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Assessment of clinical profile of patients with non-radiographic axial spondyloarthropathy in a tertiary health-care center

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ABSTRACT

Background: Axial spondyloarthritis (axSpA) is an inflammatory and immune-mediated condition comprising clinically differentiated ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA). Clinically, as the name suggests, non-radiographic axial spondyloarthritis (nr-axSpA) has an absence of definitive plain X-ray evidence of structural damage to the sacroiliac joint. **Aims and Objectives:** The aim of the study was to assess and evaluate the clinical profile of patients with non-radiographic axial spondyloarthropathy. **Materials and Methods:** This study was conducted in the department of Medicine over 18 months in a tertiary health care institution, being a prospective and observational type done with 43 subjects. **Results:** We observed a major improvement as per ASDAS criteria present among 53.49% of subjects, followed by clinically significant improvement among 27.91% of subjects. About 18.60% of subjects did not show any improvement. About 9.3% of subjects showed radiological progression. Out of eight cases that did not show improvement, all presented with low back pain and morning stiffness. About 62.5% had peripheral arthritis. About 87.5% had Schober's test positive, FABER test (62.50%) and sacroiliac joint tenderness found among 7.5% of subjects. A total of 4 (9.3%) patients showed radiological progression. All of them have low back ache and morning stiffness, and three of them having peripheral arthritis at presentation. We found that patients who showed progression had higher mean ESR and CRP (45 and 36.5, respectively) values and a very high disease activity as per ASDAS and BASDAI criteria. **Conclusion:** There is a great scope and need for research to differentiate the magnetic resonance imaging (MRI) changes in the normal population against the ones patients with spinal diseases to be able to use MRI with precision in patients with non-radiographic axial spondyloarthropathy (nr-axSpA). As assessed, currently physiotherapy and NSAIDS are first line therapy for patients suffering from non-radiographic axial spondyloarthropathy.

Key words: Ankylosing spondylitis; X-ray; Sacroiliac joint; Non-radiographic axial spondyloarthropathy

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INTRODUCTION

Axial spondyloarthritis (axSpA) is an inflammatory and immune-mediated condition comprising of clinically differentiated ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA).[1] Clinically, as the name suggests, non-radiographic axial spondyloarthritis lacks definitive plain X-ray evidence of structural damage to the sacroiliac joint.[2] Due to the subjectivity of radiological interpretation of involvement of sacroiliac joint, differentiating AS and nr-axSpA is not very accurate. Patients with nr- axSpA usually present with back pain due to involvement of the SI joint. They can also present with complaints such as dactylitis, peripheral arthritis, enthesitis, anterior uveitis, psoriasis, Crohn's disease, or ulcerative colitis.[3] Over period, there has been an increased understanding of nr-axSpA but still, there remains

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difficulty in differentiating axSpA from common mechanical backache, also accounting lack of accurate diagnostic criteria leading to an increased burden on patients and health-care systems.[4,5] This factor adds further in nr-axSpA wherein the disease burden at personal and societal levels is similar to that in RA and SpA conditions with a rise in the cost of treatment due to lesser comparative productivity in the assessment and management aspect of the disease.[6] There is a lot of scope for improvement in understanding and management of nr-axSpa to prevent its conversion to AS, lessen the risk of complications like a fusion of the spine or fractures, prevent deterioration of range of motion, and therefore diminishing the financial impact of the same on patients, health care institutions and thus the society.[7]

This study was undertaken to assess the patients with newly diagnosed nr-axSpA clinically and to compare the same with that of patients with radiographic AS. We also studied the laboratory profile of patients suffering from nr-axSpA and their outcome over 3 months.

Aims and objectives

The aim of the study was to assess and evaluate the clinical profile of patients with non-radiographic axial spondyloarthropathy.

MATERIALS AND METHODS

This was a prospective type of observational study carried out at the medicine department of a tertiary health-care center conducted over 18 months. We proceeded with the study only after obtaining clearance from the Ethics Committee of the institution and permission from the appropriate authority. The sample size was calculated to be 43 patients. Newly diagnosed treatment naïve patients with non-radiographic spondyloarthropathy in the age group between 18 and 45 years, willing to give their consent were a part of the study. Pregnant and lactating females and those allergic to drugs of the sulfa group were not included.

