Microalbuminuria as an Earliest Predictor of Diabetic Nephropathy

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Abstract: *Diabetes mellitus is major health problem worldwidwe,characterised by persistent hyperglycaemia due to defect in insulin secretion, insulin action or both. Diabetic nephropathy is one of the major complications of diabetes mellitus.The present study aimed to asses urine microalbumin in patients of diabetes mellitus and diabetic nephropathy. This cross sectional study was undertaken in the Department of Biochemistry GMC and super speciality hospital Nagpur, Maharashtra.Urine microalbumin was assessed in diabetes mellitus (n=50), diabetic nephropathy (n=50) and healthy individuals(n=50).Mean of biochemical parameter were compared by performing repeated measures one way ANOVA(F-test) and Post hoc multiple comparison of mean of three groups by Bonferroni t-test.Urinemicroalbuminwas significantly higher in diabetes mellitus with diabetic nephropathy and diabetes mellitus without diabetic nephropathy patients as compared to control (p<0.001).There was slightly higher urine microalbumin observed in diabetes mellitus without diabetic nephropathy as compared to control. The difference was statistically non significant (p>0.05).Microalbuminuria is risk factor for diabetic nephropathy.so regular screening for microalbuminuria should be done to delay complication of diabetes mellitus*
Keywords: *Diabetes mellitus, Diabetic nephropathy, Urinemicroalbumin, microalbuminuria*

I. Iintroduction

The term diabetes mellitus describes a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both.[1]Diabetes leads to various complications such as coronary artery disease, peripheral vascular disease, stroke, neuropathy, diabetic nephropathy, retinopathy and diabetic foot. The global prevalence of diabetes mellitus is expected to increase from 4% in 1995 to 5.4% by the year 2025.[2] Diabetic nephropathy is one of the major complications of diabetes mellitus.

The classical definition of diabetic nephropathy is a progressive rise in urine albumin excretion, increasing blood pressure, leading to declining glomerular filtration and eventually end stage renal disease (ESRD). [3]Diabetes is the most common cause of kidney failure. Chronic kidney disease (CKD) and kidney failure can occur in uncontrolled as well as in controlled diabetes. ESRD is the final stage of chronic kidney disease. [4]The prevalence of diabetic nephropathy in India was less (8.9% in Vellore, 5.5% in Chennai) as compared to Asian Indians (22.3%) in the UK.[5] The prevalence of diabetic nephropathy in chronic renal failure patients in India was 30.3% followed by chronic interstitial nephritis (23%) and chronic glomerulonephritis (17.7%).[6]The impairment in kidney function over the time has been associated with initial glomerular filtration rate, initial urinary albumin excretion rate (UAE), hyperglycaemia and old age.[7]Microalbuminuria is a marker for diabetic nephropathy and cardiovascular disease in patients with both type I and type II diabetes mellitus.[8-11] The urine dipstick is a relatively insensitive marker for proteinuria, not becoming positive until protein excretion exceeds 300 to 500 mg/day so using a specific assay for albumin is a more sensitive technique.

One of the earliest markers of diabetic nephropathy is the presence of small amount of the protein albumin in the urine. This is called MAU or microalbuminuria (urinary albumin excretion of 30-300 mg/24 hours).The aim of the present study was to study the urine microalbumin in patients of diabetic nephropathy.

II. Materials And Method:

The present study has been carried out in Govt. medical college and hospital, Nagpur, India Jaunary 2011 to July 2012. The study protocol was approved by the Institutional Ethical Committee. Informed written consent was obtained from all the study subjects enrolled in the study. Study sample was consisted of total of 150 individuals; 50 diagnosed cases of diabetes mellitus with diabetic nephropathy irrespective of type I and type II diabetes (Cases) in the age group of 30-70 years and 50 patients of diabetes mellitus of either sex, admitted in kidney unit of medicine department in the institute and Nehrology department in GMC and super speciality hospital, Nagpur and 50 age and sex matched controls were also selected for study.

2.1 Inclusion criteria
- Age > 30 yrs and < 70 yrs
- Registered cases of diabetic mellitus with and without diabetic nephropathy irrespective of type I and type II diabetes mellitus.

