A study of prevalence of microalbuminuria in recently detected type 2 diabetes and its relation to hypertension, dyslipidaemia and obesity

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ABSTRACT

Background: Microalbuminuria is one of the earliest markers of diabetic nephropathy, and if not recognized and treated early it may lead to diabetic nephropathy resulting in chronic renal failure. **Aims and Objective:** The aim of the current study was to find out the prevalence of microalbuminuria among newly detected Type 2 diabetic patients and also compare prevalence of microalbuminuria in patients with or without hypertension, dyslipidaemia and obesity. **Materials and Methods:** In this retrospective study, we analysed 90 patients with new onset type 2 diabetes mellitus. We divided the patients into two groups, group 1 with comorbidities like hypertension, dyslipidaemia and obesity (50 patients) and group 2 without comorbidities (40 patients). We analysed urinary microalbumin level in all patients and compared the prevalence of microalbuminuria between group 1 and group 2. **Results:** In our cohort of 90 patients, urinary microalbuminuria was found in 30 patients (33.3%). When we divided these nephropathy patients to group1 and group 2, we observed that group 1 with comorbidities had higher percentage of nephropathy patients i.e 24 out of 50(48%). Group 2 with 40 patients had only 6 patients with microalbiminuria ie 6 out of 40(15%). Incidence of microalbiminuria was higher in patients with hypertension, dyslipidaemia and obesity. **Conclusions:** We conclude that incidence of microalbiminuria is much more common in newly diagnosed type 2 diabetes. We also conclude that hypertension, obesity and hypercholesterolemia are risk factors for nephropathy and urinary microalbuminuria appears to be much more sensitive than serum creatinine as screening tool to detect diabetic nephropathy.

Key words: Diabetic nephropathy; Hypertension; Hypercholesterolemia; Microalbuminuria

INTRODUCTION

Diabetes Mellitus (DM) is one of the most common non communicable diseases in developed nations. But now a days it is becoming very common in developing countries, may be because of change in lifestyle and economic prosperity. India is second only to China in number of diabetes cases and has been rightly called "Diabetes capital of the world. If number increases in the same pattern, number of patients with diabetes expected to cross 79.4 million by year 2030.[1]

By the time patient is diagnosed to have diabetes, he/she is already developed complications like diabetic nephropathy, retinopathy and neuropathy, so rightly called the silent killer. In India diagnosis is usually delayed compared to developed nations may be due to ignorance, delayed presentation, alternative forms of treatment and lack of facilities in rural area. Microalbuminuria, may start very early in the disease and is one of the first markers for diabetic nephropathy and is an independent risk factor for development of cardiovascular complications. Microalbuminuria is defined as the excretion of 30-300 mg of albumin per 24 hours or

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30-300 mcg/mg creatinine in spot urine sample.[2] Albumin below 30 mg per 24 hours or less than 30mcg/gm of creatinine is considered as normoalbuminuria. We know that diabetic nephropathy and microalbuminuria are one of the strong predictors of cardiovascular and overall morbidity and mortality in patients of diabetes, and hence we need to give importance to early detection of same. Usually urinary microalbuminuria represents a more generalized vascular damage than just renal microvascular damage alone. We have noticed exponential increase in number of patients with end stage renal disease in last decade due to increase in incidence of diabetes. About 30% type 2 diabetic patients with microalbuminuria progress to overt nephropathy if no treatment is given.[2] The mortality rate in patients with proteinuria found to be 40 times more compared to patient without proteinuria and diabetic patient with renal disease has 17 times higher mortality rate compared to non-diabetic person.[3] It was proved that patients of Asian origin (52.6%) have more prone to develop diabetic end stage renal disease compared to Caucasian population (36.2%). Many research papers found that incidence and prevalence of nephropathy varies between geographic locations and ethnicity like they have shown that risk is more in Mexican Americans, Asians, Pima Indians and African people.[4]

Urinary microalbuminuria is an important clinical parameter since early diagnosis and treatment at this stage can revert the pathological process in the kidney to normal. This is more important in India because diagnosis of diabetes is much more delayed in India compared to western world. A study is indicated to find out what is the prevalence of diabetic microalbuminuria, what are the risk factors and if targeting these factors benefit the patients or not. Hence, this study aims at determining the prevalence of urinary microalbuminuria and impact of risk factors like Hypertension, Obesity and Hypercholesterolemia on albuminuria.

