

Screening for osteoporosis in thalassemia and chronic kidney disease patients using DEXA: A prospective observational study

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Abstract

Background: Osteoporosis is a frequent, underdiagnosed complication of both Thalassemia and Chronic Kidney Disease (CKD), yet comparative dual-energy X-ray absorptiometry (DEXA) data across these two conditions from the same institution are limited.

Objective: To assess and compare bone mineral density (BMD) using DEXA in patients with Thalassemia and CKD, and to correlate DEXA findings with clinical and anthropometric parameters.

Materials and Methods: This prospective observational study enrolled 212 patients (107 Thalassemia, 105 CKD) at a tertiary care hospital in Jamnagar, Gujarat, over 18 months. DEXA of the lumbar spine (L1-L4) and proximal hip was performed as per ISCD 2023 protocols, with BMD classified using Z-scores. Statistical analysis used Student's t-test, the chi-square/Fisher's exact test, and correlation analysis (SPSS v27.0; $p < 0.05$ considered significant).

Results: Low BMD for age ($Z \leq -2.0$) was found in 56.6% of patients and osteopenia in 41.0%; only 2.4% had normal BMD. CKD patients had significantly lower BMD than Thalassemia patients at the lumbar spine (0.777 vs 0.833 g/cm², $p < 0.001$) and hip (0.818 vs 0.856 g/cm², $p < 0.001$), with more negative Z-scores at both sites ($p < 0.001$ and $p = 0.0002$ respectively). Thalassemia major patients had a nearly 19-fold higher prevalence of low BMD than non-major patients (75.6% vs 4.0%, $p < 0.001$). Fracture history was present in 53.8% overall (CKD 70.5% vs Thalassemia 37.4%, $p < 0.001$), and 86.8% of patients with fractures had low BMD ($p < 0.001$).

Conclusion: Reduced BMD is near-universal in both Thalassemia and CKD, with CKD patients showing disproportionately greater age-adjusted bone loss. Thalassemia major and fracture history are important risk markers. Routine DEXA screening should be incorporated into follow-up protocols for both conditions.

Keywords: Osteoporosis, thalassemia, chronic kidney disease, dual-energy X-Ray absorptiometry, bone mineral density, Z-score

Introduction

The skeletal system is a dynamic, metabolically active tissue that undergoes continuous remodelling to maintain structural integrity and mineral homeostasis. Osteoporosis, defined by the World Health Organization as a reduction in bone mass with micro-architectural deterioration leading to increased skeletal fragility and fracture risk,^[1] is classically associated with ageing and postmenopausal hormonal decline, but frequently occurs as a secondary complication of chronic systemic disease. Among patients with Thalassemia and Chronic Kidney Disease (CKD), secondary osteoporosis is a common, often underdiagnosed cause of morbidity, chronic pain, and reduced quality of life.

In Thalassemia, chronic haemolytic anaemia drives erythroid marrow expansion that mechanically compromises trabecular and cortical bone, while transfusion-related iron overload is directly toxic to osteoblasts and promotes osteoclastogenesis.^[2, 3] Iron deposition within endocrine glands further causes hypogonadism, growth hormone deficiency, and hypoparathyroidism, preventing attainment of peak bone mass during adolescence.^[4] Bone disease remains common despite advances in transfusion and chelation protocols.^[2-4]

In CKD, progressive loss of renal phosphate excretion and impaired calcitriol synthesis lead to secondary hyperparathyroidism and the spectrum of CKD-Mineral and Bone Disorder (CKD-MBD).^[5] The 2017 KDIGO guideline update confirmed that DEXA-measured bone mineral

density (BMD) independently predicts incident fractures in CKD stages G3a-G5D.^[6]

Dual-energy X-ray absorptiometry (DEXA) remains the reference standard for BMD assessment in these populations, with Z-scores - rather than T-scores - recommended for comparison against age-, sex-, and ethnicity-matched norms in a predominantly young-to-middle-aged population, per the 2023 International Society for Clinical Densitometry (ISCD) Official Positions.^[7] Despite the recognised burden of skeletal disease in both conditions, prospective comparative DEXA data evaluating Thalassemia and CKD together within the same institutional cohort remain limited, particularly from India.

