



Original Article

Metabolic Disruptions in Serum Calcium and Phosphate Levels Among Pre-Diabetic and Type 2 Diabetic Patients

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ABSTRACT

Diabetes mellitus is a metabolic disorder classified by persistently raised blood sugar levels. **Objective:** To identify diabetes mellitus disturbances in serum calcium and phosphate levels. However, the exact mechanisms underlying this association were not fully understood. **Methods:** It was a cross sectional study. It was conducted at Isra University Hospital, Hyderabad from March 2023 to August 2023. 170 patients were selected with 85 patients in each group. Group A included patients with diabetes and Group B included patients with prediabetes with fasting blood glucose levels of 101-125 mg/dl or HbA1c levels of 5.7-6.4%. Fasting blood glucose levels, HbA1c levels, total serum calcium levels and serum phosphate levels were compared. Data were assessed by using SPSS version 24.0. P-values of ≤ 0.05 will be statistically significant. **Results:** This study has shown that in both in Group A and Group B, the mean age was 47.2 ± 8.4 years and 48.5 ± 7.6 respectively (p value=0.62). Group A exhibited a mean fasting plasma glucose level of 109.34 mg/dl ± 17.92 and Group B 140.59 mg/dl ± 31.03 . Group A displayed a mean serum phosphate level of 3.79 mg/dl ± 1.31 , while Group B exhibited mean level of 4.43 mg/dl ± 1.04 ($p=0.03$). Group A demonstrated a mean serum calcium level of 8.41 mg/dl ± 1.03 , whereas Group B had serum calcium level of 8.01 mg/dl ± 0.98 ($p=0.02$). **Conclusions:** The findings underscore the intricate relationship between metabolic disorders and mineral homeostasis, highlighting the potential implications for clinical management and risk stratification in diabetic patients.

INTRODUCTION

Diabetes mellitus is a persistent endocrine disorder that is identified by high blood sugar. The inadequate insulin secretion causes type II diabetes as well as tissues that are insensitive to insulin are playing a crucial role in disease causation [1]. The International Diabetes Association (IDF) has revealed that during 2019 more than 460 million people aged between 21 and 80 years were suffering diabetes mellitus globally especially the Type 2 type [2]. In the years between 1990 and 2017, there was 102.9% rise in new cases of diabetes mellitus occurring across all countries, such that number increased from 11,303,084 cases registered

during the year 1990 to 22,935,630 incidences seen by the end of 2017 while Age Standardized Incidence Rates advanced by 234-285/100000 person-years [3]. Physical inactivity, BMI, blood pressure, age & sex are all highly correlated with Diabetes Mellitus. Hence, it has been established that owing to the escalating obesity levels worldwide, cases of diabetics will be more numerous in the next few years as per projections [4]. Diabetes mellitus can also affect the serum levels of calcium and phosphate. Calcium homeostasis is regulated by insulin because it brings in calcium into cells including bone cells and keeps it

out of the bone. Insulin resistance and impaired insulin secretion in DM can interfere with this equilibrium and result in changes in calcium metabolism [5]. Some studies suggest that individuals with DM2 may have lower serum calcium levels compared to non-diabetic individuals. However, the exact mechanisms underlying this association are not fully understood. In addition, Insulin resistance and hyperglycemia in DM2 can affect phosphate levels indirectly through their impact on insulin signaling pathways [6]. Studies have reported conflicting findings regarding serum phosphate levels in individuals with DM2. A study aimed to evaluate the serum levels of calcium and phosphate in diabetics, pre-diabetics, and non-diabetics has revealed that Calcium and Phosphorus Levels in diabetic patients were around 1.97 ± 0.16 mmol/l and 0.76 ± 0.07 mmol/l respectively. While in pre-diabetics the Serum Calcium (Ca) levels were 2.15 ± 0.18 mmol/l and Serum Phosphate (PO_4) levels were 0.93 ± 0.06 mmol/l. In non-diabetic group Serum Calcium (Ca) levels were 2.33 ± 0.10 mmol/l and Serum Phosphate (PO_4) levels were 1.19 ± 0.20 mmol/l highlighting that as glycemic control deteriorates; blood calcium and phosphate levels tend to fall [7]. While some studies have shown higher serum phosphate levels in DM2 patients, others have found no significant difference compared to non-diabetic individuals. Several factors contribute towards the disturbances in calcium and phosphate levels in blood in diabetes mellitus, particularly type 2 diabetes (DM2), can be influenced by. Persistent high blood sugar levels may lead to increased urinary excretion of calcium and phosphate, resulting in lower serum levels. It can also disrupt insulin signaling pathways involved in calcium and phosphate homeostasis [8]. The kidneys have an important contribution in maintaining calcium and phosphate balance through filtration, reabsorption, and excretion processes. Disruption of these mechanisms can alter calcium and phosphate quantities in blood. Examples of drugs used in the management of diabetes which affect calcium and phosphate concentrations include Thiazolidinedione's (TZDs) [9]. The literature has notable omissions. There are few longitudinal studies that look at how disturbances in serum calcium and phosphate levels develop over time [10]. The pathophysiology of prediabetes and DM2 is still not well understood as far as the underlying mechanisms connecting disruptions of calcium and phosphate metabolism to it are concerned. However, chronic inflammation and oxidative stress contribute significantly to the pathogenesis of prediabetes as well as DM2 [11, 12]. It is not well-understood what happens specifically when conditions such as inflammation and oxidative stress interact with serum calcium or phosphate production though there are findings implying that these things may influence them in some way. Minimal data have examined contrasting groups of drugs used for diabetes

prevention regarding their influence over these two parameters.

