STUDY ON CLINICAL PROFILE, OUTCOME AND HLA-B27 ASSOCIATION IN JUVENILE IDIOPATHIC ARTHRITIS- ENTHESITIS RELATED ARTHRITIS

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ABSTRACT

BACKGROUND

Juvenile Idiopathic Arthritis (JIA) is defined as arthritis in one or more joints persisting for 6 weeks or more, which begins before the 16th birthday and has no other known cause. In contrast to the western literature only 11% - 16% of patients with JIA have ERA, In India it is probably the commonest subtype of JIA seen clinically. Data on outcome of ERA patients from India are scarce.

This study was taken up to assess the clinical profile, outcome, incidence of Juvenile ankylosing spondylitis, HLA-B27 association of Juvenile idiopathic arthritis- enthesitis related arthritis.

MATERIALS AND METHODS

History, clinical examination, radiological imaging like musculoskeletal x-rays, musculoskeletal USG, CT, MRI of sacroiliac joints, biochemical investigations and immunological investigations (HLA-B27) were done for all patients.

Material and Selection- Inpatients and outpatients of Institute of Rheumatology, Rajiv Gandhi Govt. General Hospital and Madras Medical College, Chennai. The study period was Jan. 2015 to Jan. 2017. The study was undertaken after obtaining approval from the Institutional Ethical Committee. An informed consent was obtained from all patients and parents.

RESULTS

The median age at the time of the study of the 50 patients with ERA was 16 years (range 9 - 33 years) and the median duration of disease was 5 years (3 months - 18 years); 49 patients were male and one patient was female. Median age at disease onset was 14 (8 - 15) years; 17 (34%) of the patients were HLA-B27 positive. Three (6%) patients were in remission at the time of the study; 15 patients (30%) had joints with limitation of motion; 18 (36%) patients had decreased anterior lumbar flexion movement by modified Schober's method.

CONCLUSION

Axial inflammation was common in HLA-B27 positive patients. Functional limitations were observed in one-third of the Enthesitis-Related Arthritis patients. JADI is a useful tool to measure articular and extra-articular damage in ERA; 70% of JIA-ERA patients had enthesitis (Two-third of the patients had enthesitis).

KEYWORDS

JADI-A, JADI-E, JIA-ERA.

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BACKGROUND

Juvenile Idiopathic Arthritis (JIA) is defined as arthritis in one or more joints persisting for 6 weeks or more, which begins before the 16th birthday and has no other known cause.¹

Enthesitis-Related Arthritis (ERA) is a subtype that has replaced, but is not exactly overlapping with, previous definitions in children such as juvenile ankylosing spondylitis or syndrome of seronegative enthesitis arthritis.

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In contrast to the western literature, only 11% - 16% of patients with JIA have ERA.^{2,3} In India it is probably the commonest subtype of JIA seen clinically. Data on outcome of ERA patients from India are scarce. This study was taken up to assess the clinical profile, outcome, incidence of Juvenile ankylosing spondylitis, HLA-B27 association of Juvenile idiopathic arthritis- enthesitis related arthritis.

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Sample Size

50

Study Design

Descriptive study.

Inclusion Criteria

Onset of arthritis before the 16th birthday and persisting for at least 6 weeks; arthritis and enthesitis, or arthritis or enthesitis with at least 2 of-

- Presence of or a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain
- Presence of HLA-B27 antigen⁴
- Onset of arthritis in a male over 6 years of age
- Acute (symptomatic) anterior uveitis
- History of ankylosing spondylitis, enthesitis related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative.

By definition, patients with psoriasis or a history of psoriasis in the patient or first-degree relative, presence of IgM rheumatoid factor and systemic JIA are not included in ERA subtype.