This study was therefore undertaken to assess bone mineral density using DEXA in patients with Thalassemia and CKD, to compare BMD and Z-scores between the two groups, and to correlate DEXA findings with clinical, anthropometric, and treatment-related parameters.

Materials and Methods

This was a hospital-based prospective observational study conducted in the Departments of Radiodiagnosis and Medicine at a tertiary care hospital, Jamnagar, Gujarat, over a period of 18 months, with the aim of assessing bone mineral density in patients with Thalassemia and CKD and correlating BMD with clinical features.

Patients presenting to the Thalassemia and Medicine/Nephrology outpatient departments who fulfilled the eligibility criteria were enrolled. Inclusion criteria were

a confirmed diagnosis of Thalassemia (major or intermedia) or CKD, willingness to provide written informed consent, and age ≥ 12 years. Patients with recent fractures or conditions affecting bone metabolism unrelated to Thalassemia/CKD, pregnancy, recent major surgery, or metallic implants within the scanning field were excluded. A total of 212 patients were enrolled (target sample size 210, based on a reference study for this design): 107 with Thalassemia (50.5%) and 105 with CKD (49.5%).

Ethical approval was obtained from the Institutional Ethics Committee prior to commencement of the study, and written informed consent was obtained from all participants or their legal guardians. The study was conducted in compliance with the Declaration of Helsinki (2013 revision) and the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017).

DEXA scanning of the lumbar spine (L1-L4) and proximal hip (total hip and femoral neck) was performed using a calibrated dual-energy X-ray absorptiometry scanner, with daily calibration using manufacturer-supplied phantoms and standardised ISCD positioning protocols. Areal BMD (g/cm^2) and Z-scores were generated automatically using age-, sex-, and ethnicity-matched reference data. Z-scores, rather than T-scores, were used for BMD classification given the predominantly young-to-middle-aged study

population, in accordance with the ISCD 2023 Official Positions.^[7] The minimum Z-score from the two sites was used for final classification: $Z > -1.0$ = normal BMD; $-2.0 < Z \leq -1.0$ = below-average BMD (osteopenia-equivalent); $Z \leq -2.0$ = low BMD for chronological age (osteoporosis-equivalent).

Data on Thalassemia subtype, chelation therapy, fracture history, bone pain, height loss, anthropometric measurements, and current medications were recorded on a predesigned case record form.

Data were analysed using IBM SPSS Statistics version 27.0. Descriptive statistics are reported as mean $\pm$ SD and frequency (%). The independent-samples Student's t-test was used for comparison of continuous variables between groups, and the chi-square or Fisher's exact test for categorical variables; Pearson's or Spearman's correlation was used as appropriate. A p-value < 0.05 was considered statistically significant.

Results

A total of 212 patients were enrolled in this prospective study, comprising 107 patients with Thalassemia (50.5%) and 105 patients with CKD (49.5%). Baseline demographic and anthropometric characteristics are summarised in Table 1.

Table 1: Demographic and Anthropometric Profile of Study Participants

Parameter	Thalassemia (n=107)	CKD (n=105)	Total (n=212)	p-value
Male, n (%)	51 (47.7%)	54 (51.4%)	105 (49.5%)	--
Female, n (%)	56 (52.3%)	51 (48.6%)	107 (50.5%)	--
Age, years (mean $\pm$ SD)	29.3 $\pm$ 5.5	65.0 $\pm$ 13.1	46.9 $\pm$ 19.6	< 0.001
Height, cm (mean $\pm$ SD)	163.1 $\pm$ 7.1	165.2 $\pm$ 5.9	164.1 $\pm$ 6.6	--
Weight, kg (mean $\pm$ SD)	55.8 $\pm$ 5.6	70.5 $\pm$ 4.2	63.0 $\pm$ 9.3	--
BMI, kg/m^2 (mean $\pm$ SD)	21.0 $\pm$ 2.3	25.8 $\pm$ 1.1	23.4 $\pm$ 3.1	< 0.001

CKD patients were significantly older (65.0 $\pm$ 13.1 vs 29.3 $\pm$ 5.5 years, $p < 0.001$) and had significantly higher BMI (25.8 $\pm$ 1.1 vs 21.0 $\pm$ 2.3 kg/m^2 , $p < 0.001$) than Thalassemia patients, reflecting the differing natural history of the two conditions.

