

ASSOCIATION BETWEEN GLYCOSYLATED HEMOGLOBIN AND MICRO-ALBUMINURIA IN PATIENTS WITH TYPE II DIABETES MELLITUS

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INTRODUCTION

Diabetes is the most common metabolic disorder around the world. It is characterised by varying degree of insulin resistance, impaired insulin secretion and increased glucose production. Diabetic nephropathy is the commonest cause of morbidity and premature mortality in patients with Insulin dependent diabetes mellitus (IDDM).^[1-2] Microalbuminuria (increased urinary albumin excretion) is the earliest sign, which can progress to overt albuminuria if left untreated, and then ultimately lead to renal failure.^[3] Improved glycemic control tend to delay the onset of microalbuminuria, but the development of cost-effective preventive strategies requires knowledge of the increase in the risk of nephropathy associated with increase in the degree of hyperglycemia.^[4-6] The current study was conducted to investigate the correlation of microalbuminuria with levels of HbA1c. This correlation can have imply on deciding how strictly the blood sugar levels of diabetic patients need to be controlled for optimum health and prevention of complications like diabetic nephropathy for indicating risk of Diabetic Nephropathy in poorly controlled diabetic patients.

MATERIALS AND METHODS

The study was conducted in Sree Balaji Medical College and Hospital on 50 IDDM patients who attended the OPD between 1/11/16 – 30/11/16. All patients were old cases and whose previous reports were available. 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).

The laboratory test included urine albumin, albumin creatinine ratio, blood HbA1c levels. Urine samples with abnormal sediments on routine analysis were discarded.

For protein estimation, 5 ml urine sample were collected in a plastic urine container. Random urine sample or 24 hrs urine sample (no preservatives added for 24 hr collection container) were tested for the presence of albumin.

A blood sample was also drawn after an overnight fasting of 10- 12 hrs. The fasting blood samples with EDTA was used to estimate HbA1c levels. It was tested on the BIO RAD D10 dual programme HPLC machine by cation exchange chromatographic technique.

The relation between prevalence of microalbuminuria and the HbA1 values were evaluated by calculation of Odd's ratio.

Values

Normoalbuminuria is defined as a ratio of albumin to creatinine less than 17 (males) and less than 25 (females). Microalbuminuria is defined as a ratio of albumin to creatinine in the intermediate range i.e 17-299 (males) and 25-299 (females). Ratio of albumin to creatinine of 300 or higher was considered to indicate overt albuminuria.

RESULTS

Among the 50 patients (duration of IDDM 2-30 yrs), who were screened for microalbuminuria during the study period, 20 had microalbuminuria, 5 had overt albuminuria and 25 had normoalbuminuria. Both the patient with microalbuminuria and those with overt albuminuria had long standing diabetes mellitus and higher HbA1 values than patients with normoalbuminuria.

The correlation between the hemoglobin A1 values was high in the patients with normoalbuminuria and with microalbuminuria, but not in those with overt albuminuria, indicating considerable stability in the degree of hyperglycemia in the first two groups. Whereas, the low correlation in the patients with overt albuminuria indicates a greater variation in the degree of hyperglycemia, as a result of intense glycemic control. So, the patients with overt albuminuria were excluded from further analyses.

To examine the association between microalbuminuria and degree of hyperglycemia, the patients with normoalbuminuria and microalbuminuria were subdivided into quintiles based on distribution of HbA1 values.

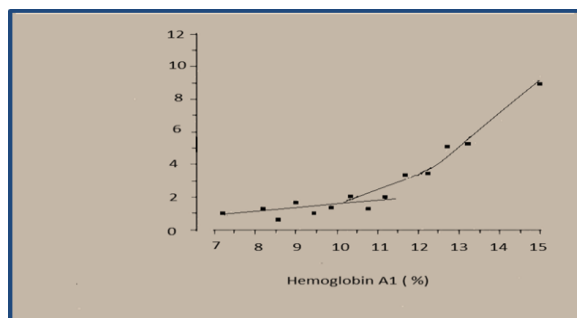
HbA1 Values (%)	Microalbuminuria (%)
5.8 – 8.7	11.6
8.8- 9.9	15.3
10- 10.7	18.2
10.8-11.8	24.4
11.9-21.4	36.2

It was seen that the prevalence of microalbuminuria was 11.6% in the lowest quintile, which increased progressively with each quintile. To examine the effect of duration of diabetes, the prevalence of microalbuminuria in each of these quintiles were examined according to the duration of diabetes mellitus.

