



CORRELATION OF SERUM CALCIUM LEVELS WITH GLYCATED HEMOGLOBIN IN TYPE 2 DIABETES MELLITUS PATIENTS- A COMPARATIVE STUDY

Biochemistry

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ABSTRACT

Background: The incidence of type-2 Diabetes Mellitus has increased world-wide making it a major public health problem. Electrolyte and mineral abnormalities are common in patients with type-2 Diabetes Mellitus. Therefore, this study was undertaken to look for the correlation between HbA1c (glycated hemoglobin) and serum calcium levels in patients with type-2 Diabetes Mellitus.

Aim: To study the correlation of serum calcium levels with glycated hemoglobin (HbA1c) levels in type-2 Diabetic patients.

Materials and Methods: A total of 130 type 2 Diabetic patients and 130 healthy non Diabetic people of age (30-55) years were included for the study. Both fasting and post prandial blood samples were collected from the two groups and were used for fasting blood sugar, HbA1c, serum calcium and post prandial blood sugar determination. Unpaired student's t-test was used to compare the results between the diabetic and non-diabetic group.

Results: The results showed a significant decrease in the serum calcium levels ($p < 0.001$) in the type 2 Diabetic patients when compared to the non Diabetic control group, whereas HbA1c levels were significantly increased in the diabetic group when compared to the non-diabetic group ($p < 0.001$). Also, type 2 Diabetic patients showed a statistically significant negative correlation ($r = -0.732$, $P\text{-value} = 0.00$) between their HbA1c and serum calcium levels.

Conclusion: Type 2 Diabetic patients with poor glycemic control are at increased risk of developing hypocalcemia when compared to those with good glycemic control

KEYWORDS

Correlation, Glycated Hemoglobin (HbA1c), Serum Calcium, type-2 Diabetes Mellitus

1. INTRODUCTION

Diabetes Mellitus is a global epidemic affecting more than 422 million people world-wide [1]. It has also been predicted that by the year 2025, India will top the list of countries with the largest number of people with Diabetes Mellitus followed by China and United States [2]. Type-2 Diabetes Mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from a relative Insulin deficiency or resistance to the action of Insulin [3]. The long term complications of Diabetes Mellitus includes; development of Diabetic retinopathy, Diabetic nephropathy and Diabetic neuropathy [4]. These complications are far less common and also less severe in people who have well controlled blood glucose levels [5]. The Diabetes control and complications trial (DCCT) and United Kingdom prospective Diabetes study have shown that the risk for developing Diabetic complications are directly related to glycemic control which is measured by glycated hemoglobin (HbA1c).

Glycated Hemoglobin (HbA1c) is routinely used to measure long term glycemic control in patients with Diabetes Mellitus [6]. Glycated Hemoglobin (HbA1c) is formed within the red blood cells at a rate directly proportional to the blood glucose level and indicates the mean blood glucose levels over the previous 10-12 weeks [7]. HbA1c values are not altered by any recent changes in diet, exercise or drug intake [8].

Skeletal system involvement is yet another complication of Diabetes Mellitus [9]. Patients with Diabetes Mellitus have increased risk of developing skeletal complications like osteoporosis, Charcot's arthropathy and Diabetic foot syndrome [10]. Bone and mineral abnormalities observed in patients with type-2 Diabetes Mellitus may be caused by Insulin resistance and hyperglycemia on the bone and bone marrow micro environment and increased concentrations of advanced glycation end products affecting the bone matrix proteins [11].

Calcium is a major mineral of the bones and teeth and also plays a major role as a second messenger in cell-signalling pathway. Calcium is necessary for insulin mediated intracellular processes in insulin-responsive tissues such as skeletal muscle and adipose tissue [12]. Changes in serum calcium levels in type-2 Diabetes Mellitus contributes to peripheral Insulin resistance via impaired Insulin signal

transduction leading to decreased GLUT-4 activity [13,14,15].

