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A study of microalbuminuria in patients with type 2 diabetes mellitus, visiting tertiary care center Sangli

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ABSTRACT

Introduction: Diabetic nephropathy is accompanied with significant micro vascular risk and is the leading cause of kidney disease. Hence there is an immense need to detect early for better quality of the care of affected patients and treat effectively those at high risk of diabetic kidney disease. Our study was aimed to assess the levels of microalbuminuria, glycated hemoglobin, urinary creatinine, urinary albumin to creatinine ratio (ACR) along with blood urea and serum creatinine in patients with type 2 DM, and to observe the incidence of microalbuminuria at tertiary care center; and correlate the presence of microalbuminuria to the duration of DM as well as with ACR.

Materials and Methods: Estimation of Blood sugar, Blood Urea, Serum Creatinine, Glycosylated hemoglobin (HbA1c), Urinary micro albumin and creatinine was done. Values of urinary creatinine, microalbumin, urinary albumin to creatinine ratio (ACR) showed highly significant ($p<0.000$) difference between the two age groups a) below 60 years and b) above 60 years of the age. Highly significant difference ($p<0.000$) was found among the results of the three groups based on duration of diabetes. We found microalbuminuria was more predominant in patients having age more than 60 years as well as in patients having more than 10 years of duration of DM.

Conclusion: Routine screening for microalbuminuria in type 2 diabetic patients will certainly helpful for early detection of renal damage and thus to minimize the burden of diabetic complications due to renal involvement. Hence addition of microalbuminuria along with diabetic profile for medical checkup will help to assess microalbuminuria at frequent intervals.

1. Introduction

The International diabetes federation estimates that there are 463 million people with type 2 diabetes. Throughout the world fifty percent of these patients (232 millions) remain undiagnosed and the number of diabetic patients predicted to increase to 700 million by 2045.[1] Nephropathy is a frequent cause of morbidity & mortality in type 2 diabetes mellitus.[2] Diabetic nephropathy is accompanied with significant micro vascular risk and is the leading cause of kidney disease. Diabetic nephropathy manifests after 10 years duration of type 1 DM, but may be exists at the time of diagnosis of type 2 DM.[3] Onset of albuminuria assists to diagnose the development of diabetic kidney disease has significant unfortunate consequences. Diabetic nephropathy may progress from microalbuminuria to macroalbuminuria with progressive loss of glomerular filtration rate (GFR) until End Stage Renal Disease (ESRD). Hence there is an immense need to detect early for better quality of the care of affected patients and treat effectively those at high risk of diabetic kidney disease.[4]

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The concept of estimation of albumin was first advised by a German Scientist, Hemann Senator in the 19^{th} century. Stage 1 diabetic nephropathy is characterized by microalbuminuria i.e. urinary albumin levels of 30 – 300 mg/24hrs.[1] Measuring 24 hrs. urine for albumin is a gold standard method for detecting albuminuria, but American Diabetes Association suggests that at least two morning samples collected within 3 months of each, should be abnormal to conclude the patient having albuminuria. Urinary albumin to creatinine ratio in spot urine samples has also been recommended. National Kidney Foundation in U.S. charted that random, untimed urine samples are suitable for initial testing of albuminuria.[5]

Due to poor healthcare infrastructure and lack of health awareness in economically developing or underdeveloped nations, people are not getting regular screening for diabetes; consequently this will result into late presenting the disease. As a result, these conditions due to disease complication are crucial to outburst the burden of diabetes.

Considering all this scenario into consideration, our study was aimed (a) to assess the levels of microalbuminuria, glycated hemoglobin, urinary creatinine, urinary albumin to creatinine ratio (ACR) along with blood urea and serum creatinine in patients with type 2 DM, and (b) to observe the incidence of microalbuminuria at tertiary care center; and correlate the presence of microalbuminuria to the duration of DM as well as with ACR.

2. Materials and Methods

2.1. Study design

Case Control study. Standard normal range was used as control values for all parameters.

2.2. Study setting

Department of Biochemistry, Bharati Vidyapeeth (Deemed to Be University) Medical College and Hospital, Sangli.

2.3. Study duration

Jan. to December 2018.

2.4. Study subjects

Patients with type 2 DM, visiting Medicine OPD, Bharati Vidyapeeth (Deemed to Be University) Medical College and Hospital, Sangli.

2.5. Inclusion criteria

Patients with type 2 DM visiting Medicine OPD, Bharati Vidyapeeth (Deemed to Be University) Medical College and Hospital, Sangli, and those who were willing to involve in the study.