Objective of this study were to find the prevalence of microalbuminuria in newly detected Type 2 DM patients and to study the effect of Hypertension, Hypercholesterolemia and Obesity on prevalence of microalbuminuria in these group of patients.

MATERIALS AND METHODS

This was a retrospective study carried out from October 2016 to September 2018 at K S Hegde Medical College and speciality hospital, a tertiary care referral centre. We had total 90 patients enrolled for the study out of which 49 patients were male and 41 were female. The mean age was 49.24 years, with 28 being the youngest and 70 being the oldest.

The criteria for diagnosing DM are the same as given by WHO and ADA based on oral Glucose Tolerance Test is as follows.[2]

A fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, or

A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT), or

A random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycaemia or hyperglycemic crisis, or

A haemoglobin A1c (HbA1c) level of 6.5% (48 mmol/mol) or higher

We have divided the patients in 2 groups. Group 1: Diabetic patients with hypertension and/or obesity and/or hypercholesterolemia (50 patients). Group 2: Diabetic patients without any of the above-mentioned factors (40 patients).

The inclusion criteria of selection of subjects were as follows- Age more than 20 years. Newly detection of diabetes or within 6 months at the time of enrolment in study.

The exclusion criteria was- Patients having type 1 diabetes of less than 20 years of age with primary and secondary renal diseases. Also patients with fever, pregnant women, urinary tract infection, congestive cardiac failure, and known case of diabetes for more than 6 months were excluded. Those patients already detected to having renal failure, Hypertensive with ACE inhibitors or angiotensin receptor blockers were also excluded from the study.

Parameters recorded

Microalbuminuria can be diagnosed from a 24-hour urine collection (between 30-299mg/24 hours) or, more commonly, from elevated concentrations in a spot urine sample (30 to 299mg/L) as done by us.

A complete history, clinical examination and investigation profile were copied from the medical records of all these patients.

BMI (Body Mass Index): BMI was measured by the formula of dividing weight in kgs by height in meter square. Patient were classified based on BMI into 4 groups[5]

BMI (Kg/m2)   ≤18.4 - Underweight

18.5-22.9 - Normal
23-24.9- Over weight
> 25 -Obese

Hypertension:- When there was a history of hypertension, drug therapy for the hypertension or blood pressure recorded was more than 140/90mmHg on 3 consecutive occasions.[5] Complete lipid profile was done for hypercholesterolemia. Then author studied both the groups for prevalence of diabetic nephropathy and analysed if there was a statistical difference in between these groups and inside the group 1 itself.

Blood sugar Control was graded based on HbA1c level as follows[6,7]:
Good control: HbA1c <7
Fair control: HbA1c 7-8
Poor control: HbA1C >8
Criteria for diagnosis of dyslipidaemia[2]
Total Cholesterol - more than 200 mg/dL
Low-density lipoproteins (LDL) - more than 100 mg/dL
Triglycerides - more than 150 mg/dL
High-density lipoproteins (HDL) Less than 40 mg/dL in male and less than 50 in female

Statistical analysis: The statistical analysis was carried out using Statistical Package of Social Science (SPSS 2015). All quantitative variables were estimated using measures mean and standard deviation. Student 's t test was used to compare means between two groups. P value was considered significant at a level of < 0.01. We obtained institutional ethical committee permission for the study.

RESULTS

In this study, out of 90 total patients, 30 patients were detected to have Diabetic nephropathy (33.3%). In group 1, out of 50 patients 24 (48%) patients had diabetic nephropathy, while in group 2; out of 40 patients 6 (15%) patients had diabetic nephropathy (Table 1).

A subgroup analysis was done within Group 1 with regards to multiple co-morbidities, showing increasing number of patients affected with increasing co morbidities (Table 2).

