Bone mineral density and bone scintigraphy in adult Saudi female patients with osteomalacia

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ABSTRACT

Objective: This prospective study was conducted to demonstrate the role of bone mineral density (BMD) and bone scan in the management of adult Saudi female patients with established diagnosis of osteomalacia.

Methods: Bone scan using Tc99m methylene diphosphonate (MDP) and BMD of the lumbar spine and femoral neck using dual x-ray absorptiometry (DXA) were performed at the time of diagnosis 6 months and one year after therapy in 96 Saudi female patients attending the metabolic bone disease clinic at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia, between January 1997 through to June 1999, aged between 20 and 73-years (mean 42 years). Alkaline phosphatase, calcium and inorganic phosphorus were measured for all patients before and after treatment. 25 Hydroxy Vitamin D was only measured with the first BMD measurements.

Results: The bone profile showed typical biochemical abnormalities of osteomalacia. The bone scan showed feature of "superscan" in all patients and "pseudofractures" in 43 patients. Bone mineral density measurements were compared with that of normal Saudi subjects matched for age and sex. The BMD was significantly low at diagnosis and showed significant improvement after therapy. The improvement of bone density in response to therapy was more evident in lumbar spine than in femoral neck bone.

Conclusion: Our results showed that BMD in adult Saudi female patients with osteomalacia was markedly affected probably due to specific constitutional and environmental factors (inadequate exercise, lack of sun exposure and lack of intake of milk and dairy products). In addition, lumbar BMD and serum calcium appeared to be better markers to monitor therapy. Bone scan helped in demonstrating disease activity, the presence of pseudofractures.

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Osteomalacia is an abnormal condition of lamellar bone characterized by loss of calcification of the matrix resulting in softening of bone due to defective mineralization and accumulation of unmineralized osteoid tissue. Vitamin D deficiency (acquired or inherited) is the most frequent cause of osteomalacia. In contrast to osteoporosis (reduction in bone mass), the bone mineral density was reported to be normal or slightly reduced.[1] However, osteomalacia can co-exist with osteoporosis, especially in elderly people with dietary vitamin D deficiency. The aim of this prospective study was to assess the value of bone mineral density (BMD) measurement and bone scan in the management of adult female patients with established diagnosis of osteomalacia. Bone mineral density measurement has been shown to be reliable and sensitive test in assessing bone density and detecting bone mineral loss.[2,3] Furthermore, bone scan using Technetium 99m methylene diphosphonate (Tc-99m MDP) is valuable in the assessment of patients with metabolic bone disease and a sensitive test for detecting related pseudofractures.[4-7]

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Methods. Ninety-six adult Saudi female patients aged between 20-73 years (mean 42 years) with clinical and biochemical diagnosis of osteomalacia attended the metabolic bone disease clinic at King Khalid University Hospital (KKUH), Riyadh, Kingdom of Saudi Arabia (KSA) were included in the study. Verbal consent was obtained from all patients after explaining the protocol. All patients received a standard therapy regime (Calcium 600 mg twice daily, Calcitriol 1 mcg/day and instructions given for regular exercise, regular sun exposure and increase dairy products intake). BMD measurement and bone scan were performed before starting treatment and BMD was repeated after 6 months and one year of therapy.

Bone profile (alkaline phosphatase, calcium and inorganic phosphorus) was assessed at each time the BMD was measured. However, 25 hydroxy vitamin D was only measured with first BMD measurement before institution of therapy protocol. Bone mineral density was measured at the lumbar spine and proximal femoral neck using DXA (GE, Wisconsin). Quality assurance, including Calibration of bone densitometer was carried out routinely every morning. Standard positioning was used for anterior and posterior scans of the lumbar spine and proximal femur. Bone mineral density results are expressed as gm/cm^2. Z-score age matched adjusted to body weight was calculated but T-score values (number of standard deviation below young adult value) was considered for analysis as recommended by World Health Organization which defines the patients with normal BMD, osteopenia or osteoporosis .The results of BMD was compared to BMD of normal Saudi female[10] similar in age (**Table 1**). Bone scans were performed few days before starting therapy. Each patient received 740 MBq (20 mCi) Tc-99m MDP intravenously. A whole body scan was performed 3 hours later. Additional spot views were obtained after completing the whole body scan if necessary.