JADI (Juvenile articular damage index) scores were calculated as described previously. The index is composed of articular (JADI-A) and extraarticular (JADI-E) damage. In the JADI-A, 36 joints or joint groups are assessed for the presence of damage: cervical spine, shoulders, elbows, wrists, individual metacarpophalangeal and proximal interphalangeal joints, hips and knees; right and left temporomandibular joints, ankle and subtalar joints and metatarsophalangeal joint of each foot are considered as a single unit.^{5,6} The damage observed in each joint is scored as 1 in case of partial damage or 2 in case of severe damage, ankylosis or prosthesis. Contractures and other joint deformities are scored when they are completely explained by prior damage and are not due to active arthritis and are present for at least 6 months. For each joint, only the most severe lesions are scored. The maximum possible JADI-A score is 72.

For JADI-E, muscle atrophy, osteoporosis with fractures or vertebral collapse, avascular necrosis of bone, significant abnormality of the vertebral curve due to leg length discrepancy or hip contracture, significant leg length discrepancy or growth abnormality of a bone segment, striae rubrae, subcutaneous atrophy resulting from intraarticular corticosteroid injection, growth failure,⁷ pubertal delay, diabetes mellitus and amyloidosis are scored as 1 if present; ocular complications like cataract or other complications of uveitis^{8,9} were scored as 1 if present, 2 if surgery was required and 3 in case of blindness.^{10,11}

Educational level achieved, loss of school years, functional status measured by HAQ-S were also recorded. For the purposes of analysis, the HAQ-S score was divided into 4 categories: 0= no disability, > 0 and ≤ 0.5= mild disability, > 0.5 and ≤ 1.5= moderate disability, and > 1.5= severe

disability^{12,13}; 100 mm Visual Analogue Scale (VAS) was used for parent/patient's assessment of their disease.

Examination included physician's global assessment on 100 mm VAS, number of active joints as defined by presence of swelling (excluding bony swelling) or any two of limitation of motion (LOM), pain, heat or tenderness and number of joints with limited range of motion (ROM); 67 joints were assessed.

Enthesitis was defined as discretely localised tenderness at the point of insertion of ligaments, tendons, joint capsules or fascia to bone. Anterior lumbar flexion was assessed using the modified Schober's method. Reduced lumbar flexion was defined as values ≤ 6.5 cm in boys and ≤ 5.5 cm in girls. Inflammatory back pain was defined as lumbosacral spinal pain at rest with morning stiffness that improved with movement. Erythrocyte Sedimentation Rate (ESR) was measured by Westergren method.

Statistical analysis was performed using the SPSS software version 17.0. Median was measured for numerical value. Age distribution, peripheral joint distribution, axial involvement, Entheseal involvement, ESR and CRP values were represented by bar chart and Histogram. Chi-square test is used to analyse the values for patients who had sacroiliac joint involvement.

RESULTS

The median age at the time of the study of the 50 patients with ERA was 16 years (range 9 - 33 years) and the median duration of disease was 5 years (3 months - 18 years). 49 patients were male and one patient was female. Median age at disease onset was 14 (8 - 15) years; 17 (34%) of the patients were HLA-B27 positive. Three (6%) patients were in remission at the time of the study; 15 patients (30%) had joints with limitation of motion; 18 (36%) patients had decreased anterior lumbar flexion movement by modified Schober's method.

At the time of the study, all patients were on NSAID; Indomethacin was the most commonly prescribed NSAID; 40 patients (80%) were on it; 21 patients (42%) had received intra-articular (IA) steroid. All patients were on DMARDs at the time of the study. Sulphasalazine was the commonest DMARD used (n= 36, 64%); 14 (28%) patients were on Methotrexate. Side effects of drug were seen in 7 patients and GI toxicity in 8 patients.

JADI-A

In JADI-A scoring, 15 patients (30%) had damaged joints. JADI-A score varied from 1 - 6. Hip was the commonest damaged joint (n= 7; 14%) followed by knees (3, 6%), ankle (3, 6%) and elbows (2, 4%).

JADI-E

2 (4%) patients had extraarticular damage with JADI-E. None of the patients had ocular damage, severe muscular atrophy, growth failure, pubertal delay and secondary amyloidosis.

