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Original Research Article

Association of microalbuminuria and glycosylated hemoglobin in type 2 diabetes mellitus

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ABSTRACT

Introduction: HbA1c is highly prognostic for long term diabetes related complications such as microalbuminuria. - Albumin is one of the most commonly assessed clinical parameters in diabetic patients. Present study was aimed a) to estimate microalbuminuria, HbA1c, urinary creatinine and urinary albumin to creatinine ratio (ACR) in patients with type 2 DM and b) to find out the correlation of glycemic control with microalbuminuria and urinary creatinine. This work is extension of our previous work on microalbuminuria in type 2 DM.

Materials and Methods: Patients with type 2 DM were involved in the study. Biochemical investigations like Blood sugar, Glycosylated hemoglobin (HbA1c), Urinary micro albumin and urinary creatinine were analyzed.

Result: There was a significant difference in the values of all parameters i) between patients and normal standard values, ii) Among the three groups based on duration of diabetes. Significantly lower values of urinary creatinine ($p<0.000$) and significantly higher values of microalbumin ($p<0.000$) and ACR ($p<0.000$) were found in patients with poor glycemic control than moderate glycemic control in our study. We observed positive correlation between microalbuminuria and glycemic control.

Discussion: Hyperglycemia in type 2 diabetes is leading to lethal effects by damaging the kidney. Early detection and prevention of nephropathy in patients with type 2 DM will be possible by frequent and timely screening the patients for HbA1c, microalbuminuria, urinary creatinine and ACR. This will definitely help to reduce the mortality rate due to diabetic nephropathy and also the economic burden of society.

1. Introduction

Diabetes mellitus is a worldwide public health problem and puts a substantial burden on healthcare resources. People having type 2 DM are more vulnerable to various forms of short and long term complications, which often lead to their early death. The chronic hyperglycemia of DM is associated with end organ dysfunction, organ damage and failure; including retina, kidney, nervous system, heart and blood vessels.[1] Older age, male gender, long duration of DM, smoking and hypertension are the risk factors for this.[2]

Mortality in diabetic patients with proteinuria is about 40 times higher than in diabetes without proteinuria. Kidney damage is a proportionately grave complication of diabetes. Estimation explored the death rate due to kidney damage is 17 times more common in diabetics than nondiabetics.[3] The early detection of proteinuria in these patients is therefore of very important.

Albumin is one of the most commonly assessed clinical parameters in diabetic patients. The role of albuminuria as a potential driver as well as well as biomarker of diabetic complications.[3] Glycated hemoglobin is the perfect and

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widely utilized biomarker of glycemic control in subjects with DM with higher concentration of glucose. Diabetic nephropathy is defined by increased urinary albumin excretion (UAE) in the absence of other renal diseases i.e. it is the indicator of early stage of kidney damage. It is categorized into two stages, a) microalbuminuria (UAE >30 – 300 μgm/min) and b) macroalbuminuria (UAE > 300 μgm/min).

HbA1c is highly prognostic for long term diabetes related complications such as microalbuminuria.[4] The risk of complications of DM is greatly reduced with intensive therapy for control of blood sugar. Long term control of blood sugar is essential for achieving low risk of complications in diabetic patients; hence glycated hemoglobin serves as an indicator for glycemic control in such patients.[4]

Present study was aimed a) to estimate microalbuminuria, HbA1c, urinary creatinine and urinary albumin to creatinine ratio (ACR) in patients with type 2 DM and b) to find out the correlation of glycemic control with microalbuminuria and urinary creatinine. This work is extension of our previous work on microalbuminuria in type 2 DM.

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 place

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

2.3. Study duration

January 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, and those who were willing to involve in the study.

2.6. Exclusion criteria

Patients with type 1 DM, type 2 DM without treatment, Secondary DM and patients with cardiac, renal disease or any other complications of DM were excluded from the study group.

2.7. Study tools

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

2.8. Methods of assay

Post prandiel blood sugar concentration was analyzed by glucose oxidase – peroxidase method by using Autoanalyzer.

Values of HbA1c and Urinary microalbumin were measured by Nephlometric method.

Concentration of Urinary Creatinine was determined by Jaffe's Method.

3. Results

Results of all biochemical analytes from patients with type 2 DM were compared with standard normal values of respective analytes using Z analysis. There was a highly significant difference ($p<0.000$) between values of all the analytes of the two groups. These results for microalbuminuria of our study are in agreement with Jayprakash.[5] (Table 1)

Based on duration of diabetes all subjects of study group were categorized into three groups. Group A – duration of diabetes up to 5 years, group B - duration of diabetes from more than 5 up to 10 years and group C - duration of diabetes from more 10 years. Post Hoc analysis of all these three group showed that, the comparison between group A and B (based on duration of DM) showed highly significant difference for urinary creatinine ($p<0.000$), microalbuminuria, ($p<0.002$) and ACR ($p<0.003$). Comparison between the parameters of group A and C showed significant difference in the values of HbA1c ($p<0.004$), microalbuminuria ($p< 0.000$), urinary creatinine ($p< 0.000$) and ACR ($p< 0.000$). When group B was compared with group C, significant difference was observed in the values of microalbuminuria ($p< 0.000$), urinary creatinine ($p< 0.001$), HbA1c ($p< 0.001$) and ACR ($p< 0.000$). Our findings were in line with Jaiprakash,[5] Osama.[6]

