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Original Article

Evaluation of the relationship between osteoporosis and musculoskeletal deformities in leprosy patients through the DXA procedure

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Abstract: The aim of the present study was to analyze the relationship between musculoskeletal deformities and osteoporosis in patients with leprosy. This study included 87 patients with leprosy who were admitted to the Leprosy, Skin and Venereal Diseases Hospital affiliated to the Association of Public Hospitals in Bakirkoy, Istanbul between the years of 2010 and 2014 and 85 healthy controls showing similar demographical characteristics with the leprosy patients. Osteoporosis-related bone density test was performed in both groups using the Dual-Energy X-Ray Absorptiometry (DXA). The mean age of the 172 patients (female: 69; male: 103) included in the study was 62.930±12.135 years. According to the T scores obtained from the DXA measurements, the osteoporotic changes occurred at a higher rate both in femoral and lumbar regions in leprosy patients as compared to non-leprosy patients (38 versus 24 and 25 versus 12, respectively). Additionally, the BMD measurements in femoral and lumbar regions were lower in leprosy patients (0.712±0.156 versus 0.830±0.108 and 0.847±0.153 versus 1.024±0.182, respectively). It was established that whereas leprosy patients tended to develop osteoporosis in femoral region, non-leprosy patients tended to develop osteoporosis in the lumbar region at a younger age. While "osteoporosis" occurred after the age of 40 years in the patients both with and without leprosy, "osteopenia" was observed to appear at younger ages (at the age of 27 years) in the patients that have leprosy. Osteoporotic changes are more common and develop at younger ages in the patients with leprosy. Early treatment that may be initiated after DXA measurement at femur may increase the quality of life of the leprosy patients by decreasing their osteoporosis-related health problems.

Keywords: Leprosy, DXA, osteopenia, osteoporosis

Introduction

Leprosy (Hansen's disease) is a chronic granulomatous latent disease that is caused by mycobacterium leprae and primarily affects skin and nerves [1, 2]. According to WHO, the global registered prevalence of leprosy in 115 countries was 232.857 in 2012 [3]. The Turkish Statistical Institute reported the number of leprosy cases in Turkey in 2004 as 2353, and prevalence rate was 3.21 per 100,000 [4].

Hands, feet, and eyes are mainly affected areas in leprosy patients [5]. However, musculoskeletal manifestations that influence vital activities and mobilizations are the most significant complications of leprosy. These complications are seen in variety of range from arthralgia (local or diffuse), arthritis (swelling within a joint), myalgia, tendinitis, contractures (in upper and lower extremities) to amputation [6]. Bone deformities in leprosy patients may be absorptive, destructive or erosive. Additionally, bony changes are divided into specific, non-specific and osteoporotic. The incidence of non-specific bone changes is higher than specific bone changes [7]. Specific bone changes, such as

nasal bone change, are caused by direct invasion of the bones by Mycobacterium leprae [8, 9]. Non-specific bone changes in leprosy are caused by destruction of nerve supply leading to sensory loss and disuse atrophy. Also, vascular changes, trauma and secondary infection contribute to non-specific changes [7].

Osteoporosis is defined by the International Osteoporosis Foundation as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [10]. If the patient has low bone mass that is not low enough to be diagnosed as osteoporosis, it is sometimes referred to as osteopenia [11].

Despite availability of various diagnostic devices, the Dual-energy X-ray Absorptiometry (DXA) is still one of the most commonly preferred methods for clinical diagnosis of osteoporosis today [12, 13]. Effects of osteoporosis in leprosy patients and the relationship between osteoporosis and leprosy-induced musculoskeletal deformities have not been investigated up to the present. The aim of this study was to evaluate the relationship between osteoporosis and musculoskeletal deformities in the patients with leprosy using the DXA procedure.

Material and methods

Following the approval of the Ethics Committee (Ethical Date/Number: 2014.08.11/2014.10.05), 87 patients with leprosy who were admitted to the Leprosy, Skin and Venereal Diseases Hospital affiliated to the Association of Public Hospitals in Bakirkoy, Istanbul between 2010 and 2014, and 85 healthy controls examined at Bakirkoy Dr. Sadi Konuk Training and Research Hospital with the pre-diagnosis of osteoporosis were enrolled into the study. Bone density and demographical characteristics were analyzed for each patient.

