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The Metabolic Architecture of Bone Health: Vitamin D, Adiposity, and DXA-Derived Skeletal Phenotypes

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Abstract

Background: Vitamin D is essential for calcium absorption, skeletal mineralization, and musculoskeletal health. However, the relationship between serum 25-Hydroxyvitamin D [25(OH) D], Body Mass Index (BMI), and DEXA-defined osteopenia or osteoporosis remains debated, particularly in populations with heterogeneous nutritional, lifestyle, and clinical risk factors.

Objective: This study evaluated the distribution of vitamin D status and Bone Mineral Density (BMD) categories and examined whether vitamin D and BMI were associated with osteopenia or osteoporosis in a diagnostic-center population in Pakistan.

Methods: A cross-sectional analysis was conducted among individuals evaluated at Islamabad Diagnostic Center, Islamabad, Pakistan, from January 2020 to March 2025. Serum 25(OH)D testing and Dual-Energy *X*-ray Absorptiometry (DEXA) or BMD assessment were reviewed. BMD categories were summarized for the lumbar spine, hip joint, and forearm. Vitamin D status was categorized as normal, insufficient, deficient, or high. Pearson correlation was used to evaluate associations between vitamin D, BMI, and bone health categories.

Results: A total of 2,202 individuals had vitamin D data. Normal vitamin D levels were reported in 1,579 (72%), insufficiency in 328 (15%), deficiency in 265 (12%), and high levels in 30 (1%). Across DEXA anatomical readings, 806 were normal, 868 were osteopenic, and 382 were osteoporotic. Osteoporosis was most frequent in the forearm, while osteopenia was common across lumbar spine and hip readings. Vitamin D showed no significant correlation with osteopenia (r=0.02, p=0.68) or osteoporosis (r=-0.03, p=0.56). BMI also showed no significant correlation with osteopenia (r=-0.01, p=0.77) or osteoporosis (r=0.04, p=0.44).

Conclusion: In this cohort, serum vitamin D and BMI were not reliable standalone predictors of DEXA-defined osteopenia or osteoporosis. Bone health assessment should integrate DEXA findings, age, sex, fracture history, hormonal status, medication exposure, nutrition, physical activity, and other clinical risk factors.

Keywords: Vitamin D; 25-Hydroxyvitamin D; Body Mass Index; Osteopenia; Osteoporosis; DEXA; Bone Mineral Density

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Introduction

Vitamin D is a fat-soluble secosteroid hormone precursor that supports calcium and phosphate homeostasis, skeletal mineralization, and neuromuscular function. Serum 25-Hydroxyvitamin D [25(OH)D] is widely used as the principal biomarker of vitamin D status because it reflects vitamin D obtained from cutaneous synthesis, diet, and supplementation [1, 2]. The Institute of Medicine and other expert bodies have emphasized the central role of vitamin D and calcium in skeletal health, while also noting uncertainty around optimal thresholds for broader disease prevention [2, 3].

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration, resulting in increased bone fragility and fracture risk. Dual-Energy *X*-ray Absorptiometry (DEXA) is the standard method for measuring Bone Mineral Density (BMD) and classifying low bone mass. A T-score of -1.0 or above is generally considered normal, a T-score between -1.0 and -2.5 indicates osteopenia or low bone mass, and a T-score of -2.5 or lower is consistent with osteoporosis in appropriate adult populations [4, 5].

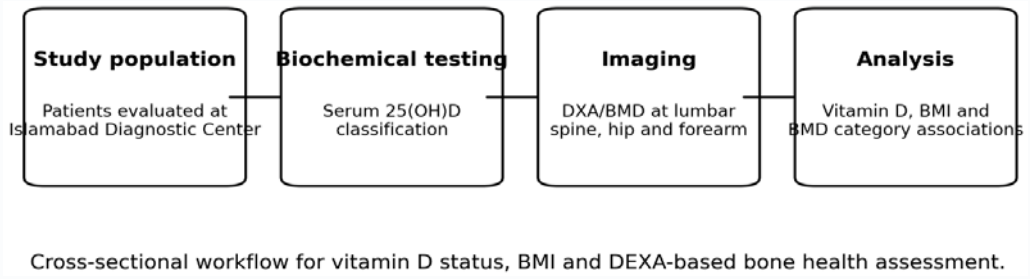

Figure 1: Cross-sectional workflow for vitamin D, BMI, and DEXA-based bone health analysis. Participants contributed to specific analyses according to availability of vitamin D, BMI, and BMD data.

