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Original Research Article

A Case Control Assessment of Glycated Haemoglobin & Total Protein and Albumin Levels in Patients with Type 2 Diabetes Mellitus

Shailesh Kumar Pankaj[1], Sujit Kumar[2], Rashmi Singh[3], C P Jaiswal[4]

[1]Tutor, Department of Pathology, NMCH, Patna, Bihar, India
[2]Tutor, Department of Physiology, NMCH, Patna, Bihar, India
[3]Tutor, Department of Community Medicine, PMCH, Patna, Bihar, India
[4]Associate Professor, Department of Pathology, NMCH, Patna, Bihar, India

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Corresponding author: Dr. Rashmi Singh
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Abstract

Aim: To evaluate the glycated haemoglobin, total protein and albumin levels in patients with type 2 diabetes mellitus.

Material & Methods: A case control study was carried out at Department of Pathology, NMCH, Patna, Bihar, India for one year to evaluate the glycated haemoglobin, total protein and albumin levels in patients with type 2 diabetes mellitus. The protocol was explained to the subjects and those who gave their informed consent were recruited for the study. A total of 122 subjects comprising of 61 diabetic subjects and 61 controls aged between 40 and 73 years were recruited for the study.

Results: The mean level of HbA1c was significantly higher in the diabetic subjects when compared with control group (9.71± 1.30Vs 5.58± 0.65; p=0.000). There were no significant differences observed between the age, the serum levels of Albumin and Total protein in the test and control subjects (p>0.05). There was no significant correlation between age, HbA1c, total protein and albumin in diabetic subjects.

Conclusion: This finding implies that there was a poor glycemic control in the diabetic subjects studied. Therefore, there is need for better management of diabetic patients through medication and use of diet and exercise.

Keywords: Glycated Haemoglobin, Albumin, Total Protein, Diabetes Mellitus (DM), Glycemic Control.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease which results from diminished or absent secretion of insulin or even by reduced tissue sensitivity to insulin resistance in Type 2 diabetes mellitus affects the metabolism of carbohydrates, lipids and proteins. [1] Type 2 diabetes mellitus is one of the leading causes of preventable death in the world, with stroke, myocardial infarction and other cardiovascular diseases being the most common causes of death for adults with diabetes. [2] A number of factors including less glycemic control, smoking, high blood pressure, elevated cholesterol levels, obesity, and lack of regular exercise are

considered to be risk factors that accelerate the deleterious effects of diabetes. [3] HbA1c gives an estimate of the average blood glucose levels of the previous three months in diabetes. Protein glycation and HbA1c have been shown to be involved in long term complications of diabetes mellitus. Glycated albumin has decreased half-life due to increased catabolic rate. [4,5]

Albumin is one of the most abundant plasma proteins. The glycation of albumin to form glycated albumin (GA) is ten times more than the glycation of hemoglobin in type 2 DM. [6] GA is a marker reflects a short-term glycemic control. One advantage of utilizing serum albumin as a measure of glycemic control is its shorter half-life of 21 days, which renders its serum concentration more sensitive to recent change in average blood glucose level than HbA1C. [7] Studies have shown decreased albumin levels associated with increased HbA1c and total protein.

Protein glycation is involved in the long-term complications of diabetes. [4,8] Plasma proteins are the primary targets of glycation following elevated levels of glucose in diabetes. [9] Amongst plasma proteins, albumin is one of the heavily glycated proteins because of its abundance, comparatively longer half-life and a higher number of free lysine and arginine residues. [10] It has been mechanistically shown that albumin competes with other proteins for glycation [11] and low albumin level was associated with increased plasma protein glycation in diabetes. [12] It has also been suggested that low plasma albumin predicts the glycated hemoglobin (HbA1c) in type 2 diabetes, [13] thus, strongly implicating albumin in regulation of plasma protein glycation and HbA1c.

Therefore, the present study evaluated the glycated haemoglobin, total protein and albumin levels in patients with type 2 diabetes mellitus.

Material & Methods

A case control study was carried out at Department of Pathology, NMCH, Patna, Bihar, India for one year to evaluate the glycated haemoglobin, total protein and albumin levels in patients with type 2 diabetes mellitus. The protocol was explained to the subjects and those who gave their informed consent were recruited for the study. A total of 122 subjects comprising of 61 diabetic subjects and 61 controls aged between 40 and 73 years were recruited for the study. The patients and controls were aged and sex matched. Subsequently, structured questionnaire was used to obtain patients' biodata and thereafter, 5mls of blood sample was collected from each patient and 1ml was dispensed into EDTA for the estimation of glycated haemoglobin, and 4ml was dispensed into plain containers for estimation of serum albumin and total protein levels.

Inclusion criteria

Known diabetic subjects aged between 40 and 73 years were recruited for the study.

