RF and Anti-CCP Antibody Tests- A comparative study in the Diagnosis of Rheumatoid Arthritis in a Tertiary Care Hospital

Ashwini Kacharu Dedwal[1], Ankita Anand[2,*], Sae Satish Pol[3], Renu Satish Bharadwaj[4]

[1, 2]Assistant Professor, [3]Associate Professor, [4]Professor & Head, Dept. of Microbiology, B.J. Govt. Medical College, Pune

*Corresponding Author:
Email: drankita.anand27@gmail.com

Abstract

Introduction: Rheumatoid arthritis (RA) is autoimmune disease associated with chronic inflammation of joints causing deformities and functional impairment. Diagnosis primarily depends on clinical manifestations because of lack of suitable diagnostic tests. Rheumatoid factor (RF) is an autoantibody specific for Fc portion of human IgG. RF has low specificity as high false positive results are common in general population. Anti CCP antibody is also useful marker to diagnose rheumatoid arthritis and included in one of the criteria of American College of Rheumatology (ACR) /European League against Rheumatism (EULAR) classification of RA. Thus the present study was planned to compare the diagnostic utility of RF and Anti CCP antibody test in Rheumatoid arthritis patients in a Tertiary Care Hospital.

Aim & Objective: To compare the diagnostic utility of RF and Anti CCP antibody test in Rheumatoid arthritis patients.

Material & Methods: A total of 72 samples were taken from clinically suspected RA patients over a period of 3 months. RF was determined by latex agglutination method (STAR DIAGNOSTICS) and Anti CCP antibody by ELISA (IMTEC ANTI CCP ANTIBODIES ELISA- GERMANY). The tests were performed as per manufacturer's instructions.

Results & Discussion: Out of total 72 samples tested, 47(58.33%) were positive. Both RF and Anti CCP Antibody was positive in 9 cases. Only RF positivity was seen in 8 cases and only Anti CCP antibody was positive in 30 cases. In present study combination of Anti CCP antibody and Rheumatoid factor together have shown positive predictive value for Rheumatoid Arthritis patients which lack specific signs and symptoms related to diagnosis of RA

Conclusion: Anti CCP antibody test and RF can be used concomitantly to diagnose Rheumatoid arthritis and can be used in clinical settings so that appropriate management can be initiated to decrease future morbidity.

Keywords: Anti CCP, RF, ELISA, RA.

Introduction

Rheumatoid arthritis (RA) is a common disease with prevalence rate 1% worldwide and more common in women than men.[1] RA is autoimmune disease with unknown etiology manifesting with chronic inflammation of joints and production of several auto antibodies leading to joint destruction, deformities and functional impairment, disability.[2,3] In RA disease auto antibodies are produces such as rheumatoid factor (RF), anti-perinuclear factor (APF), ANCA, anti-RA33, anti-flaggerin anti-bodies, anti-keratin antibodies (AKA), anti-cyclic citrullinated peptide antibodies (CCP), etc.[4] Among the various auto antibodies, RF and anti-CCP antibodies are considered useful serological diagnostic markers for RA.[3] Rheumatoid factor (RF) is IgM autoantibody directed against the Fc portion of IgG. Anti-cyclic Citrullinated peptide antibody (Anti-ccp) is autoantibody that is formed after Citrullination.[3,5]

For serological diagnosis of RA routinely serum RF determination have high sensitivity, with low specificity, particularly in the early course of the disease.[6] Anti-CCP auto antibodies are recently used for diagnosis of RA and is useful to predict the severity of the disease.[7] Anti-CCPs has been recently added as one of the criteria in the American College of Rheumatology (ACR) /European League against Rheumatism (EULAR) classification of RA.[8] Some studies have shown that Anti- CCP antibodies have moderate sensitivity and high specificity for diagnosis of RA, when compared with RF.[9]

Diagnosis of RA primarily depends on clinical manifestations because of lack of suitable diagnostic tests. Although RF and X-ray imaging have important diagnostic value, there is no specific biomarker for the diagnosis of RA at present but anti-CCP antibody detection could improve the specificity of RA diagnosis. Thus the present study was planned to compare the diagnostic utility of RF and Anti CCP antibody test in Rheumatoid arthritis patients in a Tertiary Care Hospital.

