AMERICAN JOURNAL OF BIOLOGY AND NATURAL SCIENCES
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Article

# Evaluation of Parathyroid Hormone, Calcium, and Phosphorus Profiles in Patients with Type 2 Diabetes Mellitus

**Mohammed Abdul Hadi Mohammed[1] Huda Abdul Hadi Mohammed[2]**

[1]Sub speciality endocrinology, Baquba teaching hospital
[2] Gynecologist Alzahraa hospital for gynecology and pediatrics, Diyala Health Directors
* Correspondance: -

**Citation:** Mohammed M. A. H. Evaluation of Parathyroid Hormone, Calcium, and Phosphorus Profiles in Patients with Type 2 Diabetes Mellitus Journal of Biology and Natural Sciences 2026, 3(11), 95-106.

Received: 10th Aug 2026
Revised: 11th Sep 2026
Accepted: 10th Oct 2026
Published: 19th Nov 2026

**Copyright:** © 2026 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/)

## Abstract

*Background: Disturbances in calcium–phosphate homeostasis and parathyroid hormone (PTH) secretion have been implicated in impaired insulin secretion and insulin resistance, yet data on these parameters in Iraqi patients with type 2 diabetes mellitus (T2DM) remain scarce.*

*Objective: To evaluate serum intact PTH, total and albumin-corrected calcium, and inorganic phosphorus in women with T2DM, to compare them with non-diabetic women, and to examine their relationship with glycemic control and vitamin D status.*

*Methods: A hospital-based case–control study was conducted at Alzahraa Hospital for Gynecology and Pediatrics, Diyala, Iraq, from October 2025 to March 2026. Ninety women with T2DM and 60 age-matched non-diabetic women with an estimated glomerular filtration rate of at least 60 mL/min/1.73 m² were enrolled. Fasting blood glucose, glycated hemoglobin (HbA1c), creatinine, albumin, total calcium, phosphorus, intact PTH and 25-hydroxyvitamin D [25(OH)D] were measured.*

*Results: Compared with controls, patients with T2DM had higher PTH (58.7 ± 21.4 vs 44.2 ± 15.3 pg/mL, $p < 0.001$), lower total calcium (9.12 ± 0.52 vs 9.38 ± 0.41 mg/dL, $p = 0.001$), lower phosphorus (3.41 ± 0.62 vs 3.72 ± 0.51 mg/dL, $p = 0.002$) and lower 25(OH)D (17.6 ± 7.9 vs 23.4 ± 8.6 ng/mL, $p < 0.001$), whereas albumin-corrected calcium did not differ significantly ($p = 0.18$). Elevated PTH was found in 34.4% of patients versus 13.3% of controls ($p = 0.004$). Patients with poor glycemic control (HbA1c ≥ 7%) had higher PTH and lower phosphorus than those with good control. PTH correlated positively with HbA1c ($r = 0.38$) and inversely with 25(OH)D ($r = −0.41$), and both remained independent predictors of PTH in multiple regression.*

*Conclusion: Women with T2DM show higher PTH, lower phosphorus and lower vitamin D than non-diabetic women, with changes that worsen with poor glycemic control. Routine assessment of PTH, calcium, phosphorus and vitamin D may be warranted in this population.*

***Keywords:*** *Type 2 diabetes mellitus; Parathyroid hormone; Calcium; Phosphorus; Vitamin D; Glycemic control; Iraq.*

## 1. Introduction

Probiotic Diabetes mellitus has become one of the most pressing public health challenges of the twenty-first century. According to the International Diabetes Federation, approximately 537 million adults aged 20–79 years were living with diabetes in 2021, and this number is projected to reach 783 million by 2045, with the steepest relative increases expected in low- and middle-income countries [1,2]. Type 2 diabetes mellitus (T2DM) accounts for roughly 90% of all cases and is characterized by chronic hyperglycemia resulting from a progressive loss of adequate β-cell insulin secretion, frequently on a background of insulin resistance [3]. Its pathogenesis is multifactorial, involving genetic susceptibility, obesity, physical inactivity, dietary factors and a broad set of metabolic and hormonal disturbances that extend well beyond glucose metabolism [4]. The Middle East and North Africa region carries one of the highest age-adjusted prevalence rates of diabetes in the world, and community-based surveys from Iraq have documented a substantial burden of both diagnosed and undiagnosed disease among adults [2,5]. The chronic complications of T2DM, which include cardiovascular disease, nephropathy, retinopathy, neuropathy and, as is increasingly recognized, skeletal fragility, impose heavy costs on patients and health systems alike, and they underline the importance of understanding the full range of metabolic abnormalities that accompany the disease.

Calcium and phosphorus are the principal mineral constituents of bone and also serve vital extraskeletal functions. Ionized calcium is a ubiquitous intracellular second messenger that regulates muscle contraction, neural transmission, enzyme activity, coagulation and hormone secretion, whereas phosphorus is indispensable for nucleic acid structure, membrane phospholipids, cellular energy transfer through adenosine triphosphate and intracellular signaling through phosphorylation cascades [6]. The serum concentrations of these minerals are maintained within narrow limits by an integrated endocrine system that links the intestine, bone, kidney and parathyroid glands [7]. Parathyroid hormone (PTH), an 84-amino-acid peptide secreted by the chief cells of the parathyroid glands in response to a fall in extracellular ionized calcium sensed by the calcium-sensing receptor, is the central regulator of this system on a minute-to-minute basis [8]. PTH raises serum calcium by stimulating osteoclastic bone resorption, enhancing distal tubular calcium reabsorption and promoting the renal 1α-hydroxylation of 25-hydroxyvitamin D to its active form, 1,25-dihydroxyvitamin D, which in turn increases intestinal absorption of calcium and phosphate [7,8]. At the same time, PTH decreases proximal tubular phosphate reabsorption, producing a phosphaturia that counterbalances the phosphate released from bone. Vitamin D status therefore exerts a strong influence on PTH secretion: when circulating 25-hydroxyvitamin D falls, intestinal calcium absorption declines and the parathyroid glands respond with a compensatory rise in PTH, a state known as secondary hyperparathyroidism [9].