Table 2: BMD Classification by Study Group (Minimum Z-Score)

BMD Category	Z-score Criterion	Thalassemia n (%)	CKD n (%)	Total n (%)
Normal BMD	$Z > -1.0$	4 (3.7%)	1 (1.0%)	5 (2.4%)
Osteopenia (below average)	$-2.0 < Z \leq -1.0$	46 (43.0%)	41 (39.0%)	87 (41.0%)
Osteoporosis (low BMD for age)	$Z \leq -2.0$	57 (53.3%)	63 (60.0%)	120 (56.6%)
Total	--	107 (100%)	105 (100%)	212 (100%)

Low BMD for age was the dominant finding, affecting 56.6% of the total cohort (60.0% of CKD vs 53.3% of Thalassemia patients; χ^2 test $p = 0.303$, not statistically significant). Only 2.4% of the entire cohort had normal BMD

Table 3: Comparison of Mean BMD and Z-Scores Between Thalassemia and CKD Groups

Parameter	Thalassemia (n=107)	CKD (n=105)	t-value	p-value
Lumbar BMD, g/cm^2 (mean $\pm$ SD)	0.833 $\pm$ 0.057	0.777 $\pm$ 0.053	7.497	< 0.001
Hip BMD, g/cm^2 (mean $\pm$ SD)	0.856 $\pm$ 0.064	0.818 $\pm$ 0.054	4.621	< 0.001
Lumbar Z-score (mean $\pm$ SD)	-1.87 $\pm$ 0.52	-2.17 $\pm$ 0.45	4.525	< 0.001
Hip Z-score (mean $\pm$ SD)	-1.53 $\pm$ 0.48	-1.77 $\pm$ 0.45	3.844	0.0002

CKD patients had significantly lower BMD than Thalassemia patients at both the lumbar spine (0.777 vs 0.833 g/cm^2 , $p < 0.001$) and hip (0.818 vs 0.856 g/cm^2 , $p < 0.001$). Age-adjusted Z-scores were also significantly more negative in CKD at both the lumbar spine (-2.17 vs -1.87, $p < 0.001$) and hip (-1.77 vs -1.53, $p = 0.0002$)

Table 4: Fracture Prevalence and Anatomical Distribution by Study Group

Parameter	Thalassemia n (%)	CKD n (%)	Total n (%)
Fracture history - Yes	40 (37.4%)	74 (70.5%)	114 (53.8%)
Fracture history - No	67 (62.6%)	31 (29.5%)	98 (46.2%)
Vertebral*	24 (60.0%)	20 (27.0%)	44 (38.6%)
Long bone*	6 (15.0%)	19 (25.7%)	25 (21.9%)
Multiple sites*	0 (0.0%)	18 (24.3%)	18 (15.8%)
Hip*	0 (0.0%)	17 (23.0%)	17 (14.9%)

(Overall fracture history: $\chi^2 = 22.04$, $p < 0.001$. *Percentage of fracture patients within each group; remaining sites - wrist, pelvis, and femoral neck - accounted for the balance and occurred only in Thalassemia patients.)

Fracture history was present in 53.8% of patients overall, significantly more common in CKD (70.5%) than Thalassemia (37.4%; $\chi^2=22.04$, $p<0.001$). Vertebral fractures predominated in Thalassemia (60.0% of fractures), while CKD showed a more diverse pattern, including hip

(23.0%) and multiple-site (24.3%) fractures, which occurred exclusively in the CKD group. Bone pain was reported in 87.3% of patients overall (100% CKD vs 74.8% Thalassemia, $p<0.001$), and height loss in 52.4% overall (70.5% CKD vs 34.6% Thalassemia, $p<0.001$).

