



SERO-PREVALENCE OF RHEUMATOID FACTOR IN SYMPTOMATIC PATIENTS PRESENTING AT A TERTIARY CARE HOSPITAL OF SOUTHERN HARYANA.

Dr Kumkum Yadav	Post Graduate Student, Dept of Microbiology, SHKM, GMC, Nalhar, Nuh, Haryana
Dr Jyoti Sangwan*	Professor, Dept of Microbiology, SHKM, GMC, Nalhar, Nuh, Haryana -122107. *Corresponding Author
Dr Manjeet Singh Dhanda	Professor, Dept of Orthopaedics, SHKM, GMC, Nalhar, Nuh, Haryana- 122107
Dr Pratibha Mane	Professor & Head, Dept of Microbiology, SHKM, GMC, Nalhar, Nuh, Haryana - 122107
Dr Pooja Singla	Associate Professor, Dept of Microbiology, SHKM, GMC, Nalhar, Nuh, Haryana - 122107

ABSTRACT **INTRODUCTION:** Rheumatoid arthritis (RA) is an inflammatory disease of the joints causing pain and stiffness, pathologically characterized by chronic synovitis. Without proper treatment, it progresses to cause joint deformity that results in significant loss of function. Detection of RA factor in patient serum is one of the most common diagnostic test being employed for this disease. Present study was carried out to study the Sero-prevalence of Rheumatoid Factor in symptomatic patients presenting at a tertiary care hospital of southern Haryana.

MATERIAL & METHODS: This observational cross-sectional study was done in Microbiology Department of SHKM GMC Nuh, Haryana, on the blood samples of suspected arthritis patients, received for the detection of RA factor over a period of six months.

RESULTS: The sero-prevalence of RA factor was found to be 7.41% with female preponderance. The symptoms such as joint swelling, morning stiffness and joint pain were the most commonly associated with RA factor (RF) positivity.

CONCLUSION: Prevalence of RA factor was 7.41%, female were more positive than male. RA factor alone is less specific as a marker for diagnosis of RA, hence other more confirmatory specific auto antibodies such as Anti- CCP needs to be added to testing armamentarium of Rheumatoid arthritis.

KEYWORDS : Rheumatoid Arthritis, Autoantibodies, Joint pain

INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown cause with a characteristic pattern of joint involvement. It is the most common form of chronic inflammatory arthritis, resulting in joint damage and disability therefore reduction in the quality of life and often systemic complication. About 1% of the world population is affected by RA. ^{1,2}Women are affected about three to five times more common than men. Incidence of disease of RA increases between 25 and 55 years of age. The presenting symptoms of RA typically result from inflammation of the joints, tendons and bursae. Patient usually complains of early morning joint stiffness lasting for more than one hour, easing with physical activity. The earliest joints involved are typically the small joints of the hands and feet. It is associated with fever, fatigue, weight loss and depression.

The pathologic hallmarks of RA are synovial inflammation and proliferation, focal bone erosion and thinning of articular cartilage. The pathogenic mechanism of synovial inflammation are likely to result from a complex interplay of genetic, environment and immunologic factors that produce a dysregulation of the immune system.

The main serological marker is RA factor (RF) which is an autoantibody reacting against Fc portion of human IgG and most often belonging to the IgM class. RF may also be of IgA, IgG or IgE isotype ^{3,4}. Presence of serum RF not only indicates disease but can appear several years before the disease become clinically apparent. Its appearance at high titer in serum is regarded as a risk factor for the later development of Rheumatoid arthritis. Increase in both IgM and IgA RF factor has been almost exclusively seen in RA patients. ^{5,6}RF positivity has also been reported in the healthy population ^{7,8} with a similar distribution between the two genders.

This study was undertaken to study the sero-prevalence of RA Factor among patients clinically suspected of Rheumatic Arthritis.

MATERIAL & METHOD:

This observational cross-sectional study was done in the serology section of Department of Microbiology, SHKM GMC Nuh, Haryana, on the blood samples of suspected arthritis patients, received for the

detection of RA factor over a period of six months (from January 2020 to June 2020). Serum was separated after centrifuging the samples at a speed of 1500 rpm for 5 minutes. The test was done by using rapid test kit (manufactured by Aspen laboratories), based on latex slide agglutination.

This method is based on an immunological reaction between human IgG bound to biologically inert latex particles and rheumatoid factor (RF) present in the test specimen. Positive and negative controls, provided along with the kits were put with every run of the test process. A positive test was indicated when agglutination is seen within two minutes of adding the latex reagent in the sera sample and a test was considered negative when there is no agglutination seen.

The sensitivity of the latex reagent has been adjusted to give agglutination when the level of RA factor is greater than 20 IU/mL.

The results obtained were analysed using computer program Microsoft Excel Version 7 (Microsoft Corporation, NY, USA)

RESULTS:

Serum samples of 310 patients were tested for RA factor over a period of six months. The prevalence of RA factor (RF) with titers greater than 20 IU/mL was found to be 7.41% (23/310) in the study population as shown in table 1. Out of 23 positive patients 13 (56.5%) were females and 10 (43.4%) were males. The prevalence was higher in females as compared to males as shown in figure 1. The age group of RA factor positive individuals was 30-40 years.

Majority samples ie 208 samples were received from orthopedics department out of which 16 (7.6%) were positive for RA factor. Joint swelling and morning stiffness were more associated with RF positivity with 10% and 8% respectively followed by fever and joint pain as shown in table no 2.

