

Research Article

Effect of glycemic control on albumin excretion in urine in diabetics

Pankil K. Shah^{1*}, Asutosh P. Chauhan²

Department of Biochemistry, GMERS Medical College, Gotri, Vadodara, Gujarat, India

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***Correspondence:**

Dr. Pankil K. Shah,

E-mail: drpks1983@gmail.com

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ABSTRACT

Background: Diabetes Mellitus (DM) is commonest endocrine disorder worldwide. It is associated with variety of complications such as retinopathy, neuropathy and nephropathy. The severity of the complications depends on treatment strategies, duration of diabetes and glycemic control. Microalbuminuria (MA) is an earliest predictor of nephropathy in patients of diabetic nephropathy and Diabetic Nephropathy is most common cause for End Stage Renal Disease (ESRD) worldwide. It accounts for >40% of patients with ESRD.

Methods: The present study investigated effect of glycemic control on microalbuminuria. We studied 150 diabetic patients with duration of diabetes more than 3 years. Investigations like glycated hemoglobin (HbA_{1c}) and fasting blood glucose were carried out to evaluate glycemic control and albumin in urine to evaluate early renal involvement.

Results: Out of 150 patients included in the study, 107 had poor glycemic control and 33 patients had good glycemic control. The HbA_{1c} less than 7% is taken as cut off point for control of diabetes. The mean value of albumin in urine was 34.5 mg/L in the group of diabetics with good glycemic control and the same was 60.7 mg/L in the group of diabetics with poor glycemic control and this change was statistically significant ($p < 0.05$).

Conclusions: It is concluded that those patients with good glycemic control have decreased risk of developing microalbuminuria.

Keywords: Diabetes mellitus, HbA_{1c}, Glycemic control, Microalbuminuria

INTRODUCTION

Diabetes Mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of the DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.¹ The World Health Organization (WHO) have reported an increase in the prevalence of diabetes worldwide particularly in developing countries and India leads the world with the highest number of diabetic subjects and this is expected to further rise in the coming years. As the disease

progresses, these patients are at increased risk for development of specific complications, including retinopathy leading to blindness, nephropathy leading to renal failure, neuropathy and atherosclerosis.² The main identified risk factors for the development of diabetic renal disease are hereditary susceptibility, increase in blood glucose levels, lipid level and blood pressure. Other suggested risk factors to be evaluated are smoking, body mass index, age, sex (male) and duration of Diabetes Mellitus.^{3,4}

Diabetic Nephropathy is a spectrum of progressive renal lesions secondary to Diabetes Mellitus ranging from renal hyperfiltration to end stage kidney disease. The earliest clinical evidence of nephropathy is the presence of microalbuminuria. It progresses to overt proteinuria over the next 7 to 10 Years. Once overt proteinuria develops,

renal function progressively declines and end stage renal failure is reached after about 10 years.⁵

Microalbuminuria is defined as the albumin excretion ranging between 20-200 mg/L. Albumin excretion in healthy individual is less than 20 mg/L. If the albumin excretion is higher than 200 mg/L of urine, patient is considered to have macroalbuminuria.^{2,6} microalbuminuria predicts development of overt diabetic nephropathy in diabetes. Microalbuminuria is present when albumin excretion of 20-300 mg/L is take place in urine. The appearance of microalbuminuria in diabetes is an important predictor for progression to clinical renal disease in patients with diabetes. It is at this stage that one can reverse diabetic renal disease or prevent its progression.² Data obtained from both IDDM and NIDDM demonstrate that 6-8% of microalbuminuria patients develop Overt nephropathy whereas less than 2% patients with normoalbuminuria develop Overt nephropathy.⁷ However most adverse effects are mediated through diverse metabolic pathways, there are four potential pathways linking hyperglycemia to changes within kidney, which can be linked to functional and structural changes characterising diabetic nephropathy. These are polyol pathway, nonenzymatic glycation, glucose auto-oxidation and de novo synthesis of diglycerol leading to protein kinase C and phospholipase A₂ activation.⁶

Activation of some metabolic pathways in turn causes dysregulation of a number of effector molecules which cause cellular damage and dysfunction. The role of these pathways and effectors have been studied in detail in overt diabetic nephropathy, but the importance of these elements individually in its initiation and the appearance of microalbuminuria are less clear.⁸

ROS Brownlee has proposed oxidative stress as a unifying mechanism whereby the above mentioned four pathways are inter-linked in the pathogenesis of diabetic complications. Hyperglycemia increases oxidative stress through overproduction of superoxide and other Reactive Oxygen Species (ROS) by the mitochondrial electron transport chain.⁹

Glycemic control is the mainstay of the diabetes management. The risk for occurrence of microvascular and macrovascular complications were shown to increase at HbA_{1C} values of 6.5% or more.¹⁰ The DCCT study demonstrated that the benefits of an improvement in glycemic control occurred over the entire range of HbA_{1C} values, suggesting that at any HbA_{1C} level, an improvement in glycemic control is beneficial. The clinical implication of this finding is that the goal of therapy should be to achieve an HbA_{1C} level as close to normal as possible, without subjecting the patient to excessive risk of hyperglycemia.¹¹ There are clear evidences that hyperglycemia is the major initiating factor in the pathogenesis of diabetic complications including microalbuminuria which can be linked to

functional and structural changes characterising diabetic nephropathy.⁸ The long-term follow-up of the patients who participated in the Diabetes Control and Complications Trial (Epidemiology of Diabetes Interventions and Complications Study) demonstrated a sustained effect of previous tight glycemic control on both development and progression of DN. Finally, long-term normoglycemia, achieved by pancreas transplantation, is able not only to prevent the development of early diabetic glomerulopathy in kidney transplant recipients but also to halt progression and induce regression of the established diabetic renal lesions in nonuremic patients.¹²

