ORIGINAL ARTICLE

Frequency of Rheumatoid Factor Positivity in Patients of Rheumatoid Arthritis Report of 95 cases from Lahore, Pakistan

MANAAL AFZAAL[1], ASMA MUNIR[2], MONA AZIZ[3], ATIYA MAHBOOB[4], MUHAMMAD ONEEB SALEEMI[5]
[1]Senior Registrar, Dept of Dermatology, Shaikh Zayed FPGMI Lahore, [2]Consultant hematologist, [3]Assoc Professor, Dept of Haematology, Shaikh Zayed FPGMI Lahore, [4]Professor, Dept of Dermatology, Shaikh Zayed FPGMI Lahore, [5]Demonstrator, Dept of Anatomy, Shaikh Zayed FPGMI
Address for correspondence: Dr. Manaal Afzaal, Senior Registrar Deptt of Dermatology, Shaikh Zayed FPGMI. Lahore. E-mail: manaal_afzaal@yahoo.com

ABSTRACT
Background: Rheumatoid arthritis is a chronic systemic autoimmune disease affecting primarily joints. Rheumatoid factors are autoantibodies reactive with Fc portion of Ig G. Presence of rheumatoid factor can be used to confirm the diagnosis in individuals with a suggestive clinical presentation.
Objectives: To determine the frequency of rheumatoid factor positivity in patients with rheumatoid arthritis**.**
Study Design: Descriptive case series.
Place and duration of study: Department of Medicine, Shaikh Zayed Medical Institute, Lahore from 01-01-13 to 30-06-13.
Subjects and Methods: Ninety five patients with rheumatoid arthritis of both genders above fifteen years of age fulfilling the ACR 2010 criteria were evaluated for presence of rheumatoid factor in blood.
Results: There were 14 (14.7%) males and 81 (85.3%) female patients, male to female ratio was 1:5.8. Mean age of the patients was 42.38 ±10.7 years. 76 (80%) tested positive for Rheumatoid Factor IgM.
Conclusion: Rheumatoid factor positivity in rheumatoid arthritis is quite common. Females are more commonly affected.

Key Words: Rheumatoid arthritis**,** rheumatoid factor.

INTRODUCTION
Rheumatoid arthritis (RA) is an autoimmune disease affecting 0.5-2% of the population[1]. Its prevalence in Pakistan is 0.9-1.98% and 0.5-1% in US. It affects women twice as often as men and incidence rises with increasing age.[2] The diagnosis of RA in early disease stages is important for preventing irreversible joint damage, consequent disability and deterioration of quality of life in later stages of disease.[3]

In the current ACR 2010 criteria for "definite rheumatoid arthritis" is based on the confirmed presence of synovitis in at least one joint, absence of an alternate diagnosis better explaining the synovitis, and achievement of a total score of ≥6 (of a possible 10) on a scoring system. The score is derived from four criteria: the number and site of affected joints (range 0-5), serological abnormality (elevated levels of rheumatoid factor (RF) or anti-citrullinated protein antibody; range 0-3), elevated acute phase response or ESR (range 0-1), and symptom duration (<6 or ≥6 weeks; range 0-1).[3] 40% of RA patients are positive for RF at clinical onset of the disease while 80% patients will eventually be seropositive as the disease advances. [4]

Rheumatoid factors are autoantibodies reactive with Fc portion of IgG. Widely utilized tests largely detect IgM RF.[5] It is the most common RF isotype in Caucasian RA populations.[6] Some studies have implicated IgA RF as especially associated with extra-articular RA and with erosive RA.[7] Simultaneous detection of IgM and IgA RF has been shown to be highly specific for RA in Iceland.[6] Presence of RF can be used to confirm the diagnosis in individuals with a suggestive clinical presentation and if present in high titre to designate patients at risk for severe systemic disease.[5]

The present study was conducted to detect the frequency of RF positivity in our RA patients.

MATERIAL AND METHODS
Ninety five patients with RA of both genders above fifteen years of age fulfilling the ACR 2010 criteria were enrolled in the study from Medical in- and outpatients' departments of Shaikh Zayed Medical Complex, Lahore. They were evaluated for age and gender. Detailed clinical history and

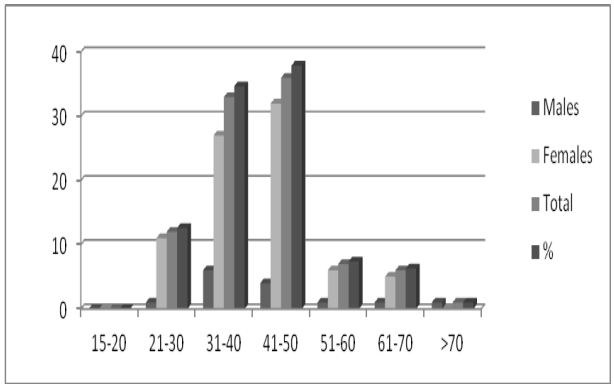
examination were performed and recorded on a predesigned performa after taking their written informed consent. Serum sample of enrolled patients were taken and tested to determine RF by doing RF – Latex test. This test is a rapid agglutination procedure, based on modification of the Singer method, [8] developed for the direct detection and the semi – quantitation on a slide, of RF in serum. The minimum detectable unit is of approximately 8 IU/ml (6-16 IU/ml), tested against a RF standard traceable to WHO Reference Material 64/1. Diagnostic specificity of this test is 98.8%.

