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Effect of Hyperglycemia in Diabetic Patients on Blood Calcium Levels

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ABSTRACT

Diabetes mellitus is a chronic disorder characterized by elevated blood glucose levels. This study aims to investigate the impact of hyperglycemia on calcium levels. The sample included 30 patients of various ages (20 patients>50 years, 10 patients < 50 years) and balanced gender distribution (15 males, 15 females). Participants were selected through questionnaire-based screening, with inclusion criteria requiring normal renal, hepatic, and parathyroid function. Measurements included blood glucose levels glycated hemoglobin (HbA1c) calcium levels and vitamin D (to confirm normal levels and exclude deficiency-related hypocalcemia. The results showed that 40% of the patients had decreased calcium levels. Moreover, a moderate inverse and statistically significant correlation was found between calcium levels and HbA1c ($P < 0.05$), and a statistically significant inverse correlation was observed between glucose and calcium levels ($P < 0.05$).

These findings suggest that glucose dysregulation may affect calcium absorption and homeostasis, potentially leading to adverse effects on bone health and cellular functions. The significance of this study lies in its contribution to the prevention of diabetes-related complications.

It is worth noting that vitamin D is essential for regulating calcium absorption and maintaining its levels within the normal range, highlighting the importance of assessing vitamin D status as part of the patients overall clinical evaluation.

KEYWORDS: Diabetes Mellitus, Hemoglobin A1c (HbA1c), Hyperglycemia, Calcium.

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1. Introduction

Diabetes mellitus is one of the most prevalent chronic diseases, defined as a group of metabolic disorders characterized by elevated blood glucose levels due to impaired insulin secretion, insulin resistance, or both [1]. As of 2021, the prevalence of diabetes in Syria among individuals aged 20-79 years is estimated to be approximately 14.9% [2]. The type of diabetes include: Type 1 diabetes (a chronic autoimmune disease), Type 2 diabetes (a common metabolic disorder caused by insufficient insulin secretion or insulin resistance), and gestational diabetes (which occurs during pregnancy in some women) [3]. This condition leads to numerous chronic complications, including diabetic retinopathy, neuropathy, nephropathy, cardiovascular diseases, dermatological conditions, infections, impaired wound healing, mental health disorders, sexual dysfunction, and acute complications such as diabetic ketoacidosis and hyperosmolar hyperglycemic state [4].

Calcium is a crucial element in the body, playing a central role in various physiological processes [5], including nerve signal transmission, muscle contraction, blood clotting, regulation of enzyme and hormone activity, intracellular signaling, cell growth and differentiation, and bone and dental health [6].

Vitamin D also plays a key role in regulating calcium absorption and maintaining calcium homeostasis in the blood [7].

Many studies have also been conducted worldwide in recent years to examine the relationship between elevated blood glucose levels and calcium concentrations in diabetic patients. A study titled (Gender based difference in glycemic control and diabetes related chronic complications among type 2 diabetic patients in Debre Berhan city public hospitals) reported significant gender differences in glycemic control, indicating that women are more susceptible to poor glucose regulation, which may exacerbate complications such as reduced calcium levels [8].

A study published under the title (Effect of glycemic control on calcium and phosphorus handling and parathyroid hormone level in patients with non-insulin-dependent diabetes mellitus), conducted on two patients with type 2 diabetes and poor glycemic control, found that after improving blood glucose levels over a period of 38 days, urinary calcium excretion significantly decreased. This finding suggests enhanced calcium absorption and stabilization in the body, potentially reducing the risk of osteoporosis related complications [9].

However, the research problem remains that the relationship between diabetes and alterations in calcium levels remains insufficiently understood, particularly due to the interaction of multiple influencing factors. The core issue lies in the need to investigate the effect of hyperglycemia on calcium levels independently of other known variables, in order to determine whether glucose imbalance alone contributes to a reduction in blood calcium levels.

Therefore, this study aims to evaluate the relationship between elevated blood glucose levels both transient and chronic (as indicated by HbA1c) and blood calcium levels in diabetic patients, while controlling for normal vitamin D status. The study seeks to determine whether disturbances in glucose homeostasis contribute to alterations in calcium levels, which may be indicative of potential complications related to bone health and cellular function.

