Section: Biochemistry

Original Research Article

EXPLORING THE LINK BETWEEN GLYCEMIC STATUS AND PARATHYROID HORMONE IN TYPE 2 DIABETES

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ABSTRACT

Background: Parathyroid hormone (PTH) is composed of 84 amino acids secreted by parathyroid cells. It plays a vital role in mineral and bone metabolism by promoting bone resorption, inhibiting urinary calcium (Ca) loss and accelerating vitamin D activation.[1] High blood glucose non-enzymatically glycates haemoglobin at numerous sites. The process of Glycation, takes 120 days. So, this property of Hb is used to track the average amount of glucose in the blood and measures a patient's glycaemic state for the past 3 months.[2]

Objectives: 1. To measure HbA1c levels in both cases and controls.
2. To measure PTH levels in cases and controls.
3. To correlate the association of HbA1c and PTH among cases and controls.

Materials and Methods: A case control study on 100 patients, out of which 50 cases of type 2 diabetes mellitus and 50 normal healthy individuals. HbA1c levels were measured using HPLC BIORAD D10 and PTH levels were measured using CLIA SIEMENS ADVIA CENTAUR XP. Spearman's rho was used to assess the correlation between HbA1c and PTH in cases and pearsons correlation analysis was done to assess the correlation between Hba1c and PTH in controls.

Results: Hundred participants (50 type 2 diabetes patients and 50 age- and sex-matched controls) were studied. HbA1c and PTH differed significantly between groups, being higher in cases. Correlations between HbA1c and PTH were weak in both groups, with large (HbA1c) and moderate (PTH) effect sizes. Higher PTH levels in higher quartiles.

Conclusion: Patients with type 2 diabetes showed significantly higher HbA1c and PTH levels than controls. However, weak correlation existed between these variables, suggesting multifactorial regulation of PTH beyond glycemia. Elevated PTH may contribute to skeletal complications in diabetes, warranting further large- scale longitudinal studies.

Keywords: HbA1c, PTH, Duration of diabetes mellitus.

INTRODUCTION

Diabetes is a metabolic disorder marked by defects in insulin secretion and function of insulin, which leads to long-term harm, organ failure, and dysfunction. Diabetes arises from multiple pathological mechanisms, such as insulin resistance and autoimmune death of pancreatic β-cells. Ninety percent of cases of diabetes are caused by T2DM, a disease that results in insulin resistance. Insulin resistance in liver, muscle, and fat cells as well as insufficient pancreatic insulin synthesis is the main causes of T2DM. Due to a combination of insufficient insulin secretory response and resistance to insulin action, T2DM can result in hyperglycemia. Diabetes can lead to both microscopic and macroscopic consequences, such as peripheral artery disease, stroke, neuropathy, retinopathy, and nephropathy.

Prevention, a healthy lifestyle that includes eating low carbohydrate, low fat, high- fibre meals, exercising moderately to vigorously, decreasing

weight, and avoiding prolonged inactivity is key to preventing type II diabetes.[3]

The HBA1C test is quick, easy to use, standardized, and less susceptible to fluctuation from pre analytical factors.[3] non-glycaemic factors that affect HbA1c are age, race, gender, erythrocyte turnover, anaemia, pregnancy, Haemoglobin variants, thyroid disease, liver disease, HIV, and kidney diseases. It has been known for a long time that different types of haemoglobin can affect the production and measurement of HbA1c. This interference depends on the type of congenital disorder that affects haemoglobin synthesis and the method used to measure HbA1c.[2]

PTH plays a central role in calcium and phosphate homeostasis by targeting two main organs, bone and kidney. In kidney it increases calcium reabsorption and inhibits phosphate reabsorption and stimulates the conversion of 25-hydroxyvitamin D3 to 1, 25 dihydroxy vitamin D3, which promotes intestinal calcium and phosphate absorption. In bone, PTH stimulates bone degradation, which leads to an increase in calcium and phosphate release. Produced by the chief cells of the parathyroid glands in response to low serum calcium concentration or high phosphate levels, PTH is cleaved to its biologically active form of 84-amino acids prior to secretion.

