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Bone Mineral Density and Trabecular Bone Score in Patients with Non-Radiographic Axial Spondyloarthropathy

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ABSTRACT

Background: spondyloarthropathies (SpA) are a group of chronic inflammatory rheumatic conditions that share multiple clinical features including axial and/or peripheral arthritis, enthesitis, absence of serum rheumatoid factor and presence of common extra articular manifestations.

Objective: the aim of this work is to study bone mineral density and trabecular bone score at patients with non-radiographic axial spondyloarthropathy.

Patients and Methods: this study is a cross sectional study in which 200 patients having chronic back pain selected from those attending the outpatient clinic and inpatient of Al-Azhar University Hospitals, Damietta and were divided into two groups: 1- (Group A, study group): (160) patients had inflammatory low back pain fulfilling Calin criteria for inflammatory low back pain. 2- (Group B, control group): (40) patients had mechanical low back pain not fulfilling criteria of inflammatory back pain.

Results: regarding results of clinical examination, there was significant increase of arthritis, dactylitis, enthesitis and psoriasis in Group A when compared to Group B (43.3%, 16.7%, 30.0%, 20.0% vs 3.3%, 0.0%, 3.3% and 3.3% respectively). In addition, there was significant increase of arthritis plus dactylitis and arthritis plus enthesitis in Group A when compared to Group B (16.7%, 30.0% vs 3.3% and 0.0% respectively).

Conclusion: results of the present study proved that, both bone mineral density and trabecular bone scores showed early changes in patients with non-radiographic axial spondylo-arthropathy. In addition, both correlated with each other and with results of axial magnetic resonance imaging. Thus, they are advocated in diagnosis of nr. SPA.

Keywords: Bone Mineral Density, Trabecular Bone Score, Non-Radiographic Axial Spondyloarthropathy.

INTRODUCTION

The spondyloarthropathy family comprises of Ankylosing Spondylitis (AS), psoriatic arthritis, reactive arthritis, inflammatory bowel disease associated SpA, juvenile SpA and undifferentiated SpA (uSpA) [(1)].

These diseases are strongly associated with the genes of the Major Histocompatibility Complex (MHC), in particular the Human Leucocyte Antigen (HLA) B27 an (HLA) B15 [(2)].

Non-radiographic axial SpA (nraxSpA) comprises those patients who may have clinical and laboratory features of SpA but do not have definite radiographic sacroiliitis and may have early MRI features on the sacroiliac joints [(3)].

Most of the studies also show that patients with axial SpA (axSpA) have a higher prevalence of than that expected in the general population [(4)]. The EULAR SpA imaging task force recommends screening for osteoporosis in SpA [(5)].

The prevalence of vertebral fractures has been shown to be increased in ankylosing spondylitis (AS) from the early stages onwards [(6)].

Osteoporotic fractures lead to increased morbidity and mortality, as demonstrated by the data on disability-adjusted life years (DALYs; i.e., the number of years lost due to ill health, disability, or early death), which are employed to estimate overall disease burden indeed, in Europe, the estimated number of DALYs lost because of osteoporosis is 2.0 million [(7)].

The standard technique for measuring bone mineral density (BMD) is dual energy X-ray absorptiometry (DXA). Measurements are usually taken in the femur and in the lumbar spine in the anterior-posterior projection [(8)].

Trabecular bone score (TBS), a new noninvasive tool for the measurement of bone microarchitecture, could be used complementary to aBMD in the evaluation of bone quality in AS patients [(9)]. It provides a surrogate estimate of bone microarchitecture, obtained using proprietary software to analyze lumbar DXA scans [(10)].

AIM OF THE WORK

The aim of this work is to study bone mineral density and trabecular bone score at patients with non-radiographic axial spondyloarthropathy.

SUBJECTS AND METHODS

Subjects:

This study is a cross sectional study in which 200 patients having chronic back pain selected from those attending the outpatient clinic and inpatient of Al-Azhar University Hospitals, Damietta and were divided into two groups:

1- (Group A): (160) patients having inflammatory low back pain fulfilling Calin criteria for inflammatory low back pain.
2- (Group B): (40) patients having mechanical low back pain not fulfilling criteria of inflammatory back pain.

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Conventional radiology for sacroiliac joint was done to all patients to exclude any radiographic finding.

Ethical considerations:

This study was approved by the Rheumatology and Rehabilitation Department Al-Azhar University and it was explained to all participants before inclusion and a written consent was taken from each one included in the study and approved by medical ethical committee in hospitals.

Inclusion criteria:

1- Patients age range from 18- 45 years old.
2- Patients have clinically features of SpA but do not have definite radiological sacroiliitis with disease duration from 3 Month to 2 years.
3- Patients have chronic Mechanical low back pain with disease duration more than 3 months.

