

Frequency of low bone mineral density in spondyloarthropathy presenting at a tertiary care hospital

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Abstract

Objective: To determine the frequency and risk factors of low bone mineral density in patients with spondyloarthropathies.

Methods: The cross-sectional study was conducted at the Rheumatology Department of a tertiary care hospital in Karachi between June and November 2014, and comprised spondyloarthritis patients whose bone mineral density of lumbar spine and hips was measured using dual energy X-ray absorptiometry scan. Variables like disease duration, diagnosis, human leukocyte antigen subtype B27, erythrocyte sedimentation rate, C-reactive protein, Bath ankylosing spondylitis disease activity Index, Bath ankylosing spondylitis functional index, Bath ankylosing spondylitis metrology index were measured along with outcomes, differentiating between osteopenia and/or osteoporosis. SPSS 21 was used for statistical analysis

Results: Of the 25 patients in the study, 16(64%) were males, 19(76%) had predominant axial involvement, and 20(80%) had duration of disease less than 10 years. Low bone mineral density at the spine and hip was found in 18(72%). Osteopenia was present in 9(36%) at hip and 8(32%) in spine, while osteoporosis was seen in 5(20%) at hip and 9(36%) in the spine. No significant association was found between bone mineral density and all the other parameters measured ($p > 0.05$ each).

Conclusion: Majority of spondyloarthritis patients had decreased bone mineral density which could be observed in early stages of the disease.

Keywords: Spondyloarthritis, Osteoporosis, Ankylosing spondylitis. (JPMA 65: 973; 2015)

Introduction

The spondyloarthropathies (SpA) are a diverse group of chronic inflammatory conditions linked by distinctive clinical, radiographical and genetic features. SpAs include ankylosing spondylitis (AS), which is regarded as the disease prototype psoriatic arthritis (PsA); reactive arthritis (ReA); enteropathic, inflammatory bowel disease (IBD)-associated SpA; and undifferentiated SpA. Inflammatory back pain (IBP) and enthesitis are hallmarks of this family of disorders that can affect both axial and peripheral joints. In European countries, the general incidence of SpA is estimated at 0.1-0.5% of the population, with onset frequently in early adulthood.¹ Because of their disabling nature, SpAs are of great economic importance.

There is paucity of data regarding bone mineral density (BMD) in SpA, but relationship between longstanding AS and loss of bone mass (osteopaenia or osteoporosis) in spine and femur is a well-recognised and important complication, with its reported incidence between ~ 20 to 60%.² Osteoporosis may contribute to spinal fractures and progressive spinal deformity, thus increasing the

mortality and morbidity related to AS/SpA. About 50% of spinal bone mass has to be lost before demineralisation becomes apparent on standard radiographs. Therefore, radiography is relatively insensitive in assessing skeletal changes. Dual Energy X-ray Absorption (DXA) is the most reliable technique for measurement of BMD.³

The aetiology of osteoporosis in SpA has not yet been completely clarified. It is thought that the immobilisation due to spinal pain and/or movement restriction is causative in the development of osteoporosis.⁴ Other factors like medications, genetic and hormonal factors may play a role.

To date, little is known about the bone mass in patients with SpA in our population. The current study was planned to determine the extent of low BMD in SpA in patients presenting to a tertiary care rheumatology clinic.

Patients and Methods

The cross-sectional study was conducted at the Rheumatology Department of a tertiary care hospital in Karachi between June and November 2014, and comprised SpA patients whose bone mineral density of lumbar spine and hips was measured using DXA scan. The patients had been diagnosed according to the Amor criteria.¹ The patients were further classified as having

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either AS, according to Modified New York criteria, Psoriatic arthritis, according to Classification of Psoriatic Arthritis (CASPAR) criteria, Reactive arthritis, enteropathic arthritis if they fulfilled Amor criteria and had evidence of inflammatory bowel disease,⁵ and undifferentiated SpA if patients had arthritis that failed to satisfy diagnostic or classification criteria for one of the other forms; axial spondylitis or peripheral spondyloarthritis.¹ Patients who were either pregnant or had used steroids for more than 2 weeks at a dose of prednisolone more than 7.5mg/day were excluded.