Vitamin D deficiency may contribute to secondary hyperparathyroidism, reduced calcium absorption, bone turnover abnormalities, muscle weakness, and fracture susceptibility. Nonetheless, the strength of association between measured serum 25(OH)D and BMD outcomes varies across studies. Meta-analyses and recent guideline reviews have challenged the assumption that vitamin D status alone reliably predicts BMD or that supplementation uniformly improves BMD in broadly unselected populations [6, 7].

BMI adds further complexity. Low BMI is a recognized risk factor for low BMD and fractures, partly due to lower mechanical loading and reduced soft-tissue protection during falls. Conversely, higher BMI may increase BMD through mechanical loading but may also be associated with lower circulating 25(OH)D because of volumetric dilution, adipose sequestration, reduced outdoor activity, or metabolic dysregulation [8, 9]. Therefore, the interaction between vitamin D, BMI, and bone health may differ according to age, sex, adiposity pattern, menopausal status, diet, physical activity, and comorbid disease.

Pakistan faces a substantial burden of vitamin D deficiency and bone health disorders, particularly among women and older adults, but diagnostic-center data are often underused. This study analyzed vitamin D status, BMI categories, and DEXA-defined BMD results from a diagnostic-center population to determine whether serum vitamin D or BMI correlated with osteopenia or osteoporosis.

Materials and Methods

Study design and setting

This was a cross-sectional observational study conducted using records from Islamabad Diagnostic Center, Islamabad, Pakistan. The study period extended from January 2020 to March 2025. The analysis focused on patients who underwent serum 25(OH)D testing and/or DEXA-based bone density assessment as part of diagnostic evaluation.

Participants and eligibility

Individuals with available vitamin D results were included in the vitamin D status analysis. Individuals with DEXA or BMD results from the lumbar spine, hip joint, or forearm were included in the bone-density analysis. Participants with incomplete records for a specific variable were excluded only from analyses requiring that variable. A subset of 51 participants with available BMI category and vitamin D status was analyzed separately for BMI-vitamin D distribution.

Vitamin D measurement and classification

Serum 25(OH)D was used to classify vitamin D status. The dataset categorized individuals as vitamin D deficient, insufficient, normal, or high. The average 25(OH)D levels reported for deficient, insufficient, normal, and high groups were 14.22 ng/mL, 24.73 ng/mL, 48.56 ng/mL, and 115.10 ng/mL, respectively.

Bone mineral density assessment

Bone health was assessed using DEXA/BMD evaluation at the lumbar spine, hip joint, and forearm. The source file described use of the Hologic Horizon Bone Densitometry System and standardized radiological protocols. BMD outcomes were categorized as normal, osteopenia, or osteoporosis according to diagnostic classification used in the reporting system.

Statistical analysis

Descriptive statistics were used to summarize vitamin D categories, BMD categories, anatomical-site distributions, and BMI subset categories. Pearson correlation coefficients were used to evaluate associations between vitamin D and osteopenia, vitamin D and osteoporosis, BMI and osteopenia, and BMI and osteoporosis. A p-value <0.05 was considered statistically significant.

Results

See Figure 1.

Vitamin D status distribution

Among 2,202 individuals with serum 25(OH)D data, 1,579 (72%) were classified as normal, 328 (15%) as insufficient, 265 (12%) as deficient, and 30 (1%) as high. Therefore, approximately 27% of the tested population had vitamin D deficiency or insufficiency. The average 25(OH)D levels were 48.56 ng/mL in the normal group, 24.73 ng/mL in the insufficient group, 14.22 ng/mL in the deficient group, and 115.10 ng/mL in the high group (Table 1 and Figure 2).

