ORIGINAL ARTICLES

BONE MINERAL DENSITY TO IDENTIFY OSTEOPENIA AND OSTEOPOROSIS IN PATIENTS OF CKD ON MAINTENANCE HEMODIALYSIS

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Abstract

Background : *Chronic renal disease changes both quality and quantity of bone through multifactorial influences on bone metabolism, leading to osteopenia, osteoporosis and increased risk of fracture. The objectives of this cross sectional study are to determine the mean bone mineral density (BMD) and to identify osteopenia and osteoporosis in patients of CKD on maintenance hemodialysis.*

Methods: *Twenty three male and 18 female patients with age between 18 and 50 years were enrolled in this study. The BMD of the lumbar vertebral spine (LV) and the neck of femur (FN) were measured in all patients. Data were analyzed using SPSS version 20.0 software and the level of significance was considered as P <0.05.*

Results: *The mean BMD in the LV (L2-L4) was 1.18 ± 0.19 gm/cm2 in male and 1.04 ± 0.13 gm/cm2 in female patients (P =0.011). The mean BMD in the FN was 0.90 ± 0.19 gm/cm2 in male and 0.77 ± 0.15 g/cm2 in female patients (P = 0.022). Based on the World Health Organization criteria, 26.0% of the male and 22.2% of the female patients in our study had normal BMD; 39.2% male and 38.9%female patients had osteopenia, while 34.8% male and 38.9% female patients had osteoporosis .This study showed a marked decrease in mean BMD in the cortical bone (FN) compared with trabecular bone (LV) (P = 0.001) as well as in female patients on maintenance hemodialysis compared with male patients . Significant negative correlation (r= -0.480; p=0.001) was found between duration of hemodialysis and bone mineral density (BMD) in lumbar spine and femoral neck.*

Conclusion: *The measurement of BMD is a good non-invasive screening test for renal bone disease and that a high number of patients with CKD stage 5 on maintenance hemodialysis have markedly decreased BMD.*

Keywords: *CKD**, BMD, Osteopenia, Osteoporosis, Hemodialysis.*

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Introduction

Disorders of bone metabolism, termed as renal osteodystrophy, are very frequent in patients with chronic kidney disease (CKD): they affect almost all patients with at least moderately impaired kidney function .[1] Renal osteodystrophy is one of the most important clinical problems in patients on maintenance hemodialysis (HD), and predominantly affects the cortical bone.[2,3] Bone disease associated with end-stage renal disease (ESRD) is a complex and multifactorial clinical entity. Along with the determinants of the various aspects of renal osteodystrophy such as secondary hyperparathyroidism, osteomalacia or adynamic bone disease, osteoporosis is another prevalent bone disorder in dialysis patients.[4] Bone strength is likely to be more severely affected during the course of chronic kidney disease (CKD) than it might be expected from normal aging process, because of the possible additional effects of renal osteodystrophy .[5,6] In addition, there is an increasing amount of evidence suggesting a potential link between bone and mineral metabolism and cardiovascular disease.[7,8] Studies also suggest that low bone density itself might be an indicator for high risk of cardiovascular events and poor overall outcome in this population.

Osteoporosis is defined as a skeletal disorder character-ized by compromised bone strength predisposing to an increased risk of fracture. The most common definition is that of the World Health Organization (WHO), which defines osteoporosis on the basis of bone mineral density (BMD) measurements applied to the lumbar spine or fem-oral neck. Large epidemiological studies in general population have identified several risk factors for osteoporosis including advancing age, female gender, white race, decreased calcium intake, gastric acid suppression therapy, sedentary lifestyle, premature loss of gonadal function, decreased estrogen secretion, thin body habitus, decreased physical activity, cigarette smoking, alcohol abuse, excess glucocorticoid exposure, and possibly some genetic factors .[9,10,11] The two main determinants of bone strength are bone density, which mainly reflects bone mass and mineralization, and bone quality, which is a composite of architecture, turnover, damage accumulation and repair. Changes in these characteristics are interdependent and will eventually affect the fragility of the bone.

