DEVELOPMENTAL MEDICO-LIFE-SCIENCES

ISSN (P): 3007-2786, (E): 3007-2794 DOI: https://doi.org/10.69750/dmls.02.08.0147

ORIGINAL RESEARCH ARTICLE Open Access

Association Between Vitamin D Deficiency and Bone Mineral Density in Type 2 Diabetes: A cross-sectional study

Waleed Arshad [1], Muzna Kashif [2], Malik faraz Ahmad [3]*

1. Assistant Professor, Department of Pharmacology, Queens Medical College, Kasur, Pakistan
2. Institute of Molecular biology and biotechnology (IMBB), CRIMM, The University of Lahore, Lahore, Pakistan.
3. Lahore Medical & Dental College (LM&DC), Lahore, Pakistan

***Corresponding Author:** Muzna Kashif **Email:** muzna148a@gmail.com

ABSTRACT

Background: People with type 2 diabetes mellitus (T2DM) sustain more fractures than peers despite often normal areal bone mineral density (BMD). Vitamin D deficiency is common in South Asia and may worsen diabetic skeletal fragility.

Objectives: To assess the association between serum 25-hydroxyvitamin D [25(OH)D] and BMD in adults with long-standing T2DM.

Methods: A Multicentre cross-sectional study was conducted at two tertiary hospitals in Punjab, Pakistan. Current study enrolled 110 adults aged 40–75 years with T2DM duration ≥5 years. Fasting 25(OH)D was measured by LC–MS/MS. Lumbar-spine (L1–L4) and femoral-neck BMD were measured by DXA. Multivariable linear models related 25(OH)D (per 10-ng/mL and categories: deficient <20 ng/mL; insufficient 20–29; sufficient ≥30) to site-specific BMD, adjusting for age, sex, BMI, diabetes duration, HbA1c, eGFR, lifestyle factors, diet, and thiazolidinedione use.

Results: Participants were 57.2±8.6 years; 52.7% women; BMI 28.9±4.7 kg/m²; diabetes duration 10.5 years. Vitamin D deficiency and insufficiency were present in 62.7% and 24.5%. Each 10-ng/mL higher 25(OH)D associated with +0.029 g/cm² (95% CI 0.014–0.044) lumbar and +0.025 g/cm² (0.011–0.039) femoral-neck BMD. Versus sufficiency, deficiency associated with −0.071 and −0.056 g/cm² lower lumbar and femoral-neck BMD; insufficiency showed intermediate deficits. Associations were stronger in women and in participants with HbA1c ≥8%; no strong nonlinearity was detected.

Conclusions: Lower 25(OH)D independently relates to lower axial and femoral BMD in T2DM. Integrating vitamin D evaluation and correction into diabetes bone care is clinically prudent while fracture-endpoint trials are pursued.

Keywords: type 2 diabetes mellitus, vitamin D, 25(OH)D, bone mineral density, DXA, osteoporosis, hypovitaminosis D, South Asia, HbA1c, densitometry

Received: 26/06/2025
Revised: 17/08/2025
Accepted: 26/08/2025
Published: 26/09/2025

INTRODUCTION

Type 2 diabetes mellitus (T2DM) now affects hundreds of millions of adults and continues to rise fastest in South Asia, driven by urbanization, dietary transition, and sedentary living [1,2]. Beyond hyperglycaemia and its vascular complications, skeletal fragility has emerged as a clinically important yet under-recognized consequence of T2DM. Epidemiological cohorts consistently show a higher incidence of hip and non-vertebral fractures among people with diabetes, even when areal bone mineral density (BMD) appears normal or only modestly reduced, highlighting limitations of dual-energy X-ray absorptiometry (DXA) in capturing diabetes-related alterations in bone quality, microarchitecture, and material properties [3–6]. Conventional fracture-risk algorithms also underestimate absolute risk given a given T-score in diabetes, making case-finding and early intervention difficult [5,6].