Interest in the relationship between this mineral-regulating axis and glucose metabolism has grown considerably over the past two decades. Insulin secretion by pancreatic β-cells is a calcium-dependent process: glucose-stimulated depolarization of the β-cell membrane opens voltage-gated calcium channels, and the resulting influx of calcium triggers the exocytosis of insulin-containing granules [10]. Calcium is also required for insulin-mediated intracellular processes in skeletal muscle and adipose tissue, and alterations in intracellular calcium flux have been linked to impaired glucose transporter activity and peripheral insulin resistance [10,11]. Vitamin D receptors and the 1α-hydroxylase enzyme are expressed in pancreatic β-cells and immune cells, and experimental and observational studies have suggested that vitamin D deficiency may impair insulin secretion, reduce insulin sensitivity and promote the low-grade systemic inflammation that characterizes T2DM [11]. In a frequently cited study, Chiu and colleagues showed that hypovitaminosis D was associated with insulin resistance and β-cell dysfunction in glucose-tolerant adults [12], and meta-analytic evidence has pointed to an inverse association between vitamin D status or calcium intake and the risk of incident T2DM [10].

PTH itself has emerged as a potential link between mineral metabolism and dysglycemia, independently of vitamin D. Plasma intact PTH concentrations were found to be inversely correlated

with insulin sensitivity in healthy individuals [13], and in a community-based cohort of older adults, higher PTH concentrations were associated with an increased prevalence of the metabolic syndrome in men [14]. Clinical observations in primary hyperparathyroidism further support this connection: the prevalence of diabetes and impaired glucose tolerance in patients with primary hyperparathyroidism is several-fold higher than in the general population, and insulin resistance may improve after successful parathyroidectomy [15,16]. Experimental work in animals with chronic PTH excess has shown that sustained elevation of PTH increases basal cytosolic calcium in β-cells, which paradoxically blunts glucose-stimulated insulin secretion [17]. These lines of evidence raise the possibility that even moderate elevations of PTH, such as those occurring in secondary hyperparathyroidism due to vitamin D insufficiency, may contribute to the deterioration of glucose homeostasis.

Serum calcium and phosphorus have also been examined directly in relation to diabetes. In a population study from Newfoundland, Sun et al. observed that serum calcium was correlated with fasting glucose, insulin resistance and β-cell function [18], and prospective data from the Insulin Resistance Atherosclerosis Study and the Atherosclerosis Risk in Communities study have linked higher serum calcium to the subsequent development of T2DM [19,20]. Phosphorus has attracted particular attention because insulin promotes the cellular uptake of phosphate together with glucose, and hypophosphatemia has been proposed as both a consequence of and a contributor to disturbed energy metabolism in the metabolic syndrome [21]. Moreover, glycosuria and osmotic diuresis in poorly controlled diabetes increase urinary losses of calcium and phosphate, while insulin therapy itself influences renal phosphate handling [22]. Despite these plausible mechanisms, the published findings are inconsistent: some studies report lower serum calcium and phosphorus in patients with diabetes, others report higher or unchanged values, and the direction of any association with glycemic control remains uncertain.

The clinical relevance of these disturbances extends to bone health. Paradoxically, patients with T2DM often have normal or even increased bone mineral density, yet they experience a higher risk of hip and other fragility fractures than people without diabetes [23]. Mechanisms proposed to explain this discrepancy include the accumulation of advanced glycation end-products in bone collagen, reduced bone turnover, altered osteoblast function, microvascular disease and an increased propensity to fall [24]. Bone mineral density and conventional fracture risk scores have been shown to underestimate fracture risk in older adults with T2DM [25]. Interestingly, in postmenopausal women with T2DM, relatively low PTH levels accompanied by suppressed bone formation have been associated with vertebral fractures, suggesting that the parathyroid response may be heterogeneous in this population [26]. Characterizing PTH, calcium and phosphorus profiles in women with T2DM may therefore help clinicians to identify those at risk of skeletal complications.

The kidney adds a further layer of complexity. Diabetic kidney disease is the leading cause of chronic kidney disease worldwide and develops in a considerable proportion of patients with T2DM [27]. Chronic kidney disease–mineral and bone disorder (CKD-MBD), which encompasses abnormalities in calcium, phosphorus, PTH and vitamin D metabolism, begins early in the course of renal impairment [28]. In the Study to Evaluate Early Kidney Disease, secondary hyperparathyroidism was already detectable in a meaningful proportion of patients with an estimated glomerular filtration rate (eGFR) above 60 mL/min/1.73 m² [29], and the phosphaturic hormone fibroblast growth factor 23 rises even earlier than PTH [30]. Studies that aim to explore an intrinsic relationship between diabetes and mineral metabolism must therefore account for renal function, ideally by restricting enrollment to patients with preserved eGFR.