This research aimed to assess serum calcium and phosphate levels in individuals with prediabetes and DM2. By comparing these parameters across different stages of glucose metabolism impairment, from prediabetes to established DM2, the study seeks to identify potential trends or patterns in disturbances of calcium and phosphate homeostasis along the continuum of diabetes development.

METHODS

It was a cross-sectional study. It was conducted from March 2023 to August 2023 at Isra university hospital Hyderabad after the authorization of Institutional ethics committee, Isra University, Hyderabad (IU/DM&DR/2023/5266). A specific criterion of inclusion and exclusion was designed. All individuals more than 21 years of age suffering from with T2DM and pre-diabetes were included in this study. Patients with chronic kidney and liver diseases, cancer, bone and mineral disorders, and drug use that interfered with the metabolism of Ca and PO_4 were excluded. The sample size was calculated by using population proportion 26.3%. The confidence interval of 95% and error margin of 6.5%. 170 patients were selected with 85 patients in each group. Group A included patients with diabetes mellitus presented in outdoor patients' department of admitted in emergency ward of Isra university hospital. Group B included patients with prediabetes with fasting blood glucose levels of 101-125 mg/dl or HbA1c levels of 5.7-6.4%. Random distribution was done in groups named as Group A (diabetes patients) and Group B (pre-diabetics). Written informed consent was taken from the participants and structured study Performa was designed to collect the data. Blood was withdrawn to measure fasting blood glucose levels, HbA1c levels, total serum calcium levels and serum phosphate levels. HbA1c was compared in both groups to establish the baseline glycemic control status of each group and to confirm the classification criteria for diabetes and prediabetes. The demographic data like age, gender and BMI was also calculated. To compare the mean values of two independent groups (Group A: patients with diabetes and Group B: patients with prediabetes), the study used an independent t-test for continuous variables such as fasting blood glucose levels, HbA1c levels, serum calcium levels, and serum phosphate levels. The results were presented as means and standard deviations. The analysis was performed using SPSS version 24.0. Demographic data are presented as percentages, calculated in Excel. A p-value of ≤ 0.05 was considered statistically significant. The findings were interpreted in the context of the study objectives and existing literature.

RESULTS

This study has shown that in Group A, the mean age was 47.2 ± 8.4 years while Group B had a slightly higher mean age of 48.5 ± 7.6 (p value=0.62). The distribution of gender within the groups was fairly balanced, with Group A consisting of 39 males (45.88%) and 46 females (54.11%), while Group B had 44 males (51.76%) and 41 females (48.23%). Group A had a mean BMI of 27.5 ± 7.6 , whereas Group B had a slightly lower mean BMI of 26.3 ± 6.4 . In Group A 31 individuals (36.47%) were diagnosed with hypertension, while in Group B had 26 individuals (30.59%) with the condition, as shown in table 1.

Table 1: Demographic Features of the Study Sample (n=170)

Variables	Group A (Mean \pm SD) / N (%)	Group B (Mean \pm SD) / N (%)
Age (Years)	47.2 ± 8.4	48.5 ± 7.6
Male	39 (45.88%)	44 (51.76%)
Female	46 (54.11%)	41 (48.23%)
Body Mass Index	27.5 ± 7.6	26.3 ± 6.4
Hypertension	31 (36.47%)	26 (30.59%)

In this study, fasting plasma glucose levels and HbA1c percentages were measured in both Group A and Group B to assess glycemic control and potential differences between the groups. Group A exhibited a mean fasting plasma glucose level of 109.34 ± 17.92 mg/dl. In contrast, Group B showed a significantly higher mean fasting plasma glucose level of 140.59 ± 31.04 mg/dl suggesting poorer glycemic control compared to Group A. Similarly, when examining HbA1c percentages, Group A displayed a mean value of $5.73\% \pm 0.39$, indicative of well-controlled blood glucose levels over time. Conversely, Group B presented a substantially higher mean HbA1c percentage of $9.41\% \pm 1.73$, suggesting poorer long-term glycemic control compared to Group A ($p=0.03$) (table 2).