Written informed consent was taken. Detailed history including low back pain (LBP), early morning stiffness, and peripheral arthritis, uveitis, enthesitis, dactylitis, and constitutional symptoms was obtained. Clinical examination including general examination and special tests such as Schober's test, FABER's test, Wall occiput distance, Sacroiliac tenderness, and chest expansion obtained. Special scores ASDAS and BASDAI were calculated. Relevant blood investigations and treatment started as per the physician's notes. The patient was asked to follow-up after 3 months, when a repeat complete physical and laboratory investigation were done (Figure 1). Data were analyzed using the Mcnemar test (for qualitative data assessment) and using the paired t-test (for quantitative data assessment).

RESULTS

Most of the subjects belonged to the age group of 26–35 years, followed by 18–25 years and 36–45 tears. The mean age group of the study subjects was 30.34±7.47 years; the median age is 30 years (Table 1).

Most of the subjects in the study were male patients (Table 2).

We observed that low backache was the most typical complaint among all subjects, followed by morning stiffness, peripheral arthritis, and fever and uveitis, fatigue, and enteritis. On assessing the patients on follow-up after 3 months, LBP was still noted among one-third of subjects, peripheral neuritis among one-fifth of subjects

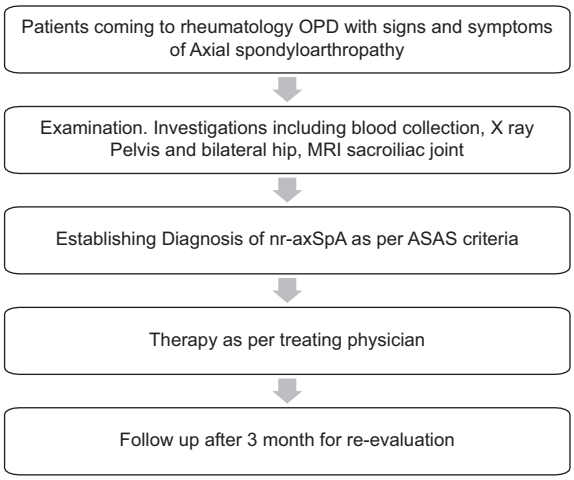

Figure 1: The step-by-step workup protocol of the study participants

Table 1: Age-wise distribution among the study subjects

Age distribution	Number of subjects	Percentage
18–25 years	12	27.91
26–35 years	20	46.51
36–45 years	11	25.58
Total	43	100.00
Mean age	30.34±7.47 years	
Median age	30 years	

Table 2: Gender-wise distribution among the study subjects

Gender-wise distribution	Number of subjects	Percentage
Male	38	88.37
Female	5	11.63
Total	43	100.00
M: F ratio	7.6:1	

while morning stiffness, enthesitis, and dactylitis was noted in fewer subjects. It was observed that the majority of the complaints were reduced significantly after 3 months (Table 3).

We also assessed the examination findings among the study subjects. This included assessment of chest expansion (>5cm), Schober's test, Faber test, sacroiliac joint tenderness, and wall occiput test. The findings improved significantly after the follow-up of 3 months (Table 4).

We also assessed X-ray pelvis with bilateral hip (NY Grading). We observed Grade 0 findings among all subjects on presentation, whereas after 3 months, there was an increase in grade among 3 subjects out of 43 to Grade 1 (Table 5).

On assessment of general examination parameter among subjects, we observed a mean pulse rate of 82.84, mean body temperature of 37.98, and mean RR of 18.12 on admission. After follow-up, the mean pulse was 95.91, mean body temperature of 37.93, and mean respiratory rate of 15.79. We also studied the hematological parameters among the study subjects. Mean levels on admission and after follow-up after 3 months are mentioned in Table 6.

The mean ASDAS score was 4.22±2.20 among the study subjects. On admission, the majority of the subjects had ASDAS score of more than 3.5. In follow-up examination, the majority of the subjects had ASDAS scores between 1.3 and 2.1 as shown in Table 7.

The mean BASDAI score was 4.57±2.31 among the study subjects. On admission, the majority of the subjects had BASDAI score of more than 4. In follow-up examination, the majority of the subjects had BASDAI score <4. The findings were statistically significant. (The Chi-square statistic is 36.4921. p<0.00001, Significant at p<0.05) - Table 8.