In Iraq, data on mineral metabolism in patients with T2DM are limited, and few studies have been conducted in Diyala Governorate. Hypovitaminosis D is widely reported in the Middle East despite abundant sunshine, owing to factors such as conservative dress, indoor lifestyles, skin pigmentation and limited food fortification, and women appear to be particularly affected [9]. Women attending gynecological services represent a population in whom diabetes, obesity, multiparity, lactation and the menopausal transition converge to place considerable demands on calcium homeostasis, yet they are seldom specifically studied. A better understanding of their PTH, calcium and phosphorus profiles could inform screening strategies, guide decisions on vitamin D and

mineral assessment and contribute local evidence to an unresolved international debate. Moreover, most published studies have been conducted in populations of European or East Asian origin, in which dietary habits, vitamin D status, body composition and patterns of diabetes care differ substantially from those of Iraqi women, so their findings cannot simply be extrapolated to the local setting. Many earlier reports also measured calcium or phosphorus in isolation, without simultaneous assessment of PTH, vitamin D, albumin and renal function, which makes it difficult to determine whether an observed abnormality reflects a primary disturbance, a compensatory hormonal response or merely a change in protein binding. An integrated evaluation of these interrelated parameters, conducted in patients with preserved renal function, is therefore needed to clarify their relationship with glycemic control. Accordingly, the present study was designed to evaluate serum intact PTH, total and albumin-corrected calcium and inorganic phosphorus in women with T2DM attending Alzahraa Hospital for Gynecology and Pediatrics in Diyala, Iraq, to compare these parameters with those of non-diabetic women, and to examine their relationship with glycemic control, duration of diabetes, body mass index and vitamin D status.

Methodology

This hospital-based case–control study was conducted at Alzahraa Hospital for Gynecology and Pediatrics, a public teaching hospital affiliated with the Diyala Health Directorate in Diyala Governorate, Iraq, over a six-month period from October 2025 to March 2026. Participants were recruited from the outpatient gynecology clinics and the internal medicine consultation service of the hospital. The study protocol was reviewed and approved by the Scientific and Ethics Committee of the Diyala Health Directorate . All participants received an explanation of the purpose and procedures of the study in Arabic, and written informed consent was obtained from each woman before enrollment. The study was carried out in accordance with the principles of the Declaration of Helsinki, and all personal data were coded and kept confidential.

The case group comprised women aged 30–65 years with an established diagnosis of T2DM for at least one year. The diagnosis had been made according to the criteria of the American Diabetes Association, namely a fasting plasma glucose of 126 mg/dL or more, a two-hour plasma glucose of 200 mg/dL or more during an oral glucose tolerance test, an HbA1c of 6.5% or more, or current treatment with glucose-lowering medication for clinically diagnosed T2DM. The control group consisted of apparently healthy women of a similar age range who attended the hospital for routine gynecological check-ups or accompanied patients, and who had a fasting blood glucose below 100 mg/dL, an HbA1c below 5.7% and no personal history of diabetes. Participants were enrolled consecutively until the required numbers were reached, and controls were frequency-matched to cases by five-year age bands.

To minimize the influence of conditions known to alter mineral metabolism, the following exclusion criteria were applied to both groups: eGFR below 60 mL/min/1.73 $m^2$; known primary hyperparathyroidism or other parathyroid disease; previous thyroid or parathyroid surgery; malignancy; chronic liver disease; malabsorption syndromes or previous bariatric surgery; current pregnancy or lactation; type 1 diabetes or secondary forms of diabetes; acute illness or hospitalization during the preceding month; use of calcium or vitamin D supplements during the preceding three months; and use of medications affecting calcium, phosphate or PTH homeostasis, including thiazide and loop diuretics, systemic glucocorticoids, bisphosphonates, denosumab, anticonvulsants, lithium, hormone replacement therapy and sodium–glucose cotransporter-2 inhibitors.

The sample size was calculated using the formula for comparing two independent means, assuming a standard deviation of serum PTH of 18 pg/mL, a minimum clinically relevant difference of 10 pg/mL between groups, a two-sided significance level of 0.05, a power of 80% and a case-to-control ratio of 1.5:1. This yielded a minimum of 64 cases and 43 controls. To allow for possible exclusions after laboratory testing and to improve the precision of subgroup analyses, 90 cases and 60 controls were finally included.

Data were collected by trained medical staff through face-to-face interviews using a structured questionnaire. The recorded variables included age, residence, parity, menopausal status (postmenopausal status being defined as the absence of menstruation for at least 12 consecutive months), family history of diabetes, duration of diabetes, current glucose-lowering treatment

(metformin alone, metformin combined with a sulfonylurea, or an insulin-based regimen), approximate daily sun exposure and use of medications. Weight was measured to the nearest 0.1 kg with participants in light clothing and without shoes, and height was measured to the nearest 0.5 cm using a wall-mounted stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured in the sitting position after at least five minutes of rest.

Venous blood samples were drawn between 8:00 and 10:00 a.m. after an overnight fast of 10–12 hours, with minimal use of the tourniquet to avoid spurious elevation of calcium. A total of 8 mL of blood was collected from each participant: 2 mL was placed in an EDTA tube for HbA1c measurement, and the remaining 6 mL was placed in a gel separator tube, allowed to clot for 30 minutes at room temperature and centrifuged at 3000 rpm for 10 minutes. Samples were processed within one hour of collection. Fasting glucose, creatinine, albumin, calcium and phosphorus were analyzed on the day of collection, whereas serum aliquots for PTH and 25(OH)D were stored at −20 °C and analyzed in batches within four weeks. Hemolyzed or lipemic samples were rejected and recollected. Laboratory personnel performing the analyses were unaware of the group assignment and clinical characteristics of the participants, and all samples from cases and controls were analyzed in the same runs using the same reagent lots wherever possible in order to minimize analytical variation.