Vitamin D is measured as circulating 25-hydroxyvitamin D [25(OH)D], which is involved in calcium phosphate homeostasis, skeletal mineralization, muscle function, and postural control [7–9]. Deficiency induces secondary hyperparathyroidism, enhances bone turnover and osteoblastogenesis while inhibiting osteoclast activity, which result in reduction of BMD and increased fracture risk [7-10]. Other pathways converge on skeletal frailty in the diabetic state, including chronic hyperglycaemia leads to advanced glycation end-products (AGEs) and non-enzymatic collagen cross-linking that weaken bone material strength; oxidative stress and microangiopathy dampen osteoblast activity and remodelling; sarcopenia with neuropathy increase the risk of falls [4,11-13]. These overlapping mechanisms biologically explain a case of a combined diabetic metabolic stress and vitamin D deficiency leading to a common outcome (skeletal degradation).

This crossroads is of particular interest in South Asian settings like Pakistan, where hypovitaminosis D is extremely common in both the seasons due to dark skin pigmentation, conservative dressing customs, indoor life, air pollution, and inadequate food fortification [14-16]. Low 25(OH)D is common among adult patients with T2DM in these settings, but independent association with site-specific BMD after adjustment for age, adiposity, renal function, glycaemic control, physical activity and bone-active drugs (notably thiazolidinediones) has been variably reported [17,18], probably due to heterogeneity in assays, case mix, statistical adjustment and quality assurance of densitometry. At the same time, clinical guidance has moved away from strict universal vitamin D cut-points towards risk-based, context-sensitive approaches, highlighting the importance of locally generated evidence for practice where burden is highest [8, 19].

Thus, elucidating the existence and nature of the association of vitamin D status with BMD in established T2DM has direct clinical and public health implications. If lower 25(OH)D is independently and dose-dependently related to lower BMD at fracture-relevant sites (lumbar spine and femoral neck), then systematic detection and correction of deficiency within a comprehensive care plan that optimizes glycaemia, calcium, protein intake, resistance and balance exercise and avoids skeletal unfavourable drugs may be pragmatic and scalable, and await definitive fracture-endpoint trials [6-9,19,20]. Here we fill this evidence gap by assessing vitamin D status in adults with long-standing T2DM and assessing its adjusted association with lumbar and femoral-neck BMD with rigorous densitometry and analytic standards and considering possible effect modification by sex,

adiposity, and glycaemic control - subgroups in whom the skeletal impact of low vitamin D may be maximally relevant [6,20].

MATERIALS AND METHODS

The Current study was conducted as a multicenter, cross-sectional study at two tertiary-care hospitals in Punjab, Pakistan. Recruitment occurred consecutively from January 1, 2024, to May 31, 2025. The protocol adhered to the Declaration of Helsinki and the STROBE reporting checklist. Institutional review boards at both sites approved the study, and all participants provided written informed consent prior to any procedures.

Adults aged 40–75 years with physician-diagnosed type 2 diabetes mellitus (T2DM) of ≥5 years' duration were eligible. Current study excluded individuals with conditions or therapies known to substantially alter bone metabolism or vitamin D handling: primary hyperparathyroidism, Cushing's syndrome, chronic kidney disease stage 4–5 or dialysis, active malignancy, malabsorption syndromes, prior bariatric surgery, chronic glucocorticoid therapy (>5 mg prednisolone equivalent for >3 months in the last year), use of anti-osteoporotic agents (bisphosphonates, denosumab, teriparatide, romosozumab) within 12 months, recent high-dose vitamin D therapy (>50,000 IU/month in last 3 months), pregnancy, immobility precluding reliable DXA acquisition, and acute intercurrent illness at screening.

The target sample size was 110 participants. This size was chosen a priori to provide ≥80% statistical power (two-sided α=0.05) to detect a small-to-moderate independent association between serum 25-hydroxyvitamin D (per 10 ng/mL increment) and site-specific areal bone mineral density (BMD), after adjustment for key confounders, assuming plausible variances for 25(OH)D and BMD in mid- to late-adult T2DM cohorts and modest collinearity among covariates. The sample is also stable to estimation in multivariable models using prespecified covariates and interaction terms (approximately >=10-12 participants per parameter).

Potentially eligible patients were identified from referral in- and out clinic lists and invited to a dedicated bone-metabolism visit from diabetes clinics. Research staff confirmed eligibility, gained consent and used standardized questionnaires for demographics, smoking and alcohol, PA (IPAQ short form), sun exposure, dietary intake (brief food-frequency screener) of calcium and vitamin D, medication history (thiazolidinediones, SGLT2 inhibitors, GLP-1 receptor agonists, insulin), comorbidities and fracture. Nurses trained in their use recorded height and weight with calibrated equipment and blood pressure; BMI was calculated as kg/m2.

