetes to prevent nephropathy but also to address the larger issue of primary prevention of diabetes, that is, reduction in the prevalence of diabetes itself by aggressive life style modifications.

References

- Burden, A.C., McNally, P.G. and Feehally, J. (1992). Increased incidence of end-stage renal failure, secondary to diabetes mellitus in Asian ethnic groups in the United Kingdom. *Diabetic Medicine*; 9:641-645.
- Centres for Disease Control and Prevention (CDCP). (2012). National Diabetes Sheet. Atlanta, Ga. US Department of Health and Human Services, <http://www.cdc.gov/diabetes/pubs>.
- Diabetes Control and Complications Trial Research Group (DCCTRG). (1993). The effect of intensive treatment of diabetes on development and progression of long-term complications in insulin dependent diabetes mellitus. *New England Journal of Medicine*; 329:977-986.
- Fabre, J., Balant., L.P. and Dayer, P.G. (1982). The kidney in maturity onset diabetes mellitus: a clinical study of 510 patients. *Kidney International*; 2:730-738.
- Hasslacher, C., Stech, W., Wahi, P. and Ritz, E. (1985). Blood pressure and metabolic control as risk factors for nephropathy in type 1 DM. *Diabetologia*; 28:6-11.
- Hypertension in Diabetes Study (HDS) (1993). Prevalence of hypertension in newly presenting type 2 diabetes and the

- association with risk factors for cardiovascular and diabetic complication. *Journal of Hypertension*; 11:309-317.
- John, L., Sunda, P.S. and Kanagasabapathy, SS. (1991). Prevalence of diabetic nephropathy in non-insulin dependent diabetes. *Indian Journal of Medical Research*; 94:24-29.
- Kimmelstiel, P. and Wilson. C. (1936). Intracapillary lesions in the glomeruli in the kidney. *American Journal of Pathology*; 12:83-97.
- Kittell. F. Diabetes Management. (2012). In Thomas, L.K. and Othersen, J.B. Nutrition Therapy for Chronic Kidney Disease, *CRC Press*: 198.
- Krolewski, A.S., Warram, J.H. and Chrisleb, AR. (1985). The changing natural history of nephropathy in type 1 diabetes. *American Journal of Medicine*; 78:785-794.
- Medical Encyclopedia (Medline plus). Diabetes and kidney disease 2015, www.nlm.nih.gov.
- Mogensen, C.E. (1984). Microalbuminuria predicts clinical proteinuria and early mortality in maturity onset diabetes. *England Journal of Medicine*; 310: 356-360.
- Mogensen, C.E. (1999). Microalbuminuria, Blood pressure and diabetes renal disease: origin and development of ideas. *Diabetologia*; 42: 263-285.
- Remuzzi, G., Bertani, T. (1990). Is glomerulosclerosis consequences of altered glomerular permeability to macromolecules? (Editorial). *Kidney International*; 38:384-394.
- Rossing, P., Hommel, E., Smidt, UM. and Parving, H.H. (1993). Impact of arterial blood pressure and albumin on the progression of DN in type 1 diabetic patients. *Diabetes*; 42:715-719.
- Stephenson, J.M., Kenny, S. and Stevens. I.K. (1995). Proteinuria and mortality in diabetes: The WHO multinational study of vascular disease in diabetes. *Diabetes Medicine*; 12:149-155.
- Tung, P. and Levin, S.R. (1988). Nephropathy in non-insulin dependent diabetes mellitus. *American Journal of Medicine*; 85:131-136.
- UK Prospective Diabetes Study (UKPDS) Group. (1998). Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS). *Lancet*; 32:1-18.
- Vijay V., Snehalatha, C. and Ramachandran, A. (1994). Prevalence of proteinuria in non-insulin dependent diabetes. *Journal of Association of Physicians of India*; 42:792-794.

Citation: Bunza F.U. and Wasagu, I.Z. Evaluation of Proteinuria in Normotensive Diabetics Attending Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria. *Sokoto Journal of Medical Laboratory Science*; 3(3): 80 - 85.

Copyright. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.