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Original Research Article

Study of microalbuminuria as early risk marker of nephropathy in type 2 diabetic subjects

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ABSTRACT

Background: Diabetic nephropathy (DN) is a common complication of diabetes mellitus that lead to end-stage of kidney disease (ESKD). Detection of early-stage can slow loss of kidney function and improve patient outcomes with use of diagnostic biomarker detection of DN. Aims and objectives of this study is to evaluate the possible association between glycated hemoglobin and urinary microalbumin as a predictor of diabetic nephropathy in type 2 diabetic patients.
Methods: Total 162 subjects were included in this study comprises uncontrolled diabetes 54 cases, controlled diabetes 54 cases and healthy controlled 54 controls. Micro albumin was measured by urinary microalbumin (turbidimetric immunoassay), glycated hemoglobin (HbA1c) measured by ion exchange resin method and fasting blood glucose estimated by GOD-POD method. The inclusion of age group was between 35 to 74 years. Statistical analysis was done by using SPSS, version 16.0. p values were calculated by ANOVA unpaired t-test. The $p<0.05$ was considered a statistically significant.
Results: Urinary microalbumin levels were statistically significant increase in type 2 diabetes mellitus with nephropathy in comparison to uncontrolled diabetes mellitus and controlled diabetes mellitus (138.9±13.7 mg/l vs 67.7±14.1 mg/l and $p<0.005$**). HbA1c, which acts as a biomarker of diabetes was significant higher diabetic nephropathy, in comparison to uncontrolled diabetes mellitus, controlled diabetes mellitus and healthy control (8.0±1.1% vs 7.1±0.9% and 5.7±0.4%).
Conclusions: The present study was demonstrated impaired glycaemic control is associated with elevations in urinary micro albumin levels and it may be considered as risk marker of diabetic nephropathy.

Keywords: Biomarker, Controlled diabetes mellitus, Glycosylated hemoglobin (HbA1c), Urinary microalbumin, Uncontrolled diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) comprises a group of metabolic disorders that share the common phenotype of hyperglycaemia. Type 2 diabetes mellitus is a leading cause of morbidity and mortality. Cardiovascular disease is the most prevalent complication and principally accounts for the overload morbidity and mortality in diabetic patients. However, micro vascular complications, as usual kidney disease and retinopathy, are generally and

contribute to the total disease load. Abnormal levels of urinary micro albumin occur in 30-40% of patients with type 2 diabetes and the presence of kidney disease increase the mortality from cardiovascular disease. Microalbuminuria, an early marker of diabetic nephropathy, is an autonomous risk factor for cardiovascular disease. The increased levels of urinary albumin secretion may represent a more generalized vascular damage than renal microvascular injury alone.[1]

Metabolic derangement syndrome is one of the causes of diabetes mellitus (DM) and it is commonly associated with permanent and irreversible functional and structural changes in the cells of the body, predominantly vascular system changes which lead in turn to the growth of well-defined clinical entities which are called the complications of diabetes mellitus, which influence the eye, kidney and the microvascular and nervous systems. During abnormal glucose homeostasis, the body fails to produce insulin due to DM, which is characterized by hyperglycaemia and impairment in all metabolisms due to a deficiency in insulin secretion.[2]

Diabetic nephropathy is a severe complication occurring in diabetic patients and it is related to an increased risk of all-cause mortality, cardiovascular disease, and development of end-stage renal disease (ESRD), requiring expensive renal replacement therapy in the form of dialysis or transplantation.[3,4]

The current statistics released by the International Diabetes Federation confirm the enormity of the diabetes epidemic and indicate that the number of patients with renal failure due to diabetes will continue to enhance dramatically. Diabetic nephropathy is the most significant long-term complications in terms of morbidity and mortality for human being patients with diabetes.[5]

Dual biomarker capacity of HbA1c (glycaemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients.[6] Best glycaemic control is important for prevention of diabetic and therapeutic approaches to the management of complications in diabetes.[7] Cholesterol, saturated fats and excessive amounts of sodium have been identified as factors of high blood pressure and Cardiovascular disease.[8]

