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Osteomalacic Myopathy and Early Gait Changes

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A B S T R A C T

Background: The incidence and prevalence of osteomalacia are vastly underestimated for at-risk populations. Increased awareness and knowledge of the disease are essential for its early diagnosis and prompt treatment.

Aim: This study aimed to establish proximal myopathy, gait abnormalities, and history of pica as early presenting symptoms of osteomalacia in young women, as well as complete remission of these symptoms on adequate supplementation.

Materials and Methods: This prospective study included 36 young women (18–32 years of age) clinically suspected and diagnosed with osteomalacia using the Uday-Hogler criteria and radiological features from December 2022 to December 2023. Baseline Harris Hip Score, visual analogue scale pain score, and power at hip extensors were also recorded. Subjects were treated with weekly vitamin D, and daily calcium and micronutrient supplementation. Adequate sun exposure was advised. Patients were followed up at four, 12, and 24 weeks post-initiation of treatment. Improvements in Harris Hip Score, visual analogue scale pain score, and power at hip extensor muscles were noted, and comparisons were made to establish statistical significance. Serum calcidiol, alkaline phosphatase, parathormone, and urine calcium levels were also monitored.

Results: Of those diagnosed with osteomalacia, 26 (72%) and 23 (63.8%) presented with symptoms of proximal myopathy with early gait changes, and history of pica, respectively; both conditions were reversible on adequate supplementation with vitamin D and calcium (p=0.001). On follow-up, patients demonstrated improvement in gait, muscle power, and ability to climb up stairs and get up from the ground over a period of 4–24 weeks. Statistical analysis showed significant improvement in all the parameters under study. Hematological studies showed gradual improvement towards normal ranges.

Conclusion: Osteomalacia should be considered as a differential diagnosis in young women with diffuse muscle and bone pain, early proximal muscle weakness, altered gait pattern, and history of pica, and the underlying disease should be investigated.

Keywords: osteomalacia, myopathy, altered gait, pica, vitamin D, calcium.

INTRODUCTION

Osteomalacia is a metabolic bone disorder associated with progressive softening of bone due to decreased mineralization of newly formed osteoid matrix at the site of bone turn-over, leading to reduced bone density [1].The condition mainly results from vitamin D deficiency, as well as deficiencies in calcium or phosphate.

Vitamin D deficiency is the most common nutritional deficiency in the world [2-8],commonly seen in adolescents, and pregnant and lactating women. Primary nutritional deficiency can result from lack of adequate sunshine in temperate regions, concealing clothing, and skin pigmentation in darker races, as well as low calcium and vitamin D consumption due to poverty or diet trends. Nutritional deficiency can also be secondary to conditions such as renal or hepatic disease, hypophosphatemia, malabsorption resulting from intestinal inflammation, cystic fibrosis, celiac disease, or gastric surgery; as well as prolonged use of drugs such as anticonvulsants, corticoids, and chemotherapy agents [9].

Osteomalacia is often asymptomatic in its early stages. As the disease progresses, it can present with non-specific symptoms such as bone pains, diffuse arthralgia and myalgia, pica (usually associated with iron and other mineral deficiencies), muscle spasms, muscle weakness and/or tenderness, altered gait, and difficulty walking [1,10,11].
In this study, we aimed to determine the earliest presenting signs and symptoms of osteomalacia in young women in order to detect the disease in its initial stages and ensure early treatment.