Exclusion criteria:

1- Patient on systemic steroid.
2- Multipara women.
3- Type 2 DM.
4- Any Patients on Bisphosphonates or any drugs affecting bone mineral density.

Patient Assessment:

1. **History taking:** personal history, history of present illness, family history & past history.
2. **General Examination**
3. **Musculoskeletal Examination**

Examination Techniques:

- Inspection – Visual examination, range of motion of joints (active and passive)
- Palpation – Joint muscle examination, use finger tips and thumbs.
- Percussion – Use ulnar surface of fist for spine examination
- Auscultation – Use stethoscope on TMJ and audible tendinous rubs
- Range of motion of all joints and spine.

Patient was seated on examination table facing the examiner.

Sacroiliac joint

- Patrick's or FABER test (flexion abduction external rotation)
- Gillet's test
- Sacroiliac distraction test
- Sacroiliac compression test
- Gaenslen's test
- Spine

4- Pain assessment

- Pain was measured using a 10 cm Visual Analogue Scale (VAS). Pain intensity is classified using a range from 0 to 10, in which 0 = no pain at all and 10 = the worst possible pain. Patients were asked to sign the place on the VAS scale that corresponded to their pain level [(11)].

5. Laboratory:-

- Complete blood count : using automated cell counter.
- ESR : using western green tubes method.
- CRP using latex agglutination test
- Rheumatoid factor using latex agglutination test
- Serum total and ionized Calcium.

6. Radiology:

Plain x-ray of both sacroiliac joint (by VILLA SISTEMI, CANADA 2006):

- Anteroposterior (AP) view and oblique view of the sacroiliac joint is one projection that makes up the sacroiliac series. Both sides are examined for comparison.
- The patient's body should be adjusted to allow the body's long axis to be parallel to the long axis of the x-ray table.
- Patient positioned supine on the imaging table with legs extended and elevate the side of interest approximately 25 to 30 degree.

7- Magnetic Resonance Imaging (MRI) for Sacroiliac joint:

Over the past three decades, MRI has proven capable of detecting preradiographic inflammatory lesions seen in SpA patients and optimism exists regarding the opportunities MRI can offer for early diagnosis of SpA [(5)].

For the sacroiliac joint, the most common sequences were T1-weighted spin-echo in combination with either a gadolinium sequence or a Short Tau Inversion Recovery (STIR) sequence. The slice orientation was either semi coronal or semi axial or a combination of both. In the spine, the MRI protocol consisted of fewer sequences. Three articles reported the use of sagittal T1-weighted spin-echo and STIR, and one used only sagittal STIR [(12)].

8. Assessment of Bone Mineral Density:

- Bone Mineral Density (BMD) measured by dual-energy X-ray absorptiometry (DEXA) on the same day of physical examination and sample withdrawal.
- It was done by Lunar Prodigy Primo DEXA system, version 17, manufactured by GE healthcare (USA).
- BMD was measured at the lumbar spine (L1_L4), the left hip (femoral neck and total proximal femur) and circumstances of the 1/3 distal radius and expressed as the number of grams of bone mineral per square centimeter (g/cm2).

9. Assessment of Trabecular Bone Score (TBS):

TBS provides a surrogate estimate of bone microarchitecture was analyzed using DXA images of the lumbar spine (L1_L4). In older adults, TBS predicts fragility fracture risk independent of BMD and clinical risk factors; it is widely used for assessment of bone microarchitecture and is incorporated into the FRAX tool to improve fracture predictive capabilities [(10)].

The software uses the posterior-anterior images, including the BMD region of interest and edge detection; thus the TBS is calculated over exactly the same region as the lumbar BMD assessment. Patients in the axSpA group were divided into three TBS groups according to the risk of fracture in a recent meta-analysis [13]**:**

- high risk: TBS below 1.23;
- medium risk: TBS 1.23_1.31;
- low risk: TBS above 1.31

Although TBS results correlate with areal bone mineral density (BMD), TBS appears to explain independent variance in fracture risk, suggesting that it measures other components of bone strength [14]**.**

- Lumbar spine DXA images were reanalyzed in an operator-independent automated manner using TBS iNight software version 2.1 (Med-Imaps, Merignac, France).

Statistical analysis of data

The collected data was organized, tabulated and statistically analyzed using statistical package for social science (SPSS) version 22 (IBM®SPSS® Inc, USA).

Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

Independent-samples t-test of significance was used when comparing between two means. Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.

Student T test was used for continuous normally distributed data and Mann-Whitney test was used for none normally distributed data. Comparing of categorical data was done using Chi square or fisher exact test used whenever appropriate. The quantitative data were examined by Kolmogrov Smirnov test for normality of data.