Table 5: BMD Comparison - Thalassemia Major vs Non-Major

Parameter	Major (n=82)	Non-Major (n=25)	t / χ^2	p-value
Lumbar BMD, g/cm ²	0.817 +/- 0.048	0.887 +/- 0.050	-6.82	<0.001
Hip BMD, g/cm ²	0.834 +/- 0.053	0.928 +/- 0.037	-8.17	<0.001
Lumbar Z-score	-1.98 +/- 0.52	-1.50 +/- 0.33	-4.24	<0.001
Hip Z-score	-1.66 +/- 0.44	-1.10 +/- 0.31	-5.89	<0.001
Low BMD (Z<=-2.0), n (%)	62 (75.6%)	1 (4.0%)	$\chi^2=37.67$	<0.001

Thalassemia major patients had significantly lower BMD than non-major patients at both the lumbar spine (0.817 vs 0.887 g/cm², $p<0.001$) and hip (0.834 vs 0.928 g/cm², $p<0.001$), with a nearly 19-fold higher prevalence of low BMD (75.6% vs 4.0%, $p<0.001$)

Table 6: BMD Parameters Stratified by Fracture History

Parameter	With Fracture (n=114)	Without Fracture (n=98)	t-value	p-value
Lumbar BMD, g/cm ²	0.766 +/- 0.047	0.851 +/- 0.043	-13.508	<0.001
Hip BMD, g/cm ²	0.825 +/- 0.056	0.852 +/- 0.066	-3.29	0.001
Lumbar Z-score	-2.28 +/- 0.48	-1.72 +/- 0.35	-9.66	<0.001
Hip Z-score	-1.76 +/- 0.48	-1.52 +/- 0.44	-3.77	<0.001
Low BMD (Z<=-2.0), n (%)	99 (86.8%)	34 (34.7%)	$\chi^2=59.09$	<0.001

Patients with a fracture history had significantly lower BMD and more negative Z-scores at both sites than those without ($p<0.001$ for all comparisons). The prevalence of low BMD was markedly higher in the fracture group (86.8% vs 34.7%; $\chi^2=59.09$, $p<0.001$), and no patient with a fracture history had normal BMD.

Among Thalassemia patients, 86.0% were receiving chelation therapy, most commonly oral Deferasirox (65.2% of those on chelation), followed by parenteral Deferoxamine (26.1%). Patients on Deferasirox had numerically better lumbar Z-scores (-1.86 +/- 0.49) than those on Deferoxamine (-2.30 +/- 0.40).

Discussion

This prospective study assessed BMD by DEXA in 212 patients with Thalassemia (n=107) and Chronic Kidney Disease (n=105) at a tertiary care hospital in Jamnagar, Gujarat. Reduced BMD was strikingly common in both groups: 56.6% had low BMD for age and 41.0% had osteopenia, leaving only 2.4% of the cohort with normal bone density. CKD patients had significantly worse absolute BMD and more negative age-adjusted Z-scores than Thalassemia patients at both the lumbar spine and hip. The osteoporosis prevalence of 53.3% in the Thalassemia group is consistent with published literature. Vogiatzi *et al.*, in a multicentre study of adult Thalassemia patients in the United States, reported osteoporosis in approximately 50% and osteopenia in 35%.^[2] Haidar *et al.* similarly noted that bone disease persists despite adequate transfusion therapy.^[4] Tzoulis *et al.* reported a 42.3% osteoporosis prevalence among adult Greek patients with beta-Thalassemia major,^[8] while Chuasuwana *et al.*, in a large Thai cohort, reported a comparable low-BMD prevalence of 62.4% by Z-score criteria.^[9] From India, Singh *et al.* reported low BMD in over 70% of Thalassemia major patients,^[10] and a previous study at the same institution reported an 81% prevalence.^[11] The marginally lower rate observed here may reflect the inclusion of non-major/intermedia patients, who had markedly better bone density.