DEXA findings by anatomical site

DEXA/BMD readings were available across three anatomical regions: lumbar spine, hip joint, and forearm. In total, 806 readings were normal, 868 indicated osteopenia, and 382 indicated osteoporosis. The forearm showed the largest number of osteoporotic readings (n = 192), whereas osteopenic readings were common in the lumbar spine (n = 295), hip joint (n = 293), and forearm (n = 280) (Table 2 and Figure 3).

Correlation of vitamin D and BMI with bone conditions

Pearson correlation analysis did not identify statistically significant relationships between vitamin D and osteopenia (r=0.02, p=0.68), vitamin D and osteoporosis (r=-0.03, p=0.56), BMI and osteopenia (r=-0.01, p=0.77), or BMI and osteoporosis (r=0.04, p=0.44). The direction and magnitude of all coefficients were weak, indicating that

Table 1: Distribution of serum 25(OH)D categories in the study population.

Vitamin D status	n	%	Mean 25(OH)D (ng/mL)
Normal	1,579	72	48.56
Insufficient	328	15	24.73
Deficient	265	12	14.22
High	30	1	115.10

Abbreviation: 25(OH)D: 25-Hydroxyvitamin D

Table 2: DEXA-based BMD categories by anatomical site.

Region	Normal (n)	Osteopenia (n)	Osteoporosis (n)	Total readings (n)
Lumbar spine	289	295	118	702
Hip joint	324	293	72	689
Forearm	193	280	192	665
Total	806	868	382	2,056

Abbreviations: BMD: Bone Mineral Density; DEXA: Dual-Energy *X*-ray Absorptiometry
Counts represent site-specific readings and should not be interpreted as unique patient counts

Table 3: Correlation analysis of vitamin D, BMI, and bone health categories.

Comparison	Pearson r	p-value	Interpretation
Vitamin D *vs* osteopenia	0.02	0.68	Not significant
Vitamin D *vs* osteoporosis	-0.03	0.56	Not significant
BMI *vs* osteopenia	-0.01	0.77	Not significant
BMI *vs* osteoporosis	0.04	0.44	Not significant

Table 4: Vitamin D status across BMI categories in the complete BMI subset.

BMI category	Deficient (n)	Insufficient (n)	Normal (n)	Total (n)
No record	5	2	4	11
Normal BMI	5	4	3	12
Obese	6	3	4	13
Overweight	6	3	5	14
Underweight	1	0	0	1
Total	23	12	16	51

neither serum 25(OH)D nor BMI explained meaningful variation in DEXA-defined bone categories in this dataset (Table 3 and Figure 4).

Vitamin D status across BMI categories

In the subset of 51 participants with available BMI category and vitamin D status, deficiency was observed across all BMI strata. Among participants with normal BMI, five were deficient, four were insufficient, and three had normal vitamin D levels. Among obese participants, six were deficient, three were insufficient, and four had normal vitamin D levels. Among overweight participants, six were deficient, three were insufficient, and five had normal vitamin D levels. The single underweight participant was vitamin D deficient. Overall, no clear monotonic pattern was observed between BMI category and vitamin D status (Table 4, Figure 5 and 6).

Discussion

This cross-sectional diagnostic-center study found that serum 25(OH)D and BMI were not significantly correlated with DEXA-defined osteopenia or osteoporosis. Although vitamin D has an established biological role in calcium absorption and skeletal mineralization, the present results suggest that a single serum vitamin D value may not be sufficient to predict bone-density classification in a heterogeneous clinical population. This finding is consistent with contemporary guideline discussions emphasizing uncertainty around optimal 25(OH)D thresholds for broad disease prevention and the need to avoid overinterpreting vitamin D testing outside specific clinical contexts [3, 7].