13% of the patients from the study group had good glycemic control (HbA1c values less than 7-10%), 45.1% had moderate glycemic control (HbA1c values between 7-10%) and 41.9% have poor glycemic control (HbA1c values above 10%). Results of Firdousi[4] are in agreement with us. (Table 2)

Significantly lower values of urinary creatinine ($p<0.000$) and significantly higher values of microalbumin ($p<0.000$) and ACR ($p<0.000$) were found in patients with poor glycemic control than moderate glycemic control in our study, which was in accordance with Dinneen[7] and Karar[8] (Table 3). We observed positive correlation between microalbuminuria and glycemic control as well

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

Parameter	N	Mean	Std. Deviation	Std. Error Mean	P value
BSL PP mg/dl	100	244.61	89.306	8.931	0.000
Microalbumin mg/dl	100	162.86	60.854	10.882	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 (mean ± SD) to normal standard as control values.
P value < 0.005 is significant.

as between HbA1c and ACR ratio. Karar,[8] Khan[9] and Muhammad[10] also observed positive correlation between microalbuminuria and glycemic control which supports our findings.(Table 3)

4. Discussion

Diabetic nephropathy is one of the most commonly observed and deadly complications of diabetes. As the burden of DM is increasing worldwide, more and more patients with diabetic nephropathy are surfacing. It has also been associated with increased morbidity and mortality. It is one of the most common cause of end stage renal disease (ESRD) and initiation of kidney transplantation. As WHO forecasted an increase in prevalence of DM around the globe, with particular importance of increasing obesity, consequently there will be exceptional increase in diabetic nephropathy worldwide.[2]

Diabetes has outstretched in India in the 21 century. Metabolic abnormalities and long term microvascular and macrovascular complications are the features of diabetes. With the extensive rise in the number of diabetes, there is a significant increase in the microvascular and microvascular complications like retinopathy, neuropathy, coronary heart diseases and cerebrovascular injuries respectively. These microvascular complications are associated with duration of diabetes and poor glycemic control. Diabetic nephropathy is a threatening disease with continuous ongoing deterioration in glomerular filtration; which will lead first into microalbuminuria and if not treated properly consequent into macroalbuminuria.[3] Therefore lowering of albuminuria is one of the most important elements in the management of diabetic kidney disease. The reversal of microalbuminuria is relatively frequent, regression of macro to micro or micro to normal is rare in type 2 DM.[11] Therefore the early detection of albumin in the urine will help to minimize the events of macroalbuminuria and eventually irreversible kidney damage.

A Reno protective effect of good glycemic control has been observed in many longitudinal and interventional studies. Already established structural changes in the kidney can be achieved by maintaining near normal blood glucose control by pancreatic transplantation in a few patients with type 1 diabetes. Elevated levels of glucose affect the antioxidant functioning system. It fastens the chemical modifications of the proteins and lipids, resulting into formation of advanced glycation end products, advanced oxidized lipid products, advanced oxidation protein products. The products of oxidation of glucose and lipid have been lodged in renal tissues of diabetic patient indicating damage. At the same time the polyol pathway stimulated by elevated blood glucose levels, consequent into renal damage. High blood glucose also reduces the activity of metalloproteases, enzymes responsible for extracellular matrix degradation.[12]

In context to above observations, findings of our study may be explained as, uncontrolled elevation of blood glucose for long time leads to glycation of protein i.e. advanced glycation product (AGE), accumulated in the basement of glomerulus leads to leakage of low molecular weight protein initially, then it will progress into microalbuminuria and finally end stage renal disease. Vincent Rigalleau and et al observed none of the patient died with no albuminuria or started dialysis; whereas most clinical events occurred in patients occurred in patients with macroalbuminuria.[13] Early diagnosis and treatment of diabetic patient aiming for good glycemic control will prevent the development of nephropathy and could also produce financial savings as well as better outcome.

5. Conclusion

Hyperglycemia in type 2 diabetes is leading to lethal effects by damaging the kidney. Early detection and prevention of nephropathy in patients with type 2 DM will be possible by frequent and timely screening the patients for HbA1c, microalbuminuria, urinary creatinine and ACR. This will definitely help to reduce the mortality rate due to diabetic nephropathy and also the economic burden of society.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

Table 2: 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

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			
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			
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 3: Comparison of microalbuminuria, urinary creatinine and ACR in patients with moderate increased HbA1c and patients with severely increased HbA1c (poor glycemic control)

	Microalbuminuria		**Urinary creatinine**		**ACR**	
HbA1c	Moderate HbA1c- 7-10% N=73	Poor control HbA1c Above 10% N= 27	Moderate HbA1c- 7-10% N=73	Poor control HbA1c Above 10% N= 27	Moderate HbA1c- 7-10% N=73	Poor control HbA1c Above 10% N= 27
Mean	142.35	254.69	107.29	84.89	161.70	350.30
Std. Deviation	96.58	98.45	26.74	25.44	143.71	197.34
Std. error of mean	11.30	18.95	3.13	4.90	16.94	37.98
P Value	0.000		0.000		0.000	

Unpaired 't' test is applied to compare the differences in means of two groups of HbA1c. P value < 0.005 is significant

Table 4: Co relationship between microalbuminuria and HbA1c

Parameter		**HbA1c**	**A:C ratio**
Microalbumin	Pearson Correlation	0.488**	0.931**
	P value	0.000	0.000

**Moderate positiveCorrelation is significant at the 0.01 level (2 tailed)
*Karl Pearson correlation is applied to find out correlation between (A) microalbumin with HbA1c and ACR
P value < 0.005 is significant

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