Association of glycosylated hemoglobin with urinary albuminuria for early detection and progression of renal damage in patients with type 2 diabetes mellitus

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ABSTRACT

Background: Regular screening of levels of glycosylated hemoglobin and microalbuminuria (MA), diabetic nephropathy can be prevented. Recent studies found some of the sensitive and specific biomarker for early detection and progression of nephropathy in type 2 diabetes mellitus (T2DM) patients. Aim and Objectives: This study was carried out to correlation of glycosylated hemoglobin with urinary albuminuria for early detection and progression of nephropathy in patients with T2DM. Materials and Methods: This was a case–control study was conducted at tertiary care institute of India. A total 300 subjects included in the present study diagnosed with T2DM according to American diabetes association criteria and the cases are sub grouped based on albumin creatinine ration, the 100 patients T2DM with normalalbuminuria (NA) (ACR Ratio: <30 mg/dL) and 100 patients T2DM with MA (ACR Ratio: 30–299 mg/dL) along with that 100 healthy subjects were included in the study. FBS, PPBS, Urea, Creatinine, Uric acid, HbA1C, and Urinary Albumin was analyzed using laboratory standard methods. Results: The plasma fasting blood sugar, post-prandial blood sugar, serum urea, creatinine, uric acid, Glycosylated hemoglobin, and urinary albumin levels were increased in two groups of T2DM Patients when compared to healthy controls. Significantly elevated levels of plasma fasting blood sugar, post-prandial blood sugar, serum urea, creatinine, uric acid, Glycosylated hemoglobin, and urinary albumin are observed in all the parameters elevated in between patients T2DM with MA when compared to patients T2DM NA. Conclusion: Elevated levels of Glycated hemoglobin as well as urinary albumin were useful for detection and progression of different stages of nephropathy in patients with T2DM and also this study suggest that continuous monitoring of these investigations were useful for treatment of different stages of T2DM.

Key words: Diabetes mellitus; Glycosylated hemoglobin; Microalbuminuria; Urinary albumin

INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance in carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action or both.¹ Long-term effects of diabetes are responsible for the macro and microvascular complications.² Diabetes requires continuous medical care with multifactorial strategies aimed at preventing and decreasing risks of chronic complications. Chronic hyperglycemia is tied to long lasting consequences that manifest in various organ dysfunctions, especially kidneys and blood vessels.³ Diabetes is the most common cause of kidney failure in the world, and it is estimated that diabetes increases the risk of end-stage renal disease (ESRD) approximately 12-fold.⁴
Diabetic nephropathy is a major microvascular complication of diabetes. Its earliest manifestation is the appearance of low amounts of albumin in the urine of patients (>30 mg/day but <300 mg/day) referred to as microalbuminuria (MA). It is easily measured but frequently overlooked as a tool for assessment of impairment of kidney functions and is associated with progression of chronic kidney disease (CKD) to more advanced stages or to ESRD. Moreover, the prevalence of diabetes related CKD has exceeded that of glomerulonephritis-related CKD to become the leading cause of CKD. To date, the diagnosis of DKD is dependent on both albuminuria and estimated glomerular filtration rate according to the relevant guidelines. However, albuminuria does not directly reflect the extent of renal injury, and few DM patients have had progressive renal decline before albuminuria and MA among some patients with DKD can be regressed back to normoalbuminuria (NA). Glycated hemoglobin (HbA1c) is commonly used as a marker of glycemic status. HbA1c was called as usual hemoglobin in patients with diabetes when it was first discovered. After that discovery, it was established that HbA1c could be used as an objective measure of glycemic control and a validated relationship between A1C and average glucose across a range of diabetes types. This study was carried out to correlation of glycosylated hemoglobin with urinary albuminuria for early detection and progression of nephropathy in patients with type 2 diabetes mellitus (T2DM).

**Aims and objectives**

This study was carried out to correlation of glycosylated hemoglobin with urinary albuminuria for early detection and progression of nephropathy in patients with T2DM.

**MATERIALS AND METHODS**

This was a case–control study was conducted at tertiary care institute of India. A total 300 subjects included in the present study diagnosed with T2DM according to American diabetes association criteria and patients above 40 years of age with a minimum duration of 5 years of diabetes from the time of diagnosis, admitted in the Department of Medicine and Surgery were recruited in the study. The cases are sub grouped based on albumin creatinine ration, the 100 patients T2DM with NA (ACR Ratio: <30 mg/dL) and 100 patients T2DM with MA (ACR Ratio: 30–299 mg/dL) along with that 100 healthy subjects were included in the study. One hundred control subjects were selected from an age-matched population on the basis of the levels of glycosylated hemoglobin <6.5% who was on regular antiglycemic therapy. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. (IEC/2020-21/357).

Patients with T2DM and age more than 40 years were included in the present study.

