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# Trabecular Bone Score and Bone Density in patients with Non-Radiographic Axial Spondyloarthritis

Authors
**Hesham Hamoud[1*], Mohamed Ghit[1], Mohamad Abdelmoez Ali[2], Islam Khaled[2]**
[1]Rheumatology Department, Al-Azhar University, Nasr City, Cairo, Egypt
[2]RheumatologyDepartment, Al-Azhar University, Damietta, Egypt
[*]Corresponding Author
**Prof. Hesham Hamoud**

**Abstract**
**Background:** *Spondyloarthritis represents a group of several inflammatory conditions. Ankylosing spondylitis and nr-axSpA are considered to belong to spondyloarthritis family of diseases.*
**Aim of the work:** *to evaluate bone mineral density (BMD) and trabecular bone scores(TBS) scores in patients suffering from non-radiographic axial spondyloarthritis (nr-axSpA).*
**Materials and Methods:** *A cross-sectional study evaluating 160 patients. Inclusion criteria involved patients 18-45 years of age, having clinical features of spondyloarthritis, and fulfilling Calin's criteria for inflammatory low back pain. Patients were divided into 3 groups; group A (nr-axSpA) patients, group B (radiographic axial spondyloarthritis (r-axSpA)) patients, and group C (mechanical low back pain).*
**Results:** *Female to male ratio was significantly higher in group A compared to group B (63.3% vs. 36.7%) and (23.33% vs. 76.7%) (p< 0.001), respectively. While disease duration was significantly higher in group B in comparison to groups A and C (47.65±7.15, 18.56±6.55, and 14.76±4.20) (p<0.001), respectively. L1-L4 and L2-L4 TBS of groups A and B were significantly lower compared to group C (p<0.001). Additionally, a statistically significant decrease in BMD scores of L1-L4, femoral neck, and total hip bones was detected in group A compared to group C (p< 0.001).*
**Conclusion:** *Patients with nr-axSpA had a lower BMD and TBS compared to r-axSpA group (B) and control group (C), and it predominantly affected more females than males (3:1).*
**Keywords:** *Spondyloarthritis, nr-axSpA, r-axSpA, BMD, TBS, Egypt.*

## Introduction

Spondyloarthritis (SpA) is a term that describes several rheumatic conditions affecting the joints and causing inflammation[(1,2)]. These rheumatic disorders include ankylosing spondylitis (AS), psoriatic arthritis (PsA), and others[(1)].

Axial spondyloarthritis (axSpA) refers to a condition that affects the axial skeleton and causes inflammation in the spine and/or sacroiliac joints (SIJs) leading to back pain and stiffness[(1,2)]. Non-radiographic axial spondyloarthritis (nr-axSpA) was identified as part of the SpA family of diseases[(3)]. Both nr-axSpA and AS are considered as 2 stages of ax-SpA[(2)]. Estimates of disease progression reveal that 5.1% of patients progress from nr-axSpA to AS within 5 years and 19% within 10 years[(3)].

Predictors that influence spinal progression vary considerably among axSpA patients with syndesmophytes being considered as the strongest predictor of radiographic spinal progression[(4)]. As the diseases progresses, inflammation leads to new bone formation as well as bone resorption causing osteoporosis. Therefore, changes in bone

mass reflect severity of the inflammation[4]. The early inflammatory phase of axSpA does not cause structural damage to the SIJs, while at later stages, structural damage is visible on X-ray scans[5].

Currently, there are no specific useful imaging techniques to diagnose and monitor osteoporosis in axSpA. Dual-energy X-ray absorptiometry (DXA) is the most widely implemented tool to measure bone mineral density (BMD)[5]. However, this technique comes with limitations associated with overestimation of results due to the presence of structural lesions. Additionally, information regarding bone micro architecture are not fully captured by BMD[5].

The trabecular bone score (TBS) is a novel non-invasive technique that is used to evaluate bone micro architecture. It facilitates the early detection of osteoporosis through evaluation of lumbar spine DXA image[6].The aim of the present study is to evaluate BMD and TBS scores in nr-axSpA patients.

## Materials and Methods

This cross-sectional study investigated 160 patients suffering from chronic low back pain. Those patients were on the follow-up period with the lower back pain clinic of Al-Azhar University hospital, Damietta, Egypt.