Verified medical history, physical examination, laboratory assessment, radiographs of the spine, and a DXA scan were obtained from all the patients. Demographics like gender and age), disease-related variables, such as time since diagnosis, disease duration (time since first symptom), and presence of peripheral arthritis and uveitis were noted. In addition, disease activity scores were obtained using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI).⁶ Laboratory assessment included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and human leukocyte antigen subtype B27 (HLA-B27) and Assessment of Spondylo Arthritis international Society (ASAS)-endorsed disease activity score (ASDAS-CRP and ASDAS-ESR)⁶ were also calculated. BMD was measured at the postero anterior (PA) lumbar spine (L2-L4), and hip by means of DXA machine (Hologic Discovery WI (S/N 86292) USA). BMD was defined according to the World Health Organisation (WHO) criteria⁷ as follows: (1) osteoporosis (T score $\leq$ -2.5 in the spine and/or hip), (2) osteopaenia (T score between -1.0 and -2.5) in the spine and/or hip, without osteoporosis), and (3) normal bone density (T score $\geq$ -1.0 both in spine and hip). For individuals below 50 years, Z-scores were used instead of T-scores.⁸ Low BMD was defined as patients having either osteopaenia and/or osteoporosis.⁹

Data was analysed using SPSS 21. Frequencies and percentages were calculated for qualitative variables like gender and smoking status. Mean $\pm$ standard deviation (SD) were calculated for quantitative variables like age and duration of symptoms.

Results

Initially, 47 patients fulfilling the criteria were registered, but 22(46.8%) were excluded as 2(4.2%) were pregnant, 11(23.4%) had been on steroids and 9(19%) declined DXA scanning. The final sample stood at 25(53.2%) patients. There were 16 (64%) males and 9 (36%) females. 23(92%) were non-smokers and all (100%) denied alcohol intake.

Table-1: Demographic, clinical and laboratory characteristics.

Demographic Variable	Patients number (%)	Mean $\pm$ SD	Range
Men	16 (64)		
Age (years)	25	37.2 $\pm$ 11.5	15 - 55
Smokers	2 (8)		
Diagnosis:			
Ankylosing Spondylitis	19 (76)		
Enteropathic SpA	3 (12)		
Juvenile SpA	1 (4)		
Undifferentiated SpA	3 (12)		
Psoriatic arthritis	0 (0)		
Predominant region involvement:			
Axial	19 (76)		
Peripheral	3 (12)		
Both	3 (12)		
Previous non-vertebral fractures	6 (24)		
Family history of SpA	5 (25)		
Years since onset of symptoms (Years)		5.1 $\pm$ 6.0	0.6 - 20
Time since diagnosis (months)		2.2 $\pm$ 2.6	0 - 10
History of anterior uveitis	4 (16)		
Backache	22 (88)		
Morning stiffness	21 (84)		
Duration of morning stiffness			
Severity of morning stiffness (0-10)		6.4 $\pm$ 3.2	0 - 10
No. of swollen joints		1.1 $\pm$ 1.7	0 - 7
Dactylitis	4 (16)		
Alternating Buttock pain	15 (60)		
Heel pain	13 (52)		
Chest pain	8 (32)		
Pain improvement with NSAIDs	21 (84)		
Patient Global assessment		7.1 $\pm$ 1.8	4 - 10
BASDAI		5.0 $\pm$ 2.1	2 - 9.6
BASFI		4.8 $\pm$ 3.0	0 - 9.9
BASMI		3.4 $\pm$ 2.1	0.56 - 9.1
MASSES		2.5 $\pm$ 3.3	0 - 13
Spinal Pain score(VAS: 0-10)		6.9 $\pm$ 3.3	0 - 10
Peripheral arthritis pain score (VAS: 0-10)		3.7 $\pm$ 3.6	0 - 10
Chest Expansion (cms)		4.1 $\pm$ 1.64	1 - 7
Modified Schober (cms)		3.9 $\pm$ 2.2	1-10
Tragus to wall distance (cms)		15.5 $\pm$ 8.3	6 - 48
Maximum intermalleolar distance (cms)		91 $\pm$ 21.7	34-127
Cervical Rotation (degrees)		68 $\pm$ 25	10- 90
Lateral spinal flexion (cms)		13.6 $\pm$ 7.8	3 - 28
Elevated CRP	19 (76)		
Elevated ESR	9 (36)		
ASDAS CRP		3.2 $\pm$ 0.83	1.5 - 4.8
ASDAS ESR		3.5 $\pm$ 1.05	2.4 - 6.7
Positive HLAB27	8(32)		
Normal Vitamin D levels	16 (64)		
X-ray sacroiliac joint			
normal	2 (8)		
Grade1	2 (8)		
Grade 2	5 (20)		
Grade 3	11 (44)		
Grade 4	3 (12)		
Syndesmophytes	7 (28)		
MRI sacroiliac joint (n=10)			
Acute sacroiliitis	7 (28)		
Chronic sacroiliitis	2 (8)		
Normal	1 (4)		

SpA: Spondyloarthropathies. NSAIDs: Non-steroidal anti-inflammatory drugs. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index. BASFI: Bath Ankylosing Spondylitis Functional Index. BASMI: Bath Ankylosing Spondylitis Metrology Index. MASSES: Maastricht Ankylosing Spondylitis Enthesitis Score. ESR: Erythrocyte sedimentation rate CRP: C-reactive protein. HLAB27: Human leukocyte antigen subtype B27. VAS: Visual analogue score. ASDAS: Ankylosing spondylitis disease activity score. MRI: Magnetic resonance imaging.

