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Original Research Article

Evaluation of Proteinuria in Normotensive Diabetics in a Tertiary Care Hospital

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Abstract
Background: *Proteinuria has been generally regarded as a marked for the degree of glomerular damage in diabetes. The levels of proteinuria correlate well with the progression for renal functions and interventions that retard the progression of diabetes renal disease also reduce proteinuria. The aim of this study is to collate information on the incidence of proteinuria among normotensive diabetic patients attending Hi-tech Medical College and Hospital, Rourkela, Odisha*
Materials and Methods: *The study involved 100 diabetics and 50 healthy controls. Proteinuria was estimated using biuret method, while fasting blood glucose using glucose oxidase method.*
Result: *The study shows that an overall 22% of the patients have diabetes related proteinuria with 17% males and 5% females. The duration of the disease < 5 years (42.0%) and > 5 years (58.0%) have 14.5% and 31.1% diabetes related proteinuria respectively. An average age of < 30 years (30%) and > 30 years (70%) have diabetes related proteinuria of (17.1%) and (24.6%) respectively. FBG differed significantly ($p<0.05$) between patients (11.01±1.03Mmol/L) and controls (4.38±0.07Mmol/L). Urinary protein excretion was significantly higher in diabetics (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±5.4mg/24hrs) and >5 years (264±9.1mg/24hrs). Statistically significant increase in proteinuria ($p<0.05$) was also observed in males (254±10.0mg/24hrs) than in females (194±29mg/24hrs).*
Conclusion: *Given the large number of individual with diabetes is increasing; the number of diabetic nephropathy 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 [1]. The levels of proteinuria correlate well with the progression for renal functions and interventions that retard the progression of

diabetes renal disease also reduce proteinuria. However, it has not yet been know 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 [1].

The association of proteinuria with diabetes mellitus was first recognized in the eighteenth century and later Kimmelstied and Wilson in 1936 who defined the condition by describing the lesions of nodular glomerulosclerosis and the association with proteinuria and hypertension in type 2 diabetes [2]. These features represent a late stage in the progression of the condition [2] Complication associated with proteinuria in diabetes include: increased risk of CVD, arterial and venous thrombosis, including renal vein thrombosis, pulmonary oedema due to fluid overload, acute renal failure due to intravascular depletion and increased risk of bacterial infection including spontaneous bacteria peritonitis [3].

According to the centers for Disease Control and Prevention in 2008, approximately 44% of new cases of kidney were caused by diabetes. About 48,374 diabetics already began treatment to ESRD, and about 202,290 diabetics with ESRD have been on long-term dialysis or had a renal transplant [4]. In 2010 United State Renal Data System Reported 29.1% of individuals with self reported diabetes had stage 2or 3 chronic kidney diseases [4]. Diabetes renal disease typically manifests after 10 years' duration in type 1, whereas approximately 3% of newly diagnosed type 2 have overt nephropathy [5].

Hypertension is strongly associated with insulin resistance, even in the absence of diabetes [6]. About 40-70% and only about 25% of type 2 diabetes and type 1 diabetes respectively have been described to be hypertensive [7]. Hypertension has been considered to be an independent risk factor for development of proteinuria [8]. Diabetes renal disease characterised by nephritic 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 [3]. During its early course, diabetes nephropathy often has no symptoms and can take 5-10 years after kidney damage begins [9]. These late symptoms include severe tiredness, headaches, a general feeling of illness, nausea, vomiting, frequent voiding, lack of appetite, itching skin and leg swelling [9].

The aim of this study is to collate information on the incidence of proteinuria among normotensive diabetic patients attending Hi-tech Medical College, Rourkela.

Material and Methods

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

An ethical clearance for this study was sought and obtained from ethical committee of the hospital prior to the commencement of this study.

Analytical Design

One hundred (100) diabetic patients and fifty (50) apparently healthy individuals (normoglycemic) as control was recruited for this study. Biuret method was employed for urinary protein estimation and blood glucose using glucose oxidase method. Systolic and diastolic blood pressure of more than 140/90 mmHg for both controls and the patients were excluded for this study.

Sample Collection

First morning void and 24 hours urine samples, and venous blood sample from both controls and patients was 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 analyzed using Microsoft Excel for Windows VII version, SPSS (Statistical Package for Social Sciences) and GraphPad Prism 6.0 version.. The values obtained were compared using students' t-test. P-value less than or equal to

0.05 (≤0.05) was considered statistically significant.

Results

A total of one hundred and fifty (150) subjects of both sexes were recruited for this study. They consisted of seventy (70) type 2 diabetics, thirty (30) type 1 diabetics and fifty (50) controls (Table l). 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 diabetes and 36% (45/150) of the total subjects were females. There was no significant difference (p>0.05) between males and females within the group as regards to age, duration of disease and glycemic status.

