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RA FACTOR AND CRP: MARKERS FOR RHEUMATOID ARTHRITIS

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ABSTRACT

Rheumatoid arthritis (RA) is chronic disease involving mostly small joints of hand and feet. Antibody – antigen reaction are used for diagnosis. The correct choice and interpretation of these tests depends on detailed knowledge of patients. The aim of our study was to assess serum CRP and RA factor as marker for RA. The study was conducted at department of microbiology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad. In total, 100 patients were included. 88% of samples were positive for CRP and 77% for RA factor. Among 88% patients, 28.4% were male and 71.6% were female whereas in 77% cases of RA, 27.2% were males and 72.8% were female. There was significant association of gender with CRP ($p < 0.05$).The frequency of positive result was high in age group 41-50 years for both CRP (30.7%) and RA factor (26.1%).The association was found significant between age group and CRP only ($p<0.01$). When the association between CRP and RA factor was determined, it was found highly significant ($p<0.001$). RA factor and CRP are the markers used for diagnosis of rheumatoid arthritis. RA factor is more specific and can be detectable in serum only in conditions of Rheumatoid Arthritis.

KEYWORDS: RA (Rheumatoid arthritis), CRP (C- reactive protein), antibody, antigen.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease, most often involving the small joints of the hands and feet, although any synovial joint can be affected. It affects 1–2% of the world population with a female-to-male ratio of 2.5:1.[1] Many of the clinical features and management strategies in RA are reverent across the spectrum of inflammatory joint disease. The clinical course is usually life-long, with intermittent exacerbations and remission and highly variable severity.[2]

Recognition of RA as early as possible is important, not only because a significant proportion of the patients develops irreversible joint damage shortly after disease onset[3] but also because of the risks associated with its treatment.[4] The diagnosis of RA depends primarily on the American College of Rheumatology (ACR) 1987 revised criteria. A patient is considered to have RA if at least four of the seven criteria have been present for at least six weeks; of which the only laboratory test criterion is the presence of serum Rheumatoid Factor (RF).[1]

Immunodiagnostic or serodiagnostic studies of antigen – antibody reaction are used for diagnosis of infectious disease, autoimmune disease, immune allergies and neoplastic disease.[5] Pathologically, autoimmune disorders are produced by autoantibodies that are directed against self-antigens example, including systemic rheumatic diseases such as rheumatoid arthritis and systemic lupus erythematosis.[6]

An increasing number of autoantibodies can be detected. Production of some of these is a common and age related phenomenon that may be exaggerated by chronic inflammation. Their mere presence, therefore often has low diagnostic specificity and little clinical relevance. If present in high concentration, however, their disease specificity often increases. It is therefore important to know how much antibodies are present (the titer or concentration in units) rather than just whether they are detectable. The correct choice and interpretation of these tests depend on detailed knowledge of the patient. Different detection and assay system exist for many of these autoantibodies, and close liaison with the local immunology service required.[7] AntiNuclear Antibody (ANA), Rheumatoid Factor (RF) and C-Reactive Protein (CRP) are among the three most frequently used as non-specific markers of autoimmunity and can occur alone or in conjugation with autoantibody specificity in rheumatic disease.[8]

MATERIALS AND METHODS

The present study was carried out in Department of Microbiology, Teerthanker Mahaveer Medical College & research Centre (TMMC&RC) Moradabad, Utter Pradesh. Total of 100 patients were included. Suspected Rheumatoid Arthritis patients and patients currently diagnosed with arthritis with or without co morbidities were included whereas patients diagnosed before 16 years of age, patients with arthritis due to other disease, such as gout, spondylitis, Reiter's syndrome, psoriasis, inflammatory bowel disease, systemic lupus erythema disease, pregnant and lactating women were excluded from the study.

Patient records were collected and a standard form was used for all relevant clinical information on demographic, clinical, laboratory, and therapeutic characteristics from the time of diagnosis until the end of the study. Patient was considered seropositive if the CRP level was more than 0.6mg/dl and seronegative if CRP was less than that. In case of RF, patients were considered seropositive if IgM RF test result was higher than 40IU/ml and seronegative if IgM RF was less than that.

RESULTS

Table: 1 Serology result of CRP and RA factor among patients

	CRP	RA
Seropositive	88(88%)	77 (77%)
Seronegative	12 (12%)	23 (23%)
Total	100	100

Table: 2 CRP and RA Distribution among Gender

Gender	CRP		RA Factor	
	Seropositive	**Seronegative**	**Seropositive**	**Seronegative**
Male	25 (28.4 %)	8 (66.7 %)	21 (27.2%)	12 (52.2%)
Female	63 (71.6%)	4 (33.3%)	56 (72.8%)	11 (47.8%)
Total	88 (100 %)	12 (100%)	77 (100%)	23 (100%)
	$\chi 2$ test	**p value=<0.001****	**$\chi 2$ test**	**p value=<0.05***

** highly significant
* significant

Table 3: Agewise CRP and RA factor results

Age	CRP		RA Factor	
	Seropositive	**Seronegative**	**Seropositive**	**Seronegative**
21-30	2 (2.3%)	3 (25%)	2(2.6%)	3 (13%)
31-40	20 (22.8%)	5 (41.8%)	20(26%)	5 (21.8%)
41-50	27 (30.7%)	1 (8.3%)	22(28.6)	6 (26.1%)
51-60	23 (26.1%)	1 (8.3%)	20(26%)	4 (17.4%)
61-70	12 (13.6%)	1 (8.3%)	10(13%)	3 (13%)
71-80	4 (4.5%)	1 (8.3%)	3(3.8%)	2 (8.7%)
Total	88 (100%)	12 (100%)	77(100%)	23(100%)
	$\chi 2$ test	**p value <0.01****	**$\chi 2$ test**	**p value >0.05**

