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Original Article

Biochemistry Section

Effect of Age and Duration of Diabetes on Levels of Microalbuminuria among Type 2 Diabetic Patients

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ABSTRACT

Introduction: Out of 10, one adult will encompass diabetes by 2030. This fact indicates that the number of people inhabiting with this disorder is predicted to rise from 366 million in 2011 to 552 million by 2030, if no critical action is taken. During the first 5 years of diabetes, thickening of the glomerular basement membrane, glomerular hypertrophy, and mesangial volume expansion occur as the GFR returns to normal. After 5–10 years of type 1 diabetes, nearly 40% of individuals begin to excrete small amounts of albumin in the urine. Microalbuminuria is present in 20-30% of all patients with type 2 diabetes mellitus, and is especially common in those with hypertension, endothelial dysfunction and other features of insulin resistance.

Aim: To estimate microalbuminuria among type 2 diabetes mellitus and to correlate age and duration of diabetis with the levels of microalbuminuria among such patients.

Materials and Methods: The case-control study was conducted in the Department of Biochemistry, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana (Ambala), India. The sample size was fifty diagnosed cases of type 2 diabetes mellitus and fifty age and sex matched apparently healthy controls. Simple random sampling method was employed. The statistical analysis was done with the help of Statistical Package for the Social Sciences (SPSS) software to validate by applying Students' t-test and Pearson correlation.

Results: Mean age of type 2 diabetic patients was found to be 51.38±7.920 years whereas, that of healthy controls was found to be 48.48±6.876 years. It was found that the prevalence of microalbuminuria was 52 %among type 2 diabetic patients. In type 2 diabetic patients, mean Fasting Plasma Glucose (FPG) and microalbuminuria were significantly higher as compared to healthy controls. Further, there was strong correlation between microalbuminuria and glycaemic control. Also, there was significant correlation of microalbuminuria with advancing age and the duration of diabetes among type 2 diabetic patients. With the increase in duration of diabetes, there was significant progression of microalbuminuria to macroalbuminuria (>300 mg/day).

Conclusion: Hence, it can be concluded that the early determination of microalbuminuria should be implemented in clinical practice for overall risk evaluation, at least in diabetic patients.

Keywords: Endothelial dysfunction, Glycemic Control, Urinary Albumin Excretion

INTRODUCTION

Microalbuminuria (MAU) is defined as Urinary-Albumin Excretion (UAE) between 30-300 mg/day, if measured in a 24 hour urine collection; 20-200 µg/min, if measured in a timed urine collection or 30-300 mg/gm, if measured with use of Urinary Albumin to Creatinine Ratio (UACR) in spot urine collection. Any urinary albumin value above these reflects the presence of macroalbuminuria or clinical proteinuria [1,2]. Diabetes mellitus (DM) is a state of metabolic disturbance caused by a complex interaction of genetics and environmental factors resulting in hyperglycaemia due to reduced insulin secretion, decreased glucose utilization, and increased glucose production. Insulin resistance and abnormal insulin secretion are central to the development of type 2 DM. During the first 5 years of DM, thickening of the glomerular basement membrane, glomerular hypertrophy, and mesangial volume expansion occur as the GFR returns to normal. After 5-10 years of type 1 DM, nearly 40% of individuals begin to excrete small amounts of albumin in the urine [1].

About 20 to 30% of all cases with DM type 2 are complicated with microalbuminuria, commonly seen with high blood pressure, endothelium injury and insulin resistance. MAU is solely a predictor of microvascular damage of the kidney and almost 5-10% of such complication advances to overt nephropathy. Furthermore, the generalized vascular damage is associated with marked increase (2 to 4 folds) in cardiovascular complication and all-cause mortality. Some studies exhibited MAU as an independent risk factor for microvascular damage, progression for diabetic nephropathy and severe renal dysfunction [3,4]. The biochemical changes include extracellular matrix expansion in the glomerular and tubulointerstitial compartments of the kidney that results into progressive glomerular sclerosis, increasing proteinuria, chronic renal failure. In case of DM type 2, MAU is more reflected by generalized vascular disease, and hence cardiovascular mortality [5]. Both hyperglycaemia and high blood pressure are the risk factors for MAU and cause increase intraglomerular pressure, thereby increasing capillary permeability. In type 2 DM, increased leakage of protein occurs, along with reduced function of compensatory tubular reabsorption of albumin. A pronounced increase in albumin filtered by the glomerulus causes excessive supply of albumin to the renal tubule, thus the tubular reabsorptive capacity exceeds, causing increased albumin excretion in the urine [6].

