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A cross-sectional study of association of Rheumatoid arthritis with sero-positivity and anaemia in a tertiary care teaching hospital

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Abstract

Background: Rheumatoid arthritis (RA) is an autoimmune disease which mistakenly attacks the joints and inflammatory changes that thicken the joints (the synovium) resulting in swelling and pain in and around the joints. It causes pain, joint deformity and also affects the quality of life. The joint is affected symmetrically. It also can affect body systems, such as the cardiovascular, respiratory systems or other systems, which manifests as extra-articular manifestations. Anaaemia in RA are documented less in India hence this study was undertaken to correlates RA with anaemia as well as its relationship with seropositivity in RA patients. **Materials and Methods:** 60 patients (age between 18-60 years) attending Medicine/Rheumatology out-patient department were included in the study (duration of 12 months) who fulfilled the criteria laid down by ACR (American College of Rheumatology)/EULAR (European League against Rheumatism) for Rheumatoid arthritis. All the subjects underwent the thorough history, clinical examination and laboratory investigations. The relevant data was analyzed with appropriate statistical methods after 12 months duration. **Results:** Extra-articular manifestations in the total subjects were found to be 41.67% where the number of subjects was mostly between 31-40 years with incidence more in the female. Extra-articular manifestations were mostly anemia which was present in 36.67% of cases. Anaemia have a statistically significant value with increase in the duration of the disease (P=0.0230). Rheumatoid Factor (RF) was found positive in 38.2% of subjects with anaemia. **Conclusion:** Anaemia need to be looked carefully as it is associated with more severity in RA. Sero-positivity and anaemia both usually indicate that the rheumatoid arthritis is severe and may affect the quality of life.

Keywords: Rheumatoid Arthritis, Rheumatoid Factor, Anaemia, Seropositivity.

INTRODUCTION

Rheumatoid Arthritis (RA) is the most common cause of inflammatory arthritis affecting around 1% of the population of India [1]. The incidence in women is thrice than the men worldwide [2]. It is the leading cause of pain, disability and poor quality of life [3]. It has a complex history and affected by age of onset, gender, genotype, phenotype and comorbid conditions [4, 5, 6]. It is marked by symmetric peripheral polyarthritis with synovium being the primary target [7]. The cause of RA remains unknown but the pathological mechanism of synovial inflammation may result due to complex interplay of genetic immunology and environmental factors [6, 8, 9].

Rheumatoid Arthritis results in a variety of extra-articular manifestations including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis and hematological abnormalities [10, 11]. It reduces lifespan by 5-10 years depending on the age of onset [12]. Mortality and morbidity increase more with systemic extra-articular manifestation, male gender, rheumatoid factor positive, chronic prednisone use, low socioeconomic status, low education and low functional capacity. The objective of the study is to find the correlation between seropositivity with extra-articular manifestations.

MATERIALS AND METHODS

Study Design

A prospective, observational, cross-sectional study conducted in Department of Medicine at a tertiary care

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teaching hospital. The duration of the study was 12 months. Adults (18-65 years of age) attending Medicine outpatient department or Rheumatology outpatient department in a tertiary care teaching hospital. During the study period, the patients were included according to ACR (American College of Rheumatology)/EULAR (European League against Rheumatism). Every patient with a total point of 6 or more is unequivocally classified as a Rheumatoid Arthritis patient provided he/she has synovitis in at least one joint and given that there is no other diagnosis better explaining the synovitis. Four areas are covered in the diagnosis.

Inclusion criteria

1. Joint involvement: Depending on the type and number of joints up to 5 joints.
2. Serological parameters including the rheumatoid factors as well as ACPA (Anti-citrullinated protein antibody) up to 3 points depending on titer level.
3. Acute phase reactants has 1 point for elevated erythrocyte sedimentation rate (ESR) or elevated C - reactive protein (CRP)
4. Duration of arthritis has 1 point for symptoms lasting six weeks or longer.

Exclusion criteria

1. Males and females less than 18 years of age.
2. Overlapping disease e.g. SLE.
3. Patients above 60 years.
4. Patient suffering from Diabetes Mellitus.
5. Patient having pre-existing renal disease or urinary tract infection.
6. Patient having pre-existing hypertension.
7. Patient suffering from congestive cardiac failure.
8. Patient suffering from the chronic liver disease.