Table-2: Bone mineral density (BMD) measured by Dual energy X-Ray absorptiometry (DXA) at different skeletal sites and different age groups.

Measurement site Age group	BMD Mean±SD	T-score Mean±SD	Z-score Mean±SD	Patients with osteoporosis/BMD below expected range for age, Number (%)*	Patients with osteopenia number (%)	Patients with normal BMD Number (%)
L1 vertebrae	0.93±0.16	-0.92±1.52	-0.75±1.41	5 (20)	7 (28)	13 (52)
<=50 years	0.94±0.16	-0.72±1.49	-0.63±1.40	4(18)	5(20)	13(52)
>50 years	0.78±0.09	-2.3±0.95	-1.6±1.48	1 (2)	2 (8)	0(0)
L2 vertebrae	0.97 ± 0.19	-0.99±1.78	-0.83± 1.72	7 (28)	8 (32)	10 (40)
<=50 years	0.99±0.19	-0.77±1.75	-0.69±1.71	5(20)	7 (30)	10 (40)
>50 years	0.81±0.12	-2.60±1.12	-1.83±1.67	2 (8)	1 (2)	0(0)
L3 vertebrae	1.0 ± 0.21	-0.90±1.84	-0.73± 1.72	7 (28)	5 (20)	13 (52)
<=50 years	1.03±0.21	-0.70±1.8	-0.60±1.70	5 (20)	5 (20)	11 (44)
>50 years	0.85±0.17	-2.3±1.43	-1.6±1.91	2 (8)	0 (0)	2 (8)
L4 vertebrae	1.01 ± 0.25	-0.87±2.14	-0.73± 2.15	9 (36)	6 (24)	9 (36)
<=50 years	1.03±0.25	-0.69±2.2	-0.61±2.2	7 (28)	6 (24)	8 (32)
>50 years	0.87±0.15	-2.2±1.30	-1.5±1.7	2 (8)	0 (0)	1 (4)
Total Lumbar spine score	0.97 ± 0.20	-0.95±1.74	-0.84± 1.72	6 (24)	9 (36)	10 (40)
<=50 years	0.99±0.20	-0.75±1.73	-0.71±1.72	4 (16)	8 (32)	10 (40)
>50 years	0.83±0.13	-2.3±1.2	-1.7±1.7	2 (8)	1 (4)	0 (0)
Femur Neck	0.80 ± 0.19	-0.83±1.61	-0.59± 1.56	4 (16)	7 (28)	13 (52)
<=50 years	0.824±0.19	-0.64±1.63	-0.50±1.64	4 (16)	4 (16)	13 (52)
>50 years	0.64±0.04	-2.1±0.28	-1.1±0.57	0 (0)	3 (12)	0 (0)
Total Hip	0.88 ± 0.21	-0.81±1.62	-0.72± 1.65	5 (20)	9 (36)	10 (40)
<=50 years	0.88±0.21	-0.70±1.71	-0.68±1.75	5 (20)	6 (24)	10 (40)
>50 years	0.77±0.03	-1.53±0.30	-0.96±0.68	0 (0)	4 (16)	0 (0)

*Data presented as the sum of patients younger than 50 years, with a Z-score ≤ -2.0 SD and patients 50 years or older with a T-score ≤ -2.5 SD.

AS was diagnosed in 19 (76%) cases, while 3(12%) had enteropathic arthritis, 2(8%) had undifferentiated SpA and 1(4%) had juvenile SpA. Predominant axial involvement was seen in 19(76%) while 3(12%) had only peripheral and 3(12%) had both axial and peripheral involvement. Duration of symptoms was less than 10 years in 20(80%) patients, while 5(20%) had disease duration ≥ 10 years (Table-1).

Overall, 18(72%) patients had low BMD either at spine or hip. Osteopenia was present in 9(36%) cases at hip and 8(32%) in the spine region, while osteoporosis was seen in 5(20%) cases at hip and 9(36%) in the spine region (Table-2).

