Mediterranean Journal of Medical Research
ISSN Online: 3080-7735
Mediterr J Med Res
doi: 10.5281/zenodo.00000000
https://mrj.org.ly

ORIGINAL RESEARCH article

Therapeutic effect of vitamin D supplementation on glycemic control in female patients with type 2 diabetes mellitus: A randomized controlled trial

Issa E.A. Amara [2, 3 *], **Ebtisam A. Benomran** [4] **Naeima A. Mohammed** [1] and **Abdurrauf M. Gusbi** [5]

[1] Department of Pharmaceutics, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya
[2] Department of Pharmacology, Faculty of Medicine, University of Zintan, Zintan, Libya
[3] Department of Pharmacology, Faculty of Medicine, University of Gharyan, Gharyan, Libya
[4] Department of Physiology, Faculty of Nursing, University of Tripoli, Tripoli, Libya
[5] Department of Pharmacy, Saraya Hamra University, Tripoli, Libya
[*] Author to whom correspondence should be addressed

Received: 20-03-2026, **Accepted:** 00-05-2026, **Published online:** 00-00-2026

HOW TO CITE THIS

Mohammed et al. Therapeutic effect of vitamin D supplementation on glycemic control in female patients with type 2 diabetes mellitus: A randomized controlled trial. Mediterr J Med Res. 2026; 3(2): 162-168. [Article number: 51]. https://doi.org/10.5281/zenodo.00000000

Keywords: HbA1c, glycemic control, cholecalciferol, Libya

Abstract: This randomized controlled trial examined the relationship between therapeutic doses of vitamin D and improvement of glycemic parameters in female patients with Type 2 Diabetes Mellitus (T2DM). 27 female patients with T2DM, aged 38-64 years, were randomly assigned to intervention (n = 15) and control (n = 12) groups at the endocrinology department of Tripoli Medical Center from 2015 to 2023. The intervention group received 50,000 IU vitamin D (cholecalciferol) weekly for 12 weeks, while controls received a placebo. Serum levels of 25-hydroxyvitamin D [25(OH)D], fasting blood glucose, HbA1c, lipid profile, and calcium were measured before and after intervention. Data were analyzed using paired t-tests and correlation analyses. Statistical significance was set at $p < 0.05$. Baseline vitamin D deficiency was prevalent: 47.0% of patients had severe deficiency, 41.0% moderate deficiency, and only 11.0% had sufficient levels. After 12 weeks of supplementation, 88.0% of patients demonstrated improved vitamin D levels. Mean serum 25(OH)D increased significantly from 12.50±12.40 nmol/L to 37.00 ± 10.00 nmol/L. About 80.0% of patients exhibited decreased HbA1c from 9.20 ± 1.80% to 7.90 ± 1.70%; $p < 0.05$. A significant inverse correlation was observed between post-intervention HbA1c and 25(OH)D levels ($r = -0.354$, $p = 0.04$). Fasting blood glucose improved from 174.44 ± 63.77 mg/dL to 144.51 ± 38.90 mg/dL. No significant changes occurred in the control group. Weekly vitamin D supplementation (50,000 IU) for 12 weeks significantly improved vitamin D status and glycemic control in female patients with T2DM, demonstrating an inverse relationship between vitamin D and HbA1c levels. Vitamin D may be a beneficial adjunct therapy for glycemic management in vitamin D-deficient diabetic patients.

Introduction

Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major global health challenge. According to the International Diabetes Federation, more than 537 million adults were living with diabetes in 2021, and this number is expected to increase substantially in the coming decades if effective preventive strategies are not implemented [1]. T2DM is characterized by chronic

hyperglycemia resulting from insulin resistance and progressive pancreatic β-cell dysfunction [2, 3]. Persistent hyperglycemia is associated with long-term complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy, which contribute significantly to morbidity and mortality among diabetic patients. Several environmental and lifestyle factors contribute to the development and progression of T2DM. These include obesity, sedentary lifestyle, unhealthy dietary patterns, cigarette smoking, and genetic predisposition [4-9]. In recent years, increasing attention has been directed toward micronutrient deficiencies as potential contributors to metabolic disorders. Among these, vitamin D deficiency has emerged as a possible modifiable risk factor associated with impaired glucose metabolism and increased risk of T2DM [10, 11].