The association of BMD with age, gender and several other factors are well documented for individuals with intact renal function. Chronic renal failure Induces pathologic conditions, such as hyperparathyroidism, metabolic acidosis, and chronic inflammation, which will have a profound effect on bone health. The majority of patients with CKD are deficient in vitamin D, most women on dialysis are amenorrheic, irrespective of their age, patients are exposed to several medications, which may have negative effects on bone. In addition, protein-energy wasting was also correlated with BMD.[12,13] The time spent on dialysis in both hemodialysis and peritoneal dialysis patients was a strong predictor of bone mineral density in particular at sites with cortical Predominance.[14]Since PTH acts mainly on cortical bone, its increase over time on dialysis could explain this association. In addition, cumulative effect of uremia on bone might also play a role .[15]

Bone biopsy is considered the gold standard for the definitive diagnosis of renal osteo-dystrophy; In clinical practice, bone biopsy is used infrequently because it is an invasive and often expensive procedure and the samples obtained require specialized processing that is not widely available. Intact parathyroid hormone (iPTH) and bone alkaline phosphatase (ALP) are reliable markers of bone turnover. [3] However, the correlation between biochemical markers of bone turnover and bone mineral density (BMD) is not clear .[3] Dual-energy Xray absorptiometry (DEXA) is a preferred method of measuring mean BMD due to its high precision and accuracy, short scan time and low radiation dose.[16] Measurement of BMD is a good non-invasive screening test for renal osteodystrophy, but cannot discriminate between the types of bone disease.[17] BMD measurement helps to assess the presence of osteopenia and osteoporosis and is considered to be the most accurate predictor of risk of bone fracture.[18]

Materials and methods

This cross sectional study was conducted in Department of Nephrology, Dhaka Medical College Hospital, Dhaka from July 2015 to June 2016. CKD stage 5 patients on maintenance hemodialysis in Dhaka Medical College Hospital, Dhaka were taken in the study.Purposive sampling method was followed as per inclusion and exclusion criteria. Male & female patients with age between 18 and 50 years and CKD patients on maintenance hemodialysis for at least 3 months were included in the study. Patients who are previously diagnosed as a case of primary hyperparathyroidism, Patients who were on medical treatment for conditions known to affect bone metabolism (such as hyperthyroidism, history of previous transplant, liver disease, collagen disease or ovarian tumor),Patients who had undergone total abdominal hysterectomy with bilateral salpingo –oophorectomy (as there is an increased risk of osteoporosis because of sudden hormonal loss or changes), Patients with history of fracture of the hip, radius or vertebra (these are the common site of osteoporotic fracture which is associated with low bone mineral density) were excluded as a case. CKD patients taking maintenance hemodialysis in nephrology department of DMCH were invited to participate. Selection of patient was done as per inclusion and exclusion criteria. After proper explanation, an informed written consent from the patients was taken. Meticulous history was taken to include inclusion criteria and to exclude exclusion criteria of each patient. General and systemic examinations were done. A standardized questionnaire was used to collect demographic data, duration and frequency of hemodialysis, clinical presentation, associated medical conditions and findings. Then the patients were assessed with investigations. BMD(Bone Mineral Density) of the lumbar vertebral spine (LV) and left femur neck (FN) area was measured in all patients by using DEXA scanner. The BMD was expressed as gm/cm2 and was calculated as ratio of weight (kg)/height (m2). Height (m) and weight was recorded using a stadiometer and a weight scale, respectively. Statistical analysis were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables, shown with cross tabulation. Student t-test was used for continuous variables. P values <0.05 was considered as statistically significant.

Operational definitions

1. **CKD stage 5:** e GFR < 15 ml/min/1.73 m^2 body surface area is defined as CKD stage 5.

2. **Maintenance hemodialysis:** CKD stage 5 patient on regular dialysis for e"8 hours / week for at least 3 months.