The patients, who had malignancy, hepatic disease, renal disease, trauma and psychiatric disease as well as those whose medical records could not be accessed were excluded from the study.

Bone Mineral Densitometry (BMD) measurements were performed with DXA. The DXA results were evaluated in three groups [≥-0.99: Normal; between "-1.0" and "-2.49": Osteopenia (Low Bone Density) and ≤"-2.5": Osteoporosis]. The BMD measurements of the controls and leprosy patients were analyzed in two categories as femoral region (femur neck total-FNTOTAL) and the average of the total of lumbar L1, L2, L3 and L4 vertebrae (lumbar total-LTOTAL). Lumbar and femoral neck regions were also evaluated in terms of T scores.

Statistical analysis

Statistical analyses were performed using the NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). Mean and Standard Deviation (SD) were calculated for all quantitative variables including age, femur neck T-score, lumbar vertebrae T-score. The Student T-Test was preferred for intergroup comparison of normally distributed variables. The Pearson Chi-Square Test and the Yates Continuity Correction Test were used for comparison of qualitative data. The effects on leprosy were also analyzed with the ROC curve analysis. The results were in 95% confidence interval and $P<0.05$ was considered statistically significant.

Results

This study was carried out with 87 patients with leprosy and 85 healthy controls with pre-diagnosis of osteoporosis. While 69 of the study subjects were female, 103 of them were male (Leprosy patients; male: 69%, female: 31% and controls; male: 50.6%, female: 49.4%). The average of the included 172 patients was 62.930±12.135 years (the average age of the leprosy patients was 64.930±14.508 years, the youngest was 21 years old while the oldest was 84 years old. The average age of the controls was 60.884±8.714 years (the youngest was 37 years old and the oldest was 78 years old) [$t (141.489) = 2.224$, $P = 0.28$]. Mean time since first diagnosis of leprosy was 15.74±6.409 years (minimum 2 years, maximum 30 years).

Although the control subjects presented with the complaints of primarily backache, heel pain, shortening of height, increased kyphosis in back, diffuse arthralgia, bone pain and fractures, there was no osteoporosis-specific symptom or sign in leprosy patients. Nevertheless, these leprosy patients mainly had the com-

Table 1. The patients diagnosed according to the femoral neck and lumbar spine T-score measurements

Patients groups	Patients	BMD regions	Normal T-Score: (-0.99 and over)		Osteopenia T-score: (-1.0 to -2.49)		Osteoporosis T-score: (-2.5 and under)		Total	
			N	%	n	%	n	%	n	%
Leprosy patients	Total	Vertebra	18	20.7	31	35.6	38	43.7	87	100
		Femur	16	18.4	46	52.9	25	28.7	87	100
	Female	Vertebra	4	14.8	11	40.7	12	44.4	27	100
		Femur	8	29.6	13	48.1	6	22.2	27	100
	Male	Vertebra	14	23.3	20	33.3	26	43.3	60	100
		Femur	8	13.3	33	55.0	19	31.7	60	100
Control patients	Total	Vertebra	30	35.3	31	36.5	24	28.2	85	100
		Femur	15	17.6	58	68.2	12	14.1	85	100
	Female	Vertebra	14	33.3	18	42.9	10	23.8	42	100
		Femur	11	26.2	27	64.3	4	9.5	42	100
	Male	Vertebra	16	37.2	13	30.2	14	32.6	43	100
		Femur	4	9.3	31	72.1	8	18.6	43	100
Total patients	Total	Vertebra	48	27.9	62	36.0	62	36.0	172	100
		Femur	31	18.0	104	60.5	37	21.5	172	100
	Female	Vertebra	18	26.1	29	42.0	22	31.9	69	100
		Femur	19	27.5	40	58.0	10	14.5	69	100
	Male	Vertebra	30	37.2	33	32.0	40	38.8	103	100
		Femur	12	11.7	64	62.1	27	26.2	103	100

plaints related to extremity deformities caused by leprosy.