Vitamin D is a fat-soluble secosteroid hormone primarily synthesized in the skin after exposure to ultraviolet B radiation, although smaller amounts can be obtained from dietary sources such as fatty fish, fortified dairy products, and supplements. After synthesis or ingestion, vitamin D undergoes hydroxylation in the liver to form 25-hydroxyvitamin D [25(OH)D], which is the major circulating form and the most reliable indicator of vitamin D status [12]. A second hydroxylation step occurs in the kidneys to produce the biologically active form, 1,25-dihydroxyvitamin D [1,25$(OH)_2$D]. Accumulating evidence suggests that vitamin D plays an important role in glucose homeostasis and insulin metabolism. Vitamin D receptors and the enzyme 1-α-hydroxylase are expressed in pancreatic β-cells and in insulin-sensitive tissues such as skeletal muscle and adipose tissue [13, 14]. Through these receptors, vitamin D may enhance insulin secretion, improve insulin sensitivity, and regulate inflammatory processes that contribute to insulin resistance [15]. In addition, vitamin D influences intracellular calcium regulation in pancreatic β-cells, which is essential for insulin secretion [16].

Observational studies have reported that individuals with low serum 25(OH)D concentrations are more likely to develop impaired glucose tolerance, metabolic syndrome, and T2DM [11, 17]. Several epidemiological studies have also demonstrated an inverse relationship between vitamin D levels and glycemic indicators such as fasting blood glucose and glycated hemoglobin (HbA1c) [17, 18]. Furthermore, vitamin D deficiency has been reported to be highly prevalent among patients with T2DM, particularly in Middle Eastern and North African populations [19]. Despite the growing evidence suggesting a relationship between vitamin D status and glucose metabolism, clinical trials evaluating the therapeutic effects of vitamin D supplementation on glycemic control have produced inconsistent results. While some randomized controlled trials have reported significant improvements [20, 21], others have observed minimal or no effects [22]. These inconsistencies may be attributed to differences in study design, baseline vitamin D status, dosage, duration of supplementation, and population characteristics. Given the high prevalence of T2DM and vitamin D deficiency in the Middle East and North Africa region, further investigation is warranted. However, data from Libya and neighboring countries remain limited. Therefore, the present randomized controlled trial aimed to evaluate the effect of vitamin D supplementation (cholecalciferol 50,000 IU weekly) on serum vitamin D levels and glycemic parameters in female patients with T2DM. Additionally, the study examined the relationship between serum 25(OH)D concentrations and indicators of glycemic control.

Materials and methods

Study design and participants: This was a randomized, double-blind, placebo-controlled clinical trial conducted at the endocrinology department of Tripoli Medical Center (TMC), Libya, from 2015 to 2023. A total of 27 female patients with T2DM, aged 38 to 64 years, were enrolled in the study.

Inclusion criteria: female patients diagnosed with T2DM for at least five years, aged between 38 and 64 years, with no history of renal or hepatic diseases based on medical records, no other significant underlying health conditions, and no use of calcium or vitamin D supplements within the six months before participation.

Exclusion criteria: included male patients, individuals with type 1 diabetes mellitus, pregnant or lactating women, those with renal or hepatic impairment, current users of vitamin D or calcium supplements, and patients with a history of parathyroid disorders.