The DEXA results showed that osteopenia was common across lumbar spine, hip, and forearm readings, while osteoporosis was most frequent at the forearm. This site-specific variation is clinically important because BMD can differ across anatomical regions due to age, cortical versus trabecular bone composition, degenerative spinal changes, prior fracture, positioning, and technical factors. Diagnostic interpretation should therefore consider the anatomical site, image quality, clinical risk profile, and fracture history rather than relying on one isolated measurement [4, 5].

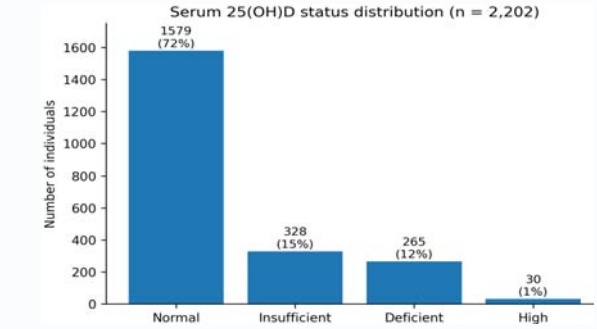

Figure 2: Distribution of serum 25(OH)D status among 2,202 individuals. Most participants were categorized as normal, while deficiency and insufficiency together accounted for more than one-quarter of the cohort.

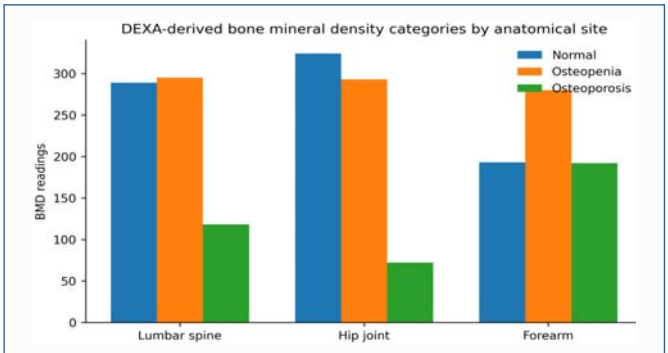

Figure 3: DEXA-derived BMD categories by anatomical site. Osteoporosis was most frequent at the forearm, while osteopenia was common across all three assessed sites.

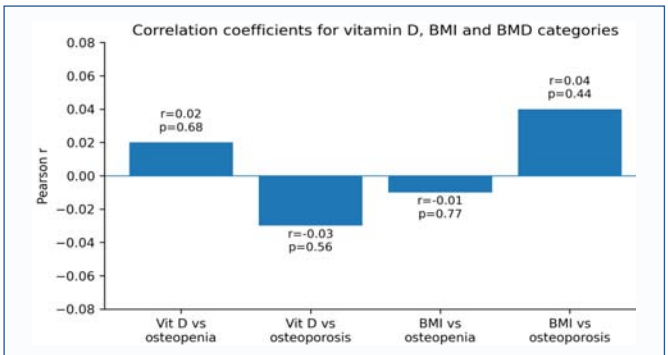

Figure 4: Correlation summary for vitamin D, BMI, and BMD categories. All correlations were weak and statistically insignificant.

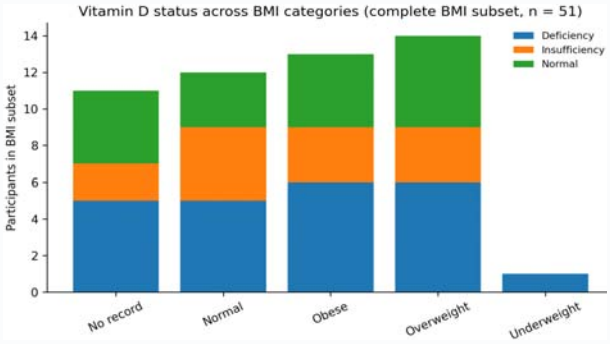

Figure 5: Vitamin D status across BMI categories in the complete BMI subset. Deficiency was present across normal, obese, overweight, and underweight categories.

