

Seroprevalence of C - Reactive Protein in Rheumatoid Arthritis Cases: A Retrospective Study in a Tertiary Care Hospital in South India

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Original Research Article

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Article History

Received: 01.11.2018

Accepted: 08.11.2018

Published: 30.11.2018

DOI:

10.36347/sjams.2018.v06i11.009



Abstract: Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune inflammatory disease that affects mainly the small joints of the hands and feet. It is one of the most common inflammatory joint diseases that compromise quality of life, cause disability and even premature mortality. RA is widely prevalent throughout the world, mainly affecting older women. Clinical manifestations consist of pain, swelling and tenderness of the small joints of the hands. Since RA is a systemic disease, patients may have accompanying constitutional symptoms such as fever, weight loss and fatigue. At initial patient evaluation complete blood count including ESR, liver function tests, kidney function tests, and CRP should be done. CRP (C-reactive protein) is an important biomarker of inflammation in RA which can help to monitor disease progression. Rheumatoid factor (RF) is detectable during the course of disease in approximately 75% to 85% of patients with RA. High titres of RF are associated with aggressive, destructive joint disease and extra-articular complications such as interstitial lung disease and rheumatoid vasculitis. The present study was undertaken to retrospectively analyse the prevalence of RF and association with CRP in patients presenting to a tertiary care hospital in South India. Of the 631 sera specimens submitted for RF test, 34 were positive i.e. there was 5.4% seroprevalence of RF in the study population. Majority of the cases i.e. 73% were females; 44% of RF positive patients were in the age group of 21-40 years, followed by 35% in the 41-60 years age group. Among the RF seropositive patients, elevated CRP levels were found in 41% of the cases. Thus the role of CRP as an acute inflammatory marker and important diagnostic indicator in RA is confirmed by the results of our study.

Keywords: Rheumatoid factor, C-reactive protein, Rheumatoid arthritis, Seroprevalence.

INTRODUCTION

Rheumatoid arthritis (RA) is a widely prevalent chronic, systemic, autoimmune inflammatory disease that affects mainly the small joints of the hands and feet with a female preponderance [1]. It is one of the most common inflammatory joint diseases that compromise quality of life, cause disability and even premature mortality. RA is widely prevalent throughout the world. The overall worldwide prevalence is 0.8% and steadily increases to 5% in women over the age of 70. RA is two to three times more common in women compared to men [2]. In India the prevalence has been estimated to be 0.7% [3]. The inflammatory process primarily affects the lining of the synovium, in contrast to osteoarthritis which primarily involves the cartilage. The inflamed synovium leads to erosions of the cartilage and bone and if the inflammatory process is unchecked, it leads to joint deformity. Clinical manifestations consist of pain, swelling and tenderness of the small joints of the hands. Since RA is a systemic disease patients may have accompanying constitutional

symptoms such as fever, weight loss and fatigue [4]. The most common form of presentation is gradual and insidious onset of joint pain and swelling occurring over weeks to months. RA is classically a polyarticular disease but occasionally it may present as a monoarthritis [5].

Extra-articular manifestations/complications of RA may involve various organs including the eyes (Keratoconjunctivitis sicca, episcleritis and scleritis). Rheumatoid nodules are firm, non-tender swellings, which develop over extensor surfaces of the body especially the elbows and are frequently adherent to the underlying periosteum. Pleuritis, pleural effusions and a slowly progressive pulmonary fibrosis associated with interstitial pattern pneumonia usually occur in RA. The most common cardiac manifestation is pericardial effusion and pericarditis, which is asymptomatic and is mostly found only on autopsies. It is increasingly recognised that the most common cause of death in patients with RA is cardiovascular disease [6].

At initial patient evaluation, complete blood count including ESR, liver function tests, kidney function tests and CRP should be done. ESR and CRP are the two most important biomarkers of inflammation in RA. These markers are usually elevated in RA patients with active disease and decline with treatment. High ESR and CRP at the onset of disease are predictive of more aggressive disease and potentially worse prognosis. The inflammatory markers ESR and CRP along with the patients' symptoms, the number of swollen joints, the number of tender joints are incorporated in to a score called as disease activity score (DAS) and is very useful to monitor disease activity over time [6, 7]. Rheumatoid factor (RF) is antibodies against the Fc portion of IgG and can be of any immunoglobulin subclass (IgA, IgG, and IgM) but is most commonly IgM. RF can be estimated in the laboratory by enzyme-linked immunosorbent assay (ELISA), or by nephelometry or by latex fixation. The cut off value for a positive RF varies depends on the methodology used in the local laboratory, but a common cut off point is greater than 45 IU/mL by ELISA or laser nephelometry, or greater than a titer of 1:80 by latex fixation [7].

RF is detectable during the course of disease in approximately 75% to 85% of patients with RA. RF is approximately 69% sensitive and 85% specific for the diagnosis of RA. The result of a positive RF should be carefully interpreted in the light of clinical findings. High titres of RF are associated with aggressive, destructive joint disease and extra-articular complications of RA, such as interstitial lung disease and rheumatoid vasculitis. As an inflammatory biomarker for RA, CRP correlates with disease activity, histological changes in the synovium and radiological progression, responding quickly to changes in disease activity [8].

