Disease Activity in Untreated Patients of Rheumatoid Arthritis in Eastern India

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ABSTRACT

Introduction: Rheumatoid Arthritis is a common chronic inflammatory disease, causing joint pain damage and disability. Assessment of disease activity is an important step in optimal management of these patients.

Aim: To describe the disease activity in untreated Indian patients with rheumatoid arthritis.

Materials and Methods: A cross-sectional observational study was done on 86 consecutive patients attending Medicine Outpatient Department (OPD) of a tertiary care hospital in eastern India and were with definite rheumatoid arthritis as per 2010 classification criteria who never received any Disease Modifying Anti Rheumatic Drugs (DMARDs) or steroids. Tender and swollen joint count out of 28 joints was measured along with Erythrocyte Sedimentation Rate (ESR) and patient's assessment of his/her global health on a Visual Analogue Scale (VAS). Disease Activity Score (DAS) for 28 joints with ESR value (DAS28-ESR) was calculated for each patient by medical calculator app based on these variables and then patients were classified into having high, moderate or Low Disease Activity (LDA) based on the DAS28-ESR values.

Results: The ratio of female: male patients were 3.5:1. The average age of the patients was 38.17 years. The mean DAS28-ESR value was 6.19 and majority of the patients (81%) were in the High Disease Activity (HDA) group. The patient reported global health assessment which was also very high (mean 64.12/100 mm).

Conclusion: Most of the untreated rheumatoid arthritis patients in our community are in a HDA group and presents with significantly higher amount of pain and disabilities. This finding underlines the need to improve the screening of arthritis in our community to reduce the number of patients who would present to health facilities with advanced disease having irreversible deformities resulting in disabilities. This would result in early increase in the number of pain free days for the patient and also reduce the overall cost of therapy.

Keywords: Disability, Disease activity score-28, Erythrocyte sedimentation rate, Indian patients

INTRODUCTION

Rheumatoid Arthritis is the most common chronic inflammatory arthritis worldwide. It is a progressive chronic inflammatory multisystem disease of unknown aetiology, characterised by symmetric polyarthritis, which causes joint damage and disability [1]. The onset is most commonly in the 3rd, 4th and 5th decades of life. It is a progressive inflammatory disease, which causes damage and disability that can be prevented by promptly initiated and effective therapy. Damage to articular and periarticular structures may result in joint destruction and deformities, the most feared complications of rheumatoid arthritis. The most common deformities due to rheumatoid arthritis affect the hands and feet of those with long standing aggressive disease [1]. The swan-neck deformity, boutonniere deformity, zeta deformity, ulnar drift, piano-key deformity, and bent-fork deformity occur in wrist and hands. In the foot, hallux valgus deformity is common. Early intervention has been shown to change the natural course of the disease, patients treated early with disease modifying drugs have been shown to have significantly more improvement in pain and disability than the ones receiving late therapy [1]. To ensure that the therapy is effective, frequent clinical assessments are also needed.

Hence, disease activity assessment is an important aspect in the management of the disease as treatment protocols depend upon the disease activity [2]. In this study, authors have tried to assess the severity of the disease on presentation in patients who were not on any kind of DMARDs or steroids. Disease activity on presentation for the patients was measured by DAS28-ESR and classified as either having LDA, Moderate Disease Activity (MDA) or HDA [3,4]. This would give us a glimpse on the spectrum of severity for the undiagnosed cases in the community.

MATERIALS AND METHODS

It was a cross-sectional descriptive study done on 86 consecutively selected patients during the period from September 2018 to August 2019. The study was carried out on 86 previously untreated adult patients attending Medicine Outpatient Department (OPD) of a tertiary care hospital in eastern India with a diagnosis of definite Rheumatoid Arthritis.

Inclusion criteria: All patients diagnosed with definite Rheumatoid Arthritis as per American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 classification criteria for rheumatoid arthritis.

Exclusion criteria: The patients already on any DMARDs or steroids were excluded from the study as DMARDs would interfere with the assessment of severity in newly diagnosed cases. Patients having other systemic diseases like uncontrolled diabetes, hypertension and any clinically significant neurologic, psychiatric, respiratory, cardiac or gastroenterological diseases were excluded from the study as they would interfere with one of the parameters of DAS28 i.e., patient's global health assessment [3,4].

A total of 112 patients were included in the study out which 26 patients were excluded on the basis of exclusion criteria. Informed consent was taken from all the participants. These patients were diagnosed as having definite rheumatoid arthritis as per ACR/EULAR 2010 classification criteria for rheumatoid arthritis 2010 [5]. The procedures followed were in accordance with the Helsinki Declaration.