MATERIALS & METHODS

This was a prospective study involving 36 women 18–32 years of age, with diagnosed primary nutritional deficiency, attending the outpatient services of the Department of Orthopedics at our hospital. The study was conducted from December 2022 to December 2023. The hospital is a rural tertiary care center attended predominantly by those of low to middle socioeconomic status.
For each patient, a detailed medical history was taken to determine the cause of primary nutritional deficiency, with special attention paid to dietary history and exposure to sunlight (duration and frequency). Each patient was probed to detect underlying medical conditions and medication use. Clinical features were noted with an emphasis on sequence of appearance of signs and symptoms.
Diagnosis of primary nutritional deficiency was made using the Uday–Hogler criteria as follows [12-14]: elevated parathyroid hormone level, elevated total or bone alkaline phosphatase level, low 24-hour urine calcium excretion, low calcium intake (usually <300 mg/day), or low calcidiol levels (<12 ng/mL). Radiologic features suggestive of osteomalacia included decreased bone mineral density, non-traumatic (fragility) fractures, and skeletal pseudofractures (i.e., Looser's zones). Bone mineral density and T-score were not calculated due to non-affordability, as the patients belonged to low to middle socioeconomic strata.
The inclusion criteria were as follows:female**,** 18–32 age group**,** primary nutritional deficiency**, and f**ulfilled the diagnostic criteria. The exclusion criteria were as follows:muscle dystrophy**,** neuro-muscular disorders**,** spine pathology leading to gait abnormality**,** skeletal deformity causing gait abnormality**,** inflammatory pathology**,** underlying systemic (secondary) cause of osteomalacia**,** and osteomalacia associated with fragility fractures. The study was approved by the ethics committee at our institute (IEC/IIMSR: F/35/2023).
Among the 36 women included in the study, all except nine (25%) patients presented with diffuse muscle pain, bone pain, and body ache, and 17 (47.2%) had lower back pain at presentation. 18 (50%) patients complained of generalized weakness. 22 (61.1%) patients gave a history of altered gait (noticed more by relatives of the patient). 24 (66.6%) patients complained of difficulty in climbing up-stairs and getting up from the ground. Dietary history frequently included poor eating habits. 23 patients(64%) gave a history of craving and eating mud or clay.
On examination, changes noted in posture included stooped posture at the hip, exaggerated lumbar lordosis, and lateral trunk tilt. Positive Trendelenburg sign was detected in 13 (36%) patients with pelvic drop, and waddling gait was noticed in nine patients (25%) with severe proximal muscle weakness. Decreased power of the proximal muscles of the lower limb (hip muscles) was found in 22 patients(61%).
All patients were clinically assessed in terms of Harris Hip Score (covering pain; use of support devices; maximum distance walked; limp; ability to put on shoes and socks; ability to climb stairs; ability to enter public transportation; sitting; absence of deformity; degrees of flexion, abduction, external rotation, adduction**),** visual analogue scale (VAS), and power of hip extensor muscles. Baseline values were recorded, and changes were monitored at 4, 12, and 24 weeks post initiation of treatment.

Diagnosis was supported by laboratory investigations, which revealed the following trends (at presentation): elevated serum total alkaline phosphatase level in all patients, with the highest recorded value of 20 times the normal level (2340 IU/L), with an average value of 1790 IU/L (normal range: 44–147 IU/L). The highest serum parathormone level detected was 1040 pg/mL, and the mean value was 820 pg/mL (normal range: 15–65 pg/mL). Serum calcidiol level was as low as undetectable, with an average value of 7 ng/mL (normal range: 30–50 mg/mL). Urine calcium levels were low, reaching 40 mg/day, with a mean value of 75 mg/day (normal: 100–300 mg/day).

Radiological evaluation revealed generalized osteopenia in 22 patients. Pseudofractures were detected in three patients (pubic rami fracture in two patients and left femur neck fracture in one patient).

Treatment and follow-up

All patients with diagnosed osteomalacia were given 60,000 IU of vitamin D3 at weekly intervals for 12 weeks [15-18]. Calcium was added at a dosage of 1 g per day in two divided doses.Adequate sun exposure was advised. Micronutrients (e.g., vitamin K2, zinc, and other micronutrients/multivitamins) were also advised to all patients.Patients with Looser's zones were advised bed rest for six weeks.
Response to treatment was evaluated clinically in terms of Harris Hip Score, VAS, and power of hip extensors at 4, 12, and 24 weeks from the start of treatment. Statistical analysis was done for the above-mentioned parameters—comparing pre-treatment and post-treatment values at 4, 12, 24 weeks—to monitor for improvement during follow-up. Serum calcium and urine calcium levels were monitored every four weeks until 24-hour urine calcium excretion was

normal.Serum calcidiol, serum parathormone, and serum alkaline phosphatase levels were determined, along with repeat X-ray, at 4, 12, and 24 weeks after starting therapy.
As the study was conducted at a tertiary care center where the study population belonged to lower socio-economic strata, inj. teriparatide and bisphosphonates were not considered as treatment options in the study.
During the study, *p*-value was measured by repeated measures analysis of variance, with $p<0.05$ considered statistically significant.

RESULTS

Age distribution

Of the 36 cases included in the study, the majority (n=19; 52.8%) were 18–25 years of age, followed by 13 (36.1%) patients 26–30 years of age, and four (11.1%) patients >30 years of age. The study sample had a mean ± standard deviation (SD) age of 25.00 ± 4.29 years, with age ranging from 18 to 32 years, as seen in Table 1.

Table 1: Age distribution of cases studied.