Inclusion criteria for the study involved patients between 18-45 years of age, having clinical features of SpA (dactylitis, psoriasis, uveitis, and arthritis), and fulfilling Calin's criteria for inflammatory low back pain (age at onset ≤40 years, insidious onset, back pain for ≥3 months, associated with morning stiffness, and improvement with exercise); the latter criteria were fulfilled if at least 4 out of 5 parameters were present[7]. Patients were excluded if they were on systemic steroids bisphosphonates, or any medications that could affect bone metabolism for the preceding year. Additionally, subjects were excluded if they had degenerative changes in the sacroiliac joints (in one or both hips), osteitis condensans ilii, or diabetes mellitus.

Sacroiliac joint X-ray was investigated for the patient population. The results revealed that 50 subjects had sacroiliitis. Out of these, 20 were excluded from the investigation due to concomitant degenerative changes in one hip (3 patients) or both hips (5 patients), sacroiliac joints involvement (2 subjects), and osteitis condensans ilii (10 patients). Afterwards, magnetic resonance imaging (MRI) results of the remaining 110 subjects were examined to detect changes in the sacroiliac joint. The results revealed that 30patients suffered from acute and chronic changes.

Subjects were then divided into 3 groups. The first group (group A) represented those patients suffering from sacroiliac joint changes as detected by the MRI (30 subjects). The second group (group B) included those patients with sacroiliitis (30 subjects), and the control group (group C) involved patients with mechanical low back pain (30 subjects).

### Magnetic Resonance Imaging for SIJs

Canadian spondyloarthritis research consortium (SPARCC) MRI score was chosen due its high inter-reader reliability and sensitivity. Moreover, it has been reported to be the most reliable scoring system[8]. The SIJs were scored using the SPARCC method based on six consecutive coronal slices representing the synovial portion of the joint. Score ranges were as follows: Bone marrow edema (BME) (0-48), depth (0-12), and intensity (0-12). The highest possible score is 72[9-11].

The depth of BME is defined as positive when 1 cm or more of continuous edema extends in a horizontal direction away from the articular surface. Each SIJ was evaluated as a whole.

### Bone Mineral Density

BMD was measured using DXA. BMD scans were performed with Lunar Prodigy Primo DXA 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 the distal forearm. It is

expressed as the number of grams of bone mineral per square centimeter (g/cm2) and T score.

**Trabecular Bone Score**

TBS provides a surrogate evaluation of bone micro architecture by analyzing DXA images of the lumbar spine (L1-L4).Patients were divided into three TBS groups according to fracture risk based on a recent meta-analysis[12,13]:

- High risk: TBS below 1.23
- Intermediate risk: TBS below 1.23-1.31
- Low risk: TBS above 1.31

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**

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); while, qualitative data were expressed as frequency and percentage.

Independent samples t-test of significance was used when comparing between two means. Chi-square (X2) 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. Comparison of categorical data was done using Chi-square or Fisher's exact test wherever appropriate. Quantitative data were examined by Kolmogrov Smirnov test for data normality.

Results were considered non-significant if $p > 0.05$, significant if $p < 0.05$, and highly significant if $p = 0.01$.

**Results**

In this cross-sectional study, 160 subjects suffering from chronic inflammatory low back pain fulfilling Calin criteria were investigated. The baseline characteristics of the study population are illustrated in table 1.

With regard to gender distribution, the ratio of female to male patients in group A (nr-axSpA) (63.3% vs. 36.7%) was significantly higher than in group B (radiographic axial SpA (r-axSpA)) (23.33% vs. 76.7%) ($p < 0.001$). Additionally, body mass index (BMI) was found to be higher in group C (control group) when compared to groups A and B ($p<0.001$).

Disease duration was significantly higher in group B in comparison to groups A and C 47.65±7.15, 18.56±6.55, and 14.76±4.20 ($p < 0.001$), respectively (table 1). Moreover, inflammatory markers such as erythrocyte sedimentation rate (ESR) were higher in groups A and B relative to group C 30.50±8.39, 31.39±8.97, and 12.13±1.72 ($p < 0.005$), respectively. Additionally, c-reactive protein (CRP) was higher in groups A and B when compared to group C ($p < 0.001$) (table 1).

The BMD and T scores of the studied subjects are presented in table 2. Results reveal a statistically significant decrease in BMD scores of L1-L4, femoral neck, and total hip bones, as well as T-scores of the same locations in group A in comparison to group C ($p<0.001$). However, group A T-scores of L1-L4 and femoral neck were significantly lower than these in group B ($p<0.001$) and significantly higher in group C than in group B ($p < 0.004$) (table 2).