Oxidative stress (OS) has been implicated in the initiation, progression and pathology of type 2 diabetes mellitus (DM) and its associated complications detect MDA can use a marker of oxidative stress in type 2 DM.[9] Other factors play an equally key role, if not more, in the pathogenesis of diabetic complications, oxidative stress plays a significant role in diabetes and its complications.[10] The alteration function of endothelium along with antioxidant/pro-oxidant imbalance in hypertension can lead to detrimental consequences and long-term adverse effects of atherosclerosis and cardiovascular disease.[11]

Microalbuminuria, occurring 10±5 years following the diagnosis of DM, is at present the earliest clinical marker identifying patients at risk to develop nephropathy.[12]

During the past decade, the incidence of the end-stage renal disease has risen dramatically, primarily due to an increase in the incidence of diabetes.[13] Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics.[14]

In this present study, we were discussed change in Microalbuminuria level in relation to diabetes with glycosylated haemoglobin and duration of diabetes to determine correlation between microalbuminuria and glycosylated haemoglobin as well as between microalbuminuria and duration of diabetes.

METHODS

The objective of the present cross- sectional study was conducted from June to December 2016 at the department of biochemistry, central clinical laboratory in career institute of medical sciences and hospital, Lucknow, India. To determine the prevalence of microalbuminuria and associated with micro vascular complications among type 2 diabetic patients. The study had 3 groups: Group A [Uncontrolled DM (n=54)], Group B [Controlled DM (n=54)] and Group C [Healthy controls (n=54)]. The inclusion of cases of controlled and uncontrolled and healthy controls in age group 35 to 74 years.

Inclusion criteria

Total 162 subjects 108 diabetic subjects aged between 35-75 years of either sex with a known history of type 2 DM chosen [based on the screening recommendation by American diabetes association (ADA)].

Exclusion criteria

Diabetic patients suffering from any other medical problems such as infections chronic kidney disease, hypertension, angina and acute coronary syndrome, coronary bypass surgery or percutaneous coronary interventions were excluded from the study.

Sample collection and storage: under aseptic conditions, 3.5ml of venous blood was collected. A sample of blood was drawn after overnight fasting of 10-12 hours. Out of this 2 ml was collected in EDTA estimation of HbA1c and 1.5 ml collected in without anticoagulant (Plain) and anticoagulant (Fluoride) estimate blood sugar fasting (3,000 rpm, for 2-3min at 37°C) and 24-hour urine store in Frozen.

Biochemical Assessments

- Glycosylated hemoglobin- Estimated using Ion Exchange Resin method.[15]

- FBSL glucose oxidase method commonly known as the GOD-PAP (end-point) method.[16]
- Microalbumin (MAL)- Estimated using by turbidimetric immunoassay method.[17]

Statistical analysis

The statistical analysis was done by using SPSS, version 16.0. One Way ANOVA method was applied to observe the association between microalbuminuria and Glycosylated Hemoglobin; duration of diabetes.

The p value of ≤ 0.0001 was considered as statistically significant.

RESULTS

Total no of 162 subjects; among 108 cases of type 2 diabetes mellitus patients who were studied (controlled and uncontrolled groups), 38% patients had a familial history of diabetes mellitus. (Table 1) shows the glycaemic control of group A, group B and group C were compared between fasting plasma glucose; glycosylated hemoglobin was compared between uncontrolled and controlled diabetic patients and healthy subjects. Shown the Mean±SD of group A (uncontrolled DM) 185.9±26.8, group B (controlled DM) 161.8±15.4 and GROUP C (healthy controls) 79.4±9.2.

Table 2 shows the Microalbuminuria increased significantly with an uncontrolled diabetes (138.9±13.7) and it correlated with controlled diabetes (67.7±14.1), which indicated a renal damage (p<0.005) and t-value 3.62; healthy control indicates the microalbumin was not seen, they were normal subjects.