2. Methodology

The study was conducted at " Qanbar Medical Laboratories in Hama " from March 1 to March 17, 2025. It included 30 patients with diabetes mellitus of varying genders (15 males, 15 females). Blood samples were collected in heparinized tubes and centrifuged at 3600 rpm for 3 minutes to separate plasma for analysis.

Diabetes and calcium analyses were performed using a spectrophotometer based on colorimetric analysis, while vitamin D levels were analyzed using liquid chromatography. The normal reference values for HbA1c, calcium, and vitamin D were as follows: HbA1c under 6%, calcium levels of 8.1 mg/dL, and vitamin D levels greater than 30 ng/mL.

3. Results

3.1.Represent cases of low calcium in diabetic patients by type and gender

Figure (1) illustrates the cases of hypocalcemia among diabetic patients according to type and gender. The chart shows that the highest proportion of hypocalcemia cases occurs in female patients with Type 2 diabetes, followed by female patients with Type 1 diabetes. In contrast, the proportion of male patients was significantly lower, not exceeding 5% of the total cases.

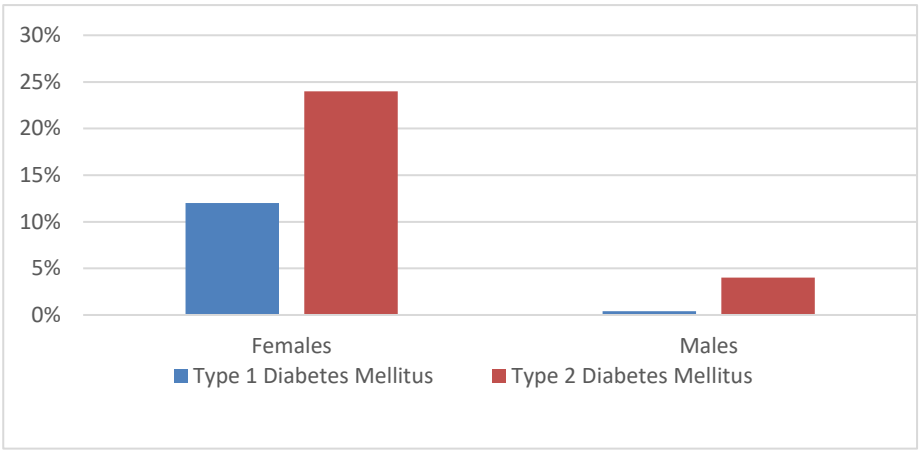

FIGURE (1): DISTRIBUTION OF HYPOCALCEMIA CASES IN DIABETIC PATIENTS CATEGORIZED BY TYPE AND GENDER

3.2.Distribution of vitamin D levels among patients

Figure (2) displays the results of vitamin D level analysis in the studied samples, with values falling within normal ranges. Given vitamin D vital role in enhancing calcium absorption from the gastrointestinal tract, it was initially considered a potential contributing factor to the observed hypocalcemia. However, the consistent and stable vitamin D levels across the target samples allowed its exclusion as a causative factor.