Probability (P-value)

- P-value <0.05 was considered significant. (Sig)
- P-value 0.01 was considered as highly significant. (HS)
- P-value >0.05 was considered non-significant. (NS)

RESULTS

The present study is a cross sectional one in which 200 patients having chronic back pain selected from those attending the outpatient clinic and inpatient of Al-Azhar University Hospitals, Damietta from November 2018 to July 2019 and were divided into two groups:

1- (Group A, Study group): (160) patients had inflammatory low back pain fulfilling Calin criteria for inflammatory low back pain.
2- (Group B, Control group): (40) patients had mechanical low back pain not fulfilling criteria of inflammatory back pain.

Conventional radiology for sacroiliac joint was done to all to exclude any radiographic finding.

Sixty patients in the Group A and ten patients from Group B were excluded as they have radiographic finding as the follow:

- 30 patients from the Group A had bilateral sacroiliitis, 20 of them were grade **III** and 10 were grade II**.**
- 20 patients from the Group A had unilateral sacroiliitis 15 of them were grade III and 5 were grade II**.**
- 20 patients from both groups had degenerative changes of hip and sacroiliac joints and osteitis condensans ilii.

MRI for sacroiliac joint was done for 100 patients of Group A which have normal X-ray for sacroiliac joint as the follow:

- 70 patients had normal MRI for sacroiliac joint and will be excluded.
- 30 patients had sacroiliitis by MRI and fulfill ASAS criteria for diagnosis of axial SpA and will be the study patients.

Table (1): Demographic characteristics of studied populations

Variable		Group A, Study group	Group B, Control group	Total	Test	P value
Age		34.50±4.93; 22- 41	26.20±3.28; 30-45	35.35±4.24; 22-45	1.57	0.12
Sex	Male	11(36.7%)	18(60.0%)	29(48.3%)	3.27	0.07
	Female	19(63.3%)	12(40.0%)	31(51.7%)		
Weight		73.37±4.55; 65-84	80.23±5.29; 70-92	76.80±5.99; 65-92	***5.38***	***<0.001****
Height		1.69±0.04; 1.62- 1.76	1.67±0.04; 1.59- 1.74	1.68±0.04; 1.59- 1.76	1.57	0.12
BMI		25.64±1.19; 23.32- 29.07	28.65±2.02; 25.01- 32.04	27.14±2.24; 23.32- 32.04	***7.02***	***<0.001****

In the present work, age ranged between 22 to 45 years, and there was no significant difference between Group A and Group B (34.50±4.93 vs 36.20±3.28 years, respectively).

In the present study, 60 subjects were included, 29 of them (48.3%) were males and 31 (51.7%) were females and there was no significant difference between both groups (males represented 36.7% and 60.0% of the study and control groups respectively).

In the present study, weight ranged from 65 to 92 kg, and there was significant decrease in study when compared to control group (73.37±4.55 vs 80.23±5.29 kg, respectively). However, subject height ranged from 1.59 to 1.76 m, and there was no significant difference between study and control groups. On the other hand, BMI ranged from 23.32 to 32.04 and there was significant decrease in study when compared to control group (25.64±1.19 vs 28.65±2.02 kg/m2, respectively).

Table (2): Results of clinical examination

		Study Group		Control Group		Total		Test	P value
		n	%	n	%	n	%		
Arthritis		13	43.3%	1	3.3%	14	23.3%	***13.41***	***<0.001****
Dactylitis		5	16.7%	0	0.0%	5	8.3%	***5.45***	***0.020****
Enthesitis		9	30.0%	1	3.3%	10	16.7%	***7.68***	***0.006****
Psoriasis		6	20.0%	1	3.3%	7	11.7%	***4.04***	***0.044****
Uveitis		3	10.0%	0	0.0%	3	5.0%	3.15	0.08(NS)
IBD		3	10.0%	1	3.3%	4	6.7%	1.07	0.30(NS)
Arthritis + dactylitis		5	16.7%	0	0.0%	5	8.3%	***5.45***	***0.020****
Arthritis + enthesitis		9	30.0%	1	3.3%	10	16.7%	***7.68***	***0.006****
Arthritis + psoriasis		2	6.7%	0	0.0%	2	3.3%	2.06	0.15
Arthritis + IBD		1	3.3%	1	3.3%	2	3.3%	0.001	1.0
Cervical Rotation	Preserved	27	90.0%	29	96.7%	56	93.3%	1.07	0.30(NS)
	Reduced	3	10.0%	1	3.3%	4	6.7%		
Tragus to wall	Negative	1	3.3%	0	0.0%	1	1.7%	1.01	0.31(NS)
	Positive	29	96.7%	30	100.0%	59	98.3%		
Lateral lumber flexion	Affected	16	53.3%	5	16.7%	21	35.0%	***8.86***	***0.003****
	Preserved	14	46.7%	25	83.3%	39	65.0%		
Schober's test	Positive	11	36.7%	4	13.3%	15	25.0%	***4.35***	***0.037****
	Negative	19	63.3%	26	86.7%	45	75.0%		
Intermalleolar Test	Positive	5	16.7%	3	10.0%	8	13.3%	0.57	0.44
	Negative	25	83.3%	27	90.0%	52	86.7%		
Chest expansion	Preserved	28	93.3%	29	96.7%	57	95.0%	0.35	0.55
	Affected	2	6.7%	1	3.3%	3	5.0%		