The parameters of the studied groups according to duration of diabetes have been summarized in (Figure-1, 2, 3). In Duration of Type 2 DM patients <5years (n=39), microalbuminuria (161.8±15.4) and HbA1c (6.0±0.5) showed a significant correlation with <5years of diabetes (p<0.002); t-value 3.96. (Figure-2) Type 2 DM patients 5-10 years (n=39), microalbuminuria (124.4 ±30.8) and HbA1c (7.1±0.5) showed a significant correlation with 5-10 years of diabetes (p<0.003); t-value 3.80. (Figure-3) Type 2 DM patients >10years (n=39), microalbuminuria (188.5±28.1) and HbA1c (8.2±1.0) showed a highly significant correlation with >10years of diabetes (p<0.001); t-value 7.79.

Table 1: Biochemical parameters in the study population (mean ± SD).

	Mean±SD		
Parameters	**Group A (54)**	**Group B (54)**	**Group C (54)**
FPG (mg/dl)	185.9±26.8	161.8±15.4	79.4±9.2
HbA1c (%)	8.0±1.1	7.1±0.9	5.7±0.4

Group A (uncontrolled DM), group B (controlled DM) and group C (healthy controls, FPG: fasting plasma glucose, HbA1c: glycosylated hemoglobin).

Table 2: Comparison of microalbuminuria between group a and group b.

	Mean±SD			
Parameter	**Group A (54)**	**Group B (54)**	**p-value**	**t-value**
Microalbumin	138.9±13.7	67.7±14.1	0.005**	3.62

Group A (uncontrolled DM), group B (controlled DM) and group C (healthy controls), microalbuminuria was not seen, they were normal subjects.

DISCUSSION

In this present study, total sample 168, type 2 diabetic patients were studied as well as positive correlation was found association between microalbuminuria and type 2 diabetes mellitus with duration of diabetes.

Epidemiological studies were showed that diabetic nephropathy is closely associated WP B et al and this correlation can be explained by a common mechanism involving tissue damage by the factors mentioned above such as HbA1c level, hypertension, dyslipidemia, duration of diabetes, cardiovascular disease, and development of end-stage renal disease (ESRD).[1]

In this study were found that microalbuminuria is a helpful predictor of renal failure in diabetic's condition as a usual risk poor glycaemic control and raised blood pressure. Duration of diabetes and additional risk factors for microalbuminuria group A (138.9±13.7) and group B (67.7±14.1) respectively, this result was showed similarity with previous study in Table 2.[18]