TBS scores of the 3 groups are illustrated in table 3. L1-L4 and L2-L4 TBS of groups A and B were significantly lower than in group C ($p<0.001$).

Results demonstrated the correlation between MRI findings and age, ESR, CRP, T-score, and TBS. A positive correlation was detected between CRP and ESR on one end and BME, depth score, and total MRI score on the other (figure 1), while a negative correlation was found between L1-L4 T-score and TBS on one side and BME, depth score, and total MRI score on the other (figure 2) and (figure 3).

**Table (1):** Baseline characteristics of the studied Groups

| Variable | | Group A (nr-ax SpA No. 30) | Group B (r-ax SpA No. 30) | Group C (Mechanical LBP No. 30) | Test* F value | P value |
|---|---|---|---|---|---|---|
| **Age (years)** | | 34.50±4.93; 18- 45 | 37.71±3.13 31-44 | 36.20±3.28; 20 -45 | 5.268 | **0.007** |
| **Sex** | Male | 11(36.7%) | 12(38.7%) | 23(76.7%) | ***4.402*** | ***0.001*** |
| | Female | 19(63.3%) | 19(61.3%) | 7(23.33%) | | |
| **Weight (kg)** | | 73.37±4.55; 65-84 | 75.52±4.09 67-82 | 80.23±5.29; 70-92 | ***17.033*** | ***0.001*** |
| **Height (m)** | | 1.69±0.04; 1.62- 1.76 | 1.69±0.04 1.62-1.76 | 1.67±0.04; 1.59- 1.74 | 1.816 | **0.169** |
| **BMI** | | 25.64±1.19; 23.32- 29.07 | 26.36±1.29 22.9-29.8 | 28.65±2.02; 25.01- 32.04 | ***31.119*** | ***0.001*** |
| **Disease duration (months)** | | 18.56±6.55; 3.00- 26.00 | 47.65±7.15 36.60 | 14.76±4.20; 6.00- 24.00 | ***406.127*** | ***0.001*** |
| **ESR (mg/dl)** | | 30.50±8.39; 15.00- 50.00 | 31.39±8.97 12-48 | 12.13±1.72; 9.00- 15.00 | ***4.801*** | ***0.010*** |
| **CRP (mg/dl)** | | 10.83±4.72; 5.00- 18.00 | 8.45±3.34 4-16 | 4.17±0.87; 3.00- 5.00 | ***30.087*** | ***0.001*** |

| ***Post hoc test (LSD)*** | **P value** | | |
|---|---|---|---|
| | **Group A VS Group B** | **Group A VS Group C** | **Group B VS Group C** |
| **Sex** | 0.001 | 0.001 | **0.001** |
| **Weight** | 0.075 | 0.001 | **0.001** |
| **Height** | 0.930 | 0.113 | **0.093** |
| **BMI** | 0.071 | 0.001 | **0.001** |
| **Disease duration** | 0.001 | 0.001 | **0.001** |
| **ESR** | 0.697 | 0.016 | **0.005** |
| **CRP** | **0.007** | **0.001** | **0.001** |

*One way ANOVA.

(nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; No: number; LBP: low back pain; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein).

**Table (2):** Bone mineral density (DXA) and T score of the studied Groups.

| | Group A (nr-ax SpA No. 30) | | | | Group B (r-ax SpA No. 30) | | | | Group C (Mechanical LBPNo. 30) | | | | One way ANOVA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** | **F** | **P value** |
| **L1-L4 (g/cm2)** | 0.93 | 0.01 | 0.90 | 0.95 | 0.86 | 0.09 | 0.64 | 0.95 | 0.81 | 0.15 | 0.60 | 1.00 | 9.584 | <0.001 |
| **L2-L4 (g/cm2)** | 0.94 | 0.01 | 0.91 | 0.96 | 1.00 | 0.00 | 1.00 | 1.00 | 1.00 | 0.00 | 0.99 | 1.00 | 289.971 | <0.001 |
| **Femoral neck ((g/cm2)** | 0.87 | 0.01 | 0.84 | 0.90 | 0.81 | 0.08 | 0.64 | 0.90 | 0.73 | 0.10 | 0.58 | 0.96 | 27.630 | <0.001 |
| **Total hip(g/cm2)** | 0.91 | 0.02 | 0.87 | 0.99 | 0.85 | 0.09 | 0.66 | 0.99 | 0.73 | 0.10 | 0.58 | 0.96 | 41.405 | <0.001 |
| **L1-L4 (T-score)** | -1.58 | 0.19 | -2.00 | -1.20 | -1.22 | 0.54 | -2.00 | 0.80 | -1.18 | 0.43 | -2.00 | -0.60 | 8.288 | 0.001 |
| **Femoral neck (T-score)** | -0.46 | 0.12 | -0.80 | -0.30 | -0.37 | 0.11 | -0.60 | -0.10 | -0.14 | 0.14 | -0.50 | 0.20 | 53.380 | <0.001 |
| **Total hip (T-score)** | -0.61 | 0.25 | -1.40 | -0.20 | -0.51 | 0.27 | -1.40 | -0.10 | -0.33 | 0.26 | -0.80 | 0.20 | 9.244 | <0.001 |