The prevalence of microalbuminuria in each of these quintiles was examined according to the post pubertal duration of diabetes which is much higher than the prevalence reported in normal subjects. It was used as the reference point for calculating the odds ratios for other combinations of hemoglobin A1 values and durations of diabetes.

It was seen that among these patients who had diabetes mellitus for 5 yrs or less, the prevalence of microalbuminuria in the lowest quintile of HbA1 was 3.6%. This was much higher than that reported in normal patients (0.9%). It was inferred that the risk of microalbuminuria increased with the duration of IDDM, except among patients who had diabetes mellitus for 25-30 yrs.

The risk of microalbuminuria also increased with the level of HbA1. The risk rose moderately between the first to fourth quintile, and then steeply in the fifth quintile. Hemoglobin A1 was then taken as a continuous variable, and the fifth quintile was treated as an outlier. The relative risk increased by a factor of 1.25 with each increase of 1 percentage point on the hemoglobin A1 scale, but in the fifth quintile, the relative risk was higher by a factor of 1.67 than that predicted by the regression line.



Relation between mean HbA1 and risk of microalbuminuria

The reference group for adjusted relative odds were the group of patients with lowest HbA1 values (5.9 – 7.9, mean 7.3). The result was that for HbA1 values below 10.1 %, the slope of relation was almost flat, whereas for values above 10.1% the prevalence of microalbuminuria rose steeply. For example, as the hemoglobin A1 values increased from 8.1 to 10.1 %, the odds of microalbuminuria increased by a factor of 1.3, but as the value increased from 10.1 to 12.1%, the odds were increased by a factor of 2.4. Maximum macro albumin positive patients had HbA1c in the range of 10.1- 12.1 %.

DISCUSSION

The risk of microalbuminuria in patients with IDDM is strongly related to both the duration of diabetes mellitus and degree of hyperglycemia (measured as level of HbA1c). In patients who have DM < 25 yrs and whose HbA1c values were between 10.1%, the risk of microalbuminuria varied little although it was higher than normal patients. But in patients with HbA1 value > 10%, the risk of microalbuminuria rose steeply. A relation between elevated hemoglobin A₁ values and an increased risk of microalbuminuria has been reported.^[7,8,9,10]

Diabetes damages the kidney through several mechanisms as suggested by the distinctly different risks of microalbuminuria in patients with low hemoglobin A₁ values and those with high values.^[11,12]

The patients who received intensive treatment had a statistically significant reduction in the cumulative incidence of microalbuminuria as compared with the patients who received conventional treatment.

At high HbA1 values, microalbuminuria is most likely caused by deleterious effects of hyperglycemia on cell functions and extracellular structures such as mesangial matrix and basement membrane.^[13,14]

So, patients and care provider should give highest priority to early detection of microalbuminuria and HbA1 values, and thus improving glycemic control to maintain HbA1 values less than 10.1%(equal to HbA1c values below 8.1%).If this is achieved, the number of patients in whom microalbuminuria develops, will decline which in turn will lower the risk of diabetic nephropathy.

CONCLUSION

Present study showed 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, the coexistence hypertension and smoking were important risk factors in early development of nephropathy.

Therefore, regular screening for microalbuminuria, along with continuous HbA1c estimation are important tools in the management of DM. Treatment of hypertension and aggressive lifestyle changes including measures to quit smoking should be given topmost priority.^[15] The rising prevalence of diabetes can produce major constraints on health care budget. This urgently calls for not only good control of diabetes to prevent nephropathy but also to address the larger issue of primary prevention of diabetes, that is, reduction in the prevalence of diabetes itself by aggressive lifestyle modifications.

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