Fasting blood glucose was measured by the glucose oxidase method, creatinine by the kinetic Jaffe method, albumin by the bromocresol green method, total calcium by the o-cresolphthalein complexone method and inorganic phosphorus by the ammonium molybdate ultraviolet method, all on a fully automated clinical chemistry analyzer (Cobas c311, Roche Diagnostics, Germany). HbA1c was measured by a turbidimetric inhibition immunoassay standardized to the National Glycohemoglobin Standardization Program. Serum intact PTH and total 25(OH)D were measured by electrochemiluminescence immunoassay on a Cobas e411 analyzer (Roche Diagnostics, Germany); the reference interval for intact PTH used by the laboratory was 15–65 pg/mL. Two levels of commercial control material were run daily for every analyte, and the laboratory participated in an external quality assessment scheme throughout the study period.

Serum calcium was corrected for albumin using the formula: corrected calcium (mg/dL) = total calcium (mg/dL) + 0.8 × [4.0 − serum albumin (g/dL)]. Hypocalcemia was defined as corrected calcium below 8.5 mg/dL and hypercalcemia as corrected calcium above 10.5 mg/dL. Hypophosphatemia and hyperphosphatemia were defined as serum phosphorus below 2.5 mg/dL and above 4.5 mg/dL, respectively. Elevated PTH was defined as an intact PTH above 65 pg/mL. Vitamin D status was classified as deficient (25(OH)D below 20 ng/mL), insufficient (20–29.9 ng/mL) or sufficient (30 ng/mL or more). Glycemic control was categorized as good when HbA1c was below 7.0% and poor when HbA1c was 7.0% or higher. The calcium–phosphorus product was calculated by multiplying total calcium by phosphorus ($mg^2/dL^2$). The eGFR was calculated with the 2021 race-free Chronic Kidney Disease Epidemiology Collaboration creatinine equation, and BMI was categorized according to the World Health Organization classification.

Data were entered and analyzed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed with the Shapiro–Wilk test and inspection of histograms. Continuous variables were presented as mean ± standard deviation and compared between two groups with the independent-samples t-test, or with the Mann–Whitney U test when the distribution was skewed. Categorical variables were presented as numbers and percentages and compared with the chi-square test, or with Fisher's exact test when any expected cell count was below five. Correlations between continuous variables in the diabetic group were evaluated with Pearson's correlation coefficient, or Spearman's rank correlation for non-normally distributed variables. Multiple linear regression analysis was performed to identify independent determinants of serum PTH in patients with T2DM, entering age, BMI, duration of diabetes, HbA1c, 25(OH)D and eGFR as independent variables; multicollinearity was checked using the variance inflation factor, and values below 2.5 were considered acceptable. A two-tailed p value below 0.05 was considered statistically significant.

**Results**

A total of 150 women were included in the final analysis, comprising 90 patients with T2DM and 60 non-diabetic controls. As shown in Table 1, the two groups were comparable in age and menopausal status. Patients with T2DM had a significantly higher BMI and, as expected, markedly higher fasting blood glucose and HbA1c. Serum albumin and eGFR were slightly but significantly lower in the diabetic group, although all participants had an eGFR of at least 60 mL/min/1.73 m². The mean duration of diabetes was 7.8 ± 4.9 years; 42.2% of patients were treated with metformin alone, 32.2% with metformin plus a sulfonylurea and 25.6% with an insulin-based regimen.

**Table 1.** Demographic and clinical characteristics of the study groups

| Variable | T2DM (n = 90) | Controls (n = 60) | p value |
|---|---|---|---|
| Age (years) | 49.6 ± 8.3 | 47.9 ± 8.1 | 0.21 |
| BMI (kg/m²) | 30.4 ± 4.6 | 27.9 ± 4.2 | 0.001 |
| Postmenopausal, n (%) | 41 (45.6) | 24 (40.0) | 0.50 |
| Duration of diabetes (years) | 7.8 ± 4.9 | — | — |
| Fasting blood glucose (mg/dL) | 168.4 ± 52.7 | 91.6 ± 10.8 | < 0.001 |
| HbA1c (%) | 8.3 ± 1.7 | 5.2 ± 0.4 | < 0.001 |
| Serum creatinine (mg/dL) | 0.78 ± 0.16 | 0.72 ± 0.14 | 0.02 |
| eGFR (mL/min/1.73 m²) | 92.5 ± 14.1 | 98.7 ± 12.6 | 0.006 |
| Serum albumin (g/dL) | 4.1 ± 0.4 | 4.3 ± 0.3 | 0.001 |
| Treatment: metformin alone, n (%) | 38 (42.2) | — | — |
| Treatment: metformin + sulfonylurea, n (%) | 29 (32.2) | — | — |
| Treatment: insulin-based, n (%) | 23 (25.6) | — | — |

Values are mean ± SD or n (%). BMI, body mass index; HbA1c, glycated hemoglobin; eGFR, estimated glomerular filtration rate.

The serum mineral and hormonal parameters of both groups are presented in Table 2. Mean intact PTH was significantly higher in patients with T2DM than in controls ($p < 0.001$). Total serum calcium and inorganic phosphorus were significantly lower in the diabetic group, as was the calcium–phosphorus product. After correction for serum albumin, however, the difference in calcium between the groups was no longer significant ($p = 0.18$). Serum 25(OH)D was significantly lower in patients with T2DM.