Hypertension was found in 53% of patients with microalbuminuria where as it was found in only 10% of patients without microalbuminuria (Table 2). Dyslipidaemia was seen in 60% patients, while obesity was seen in 70% of patients with microalbuminuria. In patients without microalbuminuria it was 15% and 25% respectively for dyslipidaemia and obesity. Thus, our study confirms that patients with comorbidities like hypertension, dyslipidaemia and obesity have higher probability of developing nephropathy compared to patients without these comorbidities.

The data shows (Table 3) that more than 50% of patients had HbA1c level of more than 8 at the time of presentation. Only one patient with HbA1c <7 had microalbuminuria (10%). In the group were HbA1c was between 7-8, we had 6 patients with microalbuminuria (21.4%). But patient with HbA1c > 8, we had 24 patients with microalbuminuria (46.1%). This confirms that patients with uncontrolled diabetes are more prone to develop microalbuminuria hence nephropathy. The data (Table 3) also shows that maximum number of (80%) patients with microalbuminuria are having their HbA1c >8 and was statistically significant (p<0.05).

Both mean systolic and mean diastolic blood pressure were in linear relationship with urinary albumin level and were found to be statistically significant ($P < 0.01$) (Table 4). This proves that patient with higher systolic and diastolic blood pressure are more likely to develop microalbuminuria compared to normal blood pressure.

The above table shows that patients with higher BMI have higher probability of developing microalbuminuria

Table 1: Patients detected with nephropathy in both groups

	Group 1 (50patients)	Group 2 (40 patients)	Total patients
With nephropathy	24(48%)	6(15%)	30
Without nephropathy	26	34	60
Total patients	50	40	90

Table 2: Patients with other co morbidities

	Hypertension	Dyslipidaemia	Obesity
Microalbuminuria (30)	16(53.3%)	18(60%)	21(70%)
No Microalbuminuria (60)	6(10%)	9(15%)	15(25%)

Table 3: HbA1c with the incidence of microalbuminuria

HbA1c	normoalbuminuria	microalbuminuria	Total no	P value
<7	10	1	11	
7-8	22	5	28	
>8	28	24	52	<0.05
Total	60	30	90	

Table 4: Mean blood pressure in relation to microalbuminuria

Blood pressure	Normoalbuminuria	Microalbuminuria	P value
Mean systolic BP (mmHg)	123.57 ±10.4	137.69±10.57	<0.05
Mean diastolic BP (mmHg)	77.4 ±5.87	84.47± 6.96	<0.05

compared to normal BMI patients (Table 5). The difference was shown to be statistically significant (P< 0.01). This shows that obesity is an independent risk factor for development of albuminuria

Table 6 shows that mean total cholesterol and LDL cholesterol are higher in patients with microalbuminuria when compared to normoalbuminuria and was found statistically significant. Though triglyceride level was higher in macroalbuminuric patients, it was not statistically significant. The findings (Table 6) reiterates the fact that control of dyslipidaemia is of paramount important in reducing the complications of diabetes especially nephropathy.

We also found that few patients had elevated creatinine level along with microalbuminuria. This proves that patient may present with renal failure at the time of diagnosis of diabetes mellitus.

DISCUSSION

Diabetic nephropathy is a dreaded complication of diabetes mellitus and early detection is of paramount importance. In this study, out of 90 total patients, total 30 patients were detected to have diabetic nephropathy ie prevalence is 33.3%. In group 1 with comorbidities like hypertension, dyslipidaemia and obesity, out of 50 patients 24 (48%) patients had diabetic nephropathy, while in group B, out of 40 patients only 6(15%) had diabetic nephropathy

In Table 7, we can see that prevalence of diabetic nephropathy varies from 15% to 54% in different studies. The variation in prevalence may be due to ethnicity, method of collection of urine albumin, number of collections, other illness, and study methodology, number of patients with hypertension, obesity and dyslipidaemia. Relatively higher prevalence of diabetic nephropathy detected in this study may be due to many reasons like ignorance of general public and delayed presentation to physician. These factors responsible for late diagnosis of DM and patient will be suffering from diabetes without treatment for years which ultimately result in higher prevalence diabetic nephropathy.