The Means±SEM of 24 hours proteinuria and first morning void in Type 1 diabetics and controls is shown in table 2. The means proteinuria (both 24hours and first morning void) in the type 1 diabetics were significantly higher (P<0.05) than the corresponding values in controls.

Tables 3 shows the Mean±SEM for proteinuria in type 2 diabetics 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 sex, 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.

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 (Mean±SEM) of the study subjects

Subject	N	Mean age	Mean DOD/Yrs	Mean FBG (Mmol/L)
Control	50	47.9±1.68		4.38±0.07
Males	35	49.31±2.0		4.25±0.07
Females	15	46.73±1.85		4.67±0.16
Type 1 DM	30	37.03±2.84	3.28±0.58	11.44±0.35
Males	20	37.50±2.29	3.01±0.46	11.37±0.59
Females	10	36.10±3.67	3.54±0.65	11.56±1.03
Type 2 DM	70	50.23±3.12	7.18±0.91	10.69±1.01
Males	50	47.54±2.28	6.98±0.84	10.59±0.81
Females	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= millimole per liter, Yrs=years, p-value is within the group.

Table 2: Proteinuria (Mean±SEM) in type 1 diabetics and controls subjects

Parameters	Males	Females	Pooled
Prot(mg/24 hrs)- Control	90.43±5.78	104±6.06	96.24±4.48
Prot(mg/24 hrs)- Type 1 Diabetics	140.75±25.18	112.5±27.29	131.33±23.81
Prot(mg/dl)(1st mv)- Control	5.9±1.16	11.93±10.75	6.91±0.98
Prot(mg/dl)(1st mv)- Type 1 Diabetics	8.84±2.86	5.47±2.03	8.28±2.46
p-values	<0.05	<0.05	<0.05

SEM=standard error of mean, Prot= proteinuria, 1st mv= first morning void, Mg/24hrs= milligram/24hours, p-value is between the groups.

Table 3: Proteinuria (Mean±SEM) in type 2 diabetics and controls subjects

Parameters	Males	Females	Pooled
Prot(mg/24 hrs)- Control	90.43±5.78	104±6.06	96.24±4.48
Prot(mg/24 hrs)- Type 2 Diabetics	143.7±26.20	127.5±22.6	136.86±27.24
Prot(mg/dl)(1st mv)- Control	7.9±1.16	11.93±10.75	6.91±0.98
Prot(mg/dl)(1st mv)- Type 2 Diabetics	10.94±0.73	9.94±3.1	10.15±2.02q
p-values	<0.05	<0.05	<0.05

SEM=standard error of mean, 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	05	16.6
<30 years of age	30	06	17.1
>30 years of age	70	16	24.6
<5 years of DOD	42	08	14.5
>5 years of 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 subjects

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

Prot= proteinuria, DOD= duration of diagnosis, mg/24hrs= milligram/24hours, p-value is between the groups.

Discussion

The present study shows the overall 22% of the patients have diabetes related proteinuria, with 17% males and 5% females. After 5 years' duration, the frequency of diabetes related proteinuria increases to 31%. Stephenson et al reported that type 1 and type 2 diabetic patients had similar prevalence rates of proteinuria [10]. In type 1 diabetes, proteinuria is associated with nephropathy and renal failure [11], while in type 2 diabetic patients proteinuria is widely associated with cardiovascular rather than renal disease [12]. Among Europeans, diabetic nephropathy is reported to develop in 35% of patients with type 1 and 3%–15% of patients with type 2 diabetes [13]. Prevalence rates would of course vary widely depending on the methodology and definitions used for proteinuria. Fabre et al reported a prevalence of 48% with abnormal protein excretion (>150 mg in 24 hours) among 510 type 2 diabetic patients [14].

Studies from the UK have shown that among migrant Asian Indians, the prevalence of both diabetic and "nondiabetic" renal disease is higher compared with Europeans [15]. John et al, in a report from Vellore in southern India found that 8.4% of patients had persistent proteinuria (over 500 mg in 24 hours.[16]

Vijay et al, working at another diabetes centre at Chennai, found a much higher prevalence of proteinuria (18.7%).[17] However the later study was confined to inpatients, that is, patients admitted to hospital. 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 our 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 [18]. The recent Diabetes Control and Complications Trial Research Group [18] and UK

Prospective Diabetes Group studies have shown the impact of blood glucose control on reducing risk of retinopathy and nephropathy [19].

Conclusion

In conclusion, given the large number of individual with diabetes is increasing, the number of diabetic nephropathy 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.

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