PTH has a dichotomous role regarding bone metabolism; continuous infusion causes a catabolic response resulting in bone loss, whereas intermittent injection leads to an anabolic response characterized by increased bone mineral density (BMD). PTH primarily utilizes the PKA pathway in exerting both its catabolic and anabolic effects. PKC activation by PTH has been associated with the activation of L-type voltage- gated calcium channels.[4]

Type 2 Diabetes mellitus reduces bone quality rather than BMD. Bone fragility in type 2 diabetes, which is not reflected by bone mineral density, depends on bone quality deterioration rather than bone mass reduction.[5]

Patients with DM are not only at risk for fracture, but also at risk for complications during osseous healing.[6]

MATERIALS AND METHODS

Study Design: Case control study

Participants: The study included 50 patients with type 2 diabetes mellitus, from june 2025 to December 2025, at the outpatient department of Endocrinology at Osmania General Hospital. All the patients were diagnosed to have diabetes mellitus according to ADA guidelines. meanwhile 50 age and sex matched healthy individuals were enrolled as controls.

Inclusion Criteria

Patients with type 2 Diabetes mellitus above 18 years of age.

Exclusion Criteria

Chronic kidney disease, Renal failure Chronic hepatic disease

Primary hyperparathyroidism Anaemia

Patients on diuretics, calcium and vitamin D supplements. Post menopausal women

Data Collection: 2ml of Venous blood samples for PTH in red topped tube and 2ml in purple topped tube for HbA1c from type 2 diabetes mellitus cases and age and sex matched healthy individuals were obtained under strict aseptic conditions from department of Endocrinology, at Osmania General hospital.

Statistical Analysis: Data analysis was done using Microsoft excel (version 2508) and the software statistic kingdom. Shapiro wilk test was used to evaluate the distribution of continuous data. For normally distributed data, descriptive statistics were reported as mean ± standard deviation and non-normally distributed data were expressed as median. correlation analysis for cases was done using spearman's rho correlation coefficient and Pearsons's correlation was used for controls. Group comparisons for HbA1c and PTH among cases and controls were done using Welch's T test. Quartile analysis was done to compare HbA1c quartiles with mean PTH.

RESULTS

A total of 100 participants were enrolled in the study out of which 50 were patients with type 2 diabetes mellitus and 50 were age and sex matched healthy individuals. Normality assessment was done using Shapiro wilk test which revealed that HbA1c in both cases and controls were non normally distributed whereas PTH showed normal distribution in cases and non normal distribution in controls. Therefore, descriptive statistics were expressed as median for non normally distributed data.

The median HbA1c level among cases and controls was 7.85 % and 5.6% respectively. The median PTH level was 26 pg/mL in controls, and mean of PTH in controls was 25.54. [Table1] Correlation analysis between HbA1c and PTH in cases showed a positive correlation between HbA1c and PTH in cases ($r = 0.0828$ $p = 0.5675$). [Figure 2]

Among controls, a small positive correlation was observed between HbA1c and PTH. ($r = 0.1971$, $p = 0.1701$). [Figure 3]

Comparison of HbA1c levels between cases and controls using Mann whitney U test demonstrated a statistically significant difference, with higher HbA1c levels observed in cases compared to controls ($z = 8.22$, $p < 0.001$). The effect size was large (0.82), indicating a substantial difference between the two groups. [Table 2]

Similarly, Mann whitney U test showed a statistically significant difference in mean PTH levels between cases and controls ($z = 5.002$, $p < 0.001$). PTH levels were significantly higher in cases compared to controls, with a moderate effect size (0.79) (Table 2).

Cases were stratified based on the quartiles of HbA1c, there was a gradual rise in the mean serum

level of PTH. The mean PTH level was lowest in the first quartile (Q1, HbA1c ≤ 6.7; 36.95 pg/mL) and rose in Q2 (41.41 pg/mL) and Q3 (42.51 pg/mL), with a slight plateau in Q4 (42.93 pg/mL). This indicates that as the glycemic burden increases, the level of PTH also rises.

Table 1: Descriptive statistics of HbA1c and PTH in both cases and controls

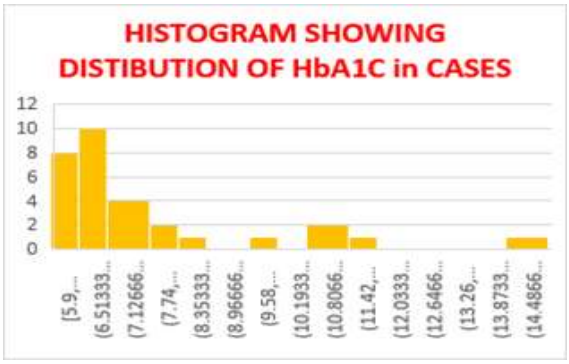
PARAMETER	MEDIAN OF CASES	MEDIAN OF CONTROLS
HbA1c	7.85	5.6
PTH	41.6	26