** highly significant

88% samples were observed to be seropositive for CRP and remaining 12% were found to be seronegative. Out of 88% seropositive samples 71.6% were female and 28.4% were male respectively. The highest seropositive results were seen in age group of 41-50 year (30.7%). In case of Rheumatoid arthritis patients, 77% samples were observed to be seropositive for RA factor and remaining 23% were found to be seronegative. Out of 77% seropositive sample 27.2% were of male and 72.8% were of female. The highest seropositive result were in age group of 41-50 (28.6%. The CRP and RA factor were significantly associated with gender ($p<0.001$** for CRP and $p<0.05$* for RA factor). When compared agewise, we could find significant association between age group and CRP only ($p<0.01$**) but not in case of RA factor ($p>0.05$).

Table 4: Association between CRP and RA

CRP	RA Factor		Total
	Seropositive	Seronegative	
Seropositive	75	13	88
Seronegative	2	10	12
Total	77	23	100
$\chi 2$ test	p value<0.001**		

** highly significant

75 samples were observed to be seropositive for both CRP and RA factor and the association between CRP and RA factor was highly significant ($p<0.001$).

DISCUSSION

In our study the highest frequency of rheumatoid arthritis patients were observed to be in 41-50 year age group with mean age of 48±12.2. The male female ratio in was 1:2.03 with 33 men and 67 women. Study of Ahmad M et.al, showed that the peak occurrence of RA was in the age group 51-65 year age was (58.69%) with male : female was 1:6.5[9]

Among the 100 patients, 77(77%) were seropositive and 23(23%) were seronegative for RA factor. In the seropositive group, the male female ratio was 1:2.6 (21 males and 56 females). The male female ratio was 1.09:1 (12 males and 11 females) in the seronegative group. The highest seropositive results were in age group of 41-50 year age (26.1%). In a Korean study done in 109 patients, 64(58.7%) were seropositive and 45(41.3%) were seronegative for the RA factor. In the seropositive group, the male female ratio was 1:4.3, with 12 men 52 women. The male female ratio was 1:6.5 in the seronegative group, with 6 men and 39 women.[10] Similarly, the results for the assessment for CRP showed 88% seropositive and remaining 12% were seronegative. . In the seropositive group, the male female ratio was 1:2.52, with 25 men 63 women. The highest CRP positive results were in 41-50 year age was 30.7%.

In our study both CRP as well as RA factor were higher in female comparing to male. This might be due to the more sensitive immune response in female than male, in most non-rheumatic conditions, titers of RF are lower than in RA.[11]The specificity of RF reaction for RA increases with serum titers.[12] This differs from recent study, because according to study by Wisal Salman et.al the highest titers of RF was found in patients with SLE are components of intracellular T cell activation. In normal health these antigens are hidden from the immune system and do not provoke an immune response. Although the triggers that lead to auto antibody production in SLE are unknown, one mechanism may be expression of novel antigen on the cell surface during apoptosis. This hypothesis is supported by the fact that environmental factors that associated with flares of lupus increase oxidative stress and subsequent apoptosis. Such factors include exposure to sun light and artificial UV light, pregnancy and infection[13] or may be due to some genetic factors, so further analysis in families having a history of RA and SLE may be helpful in predicting the detection of immune response and precise genetic susceptibility to RA and SLE, it will also be useful to include other gene markers like α1 anti trypsin, which are thought to be associated with severe seropositive RA and SLE. Studies have shown that the prevalence of RF and other auto antibodies in general population tends to decline beyond the age of 70- 80 years.[14] This decrease may be related to an increased mortality rate among autoantibody-positive individuals.

Amos et al. reported that RA patients with high ESR and CRP have serious radiological changes including bony erosion, regardless of RF status.[15] It was later revealed in a study that the seropositive group shows a higher inflammation degree, lower hemoglobin level, and increased WBC and platelet levels than the seronegative group.[16] However, there were no statistically significant differences between groups except that all RF positive patients showed progression on follow up X-Rays in the Korean study.

Combined diagnostic approach to Rheumatoid arthritis using anti-cyclic citrullinated peptide antibodies and rheumatoid factor revealed that anti CCP antibody was positive in 81.8% of the patients with titres equal to or above 800 units/ml while RF was positive in 77.2%.[17] In a meta-analysis published in 2007 it was found that anti CCP antibody displays sensitivities comparable to that of RF (approx. 80%) but with superior specificity (98%).[18] Anti-CCP antibody represents a superior serological marker for RA as it is highly specific for the disease,[72] able to distinguish RA from other arthritis that mimic RA,[19] detectable very early in disease and also helpful in predicting disease outcome[20] thus helping in earlier and focused anti-rheumatoid therapy.

CONCLUSION

RA factor and CRP are the markers used for diagnosis of rheumatoid arthritis. RA factor is a better marker of Rheumatoid Arthritis though CRP positive cases (90%) were greater than RA positive cases (77%). This is because CRP is nonspecific and its level can increase in any other inflammatory conditions also whereas RA factor is more specific and can be detectable in serum only in conditions of Rheumatoid Arthritis.

From previous studies we can also conclude that anti-CCP antibody detection may be used in combination with RF for an optimal early diagnostic strategy of RA.

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