Of those who had low BMD at spine, 14 (82.4%) were males, 14 (82.4%) were of age below 50 years, 13 (68.4%) cases had a disease duration of less than 10 years, 13 (76.5%) had predominant Axial disease, 12 (63.2%) had AS, 11 (64.7%) had a high BASDAI score, 9 (52.4%) had moderate to severe restriction in modified Schober's test, 13 (86.7%) had a high ASDAS-CRP value, 7 (63.6%) had no syndesmophytes and 8 (88.9%) were tested positive for HLA-B27 allele.

Of those who had a low BMD at hip 10 (71.4%) were males, 11 (78.6%) were of younger age group, 10 (71.4%)

had a disease duration of less than 10 years, 11 (78.6%) had predominant axial disease, 10 (71.4%) had AS, 8 (57.1%) had a high BASDAI score, 8 (57.1%) had moderate to severe restriction in modified Schober's test, 11 (91.7%) had a high ASDAS-CRP value, 5 (55.6%) had no syndesmophytes and 5 (71.4%) tested positive for HLA-B27 allele.

Discussion

BMD determined by DXA is a sensitive and objective method for an early diagnosis and for assessment of disease progression in SpAs.¹⁰ This study showed a reduction in BMD on DXA scanning affecting both the axial and peripheral skeleton in majority of patients with SpA. All patients with low BMD in our study were undiagnosed (osteoporosis/Osteopenia) prior to this study. Our study is the first to report on BMD status in Pakistani SpA population, but few reports are available from other regions on AS patients.^{2,9}

We found that 72% patients had low BMD. This high frequency was not to be expected in a relatively young and predominantly male population. A study⁹ also showed a high prevalence (47%) of low BMD in both femur and lumbar spine in SpA patients with early disease. The reason for higher frequency in our group may be in part due to the reason that our study included

patients irrespective of their disease duration. Also, no other reports on low BMD prevalence in SpA are available, especially from Asia, so ethnicity may have a role to play. Majority of our cases had AS, out of which 68.4% had a low BMD which is comparable to the reported prevalence of osteoporosis in AS which has varied from 19% to 62%.²

Our results also revealed almost equal frequency of low BMD at spine and femur, 56% and 68% respectively. Previous studies have concluded mixed results. One study¹¹ found that osteoporosis in AS is predominantly confined to the axial skeleton, while another¹² found no such difference. The cause of SpA-associated osteoporosis remains controversial. It has been suggested that local or systemic inflammatory cytokine release may be implicated in bone loss. Recent reports indicate that the Receptor activator of Nuclear factor kappa B/Ligand (RANK/RANKL) and Osteoprotegerin (OPG) system and the activated osteoclasts may be a key player in the pathogenesis of diffuse bone loss in SpA.¹³ The theory that osteoporosis is a general process affecting the whole skeleton in SpA was supported by a study of bone biopsies from the iliac crest of AS patients, showing trabecular thinning and low trabecular peripheral bone volume strongly correlated with lumbar spine BMD measured using Quantitative CT (QCT) scans.¹⁴

Risk factors for secondary osteoporosis like steroid use and immobility were already excluded in our study. Only two patients were post-menopausal, one had low BMD and the other had normal BMD.

Due to limited number of patients, this study did not have enough power to assess the association with disease-specific risk factors like the disease activity scores (BASDAI, ESR, CRP, ASDAS-ESR, ASDAS-CRP), functional status (BASFI, BASMI), subtype of SpA and disease duration. However, when an analysis was done, it failed to establish any correlation with low BMD in our study. Other studies^{9,15} have also reported no such associations. In contrast, some studies^{2,16} revealed that factors like high disease activity (BASDAI) and inflammation are of influence on BMD.

The fact that the various studies performed on AS patients within different populations show an almost equally high prevalence of low BMD strengthens the hypothesis that high prevalence of low BMD is already present at the early stages of AS.² This may be true for other SpA as the sub-types share a common immune mediated pathway suggesting that osteoporosis is part of the inherent pathogenesis of SpA likely by cytokine mediated activation of osteoclasts.

When osteoporosis is added to the disease burden of SpA, risk of vertebral and non-vertebral fractures increases, causing high morbidity and reduced quality of life.² The link between decreased BMD and fracture risk has been established in few studies.^{17,18} However, in practice, this under-recognised secondary osteoporosis in patients suffering from SpAs may represent a real public health concern because of an increased risk of fractures and a lower quality of life with important socioeconomic impact. All of these imply the necessity of an early diagnosis and a comprehensive therapy of the primary rheumatic disease as well as of the secondary osteoporosis.

Conclusion

Majority of SpA patients have decreased BMD values at both the lumbar spine and femoral neck, which can be observed in early stages of the disease. We recommend early screening with DXA scan in all patients diagnosed with SpA irrespective of their disease duration and severity as it provides an opportunity to intervene early and with timely treatment may alter the natural history of this condition.

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