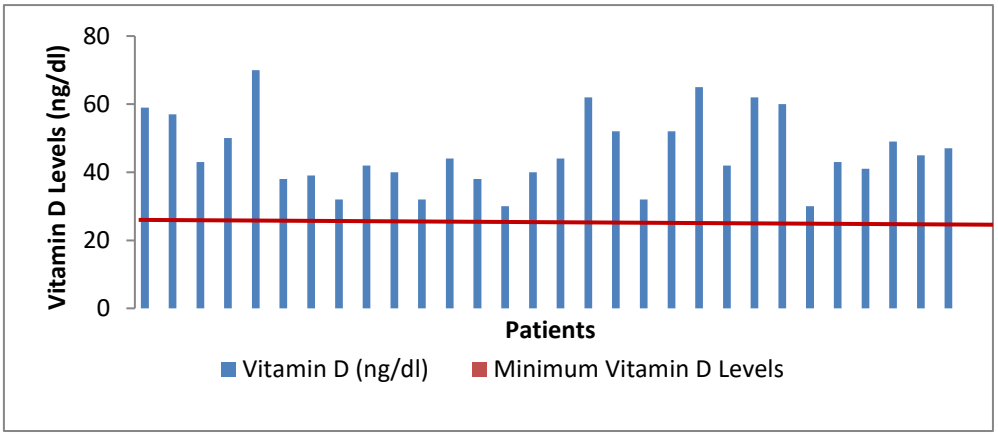

FIGURE (2): DISTRIBUTION OF VITAMIN D LEVELS AMONG PATIENTS

3.3.The relationship between calcium and HbA1c

Figure (3) demonstrates a moderate inverse relationship between calcium levels and HbA1c concentration in diabetic patients. This visual tendency was supported by Spearman's rank correlation analysis (P-value=0.00648, ρ=−0.486), confirming that higher HbA1c levels are significantly associated with lower calcium levels. These finding suggest that poor glycemic control (HbA1c) may disrupt calcium homeostasis, underscoring the metabolic consequence of chronic hyperglycemia on mineral balance in diabetes.

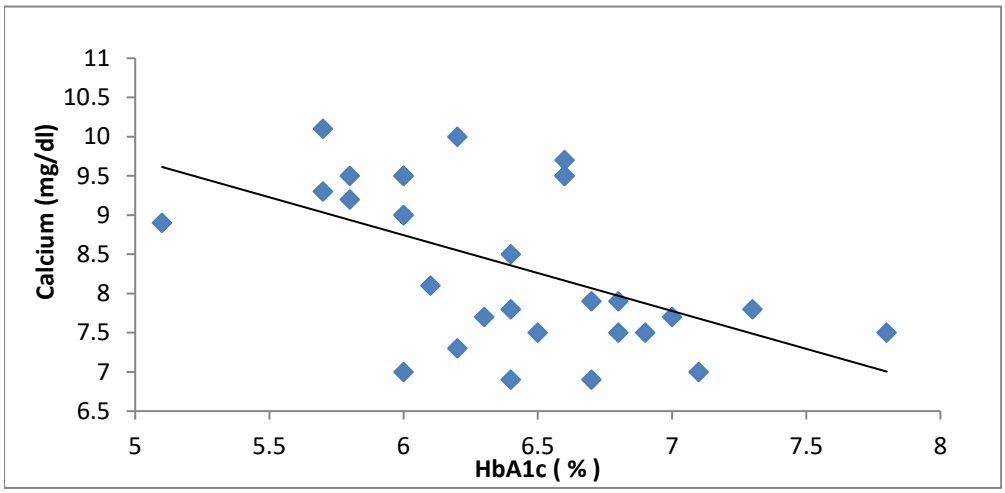

FIGURE (3) : GRAPHICAL REPRESENTATION OF CALCIUM AND (HBA1C) RESULTS

3.4.The relationship between calcium and glucose

Figure (4) show a significant inverse relationship between serum calcium levels and blood glucose concentration in diabetic patients. Spearman's correlation analysis ($\rho = -0.539, P - value = 0.000012 < 0.001$) statistically confirmed that elevated glucose levels are significantly associated with decrease calcium levels. These findings indicate that poor glycemic control may disrupt calcium homeostasis.

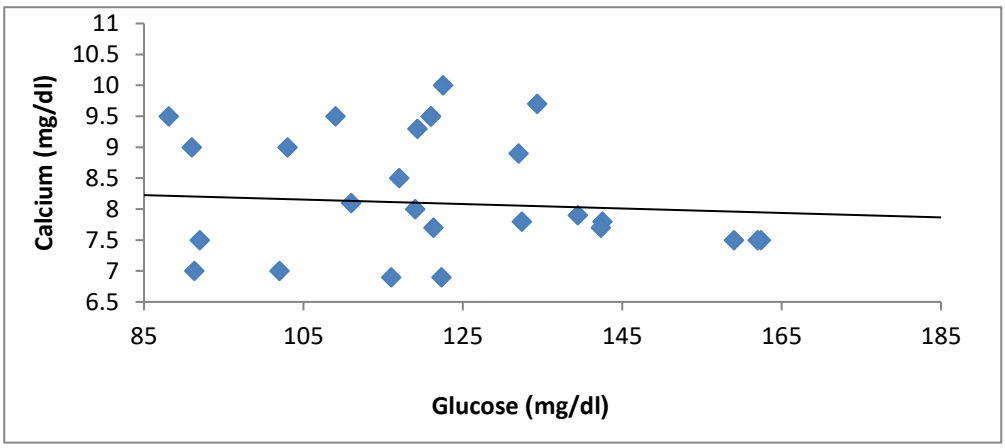

FIGURE (4) : GRAPHICAL REPRESENTATION OF CALCIUM AND GLUCOSE RESULTS.