Randomization and intervention: Participants were randomly assigned to two groups using a computer-generated random allocation sequence. Allocation concealment was ensured by sealed, opaque envelopes that were opened only after participant enrollment. Intervention group (n = 15): Received oral vitamin D3 (cholecalciferol) 50,000 IU tablet once weekly for 12 weeks. Control group (n = 12): Received placebo tablets once weekly for 12 weeks, matching the duration of the intervention group (to mitigate risks associated with no treatment)

Laboratory measurements: Blood samples were collected from all participants using red and grey vacutainers. Red-capped vacutainers were used for estimating total plasma vitamin D [25(OH)D], HbA1c, lipid profile (total cholesterol, triglycerides, HDL, LDL), and calcium levels. Grey-capped vacutainers were used for fasting blood glucose (FBG) estimation after an overnight fast. All parameters were assessed using the Cobas 6000 analyzer series before and after the 12-week intervention period.

Ethical considerations: Oral informed consent was obtained from all patients before participation. The study was approved by the Ethical Committee of Tripoli Medical Center.

Statistical analysis: Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics, including mean and standard deviation (SD), were employed to summarize the data. Paired t-tests were used to evaluate the significance of changes within groups before and after intervention. Correlation tests (Pearson's correlation coefficient) were conducted to assess relationships between variables. A p-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics: A total of 27 female patients with T2DM were enrolled, with a mean age ranging from 38 to 64 years. Baseline assessment revealed that 47.0% of diabetic patients had severe vitamin D deficiency, 41.0% had moderate deficiency, and 11.0% had sufficient levels of vitamin D.

Changes in vitamin D status: Following 12 weeks of vitamin D supplementation, 88.0% of patients in the intervention group demonstrated improvement in their vitamin D levels. Serum 25(OH)D increased significantly from 12.50 ± 12.40 nmol/L at baseline to 37.00 ± 10.00 nmol/L post-intervention ($p < 0.05$) **Figure 1**).

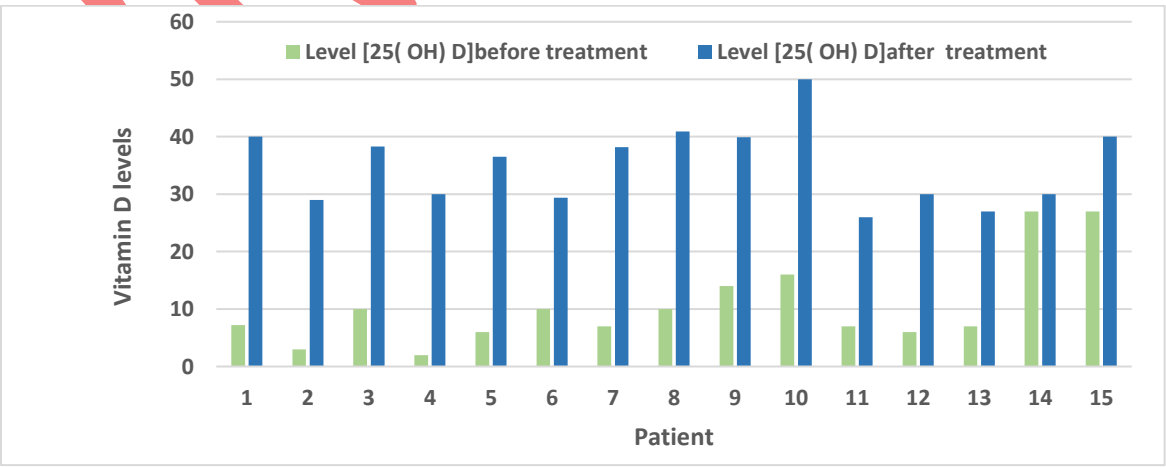

Figure 1: Vitamin D levels before and after 12 weeks of supplementation
A bar graph showing mean 25(OH)D levels increasing from 12.5 nmol/L to 37.0 nmol/L.

Changes in glycemic parameters: Around 80.0% of patients in the intervention group exhibited a significant decrease in HbA1c after treatment. Mean HbA1c decreased significantly from 9.20 ± 1.80% at baseline to 7.90 ± 1.70% post-intervention ($p < 0.05$) (**Table 1, Figure 2**). Fasting blood glucose also showed improvement, decreasing from 174.44 ± 63.77 mg/dL to 144.51 ± 38.90 mg/dL.

