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Original article

Relationship between vitamin D status, glycemic control and chronic diabetic complications in type 2 diabetes mellitus: a retrospective study

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Summary

Introduction. Vitamin D deficiency is common worldwide and has been associated with disturbances in glucose metabolism, although evidence remains inconsistent. This study evaluated serum 25(OH)D levels and their crude associations with glycemic control and chronic diabetic complications in patients with type 2 diabetes mellitus (T2DM).

Methods. This retrospective study included 170 adults with T2DM treated between January 2023 and June 2024. Participants were categorized according to serum 25(OH)D concentration into a low vitamin D group (≤30 ng/mL) and a normal vitamin D group (≥31 ng/mL). Collected data included age, sex, body mass index (BMI), diabetes duration, treatment modalities, fasting plasma glucose (FPG), 2-hour postprandial glucose (PPG), HbA1c, and documented complications (retinopathy, neuropathy, diabetic kidney disease, and atherosclerotic cardiovascular disease). Normality was assessed using Q–Q plots and the Shapiro–Wilk test. Group comparisons were performed using Student's t-test or non-parametric equivalents, and correlations were evaluated using Pearson or Spearman coefficients. No multivariable regression analyses were conducted.

Results. Patients with lower 25(OH)D levels had significantly longer diabetes duration, higher BMI, and higher HbA1c, FPG, and PPG values. Weak negative correlations were observed between 25(OH)D and glycemic parameters (r = –0.13 to –0.25). The prevalence of chronic diabetic complications was significantly higher in the low vitamin D group. All findings were unadjusted.

Conclusion. Lower 25(OH)D levels were associated with poorer glycemic parameters and a higher prevalence of chronic diabetic complications in T2DM. However, given significant group differences and the lack of adjustment, causality cannot be inferred.

Keywords: vitamin D, type 2 diabetes, glycemic control

Introduction

Vitamin D is a fat-soluble steroid hormone essential for calcium homeostasis, bone metabolism, and multiple extra-skeletal processes [1, 2]. Dietary vitamin D is found in fish liver oil, fatty fish, mushrooms and fortified foods, whereas cutaneous synthesis occurs via sunlight exposure. Following intake or synthesis, vitamin D is converted in the liver to 25-hydroxyvitamin D [25(OH)D], the principal circulating form and standard clinical biomarker [1].

Vitamin D deficiency is highly prevalent globally, affecting diverse regions and populations [3]. Earlier guidelines defined deficiency as < 20 ng/mL and insufficiency as < 30 ng/mL, but recent recommendations highlight insufficient evidence for strict thresholds [4].

Beyond its skeletal role, vitamin D has been implicated in glucose homeostasis, insulin secretion, β-cell function and inflammation [5, 6]. Observational studies suggest that low vitamin D may be associated with obesity, metabolic syndrome and increased risk of type 2 diabetes mellitus (T2DM) [6]. However, prospective cohort analyses and Mendelian randomization studies do not confirm a causal relationship between vitamin D and T2DM development [7–9].

Low vitamin D has also been associated with microvascular and macrovascular complications in T2DM, including nephropathy, neuropathy, retinopathy and cardiovascular disease [10–12]. However, significant methodological variability persists, and adjusted analyses often attenuate these associations.

This study aimed to evaluate vitamin D status and to examine crude (unadjusted) associations between serum 25(OH)D levels, glycemic control parameters and the presence of chronic diabetic complications in adults with type 2 diabetes mellitus.

Methods

This retrospective study included 170 consecutive adults with type 2 diabetes mellitus treated at the University Clinical Centre of Republic of Srpska from January 2023 to June 2024. All patients who met the inclusion criteria during this period were included.

Patients were categorized according to serum 25(OH)D concentration into two groups: low vitamin D (≤ 30 ng/mL) and normal vitamin D (≥ 31 ng/mL). Exclusion criteria were type 1 diabetes, chronic kidney or liver disease, pregnancy and alcoholism.

Collected data included age, sex, body mass index (BMI), diabetes duration, treatment modalities, fasting plasma glucose (FPG), 2-hour postprandial glucose (PPG), HbA1c, and documented complications: retinopathy, neuropathy, diabetic kidney disease and atherosclerotic cardiovascular disease (ASCVD).

Normality of continuous variables was assessed using Q–Q plots and the Shapiro–Wilk test. Quantitative variables were described as mean ± standard deviation, and categorical variables as frequencies. Group differences were analyzed using Student's t-test or non-parametric equivalents when appropriate. Correlations between 25(OH)D and clinical variables were evaluated using Pearson or Spearman coefficients.

