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Original Research Article

An Observational Study to Assess the Association of Microalbuminuria and Glycosylated Hemoglobin in Type 2 Diabetes Mellitus

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Abstract

Aim: The present study was planned to assess the association of microalbuminuria with glycosylated hemoglobin in type 2 DM patients.

Methods: The present study was conducted in the Department of Biochemistry, JNKTMCH, Madhepura, Bihar, India for the period of one year. Hundred patients were selected in the present study.

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. Microalbumin levels (g/day) were found to be highest i.e., 0.449 ± 0.160 g/ day in diabetic subjects with duration of diabetes more than four years, statistically significant ($P < 0.001$).

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.

Keywords: Microalbuminuria, glycemic control, Diabetes Mellitus, microvascular, macrovascular, Glycated hemoglobin, serum urea

Introduction

Diabetes mellitus is the leading cause of end‑stage renal disease (ESRD) in several countries. [1] It is also the cause of chronic hemodialysis and renal transplantation. Several studies have suggested that detection of early changes in renal function via microalbuminuria tests prevent further progression of the disease. [2‑5] Microalbuminuria is common (prevalence rates of 10-48%) and is a well‑established risk factor for macrovascular diseases in type 2 diabetics. Microalbuminuria defined as urinary albumin excretion rate of 20-200 µg/min or urinary protein excretion rate of 30-300 µg/min predicts future development of overt nephropathy. [6]

As microalbuminuria can be reversed and the future development of overt diabetic nephropathy significantly reduced, screening for microalbuminuria and timely therapeutic intervention has become standard of care worldwide.

Microalbuminuria is also considered to be a predictor for cardiovascular disease both among diabetic and non‑diabetic subjects, [7,8] and is one of the components of the metabolic syndrome (insulin resistance syndrome). [9]

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. [10] Glycated hemoglobin is the perfect and 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. 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. [11]

The present study was planned to assess the association of microalbuminuria with glycosylated hemoglobin in type 2 DM patients.

Methods

The present study was conducted in the Department of Biochemistry, JNKTMCH, Madhepura, Bihar, India for the period of one year. Hundred patients were selected in the present study.

Inclusion criteria

Patients with type 2 DM visiting Medicine OPD, and those who were willing to involve in the study.

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.

Study tools

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

Methods of assay

Post-prandial 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.

Statistical analysis

Student's t test has been used to find the significance of study parameters on continuous scale between two groups and to test the homogeneity samples based on age (or continuous parameters) and Chi‑square test to test the homogeneity of samples based on parameters on categorical scale between two groups. Pearson correlation between duration and microalbumin is computed to find the relationship. The Statistical Software SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs and tables.

Results

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	240.60	89.305	8.930	0.000
Microalbumin mg/dl	100	162.88	60.855	10.880	0.000
HbA1c % of Hb	100	8.602	1.560	0.1560	0.000
Urinary Creatinine mg/100 ml of urine	100	101.25	28.102	2.8102	0.000
A:C ratio	100	213.12	180.058	18.0970	0.000

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.

Table 2: Microalbumin in relation to duration of diabetes (in years)

Bio‑chemical parameters Duration of diabetes (years)	Mean±SD	P value
Microalbumin (g/day)		
1-2	0.156±0.049	<0.001
2-4	0.228±0.016	
>4	0.449±0.160	

Microalbumin levels in relation to duration of type 2 diabetes were represented in Table 2. Microalbumin levels (g/day) were found to be highest i.e., 0.449 ± 0.160 g/ day in diabetic subjects with duration of diabetes more than four years, statistically significant ($P < 0.001$).

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=70	Poor control HbA1c Above 10% N= 30	Moderate HbA1c- 7-10% N=70	Poor control HbA1c Above 10% N= 30	Moderate HbA1c- 7-10% N=70	Poor control HbA1c Above 10% N= 30
Mean	142.38	254.66	107.23	84.86	161.69	350.50
Std. Deviation	96.54	98.42	26.74	25.45	143.77	197.33
Std. error of mean	11.30	18.92	3.17	4.90	16.94	37.93
P value	0.000		0.000		0.000	

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 as well as between hba1c and ACR ratio.

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. [12]

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. [10] 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.13 Therefore the early detection of albumin in the urine will help to minimize the events of macroalbuminuria and eventually irreversible kidney damage.

The level of HbA1c has been widely accepted as an indicator of mean daily blood glucose concentration over the preceding 8–12 weeks. In the present study, levels of HbA1c are higher in diabetics than in controls, and the elevations are of high statistical significance ($P < 0.001$). In this present study, it is found that diabetics with poor glycemic control had higher microalbumin levels compared with those of diabetics with good glycemic control, and this finding is in agreement with several other studies. [13-17]

This study also highlights that there is a significant correlation between microalbumin levels and HbA1c in cases. Studies have confirmed that there is an association of microalbumin levels with well‑established risk factors such as age and poor glycemic control (HbA1c). Similarly, the present study reveals that the diabetics' subjects having poor metabolic control are more prone to renal damage, and thus elevated microalbumin levels. Microalbumin levels are found to be higher in cases than in controls, and are found to be statistically significant ($P < 0.001$). The increased microalbumin levels in diabetic subjects may be due to an altered glomerular filtration barrier, at the podocyte level. Damage to the podocyte may be explained by the fact that there is an increase in the extracellular release of reactive oxygen species.

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. [18]

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 [19] and Karar. [20] 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. [21]

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.

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