In the CKD group, 60.0% had osteoporosis and 39.0% osteopenia, with only one patient (1.0%) having normal BMD, consistent with the near-universal burden of CKD-MBD reported in advanced renal disease.^[5] Patel *et al.* confirmed early-onset mineral metabolism disturbances in Indian CKD patients that worsen with disease stage,^[12] and Etta *et al.* demonstrated high-turnover bone disease markers in the majority of newly diagnosed Indian CKD patients even before dialysis initiation.^[13]

A key finding of this study was that CKD patients had significantly lower BMD and more negative Z-scores than Thalassemia patients at both sites, even after age adjustment. This is consistent with reports that fracture risk in CKD is two- to four-fold higher than in the general population and rises with advancing disease stage,^[5] and with international guidance identifying CKD-associated osteoporosis as a distinct complication warranting active management.^[6, 14]

The pattern of skeletal involvement differed by site between the two diseases: Thalassemia showed predominant lumbar spine (trabecular) involvement, consistent with marrow-expansion-driven bone loss,^[2, 4] whereas CKD showed severe involvement at both the lumbar spine and hip, reflecting additional cortical bone loss driven by secondary hyperparathyroidism.^[5, 14] These findings support scanning both sites for comprehensive fracture-risk assessment.^[7]

Within the Thalassemia group, major patients had a nearly 19-fold higher prevalence of low BMD than non-major/intermedia patients, consistent with the established role of transfusion-related iron overload and endocrine failure in disease pathogenesis.^[3] Voskaridou and Terpos identified hypogonadism as the strongest independent predictor of reduced BMD in Thalassemia major,^[15] supporting universal DEXA screening in this subgroup.

Fracture history was strongly associated with reduced BMD: patients with fractures had significantly lower BMD and more negative Z-scores than those without, and no patient with a fracture history had normal BMD. Vertebral fractures predominated in Thalassemia, while CKD patients showed a

more diverse fracture pattern, including hip and multiple-site fractures that occurred exclusively in this group, consistent with the two- to four-fold higher hip fracture risk reported in CKD.^[5] These data support DEXA as an effective tool for fracture-risk stratification, in line with KDIGO 2017^[6] and ISCD 2023^[7] recommendations.

Among Thalassemia patients on chelation therapy, those receiving oral Deferasirox had better lumbar Z-scores than those on parenteral Deferoxamine, consistent with reports of superior iron-clearance efficacy with Deferasirox.^[16] Abdalbary *et al.* emphasised that initiation of anti-resorptive therapy should not be delayed in symptomatic patients with established low BMD,^[17] which is relevant given that a subset of patients in both groups with documented low BMD were not receiving any bone-protective medication.

This study has several limitations. It was conducted at a single centre, which may limit generalisability to other populations. Systematic biochemical parameters (serum ferritin, intact PTH, 25-hydroxyvitamin D, calcium, phosphate) and CKD staging were not captured, precluding correlation of BMD with markers of bone turnover and mineral metabolism. The inherent age difference between the two groups cannot be fully eliminated by Z-score adjustment alone. The Trabecular Bone Score, which provides additional information on bone microarchitecture,^[18] was not performed. Longitudinal studies incorporating biochemical profiling, CKD staging, and serial DEXA measurements are needed to validate and extend these findings.

Conclusion

Reduced bone mineral density is a near-universal complication in both Thalassemia and Chronic Kidney Disease, with CKD patients showing disproportionately greater, age-adjusted bone loss than Thalassemia patients. Thalassemia major and a history of low-trauma fracture are strong markers of severely reduced BMD. These findings support the routine incorporation of DEXA screening of the lumbar spine and hip into follow-up protocols for Thalassemia major patients from age 12 years (or transfusion initiation) and for CKD patients from stage G3 or the onset of bone-related symptoms, combined with biochemical monitoring and timely institution of bone-protective therapy, to reduce the burden of fractures and skeletal morbidity in these high-risk populations.

Declarations

Source of Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the Institutional Ethics Committee (IEC) of Shri M.P. Shah Medical College & Guru Gobind Singh Government Hospital, Jamnagar, Gujarat, prior to commencement. The study was conducted in accordance with the Declaration of Helsinki (2013 revision) and the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017).

Informed Consent

Written informed consent was obtained from all participants, or from their legal guardians where applicable, prior to enrolment in the study.

Author Contributions

All authors contributed equally to the study concept and design, data collection and analysis, manuscript preparation, and final approval of the version submitted for publication.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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