ORIGINAL ARTICLE

A STUDY TO COMPARE CLINICAL FEATURES AND LABORATORY FINDINGS OF SEROPOSITIVE AND SERONEGATIVE CASES OF RHEUMATOID ARTHRITIS

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disease of marked by a symmetric, peripheral polyarthritis. RA patients who test positive in stated titres either for Rheumatoid factor (RF) / Anti-CCP antibody are classified as sero-positive & who test negative as sero-negative. This study aims to find out the comparison of clinical features & laboratory findings in both cases of Rheumatoid Arthritis.

Methodology: It was cross-sectional study ,conducted in the Rheumatology OPD of Medical College, Kolkata during a period of 1 year among 100 adult literate persons - 50 were diagnosed as seropositive RA (either RF &/or Anti-CCP antibody positive) , other 50 patients were seronegative RA. Both groups were evaluated regarding demographic profile, clinical evaluation, and disease activity.

Results: Distribution of study population regarding joint deformity, Xray and extra articular manifestation showed significance among seropositive and seronegative patients (p significant). Tender and swollen joint count were not significant but ESR and DAS28 score were found to be clinically significant.

Conclusion: This study highlights that seropositive RA patients have higher disease activity, greater joint deformity, X-ray changes & extra-articular manifestations, it also demonstrates the higher preponderance of serious disease (detected clinically & laboratory findings) in seropositive RA patients in Eastern India.

Keywords: Rheumatoid Arthritis (RA), Rheumatoid Factor, AntiCCP antibody, Sero-positive & negative RA

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. For clinical practice, experts generally agree that rheumatoid inflammation should be controlled as soon as possible and as completely as possible, and that control should be maintained for as long as possible, consistent with patient safety.[1] With the goal of treatment to attain and sustain low disease activity or even remission, the management of RA should clearly include systematic and regular quantitative evaluation of rheumatoid inflammation.[2] Estimation of Rheumatoid Factor which is autoantibody (IgM) against Fc portion of IgG is found in 70-80% of RA patients. Another sero-marker anti-CCP (cyclic cirtrullinated peptide /ACPA) antibody detection by ELISA is more specific (if > 40) for diagnosing RA in very early state, before synovitis , joint destructions & other features develop. Traditionally, RA patients who test positive in stated titres either for RF / anti- CCP antibody are classified as seropositive & who test negative are classified as seronegative. Hence we planned this cross-sectional study to compare the clinical features & laboratory findings of seropositive & seronegative cases of RA in a tertiary care hospital of Eastern India (Medical College & Hospital, Kolkata).Most of the studies done comparing these two subsets of patients have been done in other countries. Hence we aim to obtain the results of seropositive / negative status on clinical & laboratory parameters of patients of RA in Eastern India. Disease activity in both the groups was measured using the tender joint count (TJC), swollen joint count (SJC), ESR, visual analogue scale (VAS) for pain assessment & DAS28 [3-5] with its disease activity. Also X-ray changes & joint deformity with extra-articular manifestations by clinical/radiological assessment were done to detect high disease activity.

METHODOLOGY

It was hospital based, cross-sectional, observational study. The study was conducted in the Rheumatology OPD of Medical College and Hospital, Kolkata, West Bengal, India during a period of 1st July 2014 to 31st August 2015. 100 adult, literate persons (≥16yrs.) having rheumatoid arthritis according to the 2010 ACR EULAR revised "Classification Criteria" [6] attending OPD of Medical College Kolkata who voluntarily gave consent to be part of this study were considered as study population . All the patients were studied on the basis of following variables - demographic evaluation, clinical evaluation, questionnaire in Bengali/English to be completed by patients themselves, 28 joint count for tender and swollen joints, estimation of ESR (Erythrocyte Sedimentation Rate) by Westergren method .Those patients with pregnancy, lactation, hypothyroidism, having severe renal, cardiac, liver, or pulmonary disease and of less than 6 wk duration were excluded from the study. Out of this total group of 100 RA patients, 50 patients were diagnosed seropositive RA (either RF &/or Anti-CCP antibody positive). The other 50 patients were diagnosed seronegative RA (both RF & anti-CCP antibody negative). Informed written consent (Bengali/ English /Hindi) was taken for each patient. They were evaluated by history taking & clinical evaluation. Data taken for each patient were name, age, sex, religion, residence (rural/urban), occupation, marital status, disease duration, formal 28 joint counts for tender and swollen joints of each patient (T.J.C. & S.J.C.), ESR, V.A.S., DAS28 Score (using DAS28 calculator), disease activity, presence of any joint deformity, presence of any extra-articular manifestation & its type, presence of any X ray abnormality in diseased joints. Ethical committee clearance was taken to conduct the study. Statistical analysis was done using SPSS 20.0 software. Demographic data, RA core data set measures, and indices of 100 patients (two groups of 50 sero-positive & 50 sero-negative patients each) were summarized.