The patients were clinically examined for the number of Tender Joints Count (TJC-28) and Swollen Joints Count (SJC-28). The 28 joints examined for each patient were bilateral proximal interphalangeal (10 joints), metacarpophalangeal (10 joints), wrist (two joints), elbow (two

joints), shoulder (two joints) and knee (two joints) joints. The ESR in mm/hour was measured for all the patients. Patients were asked to mark on a VAS of 0-100 mm for the patient's global health assessment (GH) with 0 being the least and 100 being the most severe disease indicator. Other necessary relevant baseline investigations like Rheumatoid factor, Anti-Cyclic Citrullinated Peptide (Anti-CCP) antibodies, complete blood count, liver function test, renal function test, lipid profile, electrocardiography, chest x-ray, fasting and post prandial blood sugar were done to reach the diagnosis and exclude any other co-morbidities.

The formula used to calculate DAS28 was as follows [3,4]:

$0.56 \times \sqrt{(TJC\text{-}28)} + 0.28 \times \sqrt{(SJC\text{-}28)} + 0.014 \times GH + 0.7 \times \ln(ESR)$. The calculation was done by using app "MD Calc Medical Calculator DAS-28 for rheumatoid arthritis with ESR (DAS28-ESR)" by putting in the respective entries.

The patients were subdivided into HDA, MDA and LDA on the basis of the following cut-offs of DAS28-ESR score [6,7]:

LDA≤3.2, 3.2<MDA≤5.1, HDA>5.1

STATISTICAL ANALYSIS

Descriptive statistics of the values were obtained by using Microsoft Excel software. The mean, range and standard deviation of the parameters were calculated.

RESULTS

Out of the 86 patients, 67 were females and 19 were males. Forty-four belonged to urban whereas 42 belonged to the rural population. The mean age of the patients was 38.17 years (range 18-61).

[Table/Fig-1] shows the distribution of the patients in the age groups of 11-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years and 61-70 years respectively. The percentage of patients in each of these age groups are 7 (8.1%), 17 (19.8%), 26 (30.2%), 22 (25.6%), 12 (14%) and 2 (2.3%), respectively.
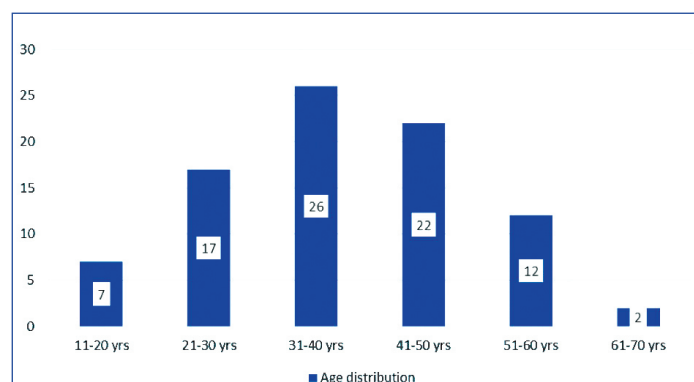
[Table/Fig-1]: Age distribution of the patients (n=86).

The mean, standard deviation, 95% confidence interval of the individual components used to calculate DAS-28 score has been described in [Table/Fig-2]. The mean TJC was 13.6, SJC 5.17, ESR was 58.27 mm/1st hour, patient reported global health assessment was 64.12 and DAS28-ESR was 6.19. The patient reported global health assessment on VAS which was significantly high (mean 64.12/100) underlining the significantly high amounts of pain and disability that the patients experience on presentation.

	Age (years)	TJC	SJC	ESR (mm)	GH	DAS28-ESR
Mean	38.17	13.6	5.17	58.27	64.12	6.19
Standard deviation	11.04	6.37	4.52	32.56	22.1	1.15
Standard error of mean	1.19	0.69	0.49	3.51	2.38	0.12
95% CI	35.79-40.55	12.22-14.98	4.19-6.15	51.25-65.29	59.36-68.88	5.95-6.43
Lowest value	18	2	0	10	25	3.56
Highest value	61	26	18	125	100	8.75
Median	37.5	12	4	50	70	6.2

[Table/Fig-2]: Descriptive statistics of the variables measured and computed.
TJC: Tender joint count; SJC: Swollen joint count; ESR: Erythrocyte sedimentation rate in mm/hour; GH: Patient's global health assessment in mm; DAS28: Disease activity score 28 joints