Age group (years)	Number of cases	% of cases
18–25	19	52.8
26–30	13	36.1
>30	4	11.1
Total	**36**	**100.0**
Mean ± standard deviation	25.00 ± 4.29 years	
Minimum – Maximum	18–32 years	

History of pica (mud/clay)

Of the 36 cases of osteomalacia included in the study, the majority (n=23; 63.8%) gave a history of mud/clay eating, which was statistically significant ($p<0.05$).

Comparison of mean pre-treatment and post-treatment Harris Hip Score

Mean ± SD Harris Hip Score at the pre-treatment stage, and 4, 12, and 24 weeks post-treatment, was 59.98 ± 13.10, 74.30 ± 10.59, 85.88 ± 8.02, and 94.93 ± 7.33, respectively, as seen in Figure 1 and Table 2. Therefore, relative to pre-treatment levels, Harris Hip Score was improved by 27.00%, 47.64%, and 64.41% at 4, 12, and 24 weeks post-treatment, respectively, with these differences being statistically significant ($p<0.05$ for all).

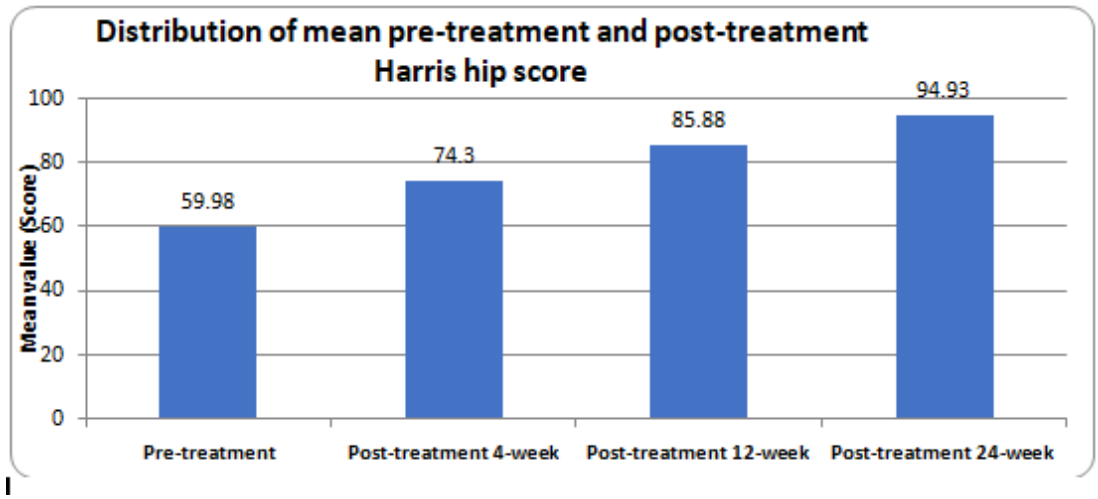

Figure 1: Distribution of mean pre-treatment and post-treatment Harris Hip Scores.

Table 2: Comparison of mean pre-treatment and post-treatment Harris Hip Scores.

	Harris Hip Score	
Follow-up	**Mean**	**SD**
Pre-treatment	59.98	13.10
4 weeks post-treatment	74.30	10.59
12 weeks post-treatment	85.88	8.02
24 weeks post-treatment	94.93	7.33
% improvement at 4 weeks post-treatment	27.00%	--
% improvement at 12 weeks post-treatment	47.64%	--
% improvement at 24 weeks post-treatment	64.41%	--
Paired comparisons	***p*-value**	
Pre-treatment vs. 4 weeks post-treatment	0.001***	
Pre-treatment vs. 12 weeks post-treatment	0.001***	
Pre-treatment vs. 24 weeks post-treatment	0.001***	

p-value determined by repeated measures analysis of variance, where $p<0.05$ is considered statistically significant. SD: standard deviation.

Comparison of mean pre-treatment and post-treatment VAS pain score

Mean ± SD VAS pain score at the pre-treatment stage, and 4 weeks, 12 weeks, and 24 weeks post-treatment, was 5.22 ± 1.31, 3.56 ± 1.13, 2.12 ± 1.08, and 0.88 ± 1.05, respectively as seen in Figure 2 and Table 3. Therefore, relative to pre-treatment levels, VAS pain score was improved by 31.00%, 60.79%, and 85.24% at 4 weeks, 12 weeks, and 24 weeks post-treatment, respectively. These differences were statistically significant ($p<0.05$ for all).