**Table 2.** Serum PTH, calcium, phosphorus and vitamin D in the study groups

| Parameter | T2DM (n = 90) | Controls (n = 60) | p value |
|---|---|---|---|
| Intact PTH (pg/mL) | 58.7 ± 21.4 | 44.2 ± 15.3 | < 0.001 |
| Total calcium (mg/dL) | 9.12 ± 0.52 | 9.38 ± 0.41 | 0.001 |
| Albumin-corrected calcium (mg/dL) | 9.04 ± 0.50 | 9.14 ± 0.39 | 0.18 |
| Inorganic phosphorus (mg/dL) | 3.41 ± 0.62 | 3.72 ± 0.51 | 0.002 |
| Calcium × phosphorus product (mg²/dL²) | 31.1 ± 6.2 | 34.9 ± 5.4 | < 0.001 |
| 25(OH)D (ng/mL) | 17.6 ± 7.9 | 23.4 ± 8.6 | < 0.001 |

Values are mean ± SD; independent-samples t-test. PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.

The frequency of abnormal values is shown in Table 3. Elevated PTH was found in 31 (34.4%) patients with T2DM compared with 8 (13.3%) controls ($p = 0.004$), and 28 of the 31 diabetic patients with elevated PTH had normal albumin-corrected calcium. Vitamin D deficiency was more frequent among diabetic women (64.4% vs 40.0%, $p = 0.003$). Hypocalcemia and hypophosphatemia were numerically more common in the diabetic group, but the differences did not reach statistical significance.

**Table 3.** Frequency of abnormal mineral and hormonal values in the study groups

| Abnormality | T2DM (n = 90), n (%) | Controls (n = 60), n (%) | p value |
|---|---|---|---|
| Elevated PTH (> 65 pg/mL) | 31 (34.4) | 8 (13.3) | 0.004 |
| Hypocalcemia (corrected Ca < 8.5 mg/dL) | 9 (10.0) | 2 (3.3) | 0.20* |
| Hypophosphatemia (< 2.5 mg/dL) | 8 (8.9) | 1 (1.7) | 0.08* |
| Vitamin D deficiency (< 20 ng/mL) | 58 (64.4) | 24 (40.0) | 0.003 |

Chi-square test; * Fisher's exact test. No participant had hypercalcemia or hyperphosphatemia.

When patients with T2DM were stratified by glycemic control (Table 4), those with poor control (HbA1c ≥ 7%, n = 58) had significantly higher PTH, lower phosphorus and lower 25(OH)D than those with good control (n = 32), whereas the difference in total calcium did not reach significance (p = 0.08).

**Table 4.** Mineral and hormonal parameters in patients with T2DM according to glycemic control

| Parameter | Good control, HbA1c < 7% (n = 32) | Poor control, HbA1c ≥ 7% (n = 58) | p value |
|---|---|---|---|
| HbA1c (%) | 6.5 ± 0.4 | 9.3 ± 1.3 | < 0.001 |
| Intact PTH (pg/mL) | 49.8 ± 17.2 | 63.6 ± 22.1 | 0.002 |
| Total calcium (mg/dL) | 9.24 ± 0.47 | 9.05 ± 0.53 | 0.08 |
| Inorganic phosphorus (mg/dL) | 3.62 ± 0.55 | 3.29 ± 0.63 | 0.012 |
| 25(OH)D (ng/mL) | 20.1 ± 7.6 | 16.2 ± 7.8 | 0.024 |

Values are mean ± SD; independent-samples t-test.

Correlation analysis within the diabetic group (Table 5) showed that PTH correlated positively with HbA1c, fasting blood glucose, duration of diabetes and BMI, and inversely with 25(OH)D. Serum phosphorus correlated inversely with HbA1c and fasting blood glucose. PTH was not significantly correlated with eGFR or with corrected calcium. In multiple linear regression analysis (Table 6), HbA1c and 25(OH)D were independent predictors of serum PTH, while age, BMI, duration of diabetes and eGFR were not; the model explained 26% of the variance in PTH (adjusted $R^2 = 0.26$, $p < 0.001$).

**Table 5.** Correlations of serum PTH and phosphorus with clinical and biochemical variables in patients with T2DM (n = 90)

| Variables | Correlation coefficient (r) | p value |
|---|---|---|
| PTH vs HbA1c | 0.38 | < 0.001 |
| PTH vs fasting blood glucose | 0.29 | 0.006 |
| PTH vs duration of diabetes | 0.24 | 0.023 |
| PTH vs BMI | 0.22 | 0.037 |
| PTH vs 25(OH)D | −0.41 | < 0.001 |
| PTH vs corrected calcium | −0.19 | 0.07 |
| PTH vs eGFR | −0.15 | 0.16 |
| Phosphorus vs HbA1c | −0.31 | 0.003 |
| Phosphorus vs fasting blood glucose | −0.26 | 0.013 |
| Total calcium vs HbA1c | −0.17 | 0.11 |

Pearson correlation coefficient.

**Table 6.** Multiple linear regression analysis of determinants of serum PTH in patients with T2DM

| Independent variable | Standardized β | t | p value |
|---|---|---|---|
| Age (years) | 0.06 | 0.63 | 0.53 |
| BMI (kg/m²) | 0.13 | 1.39 | 0.17 |
| Duration of diabetes (years) | 0.10 | 1.04 | 0.30 |
| HbA1c (%) | 0.27 | 2.82 | 0.006 |
| 25(OH)D (ng/mL) | −0.34 | −3.62 | < 0.001 |
| eGFR (mL/min/1.73 m²) | −0.07 | −0.74 | 0.46 |

Dependent variable: intact PTH (pg/mL). $R^2 = 0.31$; adjusted $R^2 = 0.26$; F-test $p < 0.001$. All variance inflation factors < 2.0.

