Original Research Article

Study of correlation of microalbuminuria with glycemic status in diabetic nephropathy at a tertiary care center

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Abstract

Background: Diabetic nephropathy (DN) develops in patients with several years' medical history of diabetes and renal failure. HbA1c is currently accepted as the most informative biomarker of glycemic control in subjects with diabetes and is highly prognostic for long-term diabetes-related complications such as microalbuminuria. In present study we aimed to correlate microalbuminuria with glycemic status in patients with diabetic nephropathy. **Material and Methods:** Present study was prospective, cross sectional type conducted in patients with Type 2 diabetis melitus with diabetic nephropathy , with HbA1c value >6.3%. **Results:** The study is conducted in 120 diagnosed cases of Type II Diabetes Mellitus with diabetic nephropathy. Mean age of patients was 53.25 ± 6.11 years. Male to female ratio was 1.26 :1. Out of total 120 patients, 64 (53%) had Normo-albuminuria while 56 (47 %) had micro-albuminuria. With increasing duration of disease, increase in patients with Micro-albuminuria was noted. In patients with less than 5 years duration 79 % patients had Normo-albuminuria while 68 % had micro-albuminuria when duration of disease was more than 15 years. In patients with glycated hemoglobin less than 8, 92 % patients had normo-albuminuria while 92 % had micro-albuminuria when glycated hemoglobin was more than 12. Duration of disease was positively corelated with micro-albuminuria. Similarly urinary albumin excretion was positively correlated with HbA1c and was statistically significant. **Conclusion:** Microalbuminuria in diabetes, which represents an earlier phase in the development of clinical nephropathy, increases with increased duration of diabetes mellitus as well as increased levels of glycated hemoglobin.
Key Words: microalbuminuria.

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INTRODUCTION

Diabetes Mellitus (DM) is a chronic, widely prevalent endocrine disease, which is characterized by hyperglycemia due to defects in insulin secretion, insulin action or both1. It is also estimated that there were 415 million people with DM worldwide in the year 2015 and this number is expected to increase to 640 million people by 20402. It is also expected that much of this increase in prevalence rate will occur in developing countries. As the number of persons with diabetes increases, the development of microvascular complications like retinopathy, nephropathy and neuropathy also rises. According to a report by the World Health Organization (WHO), the prevalence rates of nephropathy after 15 years of diabetes ranged between 17.7 and 56.6% in men and between 11.9 and 71% in women3. Diabetic nephropathy (DN) develops in patients with several years' medical history of diabetes and renal failure. However, research shows that patients with type 1 diabetes progress early to ESRD as compared to those with type 2 DM. HbA1c is currently accepted as the most informative biomarker of glycemic control in subjects

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with diabetes and is highly prognostic for long-term diabetes-related complications such as microalbuminuria[4]. Microalbuminuria has also emerged as an important risk factor for left ventricular hypertrophy, myocardial infarction, stroke, peripheral vascular diseases and retinopathy, independent of blood pressure. In present study we aimed to correlate microalbuminuria with glycemic status in patients with diabetic nephropathy.

MATERIAL AND METHODS

Present study was prospective, cross sectional type conducted in out-patient department of Medicine, XXX medical college, XXXX. Study duration was 6 months (April 2019 to September 2019). Institutional ethical committee permission taken for present study.

Inclusion criteria - Patients with Type 2 diabetis melitus, with HbA1c value >6.3%, with diabetic nephropathy willing to participate in present study.

Diabetic nephropathy is defined by increased urinary albumin excretion (UAE) in the absence of other renal diseases. It is categorized into two stages: microalbuminuria (UAE ≥ 20 microg/min and ≤ 199microg/min) and macroalbuminuria (UAE≥200 microg/ min)5.

Exclusion criteria - Patients with overt albuminuria (>350 mg/ day), congestive cardiac failure, urinary tract infection, pregnant patients, patients confined to bed for more than two weeks, and patients on ACE inhibitors for hypertension were excluded from the study.