4. Discussion

Through the practical study conducted on a sample of 30 diabetic patients of both types, encompassing both genders and various ages at Qanbar Medical Laboratories, the following conclusions were drawn:

It was observed that the majority of diabetic patients (66.66%) were aged above 50 years, while (33.33%) comprised younger individuals. These findings are consistent with a previous study which reported a 19.3% prevalence of diabetes among the elderly in 2019, with expectations of an increase in the coming years. These data confirm that aging is a major risk factor for diabetes, highlighting the importance of early prevention and targeted health interventions for this age group [10].

Consistent with these results, a separate study revealed that 85% of Type 2 diabetic patients suffer from overweight or obesity, reinforcing the link between obesity and increased risk of Type 2 diabetes [11].

This contradicts to the study which showed that the relationship between obesity and type 2 diabetes is not as clear as commonly believed. Although obesity is considered an important factor in the development of diabetes, this study suggests that other factors may play a greater role such as: physical inactivity, age-related declaim in pancreatic function (particularly after age 45), ethnicity (with higher risk observed in Asian populations), history of gestational diabetes and polycystic ovary syndrome (where hormonal Imbalance lead to insulin resistance) [12].

From Figure 3, the analysis of the relationship between blood calcium levels and glycosylated hemoglobin (HbA1c) revealed a moderate inverse correlation (P-value=0.00648, $\rho = -0.486$), suggesting that poor glycemic control is associated with decreased calcium levels. This finding is consistent with a study which demonstrated a statistically significant inverse relationship between calcium levels and HbA1c. the study was conducted on a cohort of 120 patients, divided into three groups based on HbA1c levels (well-controlled). Results revealed that the mean calcium level in the high HbA1c group was significantly lower compared to the other two groups ($p<0.05$), indicating a statistically significant association between elevated HbA1c and reduced serum calcium levels [13].

A complementary study confirmed a significant inverse correlation between HbA1c levels and calcium levels in pediatric patients with Type 1 diabetes mellitus, with a correlation coefficient of -0.445 and a p-value of 0.026, indicating moderate statistical significance [14].

Conversely, a study reported a positive correlation between calcium and HbA1c, where higher calcium levels were associated with increased HbA1c. This result clearly contradicts the findings of our study, which demonstrated an inverse relationship between these two variables.

The discrepancy in results can be attributed to differences in epidemiological setting, environmental and nutritional factors that may influence metabolic outcomes, as well as variation in study methodologies and sample characteristics. Moreover, longitudinal studies such as the Furukawa study may capture changes over time that are not evident in cross-sectional or small-scale studies [15].

Furthermore, a subsequent study did not establish a statistically significant relationship between these markers, supporting the hypothesis that environmental or biochemical factors may indirectly modulate this association [16].

A complementary supporting study confirmed a clear inverse relationship between HbA1c and calcium, reinforcing the observation that poor blood sugar control corresponds with lower calcium levels. These findings further support the hypothesis that chronic glycemic imbalance does not only affect glucose-related indicators, but also extends to vital mineral elements in the body, such as calcium-even when vitamin D levels remain within the normal range. This suggests the presence of a physiological interplay between glycemic regulation and mineral metabolism, highlighting the importance of regularly monitoring calcium levels in diabetic patients, especially those with persistently elevated HbA1c levels [17].