Regarding results of clinical examination, there was significant increase of arthritis, dactylitis, enthesitis and psoriasis in study when compared to control group (43.3%, 16.7%, 30.0%, 20.0% vs 3.3%, 0.0%, 3.3% and 3.3% respectively). In addition, there was significant increase of arthritis plus dactylitis and arthritis plus enthesitis in study when compared to control group (16.7%, 30.0% vs 3.3% and 0.0% respectively).

However, the difference between study and control groups regarding uveitis, IBD, cervical rotation, tragus to wall, intermalleolar test and chest expansion, was statistically non-significant. On the other side, lateral lumbar flexion was highly and significantly affected in study when compared to control group (53.3% vs 16.7% respectively). In addition, positive Schober's test was significantly higher in study when compared to control group (36.7% vs 13.3% respectively).

Table (3): Total and Ionized calcium among studied populations

		Mean	SD	Min.	Max.	t	p
Total calcium	Study	9.51	0.64	8.00	10.40	1.85	0.07
	Control	9.81	0.59	8.30	11.00		
	Total	9.66	0.63	8.00	11.00		
Ionized calcium	Study	4.67	0.32	4.00	5.20	***2.13***	***0.037****
	Control	4.83	0.27	4.10	5.30		
	Total	4.75	0.31	4.00	5.30		

Total calcium ranged from 8.0 to 11.0mg/dl, while ionized calcium ranged from 4.20 to 5.30 mg/dl and there was no significant difference between study and control groups as regard to total calcium, while ionized calcium was significantly decreased in study when compared to control group (4.67±0.2 vs 4.83±0.27 mg/dl respectively).

Table (4): Bone mineral density (DEXA) among studied groups

		Mean	SD	Min.	Max.	t	p
L1-L4 (g/cm2)	Study	0.93	0.01	0.90	0.95	***22.39***	***<0.001****
	Control	0.99	0.01	0.97	1.00		
	Total	0.96	0.03	0.90	1.00		
L2-L4(g/cm2)	Study	0.94	0.01	0.91	0.96	***24.27***	***<0.001****
	Control	1.00	0.00	0.99	1.00		
	Total	0.97	0.03	0.91	1.00		
Femoral neck	Study	0.87	0.01	0.84	0.90	***6.36***	***<0.001****
	Control	0.89	0.02	0.86	0.93		
	Total	0.88	0.02	0.84	0.93		
Total hip	Study	0.91	0.02	0.87	0.99	***3.82***	***<0.001****
	Control	0.93	0.02	0.89	0.96		
	Total	0.92	0.02	0.87	0.99		
L1-L4 (T-score)	Study	-1.58	0.19	-2.00	-1.20	***19.57***	***<0.001****
	Control	-0.81	0.09	-0.90	-0.60		
	Total	-1.20	0.41	-2.00	-0.60		
L2_L4 (T-score)	Study	-1.71	0.20	-2.00	-1.20	***15.38***	***<0.001****
	Control	-0.91	0.21	-1.50	-0.50		
	Total	-1.31	0.45	-2.00	-0.50		
Femoral neck (T-score)	Study	-0.46	0.12	-0.80	-0.30	***11.20***	***<0.001****
	Control	-0.13	0.11	-0.50	0.20		
	Total	-0.29	0.20	-0.80	0.20		
Total hip (T-score)	Study	-0.61	0.25	-1.40	-0.20	***4.29***	***<0.001****
	Control	-0.33	0.26	-0.80	0.20		
	Total	-0.47	0.29	-1.40	0.20		

Bone mineral density was significantly decrease at L1-L4, L2-L4, femoral neck and total hip in study when compared to control group. In addition, T score was significantly decreased in study group when compared to control group at all sites.