Scans were assessed qualitatively by 2 experienced nuclear medicine physicians. Focal abnormalities were considered as pseudofractures and usually accompanied with typical appearance of metabolic bone disease (Increased uptake in axial skeleton long bones, periarticular areas, skull, mandible, costochondral junctions, sternum and absent kidneys) what has been described as a "superscan".

Results. The bone profile showed typical biochemical abnormalities of osteomalacia {a mean serum calcium of 1.992 mmol/L (Normal 2.1-2.6), a mean serum phosphorus of 0.907 mmol/L (Normal 0.8-1.4) and a mean alkaline phosphate of 441.98 U/L (normal 43-154)}. The 25 hydroxy vitamin D mean levels were less than 10 ng/ml (normal 18-45). The bone scan showed marked increased uptake in the whole skeleton with faintly or non visualized kidneys and soft tissue (superscan) in all patients (**Figure 1**). Multiple focal areas of increased uptake were seen in 43 patients and were considered as pseudofractures. Bone mineral density measurements were compared with that of normal Saudi subjects matched for age and sex. The BMD measurements (mean + SD in gm/cm^2) at diagnosis, 6 months and one year after treatment were for the lumbar spine 0.781 + 0.156, 0.882 + 0.827 and 1.179 + 0.112 with T-scores -3.01, -2.45 and -0.62. For the femoral neck, it was 0.666 + 0.177, 0.7545 + 0.222 and 0.783 + 0.131 with T-scores -2.44, -1.90 and -1.20.

The bone density of the lumbar spine (**Figure 2a** and femoral neck **(Figure 2b)** was markedly decreased being more profound in lumbar spine than femoral neck. The improvement of bone density in response to therapy was more evident in lumbar spine than in femoral neck both on 6 and 12 months follow up. **Table 1** summarizes the results of the BMD measurements at the time of diagnosis and at follow up. Most patients showed normalization of bone profile markers after one year of therapy.

Discussion. The clinical and radiological spectrum of osteomalacia is highly variable depending on the age, etiology, duration and severity of the demineralization.[11-16] As bone mineral is mostly made of calcium and phosphate, osteomalacia may arise from either primary calcipenia or phosphopenia. Osteomalacia is not infrequently seen in current medical practice, particularly in Saudi females. Therefore, radiologists and clinicians alike should have a high index of suspicion. However, occasionally, in patients with osteomalacia this may present a diagnostic dilemma. Bone scanning and bone mineral density (BMD) has been shown to be of value in the assessment of patients with osteomalacia.[5-8,10]

As of the profound bone mineralization defect, bone density is markedly reduced in patients with osteomalacia.[4,10] Others reported that BMD is usually normal or slightly reduced in patient with osteomalacia.[1] Bone mineral density measurement is easily performed and has shown to be very reliable and sensitive in assessing bone density. Cosman et al[3] has demonstrated a significant correlation between quantitative histological measurements and BMD of the spine and different regions of the hips in patients with various metabolic bone diseases including osteomalacia. Although non-specific for diagnosis, serial BMD measurements are shown to be of value in monitoring the therapeutic response. Repeated measurements will allow estimation of the rate of bone mineralization. Our results showed

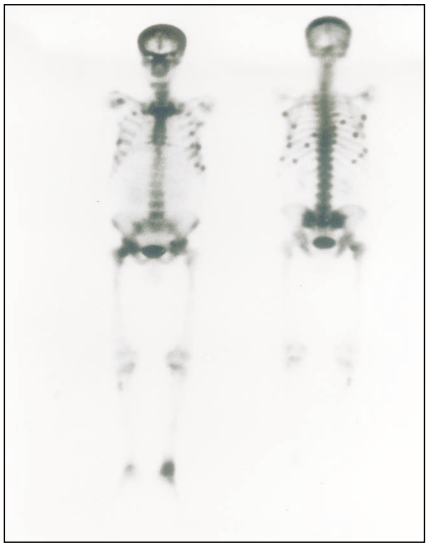

Figure 1 - Tc-99m methylene diphosphonate whole body bone scan showing diffusely increased skeletal uptake with faintly seen kidneys (superscan) and multiple focal areas of increased uptake in multiple ribs and lower end of left tibia representing pseudofractures.