Enthesitis

Ultrasound detect enthesitis in two asymptomatic individuals. Polyenthesitis were present in 11 patients.

Disease Activity

Parent's/patient's global assessment on visual analogue scale (VAS) ranged from 0 - 100 mm. Median score of physician's global assessment in VAS was 30 mm (range 10 - 90 mm). Number of active joints varied from 1 - 12 (median 2.0). Duration of EMS ranged from nil to 1 hour and Median ESR was 40 (5 - 124) mm/hour.

Disability

Mild disability in 11 (22%) patients. Median HAQ-S was 1.0 (1 - 3).

4 (8%) patients lost some years of education due to disease ranging from 2 - 10 years.

HAQ-S had correlation with limitation of spinal mobility by modified Schober's method.

HLA-B27

HLA-B27 was positive in 17 (34%) patients, 16 (35%) were male and 1 (2%) was female.

Sacroiliac Joint Involvement

18 (36%) patients had sacroiliac joint involvement in both clinical and in radiological investigations. Among these patients, 12 (24%) patients were HLA-B27 positive and 6 (12%) patients were HLA-B27 negative.

Number of Joints with LOM	Frequency (N= 50)	Percentage
0	35	70
1	1	2
2	6	12
3	2	4
4	2	4

Table 1. Frequency of Number of Joints with Limited Range of Motion (LOM)

JADI Score	Frequency (N= 50)	Percent
0	35	70
2	2	4
3	4	8
4	5	10
5	2	4
6	2	4

Table 2. Frequency of Juvenile Arthritis Damage Index-Articular (JADI-A) Score

Type of Enthesitis	Frequency (N= 35)	Percentage
Achilles enthesitis	21	58.4
Plantar fasciitis	12	33.6
Knee enthesitis	6	16.8
Spine enthesitis	1	2.8
Elbow enthesitis	1	2.8

Table 3. Active Enthesitis was Present in 70% of the Patients

Polyenthesitis were present in 11 patients.

DISCUSSION

Our study shows 70% of patients had enthesitis compared to 60% of patients had enthesitis in Sarma P, Misra R, Amita Agarwal A et al, Lucknow study. Presence of enthesitis had a highly significant correlation with HAQ-S in our study.

15 ERA patients had articular damage and 2 patients had extra-articular damage at a median duration of disease of 5 years. Moderate limitation of movement of lumbar spine was present in 18 (36%) patients; 5 (10%) patients continued to have active disease; 4 (8%) patients lost some years of education due to disease ranging from 2 - 10 years.

More than 60% of patients lost some years of education in Lucknow study.

15 patients had damaged joints in JADI-A. Hip was the commonest joint damaged in our study followed by knees, ankles and elbow. In Lucknow study hip, knees, ankle and cervical spine were more often involved. JADI-A score in our study is lower compared to the Lucknow study.

Sulphasalazine^{14,15} was the commonest DMARD used in our study in contrast to Lucknow study, in which methotrexate was the commonest DMARD.¹⁶

The limitation of application of JADI in ERA is absence of scoring for spinal involvement. Limitation of spinal mobility had high correlation with HAQ-S. Inclusion of limitation of spinal movement in JADI may be helpful to detect early damage in ERA.

In our study, 18 (36%) patients had decreased anterior lumbar flexion movement by modified Schober's method. In Lucknow study among the 49 patients, one-third had limitation of lumbar spine movement by modified Schober's method.¹⁶

HLA-B27

HLA-B27 was positive in 17 (34%) patients, 16 (35%) were male and 1 (2%) was female.

Sacroiliac Joint Involvement

18 (36%) patients had sacroiliac joint involvement in both clinical and in radiological investigations. Among these patients, 12 (24%) patients were HLA-B27 positive and 6 (12%) patients were HLA-B27 negative.