Decreased levels of serum calcium in type-2 Diabetes Mellitus patients may be due to hyperglycemia which causes excessive urinary loss of calcium proportional to the degree of glucosuria [16]. In response to urinary calcium loss, parathyroid hormone (PTH) secretion is mildly stimulated to maintain serum calcium concentrations. Bone formation is suppressed in the hyperglycemic state and urinary calcium loss in Diabetes is derived from the bone [17].

The aim of this study is to study the correlation of serum calcium and Glycated Hemoglobin (HbA1c) levels in patients with type-2 Diabetes Mellitus. This is to demonstrate how glycemic control can affect serum calcium levels in type-2 Diabetic patients.

2. MATERIALS AND METHODS

Study population

The study population consisted of two groups. Group-1 included type-2 Diabetic patients ($n = 130$) and Group-2 consisted of healthy non-Diabetic people ($n = 130$). The study was a comparative study.

Inclusion criteria

130 type-2 Diabetic patients of age group (30-55 years) with disease duration of less than 5 years were included for the study. They were recruited from the medicine op and NCD clinic after getting permission from the medicine department. Another 130 normal healthy people without Diabetes formed the non-Diabetic group which included people coming for routine health check up to the master health op.

Exclusion criteria

Patients with known history of (cardiovascular disease, respiratory disease, skeletal muscle injury, renal failure, bone and endocrine diseases) and terminally ill patients were excluded from the study.

Parameters studied

Serum Calcium, Glycated Hemoglobin (HbA1c), Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS)

Study method

Ethical committee approval was obtained for the study. Written

informed consent was obtained from all the participants of the study. All the participants were clearly explained about the procedure of the study. 5 ml of peripheral venous blood was collected from both the diabetic and non-diabetic group under strict aseptic conditions in the fasting and postprandial state. This sample was divided into two portions. The first part (2ml) was transferred to an EDTA tube and used for HbA1c analysis. HbA1c percentage was analysed by particle enhanced immuno-turbidimetric test method using HbA1c XL System Pack kit. EM-360 Fully automated clinical chemistry analyser was used for HbA1c determination. The second part (3ml) was allowed to clot at 37°C for 3 minutes and then centrifuged for 10 minutes. After separation, the serum samples were used for calcium, fasting and post prandial blood glucose determination. Erba Chem 5 plus V2 Semi automated clinical chemistry analyser was used for serum Calcium measurement. Serum Calcium levels were analysed by Arsenazo-III method. Both fasting and post prandial blood glucose levels were determined by enzymatic kit methods.

Statistical method of analysis

Statistical analysis was done using SPSS statistical package version 21. Data was expressed in terms of Mean ± SD. Unpaired student's t-test was used to compare the results between the diabetic and non-diabetic group. Pearson's correlation coefficient was used to correlate serum calcium levels with HbA1c levels in type-2 Diabetic patients. Statistically significant variation was considered when p value was less than 0.05.

3. RESULTS

Table 1: Comparison of mean values of HbA1c and serum Calcium between Diabetic and non-Diabetic group

	Diabetic Group (n= 130)	Non-Diabetic Group (n= 130)	P-Value
HbA1c (%)	8.41± 1.45	5.37± 0.29	0.000**
Serum Calcium (mg/dL)	8.53± 0.31	9.54± 0.44	0.000**
FBS (mg/dL)	193.39± 58.22	89.44± 10.98	0.000**
PPBS (mg/dL)	255.48± 70.24	111.11± 6.41	0.000**

** Highly Significant (p < 0.001)

*Significant (p < 0.05)

FBS - Fasting Blood Sugar; PPBS – Post Prandial Blood Sugar; HbA1c – Glycated Hemoglobin

Table 1 shows that mean values of Serum Calcium were significantly lower in the Diabetic group when compared to the non-Diabetic control group (P-value < 0.001); while mean values of HbA1c, FBS and PPBS were significantly higher in the Diabetic group (P-value < 0.001).