2.6. Exclusion criteria

Following patients were excluded from the study

1. Patients with type 1 DM.
2. Secondary DM.
3. Patients with cardiac, renal disease or any other complications of DM.

2.7. Study tools

Laboratory Investigations – Blood sugar, Blood Urea, Serum Creatinine, Glycosylated hemoglobin (HbA1c), Urinary micro albumin and urinary creatinine.

2.8. Methods of assay

Blood sugar, Blood Urea, serum creatinine – Autoanalyzer method.

Urinary microalbumin – Nephlometric method

HbA1c - Nephlometric method

Urinary Creatinine – Jaffe's Method.

The urine albumin (microalbumin) to urinary creatinine was calculated by the formula[6]

Microalbumin to creatinine ratio = Microalbumin in mg/L/Urinary creatinine in mg/dl = X 100

3. Results

In the present study with gender analysis we observed 76% males and 24% females with the incidence of type 2 DM. Similar incidence of male predominance was observed by Prajakta Warjukar[1] and Tauseef Ahmed.[7]

39% patients with type 2 DM belongs to age group above 60 years of the age while 61% belongs to age group below 60 years. These observations are supported by Asad Ullah.[8] The incidence of microalbuminuria in patients with age group below 60 years of the age was 72.5% while in 22.5% patients there was no microalbuminuria and 5% of this age group had macro albuminuria. (Values above 300 mg/dl). From the age group above 60 years all patients have proteinuria. 81.7% have microalbuminuria and 18.3% have macroalbuminuria.

When we categorized the patients based on the duration of DM, it was observed that 23% had 5 years duration, 56% had more than 5-10 years of duration and 21% had more than 10 years duration of DM. These findings are in line with Allawi[9] and Varghese.[10]

Results of all biochemical parameters in patients with type 2 DM, from our study group were compared with normal control values using 'Z' analysis. There is a highly significant difference ($p<0.000$) between values of both these groups. These results for microalbuminuria of our study were in agreement with the other researchers.[8]

Unpaired 't' test was applied for comparison between the two groups based on the age. Group a) below 60 years and b) above 60 years of the age. Values of urinary creatinine,

Table 1: Comparison of concentration of microalbumin, blood urea, serum creatinine, urinary creatinine, HbA1c and ACR between patients with type 2 DM and normal standards

Parameter	N	Mean	Std. Deviation	Std. Error Mean	P value
BSL mg/dl	100	244.61	89.306	8.931	0.000
Microalbumin mg/dl	100	162.86	60.854	10.882	0.000
Blood Urea mg/dl	100	36.4	10.457	1.046	0.000
Serum creatinine mg/dl	100	1.136	0.254	0.0254	0.000
HbA1c % of Hb	100	8.601	1.558	0.1559	0.000
Urinary Creatinine mg/100 ml of urine	100	101.24	28.103	2.8103	0.000
A:C ratio	100	213.13	180.057	18.0965	0.000

'Z' test applied for comparison of study group results to standard control values
P Value < 0 005 is significant

Table 2: Comparison of all Biochemical parameters according to age of the patient. Group a) Age below 60 yrs. b) Age above 60 yrs

Parameter	Age group	N	Mean	Std. deviation	Std. error mean	P value
BSL PP mg/dl	<= 60 yrs	61	249.77	82.40	10.55	0.492
	>60 yrs	39	236.54	99.74	15.97	
Microalbumin mg/dl	<= 60 yrs	61	147.23	100.300	12.84	0.004 #
	>60 yrs	39	212.49	110.91	17.76	
Sr. creatinine mg/dl	<= 60 yrs	61	1.11	0.21	0.03	0.182
	>60 yrs	39	1.18	0.30	0.05	
BUL mg/dl	<= 60 yrs	61	34.85	8.54	1.09	0.090
	>60 yrs	39	38.82	12.65	2.03	
HbA1c % of Hb	<= 60 yrs	61	8.44	1.56	0.20	0.209
	>60 yrs	39	8.85	1.54	0.25	
Ur. Creatinine mg/100ml of urine	<= 60 yrs	61	109.27	24.49	3.14	0.000 #
	>60 yrs	39	88.69	29.08	4.66	
A:C ratio	<= 60 yrs	61	158.13	135.85	17.54	0.000 #
	>60 yrs	39	297.76	206.96	33.14	

Unpaired't' test is applied for comparison between two age groups
P value < 0.005 is significant.

microalbumin, urinary albumin to creatinine ratio (ACR) showed highly significant difference between these two age groups (p<0.000). The values of all these parameters increased in patients with age group above 60 yrs except urinary creatinine, value of which was decreased. Our results are in accordance with N K Chowta [11] who observed increased microalbumin with increasing age. Concentration of HbA1c, Urea, and serum creatinine values also differ between these two groups, but this difference was non-significant.(Table 2)