**Discussion**

The present study shows that women with T2DM attending Alzahraa Hospital for Gynecology and Pediatrics had a distinct mineral profile compared with non-diabetic women of similar age. Serum intact PTH was higher, total calcium and inorganic phosphorus were lower, and 25(OH)D concentrations were markedly reduced. Approximately one-third of the diabetic women

had PTH above the upper reference limit, the large majority of them with normal albumin-corrected calcium, a pattern consistent with secondary rather than primary hyperparathyroidism. Within the diabetic group, poor glycemic control was associated with higher PTH and lower phosphorus, and in multivariable analysis both HbA1c and vitamin D status emerged as independent determinants of PTH, whereas renal function within the preserved range did not.

The elevation of PTH among our patients agrees with the observation of Chiu et al., who reported that plasma intact PTH was inversely correlated with insulin sensitivity [13], and with the community-based data of Reis et al., in which higher PTH accompanied the metabolic syndrome [14]. The direction of causality, however, cannot be established from the present design. One explanation is that vitamin D deficiency, which was highly prevalent among our diabetic women, drives a compensatory increase in PTH [9]; the strong inverse correlation between PTH and 25(OH)D in our data supports this view. Similar inverse relationships between vitamin D and insulin resistance or β-cell dysfunction have been reported in individuals at risk of diabetes [31] and in non-diabetic adults [32]. A second, complementary explanation is that PTH itself contributes to dysglycemia. Experimental studies have shown that chronic PTH excess raises basal cytosolic calcium in β-cells and impairs insulin release [17], and the high prevalence of glucose intolerance in primary hyperparathyroidism, together with its partial reversibility after parathyroidectomy, lends clinical support to this mechanism [15,16]. The fact that HbA1c remained associated with PTH after adjustment for 25(OH)D in our regression model suggests that the link between PTH and glycemia is not explained entirely by vitamin D status, although residual confounding by unmeasured factors cannot be excluded.

Our findings differ from those of Yamamoto et al., who described relatively low PTH levels, accompanied by suppressed bone formation, in postmenopausal Japanese women with T2DM, particularly in those with vertebral fractures [26]. Several factors may account for this discrepancy. Hyperglycemia and the magnesium depletion that frequently accompanies it may blunt PTH secretion in some patients, and populations with adequate vitamin D status may not exhibit the secondary hyperparathyroidism that is common where hypovitaminosis D is widespread. Our cohort was younger, included premenopausal women and had a high prevalence of vitamin D deficiency, conditions that favor a compensatory rise in PTH. It is therefore likely that the parathyroid response in T2DM is heterogeneous and is shaped by the background vitamin D, magnesium and renal status of the population studied, as well as by the stage of skeletal involvement [24].

The high frequency of vitamin D deficiency in our diabetic women, nearly two-thirds, is notable even in a region where deficiency is common in the general population. Vitamin D may influence β-cell function through vitamin D receptors and the local activation of 25(OH)D, may modulate insulin receptor expression and may exert anti-inflammatory effects relevant to insulin resistance [11,33]. Early clinical observations, including improvements in glucose tolerance after vitamin D repletion in deficient individuals [34], encouraged considerable interest in supplementation. Nevertheless, the large randomized D2d trial did not show a significant reduction in progression from prediabetes to diabetes with vitamin D3 supplementation in a population that was largely vitamin D replete at baseline [35]. These data caution against assuming that the associations observed in our study are causal, or that the correction of deficiency would by itself improve glycemia. They do, however, support evaluation of vitamin D status and PTH in women with diabetes because of the well-established skeletal consequences of deficiency and secondary hyperparathyroidism [9,33].

The lower total calcium in our diabetic group deserves careful interpretation. Because approximately 40% of circulating calcium is bound to albumin, the slightly lower serum albumin in the diabetic women would be expected to reduce total calcium without necessarily altering the physiologically active ionized fraction [36]. Indeed, after albumin correction, the difference between groups lost statistical significance. This contrasts with prospective data linking higher serum calcium to incident diabetes [18–20]. Those studies, however, largely examined normoglycemic or prediabetic individuals, in whom subtle elevations of calcium may reflect early dysregulation of the PTH–vitamin D axis or of calcium signaling, whereas our patients had established diabetes of several years' duration. In established and poorly controlled diabetes, glycosuria and osmotic diuresis promote

urinary calcium loss [22], and a compensatory rise in PTH would be expected to maintain ionized calcium within the reference range at the cost of increased bone resorption. The finding that most diabetic women with elevated PTH had normal corrected calcium is also clinically important. Current international guidance emphasizes that secondary causes, particularly vitamin D deficiency and reduced renal function, must be excluded before a diagnosis of normocalcemic primary hyperparathyroidism is considered [37]. In practice, women with T2DM and an isolated rise in PTH should therefore undergo vitamin D repletion and repeat testing rather than immediate referral for parathyroid imaging or surgery.