| | **P value** | | |
|---|---|---|---|
| | **Group A VS Group B** | **Group A VS Group C** | **Group B VS Group C** |
| **L1-L4 (g/cm2)** | **0.020** | **0.001** | **0.045** |
| **Femoral neck(g/cm2)** | **0.004** | **0.001** | **0.001** |
| **Total hip(g/cm2)** | **0.006** | **0.001** | **0.001** |
| **L1-L4 (T-score)** | **0.001** | **0.001** | **0.702** |
| **Femoral neck (T-score)** | **0.004** | **0.001** | **0.001** |
| **Total hip (T-score)** | **0.125** | **0.001** | **0.008** |

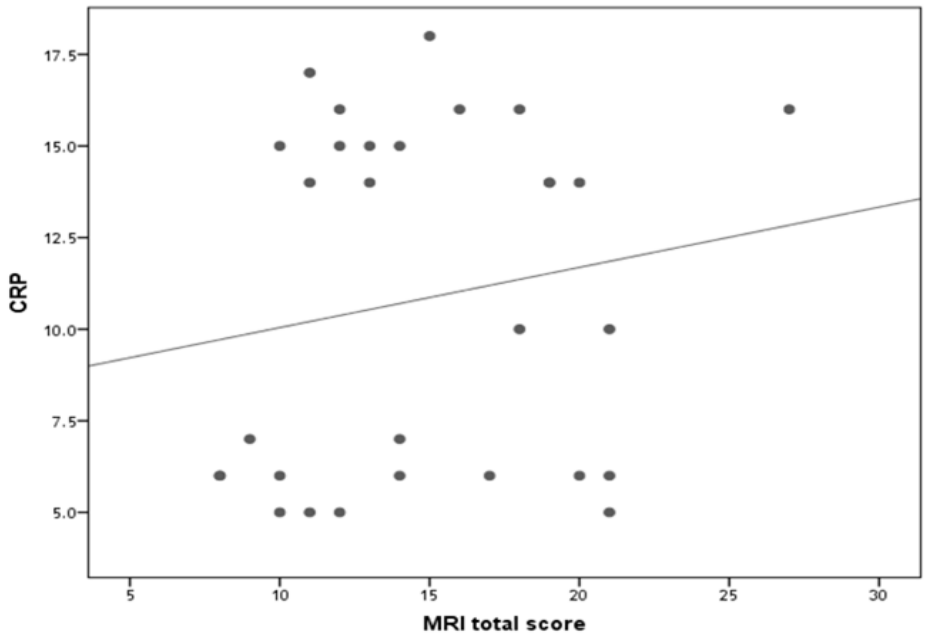
(nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; No: number; LBP: low back pain; SD: standard deviation).

**Table (3):** TBS of the studied Groups

| | Group A (nr-ax SpA No. 30) | | | | Group B (r-ax SpA No. 30) | | | | Group C (Mechanical LBP No. 30) | | | | One way ANOVA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | F | P value |
| **L1-L4** | 1.28 | 0.04 | 1.21 | 1.36 | 1.29 | 0.04 | 1.22 | 1.37 | 1.33 | 0.02 | 1.29 | 1.36 | 14.093 | 0.001 |
| **L2-L4** | 1.27 | 0.05 | 1.19 | 1.35 | 1.28 | 0.05 | 1.21 | 1.36 | 1.31 | 0.02 | 1.28 | 1.35 | 12.959 | 0.001 |
| | **Group A VS Group B** | | | | **Group A VS Group C** | | | | **Group B VS Group C** | | | | | |
| **L1-L4** | **0.220** | | | | **0.001** | | | | **0.001** | | | | | |
| **L2-L4** | **0.144** | | | | **0.001** | | | | **0.001** | | | | | |