ANOVA analysis of variance was applied for the comparison of all the parameters among the three groups formed based on duration of DM. Group A) Up to 5 years duration of DM, group B) More than 5 years to 10 years of duration of DM, group C) more than 10 years of duration of DM. This analysis explored highly significant difference (p<0.000) among the results of these three groups.(Table 3)

Post Hoc analysis between these three groups was based on duration of DM revealed that when the group A was compared with group B, there was a highly significant difference in the values of serum creatinine (p<0.001), urinary creatinine (p<0.000), urinary microalbumin (p<0.002), ACR (p<0.003). When group A was compared with group C, there was a significant difference in the values of HbA1c (p<0.004), microalbumin (0.000), urinary creatinine (p<0.000) and ACR (p< 0.000).When results of group B and group C were compared, there was a significant difference in the values of HbA1c (p<0.001), microalbumin (0.000), urinary creatinine (p<0.001) and ACR (p< 0.000).These findings are in agreement with Osama Gheith. [12]

We found microalbuminuria was more predominant in patients having age more than 60 years as well as in patients having more than 10 years of duration of DM. Our findings were in agreement with Udit Narang and co workers. [13] We observed positive correlation between microalbuminuria and ACR which was statistically highly significant.

4. Discussion

Recently India leads the world with the largest number of diabetic subjects and this is expected to further rise in the coming years. Therefore researches on diabetic complications have more importance to assess the burden of diabetes. [10]

Table 3: Comparison of all parameters among the three groups based on the duration of diabetes. Group A) up to 5yrs. B) From above 5 to 10 yrs. C) More than 10yrs.

	Duration of DM	N	Mean	Std. deviation	Std. error	P value
BSL PP mg/dl	<= 5 yrs.	23	226.35	78.81	16.43	0.001
	6-10 yrs.	56	228.13	93.32	12.47	
	>10 yrs.	21	308.57	57.09	12.46	
	Total	100				
BUL mg/dl	<= 5 yrs.	23	97.10	92.12	19.21	0.000
	6-10 yrs.	56	171.18	98.55	13.17	
	>10 yrs.	21	259.47	89.95	19.63	
	Total	100				
Serum Creatinine mg/dl	<= 5 yrs.	23	0.99	0.14	0.03	0.003
	6-10 yrs.	56	1.20	0.28	0.04	
	>10 yrs.	21	1.13	0.21	0.05	
	Total	100				
Urinary Creatinine mg/100 ml of urine	<= 5 yrs.	23	31.30	9.36	1.95	0.026
	6-10 yrs.	56	38.14	10.34	1.38	
	>10 yrs.	21	37.33	10.56	2.30	
	Total	100				
Microalbumin mg/dl	<= 5 yrs.	23	97.10	92.12	19.21	0.000
	6-10 yrs.	56	171.18	98.55	13.17	
	>10 yrs.	21	259.47	89.95	19.63	
	Total	100				
HbA1c % of Hb	<= 5 yrs.	23	8.33	1.52	0.32	0.002
	6-10 yrs.	56	8.32	1.45	0.19	
	>10 yrs.	21	9.66	1.49	0.32	
	Total	100				
ACR	<= 5 yrs.	23	121.51	14.52	3.03	0.000
	6-10 yrs.	56	103.67	27.16	3.63	
	>10 yrs.	21	72.59	17.28	3.77	
	Total	100				

The overall prevalence of microalbuminuria is up to 35% in both type of diabetes; type 1 & type2. However persons with type 2 DM exhibit the higher prevalence. Diabetic nephropathy usually manifests after 10 years duration of type 1 DM, but may present at diagnosis of type 2 DM. After being diagnosed with diabetes, 2% of persons present microalbuminuria per year, having increased plasma creatinine level or requiring renal replacement.[3] Diabetic nephropathy may also manifest as a reduced glomerular filtration rate. Therefore an absolute goal is early detection of risk resulting into the probability of intervention before advanced kidney damage has occurred. Hence screening of blood urea, serum and urinary creatinine, microalbuminuria along with HbA1c was carried out in this project.