All data was entered and analyzed by using SPSS-17.0. Demographic variables were reported as frequency and percentages. Numerical data was reported as Mean ± SD.

RESULTS

Ninety five cases of RA fulfilling the ACR 2010 criteria were included in the study. 81(85.3%) were females and 14 (14.7%) were males. Female to male ratio was 5.8:1. Age ranged from 20 to 74 years. Mean age for the case series was 42.38±10.67 years. Mean age for females was 42.22±10.50# years and for males it was 43.29±12.3 years. Most of the patients were in the age group of 31-50 years (Figure -1).

Figure 1: Age and gender distribution of patients with RA (n= 95)



Seventy six of ninety five (80%) patients were found to have positive RF. 63 (66.3%) were females and 13 (13.68%) were males. Female to male ratio was 4.84:1 (Figure 2). Age ranged from 20 to 70 years. Mean age for these patients was 41.58±10.23 years. The maximum number (39.5%) of patients were in 41-50 years age group followed by 31-40 years age group (32.9%) (Table 1 and 2).

Figure 2: Gender distribution of RA patients with positive & negative RF (n=95)

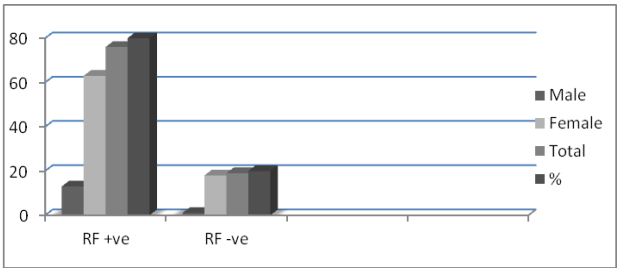


Table 1: Age and gender distribution of patients with RA (n=95)

RF	Gender	Age range	Mean±SD
Positive	M (n=13)	27-60	40.9± 8.8
	F (n=63)	20-70	41.7±10.6
	Total (n=76)	20-70	41.6± 10.2
Negative	M (n=1)	74	74
	F (n=18)	30-64	44± 10.2
	Total (n=19)	30-74	45.6± 12

Table 2: Age and gender distribution of RA patients with positive RF (n=76)

Age group	Males	Females	Total	%
15-20	0	0	0	0
20-30	1	10	11	14.5
31-40	6	19	25	32.9
41-50	4	26	30	39.5
51-60	1	6	7	9.2
61-70	1	2	3	3.9

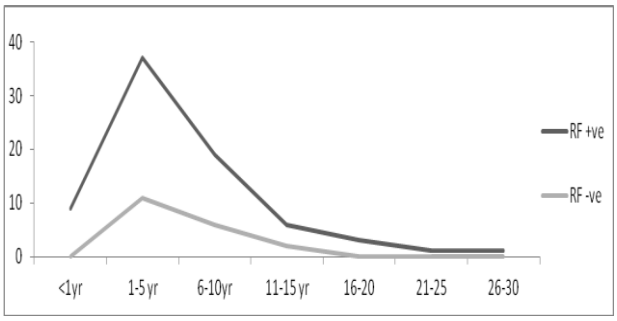
The duration of disease in RA patients varied from 2 months to 30 years (mean 6.1±5.4 years). In those with positive RF it ranged from 0.2-30 years (mean 6.2±5.8). (Table 3)

Table 3: Duration of disease in RA patients (n=95)

RF	Gender	Duration range (yrs)	Mean ±SD
Positive	M (n=13)	0.2-18	5.7±6.3
	F (n=63)	0.3-30	6.2±5.7
	Total (n=76)	0.2-30	6.2±5.8
Negative	M (n=1)	1.0	1.0
	F (n=18)	1-12	5.9±3.5
	Total (n=19)	1-12	5.6±3.6
Total	(n=95)	0.2-30	6.1±5.4

At presentation 60.5% RF positive patients had disease for 5 years. (Figure 3)

Figure 3: RF status and duration of disease in study population (n=95)



DISCUSSION

RA is a common chronic inflammatory disease of synovial joints, characterized by symmetrical, destructive and deforming polyarthritis with systemic disturbances and extra-articular manifestations. [9] RA has a significant social, economical and psychological impact on patients and their families. Early intervention is crucial in preventing irreversible joint damage. Thus, it is important to diagnose RA at an early stage.[10]

RF, auto antibodies reactive with the Fc portion of IgG, are found in 75% of patient with RA. IgM is the most frequently studied RF isotype.[6] RF is found in 5% of healthy persons. The frequency of RF in general population increases with age and 10-20% of individuals over 65 years old have a positive test. RF is also positive in systemic lupuserythematosis, Sjögren's syndrome, chronic liver diseases, sarcoidosis, interstitial pulmonary fibrosis, hepatitis B, tuberculosis, malaria, leprosy and syphilis.[5]

Presence of RF can be employed to confirm a diagnosis in individuals with a suggestive clinical presentation. We carried out this study to detect presence or absence of RF (positive or negative) in 95 patients of RA.