While the age of onset of osteopenia in lumbar region was 27 (between the ages of 27 and 82 years), the age of onset of osteoporosis was 53 (between the ages of 53 and 84 years) in the patients with leprosy. Additionally, the age of onset of osteopenia in femoral region was found 27 (between the ages of 27 and 82 years) whereas the age of onset of osteoporosis in femoral region was 44 (between the ages of 44 and 84 years).

When it came to the patients in control group, the age of onset of osteopenia in lumbar region was found 42 (between the ages of 42 and 75 years) and the age of onset of osteoporosis in lumbar region was 45 (between the ages of 45 and 78 years). Furthermore, the age of onset of osteopenia in femoral region was 42 (between the ages of 42 and 75 years), the age of onset of osteoporosis was determined as 55 years (between the ages of 55 and 78 years).

Table 1 shows the patients that were diagnosed with osteopenia or osteoporosis in both leprosy and control groups according to the T scores obtained from DXA measurements. Considering the DXA results, while rate of osteopenia-related changes was the highest in femoral neck region both in leprosy patients and controls, but the rate of osteoporosis-related changes was the highest in lumbar regions (**Table 1**). Osteopenic changes was observed to be higher in femoral region both in male and female patients (58% and 62.1%), osteoporotic changes occurred at a higher rate in vertebral region in both females and males (31.9% and 38.8%) (**Table 1**).

According to DXA measurements, the difference between the patients in leprosy group and control group with normal and non-normal T scores (osteopenia and osteoporosis) in both femoral neck and lumbar spine regions was not statistically significant ($P>0.05$). However, the difference between the patients in leprosy group and control group with normal T score (including osteopenia) and with non-normal T scores (osteoporosis) in both femoral neck and lumbar spine regions was statistically significant ($P<0.05$) (**Table 2**).

Regarding the BMD measurements, the average of both LBMD and FNBMD measurements

Table 2. According to the femoral neck and lumbar spine T-score measurements in comparison with those of non-osteoporotic changes

BMD regions	Patients groups	T score Normal n%	T score Osteopenia and Osteoporosis n%	p	T score Normal and LBD-Osteopenia n%	T score Osteoporosis n%	P
LUMBAR	Lepra (N = 87)	19 (21.8)	68 (78.2)	0.073	49 (56.3)	38 (43.7)	0.035
	Control (N = 85)	29 (34.1)	56 (65.9)		61 (71.8)	24 (28.2)	
	Total (N = 172)	48 (27.9)	124 (72.1)		110 (64.0)	62 (36.0)	
FEMUR	Lepra (N = 87)	16 (18.4)	71 (81.6)	0.942	62 (71.3)	25 (28.7)	0.020
	Kontrol (N = 85)	16 (18.8)	69 (81.2)		73 (85.9)	12 (14.1)	
	Total (N = 172)	32 (18.6)	140 (81.4)		135 (78.5)	37 (21.5)	

LBD: Low Bone Dansisity.

Table 3. Comparison of average, LBMD, FNBMD, LTOTAL-T Score, FNTOTAL-T Scores between leprosy and control groups

	LBMD Mean ± SD (min.-max.) gr/cm^2	FNBMD Mean ± SD (min.-max.) gr/cm^2	LTOTAL-T Score Mean ± SD (min.-max.)	FNTOTAL T Score Mean ± SD (min.-max.)
Leprosy patients (n = 87)	0.847±0.153 (0.52-1.25)	0.712±0.156 (0.46-1.33)	-2.10±1.29 (-4.80-1.30)	-1.91±1.10 (-4.50-1.10)
Control patients (n = 85)	1.024±0.182 (0.72-1.51)	0.830±0.108 (0.57-1.09)	-1.509±1.465 (-4.30-2.00)	-1.638±0.832 (-3.50-0.30)
Total (N = 172)	0.934±0.190 (0.52-1.51)	0.770±0.147 (0.46-1.33)	-1. 808±1.409 (-4.80-2.00)	-1.778±0.984 (-4.50-1.10)
T	-8.877	-5.719	-2.808	-1.859
Df	170	153.489	170	160.068
p*	0.000	0.000	0.006	0.065
95% CI (upper/lower)	(-0.227/-0.126)	(-0.158/-0.076)	(-1.007/-0.175)	(-0.569/-0.017)