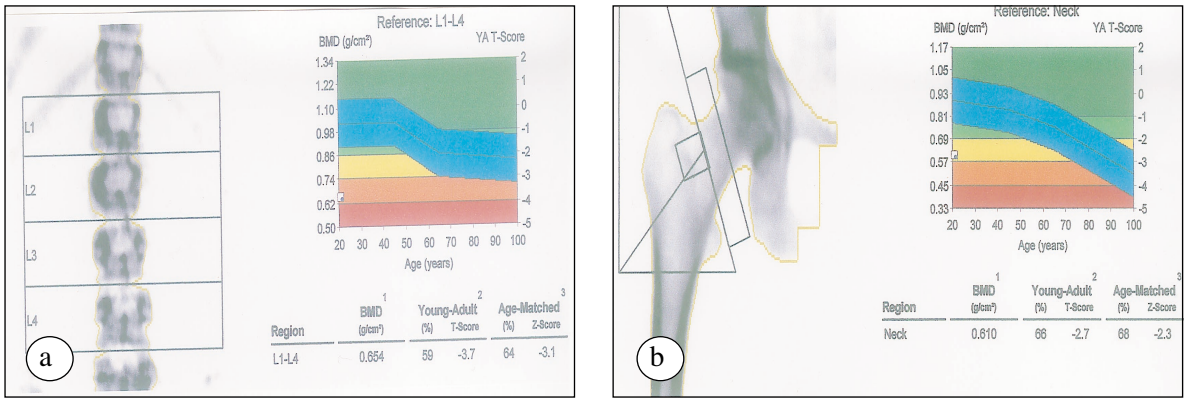

Figure 2 - Bone densitometry dual x-ray absorptiometry scan in a patient with osteomalacia. **(a)** Severe lumbar spine osteopenia with a T-score -3.7. **(b)** Femoral neck osteopenia with T-score -2.7 standard deviation.

	Normal	At dx baseline	At 6 months	At 12 months
Lumbar spine	1.143 ± 0.105 (T=+0.91)	0.781 ± 0.156 (T=-3.01)	0.882 ± 0.287 (T=2.45)	1.179 ± 0.112 (T=-0.62)
Femoral neck	0.959 ± 0.100 (T=+1.12)	0.666 ± 0.177 (T=-2.44)	0.754 ± 0.222 (T=-1.90)	0.783 ± 0.131 (T=-1.20)

dx - dual x-ray absorptiometry

Table 1 - Body mineral density of lumbar spine and femoral neck at time of diagnosis and follow up as well as normal body mineral density of normal Saudi females.

marked reduction in BMD values on baseline study in the lumbar spine and the femoral neck (the lumbar spine being more affected than femoral neck). These findings may be attributed to the profound deficiency in vitamin D in our patients population to the low bone density in healthy Saudi population compared to their counterparts of Western countries[10] and to the possible association of osteoporosis with osteomalacia especially in elderly patients with dietary vitamin deficiency.

Changes in BMD values and biochemical markers at 6 month follow up studies showed partial changes in most patient in both regions and that was attributed to the noncompliance of some patients with the recommended therapy protocol. In addition, the patients were questioned for possible chronic disease (malabsorption, celiac disease for example) and only 3 patients were found to suffer from celiac disease.

Patients were asked to comply better with recommended therapy and repeated studies after 12 months showed normalization of BMD of lumbar spine in most of the patients while the improvement of BMD in femoral neck was adequate but less than in lumbar spine. The bone profile also showed normalization of serum calcium but improvement in other parameters was less evident. The repeat bone scan at 12 months showed reduced global skeletal uptake and decrease in intensity and number of lesions described as pseudofractures on baseline study.

Our results showed that BMD in adult Saudi female patient with osteomalacia was markedly affected probably due to specific constitutional and environmental factors. In addition, lumbar BMD appeared to be better marker to monitor therapy than femoral neck BMD. Bone scans helped in demonstrating disease activity and presence of pseudofractures and its response to therapy.

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