RESULTS

The mean age of the patient in seropositive group was 43.22 ± 11.13years and the mean age of seronegative group was 44.66 ± 13.81 years (p value not significant). There were 78 females and 22 males with male /female ratio 1:3.54 (p value 0.14) .The distribution of study population according to residential staus (Rural/Urban) and religion showed no clinical significance (p value 0.812 & 0.975) (Table 1)

Distribution of study population according to duration treatment in months showed no clinical significance. On clinical examination and investigation, tender and swollen joint count were clinically not significant but ESR and DAS28 score were found to be clinically significance (p value significant).

Table 1: The distribution of study population according to religion, sex and residence

Variable		Sero positive (%) (n=50)	Sero negative (%) (n=50)	Total (%)	p-Value
Religion	Christian	1 (2)	1 (2)	2 (2)	0.975
	Hindu	35 (70)	36 (72)	71 (71)	
	Muslim	14 (28)	13 (26)	27 (27)	
Sex	Female	42 (84)	36 (72)	78 (78)	0.14
	Male	8 (16)	14(28)	22 (22)	
Residence	Rural	38 (76)	39 (78)	77 (77)	0.812
	Urban	12 (24)	11 (22)	23 (23)	

Table 2: Distribution of study population according to duration of treatment, clinical examination, investigation & activity index

Variables	Seropositive (Mean ± SD)	Seronegative(Mean ± SD)	p Value
Duration of treatment	11.86 ± 15.48	12.2 ± 13.22	0.906
T. J. C	8.2 ± 5.09	6.66 ± 5.72	0.18
S. J. C.	3.54 ± 4.05	2.62 ± 4.38	0.28
E.S.R.	44.16 ± 13.04	34.92 ± 15.99	**0.02**
DAS 28 Score	5.14 ± 1.17	4.48 ± 1.52	**0.06**

Table 3: Distribution of study population according to disease severity as obtained by DAS28

Disease Activity	Seropositive (%)	Seronegative (%)	Total	p-Value
Remission	1 (2)	7 (14)	**8 (8)**	0.049
Low	5 (10)	9 (18)	**14 (14)**	
Moderate	21 (42)	20 (40)	**41 (41)**	
High	23 (46)	14 (28)	**37 (37)**	
Total	**50 (100)**	**50 (100)**	**100 (100)**	

Table 4: distribution of study population regarding joint deformity , extra articular features and x ray abnormalities

Parameters	Seropositive (%)	Seronegative (%)	Total (%)	p-Value
Joint deformity				
Absent	28 (56)	43 (86)	71 (71)	**0.001**
Present	22 (44)	7 (14)	29 (29)	
Extra-articular manifestations				
Absent	30 (60)	44 (88)	74 (74)	**0.001**
Present	20 (40)	6 (12)	25 (25)	
X-Ray abnormality				
Absent	22 (44)	35 (70)	57 (57)	**0.009**
Present	28 (56)	15 (30)	43 (43)	

In distribution of study population regarding joint deformity , Xray features and extra-articular manifestation showed significance among seropositive and seronegative study population. (table 4)