Table (5): Correlation between DEXA and Age, ESR, CRP and TBS

	L1-L4 (t-score)	L2-L4 (t-score)	Femoral neck (t-score)	Total hip (t-score)
	r	r	r	r
Age	0.127	0.112	0.145	-0.079
ESR	***-0.739****	***-0.674****	***-0.706****	***0.508****
CRP	***-0.592****	***-0.520****	***-0.638****	***-0.483****
L1-L4 (TBS)	***0.506****	***0.531****	***0.618****	0.196
L2-L4 (TBS)	***0.457****	***0.496****	***0.592****	0.178
Femoral neck (TBS)	***0.451****	***0.511****	***0.601****	0.171
Total hip (TBS)	***0.538****	***0.521****	***0.642****	***0.336****
***. Correlation is significant at the 0.01 level*				

In the present study, there was negative (inverse) significant correlation between L1-L4, L2-L4, femoral neck and total hip t score and each of ESR and CRP. In addition, there was significant proportional correlation between t score of L1-L4, L2-L4 and femoral neck score from one side and each of TBS of L1-L4, L2-L4, femoral neck and total hip from the other side. In addition, there was positive correlation between total hip t score and total hip TBS, while total hip t-score was no significantly correlated with each of TBS of L1-L4, L2-L4 and femoral neck. However, there was no significant correlation between age and each of L1-L4, L2-L4, femoral neck and total hip t scores from the other side.

Table (6): Correlation between MRI findings and each of Age, ESR, CRP and Bone mineral density (t score) and TBS

	Score for BME	Score for Depth	Score for intensity	Total score
	r	r	r	r
Age	-0.03	0.03	-0.11	-0.024
ESR	***0.535***	***0.555***	***-0.262****	***0.539***
CRP	***-0.465***	***-0.518***	***0.345***	***-0.498***
L1-L4 (t-score)	***-0.71***	***-0.73***	***-0.31****	***-0.71***
L2-L4 (t-score)	***-0.55***	***-0.51***	-0.15	***-0.52***
Femoral neck (t-score)	***-0.53***	***-0.56***	***-0.29****	***-0.54***
Total hip (t-score)	***-0.52***	***-0.43***	-0.23	***-0.49***
L1-L4 (TBS)	***-0.35***	***-0.39***	-.158	***-0.36***
L2-L4 (TBS)	***-0.33****	***-0.36***	-.161	***-0.34***
Femoral neck (TBS)	***-0.27****	***-0.30****	-.165	***-0.29****
Total hip (TBS)	***-0.34***	***-0.39***	***-0.26****	***-0.37***

***. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).*

In the present work, there was positive (proportional), significant correlation between scores for BME, depth, intensity and total MRI score with each of ESR and CRP. In addition, there was negative (inverse) correlation between each of bone mineral edema, score for depth and total MRI score from one side and each of all variables of bone mineral density and all variables of TBS. In addition, score of intensity was correlated inversely with each of L1-L4 t-score, femoral neck t-score and total hip TBS. On the other hand, there was no significant correlation between age with each of BME, depth, intensity or total MRI score.

Table (7): Relation between articular manifestations (clinically) and MRI scoring

		Mean	S. D	Min.	Max.	t	p
Bone marrow edema	Articular manifestations	10.85	3.73	4.00	16.00	***3.36***	***0.001****
	Negative	7.91	2.56	4.00	14.00		
	Total	8.60	3.10	4.00	16.00		
Depth	Articular manifestations	4.00	1.92	1.00	8.00	***4.94***	***<0.001****
	Negative	2.00	1.09	1.00	5.00		
	Total	2.46	1.56	1.00	8.00		
Intensity	Articular manifestations	1.14	0.86	0.00	3.00	1.84	0.070(ns)
	Negative	0.72	0.71	0.00	3.00		
	Total	0.82	0.77	0.00	3.00		
Total score	Articular manifestations	16.00	6.11	5.00	27.00	***3.85***	***<0.001****
	Negative	10.63	4.00	5.00	21.00		
	Total	11.88	5.07	5.00	27.00		

In the present work with articular manifestations, there was statistically significant increase of bone marrow edema, depth and total MRI score when compared to cases with no articular manifestations (N.B, by articular manifestations, we mean arthritis and dactylitis).

Table (8): Relation between extra-articular manifestations (clinically) and MRI scoring

		Mean	S. D	Min.	Max.	t	p
Bone marrow edema	Extra-Articular manifestations	9.78	3.14	4.00	14.00	***1.97***	***0.05****
	Negative	8.10	2.99	4.00	16.00		
	Total	8.60	3.11	4.00	16.00		
Depth	Extra-Articular manifestations	3.06	1.59	1.00	6.00	***1.96***	***0.05****
	Negative	2.21	1.51	1.00	8.00		
	Total	2.47	1.57	1.00	8.00		
Intensity	Extra-Articular manifestations	0.78	0.73	0.00	2.00	0.25	0.80
	Negative	0.83	0.79	0.00	3.00		
	Total	0.82	0.77	0.00	3.00		
Total score	Extra-Articular manifestations	13.61	5.03	5.00	21.00	1.75	0.08
	Negative	11.14	4.97	5.00	27.00		
	Total	11.88	5.07	5.00	27.00		

When correlating MRI scores with extra-articular manifestations, patients with extra-articular manifestations had significantly higher bone marrow edema and depth scores when compared to patients with non-extra-articular manifestations.