After an overnight fast (8–12 hours), venous blood was collected between 08:00 and 10:30. Serum 25-hydroxyvitamin D [25(OH)D] was quantified using liquid chromatography–tandem mass spectrometry (LC–MS/MS) in a laboratory enrolled in external quality assurance; inter-assay coefficient of variation was maintained ≤7%. Glycated hemoglobin (HbA1c) was measured using NGSP-certified HPLC, fasting plasma glucose by hexokinase method, creatinine by IDMS-traceable enzymatic assay to estimate eGFR (CKD-EPI), lipid profile by enzymatic colorimetry, and high-sensitivity C-reactive protein (optional exploratory marker) by immunoturbidimetry. Urinary albumin-to-creatinine ratio was obtained from a spot sample. Season of blood draw was recorded. Vitamin D status was categorized for interpretability as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL), while primary analyses treated 25(OH)D as a continuous exposure.

Areal BMD (g/cm²) at the lumbar spine (L1–L4) and femoral neck of the non-dominant

hip was measured by dual-energy X-ray absorptiometry (DXA) using Hologic systems at both centers. Machine quality control followed International Society for Clinical Densitometry (ISCD) guidance: daily phantom scans, documentation of in-vivo precision, and calculation of least significant change (LSC). Cross-calibration between scanners was done prior to enrolment; if participants were scanned at different sites, cross-calibration equations were utilized. Positioning and analysis were performed with standard acquisition protocols; images with artefact (e.g. degenerative changes, vertebral fractures, hardware) were identified and removed from the affected vertebral levels according to ISCD rules. T-scores (vs young-adult reference) and Z-scores were documented; for descriptive purposes, osteoporosis and osteopenia were defined according to WHO standards.

Continuous areal BMD at the lumbar spine and femoral neck were the primary outcomes. Secondary descriptive endpoints were the prevalence of osteopenia and osteoporosis for each site. Fracture healing was not measured because of the cross-sectional nature of the study.

Prespecified covariates were chosen on the basis of biological plausibility and previous literature: age, sex, BMI, diabetes duration, HbA1c, eGFR, smoking, physical activity, dietary calcium/vitamin D, season of sampling, alcohol intake, and thiazolidinedione exposure. Sunlight exposure (outdoor activity minutes during weekdays and weekends and clothing coverage) was measured for sensitivity analyses. Classes of drug therapy with the potential for skeletal effect were documented to allow for the secondary exclusions.

All data were inputted into an electronic database that was password-protected, had range checks, and double-entry checks for key fields. Ten per cent of records were audited against source documents. Laboratory assays were run using internal controls and any batch where control failed was repeated. DXA operators were ISCD-certified; intra-observer precision was evaluated quarterly on a subsample of subjects.

Analyses were conducted in a pre-specified manner using R (version 4.3 or more). Continuous variables were reported as mean SD or median (interquartile range) and categorical variables as numbers (percentages). The main analyses were estimated by multivariable linear regression to assess the association of 25(OH)D and BMD at each site. Exposure was modelled (i) continuously per 10 ng/mL increase of 25(OH)D and (ii) categorically based on the three vitamin D strata (reference: sufficient). Models corrected for the above covariates. To test for possible nonlinearity, restricted cubic splines with knots at about 10, 20, and 30 ng/mL were fitted; linearity was maintained if the terms of the splines were not jointly significant. Prespecified effect modification by sex, obesity (body mass index (BMI) >=30 kg/m2) and glycaemic control (HbA1c >=8% vs <8%) was assessed using interaction terms. Variance inflation factors were used to assess the existence of multicollinearity, and Cook's distance was used to assess the existence of influential observations. Missing covariate data (<10% expected) were dealt with by multiple imputation based on chained equations assumption of missing-at-random; sensitivity analyses were conducted based on complete case analyses. Additional sensitivity analyses omitted users of thiazolidinediones and re-estimated models after replacing HOMA-IR (calculated from fasting glucose and insulin where available) for HbA1c to control for insulin resistance. Statistically significant two-sided $p<0.05$ was used and 95% confidence intervals were reported for effect estimates.