Table 1: Glycemic parameters before and after intervention

Parameter	Before treatment (Mean ± SD)	After treatment (Mean ± SD)	p-value
HbA1c (%)	9.20±1.80	7.90±1.70	< 0.05
FBG (mg/dL)	174.44±63.77	144.51±38.90	< 0.05

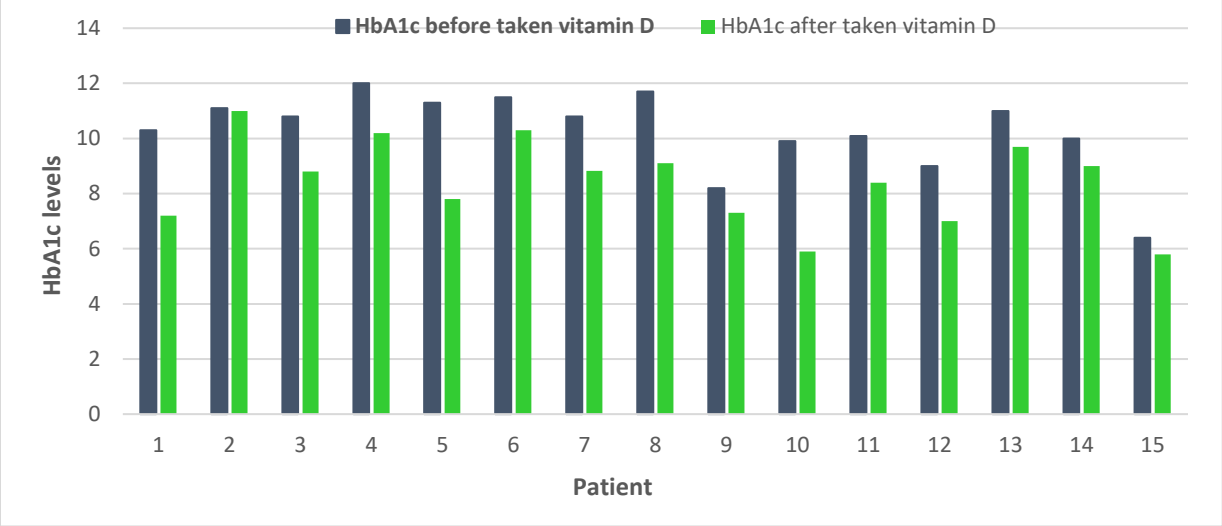

Figure 2: HbA1c levels before and after 12 weeks of vitamin D supplementation
A bar graph showing mean HbA1c decreasing from 9.2% to 7.9%.

Correlation between vitamin D and glycemic control: A significant inverse correlation was observed between post-intervention HbA1c and 25(OH)D levels ($r = -0.354$, $p = 0.040$), indicating that higher vitamin D levels were associated with better glycemic control.

Changes in lipid profile and calcium: Vitamin D supplementation resulted in modest improvements in lipid parameters and a significant increase in serum calcium levels (from 8.21 ± 1.25 mg/dL to 9.24 ± 0.90 mg/dL; $p < 0.05$) (**Table 2**).

Table 2: lipid profile and calcium levels before and after intervention

Parameters	Before treatment (mean ± SD)	After treatment (mean ± SD)
Total cholesterol (mg/dL)	177.49 ± 33.88	161.99 ± 30.57
Triglycerides (mg/dL)	150.0 ± 80.44	116.63 ± 48.55
HDL (mg/dL)	50.96 ± 21.04	47.74 ± 15.76
LDL (mg/dL)	133.25 ± 108.69	105.28 ± 36.09
Calcium (mg/dL)	8.21 ± 1.25	9.24 ± 0.90

Control group findings: No significant changes were observed in the control group for any measured parameters. Mean HbA1c remained relatively unchanged (7.98 ± 1.67% to 8.14 ± 1.68%), and vitamin D levels showed no significant improvement (10.08 ± 6.66 nmol/L to 9.97 ± 6.62 nmol/L) (**Table 3**).