3. **Frequency of hemodialysis:** It means how many times/session a patient getting hemodialysis per week.

4. **Duration of dialysis:** It is the time interval since the beginning of dialysis to the date of interview of the patients (measured in months).

5. **Osteopenia and osteoporosis:** The defining feature of osteoporosis is reduced bone density, which causes a micro-architectural deterioration of bone tissue and leads to an increased risk of fracture. Osteoporosis can occur because of a defect in attaining peak bone mass and/or because of accelerated bone loss. Osteoporosis is diagnosed when the T-score value falls to -2.5 or below, whereas osteopenia is diagnosed when the T-score lies between -1.0 and -2.5. The T-score is a measure of how many standard deviations the patient's BMD value differs from that of a young healthy control.

6. **DEXA:** Dual energy X-ray absorptiometry (DEXA) works on the principle that calcium in bone attenuates passage of X-ray beams in proportion to the amount of mineral present. The DEXA provides an image of the region studied, a BMD measurement (expressed as grams of hydroxyapatite/cm^2) and T-score and Z-score values.

7. **Bone density (or bone mineral density)** :It is a medical term normally referring to the amount of mineral matter per square centimeter of bones. Bone density (or BMD)

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is used in clinical medicine as an indirect indicator of osteoporosis and fracture risk.

T-score: Most commonly, DEXA test results are compared to the ideal or peak bone mineral density of a healthy 30-year-old adult and a T-score is the result. A score of 0 means BMD is equal to the normal for a healthy young adult. Differences between the patients BMD and that of the healthy young adult normal are measured in units called standard deviations (SDs). The more standard deviations below 0, indicated as negative numbers, the lower the BMD and the higher the risk of fracture.

WHO Definition Based on Bone Density Level

Level	Definition
Normal	Bone density is within 1 SD (+1 or "1) of the young adult mean.
Low bone massosteopenia	Bone density is between 1 and 2.5 SD below the young adult mean ("1 to "2.5 SD).
osteoporosis	Bone density is 2.5 SD or more below the young adult mean ("2.5 SD or lower).
Severe (established) osteoporosis	Bone density is more than 2.5 SD below the young adult mean, and there have been one or more osteoporotic fractures.

Results

This was a hospital based cross sectional study conducted on 41 patients with CKD stage 5 on maintenance hemodialysis (HD), in the department of Nephrology of Dhaka Medical College and Hospital, Dhaka. The results are presented by the following tables and graphs .

Table-I

Demographic parameters and clinical characteristics of male and female patients on hemodialysis (n=41)

	Male	Female
Number of patients	23	18
Age (years)	41.8±8.2	38.7±10.7
Weight (kg)	55.9±7.0	51.8±12.3
Height (cm)	154.8±33.8	147.7±36.9
Body mass index (kg/m^2)	21.4±3.1	22.4±4.5

*Values are mean ± SD

Table I shows demographic parameters and clinical characteristics of male and female patients on hemodialysis. Total number of patients were 41. Among them 23 were male and 18 were female .Mean age,weight, height, body mass index of male and female patients are depicted on the table.

Table II

Number and percentage of normal bone, osteopenia and osteoporosis in study population (n=41)

Bone mineral density (BMD)	Male(n=23)		Female(n=18)		Total(n=41)		p value
	N	%	n	%	n	%	
Normal (T score >-1.0)	6	26.0	4	22.2	10	24.4	
Osteopenia (T score -1.0 to -2.5)	9	39.2	7	38.9	16	39.0	0.998[ns]
Osteoporosis (T score <-2.5)	8	34.8	7	38.9	15	36.6	

ns= not significant
p value reached from chi square test

Table shows normal BMD was found in ten (24.4%)patients among them 6(26.0%) patients were male and 4(22.2%) were female. Osteopenia was found in sixteen (39.0%) patients, among them 9(39.2%) patients were male and 7(38.9%) were female. Osteoporosis was found in fifteen (36.6%) patients among them 8(34.8%) patients were male and 7(38.9%) were female. The difference was statically not significant (p=>0.05) between groups.