[Table/Fig-3] shows the distribution of the patients in the HDA, MDA and LDA group. The majority of the patients were found to be in the HDA group and no patient was in LDA group. The patients were then treated as per the standard guidelines (American College of Rheumatology 2015) [2].
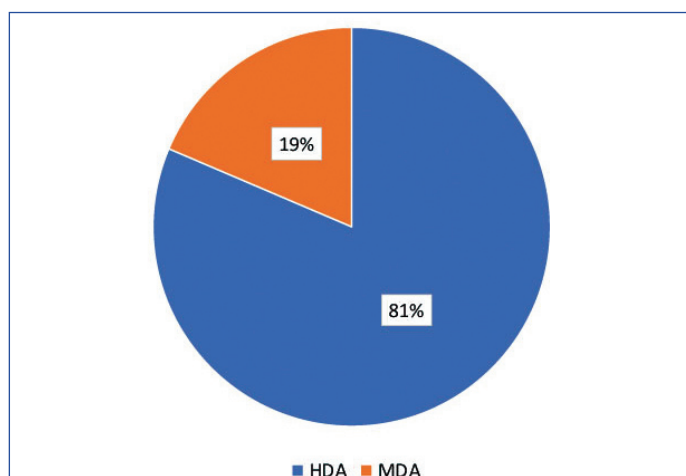
[Table/Fig-3]: Spectrum of disease activity among newly diagnosed rheumatoid arthritis patients.

DISCUSSION

This was a cross-sectional study on DMARD naïve Rheumatoid Arthritis patients attending Medicine OPD. The DAS was validated as a tool for assessment of disease activity in patients with rheumatoid arthritis. Calculation of DAS was a very cumbersome process for routine clinical practice. The DAS then underwent mathematical modifications to lead to the development of DAS-28 which included evaluation of 28 joints of the body. The DAS28-ESR was developed and accepted in 1993 as a standard method to assess disease activity of patients suffering from rheumatoid arthritis. It includes counting of tender joints and swollen joints out of a total of 28 joints clinically [3,4,6,7]. The other variables required in this tool are the patient's own assessment of his/her health status in a VAS and the laboratory value of ESR. This tool has stood the test of time to establish itself as a gold standard measure to assess disease activity. Several modifications of this tool like DAS28-CRP, Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) have been developed [8-10]. These modifications have gradually led to replacement of ESR by CRP as in DAS28-CRP or SDAI and replacement of the laboratory parameter by complete clinical assessment as in CDAI [11-13].

From the results obtained out of this study, it was found that the female: male ratio of the patients was about 3.5:1. The mean age of the patients in this study was 38.17 years with patients ranging from 18 years to 61 years of age. The worldwide prevalence of RA was found to be about 0.8% (range 0.5-1%) [1]. Studies in India on prevalence of rheumatoid arthritis reported figures of 0.5% in one study and 0.7% in rural population in another study [14,15]. Women are affected almost three times more commonly than men in the studies with female: male ratio ranging from 2:1 to 4:1. The basis of gender defect is not known but presumably is related to effects of the hormonal milieu on immune function. Oestrogens have a generally stimulatory effect on the immune system, and this may be a factor in the increased female to male ratio. The relative risks of developing RA in women appear to fluctuate with different stages of the reproductive cycle throughout their lives, from menarche to menopause. There is tendency of RA to improve during pregnancy

and oral contraceptive use [16]. At least 75% find substantial relief of symptoms during pregnancy, although in the postpartum state the disease activity often recurs. Another relationship is that Rheumatoid Arthritis exhibits a lower penetrance in men. Men are more likely to have erosive joint disease [17].

The mean value of DAS28-ESR for our sample of patients was 6.19. An important data which was obtained from the present study was that majority of the untreated patients in the community belonged to the HDA group. The main purpose of this study was to describe the disease and its severity in the untreated group presenting to a hospital for treatment. Other studies from India also had similar findings like present study [18,19]. A 42-65% of the patients were found to be in the HDA group in one of these studies [19]. In another study, where DMARD treatment was delayed by more than two years, more than 84% of patients had HDA [18]. A study from eastern India showed 34% patients had HDA followed by 39% with LDA on presentation [20]. Another study from southern India showed a grim scenario with 97% of treatment naïve patients in HDA group [21]. Present study hence highlights the need to screen the general population for inflammatory arthritis as otherwise the patients being mostly women generally ignore their health issues and present late in the course with already advanced diseases resulting in increased morbidities and deformities.

Earlier detection in milder stages of the disease would help us to reduce the health expenditure as more severe diseases are likely to require multiple DMARDs and also biological therapies which are extremely expensive and mostly out of reach of common Indian population. Early detection and treatment also reduces the loss of working days for the patients in particular and the community in general.

Limitation(s)

The number of patients selected for the present study was small and was conducted in one centre. Larger multicentric studies especially community-based studies would provide a better understanding of the burden of disease and the disease activity in the community.