Table (9): Correlation between VAS and other studied variables

	VAS	
	r	p
Age	0.028	0.834
ESR	0.062	0.636
CRP	-0.058	0.658
Bone marrow edema	0.195	0.136
Depth	***0.336****	***0.009***
Intensity	0.185	0.157
Total score	0.251	0.053
L1-L4 (t-score)	-0.202	0.123
L2_L4(t-score)	-0.144	0.271
Femoral neck (t-score)	-0.130	0.321
Total hip (t-score)	***0.279****	***0.031***
L1-L4 (TBS)	-0.221	0.090
L2-L4 (TBS)	-0.206	0.115
Femoral neck (TBS)	-0.143	0.275
Total-hip (TBS)	-0.149	0.255
***. Correlation is significant at the 0.01 level (2-tailed).*		
**. Correlation is significant at the 0.05 level (2-tailed).*		

Visual analogue scale was significantly and proportionally correlated with depth score on MRI and total hip t-score.

Table (10): Correlation between MRI scoring and duration of the disease

Correlations

	Disease duration	
	r	p
Bone marrow edema score	-.222	.089
Depth score	-.179	.171
Intensity score	***-.341****	***.008***
Total MRI score	-.243	.062

*. Correlation is significant at the 0.01 level (2-tailed).

In the present study, there was negative (inverse), significant correlation between disease duration and MRI intensity score. Otherwise, no significant correlation was found between disease duration and each of bone marrow edema score, depth score or total MRI score.

Table (11): Relation between acute and chronic changes with disease duration

		Mean	SD	Minimum	Maximum	t	p
Subchondral sclerosis	Positive	4.00	1.41	3.00	5.00	***2.29***	***0.026****
	Negative	7.24	1.98	3.00	14.00		
Periarticular fat deposition	Positive	6.17	2.23	3.00	9.00	1.23	0.22
	Negative	7.24	2.01	3.00	14.00		
Bone marrow Edema	Positive	7.18	2.15	3.00	12.00	0.14	0.89
	Negative	7.11	2.00	3.00	14.00		

In the present work, disease duration was significantly shorter in patients with when compared to those without subchondral sclerosis (4.0±1.41 vs 7.24±1.98 months respectively). On the other side, there was no significant difference between patients with periarticular fat sclerosis or bone marrow edema when compared to negative patients.

DISCUSSION

The present study was designed to estimate bone mineral density and trabecular bone score for patients with non-radiographic axial spondyloarthropathy.

Axial spondyloarthritis (SpA) is a chronic inflammatory disease predominantly affecting the sacroiliac joints and spine. The disease comprises 2 subpopulations: those with radiographic axial SpA (also known as ankylosing spondylitis) and those with nonradiographic axial SpA, who have been reported to have a similar disease burden **[15].**

The present study included 200 patients; conventional radiology for sacroiliac joint was done to all to exclude radiographic finding.

Thirty of them had inflammatory low back pain who met the assessment of spondyloarthritis international society criteria for axial SpA as a nraxspa by having sacroilliits by MRI (Group A, Study group); the other thirty persons presented with chronic mechanical low back pain after exclusion of any radiographic finding (Group B, control group).
The study was approved by the Rheumatology and Rehabilitation Department Al-Azhar University and it was explained to all participants before inclusion and a written consent was taken from each one included in the study and approved by medical ethical committee in hospitals.

All participants underwent full history taking, physical examination, laboratory investigations and radiological examination as well as imaging. Bone mineral density was measured for all participants. In addition, trabecular bone score was documented for every patient.

In the present work, age ranged from 22 to 45 years, and there was no significant difference between study and control groups (34.50±4.93 vs 36.20±3.28 years, respectively). In addition, 29 patients (48.3%) were males and 31 (51.7%) were females. These results are incomparable to those reported by **Kang *et al.* [16]** who reported that, the mean age of the patients in both groups was 39 (11) years, and 78% were males and could be attributed to different inclusion criteria. In addition, **Deodhar *et al.* [15]** reported that, the mean age in placebo group was 37.4 ± 10.8 compared to 37.3 ± 10.5 in the study group. These results are in line with the present study. However, most of their patients were females; a finding that corresponds with that of the present work. Furthermore, results of the present work disagree with **Burgos-Varga *et al.* [17]** who reported that, patients with nr-axSpA had a mean age of 34.75 years (SD 10.03); 36.47 % were females.