In present study we found microalbuminuria was more predominant in patients having age more than 60 years as well as in patients having more than 10 years of duration of DM. Diabetes Mellitus and hypertension share common pathways, one of these is insulin resistance. These pathways interact and influence each other.[14] In DM elevated blood glucose travels through the body; it may cause widespread damage including blood vessels and kidneys. These organs play a key role in maintaining healthy blood pressure. If they are encountered by this damage, blood pressure can elevate, increasing the risk of further injury and complications. Intrarenal arteriosclerosis is the chief cause of renal impairment in type 2 diabetes mellitus and this may cause eGFR declines in these patients.[15] Pappitha Raja found a positive correlation between albuminuria and dysregulation of glomerular pore size.[16] On the basis of these references, findings of our study may be explained as follows…Long term duration of DM often cause subclinical hypertension, which results into increased glomerular circulation pressure and eventually damage the glomerulus. This damage may consequent into leakage of low molecular weight protein (microalbumin). Older age is one of the risk factor risk factor for such type of damages. If not treated timely or not followed up properly this may progress further as end stage renal disease. Therefore to reduce the damage of the kidney and minimize the economic burden of these diabetic complications, routine screening of type 2 DM patients for microalbuminuria will be most promising for saving the kidneys and obviously for uplifting the quality of life.

Table 4: Comparison of all biochemical parameters as per duration of diabetes mellitus

Dependent variable	Duration group (I) years	Duration group (J) years	Mean difference (I-J)	Std. error	P value
BSL - PP	<=5	<=5			
		6-10	-1.777	20.148	0.932
		>10	-82.224*	25.286	0.002
	6-10	<=5	1.777	20.748	0.932
		6-10			
		>10	-80.446	21.437	0#
	>10	<=5	82.224	25.286	0.002#
		6-10	80.446	21.437	0#
		>10			
Microalbumin	<=5	<=5			
		6-10	-74.0883*	23.6246	0.002#
		>10	-162.3710*	28.7913	0#
	6-10	<=5	74.0883*	23.6246	0.002#
		6-10			
		>10	-88.2827*	24.4091	0#
	>10	<=5	162.3710*	28.7913	0#
		6-10	88..2827*	24.4091	0#
		>10			
Sr. Creatinine	<=5	<=5			
		6-10	-0.2130	0.0599	0.001#
		>10	-0.1416	0.073	0.055
	6-10	<=5	0.2130*	0.0599	0.001#
		6-10			
		>10	0.0714	0.0619	0.251
	>10	<=5	0.1416	0.073	0.055
		6-10	-0.0714	0.0619	0.251
		>10			
Blood Urea	<=5	<=5			
		6-10	-6.839*	2.52	0.008
		>10	-6.029	3.071	0.052
	6-10	<=5	6.839*	2.52	0.08
		6-10			
		>10	0.81	2.603	0.757
	>10	<=5	6.029	3.071	0.052
		6-10	-0.81	2.603	0.757
		>10			
HbA1c	<=5	<=5			
		6-10	0.0082	0.3652	0.982
		>10	-1.3311*	0.4451	0.004#
	6-10	<=5	-0.0082	0.3652	0.982
		6-10			
		>10	-1.3393*	0.3773	0.001#
	>10	<=5	1.3311*	0.4451	0.004#
		6-10	1.3393*	0.3773	0.001#
		>10			

Table 5:

Dependent variable	Duration group (I) years	Duration group (J) years	Mean difference (I-J)	Std. error	P value
Urinary Creatinine	<=5	<=5			
		6-10	17.84654*	5.6883	0.002#
		>10	48.92213*	6.93233	0#
	6-10	<=5	-17.84654*	5.6883	0.002#
		6-10			
		>10	31.07560*	5.87717	0#
	>10	<=5	-48.92213*	6.93233	0#
		6-10	-31.07560*	5.87717	0#
		>10			
ACR	<=5	<=5			
		6-10	-13.99439*	37.22032	0.003#
		>10	-301.58743*	45.24086	0#
	6-10	<=5	113.99439*	37.22032	0.003#
		6-10			
		>10	-187.59304	38.44978	0#
	>10	<=5	301.58743*	45.24086	0#
		6-10	187.59304*	38.44978	0#
		>10			

Post hoc analysis of all parameters as per duration of DM
P value < 0 005 is significant

Table 6: Correlation of microalbumin to ACR

Microalbumin		ACR
	Karl Pearson correlation	0.931**
	P value	0.000

**- significantly positive correlation between microalbumin and ACR.

5. Conclusion

Routine screening for microalbuminuria in type 2 diabetic patients will certainly helpful for early detection of involvement of kidney and thus to minimize the burden of diabetic complications due to renal involvement. As well as, increasing age also increases the risk of nephropathy in patients with type 2 diabetes mellitus. Hence addition of microalbuminuria along with diabetic profile for medical checkup will help to assess microalbuminuria ate frequent intervals. This can reduce the mortality rate because reversal of microalbuminuria to normal urine without protein is possible when microalbumin is detected before it was converted to macroalbuminuria.

6. Conflict of Interest

None.

7. Source of Funding

None.

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