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Evaluation of Glycated Hemoglobin and Risk of Microalbuminuria in Patients with Type 2 Diabetes Mellitus

Medical Science

KEYWORDS : Glycated Hemoglobin, Type 2 DM, MAU and DN.

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ABSTRACT

Nephropathy is one of the complications of type 2 diabetes mellitus that could lead to end-stage renal disease. Persistent microalbuminuria is the best predictor of high risk of developing diabetic nephropathy. The relation between HbA1c and microalbuminuria with the duration of diabetes is not clear. A total of 120 subjects were studied. The study included patients in the age group ranging from 25-75 years with mean age of 51.41 years. A positive correlation of microalbuminuria with duration of diabetes and level of glycaemic control (measured by HbA1c levels), which is in accordance with many previous reports. Also, presence of concomitant hypertension and smoking were important risk factors in early development of nephropathy.

Introduction:

In the ancient Sanskrit Literature, diabetes mellitus was described as "honey-urine disease," associated with gross emaciation and wasting. Diabetes is a global endemic with rapidly increasing prevalence in both developing and developed countries.1In Indian population, 61.3 million people had diabetes in 2011, which is expected to reach 101.2 million by 2030 (International Diabetes Federation) now placing India at second position in world diabetic prevalence.2

Diabetes mellitus is the leading cause of end−stage renal disease (ESRD) in several countries.3 Diabetic nephropathy (DN) is one of the most common complications, and an important cause of renal failure.4 Microalbuminuria is the earliest clinically detectable stage of diabetic kidney disease at which appropriate interventions can retard, or even reverse, the progress of nephropathy.5 Glycosylated haemoglobin (GHb) is a useful index of mean glycaemia during the preceding 120 days.6 It is also a predictor of complications as measures reducing HbA1c correspondingly reduce the risk of complications.7

Hence, the aim of this study was to observe the relationship between duration of diabetes, degree of hyperglycemia and the incidence of microalbuminuria in patients with type 2 diabetes mellitus.

Material and methods:

The present study was conducted in Department of Pathology, Srinivas Institute of Medical Science and Research Centre, Mangalore, India. Randomly selected 120 known type 2 diabetic patients attending both outpatient and inpatient departments during the period from November 2013 to October 2014. A detailed history was taken and thorough physical examination of all the patients was done, followed by HbA1c estimation and tests for proteinuria (both microalbumin and macroalbumin). Blood samples were taken in EDTA vacutainers for HbA1c. It was tested on the BIO RAD D10 dual programme HPLC machine by cation exchange chromatographic technique For protein estimation, random urine sample was taken. All samples were tested for presence of albumin by URITRACE 10 PA reagent strips. (Based on the principle of protein error of PH indicator). Albumin negative samples were then tested for microalbumin by the NYCO CARD microalbumin test kit following the principle of sandwich format immunommetric assay. Statistical analysis was done by applying Karl Pearson's correlation using Statistical Programme for Social Sciences (SPSS) version 18. p value of <0.05 was considered statistically significant.

Results and Discussion:

A total of 120 subjects were studied. The study included patients in the age group ranging from 25-75 years with mean age of 51.41 years. The first detectable sign of kidney damage is the appearance of microalbuminuria.8 This allows early intervention with the goal of delaying the onset of overt diabetic nephropathy.9 To maximize prevention of microalbuminuria development, blood pressure should be maintained at less than 130/80 mm Hg, and HbA1c should be kept below 7%.7 The level of glycaemic control also plays an important role in the transition from normoalbuminuria to microalbuminuria to macroalbuminuria.10

Table 1: Demographic Profile according to status of proteinuria

Variables	ALBUMINURIA					
	NORMO	%	MICRO	%	MACRO	%
No. of PATIENTS	30	25	50	41.66	40	33.33
Male:Female	12:18	40:60	35:15	70:30	10:30	25:75
MEAN AGE (Yrs)	44.01	-	49.2	-	61.03	-
MEAN DURATION (Yrs)	5.0	-	7.90	-	11.01	-
HYPERTENSIVES	14	46.66	28	56.0	18	45.0
SMOKERS	12	40.0	26	52.0	19	47.5
MEAN AbA1c %	6.95	-	8.86	-	10.05	-

Fig-1: Pie chart represents the No. of subjects in different groups:

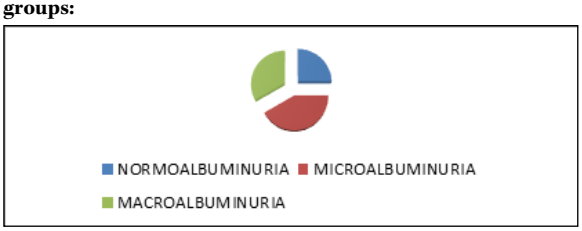

Table 2: Correlation of protienuria with duration of diabetes:

DURATION OF DIABETES	WITHOUT PROTEINURIA		ALBUMINURIA				TOTAL
			MICRO		MACRO		
	Cases	%	Cases	%	Cases	%	
0-10	22	73.33	40	80.0	37	95.5	99
11-20	6	20.00	7	14.0	2	5.0	15
21-30	2	6.66	2	4.0	1	2.5	5
>30	0	0.0	1	2.0	0	0.0	1
Total	30	100	50	100	40	100	120

Table 3: Status of Proteinuria according to HbA1c level:

HbA1c (%)	WITHOUT PROTEINURIA	ALBUMINURIA		TOTAL
		MICRO	MACRO	
Up to 7.0	19	0	0	19
7.1-7.5	7	0	0	7
7.6-8.0	2	3	0	5
8.1-8.5	1	22	0	23
8.6-9.0	1	18	0	19
9.1-9.5	0	2	5	7
9.6-10.0	0	1	25	26
10.1-10.5	0	1	2	3
10.5-11.0	0	0	4	4
11.1-11.5	0	1	2	3
11.6-12.0	0	1	1	2
>12	0	1	1	2
Total	30	50	40	120

Hence, two important recommendations for the follow-up of diabetics include monitoring of glycaemic status by HbA1c and screening for nephropathy with

urine microalbumin to assess disease progression and to detect potential progression towards end organ damage.11 The age range of patients in our study was 25-75 years with the mean age of 51.41 years. Similar mean age was observed in various other studies by Chowta NK et al, Kanakmani J et al, Maskari FA et al.10,12,13 Although the exact reason why the residents of developing countries, especially Asian, are more prone to diabetes at a younger age remains speculative, there is growing evidence to support the concept of the 'Asian Indian Phenotype'. The term refers to the peculiar metabolic features of Asians characterized by a propensity to excess visceral adiposity, elevated serum triglycerides and an increased ethnic susceptibility to diabetes.8 Microalbuminuria is a useful predictor of renal failure in diabetics. The causal risk factors for microalbumin are poor glycaemic control and raised blood pressure. Duration of diabetes, male sex and smoking as additional risk factors for microalbuminuria.14

In our study, 25% cases were normoalbuminurics, 74.99% were proteinurics, of which 41.66% had microalbuminuria and 33.33% macroalbuminuria . Similar results were obtained in many other studies by Jha P et al, Al Sheikh et al, Muraliswaran P et al etc.7,14,15 High microalbumin levels can be due to irregular treatment and poor glycaemic control. The level of glycaemic control is a strong factor influencing the transition from normoalbuminuria to microalbuminuria.7 A lower percentage of microalbumin was also seen in a number of studies by Chowta NK et al, Kanakmani J et al, Verghese A et al7,12,16 while few studies by Maskari FA et al and Choo Kang E et al13,17 showed a higher percentage of microalbuminuria. This variation can be due to difference in ethnic susceptibility to nephropathy.18

In this study, maximum number of microalbumin positive patients (80.0%) had longer duration of diabetes (0-10 years) and higher HbA1c levels (8.1-9.0%) as compared to normoalbuminurics. This is in accordance to other studies by Al Sheikh et al, Maiti A et al, Afkhami M et al.14,19,20 This can be explained by the fact that higher HbA1c indicates persistent hyperglycaemia which leads to excessive protein glycosylation and subsequent deposition of these advanced glycated end products in the glomerulus. This results in glomerular hypertrophy and thickening of glomerular basement membrane, eventually leading to leakage of protein.18 In contrast, in the study by Chowta N K et al21 maximum number of microalbumin positive patients had duration of diabetes more than 15 years. This can again be due to variation in glycaemic controls of the cases studied. The causal risk factors for microalbumin are poor glycaemic control and raised blood pressure.17 Studies show that once microalbuminuria is present, it is most likely to progress to protienuria in approximately 20-50% of the subjects and is accelerated by the presence of hypertension. Smoking has been described to be a major risk factor for the development of microalbuminuria. In our study, of the total microalbumin positive patients, 28(56.0%) were also hypertensive and 26(52.0%) were smokers. This is in agreement with many earlier studies.14,15,17,18,20

Diabetes itself is not a high mortality condition, but is a major risk factor in other causes of death and has a high attributable burden of disability.21 Diabetic nephropathy, a common sequelae of uncontrolled diabetes, greatly affects the quality of life and contributes to decreased life expectancy.22 From this study, it seems that if glycemic control is maintained at early stages of diabetes, chances of microalbuminuria is less.

CONCLUSION:

These findings suggest that, positive correlation of microalbuminuria with duration of diabetes and level of glycaemic control (measured by HbA1c levels), which is in accordance with many previous reports. Also, presence of concomitant hypertension and smoking were important risk factors in early development of nephropathy. Finally, the sample size (the number of cases) is so small that these results cannot be applied to the whole population of individuals suffering from type 2 diabetes mellitus. Despite its role as an independent predictor of renal and cardiovascular outcomes, the importance of monitoring microalbuminuria and to act as a modifiable risk factor is still underestimated. Therefore, large−scale clinical trials to establish a relation between elevated microalbumin levels and type 2 diabetes mellitus are worth undertaking.

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