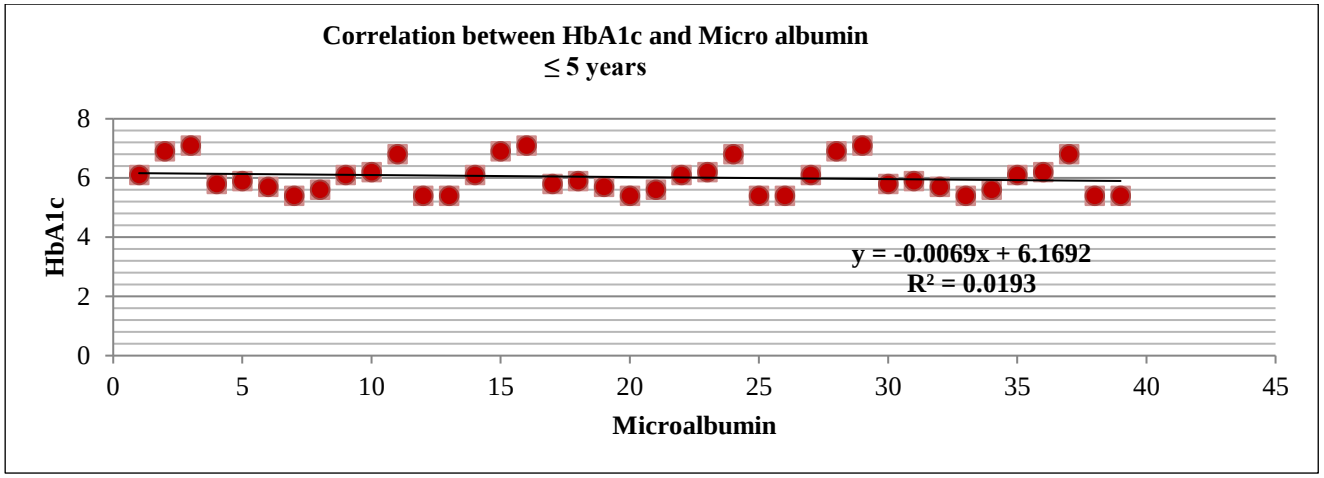

Figure 1: Scatter diagram of correlation between HbA1c and micro albumin ≤ 5 years cases.

Figure 1, 2 and 3 showed correlation between microalbuminuria and HbA1c duration of diabetes <5years (0.002**), 5-10years (0.003**) and >10years (0.001**) between positive association statistically significance, whereas the same study was done by Maiti A et al during last decades study were showed a significant and positive correlation between microalbuminuria and duration of diabetes as well as microalbumin and HbA1c.[19]

Present study showed similarity and positive correlation with Raile K et al, diabetes duration is one of the strongest risk factors for diabetic nephropathy along with glycaemic control, blood pressure and blood lipid levels.[20,21]

We were showed a positive correlation between microalbumin and HbA1c with duration of diabetes, which is consistent with the similar findings of past study.[22-23] In this study, duration of diabetes is a strong prediction for the development of abnormal albuminuria in type 2 diabetes mellitus.

This study is supported by WHO Consultation.[21] Hence, recommendations for the diabetics comprise monitoring of glycaemic status by HbA1c screening by ion exchange resin method with urinary microalbumin estimated by turbidimetric method to assess disease development and to detect prospective development towards end stage of renal damage.[21] The present studies were showed that the duration of diabetes is a strong predicts biomarker of urinary microalbumin same study was done.[18,19,21-23]