Sample Size

As this is a preliminary study formal sample size is not calculated. Keeping in mind the availability of patients it is decided to include 60 patients (age between 18-60 years) attending Medicine out-patient department or Rheumatology out-patient department for the study duration of 12 months after approval from Ethics committee. Informed consent was taken from all patients. In a case of the patient being incompetent, the primary caregiver staying with the patient will be approached for the same.

All the cases were subjected to a thorough history, clinical examination and laboratory investigations. Patient's demographic data were collected at the time of visit to the Medicine/Rheumatology out-patient department.

Socio-demographic Clinical profile data

A structured proforma was used to record certain the demographic variables such as age, gender, education, occupation, religion, type of family, the income of the patient and family. Blood routine examination, Random blood sugar (RBS), Serum Creatinine, BUN, SGOT, SGPT, Serum Uric Acid, ESR, CRP, Fasting Lipid Profile, Iron Profile, Urine routine examination, Rheumatoid Factor were examined in all patients. ANA, Anti-CCP antibody, Chest X-Ray, Joint X-Ray, ECG, Ultrasound W/A, CT Thorax, Nerve conduction velocity test and ECHO had been done in selected patients, if clinically needed.

Assessment of disease activity and damage were done as follows:

1. Tender Joint Count: ACR tender joint counts include an assessment of 28 joints including PIPs (n=10), MCPs (n=10), Wrists (n=2), Elbows (n=2), Shoulders (n=2) and Knees (n=2)
2. Swollen Joint Count: To check for fluctuance of the swollen joints. ACR tender joint counts include an assessment of 28 joints mentioned above.
3. Patient's assessment of pain: A horizontal visual analog scale (usually 10 cm) is used for assessment of the patient's current level of pain.
4. Patient global assessment of disease activity: It was assessed for the patient's overall prognosis regarding arthritis. It was assessed according to an acceptable method for determination by asking the question from the arthritis impact management scale (AIMS).
5. Physician global assessment of disease activity: A visual analog scale (0-10 cm) measure the physician's global assessment of current disease activity.
6. Acute Phase Reactant Value for ESR or CRP level.

Quantification of Current Disease Activity

Disease Activity Score-28 (DAS28) combines single measure into an overall, continuous measure of Rheumatoid Arthritis disease activity. The use of a single index has advantages because the simultaneous interpretation of several measures of RA disease activity which includes 28 tender joints count, 28 swollen joint counts, erythrocyte sedimentation rate and general health assessment on a visual analog scale. It can also calculate C-reactive protein (CRP) instead of ESR.

Response Scale of 28 tender joints count (28TJC) and 28 swollen joint counts (28SJC) both range from 0 to 28. ESR may range from 0 to 150 and general health (GH) ranges from 0 to 100. The range of the DAS28 is 0-9.4. The levels of RA disease activity can be interpreted as scoring of DAS28. High disease activity if DAS is more than 5.1, low disease activity if DAS is less than 3.2 and remission if the score is less than 2.6. The EULAR response criteria are also based on the DAS-28 and are expressed in terms of both the change in disease activity.

Ethical consideration

Ethical clearance was taken from the Institutional Ethical Committee.

Statistical analysis

Data was compiled using Microsoft Excel and analyzed using SPSS Version 21. Quantitative variables were expressed as numbers and percentages. Normality distribution of data was first determined by Kolmogorov–Smirnov test. As data were found to be normally distributed, the parametric analysis was used throughout the analysis. Chi-square test was used to study the correlation between Rheumatoid Arthritis, anaemia and inflammatory markers. P-values less than 0.05 were considered statistically significant for all tests.

RESULTS

In the study, Table 1 presents the age distribution of all patients present with Rheumatoid Arthritis. The prevalence of extra-articular manifestations in the total subjects was found to be about 42.67%. The age at onset ranged from 19 to 65 years with a mean age of 42.07±10.6 years. Maximum incidence was between 31-40 years (38.33%). The age of onset in female ranged from 19 to 60 years with mean age of 39.18 years and in the male, the age of onset ranged from 28 to 65 years with mean age of 50.73 years. The incidence of RA was found more in the females (nearly three-fourth) than male.

In Table 2, the subjects showed the extra-articular manifestation of the disease. Anaemia was present in 36.67 of cases and constitutional symptoms were present in 33% of cases. Peripheral neuropathy was present in 31.7% of the subjects. Pulmonary manifestations and dyslipidemia were present in 23.3% each of all the subjects. In Table 3, anaemia increase with the duration of the disease with statistically significant value (P=0.023). It was found that duration of the disease has a positive correlation with anaemia if the duration of the disease

was more than four years. Nearly 48.1% of patients have duration of anaemia between two to five years. As regards to prevalence of extra-articular manifestations with regards to serostatus. It was found that Rheumatoid Factor (RF) was found positive in 38.2% of the total subjects with anaemia. [Table 4]

Table 1: Age distribution of patients with Rheumatoid Arthritis (RA).