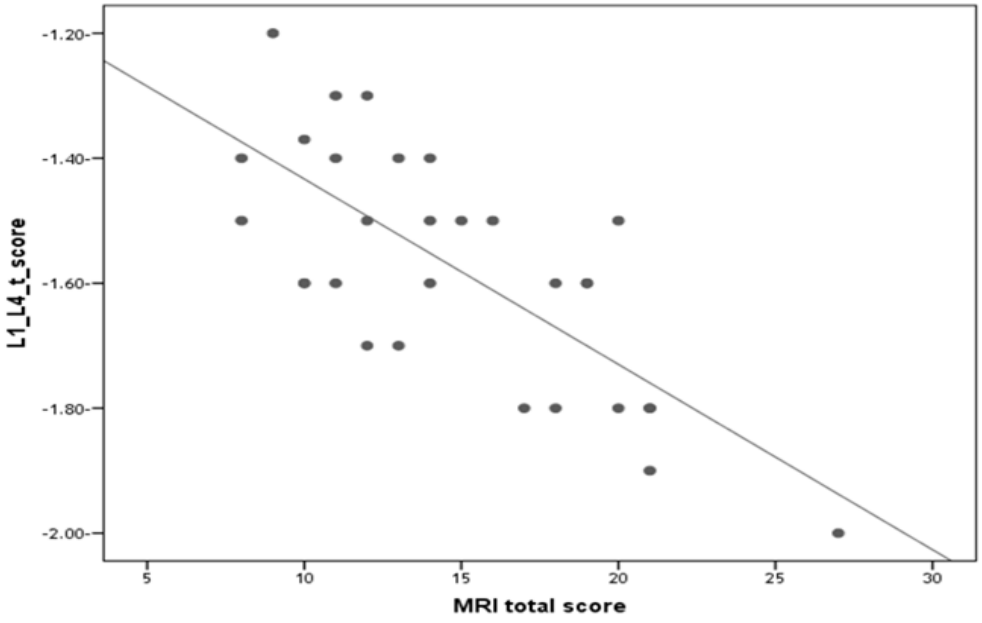
(nr-axSpA: non-radiographic axial spondyloarthritis; r-axSpA: radiographic axial spondyloarthritis; No: number; LBP: low back pain; SD: standard deviation; TBS: trabecular bone score).