Table 2: Assessment of Blood Glucose Levels and HbA1c Levels

Variables	Group A (Mean \pm SD)	Group B (Mean \pm SD)
Fasting Plasma Glucose Levels (mg/dL)	109.34 ± 17.92	140.59 ± 31.04
HbA1c (%)	5.73 ± 0.39	9.41 ± 1.73

In this investigation, serum phosphate and serum calcium levels were assessed in both Group A and Group B to explore potential variations in mineral metabolism between the two cohorts. Group A displayed a mean serum phosphate level of 3.79 ± 1.31 mg/dl, while Group B exhibited a slightly higher mean level of 4.43 ± 1.04 mg/dl ($p=0.03$). This suggests that individuals in Group B had elevated serum phosphate levels compared to those in Group A. Furthermore, when examining serum calcium levels, Group A demonstrated a mean level of 8.41 ± 1.03 mg/dl, whereas Group B had a slightly lower mean level of 8.01 ± 0.98 mg/dl ($p=0.02$). This indicates a trend towards lower serum calcium levels in Group B compared to Group A as shown in table 3.

Table 3: Comparison of Serum Calcium and Serum Phosphate in Group A and Group B

Variables	Group A (Mean \pm SD)	Group B (Mean \pm SD)
Serum Phosphate (mg/dL)	3.79 ± 1.31	4.43 ± 1.04
Serum Calcium (mg/dL)	8.41 ± 1.03	8.01 ± 0.98

DISCUSSION

Diabetes is a disorder characterized by deranged levels of glucose in the blood. This can be due to either insulin deficiency or resistance of the action of insulin and often both of them. It is an important health problem that affects many people across the globe especially in the management of healthcare including patients themselves [13]. Insights concerning metabolic profiles and demographic features of Group A and Group B can be deduced from findings of the aforementioned research, revealing the possible variation in health parameters between them. About demographic characteristics, these two groups were similar in that they had the same levels when it came to age and sex distribution, without any major disparities being noticed. This means that demographic factors are not likely to affect health differences between the two groups. In terms of metabolic parameters, Group B (type II diabetes patients) showed significantly increased levels of fasting plasma glucose as well as HbA1c than in Group A (pre diabetes patients). Thus, depriving them might be worsening the glycemic controls as well increasing numbers suffering from this condition in comparison with those from Group A. The results of this study show that people belonging to Group B may suffer from diabetes more often and to a larger extent. According to the data, the high values of fasting plasma glucose and HbA1c in Group B have underlined the significance of efficient management of diabetes and measures aimed at improving glycemic control among these people [14]. Additionally, there was a noticeable distinction when it came to levels of phosphate and calcium in the blood serum of the two groups. Talking about the serum test results, group B showed higher amounts of serum phosphate while having slightly decreased serum calcium levels in contrast with group A. These disparities could also reflect any potential variations that exist within our bodies' way of processing substances like minerals based on their own contexts. Further investigation is warranted to elucidate the factors contributing to these differences and their implications for overall health and disease risk in the respective populations [15]. Moreover, blood calcium levels in type 2 diabetes mellitus patients significantly reduce, with an inverse correlation between duration and age of diabetes mellitus [16]. The findings of this study are also comparable with the findings of a study conducted in Bangladesh. It has revealed that in Type 2 diabetes mellitus patients have considerably lower serum calcium levels (8.46 ± 0.63 vs 8.86 ± 0.64 mg/dl) than healthy controls [17].

The deranged calcium and phosphate levels in type II diabetes mellitus can lead to diabetic osteopathy. Studies have shown that those with Type II Diabetes mellitus had impaired bone remodeling processes [18]. Various factors are involved in alteration in serum mineral levels. Gut microbiota alterations can affect the absorption of serum calcium and it can play a role in both diabetes mellitus and osteopathogenesis, potentially contributing to bone health and diabetic osteopathy [19]. Another study has highlighted that the hypocalcemia (serum calcium level less 2.15 mmol/L) was detected in 73.6% of patients with type 2 diabetes mellitus. The prevalence of electrolyte abnormality entails that thorough investigation must be exerted to find out the causative factors behind these derangements [20]. This study employs a cross-sectional design, it only provides an assessment of calcium and phosphate levels at a single point in time. This limits the ability to establish causal relationships between disturbances in serum calcium and phosphate levels. There may be confounding variables, such as diet, physical activity levels, medication use, or comorbidities. Moreover, the small sample size can affect the generalizability of the outcomes of this study. Detection of abnormal levels of calcium and phosphate in the serum can be an early warning for the onset of metabolic dysfunction among individuals who are at risk for diabetes. With this information, medical professionals (doctors, nurses, etc.) can prevent this from happening by making changes in lifestyles like diet or drugs that prevent or control diabetes [21]. The study may stimulate further research into the mechanisms underlying disturbances in serum calcium and phosphate levels in diabetes. This could lead to the development of novel therapeutic interventions aimed at restoring metabolic balance and improving outcomes for diabetic patients.

CONCLUSIONS

In conclusion, the findings underscore the intricate relationship between metabolic disorders and mineral homeostasis, highlighting the potential implications for clinical management and risk stratification in diabetic patients. Further research is warranted to elucidate the underlying mechanisms driving these disturbances and to explore their prognostic significance in the context of diabetes-related complications.

Authors Contribution

Conceptualization: AFQ

Methodology: NUR

Formal analysis: SM, RA

Writing, review and editing: MP, MM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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