Table 2: Comparison of HbA1c and PTH among cases and controls using Mann whitney u test

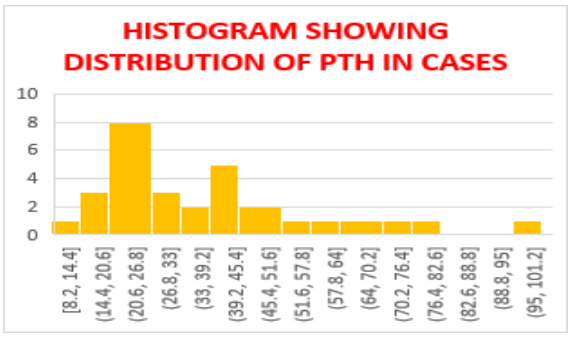
PARAMETER	P VALUE	Z VALUE	EFFECT SIZE
HbA1c	< 0.001	8.22	0.82
PTH	< 0.001	5.002	0.79

Table 3: Comparison of HbA1c quartiles with mean PTH, where Q3 and Q4 showing high Mean PTH levels

HbA1c Quartile	HbA1c Range	Mean PTH
Q1	≤ 6.7	36.95
Q2	6.8 – 7.8	41.41
Q3	7.9 – 9.8	42.51
Q4	9.9 – 15.1	42.93



A



B

Figure 1: A showing non normal distribution with right positive skew of HbA1C cases, B showing non normal distribution of PTH in cases

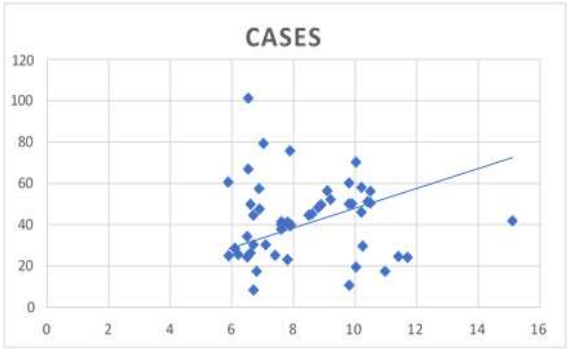


Figure 2: scatter plot showing positive correlation between HbA1c and PTH in cases r = 0.0828 p = 0.5675

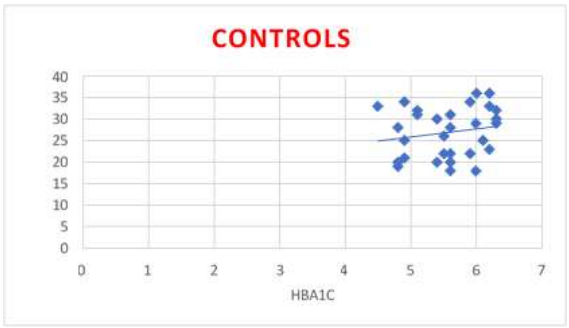


Figure 3: scatter plot showing weak positive correlation between HbA1c and PTH r = 0.1971, p = 0.1701

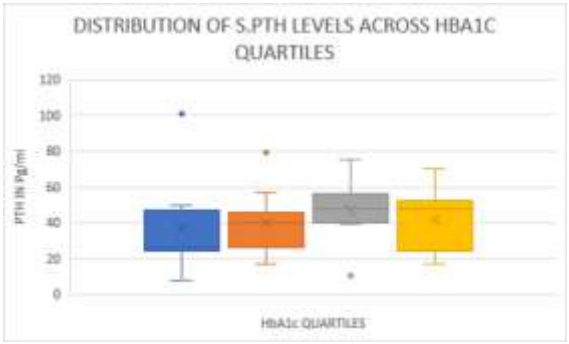


Figure 4: Box-and-whisker plot showing the distribution of serum parathyroid hormone (PTH) levels across HbA1c quartiles. The box represents the interquartile range, the central line denotes the median, and the whiskers indicate minimum and maximum values

DISCUSSION

The present study was done to explore the relationship between glycemic status and parathyroid hormone (PTH) levels in patients with type 2 diabetes mellitus. The findings of this study demonstrated that patients with type 2 diabetes mellitus had significantly higher levels of HbA1C and PTH than healthy controls, indicating effect of poor glycemic status on parathyroid function.