Table 3: Control group parameters before and after placebo

Parameter	Before placebo (mean ± SD)	After placebo (mean ± SD)	p-value
HbA1c (%)	7.98 ± 1.67	8.14 ± 1.68	NS
25(OH)D (nmol/L)	10.08 ± 6.66	9.97 ± 6.62	NS
FBG (mg/dL)	154.5 ± 71.34	156.6 ± 70.99	NS

NS = not significant

Discussion

The primary objective of this study was to evaluate the effect of vitamin D supplementation on glycemic parameters in female patients with T2DM. The results demonstrated a significant inverse relationship between vitamin D levels and HbA1c, suggesting that maintaining adequate vitamin D status may contribute to improved glycemic control. This finding is consistent with previous evidence highlighting the potential role of vitamin D in glucose metabolism and diabetes management [1, 23-27]. The present randomized controlled trial showed that weekly cholecalciferol supplementation over 12 weeks significantly increased serum 25-hydroxyvitamin D levels. More importantly, a significant reduction in HbA1c and fasting blood glucose was observed in the intervention group, alongside a clear inverse correlation between vitamin D status and HbA1c. Similar improvements in glycemic control have been reported in other clinical trials and meta-analyses, supporting the beneficial effect of correcting vitamin D deficiency in patients with T2DM [5, 23, 28].

Vitamin D deficiency was highly prevalent among participants at baseline, with most showing moderate to severe deficiency. This aligns with previous reports indicating a high prevalence of vitamin D deficiency in individuals with T2DM, particularly in Middle Eastern populations, despite abundant sunlight exposure. Contributing factors include limited sun exposure, clothing practices, and dietary insufficiency, with reported deficiency rates reaching 60.0-90.0% in this region [11, 29]. The observed reduction in HbA1c is clinically significant, as even small decreases in HbA1c are associated with reduced risk of diabetic complications. Prior studies and meta-analyses have similarly shown that vitamin D supplementation can lead to modest but meaningful improvements in glycemic markers, particularly in deficient individuals [16, 28]. Several biological mechanisms may explain these effects. Vitamin D receptors are present in pancreatic β-cells, skeletal muscle, and adipose tissue, indicating a role in glucose homeostasis. Vitamin D enhances insulin secretion by regulating intracellular calcium in β-cells and may improve insulin sensitivity in peripheral tissues [13, 30]. Additionally, vitamin D exerts anti-inflammatory effects by suppressing pro-inflammatory cytokines such as TNF-α and IL-6, thereby reducing insulin resistance [24, 31]. Another proposed mechanism involves modulation of the renin-angiotensin system, where vitamin D suppresses renin expression, potentially improving β-cell function and insulin sensitivity [21]. These combined effects may explain the improvement in glycemic control observed in this study. Although lipid profile changes were not statistically significant, slight improvements were observed. Previous research suggests vitamin D may influence lipid metabolism indirectly through improved insulin sensitivity and reduced inflammation, potentially contributing to cardiometabolic benefits [11, 32]. Despite these findings, limitations should be acknowledged. The relatively small sample size and inclusion of only female participants limit generalizability. Additionally, the short intervention duration (12 weeks) may not fully reflect long-term metabolic effects. Other influencing factors, such as sun exposure, diet, and physical activity, were not controlled, which may affect vitamin D status and metabolic outcomes [20, 31]. Future research should focus on larger multicenter randomized trials including both genders and longer follow-up periods to confirm these findings. Determining optimal dosing strategies and identifying populations most likely to benefit from supplementation remain important areas for further investigation. Overall, this study adds to the growing body of evidence suggesting that vitamin D supplementation may serve as a beneficial adjunctive strategy for improving glycemic control in patients with T2DM.