There were several methodological differences across these studies (e.g., inclusion and exclusion criteria, country), but it is unclear which of these factors would help to explain the differences in results. Further research is necessary.

As regard associated diseases and risk factors, smoking was reported in 33.3% of all studied populations, hypertension in 23.3%, history of fracture in 11.7% and family history for axial spa in 6.7% and there was significant increase of family history of axial spa in study when compared to control group (13.3% vs 0.0% respectively). On the other side, smoking, hypertension and history of fracture were comparable between study and control groups (no significant difference). In their study, **Neumann *et al.* [18]** reported that, 37.6% were former or current smokers, with no significant difference between study and control subjects. Our results go in agreement with this study. In addition, smoking prevalence appears to be increased in patients with axSpA, with reported incidence up to 30 and 40% **[19].**

Regarding the results of clinical examination, there was significant increase of arthritis, dactylitis, enthesitis and psoriasis in study when compared to control group (43.3%, 16.7%, 30.0%, 20.0% vs

3.3%, 0.0%, 3.3% and 3.3% respectively). In addition, there was significant increase of arthritis plus dactylitis and arthritis plus enthesitis in study when compared to control group (16.7%, 30.0% vs 3.3% and 0.0% respectively). However, the difference between study and control groups regarding uveitis, IBD, cervical rotation, tragus to wall, intermalleolar test and chest expansion, was statistically non-significant. On the other side, lateral lumbar flexion was highly and significantly affected in study when compared to control group (53.3% vs 16.7% respectively). In addition, positive Schober's test was significantly higher in study when compared to control group (36.7% vs 13.3% respectively). In agreement with results of the present work, **Neumann *et al.*** [18] reported that, 12.9% of the patients had psoriasis, 7.9% had anterior uveitis, and 6.9% had IBD in their medical history. In addition, peripheral arthritis in general was found to be around 54%. Similar observations were also made for the prevalence of psoriasis, with 10.7%for nr-axSpA [20].

Response to NSAIDs in the present study was good in 75.0% and poor in 25.0% and there was significant difference between study and control groups (the good response was significantly increased in study when compared to control group; 90.0% vs 60.0% respectively).

NSAIDs have been used for many years for patients with axSpA and have been shown to improve disease activity and function [21]. Both traditional and cyclooxygenase (COX) 2 inhibitors are effective but these agents are known to be associated with adverse cardiovascular, renal and gastrointestinal events [22].

Regarding disease duration, it ranged from 3 to 26 months; and there was significant decrease of disease duration in study when compared to control group (14.76±4.20 vs 18.56±6.55 months, respectively). These results are comparable to those reported by **Prabhakar and Singh** [23] who reported that, patients with AS, as compared with nr-axSpA had a longer disease duration 4.5 vs. 2.0, p-value 0.023. In addition, **Sieper *et al.*** [24], showed that patients with AS had a longer disease duration.

Regarding inflammatory markers, ESR ranged from 9 to 50 and CRP ranged from 3 to 18 and there was significant difference between study and control groups. These results are incomparable to those reported by **Sieper *et al.*** [24] who reported that, there was no significant difference between AS and nr-AxSPA regarding ESR and CRP. In addition, **Turina *et al.*** [25] reported that, serum CRP and ESR levels are not elevated in patients with early axSpA versus patients with back pain from different origins, which is disagree with our present work.

Total serum calcium ranged from 8.0 to 11.0mg/dl, while ionized serum calcium ranged from 4.20 to 5.30 mg/dl and there was no significant difference between study and control groups as regard to total calcium level, while ionized calcium was significantly decreased in study when compared to control group (4.67±0.2 vs 4.83±0.27 mg/dl respectively). **Akgol *et al.*** [26] reported that, there was no significant difference between nr-Axial Spa and other causes of low back pain as regard to total serum calcium as in the present work. However, the research could not identify any study determining ionized calcium in nr-Spa patients.

Bone mineral density was significantly decreased at L1-L4, L2-L4, femoral neck and total hip in the study when compared to the control group. In addition, T score was significantly decreased in the study group when compared to the control group at all sites. **Akgol *et al.*** [26] reported that, patients with axial SpA have lower bone mass compared with age- and sex-matched patients with mLBP. Also, nr-axSpA patients with inflammatory lesions on spinal MRI had lower BMD at the spine and hip, indicating inflammation has a negative effect on bone mass. They added, BMD values and T and Z scores at L1-L4 and L2-L4 were lower in nr-axSpA compared with patients with mLBP, whereas BMD, T and Z scores were similar at the proximal femur.