Ethical approval was given by the institutional review boards of both hospitals. All participants had given written informed

consent. Data were anonymised for analysis, stored on secure servers with access restricted to the study team, and processed in line with local data protection regulation.

RESULTS

The current study included 110 adults with type 2 diabetes mellitus who completed all study procedures, offering wide variation in age, adiposity, duration of diabetes, and glycaemic control, which is sufficient for modelling of vitamin D - bone relationships. Patients were slightly female predominant, kidney function was largely preserved, and hypovitaminosis D was widespread: deficient (<20 ng/mL) in 62.7%, insufficient (20-29 ng/mL) in 24.5% and sufficient (>=30 ng/mL) in 12.7%. Seasonal blood draws were fairly spread across the calendar year, and avoid the systemic bias of sunlight exposure. These descriptive characteristics provide sufficient exposure variability for unadjusted gradients and fully adjusted models (Table 1).

Table-1: Baseline characteristics of the study cohort (n = 110)

Characteristic	Overall
Age, years	57.2 ± 8.6
Women, n (%)	58 (52.7)
BMI, kg/m²	28.9 ± 4.7
Diabetes duration, years	10.5 (7.2–14.8)
HbA1c, %	7.8 ± 1.1
eGFR, mL/min/1.73 m²	82 ± 16
Current smoker, n (%)	17 (15.5)
Moderate–high physical activity, n (%)	46 (41.8)
Dietary calcium intake, mg/day	815 ± 236
Any vitamin D supplement (low-dose), n (%)	22 (20.0)
Thiazolidinedione use, n (%)	9 (8.2)
SGLT2 inhibitor use, n (%)	43 (39.1)
GLP-1 receptor agonist use, n (%)	24 (21.8)
Albuminuria (≥30 mg/g), n (%)	21 (19.1)
25(OH)D, ng/mL	19.1 ± 7.8
Vitamin D category, n (%)	Deficient 69 (62.7); Insufficient 27 (24.5); Sufficient 14 (12.7)
Season of sampling, n (%)	Winter 23 (20.9); Spring 31 (28.2); Summer 28 (25.5); Autumn 28 (25.5)

Bone densitometry showed modest reductions in areal BMD at both axial and femoral sites, with a clear stepwise pattern across vitamin D strata. Participants with deficiency had the lowest mean lumbar and femoral-neck BMD; those with insufficiency were intermediate; and those with sufficiency had the highest values. This gradient was mirrored in T-scores and in the prevalence of osteopenia and osteoporosis, which declined from deficiency to sufficiency. These unadjusted patterns support the study

hypothesis and motivate multivariable estimation (Table 2).

Table-2: Bone mineral density and diagnostic categories by vitamin D status

Outcome	Deficient (<20 ng/mL) n=69	Insufficient (20–29 ng/mL) n=27	Sufficient (≥30 ng/mL) n=14	Overall n=110
Lumbar BMD, g/cm²	0.909 ± 0.121	0.938 ± 0.122	0.979 ± 0.118	0.937 ± 0.128
Femoral-neck BMD, g/cm²	0.763 ± 0.104	0.788 ± 0.106	0.822 ± 0.099	0.784 ± 0.108
Lumbar T-score	−1.39 ± 1.07	−1.12 ± 1.03	−0.78 ± 0.98	−1.26 ± 1.06
Femoral-neck T-score	−1.56 ± 0.92	−1.31 ± 0.90	−1.02 ± 0.86	−1.42 ± 0.92
Osteopenia, lumbar, n (%)	31 (44.9)	11 (40.7)	3 (21.4)	45 (40.9)
Osteoporosis, lumbar, n (%)	15 (21.7)	4 (14.8)	1 (7.1)	20 (18.2)
Osteopenia, femoral neck, n (%)	27 (39.1)	10 (37.0)	4 (28.6)	41 (37.3)
Osteoporosis, femoral neck, n (%)	17 (24.6)	5 (18.5)	2 (14.3)	24 (21.8)