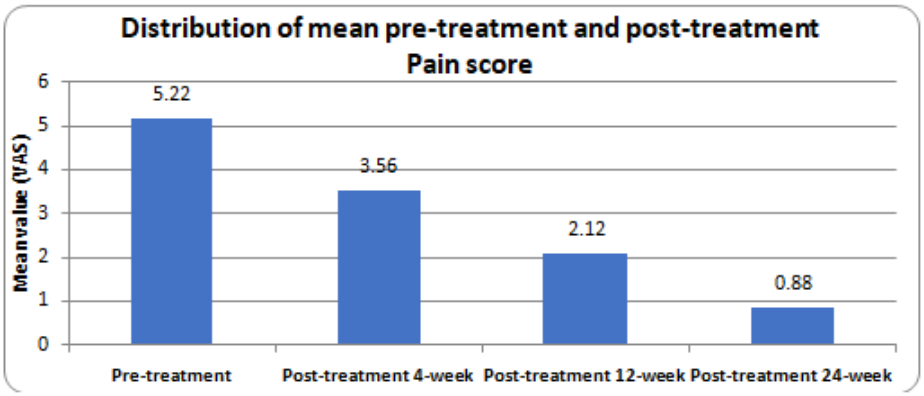

Figure 2: Distribution of mean pre-treatment and post-treatment visual analogue scale pain scores.

Table 3: Comparison of mean pre-treatment and post-treatment visual analogue scale pain scores.

	Pain score (VAS)	
Follow-up	**Mean**	**SD**
Pre-treatment	5.22	1.31
4 weeks post-treatment	3.56	1.13
12 weeks post-treatment	2.12	1.08
24 weeks post-treatment	0.88	1.05
% improvement at 4 weeks post-treatment	31.30%	--
% improvement at 12 weeks post-treatment	60.79%	--
% improvement at 24 weeks post-treatment	85.24%	--
Paired comparisons	***p*-value**	
Pre-treatment vs. 4 weeks post-treatment	0.001***	
Pre-treatment vs. 12 weeks post-treatment	0.001***	
Pre-treatment vs. 24 weeks post-treatment	0.001***	

p-value determined by repeated measures analysis of variance, where $p<0.05$ is considered statistically significant. VAS: visual analogue scale, SD: standard deviation.

Comparison of mean pre-treatment and post-treatment power (hip extensor) scores

Mean ± SD of power (hip extensor) scores at the pre-treatment stage, and 4, 12, and 24 weeks post-treatment, was 3.72 ± 0.45, 4.32 ± 0.64, 4.70 ± 0.64, and 4.79 ± 0.54, respectively, as seen in Figure 3 and Table 4. Therefore, relative to pre-treatment levels, power (hip extensor) score was improved by 16.18%, 26.51%, and 29.29% at 4, 12, and 24 weeks post-treatment, respectively. These differences were statistically significant (p<0.05 for all).

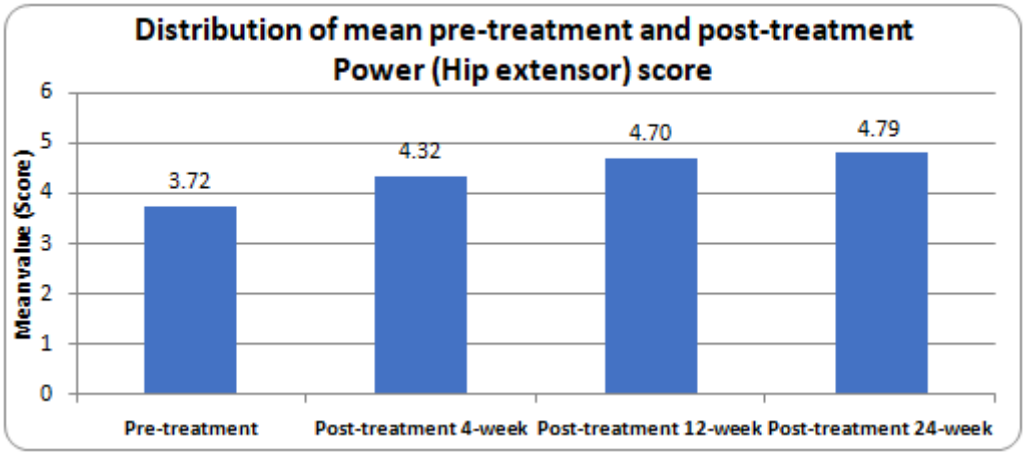

Figure 3: Distribution of mean pre-treatment and post-treatment power (hip extensor) scores.

Table 4: Comparison of mean pre-treatment and post-treatment power (hip extensor) scores.