Due to the retrospective design of the study and the limited number of available covariates, no multivariable regression analyses were performed.

Results

A total of 170 patients were included, with a mean age of 61.9 ± 9.0 years, of whom 55% were women. Patients in the low 25(OH)D group were older on average, had significantly longer duration of diabetes and higher BMI values compared with those in the normal 25(OH)D group (Table 1).

Regarding glycemic control, patients with lower 25(OH)D concentrations had statistically significantly higher fasting plasma glucose, 2-hour postprandial glucose and HbA1c values. These differences occurred in parallel with longer disease duration and higher BMI, both well-established contributors to suboptimal glycemic regulation [13, 14].

Correlation analysis showed significant negative associations between 25(OH)D levels and FPG, PPG, HbA1c and BMI. Despite statistical significance, the magnitude of these correlations was weak (r values between –0.13 and –0.25), suggesting limited clinical impact. Similar weak associations have been reported in previous studies, with effect sizes often diminishing after adjusting for confounders such as obesity, age and duration of diabetes [15–17].

Prevalence of chronic diabetic complications (retinopathy, polyneuropathy, diabetic kidney disease and atherosclerotic cardiovascular disease) was numerically and statistically significantly higher among patients with lower 25(OH)D levels, consistent with earlier literature describing similar crude associations in T2DM [18–23]. Nevertheless, in the absence of adjustment for confounders, these findings must be interpreted with caution.

Table 1. Demographic, clinical and laboratory parameters according to vitamin D status

Variable	Group I (Low 25(OH)D) ≤ 30 ng/mL	Group II (Normal 25(OH)D) ≥ 31 ng/mL	p-value
Age (years)	64.6 ± 9.7	59.2 ± 8.3	ns
Duration of diabetes (years)	10.2 ± 3.2	8.6 ± 3.6	< 0.05
HbA1c (%)	9.2 ± 1.1	8.4 ± 1.4	< 0.05
Fasting plasma glucose (mmol/L)	9.5 ± 1.5	8.1 ± 2.3	< 0.05
2-hour postprandial glucose (mmol/L)	11.3 ± 2.2	9.8 ± 2.5	< 0.05
BMI (kg/m²)	32.2 ± 5.3	29.4 ± 1.8	ns
25(OH)D (ng/mL)	21.0 ± 5.5	34.5 ± 2.5	< 0.01

**Abbreviations and footnotes. Values are presented as mean ± standard deviation unless otherwise indicated. ns = not significant (p ≥ 0.05); BMI = body mass index. Group comparisons were performed using Student's t-test or appropriate non-parametric tests. All p-values are unadjusted. Statistical significance was set at p < 0.05 (two-tailed).*

Discussion

In unadjusted analyses, lower serum 25(OH)D concentrations were accompanied by poorer glycemic parameters, higher body mass index (BMI), and longer duration of diabetes in adults with type 2 diabetes mellitus. These crude findings are consistent with several previous observational studies reporting similar unadjusted associations between lower vitamin D status and worse glycemic outcomes [6, 7, 13].

The literature proposes several biological mechanisms that could potentially explain such associations, including the presence of vitamin D receptors on pancreatic β-cells, modulation of intracellular calcium flux important for insulin secretion, and anti-inflammatory effects that may influence insulin sensitivity [7, 13]. Although these mechanisms are biologically plausible, large-scale Mendelian randomization studies and randomized controlled trials have not consistently supported a causal role of vitamin D in glucose metabolism or the development of type 2 diabetes [8, 9].

Patients with lower 25(OH)D levels in this cohort also exhibited a significantly higher

prevalence of chronic diabetic complications. This pattern aligns with earlier reports describing crude associations between vitamin D deficiency and retinopathy, neuropathy, nephropathy, and macrovascular disease [18–23]. However, such associations are highly susceptible to confounding. Patients with long-standing diabetes, higher BMI, and poorer glycemic control are simultaneously at increased risk for both complications and lower vitamin D levels.

Nearly half of the patients with low vitamin D levels were receiving supplementation, but the doses (most commonly 2000 IU/day) were often insufficient to achieve normal serum concentrations. Previous studies indicate that individuals with obesity may require two to three times higher doses due to increased sequestration of vitamin D in adipose tissue [14]. Randomized trials have yielded mixed results regarding whether vitamin D supplementation improves glycemic control, with some suggesting benefit only at higher doses or in patients with marked vitamin D deficiency [26–28].