*Student t test (independent samples t test); (min: minimum; max: maximum); (CI: Confidence Interval); (LBMD = LUMBAL BMD, FNBMD = FEMUR NECK BMD, LTOTAL = L1-L4 T SCORE, FNTOTAL = FEMUR NECK T SCORE).

was statistically significantly lower in leprosy patients as compared to healthy controls (P = 0,000). When the T score measurements were analyzed, the average of T scores in lumbar region was statistically significantly lower in the patients with leprosy in comparison with the average of the T scores of the controls (P<0.05). However, no statistically significant difference was found between the groups regarding the average of T scores in the femoral neck region (P>0.05) (**Table 3**).

ROC analysis was applied for LBMD, FNBMD, LTOTAL and FNTOTAL in prediction of leprosy cases. In the ROC analysis, the areas under the curve for LBMD and FNBMD were found to be more valuable for LTOTAL and FNTOTAL. The areas under the ROC curve were as follows: 76.4% with a standard error of 3.6% for LBMD, 78.7% with a standard error of 3.6% for FNBMD, 61.1% with a standard error of 4.3% for LTOTAL, and 59.1% with a standard error of 4.4 for FNTOTAL (**Figure 1**).

Discussion

Leprosy patients have different clinical signs ranging from skin to bone lesions [14]. There is not enough data on the features of osteopenia or osteoporosis in leprosy patients, and moreover, there is no information about the relationship between osteoporosis and musculoskeletal deformities in leprosy patients up to date.

Osteoporosis is the most common bone disease both in men and women [15]. It is characterized by low bone mineral density and abnormal bone structure [16]. Early diagnosis of osteoporosis is important for evaluation of fracture risk and treatment [17]. DXA is an effective clinical tool to evaluate skeletal bone mineral density, especially in lumbar spine and proximal femur [12, 13, 18, 19].

In the study that Makhdoom et al. performed DXA scan on 330 patients, 39.10% of the males were normal, 47.80% were osteopenic and 13% of the males had osteoporosis. They found that 23.50% of all patients were normal, 45.60% had osteopenia and 30.90% had osteoporosis [15].

Unlike Makhdoom et al., we found the osteoporotic changes in the femoral region to be higher in males as compared to females in this study. Additionally, the osteoporotic changes in verte-