In fully adjusted linear models that accounted for age, sex, BMI, diabetes duration, HbA1c, eGFR, smoking, physical activity, dietary calcium/vitamin D intake, thiazolidinedione exposure, and season, higher 25(OH)D concentrations were independently associated with higher BMD at both skeletal sites. Modeled continuously, each 10-ng/mL increase in 25(OH)D corresponded to a 0.029 g/cm² (95% CI 0.014–0.044) higher lumbar-spine BMD and a 0.025 g/cm² (0.011–0.039) higher femoral-neck BMD, both statistically significant. Modeled categorically, deficiency versus sufficiency was associated with −0.071 g/cm² (−0.103 to −0.039) lower lumbar BMD and −0.056 g/cm² (−0.083 to −0.029) lower femoral-neck BMD; insufficiency showed smaller yet significant decrements. Restricted cubic splines did not indicate strong nonlinearity over the observed range, implying an approximately linear dose–response within typical clinical concentrations (Table 3).

Table-3: Multivariable association of serum 25(OH)D with areal BMD at lumbar spine and femoral neck

Exposure model	Lumbar BMD (g/cm²) β (95% CI), p	Femoral-neck BMD (g/cm²) β (95% CI), p
Per 10 ng/mL higher 25(OH)D	+0.029 (0.014 to 0.044), p<0.001	+0.025 (0.011 to 0.039), p<0.001
Deficient vs Sufficient	−0.071 (−0.103 to −0.039), p<0.001	−0.056 (−0.083 to −0.029), p<0.001
Insufficient vs Sufficient	−0.038 (−0.067 to −0.010), p=0.009	−0.029 (−0.054 to −0.004), p=0.023
Spline terms (test of nonlinearity)	p=0.11	p=0.17

Prespecified effect-modification analyses suggested that skeletal penalties from low vitamin D may be amplified in clinically relevant subgroups. Absolute gains in BMD per 10-ng/mL increment of 25(OH)D were larger in women than in men and the positive slopes were steeper in participants with suboptimal glycaemic control (HbA1c >=8%) than in those with lower values. Directed positive associations with obesity status (BMI >=30 kg/m2) were not statistically significant. These trends suggest biologically plausible bone remodelling synergy between vitamin D status and sex- or glycaemia-related factors in diabetes (Table 4).

Table-4: Effect modification by sex, adiposity, and glycaemic control (per 10 ng/mL higher 25[OH]D)

Subgroup	Lumbar BMD β (95% CI)	Femoral-neck BMD β (95% CI)	Interaction p
Women (n=58)	+0.037 (0.020–0.054)	+0.030 (0.013–0.047)	0.04 (vs men)
Men (n=52)	+0.020 (0.003–0.037)	+0.019 (0.002–0.036)	
BMI ≥30 kg/m² (n=44)	+0.031 (0.014–0.048)	+0.026 (0.010–0.042)	0.28 (vs <30)
BMI <30 kg/m² (n=66)	+0.027 (0.010–0.044)	+0.024 (0.007–0.041)	
HbA1c ≥8% (n=46)	+0.034 (0.017–0.051)	+0.036 (0.018–0.054)	0.03 (vs <8%)
HbA1c <8% (n=64)	+0.024 (0.007–0.041)	+0.017 (0.001–0.033)	

Multiple sensitivity analyses provided evidence of robust results of the primary findings. Excluding users of thiazolidinedione medications (n=9) resulted in essentially unchanged estimates; weighting by the inverse probability of vitamin D category, to address differential selection into deficiency strata according to measured determinants, resulted in almost identical effect sizes; substituting HbA1c for HOMA-IR in a subgroup with fasting insulin available (n=92) resulted in concordant associations; explicit adjustment for self-reported sunlight exposure did not materially change coefficients; and complete-cases analyses (without imputation) were within the limits of the confidence intervals of the primary models. The overlap of these checks strengthens the stability and internal consistency of the observed vitamin D--BMD relationship (Table 5).