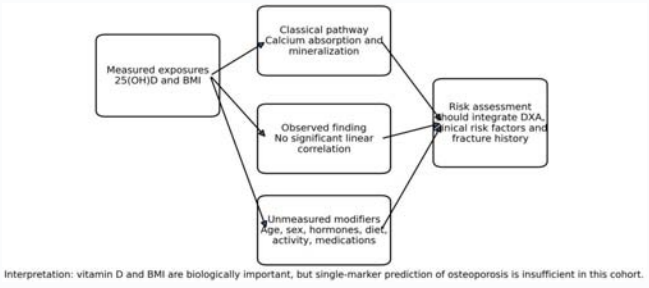

Figure 6: Interpretive model showing why vitamin D and BMI alone may be insufficient predictors of osteoporosis risk. Comprehensive assessment requires DEXA findings and broader clinical risk profiling.

The absence of significant correlation between vitamin D and bone-density category does not negate the importance of vitamin D. Deficiency can impair calcium absorption, contribute to secondary hyperparathyroidism, increase bone turnover, and worsen muscle function, particularly in frail or older adults [1, 2, 10]. However, BMD is influenced by multiple determinants, including genetics, sex hormones, age, menopause, chronic inflammation, kidney disease, medications such as glucocorticoids, nutritional intake, smoking, alcohol exposure, and physical activity. These unmeasured factors may explain why vitamin D alone was not a strong predictor in this cohort.

Similarly, BMI showed no significant correlation with osteopenia or osteoporosis. BMI is a crude anthropometric measure and does not distinguish between fat mass, lean mass, fat distribution, sarcopenia, or mechanical loading patterns. Higher BMI may increase BMD through loading but may also impair vitamin D bioavailability or increase fall-related morbidity. Conversely, low BMI may indicate frailty or malnutrition, but not all low-BMI individuals have osteoporosis. These competing mechanisms may produce weak aggregate correlations in cross-sectional datasets [8, 9].

The BMI subset showed vitamin D deficiency across all BMI categories, including normal, obese, overweight, and the single underweight category. This supports the interpretation that vitamin D status in Pakistan may reflect a combination of sun exposure, dietary intake, clothing practices, supplementation, indoor lifestyle, air pollution, age, sex, and metabolic factors rather than BMI alone. The finding also warns against assuming that normal BMI excludes vitamin D deficiency or bone health risk.

This study has several strengths, including a large vitamin D testing denominator, DEXA readings across multiple anatomical sites, and a practical diagnostic-center setting. Important limitations include cross-sectional design, absence of patient-level longitudinal follow-up, limited BMI subset size, possible overlap of site-specific DEXA readings within the same patients, lack of fracture outcome data, and lack of adjustment for age, sex, menopause, diet, physical activity, medication use, parathyroid hormone, calcium, phosphate, and kidney function. Future work should use patient-level multivariable models and fracture outcomes to determine whether vitamin D, BMI, and other biomarkers improve risk prediction beyond DEXA alone.

Conclusion

This study demonstrates that vitamin D status and BMI were not significantly associated with DEXA-defined osteopenia or osteoporosis in the analyzed population. Although vitamin D remains biologically important for skeletal health, bone-risk assessment should not rely on vitamin D or BMI alone. A comprehensive approach integrating DEXA, fracture history, age, sex, hormonal status, lifestyle, nutrition, comorbidities, and medication exposure is necessary for accurate osteoporosis risk assessment and prevention.

Declarations

Ethics approval and consent to participate: The source study reported informed consent and institutional review board approval from Islamabad Diagnostic Center. The exact approval number should be inserted before submission.

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Conflict of Interest

The authors should declare any potential conflicts of interest before submission.

Data Availability

Aggregated data are included in the manuscript. Patient-level data are not publicly available because of privacy considerations.

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