Table 1: Sero-prevalence of RA factor in the serum

RA factor SAMPLES	POSITIVE	NEGATIVE	TOTAL
	23 (7.41%)	287(92.58%)	310(100%)

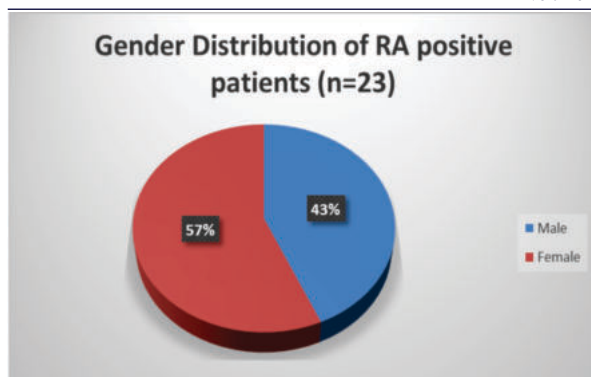


Table 2: Presenting symptoms in relation to RA positivity.

S. No.	Types of symptoms	Total	Positive	Percentage
1.	Fever	55	4	7.2%
2.	Joint pain	205	16	7.8%
3.	Joint swelling	10	1	10%
4.	Morning stiffness	25	2	8.0%
5.	Limitation of movements	15	0	0%
TOTAL		310	23	7.41%

DISCUSSION:

The present study has shown that more females produced RA factor than male. It can be explained by the involvement and influence of female sex hormones on autoimmunity. Female hormones play a role in the initiation and/or worsening of the disease as seen by the risk induced by estrogen-progestin pills, pregnancy and the postpartum period. Rheumatoid factor was present in people between 30-40 years and absent beyond 70 years. Similar pattern was obtained by Vardhan et al from Uttar Pradesh.⁹

The sero-prevalence of Rheumatoid factor in the present study was found out to be 7.41%. The findings are similar to the prevalence reported by Etienne philemon atabonkeng et al 2015,¹⁰ from Cameroon, where in they reported prevalence of RA to be 5.4% and to various other studies such as, studies by Varad vardhan bisen et al 2018 Uttar Pradesh⁹ where the sero-prevalence of RA was found to be 14.3%. Chandrashekhar et al observed a prevalence of 7% similar to our study.¹¹

RF positive patients with rheumatoid arthritis may experience more serious and erosive joint disease and extra articular manifestations than those who were R.F. negative.⁹ This is corroborated by present study findings wherein it was observed that joint swelling, morning stiffness and joint pain were the most commonly seen in RF positive patients.

Since majority of symptomatic patients (93.6%) were RF negative, there is a great possibility of missing out on positive patients, this is further explained by the low sensitivity of RA kits to the tune of 60-95%.⁹ Therefore, these suspected cases should also be tested for antibodies to citrullinated peptides such as anti-CCP ELISA which is more specific for detecting RA but the routine availability is an issue.¹²

Limitation:

This was a cross-sectional study, only for six months during COVID-19 times, so total no of cases were less which is a drawback of the study.

CONCLUSION:

This study was done to estimate the sero-prevalence of RA factor antibodies. Prevalence of RA factor was 7.41%, female were more positive than male. RA factor alone is less specific as a marker for diagnosis of RA, hence other more confirmatory specific auto antibodies such as Anti-CCP needs to be added to testing in order to increase the specificity of the test, especially for early suspected RA patients. However, the RA factor test is cheaper and easy to perform even in rural settings.

Acknowledgement: None

Source of Support: Nil

REFERENCES:

1. Scott DL, Wolfe F, Huizinga TW. Rheumatoid arthritis. *Lancet*, 2010; 376 (9746): 1094-108.
2. Carmona L, Cross M, Williams B, Lasserre M, March L. Rheumatoid arthritis. *Best pract. Res. Clin. Rheumatol*, 2010; 24: 733-45.
3. Bonnotte B. Pathogenic mechanism of autoimmune diseases. *Rev Med Interne* 2010; 31; 292-5.
4. Nell VPK, Machold KP, Stamm TA, et al. Autoantibody profiling as early diagnostic and prognostic tool for rheumatoid arthritis. *Ann Rheum. Dis.*, 2005; 64(12): 1731-36.
5. Jonsson T, Steinsson K, Jonsson H, Geirsson AJ, Thorsteinsson J, et al. Combined elevation of IgM and IgA rheumatoid factor has high diagnostic specificity for rheumatoid arthritis. *Rheumatol. Int.* 1998; 18: 119-22.
6. Jonsson T, Valdimarsson H. What about IgA rheumatoid factor in rheumatoid arthritis? *Annals Rheum. Dis.* 1998; 57(1): 63-64.
7. M. Borretzen, C. Chapman, J.B. Natvig, and K.M. Thompson, "differences in mutational patterns between rheumatoid factors in health and disease are related to variable heavy chain family and germ line gene usage." *European journal of immunology*, vol 27, no 3 pp. 735-741, 1997.
8. J.F. Simard and M. Holmqvist "Rheumatoid factor positivity in the general population", *British Medical Journal* vol 345, article e5841, 2012.
9. Varad Vardhan Bisen, "Seroprevalence of Rheumatoid Factor in tertiary care hospital" *Ijlsr*. 2015 (4) 2076-79.
10. Etienne PA, Dieudonn EA, et al. Evaluation of the Prevalence of Rheumatoid Factor in Five Regions of Cameroon. *Arch. Rheumatol.*, 2015; 30(5): 226-30.
11. Chandrasekhar S, Koripella R. Seroprevalence of Rheumatoid Factor in Arthritis Cases in a Tertiary Care Hospital. *Int. J. Curr. Microbiol. App. Sci.*, 2017; 6(12): 1925-28
12. Nishimura K, Sugiyama D, Kogata Y, et al. Meta analysis: diagnostic accuracy of anti-citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis. *Ann. Intern. Med.*, 2007; 146(11): 797-808.