DISCUSSION

In this study we have found that mean age of the study population was 43.22 years in seropositive group & 44.66 years in seronegative group (p value not significant). This shows that both the groups were statistically well-matched with respect to demographic parameters for a comparative study about clinical & laboratory parameters between them. This is in agreement to the study on RA patients by Sahatciu Meka V, in which all patients were in 25-60 years of age (mean age in this study being 43.22). Also epidemiological characteristics such as education, residence, economic & living conditions inabove-mentioned study did not show any significant statistical difference regarding serostatus as in our study.[7] ESR mean value in seropositive group was 44.16mm, whereas in seronegative group was 34.92mm (p-value was 0.002). DAS28 Score mean value in seropositive group was 5.14, whereas in seronegative group was 4.48 (p-value was 0.016). This is in agreement to study on RA patients by Sahatciu Meka V which found elevated average values of E.S.R., C.R.P. & erythrocytes in Seropositive patients, especially female seropositive patients with p-value < 0.01 without correlation to disability & duration of disease.[8] In Disease activity parameter (based on DAS28 Score), in seropositive group 23 patients were in high disease activity & only 1 patient was in remission. In seronegative group 14 patients were in high disease activity & 7 patients were in remission. Between the two groups, p-value was 0.049 which was significant. This is in agreement to study on RA patients by Sahatciu Meka V which found exacerbations, progressive continual course & bad prognosis more common in seropositive patients & partial remission to be more common in seronegativepatients.[9] In joint deformity parameter, in seropositive group 22 patients had joint deformity (44% of group) as compared to only 7 patients in seronegative group (14% of group). In this respect, between the two groups, p-value was significant. This is in agreement to the study on RA by Edelman J & Russell AS which stated that major differences detected between the two groups on "blind' assessment were a greater tendency to deformity, a greater degree of erosion and the presence of subcutaneous nodules in the seropositive group. Seronegative and seropositive rheumatoid arthritis appear to have very similar clinical features, but differing degrees of severity.[10] In X-ray abnormality parameter, in seropositive group 28 patients had X-ray skeletal abnormality (56% of group) as compared to 15 patients in seronegative group (30% of group). In this respect, between the two groups, p-value was significant. This is in agreement to the study by Lindqvist E et al which stated that presence of RF & ACPAs are predictors of radiographicdamage.[11] In extra-articular manifestations parameter, in seropositive group 20 patients had extra-articular manifestations (40% of patients) as compared to only 6 patients in seronegative group (12% of patients). In this respect, between the two groups, p-value was significant. Anaemia, subcutaneous nodules, episcleritis, interstitial lung disease, ischaemic heart disease, peripheral neuropathy, secondary Sjogren Syndrome & small airway disease were the extra-articular manifestations noted. Among them, anaemia was noted to be most common, with 10 patients detected with it in seropositive group & 4 patients in seronegative group. Turesson C et al had found Subcutaneous nodules(31.2 %) as most common extraarticular manifestation in RA patient, followed by Secondary Sjogren Syndrome (9.6%), pulmonary fibrosis(5.0%), pericarditis(2.6%), pleuritis(1.9%) & episcleritis(0.75). [12]

LIMITATIONS

First, this study was conducted in only one center, and it would be desirable to extend these studies to a larger number of rheumatologists at multiple-centers. Second, a larger sample size would have increased the power of this study. Thirdly, this study depends largely on DAS28 to assess disease activity.DAS28 has its inherent disadvantages such as exclusion of ankle, foot & T-M joint etc. It also depends largely on E.S.R. which may be secondarily

elevated in other associated conditions. CRP-DAS28 is always not available being costlyinvestigation.

CONCLUSION

This study highlights that seropositive RA patients have higher disease activity, greater joint deformity, X-ray changes & extra-articular manifestations, which were more frequent & serious, than in seronegative patients. There are numerous studies worldwide amongst published literature, which compare these two distinct subsets of RA patients taking into account the various epidemiological, clinical & laboratory parameters enlisted in this study. This study corroborates the data published in them & shows similar results. But the above-mentioned studies have compared the parameters individually & didn't compare all parameters for each patient. But this study enlists the various comparable parameters amongst the two subsets (in a total of 100 patients) into one document & demonstrates the higher preponderance of serious disease (detected clinically & by laboratory findings) in seropositive RA patients in Eastern India.

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