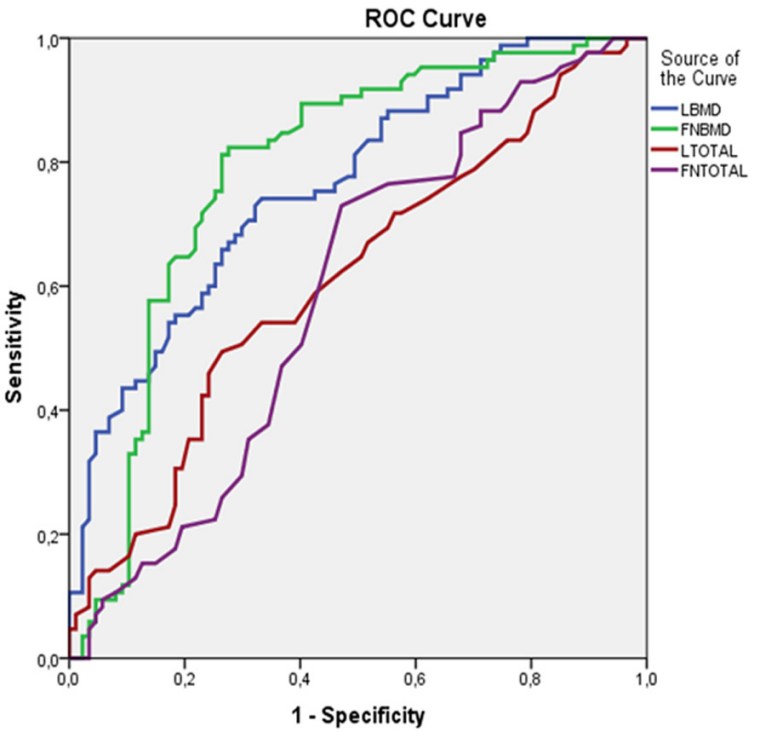

Figure 1. ROC curve in prediction of leprosy patients. LBMD Area = 0.236; Std. Error = 0.036; P = 0.000; 95% CI (Lower-Upper) = 0.166-0.306; FNBMD Area = 0.213; Std. Error = 0.036; P = 0.000; 95% CI (Lower-Upper) = 0.142-0.285; LTOTAL Area = 0.389; Std. Error = 0.043; P = 0.012; 95% CI (Lower-Upper) = 0.305-0.473; FNTOTAL Area = 0.409; Std. Error = 0.044; P = 0.039; 95% CI (Lower-Upper) = 0.323-0495.

bral region were higher in males. Moreover, whereas the highest osteopenic signs were observed in the femoral region, the highest osteoporotic signs were in lumbar region in patients of both genders (females and males) either with or without leprosy.

Osteoporosis frequently occurs in elderly patients and in women aged over 40 years [15]. In the present study, "osteoporosis" developed after the age of 40 years in both leprosy and non-leprosy patients, but "osteopenia" developed at earlier ages (at the age of 27 years) in leprosy patients as compared to non-leprosy patients. It was also identified that osteoporosis developed at earlier ages in femoral region in the patients with leprosy while it developed at earlier ages in lumbar region in the patients without leprosy.

Joint and skeletal pain is the major complaint of osteoporotic patients [15]. Accordingly, the controls in this study presented with diffuse complaints related to bones and joints; however, there was no complaint or symptom in the leprosy patients specific to osteoporosis.

Ishikawa S et al. reported in the study they performed on leprosy patients the cutoff value for osteoporosis in the respective BMD of L2-L4; 0.747 g/cm^2 and neck; 0.581 g/cm^2 in the Japanese women [5]. In a study of Turkish origin, 4063 DEXA measurements were performed on 2763 women aged between 20 and 79 years, and the LBMD mean value was found 0.989±0.191 while the FNBMD mean value was 0.826±0.165 [20].

In this study the LBMD and FNBMD values of leprosy patients were found to be lower than of the patients in control group. Also, these values were found to be lower than the values that Baykara obtained in his study (0.847 and 0.712 versus 1.024 and 0.830). Lumbar and femoral T scores of leprosy patients were found to be lower than of the control patients in this study, (-2.10±1.29 and -1.91±1.10 versus -1.509±1.465 and -1.638±0.832).

In the present study, the average of the LBMD, FNBMD, LTOTAL T scores of the leprosy group was significantly lower than the average of the relative scores of the control group; however, there was no significant difference between groups regarding the average FNTOTAL T score. The average of the LBMD and FNBMD measurements were statistically significantly lower in the leprosy group as compared to the control group. Whereas the average of the LTOTAL T scores of the leprosy patients was statistically significantly lower than the control group, the average of the FNECK T scores did not show a statistically significant difference between the groups. When the T scores obtained from the DXA measurements were considered, the osteoporotic changes developing both in lumbar and femoral regions were more common in

leprosy patients as compared to non-leprosy patients. Additionally, the BMD measurements performed both at femur (FNBMD) and lumbar region (LBMD) were found to be lower in the patients with leprosy.

The present study indicated that osteoporotic changes developed earlier and at a higher amount in leprosy patients in comparison with the non-leprosy patients. Osteoporotic events appearing in leprosy patients, who already suffer from several health problems due to presence of bone deformities, may further contribute to worsening of quality of life of such patients. DXA scan to be performed on femoral region rather than lumbar region may help earlier detection of osteopenic changes as well as osteoporotic signs. Early diagnosis and appropriate therapy have the potential to increase the quality of life by decreasing the risk for osteoporosis-related fractures.

Conclusions

Osteoporotic changes are seen at an earlier age and at a higher amount in leprosy patients. Early treatment that may be initiated after DXA measurement at femur may increase the quality of life of the leprosy patients by decreasing their osteoporosis-related health problems.

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Disclosure of conflict of interest

None.

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