As, the incidence of DM is increasing, there is always a chance to develop complications, especially the renal functions among such people, if precautions are not taken on time. Various factors are associated with the diabetic complications such as poor awareness, lack of proper care and life style modifications. Also, there is less data to emphasize on such measures in the study area, to minimize overall co-morbidity and mortality. Thus, the present study was designed to assess microalbuminuria among patients of type 2 diabetes mellitus, and to correlate the degree of microalbuminuria with age and diabetic duration among such patients.

MATERIALS AND METHODS

The present case-control study was conducted in the Department of Biochemistry, MMIMSR (Maharishi Markandeshwar Institute of Medical Sciences and Research), Mullana (Ambala), India. Simple

random sampling method was adopted for the selection of patients and sample size was calculated by the formula given below [7].

$$N = z^2p\ (1\text{-}p)/e^2$$

Here, N is the required size of sample; z = confidence level; p = anticipated prevalence and e = absolute precision

This institutional study was carried out from January to April 2012. Type 2 diabetic patients were taken from Medicine outpatient and indoor patient departments. The study was approved by the ethics committee of the institution. Detailed proforma with written consents were taken from each subject. Subjects of the age group 40 to 60 years and those willing to participate in the study were included. Subjects with any endocrinal disorder like thyroid abnormalities, on steroid therapy, urinary tract infections and gestational diabetes were excluded from the study. Subjects included for the study were categorized into 2 groups: Group 1 had 50 (fifty) type 2 diabetic patients and Group 2 had 50 (fifty) age and sex matched apparently healthy controls. The cases were diagnosed as type 2 diabetes mellitus with the help of following criteria.

Criteria for Diabetes Mellitus [1]: Fasting plasma glucose level ≥ 126 mg/dL

Post prandial plasma glucose level ≥200 mg/dL.

Five mL of venous blood was collected in a vial containing ethylenediamine tetraacetate (EDTA). Fasting plasma glucose was measured by Glucose Oxidase/Peroxidase (GOD/POD) method [8].

Expected Values

Fasting plasma Glucose : 60 to 100 mg%

Postprandial plasma Glucose : < 140 mg%

A 24-hours urinary albumin for microalbuminuria was estimated by Pyrogallol red method [9] with normal range of 30- 300 mg/day.

STATISTICAL ANALYSIS

Data obtained were analysed as per standard statistical methods with the help of SPSS version 21.0 software. Mean and standard deviation for all parameters were calculated. Correlation between various parameters was calculated by using Pearson correlation coefficient.

RESULTS

In the present study, all the subjects were between 40-60 years of age. Mean age of type 2 diabetic patients was found to be 51.38±7.920 years whereas, that of healthy controls was found to be 48.48±6.876 years. Sex-wise distribution of male/female T2DM patients was 21/29 and that of healthy controls was 30/20. In type 2 diabetic patients, mean FPG and microalbuminuria values were higher as compared to healthy controls which were found to be highly significant [Table/Fig-1].

Parameters	Group	N	Mean±SD Deviation	p-value
Age (Years)	Healthy Control	50	48.48±6.876	>0.001
	Type 2 Diabetic patients	50	51.38±7.920	
FPG (mg%)	Healthy Control	50	80.30±7.733	<0.001
	Type 2 Diabetic patients	50	189.76±78.494	
Microalbuminuria (mg/day)	Healthy Control	50	13.73±5.372	<0.001
	Type 2 Diabetic patients	50	379.18±691.147	

[Table/Fig-1]: Comparison of mean value, standard deviation and p-value of age, FPG and microalbuminuria between the healthy control and type 2 diabetic patients.

In present study, males and females were almost equally affected with microalbuminuria in the range of 30-300 mg/day (male: female ratio being 1:1). However, males were commonly affected in progression of microalbuminuria to macroalbuminuria i.e., >300 mg/day, male: female ratio being 1.75: 1 [Table/Fig-2].

Range of Microalbuminuria (mg/day)	Healthy Control		Type 2 Diabetic Patients	
	Male	Female	Male	Female
Below 30	30	20	9	15
30-300	Nil	Nil	7	8
>300	Nil	Nil	7	4
Total	30	20	23	27

[Table/Fig-2]: Sex-wise Distribution of Microalbuminuria in patients of Type 2 diabetes mellitus. Macroalbuminuria (>300 mg/day) was more pronounced among male T2DM patients.

