

Prevalence of Nephropathy in Presymptomatic Phase of Undiagnosed Type-2 Diabetes Mellitus

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ABSTRACT

Background: This study was conducted to find out nephropathy in asymptomatic and previously undiagnosed patients of type 2 diabetes mellitus.

Method: A cross sectional descriptive study comprising of 300 subjects was carried out over a period of 3 year at our institute. Blood samples for fasting, postprandial blood sugar and renal function were collected; urine analysis for proteinuria; and HbA1c and body mass index estimated were carried out. All the subjects were evaluated for other confounding factors like smoking and hypertension.

Results: Diabetic nephropathy was detected in 75 out of 300 newly diagnosed DM patients. Macroalbuminuria and microalbuminuria was seen in 66 and 9 patients respectively. Forty one (24.1%) out of total 165 male patients; and 34 (25.1%) out of total 135 female patients had nephropathy. In our study diabetic nephropathy had statistically significant association with both HbA1c (p-0.001) and hypertension (p-0.001). BMI had no significant association with nephropathy (p-0.625).

Conclusion: This study shows significantly high prevalence of diabetic nephropathy among undiagnosed asymptomatic diabetic patients. The findings highlight the requirement for regular health evaluation and laboratory workup especially to look for asymptomatic hyperglycemia to detect and treat DM in early stage and prevent complications.

Keywords: Nephropathy, Undiagnosed, Presymptomatic, Diabetes Mellitus (DM), Microvascular Complications,

INTRODUCTION

Diabetes mellitus, a group of metabolic disease characterized by hyperglycemia, leads to significantly higher morbidity and mortality in diabetic patients compared to general population. ⁽¹⁾ DM is one of the largest health problems affecting the world. Population affected with DM is rising all over the world especially in middle and low income countries like India. The number of people with DM has gone up from 108 million in 1980 to 422 million in 2014. ⁽²⁾ There is variable prevalence of diabetes mellitus in different geographic regions. Compared to other regions Asian countries have higher (>10%) prevalence of DM in general population. ⁽³⁾

If diabetes mellitus remains untreated, it leads to various microvascular and macrovascular complications. Problem is further compounded by the fact that DM does not cause overt symptoms in early stage. As a result, many patients who have developed hyperglycemia remain symptom free for several years. During this presymptomatic phase of DM, many individuals develop one or other diabetes related vascular complications. Subsequently, after a variable period of several years asymptomatic hyperglycemia leads to overt symptoms or various symptomatic vascular complications. ⁽⁴⁾ Sizeable number of individuals in presymptomatic phase of hyperglycemia develops various microvascular or macrovascular complications. Microvascular complications due to DM may affect peripheral nervous system,

kidney or retina. During presymptomatic phase of hyperglycemia neuropathy has been seen in up to 44.24%, retinopathy in up to 24% and nephropathy in up to 50% individuals. (5)

Diabetic nephropathy remains a major cause of morbidity and mortality for persons with either T1DM or T2DM. Studies have shown variable prevalence of diabetic nephropathy at the time of diagnosis of DM. Diabetic nephropathy at the time of first diagnosis of DM has been reported from 2.8% to 20% in patients with newly diagnosed type 2 diabetes mellitus; (6,7) and a further 30% to 40% develop diabetic nephropathy, mostly within 10 years of diagnosis. Nephropathy is the commonest complication in diabetic patients and leading cause of death among end stage renal disease patients. (8-9)

In order to prevent complications, it is imperative that diabetes mellitus or presymptomatic hyperglycemia be detected in the early stage itself. Then only diabetic complications can either be prevented or treated to decrease the pace of progression of the disease and its further complications.

OBJECTIVES

This study was conducted to ascertain the prevalence of diabetic nephropathy in patients who were previously asymptomatic and were first time diagnosed to have type 2 diabetes mellitus.

METHODOLOGY

Adult patients who were admitted or who attended the outdoor department of general medicine at our institute and found to have hyperglycemia without prior diagnosis of diabetes mellitus were included in the study. It was a cross-sectional descriptive study carried out over a period of 3 years from July 2015 to June 2018. Total of 300 patients with first time hyperglycemia comprised the study sample size. Patients with prior diagnosis of DM and other confounding factors likely to alter kidney function or urinary protein like pregnancy, acute or chronic kidney disease

and urinary tract infection were excluded from the study.