CONCLUSION(S)

Disease activity measurement is pivotal to treat the patients with rheumatoid arthritis as per standard treatment guidelines which are based on DAS. Present study has attempted to get a view of the disease spectrum in the untreated patients. It has highlighted that most of the patients suffer from HDA, therefore, giving rise to significant disability in their daily activities at the time of their initial presentation.

REFERENCES

[1] Shah A, St. Clair EW. Rheumatoid Arthritis. In: Larry JJ editor. Harrison's Principles of Internal Medicine. 20th ed. Mc Graw Hill Education; 2018: 2527-2540.

[2] Singh JA, Saag KG, Bridges SL, Akl EA, Bannuru RR, Sullivan MC, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheum. 2016;68(1):01-26.

[3] Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials.The Committee on Outcome Measures in Rheumatoid Arthritis Clinical Trials. Arthritis Rheum. 1993;36:729-40.

[4] Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38:44-48.

[5] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. 2010 Rheumatoid Arthritis Classification Criteria An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative. Arthritis & Rheumatism. 2010;62(9):2569-81.

[6] van der Heijde DM, van 't Hof MA, van Riel PL, Theunisse LA, Lubberts EW, van Leeuwen MA, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis. 1990;49:916-20.

[7] Boers M, Tugwell P, Felson DT, van Riel PL, Kirwan JR, Edmonds JP, et al. World Health Organization and International League of Associations for Rheumatology core endpoints for symptom modifying antirheumatic drugs in rheumatoid arthritis clinical trials. J Rheum. 1994:86-89.

[8] Aletaha D, Ward MM, Machold KP, Nell VPK, Stamm T, Smolen JS. Remission and active disease in rheumatoid arthritis: Defining criteria for disease activity states. Arthritis Rheum. 2005;52:2625-36.

[9] Smolen JS, Breedveld FC, Schiff MH, Kalden JR, Emery P, Eberl G, et al. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. Rheum (Oxford) 2003;42:244-57.

[10] Aletaha D, Stamm T, Smolen JS. Validation of the Simplified Disease Activity Index (SDAI) in an observational cohort of patients with rheumatoid arthritis. Ann Rheum Dis. 2004:111.

[11] Aletaha D, Nell VPK, Stamm T, Uffmann M, Pflugbeil S, Machold K, et al. Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: Validation of a clinical activity score. Arthritis Rheum. 2005;7:R796-806.

[12] Smolen Joseph S, Aletaha D. Activity assessments in rheumatoid arthritis. Current Opinion in Rheum. 2008;20:306-13.

[13] Aletaha D, Smolen J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): A review of their usefulness and validity in rheumatoid arthritis. Clin Exp Rheum. 2005;23(Suppl. 39):S100-08.

[14] Chopra A, Patil J, Billempelly V, Relwani J, Tandle HS. Prevalence of rheumatic diseases in a rural population in Western India: A WHO-ILAR COPCORD Study. JAPI. 2001;49:240-46.

[15] Malaviya AN, Kapoor SK, Singh RR, Kumar A, Pande I. Prevalence of rheumatoid arthritis in the adult Indian population. Rheum Int. 1993;13:131-34.

[16] Masi AT, Feigenbaum SL, Chatterton RT. Hormonal and pregnancy relationships to rheumatoid arthritis: Convergent effects with immunologic and microvascular system. Semin Arthritis Rheum. 1992;25:1.

[17] Weyand CM, Schmidt D Wagner U, Goronzy JJ. The influence of sex on phenotype of rheumatoid arthritis. Arthritis Rheum. 1998;41:817.

[18] Shah A, Kini S, Londhey V. Use of Disease Activity Score (DAS28) and Routine Assessment of Patient Index Data 3 (RAPID3) for Assessment of Rheumatoid Arthritis Disease Activity, in the Indian Setting. J Assoc Physicians India. 2019;67(7):58-60.

[19] Borukar SC, Chogle AR, Deo SS. Importance of disease activity indices in Indian Rheumatoid Arthritis (RA) patients of western region. Lupus Open Access. 2016;1:117.

[20] Das AK, Sarkar RN, Das CK, Baisya R, Bhattacharjee U, Biswas P, Bhattacharya A. A comparison of 3 rheumatoid arthritis disease activity indices in routine clinical practice. Indian J Rheum. 2017;12:209-13.

[21] Kumar BS, Suneetha P, Mohan A, Kumar DP, Sarma KV. Comparison of Disease Activity Score in 28 joints with ESR (DAS28), Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire Disability Index (HAQ-DI) & Routine Assessment of Patient Index Data with 3 measures (RAPID3) for assessing disease activity in patients with rheumatoid arthritis at initial presentation. Indian J Med Res. 2017;146(Suppl S2):57-62.

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