Diabetes mellitus is one of the major public health problems and India has the largest number of people suffering from diabetes. In normoglycemic subjects, a small proportion of hemoglobin A is attached to carbohydrate moiety thus creating HbA_{1C}. In chronic hyperglycemia, such as in Diabetes Mellitus, the proportion of hemoglobin that is glycosylated is increased substantially. HbA_{1C} has been firmly established as an index for long term blood glucose concentrations and reliable measure for assessing and monitoring glycemic control in patients with Diabetes Mellitus. It is an effective way to monitor glycemic control as it gives the average blood glucose level of preceding 6 to 8 weeks and is not subjected to the wide fluctuations as observed when assaying blood glucose concentrations.²

Nonenzymatic reactions between sugars and the free amino groups on proteins, lipids and nucleic acids result in molecular dysfunction through the formation of advanced Glycation End Products (AGE). AGEs have a wide range of chemical, cellular and tissue effects through changes in charge, solubility and conformation that characterize molecular senescence.¹³

The aim of present study was to evaluate effect of glycemic control on albumin excretion in urine in patients of diabetes mellitus.

METHODS

The study population

The present study was conducted at Medicine OPD. Patients suffering diabetes and on treatment for more than 3 years were included in the study. As the study was conducted in general hospital, Patients coming middle & lower socioeconomic status were included in the study. Due to large variation in socioeconomic status, it was not taken as criteria for selection of patient. Patients were advised to take anti-diabetic diet.

Sample collection and preparation

Patients suffering from hypertension, coronary heart disease, urinary tract infection and acute febrile illness were excluded. 150 cases of diabetes mellitus were

studied. Laboratory investigations like HbA_{1C} and Fasting Blood Sugar (FBS) and albumin excretion in urine were carried out. Blood for sugar estimation was collected in fluoride container. Whole blood collected for HbA_{1C} estimation. Spot urine is collected for albumin estimation in urine.

Measurement

FBS was estimated by GOD-POD (Glucose oxidase-Peroxidase) method.¹⁴ HbA_{1C} estimation is done by immunoturbidimetric latex method.¹⁵ Albumin estimation in urine done by turbidatex method.¹⁶ HbA_{1C} less than 7% as good glycemic control and albumin excretion less than 20 mg/L were considered as normoalbuminuria.¹⁷

RESULTS

The 150 diabetic patients that are included in the study are investigated for glycated hemoglobin (HbA_{1C}(%). Out of the 150 patients included in the study, 80 patients have good glycemic control, and 70 patients have poor glycemic control. The statistical analysis was done by 't' test. The values were expressed as Mean \pm SD. Then the two groups were compared statistically for albumin excretion in urine. Interpretation was done according to p value i.e. *p<0.05 is considered significant, **p<0.001 is considered highly significant and p \geq 0.05 is considered not significant.

Table 1: Comparison of albumin excretion in urine in patients of diabetes mellitus in both groups.

Parameters	Reference value	Good glycemic control (n=80)			Poor glycemic control (n=70)		
		Min.	Max.	Mean \pm SD	Min.	Max.	Mean \pm SD
Albumin in urine (mg/L)	Less than 20 mg/L	12	92	31 \pm 19	10	200	60.7 \pm 30

t value= 7.36, p value <0.0001

Table 2: Incidence of microalbuminuria in the two groups.

Glycemic control/ Albumin excretion in urine	Micro-albuminuria	Normo-albuminuria	Total patients
Good glycemic control	43 (53%)	37 (43%)	80
Poor glycemic control	64 (91%)	6 (9%)	70
Total	107	43	150

DISCUSSION

Among In the present study, Albumin excretion in urine ranges from 12 to 92 mg/L with mean value of 31 mg/L in patients with good glycemic control. While the range was 10-200 mg/L in patients with Poor glycemic control with mean of 60mg/L and this change was statistically significant (p<0.05). It suggests that the patients with good glycemic control has decreased Albumin excretion in urine as compared to that of poor glycemic control. The incidence of microalbuminuria in the two groups of the patients of diabetes mellitus. Out of 80 patients with good glycemic control, 43 (53%) had microalbuminuria & 37 (43%) had normoalbuminuria While out of 70 patients with poor glycemic control 64 (91%) had microalbuminuria & 06 (9%) had normoalbuminuria. So there is a lower incidence of microalbuminuria in patients with good glycemic control.

The Diabetes Control and Complications Trial (DCCT), the Kumamoto Study and The United Kingdom Prospective Diabetes Study (UKPDS) have shown that maintaining blood glucose concentration as much close to normal as possible in diabetic patients will decrease the incidence of microvascular complications.¹⁰ The DCCT and the UKPDS have demonstrated in type 1 and type 2 diabetes, that intensive glycemic control significantly reduces risk for development of microalbuminuria.^{18,19}

CONCLUSION

The study analysis of patients with diabetes for glycemic control and microalbuminuria suggests that long term glycemic control certainly beneficial to diabetics which will certainly delay the outcomes like early renal changes and variety of complications associated with the disease. This will not only improve the quality of life of diabetic patients but also hopefully boost their morale too. Further research is necessary to establish this fact and national health guidelines for the treatment and prevention of complications associated with diabetes mellitus need to be designed and implemented thereafter.

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