Table 2: Correlation between HbA1c and serum Calcium levels in Diabetic Group

	Serum Calcium (mg/dL)
HbA1c (%)	Pearson correlation -0.732**
	Sig. (2-tailed) 0.00
	N 130

**Correlation is significant at the 0.01 level

Table 2 shows that Serum Calcium levels have a strong negative correlation with HbA1c levels in the Diabetic group (r = -0.732, P-value = 0.00).

Figure 1: Bar Diagram showing comparison of mean values of HbA1c and serum Calcium between Diabetic and non- Diabetic group

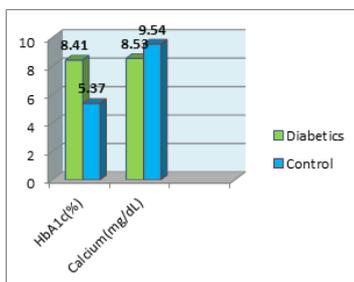


Figure-1. Bar Diagram shows decrease in the mean Serum Calcium levels and increase in mean HbA1c values in the Diabetic group when compared to the non-Diabetic group.

Figure-2: Scatter diagram showing the Correlation between HbA1c and serum Calcium levels in Diabetic Group

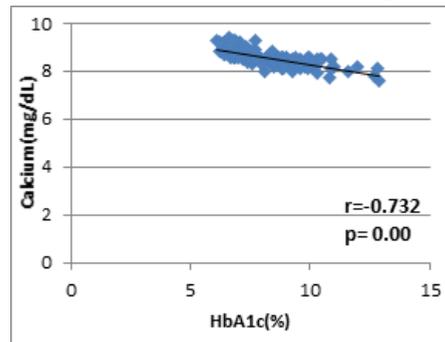


Figure 2. Scatter diagram shows a statistically significant negative correlation between HbA1c and Serum Calcium levels in the Diabetic group (r = -0.732, P-value = 0.00).

4. DISCUSSION

In the present study, we have evaluated the levels of serum calcium in type-2 Diabetic patients and its correlation with HbA1c levels. Results in our study have shown that serum calcium levels were significantly decreased (p < 0.001) in type-2 Diabetic patients when compared to the non-Diabetic control group. The mean level of HbA1c in patients with type-2 Diabetes Mellitus in our study was (8.41 ± 1.45) and they were significantly higher (p < 0.001) than those of the non-Diabetic controls with mean value (5.37 ± 0.29) as shown under (table-1 and figure-1). The findings in our study are in accordance with the study done by Najeeb et al [18]. who also showed statistically significant decrease in serum calcium and increase in HbA1c in type 2 Diabetic patients when compared to non-Diabetic controls (p < 0.001). Similar findings were also observed in another study done by Kanchana N and Saikumar P [19]. However in contrast to our study, Nuha E. Abubaker and Mohammed Nasir [20] had shown that there was no statistically significant difference in serum calcium levels between the Diabetic and non-Diabetic control group (p > 0.05).

The decrease in serum calcium levels in type 2 Diabetic patients observed in our study may be due to several factors; reduction in Insulin levels with impaired bone formation as a result of decreased osteoblastic activity thus resulting in impaired calcium homeostasis, associated hyperglycemia which increases the calcium and glucose excretion in urine proportional to the degree of glucosuria. The increase in HbA1c levels observed in patients with type-2 Diabetes Mellitus in our study may be due to poor glycemic control.

In our study, a statistically significant negative correlation (r = -0.732, P-value = 0.00) between HbA1c and serum Calcium levels was observed in the type 2 Diabetic patients as shown under (table-2 and figure-2). These findings are in agreement with the study done by Safaa Abed EL et al [21]. who showed a significant negative correlation (r = -0.56, P-value = 0.00) between HbA1c and serum Calcium levels in the Diabetic Group.

5. CONCLUSION

We conclude that, in type 2 Diabetic patients, serum calcium levels are very much affected by poor glycemic control with a significant negative correlation between HbA1c and serum calcium levels. The better the glycemic control, as reflected by HbA1c, the better would be the serum calcium level. Therefore, it can be concluded that, a good glycemic control in type 2 Diabetic patients will contribute in improving the serum calcium level and lessen the associated risk of developing diabetic complications.

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