This study had several important limitations. It was retrospective and relied on data extracted from medical records, which preventing comprehensive control of all relevant confounders. The two groups differed significantly at baseline in diabetes duration (10.2 vs 8.6 years) and BMI (32.2 vs 29.4 kg/m^2), both of which are strong independent predictors of poor glycemic control and complication development. No multivariable analyses were performed to evaluate whether 25(OH)D levels had any independent association with the studied outcomes after accounting for these and other factors. Data on vitamin D supplementation were incomplete and did not include information on dose, duration of use, or achievement of target concentrations.

Consequently, the observed differences in glycemic parameters and complication prevalence are most likely attributable, at least in large part, to differences in baseline clinical characteristics rather than to a direct effect of vitamin D status.

Conclusion

In this retrospective study, lower 25(OH)D levels were accompanied in unadjusted analysis by higher values of HbA1c, fasting plasma glucose, and 2-hour postprandial glucose, as well as by a higher prevalence of chronic diabetic complications. However, patients with lower 25(OH)D concentrations also had significantly longer diabetes duration and higher BMI — two of the strongest known risk factors for poor glycemic control and development of diabetic complications.

Given the retrospective design and lack of adjustment for important confounders, no conclusion could be drawn regarding an independent causal role of low 25(OH)D levels in worsening glycemic control or increasing complication risk. The present results demonstrate an association but do not establish causality. Prospective studies with appropriate multivariable adjustment are required to determine whether vitamin D status has any independent clinical relevance in the management of type 2 diabetes mellitus.

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Ethical approval. The Ethics Committee of the University Clinical Center of Republic of Srpska, Banja Luka, Republic of Srpska, Bosnia and Herzegovina, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

*Author contributions: IR, AM, MK, MG drafted this manuscript and collected the sample. IR, MK, MG, MB analyzed the data. IR and AM are responsible for the integrity of the work as a whole. All authors read and approved the final manuscript.

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Povezanost nivoa vitamina D, regulacije glikemije i hroničnih komplikacija dijabetesa: retrospektivna studija

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Uvod. Deficit vitamina D je rasprostranjen širom svijeta i povezan je sa poremećajima metabolizma glukoze, iako su dokazi neujednačeni. Cilj ove studije bio je da se procijene vrijednosti serumskog 25(OH)D i njihove grube povezanosti sa glikemijskom kontrolom i hroničnim dijabetičkim komplikacijama kod pacijenata sa dijabetes melitusom tipa 2 (T2DM).

Metode. Ova retrospektivna studija obuhvatila je 170 odraslih pacijenata sa T2DM liječenih u periodu od januara 2023. do juna 2024. godine. Ispitanici su podijeljeni prema koncentraciji serumskog 25(OH)D na grupu sa niskim nivoom vitamina D (≤30 ng/mL) i grupu sa normalnim nivoom vitamina D (≥31 ng/mL). Prikupljeni su podaci o starosti, polu, indeksu tjelesne mase (BMI), trajanju dijabetesa, terapiji, vrijednostima glukoze natašte (FPG), dvočasovne postprandijalne glukoze (PPG), HbA1c, kao i o dokumentovanim komplikacijama (retinopatija, neuropatija, dijabetička bolest bubrega i aterosklerotska kardiovaskularna bolest). Normalnost raspodjele procijenjena je pomoću Q–Q grafika i Shapiro–Wilk testa. Za poređenje grupa korišćen je Studentov t-test ili neparametrijski ekvivalenti, dok su korelacije procijenjene Pearsonovim ili Spearmanovim koeficijentom. Nisu sprovedene multivarijantne regresione analize.

Rezultati. Pacijenti sa nižim nivoima 25(OH)D imali su značajno duže trajanje dijabetesa, viši BMI i više vrijednosti HbA1c, FPG i PPG. Uočene su slabe negativne korelacije između 25(OH)D i glikemijskih parametara (r = –0,13 do –0,25). Prevalencija hroničnih dijabetičkih komplikacija bila je značajno veća u grupi sa niskim nivoom vitamina D. Svi rezultati bili su neprilagođeni.

Zaključak. Niži nivoi 25(OH)D bili su povezani sa lošijim glikemijskim parametrima i većom prevalencijom hroničnih dijabetičkih komplikacija kod pacijenata sa T2DM. Međutim, zbog značajnih razlika između grupa i izostanka prilagođavanja na konfuzne faktore, uzročno-posljedična povezanost se ne može potvrditi.

Ključne riječi: vitamin D, dijabetes tipa 2, glikemijska kontrola