Conclusion: This randomized controlled trial demonstrates that weekly supplementation with 50,000 IU vitamin D for 12 weeks significantly improves vitamin D status and glycemic control in female patients with T2DM. The significant inverse correlation between vitamin D and HbA1c levels suggests that vitamin D plays a beneficial role in glucose homeostasis. Given the high prevalence of vitamin D deficiency among diabetic patients in Libya, routine screening for vitamin D deficiency and appropriate supplementation should be considered as part of comprehensive diabetes management.

References

1. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: A systematic review. European Journal of Clinical Nutrition. 2011; 65(9): 1005-1015.
2. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: A systematic review. Diabetes Care. 2007; 30(3): 744-752.
3. Elmiladi SA. Presentation and character for adult patients with diabetes in Libya. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2022; 2(1): 79-86. doi: 10.5281/zenodo.6399891
4. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: A systematic review and meta-analysis. JAMA. 2007; 298(22): 2654-2664.
5. Kelly A, Brooks LJ, Dougherty S, Carlow DC, Zemel BS. A cross-sectional study of vitamin D and insulin resistance in children. Archives of Disease in Childhood. 2011; 96(5): 447-452.
6. Walli RR, Derbal AAA, Altabib MN. Body mass index and vitamin D in Libyan women. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2024; 4(2): 64-68. doi: 10.5281/zenodo.12171291
7. Rafi IK, Aktaruzzaman Md. Lifestyle and nutritional deficiencies associated with vegetarian diets. Mediterranean Journal of Medical Research. 2025; 2(2): 20-25. doi: 10.5281/zenodo.15336103
8. Ahmed R, Uddin MM, Hoque. Nutraceuticals: Food-based therapeutics and health benefits. Mediterranean Journal of Medicine and Medical Sciences. 2025; 1(1): 22-30. doi: 10.5281/zenodo.15771921
9. El-hemali JG, Sherif FM. Pre-diabetes and its associated risk factors in Libya: Future needs for public health care. Research and Reviews on Healthcare. 2018; 1(1): 1-2. doi: 10.32474/R10.32474/RRHOAJ.2018.01.000102
10. Nasri H, Behradmanesh S, Maghsoudi AR, Ahmadi A, Nasri P, Rafieian-Kopaei M. Efficacy of supplementary vitamin D on improvement of glycemic parameters in patients with type 2 diabetes mellitus: A randomized double blind clinical trial. Journal of Renal Injury Prevention. 2014; 3(1): 31-34.
11. Palomer X, Gonzalez-Clemente JM, Blanco-Vaca F, Mauricio D: Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes, Obesity and Metabolism. 2008; 10: 185-197.
12. Isaia G, Giorgino R, Adami S: High prevalence of hypovitaminosis D in female type 2 diabetic population. Diabetes Care. 2001; 24: 1496.
13. Baynes KC, Boucher BJ, Feskens EJ, Kromhout D: Vitamin D, glucose tolerance and insulinaemia in elderly men. Diabetologia. 1997; 40: 344-347.
14. Pietschmann P, Schernthaner G, Woloszczuk W: Serum osteocalcin levels in diabetes mellitus: analysis of the type of diabetes and microvascular complications. Diabetologia. 1988; 31: 892-895.
15. Chun RF, Peercy BE, Orwoll ES, Nielson CM, Adams JS, Hewison M. Vitamin D and DBP: The free hormone hypothesis revisited. The Journal of Steroid Biochemistry and Molecular Biology. 2014; 144: 132-137.
16. Talaei A, Mohamadi M, Adgi Z. The effect of vitamin D on insulin resistance in patients with type 2 diabetes. Diabetology and Metabolic Syndrome. 2013; 5(1): 8.
17. Amar B Elhussein, Walid G Babikr, Mariam I Alsayed, Omar E Fadlelseed: The association between vitamin D level and glycemic control in type 2 diabetic patients in Najran Area, Saudi Arabia. 2020.
18. American Diabetes Association. Standards of medical care in diabetes-2010. Diabetes Care. 2010; 33(Suppl 1): S3-S62.
19. Pittas G, Lau J, Hu FB, Dawson-Hughes B. Review: the role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. Journal of Clinical Endocrinology and Metabolism. 2007; 92(6): 2017-2029.
20. Maestro B, Campi´on J, D´avila N, Calle C. Stimulation by 1,25-dihydroxyvitamin D3 of insulin receptor expression and insulin responsiveness for glucose transport in U-937 human promonocytic cells. Endocrine Journal. 2000; 47(4): 383-391.
21. Cheng Q, Li YC, Boucher BJ, Leung PS. A novel role for vitamin D: Modulation of expression and function of the local renin-angiotensin system in mouse pancreatic islets. Diabetologia 2011; 54: 2077-2081.