Written informed consent was taken from patients for participation in present study. Demographic, history (medical, family, dietary), clinical details (duration of disease, complications) were collected at the time of participation in present study. A thorough physical examination was done. All relevant laboratory, clinical records, drug intake were reviewed. Other causes for microalbuminuria like heavy metal poisoning, connective tissue disorders, and chronic NSAIDs use were also ruled out in the selected patient

HbA1c was estimated using NyCocard boronate affinity assay. Before performing microalbumin test, the urine sample was tested by uristrip method to exclude overt proteinuria from this study. Microalbuminuria was diagnosed if albumin was between 20-200 mg/L. Microalbumin was measured in spot urine sample using NyCocard immunometric assay. Statistical analysis was done using SPSS, Pearson's correlation was applied to observe associations of microalbuminuria with duration of diabetes and HbA1c level. All p-values <0.05 were considered as statistically significant.

RESULTS

The study is conducted in 120 diagnosed cases of Type II Diabetes Mellitus with diabetic nephropathy, irrespective of duration of Diabetes and sex taken randomly from the Outpatient and admitted patients under department of Medicine. Microalbuminuria includes a range of urinary excretion of albumin of 20 to 200 mg/L or 20 to 200 µg/min. While normo-albuminuria considered as urinary excretion of albumin less than 20 mg/L or less than 20 µg/min. patients with macroalbuminuria were already excluded. Patients were from age group of 40-60 years, mean age of patients was 53.25 ± 6.11 years. Male to female ratio was 1.26 :1. Out of total 120 patients, 64 (53%) had Normo-albuminuria while 56 (47 %) had micro-albuminuria (Table 1).

Table 1: Gender wise distribution of proteinuria

	Normo-albuminuria	Micro-albuminuria	Total
Male	36 (54 %)	31 (46 %)	67
Female	28 (53 %)	25 (47 %)	53
Total	**64 (53 %)**	**56 (47 %)**	**120**

Urinary albumin excretion was compared with duration of diabetes. With increasing duration of disease, increase in patients with Micro-albuminuria was noted. In patients with less than 5 years duration 79 % patients had Normo-albuminuria while 68 % had micro-albuminuria when duration of disease was more than 15 years. (Table 2).

Table 2: Prevalence of microalbuminuria in relation to duration of T2DM

Duration (years)	Normo-albuminuria	Micro-albuminuria	Total
<5 years	22 (79 %)	6 (21%)	28
≥5-10 years	16(64 %)	9 (36%)	25
≥10-15 years	15 (45 %)	18 (55%)	33
≥15 years	11 (32 %)	23 (68%)	34
Total	**64 (53 %)**	**56 (47 %)**	**120**

We compared urinary albumin excretion with glycemic status of patients (HbA1c – glycated hemoglobin). With increasing values of glycated hemoglobin, increase in patients with micro-albuminuria was noted. In patients with glycated hemoglobin less than 8, 92 % patients had normo-albuminuria while 92 % had micro-albuminuria when glycated hemoglobin was more than 12 (Table 3).

Table 3: Prevalence of microalbminuria in relation to HbA1c level in T2DM

HbA1c level (%)	Normoalbuminuria	microalbuminuria	Total
<8	45 (92 %)	4 (8 %)	49
8.1-10	13 (54 %)	11 (46 %)	24
10.1-12	4 (18 %)	18 (82 %)	22
≥12	2 (8 %)	23 (92 %)	25
Total	**64 (53 %)**	**56 (47 %)**	**49**

We statistically compared urinary albumin excretion with duration of disease and HbA1c levels. Mean duration (years) of disease was 7.32 ± 3.19 in Normo-albuminuria patients while it was 9.27 ± 4.98 years in patients with micro-albuminuria. Duration of disease was positively corelated with micro-albuminuria. Similarly urinary albumin excretion was positively correlated with HbA1c and was statistically significant.