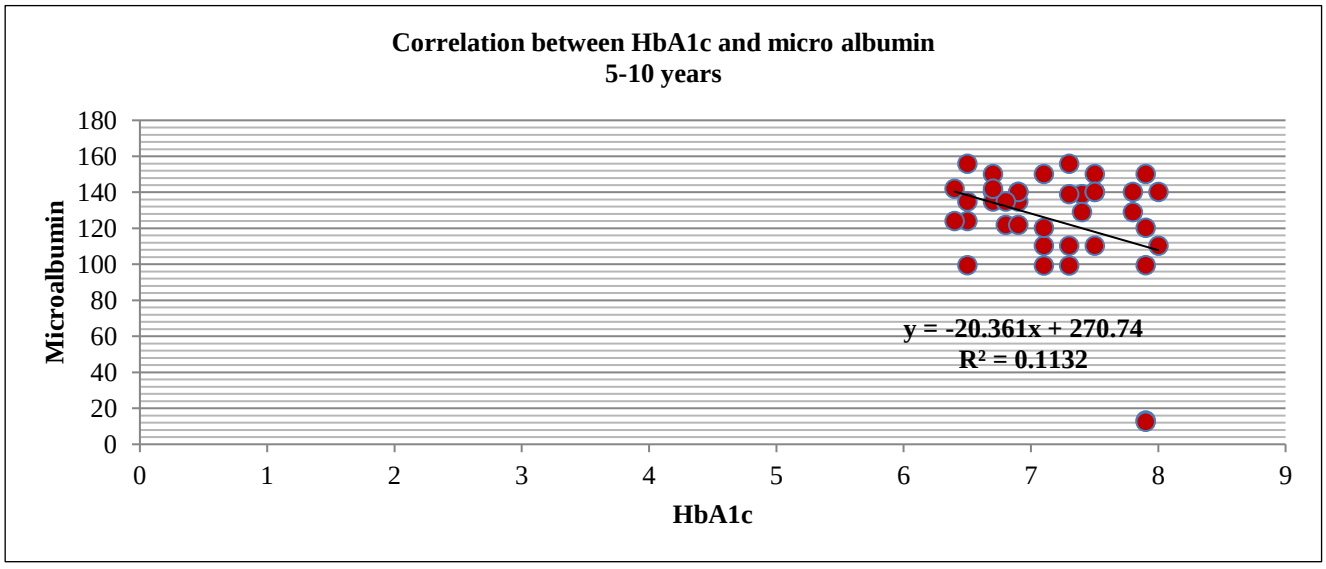

Figure 2: Scatter diagram of correlation between HbA1c and micro albumin 5-10 years cases.

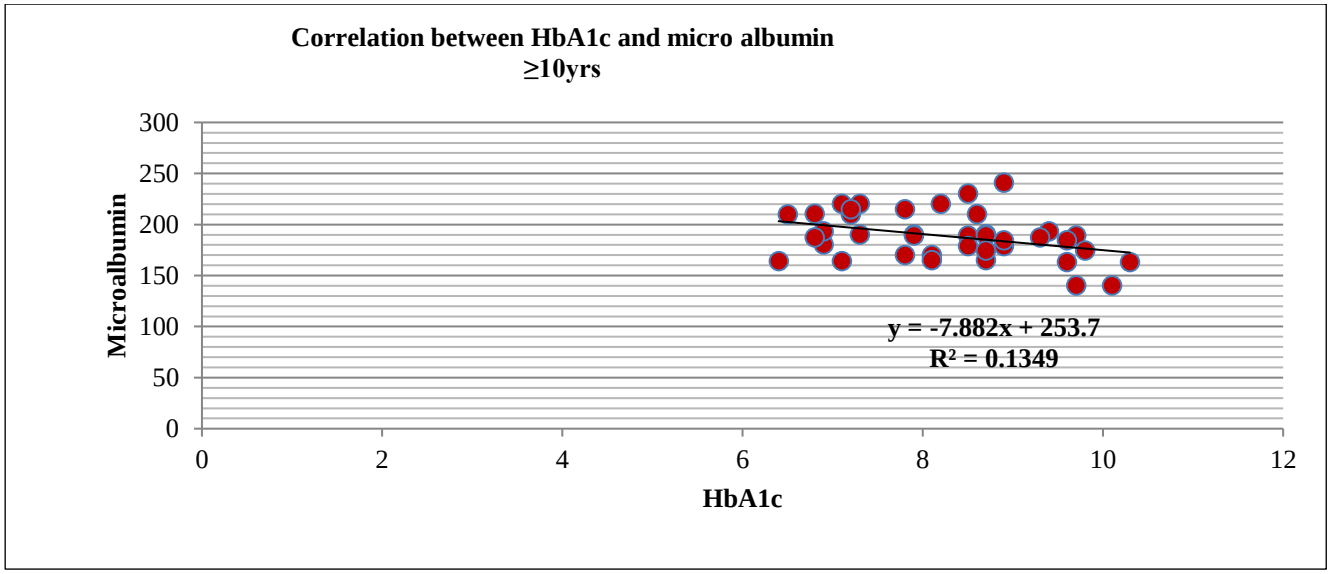

Figure 3: Scatter diagram of correlation between HbA1c and micro albumin ≥10 yrs cases.

CONCLUSION

Microalbuminuria has been considering as the earliest marker for should start with early diagnosis of kidney damage.

The current study was showed a positive correlation of microalbuminuria with duration of diabetes and level of glycemic control (measured by HbA1c levels). Urinary biomarker was significantly elevated in microalbuminuria in uncontrolled type 2 diabetic patients compared with controlled diabetes subjects and could be used as marker of diabetic nephropathy (DN) at a very early stage even before the improvement of urinary microalbumin, the current gold standard for early diagnosis.

Present study, we were investigated on the bases of our result, evaluation of microalbuminuria in diabetes patients to emphasize the need for routine screening of glycemic control of risk factors.

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Ethical approval: Not required

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