Method of Collection of Data: Blood sugar (fasting and postprandial), urine analysis for proteinuria (microalbuminuria or macroalbuminuria), HbA1c and renal function test were carried out. Microalbuminuria was estimated by nephelometry. Microalbuminuria was defined as a mean urine albumin concentration more than or equal to 25 mg/day by nephelometry on three consecutive days. Body Mass Index (in kilograms by height in metres squared) and gender of the patients were noted. Associated medical conditions like hypertension, history of any addiction like smoking or alcohol were recorded. All the data was analysed with SPSS software. Various statistical parameters were calculated. Statistical association and its significance between various variables were calculated using student's t test and chi square test.

RESULTS

The age distribution of our study sample was from 25 years to 81 years. The mean age of the patients was 49.15 and the Standard deviation was 12.574. Half of the patients are clustered between 34-58 years of age. Out of a total of 300 patients with newly detected diabetic patients, 55% (165) were males and 45% (135) were females.

In our study there were 125 patients who had history of smoking. All smokers were male (125 out of 165 male patients). Twenty five percent patients (75 out of 300 patients) had diabetic nephropathy. There was no significant difference in the incidence of nephropathy between the diabetic individuals who smoke and the diabetic individuals who did not smoke (p-value: 0.259).

Out of 300 patients 87 had hypertension. Seventy two patients had stage-1 hypertension and 15 had stage-2 hypertension; and 129 had pre-hypertension. Eighty four patients had normal blood pressure. Out of 87 hypertensive patients 45

had diabetic nephropathy but out of 213 normotensive patients only 30 had nephropathy. Diabetic patients with associated hypertension had higher prevalence of nephropathy (p-value less than 0.001) as compared to those diabetic patients who did not have associated hypertension. Table No. 1

Table No. 1: Relationship between Hypertension and Diabetic Nephropathy

	Hypertension	Diabetic Nephropathy	
		Absent	Present
NO	213	183	30
YES	87	42	45
Total	300	225	75

Table No.2: BMI and its association with Nephropathy

BMI groups	No.	Mean	Std. Deviation	Diabetic Nephropathy	
				A	P
<18	3	17.5	0	3	0
>30	24	32.51	0.488	17	7
19-25	117	23.01	1.692	91	26
26-30	156	25.92	1.001	114	42
Total	300	24.73	3.187	225	75
Chi-Square Value				1.761	
p-value				0.625	

In our study 156(52%) patients were overweight, 24(8%) were obese, 1% were underweight and 39% were normal. There

Table No. 3: Relationship between gender and nephropathy

Gender	Total	Nephropathy					
		Microalb		Macroalb		Absent	
Female	135	27	20.0	7	5.1	101	74.8
Male	165	39	23.6	2	1.2	124	75.1

Microalb=Microalbuminuria; Macroalb=Macroalbuminuria

HbA1c analysis showed that 96% (288 out of total 300 patients) had HbA1c above 6.5. Twelve patients (4 percent of the patients) had a HbA1c of less than 6.5, 99 patients (33 percent of the patients) had a HbA1c between 6.5 and 7.4, 87 patients (29 percent of the patients) had a HbA1c between 7.5 and 8.4, 48 patients (16 percent of the patients) had a HbA1c between 8.5 and 9.4 and 54 patients (18 percent of the patients) had a HbA1c greater than or equal to 9.5. Table No. 4

Table No. 4: HbA1c distribution trends

HbA1c	N	Mean	Std. Deviation
<6.5	12	5.986	.0577
6.5- 7.4	99	9.991	.2753
7.5- 8.4	87	7.899	.1478
8.5- 9.4	48	8.908	.1624
>9.5	54	9.887	1.0410
Total	300	8.534	1.3912

was no statistically significant association between BMI and prevalence of diabetic nephropathy in our study (p value: 0.625).(Table No. 2)

Data was analysed to find out relationship between gender and diabetic nephropathy. Out of 300 subjects 75 had evidence of diabetic nephropathy. Among patients detected to be diabetic nephropathy (25 % of our study population) 66 had microalbuminuria and 9 had macroalbuminuria. Out of 165 male patients 41 (24.8%) had nephropathy. Out of 41 male diabetic patients with nephropathy, 39 (23.6%) had microalbuminuria, 2 (1.2%) had macroalbuminuria. Out of 165 male patients with diabetes mellitus 124 (75.1%) had no proteinuria. Among 135 female patients 34 (25.1%) had diabetic nephropathy. Among 34 diabetic female patients with associated nephropathy 27 (19.9%) had microalbuminuria, 7 (5.1%) had macroalbuminuria. Out of total of 135 female diabetic patients 101 (74.8%) patients had no proteinuria. Table No. 3