Materials & Methods

This was a prospective laboratory based study.
Inclusion criteria: a total of 72 samples from clinically suspected RA patients over a period of 3 months between 20 and 60 years of age from both genders were included in this study.

Exclusion criteria: Patients of chronic renal failure, malignancy, diabetes mellitus, HIV, HBV and HCV, and pregnant women.

RF was determined by latex agglutination method (STAR DIAGNOSTICS) and Anti CCP antibody was detected by ELISA (IMTEC ANTI CCP ANTIBODIES ELISA-GERMANY). The tests were performed as per manufacturer's instructions.

RF was considered positive at values greater than 8 IU/ml. Data was analysed on MS Excel sheet and SPSS software.

Results

72 patients comprising of 49(68%) females and 23(32%) males with male to female ratio of 1:2. Most common age group was 21-40 (40%) followed by 41-60 (32%), 61-80(14%), above 80(1%) and 1-20(13%).

Out of total 72 samples tested, 47(58.33%) were positive. RF was seen in 17(23.61%) and Anti CCP Antibody was seen in 39(54.16%) of cases. (Fig. 1)

Both RF and Anti CCP Antibody positive in 9, only RF positive in 8 and only Anti CCP antibody positive in 30 cases. (Fig. 3)

Out of 55 RF seronegative samples 30(54%) were Anti CCP positive and 25(46%) were Anti CCP negative. In 17 RF seropositive samples 9(52%) were Anti CCP positive and 8(48%) were Anti CCP negative. (Fig. 2)
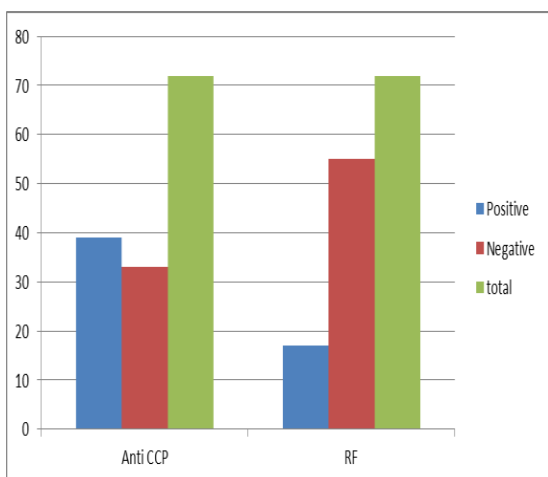

Fig. 1: Comparison of positivity of RF and Anti CCP antibody in clinically suspected RA cases
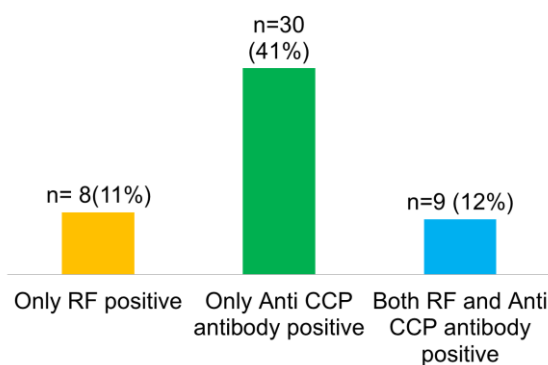

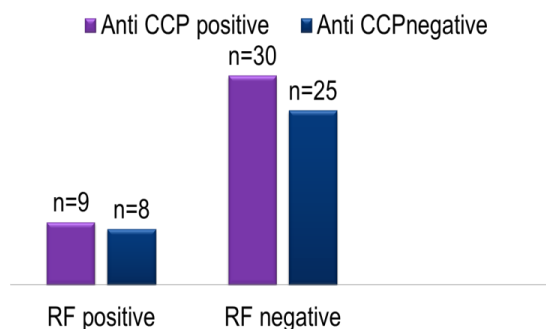**Fig. 2: Comparison of positivity of RF and Anti CCP Antibody n=72**

Fig. 3: Comparison of Anti CCP in RF positive and negative samples

Discussion

In the present study total 72 patients were included with male to female ratio of 1:2 and most common age group was 21-60 (72%). RF was seen in 17(23.61%) and Anti CCP Antibody was seen in 39(54.16%) of cases.