In the present study female gender predominance (male: female ratio 1:5.8) was found. It is consistent with other studies [2,9,11,12,13]. In present study age of patients at initial visit varied from 20-74years with a mean of 42.38±10.67 years. In other studies [12,13] mean age of patients was 51.4±12.4years and 28 years which are quite different from that of our patients. The mean age of our female patients was 42.2±10.5 years which is almost similar to the age reported by Safeer M et al[5]. Mean age of our male patients was 43.29±12.3 years which is quite different from 39 years reported by Safeer M et al.[5]

72.63% patients in current series of RA patients and 72.36% of RA patients with positive RF belonged to third and fourth decade of life. It is very similar to reported age groups of other studies. [2,9,12]

In present study seventy six (80%) patients were RF positive. A study conducted by Bas et al[14] RF was positive in 88% of patients with RA which is slightly higher as compared to our study. In another study[11] RF was found to be positive in 74.4% patient which is lower than that in our cases. In our study 66.3% females and 13.68% males were positive for RF. In a study conducted by Safeer M et al[5], 69% female patients were positive and all male patients were negative for RF.

The duration of the disease in our RA patients with positive RF varied from two months to thirty years (mean 6.1±5.4 years) which is quite high from that reported by Johnson PM[13] in which the mean duration of symptoms before inclusion was 12±7 months.

CONCLUSION

RA is a progressive, chronic inflammatory disease which generally leads to progressive joint destruction and consequent disability and reduction of quality of life if not treated promptly and adequately. Detection of RF may help to diagnose and manage RA at an early stage to reduce the associated morbidity and mortality.

REFERENCES

1. Neovius M, Simard JF, Askling J. Nationwide prevalence of rheumatoid arthritis and penetration of disease-modifying drugs in Sweden. Ann Rheum Dis 2011;70:624-9.
2. Alam SM, Kidwai AA, Jafri SR, Qureshi BM, Sami A, Qureshi HH, et al. Epidemiology of rheumatoid arthritis in a tertiary care unit, Karachi, Pakistan. J Pak Med Assoc 2011;61(2):123-6.
3. 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 Rheum2010;62:2569-81.
4. Kuriya B, Cheng CK, Chen HM, Bykerk VP. Validation of a prediction rule for development

of rheumatoid arthritis in patients with early undifferentiated arthritis. Ann Rheum Dis2009;68:1482-5.
5. Safeer M, Rahman U, Ahmad N, Rehman J, Ubaidullah, Nasir M. Rheumatoid factor and rheumatoid arthritis. KJMS,2011; 3(2): 67-9.
6. Vallbracht I, Rieber J, Oppermann M, Forger F, Siebert U and Helmke K. Diagnostic and clinical value of anti-cyclic citrullinated peptide antibodies compared with rheumatoid factor isotypes in rheumatoid arthritis. Ann Rheum Dis 2004; 63(9): 1079-84.
7. Jonsson T, Arinbjarnarson S, Thorsteinsson J, Steinsson K, Geirsson AJ, Jonsson H, et al. Raised IgA rheumatoid factor but not IgM RF or IgG RF is associated with extra-articular manifestations in rheumatoid arthritis. Scand J Rheumatol 1995; 24(6): 372-5.
8. Singer JM and Plotz CM. Am J Med1956. 21:888.
9. Qayyum A, Mehmood A, Ahmad N. The articular involvement in Rheumatoid Arthritis- A prospective study. Biomedica 2004; 20: 85-9.
10. Cush JJ. Early arthritis clinics: If you build it will they come? J Rheumatol 2005; 32(2): 203-7.
11. Vollenhoven RF. Sex differences in rheumatoid arthritis: more than meets the eye. BMC Medicine 2009; 7:12.
12. Shaukat MK, Sial NA, Abrar M. rheumatoid arthritis- presentation and outcome of management. JUMDC 2011; 2(1): 17 -22.
13. Johnson PM, Eberhardt K. Hand deformities are important signs of disease severity in patients with early rheumatoid arthritis. Rheumatology 2009; 48 (11): 1398-1401.
14. Bas S, Perneger T, Kunzle E and Vischer T. Comparative study of different enzyme immunoassays for measurement of IgM and IgA rheumatoid factors. Ann Rheum Dis. Jun 2002; 61(6): 505–10.