Further analysis was carried out to find out association between level of HbA1c and diabetic nephropathy. It was found that with increasing level of HbA1c there was higher prevalence of diabetic nephropathy (p value <0.001).Table No. 5

Table No. 5: Relationship between HbA1c and diabetic nephropathy

HbA1c groups	Total	Diabetic Nephropathy	
		Absent	Present
<6.5	12	12	0
6.5- 7.4	99	84	16
7.5- 8.4	87	71	12
8.5- 9.4	48	32	15
>9.5	54	26	32
Total	300	225	75

DISCUSSION

Diabetes mellitus is emerging as a medical emergency all over the world especially in Asian-Pacific region with rapidly increasing prevalence of diabetes mellitus in the population. Currently 415 million people in the world are diabetic and this figure is likely to increase to 642 million by the year 2040. ⁽¹⁰⁾ Diabetes mellitus is a major health problem all over the world. DM leads to various microvascular and macrovascular during its natural course. With increasing duration of the disease diabetic complications also increase. This is especially important because many individuals remain asymptomatic in the early stage of DM. During this presymptomatic phase of hyperglycemia of several years significant number of patients develops various vascular complications. This study was carried out over a period of 3 years including 300 newly detected type 2 diabetes patients (165 male and 135 female) to find out the prevalence of nephropathy at initial diagnosis of type 2 diabetes. The mean age of the diabetics in our study was 49.15 ± 12.574 . The maximum incidence of diabetes was seen in patients who were between 35-55 years of age. The mean age in our study correlates closely to the studies done by Manish et al (mean age 56). ⁽¹¹⁾

In our study 52% of patients were overweight and 8% were obese. 53.5% (33.8% females and 19.7% males) were overweight and 11.3% (8.5% men and 2.78% women) were underweight in Nambuya AP et al study. ⁽¹²⁾ The mean fasting blood glucose in our study was 176.15 with a standard deviation of 55.9 and the average PPBS was 283.7 with a standard deviation of 73.8. In the study done by Cathlineau et al, the mean FBS was 182 with a standard deviation of 48 and the PPBS was 209 with a standard deviation of 68. ⁽¹³⁾ Once the diabetic nephropathy develops in diabetic patients it leads to progressive decline in renal function and ultimately causes end stage renal disease. Patients with kidney disease have higher

incidence of cardiovascular morbidity and mortality compared to those individuals who do not have nephropathy. ⁽¹⁴⁾ It is imperative to detect and diagnose diabetes in early stage to prevent complications. Due to several year of presymptomatic hyperglycemia significant number of people develops various microvascular diabetic complications including nephropathy before the diagnosis of DM. Studies have shown variable rate of prevalence 24%, 2.8% and 20% of diabetic nephropathy at the time of initial diagnosis of type 2 DM; ⁽⁵⁻⁷⁾ and a further 30% to 40% develop diabetic nephropathy, mostly within 10 years of diagnosis. In our study the overall incidence of Nephropathy (both microalbuminuria and macroalbuminuria combined) was 25%. There is huge variability in the rate of prevalence of nephropathy in newly detected diabetic patients from Asian-Pacific region ranging from 14.2% in Iran, 24.2% in Pakistan, to 36.3% in India. ⁽¹⁵⁾ Some studies have shown much higher prevalence of diabetic nephropathy (47.4%) at the time of diagnosis of DM. ⁽¹⁶⁾ Ramachandra et al found nephropathy in 16.5% of patients. ⁽¹⁷⁾

Hypertension is more common in diabetic compared to general population. The prevalence of hypertension in newly diagnosed diabetic cases in our study was 29% (87 out of total 300 patients). Presence of hypertension had significant association with prevalence with diabetic nephropathy. Further analysis of data revealed no significant association between smoking, body mass index and prevalence of nephropathy in newly diagnosed type 2 diabetes patients in our study.

CONCLUSION

This study highlights that significant number of patients develop microvascular complications in presymptomatic phase of hyperglycemia. Our study shows that before being diagnosed as diabetic one quarter of patients had already developed nephropathy during asymptomatic period of hyperglycemia. There is need for regular

community and hospital based programs to screen individual to detect asymptomatic hyperglycemia so that complications due to diabetes can either be prevented or treated in early stage itself. This may help in decreasing the burden of diabetes related morbidity and mortality.

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