Table III(a)

Number and percentage of normal bone, osteopenia and osteoporosis in lumbar spine in male and female patients (n=41)

	Total	Normal		Osteopenia		Osteoporosis		P
		n	%	n	%	n	%	value
Male	23	11	47.8	8	34.8	4	17.4	0.203[ns]
Female	18	6	33.3	11	61.1	1	5.6	

ns= not significant

p value reached from chi square test

Table III(b)

Number and percentage of normal bone, osteopenia and osteoporosis in femoral neck in male and female patients (n=41)

	Total	Normal		Osteopenia		Osteoporosis		P value
		n	%	n	%	n	%	
Male	23	7	30.4	11	47.8	5	21.7	0.675[ns]
Female	18	4	22.2	8	44.4	6	33.3	

ns= not significant

p value reached from chi square test

Table III(a) shows in lumbar spine, normal bone mineral density (BMD) was found in 11(47.8%) male patients, osteopenia was found in 8(34.8%) and osteoporosis was found in four(17.4%) patients . In female group normal bone mineral density was found in 6(33.3%) patients, osteopenia was found in 11(61.1%) and osteoporosis in 1(5.6%) patient .The difference was statically not significant (p=>0.05) between groups.

Table III(b) shows in femoral neck,, normal bone mineral density (BMD) was found in 7(30.4%) male patients, osteopenia was found in 11(47.8%) and osteoporosis was found in five(21.7%) patients and in female group normal bone mineral density was found in 4(22.2%) patients, osteopenia was found in 8(44.4%) and osteoporosis in 6(33.3%) patient. The difference was statically not significant (p=>0.05) between groups

Table IV

Comparison of mean ±SD of bone mineral density Lumbar spine (L2-L4) and Femoral neck in male and females patients (n=41).

Mean bone mineral	Lumbar spine (L2-L4)			Femoral neck		P-value
density (gm/cm^2)	n	Mean±	SD	Mean±	SD	
Males	23	1.18	±0.19	0.90	±0.19	0.001[s]
Females	18	1.04	±0.13	0.77	±0.15	0.001[s]
P-value	0.011[s]	0.022[s]				

s=significant

P value reached from unpaired t-test

Table shows in male patients mean bone mineral density was found 1.18 ± 0.19 gm/cm^2 in lumbar spine and 0.90 ± 0.19 gm/cm^2 in femoral neck. In female patients mean bone mineral density was 1.04 ± 0.13 gm/cm^2 and 0.77 ± 0.15 gm/cm^2 in lumbar spine and femoral neck respectively. The mean bone mineral density as statistically significant ($p<0.05$) when compared with male and female group. There was also significant difference ($p<0.05$) in mean bone mineral density was found when compared with lumbar spine and femoral neck in both male and female group.
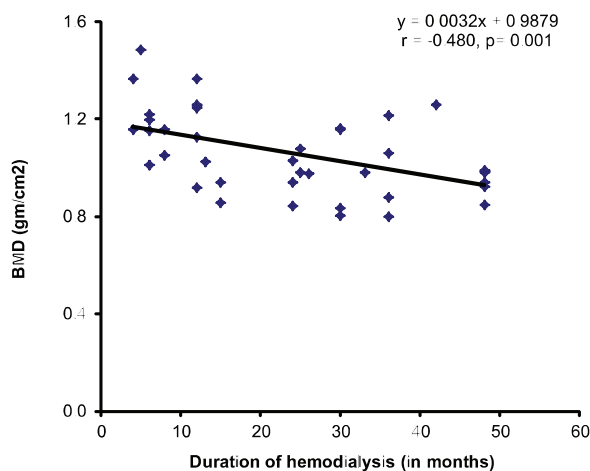
$$y = 0.0032x + 0.9879$$
$$r = -0.480, p = 0.001$$