We also assessed the severity according to the ASDAS score. We observed that the most of the subjects had very high disease severity (81.40%), followed by high disease severity among 18.60% of study subjects.

It was observed that most subjects with greater ASDAS score had greater BASDAI scores. The difference was found to be statistically significant as shown in Table 9 (The Chi-square statistic is 8.412. p=0.003728 (Significant at p<0.05.)

We observed significant improvement among 53.49% of subjects, followed by clinically meaningful improvement among 27.91% of subjects. At the same time, 18.60% of subjects did not show any improvement. Out of eight cases did not show improvement, all presented with LBP and morning stiffness. About 62.5% had peripheral arthritis.

Table 3: Comparison of clinical presentation on admission and after 3 months

Clinical presentation	On admission		After 3 months		Significance
	Number	%	Number	%	
LBP	43	100.00	13	30.23	--
Morning stiffness	41	95.35	4	9.30	63.81, <0.0001
Fever	11	25.58	1	2.33	9.68, 0.0018
Fatigue	5	11.63	0	0.00	--
Weight loss	0	0.00	0	0.00	--
Peripheral arthritis	23	53.49	8	18.60	11.34, 0.00075
Uveitis	11	25.58	0	0.00	0
Enthesitis	5	11.63	1	2.33	2.86, 0.09
Dactylitis	2	4.65	1	2.33	0.34, 0.556
Pallor	0	0.00	0	0.00	0
Cyanosis	0	0.00	0	0.00	0
Icterus	0	0.00	0	0.00	0
Clubbing	0	0.00	0	0.00	0
Lymphadenopathy	0	0.00	0	0.00	0

LBP: Low back pain

Table 4: Examination findings of the patients

Examination findings	On admission		After 3 months		Significance
	Number	%	Number	%	
Chest expansion (>cm)	19	44.19	42	97.67	29.83, <0.0001
Schober'stest	38	88.37	12	27.91	32.29, <0.0001
Faber test	30	69.77	5	11.63	30.11, <0.0001
Sacroiliac joint tenderness	36	83.72	25	58.14	6.82, 0.008
Wall occiputtest	8	18.60	6	13.95	0.34, 0.559

Table 5: X-ray pelvis with bilateral hip findings

X-ray Pelvis wit bilateral hip (Ny grading)	On admission		After 3 months	
	Number	%	Number	%
Grade 0	43	100.00	40	93.02
Grade 1	0	0.00	3	6.98

Table 6: Routine hematological investigations

Hematological investigations	On admission	After 3 months
Hemoglobin	12.78	13.20
TLC	8250.00	8220.70
Platelet	2.61	2.74
BUN	10.99	10.85
Serum creatinine	1.08	1.10
TP	7.98	8.08
Albumin	3.69	3.74
Total Bilirubin	0.86	0.81
Direct Bilirubin	0.45	0.84
SGOT	35.05	29.72
SGPT	25.23	25.74
ALP	158.58	169.37
RBS	92.84	90.95
Uric acid	4.81	4.66
CRP	34.51	14.04
ESR	33.42	16.61

Table 7: ASDAS score of the patients

ASDAS score	On admission		After 3 months	
	Number	%	Number	%
<1.3	0	0.00	2	4.65
1.3–2.1	0	0.00	21	48.84
2.1–3.5	8	18.60	16	37.21
More than 3.5	35	81.40	4	9.30
Total	43	100.00	43	100.00

Table 8: BASDAI score of the patients

BASDAI score	On admission		After 3 months	
	Number	%	Number	%
<4	16	37.21	43	97.67
More than 4	27	62.79	1	2.33
Total	43	100.00	43	100.00

The Chi-square statistic is 36.4921. p<0.00001. Significant at p<0.05.

About 87.5% had Schober's test positive, FABER test (62.50%), sacroiliac joint tenderness found among 87.5% subjects, and wall occiput test positive among 12.5% subjects. Magnetic resonance imaging (MRI) findings of the patients are depicted in Table 10.

Four patients who had normal MRI at first progressed to show evidence of spondyloarthropathy on follow-up (MRI progression). All four patients had lower backache and morning stiffness and 3 (75%) had peripheral arthritis on presentation. They were also found to have raised mean CRP and ESR values, with mean values of 45 and 36.5, respectively, and ASDAS and BASDAI mean score of 3.76 and 5.3, respectively, suggesting very high disease activity.