22. Maestro B, Molero S, Bajo S. Transcriptional activation of the human insulin receptor gene by 1,25-dihydroxyvitamin D(3). Cell Biochemistry and Function. 2002; 20: 227-232.
23. Kumar K, Bordoloi T, Narang S, et al. Effect of vitamin D supplementation on glycemic control in newly diagnosed patients with type 2 diabetes mellitus: a randomized controlled trial. Cureus. 2024; 16(9): e70224.
24. Akhter A, Alouffi S, Shahab U, et al. Vitamin D supplementation modulates glycated hemoglobin in diabetes mellitus: a systematic review. Archives of Biochemistry and Biophysics. 2024; 753: 109911.
25. Elhadi AA, Ahmed AA. Correlation of vitamin D with glycemic control and body mass index in patients with type II diabetes mellitus. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2022; 2(1): 28-36. doi: 10.5281/zenodo.6399450
26. Ahmed AA, Alapid AA, Ahmed ZM, Moudah NJ, Salim HM. Correlational study of vitamin D deficiency and dyslipidemia among adult Libyan population. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2025; 5(2): 96-103. doi: 10.5281/zenodo.15381077
27. Laflof KBA. Vitamin D, calcium, and hematological levels in healthy Libyan subjects. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2025; 5(3): 94-100. doi: 10.5281/zenodo.17210995
28. Zhang XJ, Wang HF, Gao X, Zhao Y. Effects of oral vitamin D supplementation on glycemic parameters in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. Biomedical and Environmental Sciences. 2025; 38(6): 716-726.
29. Holick MF. Vitamin D deficiency. The New England Journal of Medicine. 2007; 357(3): 266-281.
30. Palomer X, González-Clemente JM, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes, Obesity and Metabolism. 2008; 10(3): 185-197.
31. Cohen-Lahav M, Douvdevani A, Chaimovitz C, Shany S: The antiinflammatory activity of 1,25 dihydroxy vitamin D3 in macrophages. The Journal of Steroid Biochemistry and Molecular Biology. 2007; 103: 558-562.
32. Gamag EA, Albakoush AM, Rashed MJ, Kassab BA, Albasha SA. Glycosylated hemoglobin in type 2 diabetic patients as a biomarker for predicting dyslipidemia. Mediterranean Journal of Pharmacy and Pharmaceutical Sciences. 2024; 4(4): 1-5. doi: 10.5281/zenodo.13993737

Acknowledgements: The author would like to thank all the participants for their involvement in this study.
Author contribution:
Conflict of interest: The authors declare the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.
Ethical issues: All authors are responsible for ethical issues, including plagiarism, informed consent, data fabrication or falsification, and duplicate publication or submission.
Trial Registration: This trial was registered with the Ethical Committee of Tripoli Medical Center.
Data availability statement: The raw data that support the findings of this article are available from the corresponding author upon reasonable request.
Author declarations: The authors confirm that they have followed all relevant ethical guidelines and obtained any necessary IRB and/or ethics committee approvals.
Generative AI disclosure: No generative AI was used in the preparation of this manuscript.