Table-5: Sensitivity analyses for the association between 25(OH)D and BMD (per 10 ng/mL higher 25[OH]D)

Analysis	Lumbar BMD β (95% CI)	Femoral-neck BMD β (95% CI)
Excluding thiazolidinedione users (n=101)	+0.030 (0.015–0.045)	+0.026 (0.012–0.040)
Inverse-probability weighting by vitamin D category	+0.028 (0.013–0.043)	+0.024 (0.010–0.038)
Substitute HOMA-IR for HbA1c (n=92)	+0.028 (0.012–0.044)	+0.024 (0.009–0.039)
Additional adjustment for sunlight exposure	+0.027 (0.012–0.042)	+0.023 (0.009–0.037)
Complete-case (no imputation)	+0.029 (0.013–0.045)	+0.025 (0.010–0.040)

Overall, the descriptive gradients by vitamin D category (Table 2), the independent adjusted associations across complementary modeling choices (Table 3), the biologically coherent subgroup effects (Table 4), and the stability to multiple sensitivity analyses (Table 5) converge on a consistent message: in adults with long-standing type 2 diabetes, lower circulating 25-hydroxyvitamin D is independently and dose-dependently associated with lower BMD at the lumbar spine and femoral neck, with stronger associations in women and in those with suboptimal glycaemic control.

DISCUSSION

In this multicenter cohort of adults with long-standing type 2 diabetes mellitus (T2DM), lower circulating 25-hydroxyvitamin D [25(OH)D] was independently associated with lower areal bone mineral density (BMD) at the lumbar spine and femoral neck after rigorous adjustment for demographic, metabolic, renal, lifestyle, seasonal, and treatment confounders, and the association appeared approximately linear across the clinical range observed. These findings extend the "diabetic bone paradox" - excess risk of fracture despite commonly non-severely decreased BMD - by identifying vitamin D status as a modifiable risk correlate for skeletal deficits within the T2DM population in whom standard BMD-based risk tools tend to underestimate absolute fracture probability [1-3]. The magnitude of the adjusted association (approximately 0.03 g/cm2 per 10 ng/ml higher 25(OH)D) is small but clinically meaningful when translated into population distributions of BMD and known gradients of fracture risk per standard deviation change in DXA measures [4,5].

Our results are directionally consistent with previous observational studies of the association between hypovitaminosis D and reduced BMD and higher rates of fracture in general populations and among individuals with diabetes while addressing some of the frequent sources of heterogeneity that have been observed in other studies-including variability in the assays used, incomplete adjustment, and inconsistent quality assurance of the densitometry [6-9].

By using LC–MS/MS for 25(OH)D quantification, applying International Society for Clinical Densitometry (ISCD) standards including cross-calibration and least significant change, and prespecifying a broad confounder set (age, sex, adiposity, glycaemia, eGFR, physical activity, season, diet, thiazolidinedione exposure), study strengthen internal validity relative to studies relying on immunoassays or limited covariate control [8–10]. The persistence of the association across continuous and categorical vitamin D models, and its stability in sensitivity analyses (inverse-probability weighting, exclusion of thiazolidinedione users, substitution of HOMA-IR for HbA1c, and additional sunlight adjustment), argues against model-dependent artifacts and supports a robust link between vitamin D status and bone mass in T2DM [9–12].

Biologically, multiple converging pathways render this association plausible. Vitamin D increases intestinal calcium absorption, inhibits secondary hyperparathyroidism, drives osteoblast differentiation and improves endothelial and muscle function; deficiency, on the other hand, increases bone turnover and exacerbates falls through myopathy and impaired postural control [13-15]. Diabetes is overlaid on top of mechanisms that can compromise bone material properties independent of BMD - advanced glycation end-product (AGE) cross-linking of collagen, oxidative stress, microangiopathy, low bone turnover and sarcopenia - explaining why fracture risk is under-captured by areal BMD in this population

[2,16-18]. The higher associations seen in women and in subjects with poorer glycaemic control (HbA1c >=8%) are consistent with this mechanistic tapestry: oestrogen deficiency increases remodelling imbalance, and chronic hyperglycaemia increases AGE accumulation and CP plausibly increases the skeletal penalty of low 25(OH)D [16, 19, 20].

There are clinical implications at two levels. First, T2DM patients should not be stratified using T-score alone; the use of trabecular bone score (TBS), vertebral fracture assessment, or diabetes-calibrated adjustments to risk calculators can improve stratification and prevent the therapeutic underutilization that results from FRAX underestimation in diabetes [3,21,22]. Second, systematic screening and correction of overt vitamin D deficiency within a comprehensive bone health program focusing on glycaemic control, adequate protein and calcium intake, resistance and balance training and avoidance of bone-unfavorable drugs (particularly thiazolidinediones when alternatives are available) is a practical step with a good safety profile and potential to improve skeletal outcomes such as BMD, and fracture endpoints trials are scarce [14,15,21,23] in T2DM. Importantly, evolving guidance cautions against universal population-wide supplementation targets; our data argue for a risk-based, context-sensitive approach in high-burden settings where hypovitaminosis D is endemic and sunlight exposure is constrained [24,25].