In this study, a significantly elevated levels of HbA1c were observed in cases compared to controls, reflecting persistent hyperglycemia in cases. This finding is consistent with the established role of HbA1c as a reliable indicator of long-term glycemic control.

PTH levels were also found to be significantly higher in cases compared to controls. These findings support previous observations suggesting diabetes is associated with disturbances in calcium homeostasis which leads to secondary alterations in parathyroid hormone. chronic hyperglycaemia may impair the intestinal absorption of calcium and bone and renal handling of calcium and phosphate,[7] resulting in decreased serum calcium levels which stimulate the expression of PTH gene in chief cells of parathyroid gland resulting in increased levels of parathyroid hormone.

Reduced bone formation may also occur, in part, due to an increase in advanced glycosylation end-products (AGEs) in bone collagen. AGEs are a broad group of molecules that accumulate as a result of the non-enzymatic glycation or glycoxidation of proteins, lipids, and nucleic acids.[8]

AGEs affect osteoblast function and binding to the collagen matrix as well as inhibit osteoblast development. In the bone matrix, the accumulation of AGEs increases the biomechanical brittleness of bone, which has lost its toughness and ability to deform before breaking.[9-13] A positive correlation between HbA1c and PTH was observed in cases $r = 0.0828$ $p = 0.5675$A and a weak positive correlation between HbA1c and PTH $r = 0.1971$, $p = 0.1701$ was observed in controls. This suggests that relationship between glycemic control and PTH levels may be influenced by multiple confounding factors such as duration of diabetes, renal function, vitamin D status, and insulin resistance.

HbA1c levels were markedly higher in cases compared to controls with the difference being highly statistically significant ($p < 0.001$) and associated with a large effect size (0.82). This finding confirms poor long-term glycemic control in the diabetic group.

In addition, serum PTH levels were significantly elevated in diabetic patients compared to controls with Mann whitney U test showing a statistically significant difference ($p < 0.001$) and a moderate to large effect size (0.79).

Analysis of patients stratified based on the quartiles of HbA1c revealed a gradual increase in serum PTH levels from lower to higher quartiles, with the lowest mean value of PTH in Q1 (HbA1c $\leq$ 6.7) and increasing levels in Q2 and Q3. Although a slight plateau was seen in the highest quartile, the overall trend suggests that deteriorating glycemic control is linked to increased levels of PTH. This is in line with the hypothesis that hyperglycemia can affect parathyroid gland function, perhaps due to abnormalities in calcium-vitamin D metabolism, insulin resistance, or chronic low-grade inflammation, as seen in type 2 diabetes mellitus.

The elevated PTH levels observed in patients with T2DM may have potential clinical relevance. Increased PTH levels are associated with reduced bone quality and increased fracture risk, Thus, monitoring PTH levels in patients with diabetes may help identify individuals at risk for skeletal complications.

CONCLUSION

This study demonstrates that patients with type 2 diabetes mellitus exhibit significantly higher HbA1c and parathyroid hormone (PTH) levels compared to healthy controls, suggesting an association between poor glycemic status and altered parathyroid function. A small correlation was observed between HbA1c and PTH within either group, indicating that PTH regulation in diabetes is likely influenced by multiple factors beyond glycemic control alone. These may include disturbances in calcium–phosphate metabolism, vitamin D status, insulin resistance, and duration of diabetes. Elevated PTH levels in diabetic patients may contribute to impaired bone quality and increased skeletal fragility, which are recognized complications of type 2 diabetes mellitus. Routine evaluation of PTH alongside glycemic markers may therefore provide additional insight into metabolic and skeletal alterations in diabetic patients. Further longitudinal studies with larger sample sizes are warranted to clarify causal relationships and clinical implications.

Limitations

This study has certain limitations that should be acknowledged. The relatively small sample size and single-center design may limit the generalizability of the findings. Important confounding factors influencing parathyroid hormone secretion, such as serum vitamin D, calcium, and phosphate levels, were not assessed. In addition, the duration of diabetes and its potential impact on hormonal variations were not evaluated. Bone mineral density and markers of bone turnover were also not included, which restricts direct interpretation of the clinical significance of elevated parathyroid hormone levels on skeletal health. Despite these limitations, the study provides useful preliminary insights into parathyroid hormone alterations in patients with type 2 diabetes mellitus.

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