Fig.-1: *Correlation between duration of hemodialysis with bone mineral density (BMD) in lumbar spine.*

Scatter diagram showing significant negative correlation (r= -0.480; p=0.001) between duration of hemodialysis and bone mineral density (BMD) in lumbar spine.
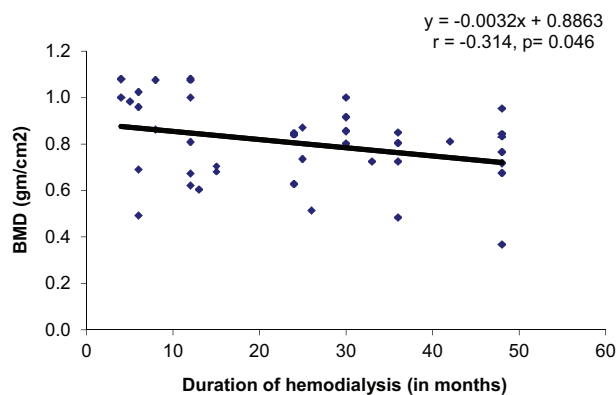
$$y = -0.0032x + 0.8863$$
$$r = -0.314, p = 0.046$$

Fig.-2: *Correlation between duration of hemodialysis with bone mineral density (BMD) in femoral neck .*

Scatter diagram showing significant negative correlation (r= -0.3.14; p=0.046) between Duration of hemodialysis and Bone mineral density (BMD) in femoral neck.

Discussion:

This cross sectional study was carried out with an aim to determine the mean BMD (Bone Mineral Density) among the study population as well as to find the correlation between duration of hemodialysis and bone mineral density. A total of 41 patients on maintenance hemodialysis in Dhaka Medical College Hospital, Dhaka who were on maintenance hemodialysis for at least 3 months between July 2015 to June 2016, were included in this study. Adult male & female patients with age between 18 and 50 years (relatively older patients of either sex were excluded in this study to minimize the effect of age related decrease in BMD) and CKD patients on maintenance hemodialysis who attended the hemodialysis unit of DMCH were enrolled in this study..

In this study it was found that, 10(24.4%) patients had normal bone mineral density (BMD) among them 6(26.0%) patients were male and 4 (22.2%) patients were female. Osteopenia was found in 16 (39.0%) patients among them 9(39.2%) patients were male and 7(38.9%) were female. Osteoporosis was found in 15 (36.6%) patients among them 8(34.8%) patients were male and 7(38.9%) were female. According to the World Health Organization (WHO) categorization based on T-score, 73.8%, 16.7% and 4% of the male patients in [19] study were classified to have normal BMD, osteopenia and osteoporosis, respectively who were on hemodialysis for longer than one year. Among the female patients, 44.9%, 28.2% and 26.9% were classified to have normal BMD, osteopenia and osteoporosis, respectively. In Saudi Arabia by [20] in patients on HD, it was found that about 65% of the patients had low BMD.[21] reported that, in HD patients, 42% had osteoporosis and 52% had osteopenia. [22] have also reported in their study that 72% of the patients had either osteopenia or osteoporosis. [23] have also reported low BMD with T score in the range of osteopenia/osteoporosis in 78% of their patients.

In this study it was observed that in lumbar spine, osteopenia was found in 8(34.8%) male and osteoporosis was found in four(17.4%) male patients and in female group osteopenia was found in 11(61.1%) and osteoporosis in1(5.6%) patient. In femoral neck, osteopenia was found in 11(47.8%) and osteoporosis was found in five(21.7%) male patients and in female group osteopenia was found in 8(44.4%) and osteoporosis in 6(33.3%) patient.