In our study none of the patients had severe muscular atrophy, growth failure, pubertal delay in contrast to Lucknow study in which three patients (6.1%) had severe muscular atrophy, pubertal delay was seen in 2 (4.1%) and secondary amyloidosis was seen in 1 (2.0%). None of the patients had ocular damage in our study similar to Lucknow study.

Our study has many limitations: numbers of patients are small, the average disease duration is only 5 years.

CONCLUSION

1. Axial inflammation was common in HLA-B27 positive patients.
2. Functional limitations was observed in one-third of the Enthesitis Related Arthritis patients.
3. JADI is a useful tool to measure articular and extraarticular damage in ERA.
4. 70% of JIA-ERA patients had enthesitis (Two-third of patients had enthesitis).

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REFERENCES

- [1] Petty RE, Southwood TR, Manners P, et al. International league of associations for rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004;31(2):390-2.
- [2] Denardo BA, Tucker LB, Miller LC, et al. Demography of a regional pediatric rheumatology patient population. Affiliated children's arthritis centers of New England. *J Rheumatol* 1994;21(8):1553-61.
- [3] Malleson PN, Fung MY, Rosenberg AM. The incidence of pediatric rheumatic diseases: results from the Canadian pediatric rheumatology association disease registry. *J Rheumatol* 1996;23(11):1981-7.
- [4] Prahalad S. Genetics of juvenile idiopathic arthritis: an update. *Curr Opin Rheumatol* 2004;16(5):588-94.
- [5] Laiho K, Savolainen A, Kautiainen H, et al. The cervical spine in juvenile chronic arthritis. *Spine J* 2002;2(2):89-94.
- [6] Rosenberg AM, Petty RE. A syndrome of seronegative enthesopathy and arthropathy in children. *Arthritis Rheum* 1982;25(9):1041-7.
- [7] Cimaz R. Osteoporosis in childhood rheumatic diseases: prevention and therapy. *Best Pract Res Clin Rheumatol* 2002;16(3):397-409.
- [8] Cassidy JT, Hillman LS. Abnormalities in skeletal growth in children with juvenile rheumatoid arthritis. *Rheum Dis Clin N Am* 1997;23(3):499-522.
- [9] Saurenmann RK, Levin AV, Feldman BM, et al. Prevalence, risk factors, and outcome of uveitis in juvenile idiopathic arthritis: a long-term followup study. *Arthritis Rheum* 2007;56(2):647-57.
- [10] Petty RE, Smith JR, Rosenbaum JT. Arthritis and uveitis in children. A pediatric rheumatology perspective. *Am J Ophthalmol* 2003;135(6):879-84.
- [11] Edelsten C, Lee V, Bentley CR, et al. An evaluation of baseline risk factors predicting severity in juvenile idiopathic arthritis associated uveitis and other chronic anterior uveitis in early childhood. *Br J Ophthalmol* 2002;86(1):51-6.
- [12] Chalom EC, Goldsmith DP, Koehler MA, et al. Prevalence and outcome of uveitis in a regional cohort of patients with juvenile rheumatoid arthritis. *J Rheumatol* 1997;24(10):2031-4.
- [13] Oen K, Malleson PN, Cabral DA, et al. Disease course and outcome of juvenile rheumatoid arthritis in a multicenter cohort. *J Rheumatol* 2002;29(9):1989-99.
- [14] Zak M, Pedersen FK. Juvenile chronic arthritis into adulthood: a long-term follow-up study. *Rheumatology (Oxford)* 2000;39(2):198-204.
- [15] Wallace CA, Huang B, Bandeira M, et al. Patterns of clinical remission in select categories of juvenile idiopathic arthritis. *Arthritis Rheum* 2005;52(11):3554-62.
- [16] van Rossum MA, Fiselier TJ, Franssen MJ, et al. Sulfasalazine in the treatment of juvenile chronic arthritis: a randomized, double-blind, placebo-controlled, multicenter study. Dutch juvenile chronic arthritis study group. *Arthritis Rheum* 1998;41(5):808-16.