2.2 Exclusion criteria
- Age < 30 yrs and >70yrs
- Patients with gestational diabetes
- Individual with urinary tract infection
- Patients with provisional diabetes or impaired glucose tolerance
- Patients having any mental disorder
- Individuals having any past medical history of various vascular complications before the diagnosis of diabetes mellitus such as ischemic heart disease, cerebral and peripheral vascular diseases, congestive heart failure and renal failure
- Those who did not consent to participate in the study.

2.3 Specimen collection and preservation:
2.3.1 Urine sample:
2ml urine sample was collected in plain bulb. Microalbumin in urine was estimated on the same day.
2.3.2 Blood sample
2ml venous blood was collected in fluroid bulb for fasting blood glucose level after an overnight fast (i.e. after 12 hours) and 1and half hour after meal for postprandial blood glucose level
2.4 Laboratory Analysis
Blood glucose level was estimated by glucose oxidase peroxidase (GOD-POD) method.Urinemicroalbumin was estimated by Pyragallol Red End Point method[12]

2.5 Statistical analysis:
- Statistical data was recorded on Microsoft Excel programme and analysed by using statistical software STATA version 10.0
- All continuous variables were presented as mean ± standard deviation.
- Categorical variables are expressed as percentages.
- Urine microalbumin in three group were compared by performing repeated measures one way ANOVA (F-test).
- Post hoc multiple comparison of mean of three groups by Bonferroni t-test.

III. Results
Table 1 shows patients of diabetic nephropathy with mean age 56.02 ± 6.92 years consisted of 34 males with and 16 females and patients of diabetes mellitus with with mean age 50.44 years consisted of 33 males and 17 females whereas mean age of controls 50.08 ± 8.42 years consisted of and 17 female .We found diabetes mellitus with diabetic nephropathy patients were of older age group as compared to diabetes mellitus without diabetic nephropathy and control group.

The number of males in cases of diabetes mellitus without diabetic nephropathy and in control group was 33 and in diabetes mellitus with diabetic nephropathy were 34. The number of females in cases of diabetes mellitus without diabetic nephropathy and in control was 17 and in diabetes mellitus with diabetic nephropathy were 16. We found higher number of males in diabetes mellitus with diabetic nephropathy as compared to female

Table 1: Age and Gender Distribution of study group

	Controls	Diabetic nephropathy patients	Diabetes mellitus patient
Age	50.08±8.42	56.02.08±6.92	50.44±9.4
Male	33	34	33
Female	17	18	17

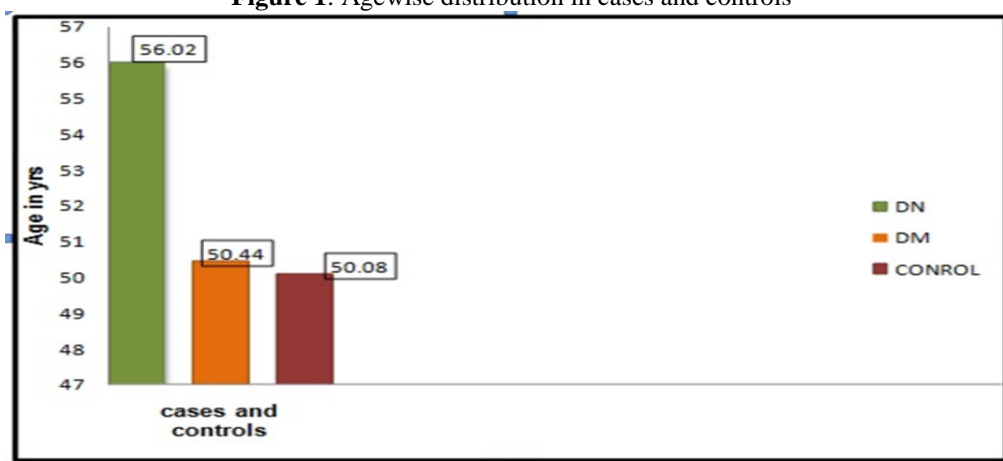**Figure 1**: Agewise distribution in cases and controls