**Figure (1):** Positive correlation between CRP and MRI total score.



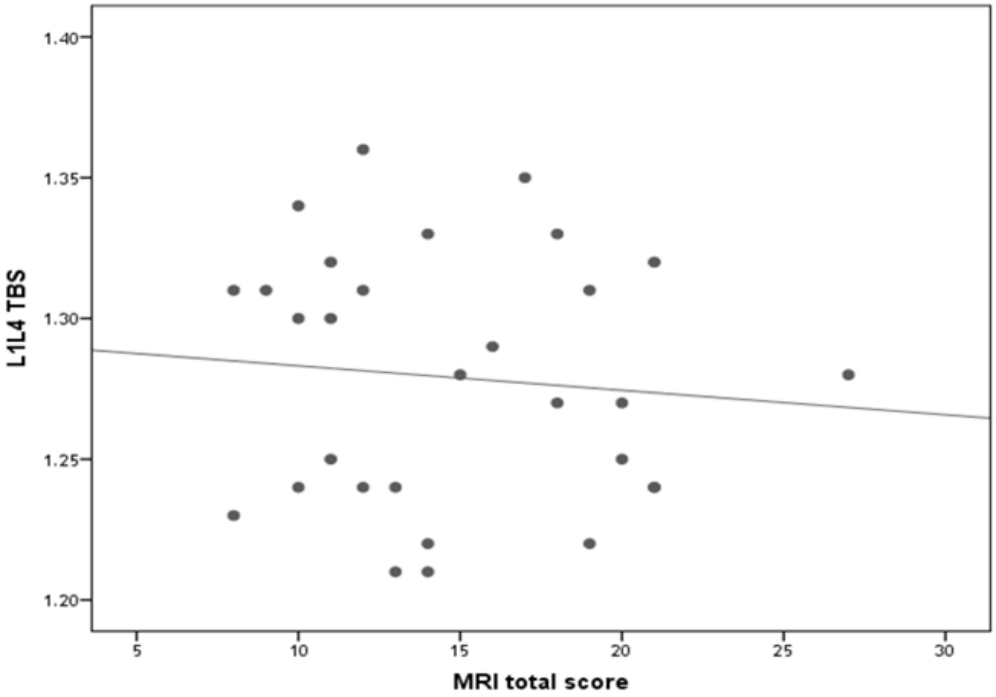

(CRP: c-reactive protein; MRI: magnetic resonance imaging).

**Figure (2):** Negative correlation between L1L4 t score and MRI total score.




(MRI: magnetic resonance imaging).

**Figure (3):** Negative correlation between L1L4 TBS and MRI total score




(MRI: magnetic resonance imaging).

**Discussion**

The aim of the current study is to assess BMD and TBS scores in nr-axSpA patients. With regard to baseline characteristics, age was not a factor contributing to differences between the study groups, since it was not significantly different between the 3 studied populations. The results obtained in our study are aligned with the findings of another study[13]. However, findings from our study reveal a higher female-to-male ratio in group A (nr-axSpA) compared to group B (r-axSpA), which is aligned with what has been reported in another study by Kiltz et al[14]. A recent review by Rusman et al attributed the higher ax-SpA burden in females to delay in diagnosis, higher disease activity, and significantly less responsiveness to treatment with tumor necrosis factor inhibitors (TNFis)[15].

Regarding disease duration, our findings indicate a longer disease duration in r-axSpA patients compared with nr-axSpA, which is in agreement with the results obtained elsewhere[16]. Moreover, the German spondyloarthritis inception cohort (GESPIC) of patients suffering from AS found that subjects with longer symptom duration had significantly worse functional scores that was maintained for over 2 years of follow-up[1].

CRP and ESR are acute-phase reactants. It has been highlighted that the former may act as a predictor of radiographic progression[17]. Additionally, higher level of CRP at baseline was found to be associated with improved treatment adherence and superior clinical outcomes[17]. Our results indicate that CRP and ESR levels were significantly higher in groups A and B relative to group C, with no significant differences between the first 2 groups. Additionally, one study demonstrated a higher level of CRP in r-axSpA compared to nr-axSpA. Moreover, CRP level was found to be correlated with MRI inflammation[18].

Results from our study reveal that patients in groups A and B had significantly lower BMI compared with group C. A study by Micheroli et al concluded that BMI affects response to TNF is in axSpA patients, in that study, results demonstrated that obesity was associated with significantly lower response to the aforementioned class of therapeutic agents[19]. Moreover, a French study conducted by Malochet-Guinamand et al found that axSpA patients with lower BMI had lower BMD[20].

A study by Akgol et al concluded that BMD at the lumbar spine was significantly lower in nr-axSpA compared to patients with mechanical low back pain[21]. The results of our study highlighted that patients in the nr-axSpA (group A) had significantly lower BMD and T-scores at L1-L4, femoral neck, and total hip compared to patients in group C (mechanical low back pain group).The inflammatory process was named to be the reason for the lower BMD in nr-SpA patients[21].

TBS is an important imaging technology in assessing bone impairment in axSpA patients. It is a non-invasive technique that provides a reliable method in identifying bone quality deterioration[22]. The results from our study demonstrated that TBS of L1-L4 and L2-L2 was lower in groups A and B compared to group C. AxSpA patients with lower TBS have been found to be more liable to have vertebral fractures, which makes the tool useful in predicting the future risk of such events[5].

In accordance with what has been described in recent literature, our study revealed the presence of a positive association between TBS and BMD scores of L1-L4, total hip, and femoral neck[23].

There are some limitations in our study. Firstly, the cross-sectional design of our study did not allow us investigate whether TBS can predict the incidence of vertebral fractures. Secondly, we did not collect information regarding the levels of vitamin D.

## Conclusion

We conclude that patients with nr-axSpA have lower BMD and TBS scores compared to patients with r-axSpA and mechanical low back pain. This puts them at a higher risk of fracture. Additionally, good clinical and radiological evaluations along with regular follow-up are warranted among patients with chronic inflammatory back pain to prevent disease progression that could lead to severe irreversible structural changes.

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