Serum phosphorus was lower in the diabetic women and correlated inversely with HbA1c and fasting glucose. Several mechanisms may contribute to this finding. Insulin and glucose drive phosphate into cells for the phosphorylation of glucose and the generation of adenosine triphosphate, and chronic perturbations of this process may lower extracellular phosphate; Haglin proposed that hypophosphatemia may be both a marker and a contributor to the disturbed energy metabolism of the metabolic syndrome [21]. Osmotic diuresis increases urinary phosphate excretion, and insulin treatment alters renal tubular phosphate handling [22]. In addition, the higher PTH observed in our patients would be expected to reduce proximal tubular phosphate reabsorption, given the well-described phosphaturic action of the hormone [7]. The combination of lower phosphorus and higher PTH in patients with poor glycemic control is consistent with these mechanisms acting together. Although the degree of hypophosphatemia in most patients was mild, phosphate depletion may impair muscle function, erythrocyte 2,3-diphosphoglycerate production and tissue oxygen delivery, and it may further compromise insulin sensitivity, potentially establishing a vicious cycle.

Renal function is a major confounder in any study of mineral metabolism in diabetes, since diabetic kidney disease is common [27] and CKD-MBD develops early in the course of renal impairment [28]. To limit this confounding, we excluded women with an eGFR below 60 mL/min/1.73 $m^2$, calculated with the race-free 2021 equation [38]. Nonetheless, abnormalities of PTH have been documented in a proportion of patients with eGFR above this threshold [29], and fibroblast growth factor 23 rises even before PTH as renal function declines [30]. Although the mean eGFR of our diabetic group was slightly lower than that of controls, eGFR was not correlated with PTH and was not an independent predictor in the regression model, suggesting that the observed PTH elevation is unlikely to be explained by early renal impairment alone. We did not, however, measure albuminuria or fibroblast growth factor 23, and a contribution of subclinical kidney disease cannot be completely ruled out.

These mineral disturbances may have implications for skeletal health. Patients with T2DM have an increased fracture risk despite preserved or increased bone mineral density [23,25], and the mechanisms are thought to involve poor bone quality, altered bone turnover and microvascular disease [24]. Secondary hyperparathyroidism preferentially increases cortical bone resorption, and in women already exposed to hyperglycemia, obesity and, in many cases, the menopausal decline in estrogen, it may add to skeletal fragility. Our findings thus provide a rationale for including PTH, calcium, phosphorus and vitamin D in the metabolic assessment of women with diabetes, particularly those with poor glycemic control, in keeping with the broader emphasis on comprehensive care in current diabetes standards [3]. Given the substantial and growing burden of diabetes in Iraq [5], even modest improvements in the detection and management of these disturbances could have meaningful public health benefits.

This study has several strengths, including the careful exclusion of women with reduced eGFR and of those using medications or supplements that influence mineral metabolism, standardized fasting morning sampling, measurement of vitamin D alongside PTH, and the use of multivariable analysis to examine independent associations. Several limitations should also be acknowledged. The case–control design does not permit causal inferences. The study was conducted in a single center and included only women, which limits generalizability to men and to other regions of Iraq. Ionized calcium, serum magnesium, 1,25-dihydroxyvitamin D, fibroblast growth factor 23, urinary calcium and phosphate excretion and markers of bone turnover were not measured, and bone mineral density was not assessed. Dietary calcium and phosphate intake and physical activity were not quantified, and seasonal variation in vitamin D may have influenced the results, although

recruitment of cases and controls occurred over the same period. Finally, the sample size, while adequate for the primary comparison, may have been insufficient to detect smaller differences in the frequency of hypocalcemia and hypophosphatemia. Larger prospective studies, ideally including interventional trials of vitamin D repletion with assessment of PTH, glycemic and skeletal outcomes, are needed to clarify the clinical significance of these findings.

**Conclusion**

Women with type 2 diabetes mellitus attending Alzahraa Hospital for Gynecology and Pediatrics in Diyala, Iraq, exhibited higher serum PTH, lower total calcium, lower phosphorus and lower 25-hydroxyvitamin D than non-diabetic women of similar age, while albumin-corrected calcium was preserved. One-third of the diabetic women had elevated PTH, mostly with normocalcemia, suggesting secondary hyperparathyroidism. These abnormalities were more pronounced in patients with poor glycemic control, and HbA1c and vitamin D status were independent predictors of PTH. Periodic assessment of PTH, calcium, phosphorus and vitamin D, together with efforts to improve glycemic control and correct vitamin D deficiency, is recommended for women with T2DM, and larger prospective studies are needed to determine whether these measures improve metabolic and skeletal outcomes.

Declarations

Conflict of interest: The authors declare no conflict of interest.

Funding: This research received no specific grant from any funding agency.

Acknowledgments: The authors thank the staff of the laboratory and outpatient clinics of Alzahraa Hospital for Gynecology and Pediatrics and all women who participated in the study.

**Refrenceses**

International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.

2. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.

3. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: Standards of Care in Diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S20–S42.

4. DeFronzo RA, Ferrannini E, Groop L, Henry RR, Herman WH, Holst JJ, et al. Type 2 diabetes mellitus. Nat Rev Dis Primers. 2015;1:15019.

5. Mansour AA, Al-Maliky AA, Kasem B, Jabar A, Mosbeh KA. Prevalence of diagnosed and undiagnosed diabetes mellitus in adults aged 19 years and older in Basrah, Iraq. Diabetes Metab Syndr Obes. 2014;7:139–44.

6. Peacock M. Calcium metabolism in health and disease. Clin J Am Soc Nephrol. 2010;5(Suppl 1):S23–30.

7. Blaine J, Chonchol M, Levi M. Renal control of calcium, phosphate, and magnesium homeostasis. Clin J Am Soc Nephrol. 2015;10(7):1257–72.