Table 9: Comparison between asdas and basdai scores

On admission	BASDAI score			
ASDAS score	<4		More than 4	
	Number	%	Number	%
<1.3	0	0.00	0	0.00
1.3–2.1	0	0.00	0	0.00
2.1–3.5	7	87.50	1	12.50
More than 3.5	11	31.43	24	68.57
Total	18	41.86	25	58.14

The Chi-square statistic is 8.412. The p=0.003728. Significant at p<0.05.

Table 10: Comparison of MRI findings on presentation and at 3months

Time of examination	MRI findings absent	MRI findings present
At Presentation	14	29
At 3 months	10	33

MRI: Magnetic resonance imaging

DISCUSSION

Non-radiographic axial spondyloarthritis is a form of axial inflammatory arthritis without significant erosive involvement of the sacroiliac joint. It can develop into ankylosing spondylitis (AS, also termed radiographic axSpA) in a specific group of people and thus can be associated with deteriorating quality of life in them. With recent advancements in MRI, there has been an improvement in the diagnosis of the condition. However, still there is less clarity in the criteria for the classification of the same among the international community. Further studies are underway to define the classification and find out appropriate modalities given the diagnosisof nr-axSpA.

Gavali et al., in the study on a comparison between clinical and laboratory profiles of nr-axSpA and AS concluded that patients with AS were older at presentation and had more extended disease duration history than those with nr-axSpA.[8]

Benchérifa et al., in the study on a comparison of disease activity parameters, disease activity and functional scores between r-axSpA and nr-axSpA, did not find any significant difference in demographic and clinical characteristics among the two with an exception of psoriasis, which was more common among r-axSpA patients.[9]

Cantarini et al., in a study on the effectiveness of Adalimumab in nr-axSpA suggested a favorable risk- benefit

profile for ADA in patients of nr-axSpA, inadequately responding to NSAIDS.[10]

Denis Poddubnyy and Sieper in their study observed that nr-axSpA is a significant differential diagnosis in patients with diagnosed backache, especially in ones with recent onset backache. Moreover, they found out that high NSAIDs intake (NSAIDs index >50) in AS was associated with slower radiographic progression. No such association was found in patients with nr-axSpA.[11]

Goswami et al., in the study on the presence of spondyloarthropathy in hypoparathyroid patients observed that spondyloarthropathy is associated with a longer duration of hypoparathyroidism and that in patients of sporadic idiopathic hypoparathyroidism, spondyloarthropathy is an important clinical entity which needs to be distinguished from AS due to difference in the management of both the conditions.[12]

McCormick et al., in the study on anti-TNF response rate in r-axSpA and nr-axSpA showed equal response rates to anti-TNF therapy in both the groups after 3-month therapy.[13]

Limitations of the study

The study was carried out in a single tertiary care institute with a sample size of only 43 patients.

Pregnant and lactating females and patients allergic to sulpha drug groups were excluded from the study.

CONCLUSION

According to the study, it is found that non-radiographic axial spondyloarthropathy has higher male predisposition particularly diagnosed in early thirties with symptoms usually responding to primary treatment within a span of 3 months. Lower back pain appears to be the most common complaint among the subjects. Similarly, there is characteristic improvement of assessment scores such as BASDAI score and ASDAS score after primary treatment of the subjects. Few patients who showed limited response to primary treatment need to be assessed further and considered for other newer treatment modalities available.

Further research is required for optimal MRI usage in nr-axSpA to differentiate SI joint changes in normal populations versus the ones with spinal diseases. First-line treatment for nr-axSpA remains NSAIDs and physiotherapy. Other treatment modalities include anti-TNF drugs, JAK inhibitors, and drugs directed at IL-17 and IL-23. Much active research is being done in the classification, imaging, and treatment of nr-axSpA; hence, the future to improve the lives of patients with nr-axSpA looks promising.

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SL- Review of literature and manuscript preparation, coordination, statistical analysis and interpretation; **SM and MN-** Concept and design of the study, Interpretation of results; **AM, HN ans SJ-** Statistical analysis and interpretation, preparation of manuscript and revision of the manuscript

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