	Power (hip extensor) score	
Follow-up	**Mean**	**SD**
Pre-treatment	3.72	0.45
4 weeks post-treatment	4.32	0.64
12 weeks post-treatment	4.70	0.64
24 weeks post-treatment	4.79	0.54
% improvement at 4 weeks post-treatment	16.18%	--
% improvement at 12 weeks post-treatment	26.51%	--
% improvement at 24 weeks post-treatment	29.29%	--
Paired comparisons	***p*-value**	
Pre-treatment vs. 4 weeks post-treatment	0.001***	
Pre-treatment vs. 12 weeks post-treatment	0.001***	
Pre-treatment vs. 24 weeks post-treatment	0.001***	

p-value determined by repeated measures analysis of variance, where p<0.05 is considered statistically significant. SD: standard deviation.

Of the 36 women included in the study, three did not follow-up for the entire duration of the study and were categorized as "loss to follow-up." Among the rest of the participants, adequate supplementation with calcium and vitamin D resulted in a spectacular resolution of muscle symptoms. Generalized weakness generally improved within the first week of therapy. Diffuse arthralgia and myalgia improved in 20 out of 24 patients within two weeks of treatment.By the end of the second week of treatment, difficulty in ambulation also improved in 16 out of 24 patients, and 15 out of 17 patients had relief from lower back pain.Posture and gait abnormalities improved gradually with improvement in proximal muscle power.With improvement in muscle power, patients were more at ease in climbing up stairs and getting up from sitting on the ground.Symptoms continued to resolve gradually over a period of 24 weeks, by which time the majority of patients were symptom-free.Only three out of 33 patients still complained of mild muscle pain and proximal muscle weakness at the 24-week follow-up.

Serum and urine calcium levels showed an upward trend starting at the first follow-up investigation at four weeks and continued to rise steadily further. Serum parathormone and alkaline phosphatase levels were lower at first follow-up and further declined to within the normal ranges at 24 weeks.

Radiological assessment showed significantly improved bone mineral density in all patients, first noted at 12 weeks follow-up and improved further at 24 weeks. In patients with Looser's zones, signs of callus formation were seen at four weeks, and union was present by the end of 24 weeks.

DISCUSSION

Osteomalacia is often asymptomatic in its early stages; with progression, it presents with non-specific symptoms such as bone pains, diffuse arthralgia and myalgia, muscle spasms, muscle weakness and/or tenderness, and difficulty walking [1,10,11].History of poor dietary habits and inadequate sun exposure is very common in such cases. History of picais uncommon but significant.

Recent studies have shown that vitamin D plays important roles in muscle growth, strength, and gait, confirming that hypovitaminosis D is strongly associated with a decrease in muscle function and performance, and an increase in disability [19,20]. Proximal muscle weakness (hip girdle and upper thigh muscles) and diffuse muscle pain often lead to instability of pelvis on standing and walking, as well as early presentation of gait abnormalities [21,22]; the hip extensor muscles are commonly affected, leading to flexion posture at hip, stooped posture, and appearance of exaggerated lumbar lordosis.Bilateral weakness of the Gluteus medius muscle eventually leads to waddling gait characterized by pelvic drop on the side of the swinging leg with compensatory lateral trunk tilt towards the limb in stance phase. Progressive difficulties in changing body position, rising from a chair, climbing up stairs, and getting up from the ground are all symptoms of myopathy resulting from osteomalacia[19,20].

Serum calcidiol level is regarded as the best marker of vitamin D status, where blood levels of <30 ng/mL and <20 ng/L indicate insufficiency and deficiency, respectively [23].Decreased muscle strength is observed at calcidiollevels of <12 ng/mL. Skeletal deformities are rare in adults [1,24].

Osteomalacic myopathy is a pure proximal motor weakness that is confirmed with nerve conduction studies (normal results). Electroneuromyogram may be normal or reveal brief-duration motor unit action potentials of normal amplitude with an increased proportion of polyphasic motor unit potentials [25]. Treatment with adequate doses of calcium and vitamin D has shown to improve symptoms and increase muscle power, improving the activities of daily living and general wellbeing of the patient [26].

The limitations in our study include a short follow-up period and limited sample size. Inj. teriparatide and bisphosphonates were not included as treatment options due to financial constraints of the patients.

CONCLUSION

Patients diagnosed with osteomalacia often suffer from proximal myopathy, leading to early gait changes, and difficulty in climbing stairs and getting up from the ground.Proximal myopathy and gait changes are completely reversible with adequate treatment**.** The majority of young women with osteomalacia elicit a history of craving and eating mud/clay (i.e., pica), which can be addressed with treatment.

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