8. Goltzman D, Mannstadt M, Marcocci C. Physiology of the calcium-parathyroid hormone-vitamin D axis. Front Horm Res. 2018;50:1–13.

9. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266–81.

10. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab. 2007;92(6):2017–29.

11. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. Diabetologia. 2005;48(7):1247–57.

12. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr. 2004;79(5):820–5.

13. Chiu KC, Chuang LM, Lee NP, Ryu JM, McGullam JL, Tsai GP, et al. Insulin sensitivity is inversely correlated with plasma intact parathyroid hormone level. Metabolism. 2000;49(11):1501–5.

14. Reis JP, von Mühlen D, Kritz-Silverstein D, Wingard DL, Barrett-Connor E. Vitamin D, parathyroid hormone levels, and the prevalence of metabolic syndrome in community-dwelling older adults. Diabetes Care. 2007;30(6):1549–55.

15. Taylor WH, Khaleeli AA. Coincident diabetes mellitus and primary hyperparathyroidism. Diabetes Metab Res Rev. 2001;17(3):175–80.

16. Procopio M, Borretta G. Derangement of glucose metabolism in hyperparathyroidism. J Endocrinol Invest. 2003;26(11):1136–42.

17. Perna AF, Fadda GZ, Zhou XJ, Massry SG. Mechanisms of impaired insulin secretion after chronic excess of parathyroid hormone. Am J Physiol. 1990;259(2 Pt 2):F210–6.

18. Sun G, Vasdev S, Martin GR, Gadag V, Zhang H. Altered calcium homeostasis is correlated with abnormalities of fasting serum glucose, insulin resistance, and β-cell function in the Newfoundland population. Diabetes. 2005;54(11):3336–9.

19. Lorenzo C, Hanley AJ, Rewers MJ, Haffner SM. Calcium and phosphate concentrations and future development of type 2 diabetes: the Insulin Resistance Atherosclerosis Study. Diabetologia. 2014;57(7):1366–74.

20. Rooney MR, Pankow JS, Sibley SD, Selvin E, Reis JP, Michos ED, et al. Serum calcium and incident type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) study. Am J Clin Nutr. 2016;104(4):1023–9.

21. Haglin L. Hypophosphataemia: cause of the disturbed metabolism in the metabolic syndrome. Med Hypotheses. 2001;56(6):657–63.

22. Raskin P, Pak CY. The effect of chronic insulin therapy on phosphate metabolism in diabetes mellitus. Diabetologia. 1981;21(1):50–3.

23. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes—a meta-analysis. Osteoporos Int. 2007;18(4):427–44.

24. Napoli N, Chandran M, Pierroz DD, Abrahamsen B, Schwartz AV, Ferrari SL. Mechanisms of diabetes mellitus-induced bone fragility. Nat Rev Endocrinol. 2017;13(4):208–19.

25. Schwartz AV, Vittinghoff E, Bauer DC, Hillier TA, Strotmeyer ES, Ensrud KE, et al. Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. JAMA. 2011;305(21):2184–92.

26. Yamamoto M, Yamaguchi T, Nawata K, Yamauchi M, Sugimoto T. Decreased PTH levels accompanied by low bone formation are associated with vertebral fractures in postmenopausal women with type 2 diabetes. J Clin Endocrinol Metab. 2012;97(4):1277–84.

27. Thomas MC, Brownlee M, Susztak K, Sharma K, Jandeleit-Dahm KA, Zoungas S, et al. Diabetic kidney disease. Nat Rev Dis Primers. 2015;1:15018.

28. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD-MBD). Kidney Int Suppl. 2017;7(1):1–59.

29. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, et al. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney Int. 2007;71(1):31–8.

30. Wolf M. Update on fibroblast growth factor 23 in chronic kidney disease. Kidney Int. 2012;82(7):737–47.

31. Kayaniyil S, Vieth R, Retnakaran R, Knight JA, Qi Y, Gerstein HC, et al. Association of vitamin D with insulin resistance and β-cell dysfunction in subjects at risk for type 2 diabetes. Diabetes Care. 2010;33(6):1379–81.

32. Liu E, Meigs JB, Pittas AG, McKeown NM, Economos CD, Booth SL, et al. Plasma 25-hydroxyvitamin D is associated with markers of the insulin resistant phenotype in nondiabetic adults. J Nutr. 2009;139(2):329–34.

33. Bouillon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, et al. Skeletal and extraskeletal actions of vitamin D: current evidence and outstanding questions. Endocr Rev. 2019;40(4):1109–51.

34. Kumar S, Davies M, Zakaria Y, Mawer EB, Gordon C, Olukoga AO, et al. Improvement in glucose tolerance and beta-cell function in a patient with vitamin D deficiency during treatment with vitamin D. Postgrad Med J. 1994;70(824):440–3.

35. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, et al. Vitamin D supplementation and prevention of type 2 diabetes. N Engl J Med. 2019;381(6):520–30.

36. Payne RB, Little AJ, Williams RB, Milner JR. Interpretation of serum calcium in patients with abnormal serum proteins. Br Med J. 1973;4(5893):643–6.

37. Bilezikian JP, Khan AA, Silverberg SJ, Fuleihan GE, Marcocci C, Minisola S, et al. Evaluation and management of primary hyperparathyroidism: summary statement and guidelines from the Fifth International Workshop. J Bone Miner Res. 2022;37(11):2293–314.

38. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. N Engl J Med. 2021;385(19):1737–49.