Exclusion criteria

Those younger than 40 or older than 73 years and non-diabetic subjects were excluded from the study.

Determination of glycated haemoglobin level

Glycated Haemoglobin level was determined using immunoturbidimetric method as described by Wolf *et al*., (1984). [13]

Estimation of serum albumin level

Serum albumin level was estimated Bromo Cresol green Method as described by Doumas *et al*., (1971). [14]

Estimation of total protein

Estimation of serum total protein level was done using Biuret Method according

to Weichsel Baum, (1946). [15]

Statistical analysis

The data were presented as mean SD and the mean values of the control and test group were compared by Students t-test and Pearson correlation using Statistical package for social sciences (SPSS) (Version 20) software. Statistical significance was tested at $P<0.05$.

Results

The mean level of HbA1c was significantly higher in the diabetic subjects when compared with control group (9.71± 1.30Vs 5.58± 0.65; p=0.000). There were no significant differences observed between the age, the serum levels of Albumin and Total protein in the test and control subjects (p>0.05).

Table 1: Levels of HbA1c, total protein and albumin in diabetic and control subjects

Parameters	Control	Diabetic subject	t- test	p- value
Age(years)	54.69±7.65	46.71±6.02	- 0.082	0.935
HbA1c (%)	4.78±0.65	7.89±1.30	1.712	0.000*
Protein (g/l)	51.08±9.8	54.08±4.6	1.649	0.104
Albumin (g/l)	32.69±5.45	34.56±6.7	0.191	0.849

Table 2 shows that there is no significant correlation between age, HbA1c, total protein and albumin in diabetic subjects.

Table 2: Correlation of HbA1c with age, total protein and albumin in diabetic subjects

Parameters	R	p-value
HbA1c Vs age	0.078	0.047
HbA1c Vs Total protein	0.096	0.571
HbA1c Vs Albumin	-0.162	0.338
Age Vs Total protein	-0.044	0.797
Age Vs Albumin	0.085	0.615
Total protein Vs	-0.007	0.966

Discussion

The results of our study showed a statistically significant negative correlation between HbA1c and serum albumin levels. This persisted despite adjusting for confounding factors like FPG age, BMI, Hb, serum creatinine, serum globulin, total protein. Notably, common clinical conditions like anemia and drugs interfering with HbA1c estimations like aspirin were excluded.

In this study, the mean level of HbA1c was significantly higher in the diabetic subjects than in control. This increase can be attributed to hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism that results from abnormalities in insulin secretion, insulin action or even both (IDF, 2015; ADA, 2016). [16,17] This finding implies that there is a poor glycemic control in the diabetic subjects under study. Furthermore, our finding shows a higher mean value of HbA1c (9.71±1.30) than the recommended cut- point (<7%) in diabetic patients (ADA, 2010). It follows therefore, that these patients may be at greater risk of long- term complications due to diabetes if the glycemic level is not properly controlled and this call for concern in the management of diabetic patients.

However, there was no significant difference between the mean serum level of Albumin in the test subjects when compared with control subjects (p>0.05). This may be as a result of Insulin resistance which is a principal cause of type 2 diabetes (Kahn, 1994) [18] and previously, serum albumin has been associated with insulin resistance (Hostmark et al., 2005; Ishizaka et al., 2007). [19,20] In diabetic patients, plasma albumin concentration has been reported to be inversely related with HbA1c levels, revealing a large proportion of poorly

controlled diabetes in patients with lower plasma albumin concentrations (Rodriguez- Segade et al., 2005; Hemangi et al., 2012). [21,22] This inverse relationship may also be explained by the fact that poorly controlled type 2 diabetes has been associated with a further decrease in insulin production and secretion by the pancreatic β-cell (Marshak et al., 1999; Kahn, 2003). [23,24] Furthermore, our finding shows no significant difference between the serum levels of total protein in the diabetic patients and control subjects ($p>0.05$). This is in contrast with the findings of (Malawadi and Adiga, 2016; Nazki et al., 2017). [25,26]

Our study in Indian subjects suggests that higher serum albumin levels may decrease HbA1c levels and that lower serum albumin levels may raise HbA1c levels as reported previously from western studies. [22] Further, we caution that our study may be interpreted as hypothesis‐generating, rather than hypothesis proving results, as this study has several limitations ‐importantly, it was a retrospective study. Also, we classified subjects into hyperglycemia and non hypergylcemia and did not group them into diabetes and non‐diabetes. [27]

Conclusion

In conclusion, the present study showed significantly higher mean levels of HbA1c in the diabetic patients compared with the control subjects. However, the mean serum of levels of Albumin and total protein did not differ significantly when compared between the diabetic patients and controls. This finding implies that there was a poor glycemic control in the diabetic subjects studied. Therefore, there is need for better management of diabetic patients through medication and use of diet and exercise.

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