From Figure 4, the analysis of the relationship between blood calcium levels and glucose revealed a significant inverse relationship ($\rho = -0.539, P - value = 0.000012 < 0.001$) ,suggesting that poor glycemic control is associated with decreased calcium levels. These findings align with an experimental study demonstrating that a 75g oral glucose load induced a significant 4.2% decrease in serum calcium levels at 120 minutes ($P<0.01$), accompanied by concurrent increases in urinary calcium excretion. These rapid metabolic alterations confirm the existence of an immediate mechanism linking acute hyperglycemia to disrupted calcium homeostasis.[18]

The observed decrease in serum calcium levels among diabetic patients may be attributed to several mechanisms, one of which is the effect of high glucose osmolarity on calcium distribution, when blood glucose rises significantly, plasma osmolarity increases. This osmotic imbalance causes water to shift from the intracellular compartment to the extracellular (plasma) compartment in an attempt to restore osmotic equilibrium. As a result, a temporary expansion in plasma volume occurs, leading to a dilutional effect on calcium concentration, despite no actual change in the total body calcium content—a condition referred to as osmotic or dilutional hypocalcemia. Another possible mechanism involves the effect of glucose on membrane potential and calcium influx into cells. Unlike potassium, cells do not have specific active transport receptors for calcium in the same way. However, during acute or chronic hyperglycemia, alterations in membrane electrical balance may occur.

These changes can promote intracellular calcium influx or increased binding of calcium to proteins in the blood, reducing the concentration of free (ionized) calcium in plasma—i.e., the biologically active form of calcium declines. Furthermore, calcium's binding to proteins and its dependence on blood pH may also contribute to reduced calcium levels. In the bloodstream, calcium exists in three forms: ionized (free), bound to albumin, and complexed with anions such as phosphate. During acidosis, which is common in uncontrolled hyperglycemia, blood pH decreases. Hydrogen ions compete with calcium for albumin-binding sites, leading to a temporary rise in free calcium. However, following treatment and normalization of pH, more calcium binds to albumin, potentially causing a rapid drop in free (ionized) calcium levels.

Following insulin administration for hyperglycemia management, glucose enters cells rapidly. This is accompanied by the intracellular shift of potassium, phosphate, and magnesium. Part of the extracellular calcium may also shift into cells due to changes in membrane charge, resulting in decreased extracellular calcium levels despite no net loss of calcium from the body.

Upon analyzing vitamin D levels in the studied samples, it was found that all values were within the normal range, indicating no deficiency of this vitamin among the study subjects. Given the vital role of vitamin D in enhancing calcium absorption from the gastrointestinal tract, it was initially considered a potential contributing factor to the observed reduction in calcium levels. However, the consistency and stability of vitamin D levels across the targeted samples allowed it to be ruled out as a causative factor, thereby reinforcing the hypothesis that the decrease in calcium levels in this case may be primarily attributed to the effects of hyperglycemia. These effects may occur through increased urinary calcium excretion or hormonal imbalances related to diabetes. Therefore, this finding suggests that the calcium disturbance is directly linked to hyperglycemia itself rather than to vitamin D deficiency or malabsorption.

One study reached results consistent with the findings of this research. It investigated patients with type 2 diabetes and found that they experienced decreased serum calcium levels, while their vitamin D levels remained within the normal range. The study concluded that hyperglycemia is the main factor in calcium metabolism disturbances, primarily through increased renal calcium loss, rather than vitamin D deficiency.[19]

However, a conflicting study was published that included 122 diabetic patients and 122 healthy controls. A comparison between the two groups revealed a significant reduction in vitamin D levels among diabetic patients compared to the controls, in addition to a decrease in calcium levels. A negative correlation was found between both vitamin D and calcium with blood glucose levels, and a positive correlation between vitamin D and calcium levels. This study suggested that vitamin D deficiency may indeed be part of the explanation for the reduced calcium levels observed in diabetic patients. [20]

5. Conclusion and recommendation

From the previous study a notable inverse correlation was observed between blood calcium levels and diabetes control indicators. This suggests that both chronic and acute hyperglycemia contribute to disturbances in calcium homeostasis, despite vitamin D levels remaining within the normal range.

The study reached a set of recommendations that could help enhance the understanding of the relationship between elevated blood glucose and calcium imbalance, these include emphasizing the importance of regularly monitoring calcium levels in diabetic patients, rising health awareness programs to promote early detection and preventive care, encouraging further scientific research to better understand the relationship between hyperglycemia and calcium levels. Additionally, raising patients awareness about the importance of maintaining regular physical activity is crucial, as it improves insulin sensitivity and supports calcium absorption.

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