In RF seronegative patients 30 (54%) of patients showed Anti CCP Antibody while 25 (46%) did not have Anti CCP Antibodies in there serum while in RF seropositive patients 9 (52%) of patients showed Anti CCP Antibodies and 8 (48%) did not show antibodies in serum. Similar findings with our study was shown by Kastbom et al,[10] Naddim Afzal et al[11] also showed that Anti CCP Antibodies in RF seronegative patients that indicates that Autoantibodies are formed early in the course of RA before RF appear in the serum.

In the present study RF seropositive patients did not show Anti CCP Antibodies this can indicate that they are RA negative and might be suffering from other diseases which causes seropositivity thus indicates that RF is not a reliable marker for RA and can be raised in in other autoimmune diseases.

Testing for the combination of anti-CCP antibodies and IgM RF may be better for excluding the diagnosis of RA than is achievable by testing for either antibody alone. Those with early arthritis who are RF or anti-CCP antibody positive are at an increased risk of developing RA and erosive joint disease, while those with neither of these markers are less likely to develop joint damage. Thus, earlier intervention with disease modifying antirheumatic drug (DMARD) therapy may be warranted in those with positive markers, while symptomatic treatment may be appropriate for those lacking both RF and anti-CCP antibodies when first seen.

In RF seronegative patients, anti-CCP can be helpful in confirming the diagnosis of RA.

Step up of anti-CCP testing in the ACR's updated 2010 RA classification criteria reveals the clinical value of these tests for the diagnosis of RA patients.[8]

However, this does not mean that anti-CCP can replace RF in diagnostic and prognostic testing for RA. We recommend that Anti CCP antibody test and RF should be used concomitantly to diagnose early RA and can be used in clinical settings so that appropriate management can be initiated to decrease future morbidity.

References

1. Klareskog L, Catrina IA, Paget S. Rheumatoid arthritis. The Lan-cet 2009;373:659-72.
2. De Rycke L, Peene I, Hoffman IE, *et al*. Rheumatoid factor and anti-citrullinated protein antibodies in rheumatoid arthritis: diag-nostic value, associations with radiological progression rate, and extra-articular manifestation. Ann Rheum Dis 2004;63:1587-93.
3. Alessandri C, Priori R, Modesti M, Mancini R, Valesini G. The role of anti-cyclic cytrullinate antibodies testing in rheumatoid arthritis. Clinic Rev Allerg Immunol 2008;34:45-9.
4. Bas S, Perneger TV, Seitz M, Tiercy MJ, Lombard RP, Guerne AP. Diagnostic tests for rheumatoid arthritis. Comparison of anti-cyclic citrullinated peptide antibodies, anti-keratin antibodies and IgM rheumatoid factor. Rheumatol 2002;41:809-14.
5. Zendman WJ, Venrooij VJW, Pruijin MJ. Use and significance of anti-CCP autoantibodies in rheumatoid arthritis. Rheumatol 2006;45:20-5.
6. Miriovsky BJ, Michaud K, Thiele GM, O'Dell JR, Cannon GW, et al. (2010) Anti-CCP antibody and rheumatoid factor concentrations predict greater disease activity in men with rheumatoid arthritis. Ann Rheum Dis 69:1292-1297.
7. Hayashi N, Kumagai S (2010) [Anti-cyclic citrullinated peptide antibodies and rheumatoid arthritis]. Rinsho Byori 58:466-479.
8. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, et al. (2010) Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis and rheumatism 62:2569-2581.
9. Lee DM, Schur PH (2003) Clinical utility of the anti-CCP assay in patients with rheumatic diseases. Ann Rheum Dis 62:870-874.
10. Kastbom A, Strandberg G, Lindroos A, Skogh T. Anti-CCP anti-body test predicts the disease course during three years in early rheumatoid arthritis. Ann Rheum Dis 2004;63:1085-9.
11. Nadeem Afzal, Sara Karim, Fazzul-E-Haque Mahmud, Waqas Sami, Maria Arif, Sarwar Abbas. Evaluation of Anti-CCP Antibody for Diagnosis of Rheumatoid Arthritis. Clin. Lab. 2011;57:895-899.
12. https://www.arthritis.org.nz/wp-content/uploads/2011/07/4203_art_RA_flyer_2-0.pdf.