TBS was significantly decreased in the study group when compared to the control group at L1-L4 (1.27±0.044 vs 1.32±0.025), L2-L4 (1.26±0.047 vs 1.31±0.025), femoral neck (1.27±0.049 vs 1.32±0.046) and at total hip (1.29±0.036 vs 1.33±0.017). These results agree with **Kang *et al.*** [16] who reported that, patients with axSpA were seen to have poor bone quality in the lumbar spine compared with matched controls. Their findings indicate that TBS may be a valuable alternative tool for the assessment of bone quality influenced by inflammation in patients with axSpA, regardless of spinal progression. Another study also showed that TBS is not affected by syndesmophytes in patients with axSpA [27].

In the present work, there was statistically significant increase of bone marrow edema, depth and total MRI score in the study group when compared to the control group. However, the difference regarding intensity was statistically non-significant. In their study, **Maksymowych *et al.*** [28] demonstrated that, structural lesions on MRI, particularly erosions, may occur in nraxSpA when radiographs are normal or inconclusive, and even in the absence of SIJ BME on MRI. Additionally, mean 23-DVU spinal scores were higher in patients with SIJ structural lesions than without.

MRI is particularly useful for the early diagnosis of axSpA [29], capable of detecting both bone marrow edema (BME) or osteitis and erosions before conventional radiography (CR) [30]. In addition, inflammation of the SIJs as detected by MRI correlates with histological and clinical finding in axSpA [31]. Thus, in the setting of suspected

axSpA, when the diagnosis cannot be established based on clinical features and CR, assessment of the SIJs by MRI should be conducted [(5)].

In the present study, there was significant proportional correlation between t score of L1-L4, L2-L4 and femoral neck score from one side and each of TBS of L1-L4, L2-L4, femoral neck and total hip from the other side. In addition, there was positive correlation between total hip t score and total hip TBS, while total hip t-score was no significantly correlation with each of TBS of L1-L4, L2-L4 and femoral neck. However, there was negative significant correlation between age, ESR and CRP from one side and each of L1-L4, L2-L4, femoral neck and total hip t scores from the other side. These results are comparable to those reported by **Ayoub *et al.*** [(32)] who reported that, TBS was positively correlated to whole body BMD ($r = 0.35$; $P < 0.01$),L1-L4 BMD ($r = 0.42$; $P < 0.001$), total hip BMD ($r = 0.46$; $P < 0.001$) and femoral neck BMD ($r = 0.48$; $P < 0.001$).

In the present work, there was negative (inverse) correlation between each of bone mineral edema, score for depth and total MRI score from one side and each of all variables of bone mineral density and all variables of TBS. In addition, score of intensity was correlated inversely with each of L1-L4 t-score, femoral neck t-score and total hip TBS. On the other hand, there was significant correlation between ESR and CRP from one side and each of BME, depth, intensity or total MRI score. These results are comparable with those reported by **Kim *et al.*** [(33)] who reported that, the scores for BMD and deep edema correlated with sCTX. The BME score showed a significant correlation with the femoral neck Z score, and total hip BMD, T score, and Z score. The depth scores also correlated with the femoral neck T and Z scores, and with total hip BMD and Z score. The ESR and CRP levels did not correlate with bone turnover markers, but the ESR did correlate with BMD, T score and Z score at all sites. CRP also showed a significant correlation with BMD and the T score and Z score at each site, but not with the femoral neck Z score. In contrast to acute inflammatory lesions, structural lesions on SIJ MRI did not correlate with variables associated with bone density.

Other studies show that bone inflammation, as assessed by MRI, is associated with low BMD in patients with nr-axSpA and IBP. These studies report that the presence of BME on MRI is the main risk factor associated with low BMD [(34)].

Few studies have reported an association between the presence of BME on SIJ MRI and BMD in patients with early inflammatory back pain. These studies included patients with IBP that did not fulfil the ASAS criteria. No study has yet examined only patients that fulfil the ASAS criteria [(34)].

In conclusion, results of the present study proved that, both bone mineral density and trabecular bone scores showed early changes in patients with non-radiographic axial spondyloarthropathy. In addition, both correlated with each other and with results of axial magnetic resonance imaging. Thus, they are advocated in diagnosis of nr.SPA.

CONCLUSION

Bone mineral density and trabecular bone scores showed early changes in patients with non-radiographic axial spondyloarthropathy. In addition, both correlated with each other and with results of axial magnetic resonance imaging. Thus, they are advocated in diagnosis of nr.SPA.

Thirty percent of patients having inflammatory low back pain may be nr-axspa so they should have good evaluation and follow up.

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