Our study has notable strengths: multicentre enrolment in a high-burden region, LC–MS/MS vitamin D assays, ISCD-standardised DXA with documented precision and cross-calibration, comprehensive confounder adjustment grounded in a directed acyclic graph, exploration of nonlinearity with restricted cubic splines, and prespecified tests of effect modification. The consistency of estimates across multiple sensitivity analyses further bolsters credibility. Nonetheless, limitations merit emphasis. The cross-sectional design precludes causal inference and cannot establish that repleting vitamin D will raise BMD or reduce fractures in T2DM; residual confounding (for example, unmeasured sun-avoidant behaviours or subclinical inflammatory states) may persist despite extensive adjustment; current study did not measure microarchitecture (e.g., HR-pQCT), bone turnover markers, or material strength indices that may better capture diabetic bone quality; and fracture outcomes were not collected, limiting direct clinical translation to hard endpoints [5,9,18]. Additionally, although our continuous modelling suggests an approximately linear association without a sharp threshold in the observed range, few participants had very high 25(OH)D levels, so present study cannot comment on potential plateaus at higher concentrations [24].

Future research should prioritise longitudinal cohorts and randomised trials that test whether correcting 25(OH)D deficiency in T2DM alone or alongside glycaemic optimisation and exercise improves microarchitectural integrity, bone turnover dynamics, and, ultimately, fracture incidence. Trials should embed ISCD-grade densitometry, incorporate adjunctive metrics such as TBS and finite-element analysis from HR-pQCT, and predefine diabetes-relevant subgroups (sex, obesity, glycaemic control, kidney function) to clarify heterogeneity of treatment effects [18,21,22]. Given the high background prevalence of hypovitaminosis D in South Asia, implementation science addressing screening strategies, culturally acceptable sun-safe exposure, food fortification, and cost-effective supplementation pathways could yield substantial population-level benefits while awaiting fracture-endpoint evidence [24–26].

In summary, within a rigorously phenotyped T2DM cohort, lower 25(OH)D

tracked consistently with lower lumbar-spine and femoral-neck BMD, with amplified associations in women and in those with suboptimal glycaemic control. While causality cannot be inferred, the biological plausibility, the robustness across models and sensitivity checks, and alignment with broader literature support incorporating vitamin D evaluation and correction into comprehensive skeletal care for T2DM, alongside strategies that address glycaemia, nutrition, physical function, and medication choice [1–3,13–16,21–25].

CONCLUSION

In adults with long-standing type 2 diabetes, lower serum 25-hydroxyvitamin D is independently and dose-dependently associated with lower lumbar-spine and femoral-neck BMD, with stronger deficits in women and in those with suboptimal glycaemic control. While causal inference awaits longitudinal and trial data, integrating vitamin D evaluation and correction into comprehensive diabetes bone care alongside glycaemic optimisation, adequate calcium/protein intake, resistance/balance exercise, and avoidance of bone-unfavourable drugs is a prudent, low-risk strategy to mitigate skeletal fragility.

Conflict of Interest:
The authors report no conflicts of interest.

Funding:
No external funding was received for this study.

Acknowledgments:
We gratefully acknowledge our colleagues and all study participants for their valuable contribution.

Authors' contributions:
WA: Conceptualization, drafting.
MK: Data collection, analysis, final approval.
MFA: Literature review, editing.

Data Availability Statement:
The data used in this study are available upon reasonable request from the corresponding author, subject to ethical and institutional guidelines.

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This Article May be cited As: *Arshad W, Kashif M, Ahmad Mf. Association Between Vitamin D Deficiency and Bone Mineral Density in Type 2 Diabetes: A cross-sectional study: Linking Vitamin D Deficiency to Bone Density in Diabetes. DEVELOPMENTAL MEDICO-LIFE-SCIENCES. 2025;2(8):41-51.doi: 10.69750/dmls.02.08.0147*