Age at onset (in years)	Number (n)	Percentage (%)
18-30	9	15.00
31-40	23	33.33
41-50	15	25.00
51-60	12	20.00
>60	1	1.67
Total	60	100
Mean= 42.07±10.6		

Table 2: Extra articular (EA) features with regards to Seropositivity.

EA Features	Seropositive		Seronegative		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Constitutional	18	90.0	2	10.0	20	33.3
Anaemia	19	86.37	3	18.19	22	36.67
Subcutaneous nodule	8	88.89	1	11.11	9	15.00
Pulmonary	13	92.86	1	7.14	14	23.33
Hepatomegaly	5	83.33	1	16.67	6	10.0
Spleenomegaly	6	85.71	1	14.29	7	11.67
Cardiovascular	4	80.0	1	20.0	5	8.33
Neurological	18	94.74	1	5.26	19	31.67
Eye	6	66.67	3	33.33	9	15.0
Sjogrens	7	77.78	2	22.22	9	15.0
Vasculitis	4	100.0	0	0.0	4	6.67
Renal	4	80.0	1	20.0	5	8.33
Osteoporosis/ Osteopenia	11	91.67	1	8.33	12	20
Lipid abnormalities	12	86.71	2	14.29	14	23.33

Table 3: Duration of disease and prevalence of Anaemia in Rheumatoid Arthritis patients.

Duration of symptoms(Months)	Total number of patients	Anaemia		P value
		Present	Absent	
≤12	12	2(16.7%)	10(83.3%)	0.0230
13-24	16	3(18.8%)	13(81.2%)	
25-60	27	13(48.1%)	14(51.9%)	
>60	5	4(80%)	1(20%)	
Overall	60	22(36.67%)	38(63.33%)	

Note: *P* value <0.05 is considered significant

Table 4: Anaemia in Rheumatoid Arthritis with regards to Seropositivity.

Anaemia	Present	Absent	Total
Seropositive	19(38.2%)	28(61.8%)	47
Seronegative	3(23.1%)	10(76.9%)	13
Overall	22(36.67%)	39(63.33%)	60
P value	0.033		

Note: *P* value <0.05 is considered significant

DISCUSSION

Rheumatoid arthritis is a chronic multisystem disabling disease with various extra-articular manifestations frequently leading to physical and psychological dependence with considerable economic consequences, occurring in about 0.75% of the adult population in India. As there is a paucity of literature on the impact of RA on anaemia in India, thus this study was untaken to evaluate anaemia in RA and correlates with duration of disease and seropositivity.

Anaemia is a frequently occurring extra-articular manifestation in patients with rheumatoid

arthritis (RA). Anaemia of chronic disease and iron deficiency anaemia are considered to be the most important causes [13]. The prevalence of anaemia in RA was found to range from 30% to 70% in cross sectional studies which is similar to our study [14].

In our study, nearly half of patients (41.7%) had one or more extra-articular manifestations with a high incidence of anemia (36.7%) followed by constitutional symptoms (33.3%), peripheral neuropathy (31.7%), pulmonary manifestations (23.3%) and dyslipidemia (23.3%). These findings were very similar to those found in another study [15]. Anaemia of RA has a close association with inflammatory mediators like RF, CRF and also elevated levels of cytokines (TNF-alpha, IL-1, and IL-6) and complement components (C1q, C3 and C4) [19]. These mediators play a direct pathogenic role in the development of anaemia [16]. It correlates well with the well-established facts that anaemia in RA has a positive correlation with seropositivity due to the inflammatory pathogenesis of the diseases [11]. anaemia appeared as a frequent and dynamic manifestation in this longitudinal study of patients with recent onset RA. It occurred rapidly after the onset of the symptoms of arthritis.

CONCLUSION

Extra-articular manifestations are present in a substantial number of RA patients which is often overlooked or missed by the physician. Anaemia is associated with more chronic course and the majority of them are more common in long duration disease. Sero-positivity also has a positive relationship with anaemia and presence of both usually indicates a more severe disease. One of the limitations of the study was that the sample size is not large and also a large-scale study with longer duration is needed to find out and further strengthen the correlations.

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