Table 2 shows urine microalbumin in cases of diabetes mellitus with diabetic nephropathy and diabetes mellitus without diabetic nephropathy group and control. There was higher level of urine microalbumin, fasting and postmeal plasma glucose observed in diabetes mellitus with diabetic nephropathy group as compared to diabetes mellitus without diabetic nephropathy and control group and the difference was statistically highly significant (p<0.001). There was slightly higher urine microalbumin observed in diabetes mellitus without diabetic nephropathy as compared to control. The difference was statistically non significant (p>0.05).
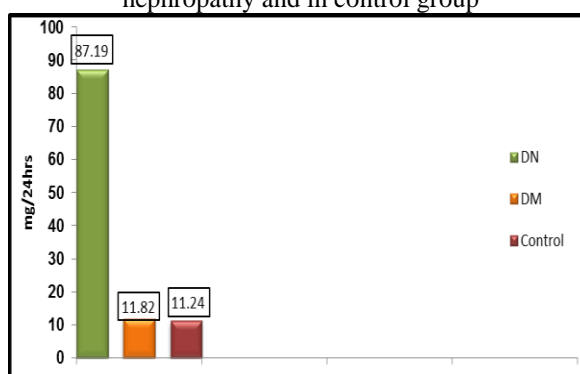
Table 2: Urinemicroalbumin in diabetes mellitus with diabetic nephropathy ,diabetes mellitus without diabetic nephropathy and in control

Variables	Diabetesmellituswith diabetic nephropathy (n=50) (Mean + SD)	Diabetes melltus without diabetic nephropathy (n=50)(Mean + SD)	Controls (n=50) (Mean + SD)
Plasma glucose F (mg%)	137.18+9.32 [a, b]	111.02+21.60 [b]	92.56+10.84
Plasma glucose PM (mg%)	181.55+30.79 [a,b]	136.26+18 [b]	116+11.06
Urine microalbumin (mg/24hr)	87.19+37.53 [a,b]	11.82+6.44 [c]	11.24+6.37

a= p<0.001 when compared with DM;b<0.001 when compared with controls ;c=p>0.05 when compared with control
SD: Standard Deviation;DM: Diabetes mellitus

Figure 2: urine microalbumin in diabetes mellitus with diabetic nephropathy, diabetes mellitus without diabetic nephropathy and in control group

IV. Discussion

Microalbuminuria is a marker for diabetic nephropathy and cardiovascular disease in patients with diabetes mellitus. Microalbuminuria is the earliest predictor of renal damage in diabetic nephropathy. Microalbuminuria is the increased passage of albumin through the glomerular filtration barrier. The Initial mechanism for development of microalbuminuria is glomerular endothelial dysfunction due to damage to its

glycocalyx layer. [13] This glycocalyx covers glomerular endothelial cell luminal surface. The glycocalyx layer is composed of glycoproteins and proteoglycans with adsorbed plasma proteins. Heparan sulphate proteoglycans (HSPGs) are responsible for the negative charge of glycocalyx. Reactive oxygen species (ROS) disrupt the glycocalyx. Removal of the glycocalyx increases vascular protein permeability through glomerular basement membrane and therefore increases albumin excretion rate.[14,15] Chowta NK et al [16] observed that there was higher number of male diabetic nephropathy patients as compared to female. Microalbuminuria patients were of older age group. Finding of this study also resembles with our study. The findings of our study are similar to those observed by Naveen et al [17]who found higher mean microalbuminuria in uncontrolled diabetes mellitus patients when compared with controlled diabetes mellitus .They also observed that the levels of HbA1c and microalbuminuria increases with duration of the disease. Our study findings are in accordance with those of Jha et al [18] who found the mean value of fasting blood glucose in microalbuminuric patients was higher as compared to normoalbuminuria

V. Conclusion

Patients with both type I and type II diabetes are at risk of diabetic nephropathy.Diabetic nephropathy develops in 20-30% of type I and type II diabetes mellitus patients.Microalbuminuria is a earliest marker for renal damage in diabetes mellitus. So detection of microalbuminuria is an indication for screening for possible vascular diseases

Acknowledgment

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