The present study was undertaken to retrospectively analyse the prevalence of RF and association with CRP in patients presenting to a tertiary care hospital in South India as there is a lack of sufficient information from our region regarding the same.

MATERIALS AND METHODS

A retrospective analysis of specimens tested in Serology section of the Clinical Microbiology Laboratory of Gandhi Hospital, attached to Gandhi Medical College, Hyderabad, and Telangana during a one and half year period, 01 January 2015 to 30 June 2016 was done. Data retrieval was done through the Health4All software application which was used as a laboratory information management system. Of the 26,552 specimens submitted for serological analysis

during this period, 631 were presumably sourced from patients with joint disorders and subjected to testing for Rheumatoid Factor (RF). Analysis for presence of C-reactive protein (CRP) was also done. Both tests were done by rapid, latex slide agglutination reactions by qualitative and semi-quantitative methods as per manufacturer's instructions and the results were tabulated. Demographic characteristics of the study population, namely age and gender, were documented and the location of the patients at the time of sample submission was noted.

RESULTS AND DISCUSSION

Of the 631 sera specimens submitted for RF test, 34 were positive implying there was 5.4% seroprevalence of RF in the study population. The RF seropositive set comprised 73% females and 27% males, thus there was a clear female preponderance. Age-wise distribution of the RF seropositive cohort revealed that 44% of RF positive patients were in the age group of 21-40 years, followed by 35% in the 41-60 years age group (refer Table 1). Our results are similar to those of another study from South India wherein 7% seroprevalence of RF was reported and the majority of patients belonged to the age-group of 20-50 years [9]. So, majority of the patients in our study were younger females rather than older females; this may possibly reflect a lower age of onset of RA in our setting or perhaps could be explained by a greater initiative taken by younger patients to seek medical attention for their symptoms while older patients, due to various reasons, may not be able to access healthcare facilities for symptoms such as joint pains which are perceived to be commonly associated with the ageing process.

Elevated CRP levels were found in 41% (14/34) RF seropositive patients. Thus the role of CRP as an acute inflammatory marker and important diagnostic indicator in RA is confirmed by the results of our study. The diagnostic role of CRP in RA has been known for the past few decades and that it is a better marker of the inflammatory response in RA than ESR [10]. More recently, it has been emphasized that CRP is the most useful marker in the prospective evaluation of patients with rheumatoid arthritis [11]. Stress-induced increases in CRP may be a particular characteristic of patients with RA with high disease activity. CRP is a well established risk factor for myocardial infarction [12]. Recently, it has been suggested that CRP is more than merely a risk factor, acting as a causal agent facilitating thrombotic occlusion and atherosclerosis [13]. Thus, the stress-induced increase in CRP in patients with RA with high disease activity over and above their high baseline levels might contribute to their increased risk for cardiovascular complications [14].

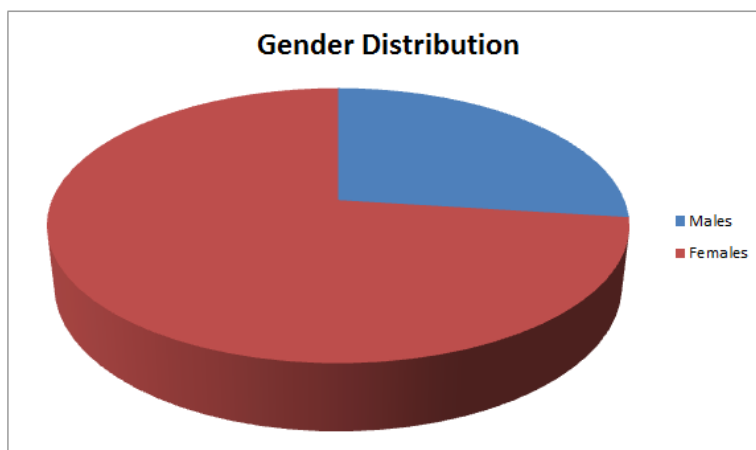


Table-1: Age-wise distribution of patients among RF seropositive cases (Total No. = 34)

Age-group (years)	No. of patients (%)
0 - 20	1 (3)
21-40	15 (44)
41-60	12 (35)
> 60	6 (18)

Patients were chiefly referred from the General Medicine units followed closely by Orthopaedics units (Table 2).

Table-2: Ward - wise distribution of patients among RF seropositive cases(Total No. = 34)

Name of the ward/unit	Percentage of patients
Orthopedics	36.5
General Medicine	39
Neurology	4.9
Gynecology	2.4

CONCLUSIONS

In conclusion, our study reveals a RF seroprevalence corresponding with similar studies from the region. The finding of elevated CRP levels in a significant proportion of RF seropositive cases reaffirms its cardinal role in the diagnostic workup of rheumatoid arthritis. Moreover, in view of the association of CRP with cardiovascular complications in RA cases, a closer monitoring of CRP levels is definitely warranted to deliver better health care and improve outcomes.

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