Microalbuminuria in type 2 diabetes mellitus was significant as it was found that out of 50 type 2 diabetic cases, 26 cases were microalbuminuric. The prevalence of microalbuminuria among type 2 diabetic patients in the present study was 52 % [Table/Fig-3].

S.No.	Microalbuminuria	Frequency
1	Positive (≥30 mg/day)	26
2	Negative (<30 mg/day)	24
3	Total	50

[Table/Fig-3]: Frequency of Microalbuminuria among T2DM patients.

Further, highly significant correlation between microalbuminuria and glycaemic control was found in the present study as shown in [Table/Fig-4].

Parameter	FPG<126	FPG>126	Total
Microalbuminuria <30 mg/day	4	20	24
Microalbuminuria ≥30 mg/day	2	24	26
Total	6	44	50

[Table/Fig-4]: Correlation between microalbuminuria and glycemic control. Higher level of microalbuminuria was found in T2DM patients with higher FPG level (poor glycemic control).
Chi-square: 49.887, df: 1, p<0.001 highly significant

Also, there was significant correlation of microalbuminuria with age and the duration of diabetes in type 2 diabetic patients, as shown in [Table/Fig-5]. With the increase in duration of diabetes, there was significant progression of microalbuminuria to macroalbuminuria (>300 mg/day).

Parameter		Age	Diabetic Duration
Microalbuminuria (mg/day)	Pearson Correlation	0.336*	0.940**
	Sig. (2-tailed)	0.017	0.000
	N	50	50

[Table/Fig-5]: Correlation of microalbuminuria with age and duration of diabetes among type 2 diabetic patients.
* Correlation is significant at the 0.05 level (2-tailed)
** Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

Microalbuminuria is highly prevalent in several disease states. Widely known is the high prevalence in individuals with diabetes. A recent worldwide survey showed that in 40% of the patients with diabetes and without known kidney disease, the levels of urinary albumin were in the microalbuminuric range [10]. Similar data (20%) were found in a large population study (Australian Diabetes, Obesity, and Lifestyle Study [Aus-Diab]) which showed that albuminuria is common among patients with established diabetes, is present before the onset of diabetes, and becomes more prevalent with worsening glucose tolerance [11]. Even after treatment a transition of 2 to 2.5% per year occurs from normo- to microalbuminuria [12,13]. The National Urban Diabetes Study showed the prevalence of diabetes in a population older than 40 years to be 23.8% in 6 cities in India, and more recently, the Chennai Urban Rural Epidemiology Study (2003-2004) estimated the prevalence in those older than 40 years to be 30.1% [14]. In contrast to these results, there was higher prevalence of

microalbuminuria among diagnosed cases of type 2 diabetes mellitus in our geographical area [Table/Fig-3].

In the present study, there was highly significant difference between FPG and microalbuminuria among type 2 diabetic cases as compared to healthy controls [Table/Fig-4]. Highly significant association between glycaemic control [Table/Fig-5] and microalbuminuria was found and the level of microalbuminuria was significantly correlated to increasing diabetic duration and age. These findings were in consistent with the study done by Suma KR et al., [15]. Another study done by Sheikh SA et al., also reported a significant correlation of microalbuminuria with duration of diabetes [16]. Mohan MM et al., also revealed poor glycemic control and age along with high blood pressure as risk factor for prevalence of microalbuminuria [17]. Furthermore, in a study done by Geetha P et al., it was reported that the incidence of MAU increased with advancement of age, duration of diabetes and blood sugar levels along with hypertension [18]. Kundu D et al., also emphasized that increasing duration of diabetes, along with higher glycaemic status was the strongest predictor of microalbumin excretion rate, and hence highlighted the need for early detection of urinary microalbumin excretion among T2DM patients [19].

LIMITATION

Parameters such as the glycosylated haemoglobin (HbA1c), homocysteine level, Body Mass Index (BMI), serum lipid profiles, degree of insulin resistance, C-reactive protein, obesity, endothelial dysfunction, and genetic factors were not taken in consideration. Also, the patients included in the present study were taken from those visiting the hospital, and hence to validate the findings, large population-based study is needed.

CONCLUSION

The study found an increased frequency of MAU among T2DM cases which is strongly correlated with the increasing duration of diabetes and advancing age along with FPG. This emphasizes the need for routine screening of such patients.

Further, the early determination of microalbuminuria should be implemented in clinical practice for all-cause morbidity and mortality, at least in all diabetic patients. The test is inexpensive, easy to obtain in the clinical setting and the results are rapidly available.

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