Table 4: Correlation microalbuminuria with duration of disease and HbA1c levels

Variable	Normo-albuminuria	Micro-albuminuria	P value
Mean duration (years)	7.32 ± 3.19	9.27 ± 4.98	Statistically significant
Mean HbA1c level (%)	7.35 ± 1.98	8.45 ± 2.09	Statistically significant

DISCUSSION

End-organ damage seen in dibetes melitus is maily due to microvascular changes. The magnitude of damage caused by these microvascular complications of diabetes stresses the need for sensitive markers of screening for retinopathy and nephropathy[6]. These microvascular complications are linked to the duration of diabetes mellitus, poor glycemic control and systolic hypertension[7]. Diabetic nephropathy also called as Kimmelsteil Wilson syndrome is characterized by a progressive increase in the excretion of protein particularly albumin, an early and continuing rise in blood pressure and a late decline in glomerular filtration rate (GFR) resulting in end stage renal disease. Staging of diabetic nephropathy is given in table-5.

Table 5: Staging of diabetic nephropathy

Stage	staging by Tervaert *et al.*	staging by Gheith *et al.*
1	Glomerular basement membrane thickening	From onset to 5 years. Borderline GFR, no albuminuria, hypertension. But kidney size increased by 20% along with an increase in renal plasma fow
2	Mild or severe mesangial expansion	From 2 years after onset with basement membrane thickening and mesangial prolieration, normal GFR and no clinical symptoms
3	Nodular sclerosis	5–10 years after onset with or without hypertension, with glomerular damage and microalbuminuria (30–300 mg/day)
4	Advanced diabetic glomerulosclerosis that includes tubulointerstitial lesions and vascular lesions	Irreversible proteinuria, sustained hypertension and GFR below 60 ml/min/1.73 m2
5		End-stage kidney disease with GFR<15 ml/min/1.73 m

Multiple studies shown that, the sensitive marker for the detection of diabetic nephropathy is to estimate excretion of microalbumin in urine10. Microalbuminuria has also emerged as an important risk factor for left ventricular hypertrophy, myocardial infarction, stroke, peripheral vascular diseases and retinopathy, independent of blood pressure. Strong evidence exists that improved glycemic control is effective at lessening the risks of nephropathy, retinopathy and neuropathy in diabetes. Although microalbuminuria is a confirmatory test for diagnosis of diabetic nephropathy, not all patients progress to macroalbuminuria. In fact, some patients may regress to normoalbuminuria[11]. Progression and regression of kidney disease in type 2 DM is highly variable as it is usually diagnosed with a secondary disorder, the onset of which is unrecorded. The UKPDS study reported microalbuminuria and reduced GFR in 38% and 29% patients respectively after a median follow-up of 15 years. In terms of progression, the same study reported a change from microalbuminurea–macroalbuminuria-ESKD at 2.8% and 2.3% per year respectively[12]. Microalbuminuria represents the simplest and most sensitive prognostic factor to evaluate the risk of overt nephropathy in diabetes, representing the first stage of progressive diabetic renal disease. However, it is not clear whether microalbuminuria represents an independent predictor or rather a marker of organ damage, since mechanisms linking microalbuminuria with end organ damage have not been fully explained[13]. Higher levels of HbA1C are associated with increased risk for development of microangiopathy in diabetic. This may be due to the fact that HbA1c has special affinity for oxygen thereby

causing tissue anoxia and plays a role in causation of micro and macroangiopathy. Shonima Venugopal and Uma M lyer showed statistically significant correlation of microalbuminuria and HbA1c level (p< 0.05)14. Manjrekar *et al* has reported gradual increase in prevalence of microalbuminuria with similar increase in HbA1c level.[15] Our results are similar with above studies. Meta-analysis for HbA1C Variability and the Risk of Renal Status Progression in Diabetes Mellitus16 indicated that HbA1C variability was independently associated with the development of microalbuminuria and the progression of renal status in both type 1 and 2 diabetes patients. Another analysis performed by Sugawara *et al*[17] also demonstrated that the intra-person standard deviation in A1C (A1C-SD) was an independent risk factor for the development of microalbuminuria in T2DM.

CONCLUSION

Microalbuminuria in diabetes, which represents an earlier phase in the development of clinical nephropathy, increases with increased duration of diabetes mellitus as well as increased levels of glycated hemoglobin. Regular screening for urinary microalbumin as well as HbA1c and good glycemic control is recommended to prevent diabetic nephropathy.

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