**Exclusion criteria**

The following criteria were excluded from the study:

1. Diabetic patients with overt albuminuria, that is, urinary albumin excretion >300 mg/24 h.
2. Diabetic patients with anemia were excluded as the level of glycosylated hemoglobin is dependent on the life span of RBCs.

From the all subjects, after overnight fasting (12h), 5mL of venous blood was collected and 2mL transferred into anticoagulant tube contain fluoride and 3 mL transferred into plain tube. The second sample was collected for PPBS. Urine samples also collected from all the subjects. The collected samples were separated by centrifugation at 3000 rpm for 5 min and stored until biochemical analysis was done. The Plasma FBS, PPBS, HbA1C, Serum Urea, Creatinine, and Uric Acid were analyzed by laboratory standard methods; Urine Albumin Creatinine Ratio was measured by immunoturbidimetric method.

**Statistical analysis**

The recorded data were compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5%, respectively.

**RESULTS**

The plasma fasting blood sugar, post-prandial blood sugar, serum urea, creatinine, uric acid, glycosylated hemoglobin, and urinary albumin levels were increased in two groups of T2DM Patients when compared to healthy controls. Significantly elevated levels of plasma fasting blood sugar, post-prandial blood sugar, serum urea, creatinine, uric acid, glycosylated hemoglobin, and urinary albumin are observed in all the parameters elevated in between patients T2DM with MA when compared to patients T2DM NA (Table 1). The plasma fasting blood sugar, post-prandial blood sugar, serum urea, creatinine, uric acid with positively correlated with HbA1C, and urinary albumin levels were in two groups of T2DM patients (Table 2).

**DISCUSSION**

Hyperglycemia is a major risk factor for diabetes mellitus due to improper production and activation of insulin from the beta cells of pancreas results insulin resistance. Diabetes associated hyperglycemia causes
The plasma fasting blood sugar, post prandial blood sugar, serum urea, creatinine, uric acid, Glycosylated hemoglobin and urinary albumin levels were increased in two groups of T2DM patients when compared to healthy controls. In between the two groups of subjects, there are increased levels of FBS, PPBS, Urea, Creatinine, Uric Acid, HbA1C, and Urinary albumin elevated in patients T2DM with MA when compared to patients T2DM with NA (P<0.05). The Pearson correlation analysis shows that HbA1C and urinary albumin were positively correlated with the plasma fasting blood sugar, post prandial blood sugar, serum urea, creatinine, uric acid in patients with two groups of T2DM. This correlation was highly significant and supported by the studies of Oellgaard et al.,18 Neil et al.,19 Wei et al.,20 Tabaei et al.,21 Bruno et al.,22 Wu et al.,23 Parvanova et al.,24 and Naveen et al.25 In the studies conducted by Pavithra et al.,26 a rise in the levels of glycosylated hemoglobin was seen along with the increase in the duration of diabetes. The increase in these values is explained by the pathogenesis of formation of glycosylated hemoglobin. Longer duration of uncontrolled diabetes pathogenetically correlates with the higher values of glycosylated hemoglobin.

A highly significant correlation was also seen with the rise in the levels of MA along with the increase in fasting plasma sugar. This indicates increased renal damage with increase in fasting plasma sugar levels. This was supported by the studies of Bruno et al.,22 Adler et al.,27 Rossing et al.,28 Parvanova et al.,29 Retnakaran et al.,29 and Parving et al.,30 MA as an indicator of nephropathy and renal damage has been concomitantly correlated with fasting plasma sugar, glycosylated hemoglobin, and occasionally with serum creatinine by many workers. The study of Retnakaran et al.,29 stated that these variables rise together if not intervened by antiglycemic drugs. However, multivariate model of the same study has found that the rise in glycosylated hemoglobin was an independent predictor of MA. Parving et al.,30 in his study suggested that at the mean level of HbA1c of 7.5%, MA could be demonstrated in 39% of the patients and overt albuminuria in 9.8% of the patients while other remained normoalbuminuric. This study suggest continuous monitoring of these investigations were useful for detection as well as prognosis of nephropathy in patients with T2DM.

### Limitations of the study

Limitation of the study is specific types of antihypertensive medication that may influence albuminuria or renal function, such as angiotensin converting enzyme 10 inhibitors or angiotensin II receptor blockers were not taken into account.

### CONCLUSION

Elevated levels of glycated hemoglobin as well as urinary albumin were useful for detection and progression of different stages of nephropathy in patients with T2DM and also this study suggest that continuous monitoring of...
these investigations were useful for treatment of different stages of T2DM.

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REFERENCES


Authors’ Contributions:
MSP- Concept and design of the study, prepared first draft of manuscript; RPP- Interpreted the results; reviewed the literature and manuscript preparation; MRS- Concept, coordination, preparation of manuscript; RRS- statistical analysis and interpretation.

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