In this study, we found 24 out of 50(48%) patients in Group 1 (those having hypertension and/or hypercholesterolemia and/or obesity) to have diabetic nephropathy. While in Group B (without any of the 3 factors), only 6 out of 40(15%) patients were detected to have diabetic nephropathy.

The microalbuminuric patients had significantly increased systolic and diastolic blood pressure compared to

Table 5 : BMI in relation to urinary microalbuminuria

	Microalbuminuria	Normoalbuminuria	P value
BMI	26.5±3.7	24.2±2.6	<0.01

Table 6: Lipid profile in patients microalbuminuria

Lipid profile	Microalbuminuria	Normoalbuminuria	P value
Total cholesterol	193.4±49.6	170.5±39.1	<0.01
LDL	125.7±40.3	101.2±30.7	<0.01
Triglyceride	165.7±48.6	144.8±45.7	Not significant

Table 7: Year wise studies showing the prevalence of diabetic nephropathy in newly detected diabetes mellitus

Author	Year of study	Prevalence
Niskanen et al[8]	1990	19%
Yajnik et al[9]	1992	23%
Ghai et al[10]	1994	25%
Cathelineau et al[11]	1997	29.6%
Vijay et al[12]	1998	21%
Viberti et al[13]	2002	15.2%
Sosenko et al[14]	2002	18%
Annemieke et al[15]	2003	26.7%
Unuigbe et al[16]	2004	49.2%
Chowta N K et al[17]	2009	37%
Bhashkar et al[18]	2011	54,09%
Debbarma et al[19]	2015	20.19%
Vitan patel et al[20]	2018	43%
Present study	2020	33.3%

normoalbuminuric subjects (P < 0.01). John et al[21] reported that male gender, elderly, longstanding diabetes, uncontrolled blood sugar and elevated blood pressure as risk factors of microalbuminuria. Agarwal et al[22] reported that diabetes patients with hypertension have 60% chance of development of nephropathy. Another study by Vijay et al[12] showed that duration of diabetes, blood pressure, age of the patient, and serum creatinine to be associated with proteinuria

This study also proves that patients with higher HbA1c at the time of presentation had higher prevalence of nephropathy (P<0.01). Patients with HbA1c > 8 had 46.1% prevalence of microalbuminuria. A study by Gupta et al[22] showed that patients with higher HbA1c had higher incidence of diabetic nephropathy.

In our study mean BMI of normoalbuminuric patients was 24.2±2.6kg/m² and that of microalbuminuric patients was 26.5±3.7kg /m². Therefore, it is beyond doubt that obese patients have higher incidence of microalbuminuria. Kohler et al showed that increased risk of microalbiminuria is

seen in patients with poor glycemic control, endogenous hyperinsulinemia, high blood pressure, elevated triglyceride levels, and obesity.[23] Thus, we conclude that diabetic patients with risk factors of hypertension and/or obesity and/or hypercholesterolemia are at a much greater risk of developing diabetic nephropathy, at the onset. Even without the risk factors, we found that the prevalence of microalbuminuria at onset of type 2 diabetes mellitus was 15%, which cannot be ignored. While the 48%% prevalence associated with these risk factors is also to be taken with great concern. We need to educate the general public, medical fraternity and government regarding early diagnosis and treatment to address this problem.

Our study has many drawbacks. Firstly, small sample size, retrospective in nature makes this study less powerful to do complete subgroup analysis of every risk factor associated with nephropathy. Further studies are needed to find out importance of each risk factor and combination of different factors on nephropathy prevalence.

This highlights the importance of performing the urinary micro albumin in all patients at the time of diagnosis and it may be the most sensitive tool to diagnose incipient diabetic nephropathy. This also brings to our notice, the common practice of doing only creatinine at diagnosis and follow up of patients with diabetes to assess renal function.

CONCLUSION

We conclude that micro albuminuria is important predictor of diabetic nephropathy and is reasonably high at the onset of diabetes mellitus. Our study also showed that its prevalence is high in type 2 DM with those associated comorbidites like hypertension, obesity and dyslipidemia.

ACKNOWLEDGEMENT

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