In another study, BMD T scores in the osteopenia / osteoporosis range were observed at the lumbar spine (LS) in 58 patients (82.8%) and at the femoral neck (FN) in 45 patients (64.3%) found by.[23]According to BMD measurements in femoral neck T score, 10.0% of patients wereOsteoporotic, 54.3%, osteopenic, and 35.7%, normal. On the other hand, in LS T score, the results were 47.1% osteoporotic, 35.7%,. osteopenic, and 17.1%, normal. No statistically significant association was found in osteopenia /osteoporosis between sexes according to FN and LS T score.

In this present study, in male patients mean bone mineral density was found 1.18 ± 0.19 gm/cm^2 in lumbar spine and 0.90 ± 0.19 gm/cm^2 in femoral neck. In female patients mean bone mineral density was 1.04 ± 0.13 gm/cm^2 and 0.77 ± 0.15 gm/cm^2 in lumbar spine and femoral neck respectively. The mean bone mineral density was significantly ($p<0.05$) higher in male subjects in lumbar spine and femoral neck. On the other hand mean bone mineral density also significantly ($p<0.05$) higher in lumbar spine with compared to femoral neck in both male and female subjects. [24] had reported lower femoral and lumbar spine BMD in females. [22] also reported that females had significantly lower BMD than males (0.361 g/cm^2 and 0.425 g/cm^2, respectively; $P <0.05$). It has been reported that the BMD is better preserved in male HD patients as compared with female HD patients .[25] Simailrly, Khan et al. (2013) [24]observed that mean BMD was significantly lower in female patients when compared with male patients at both the LV level (1.155 ± 0.026 g/cm2 vs 1.050 ± 0.025 g/cm2, $P = 0.16$) and the FN area (1.010 ± 0.023 g/cm2 vs. 0.784 ± 0.020 g/cm2, $P = 0.00$) . When the mean BMD measured at L2-L4 was compared with BMD measured in the FN the BMD was higher at L2-L4 than in the FN $(P = 0.000)$ .The reason for this difference is not very clear, but may be explained by significant abnormalities associated with hypophysis/gonadal function in uremic women.[26] Another possible contributing factor may be less exposure of studied females to sun light compared with males. In summary, gonadal dysfunction, less exposure to sunlight and less physical activity might all contribute to relatively lower BMD in female patients on HD. [26]observed that in patients on HD, the BMD was higher in the L2–L4 region than in the FN (males: 1.156 ± 0.306 g/cm^2 vs 0.849 ± 0.160 g/cm^2, respectively, $P<0.05$; females: 1.020 ± 0.218 g/cm^2 vs 0.790 ± 0.140 g/cm^2, respectively, $P < 0.05$), which are closely resembled with the present study.

Patients on HD have significantly lower BMD values in cortical bone areas, cortical thickness, moment of inertia and polar moment of inertia than age-matched controls.[24] The relatively high BMD in the lumbar vertebrae is probably due to the effect created by spinal osteophytes and aortic calcification, which may spuriously elevate the lumbar BMD .[27]

In this current study it was observed that there was significant negative correlation (r= -0.480; p=0.001) between duration of hemodialysis and bone mineral density (BMD) in lumbar spine and femoral neck. [14] reported that radial-BMD correlated negatively with the duration on HD in male patients, whereas female patients showed strong and negative correlations between patient age and each of the absolute BMD values.[28] found a significant correlation between BMD and the duration on HD in male patients only.[29] Observed that prolonged HD will cause skeletal complications. In contrast, [30] and [31] reported that BMD did not correlate with the duration on HD, patient age or with any other biochemical parameters.

Conclusion:

This study was undertaken to determine osteopenia and osteoporosis CKD (stage 5) patients on maintenance hemodialysis. The measurement of BMD is a good non-invasive

screening test for renal bone disease and that a high number of patients with CKD stage 5 on maintenance hemodialysis have markedly decreased BMD. Female patients on HD are more vulnerable to bone loss at a higher rate and BMD relatively preserved in the lumbar vertebrae as compared with the femoral neck area. Duration of hemodialysis for a longer period increase the risk to develop low BMD in both lumbar spine and femoral neck.

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