

The physiological evaluations of C-reactive protein, anti-cyclic citrullinated peptide antibody and RF in the rheumatoid arthritis patients of Al-Nassyria hospitalTalib F. Abbas ^{*1}**Abstract**

The assessment of autoantibody before clinical onset of Rheumatoid Arthritis, has been helped in establishing early diagnosis. Recent studies on RA described many inflammatory conditions that precede joints inflammations. Anti-CCP and IgM-RF were evaluated in 10-RA patients and in same number as control. Anti-CCP was detected by ELISA and IgM-RF using latex agglutination test, while the CRP was measured by latex turbidimetric immunoassay, and the ESR was measured by Westergren method. The values of Anti-CCP antibody is more sensitive than the other tests, in 50% were positive, and 50% negative. CRP measures were fluctuated around 37% positive and 63% were negative. ESR values have been shown a significant increase in 90% positive, whereas 10% negative. RF show a significant increase by 60% positivity. The positive value was higher for anti-CCP antibodies in comparison to other markers for RA patients. Interestingly, there were not significant relation between anti-CCP antibody titers and inflammatory markers such as ESR and CRP. However, there is a tighten relation between Anti-CCP and RF had been confirmed.

Keywords: Rheumatoid Arthritis; Anti-CCP; RF^{*}Corresponding Author: Talib F. Abbas: tlb_abbas77@yahoo.com¹ College of Pharmacology/Muthanna University

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Copyright © 2015 TA. This is article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**Introduction**

Physiological suppression and enhancement of some parameters become the crucial role in evaluation of the patient's state of Rheumatoid Arthritis (RA). It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility if not adequately treated. RA is a common autoimmune disease (AID) caused

by inflammation of synovial with swelling and fibrous tissues formation [1]. Gender, heredity and genes largely determine a person's risk of developing RA. It is associated with inherited type of antigen call human leukocyte Antigen gene (HLA) gene [2]. Vitamin D supplementation has been decreased the risk for RA [3]. Complication of RA may be developed to peripheral

neuropathy; an erosion can give rise to vertebrate slipping over one another and compressing the spinal cord. X-rays of the hands and feet are generally performed as diagnostic step. Magnetic resonance imaging (MRI) and ultrasonography are also used. Colour doppler and power doppler ultrasound are useful in assessing synovial inflammation [4]. When RA is clinically suspected, immunological studies are required such a testing for the presence of rheumatoid antibodies.

The shift to earlier, aggressive treatment would be facilitated by more sensitive and specific early diagnostic tests. However, this remains challenging given the limitations of current diagnostic tools and intervention practices [5]. Clinical evidence, laboratory tests, and imaging tests are used to diagnose patients suspected of RA [6]. However, clinical examinations often fail to identify patients with early RA due in part to heterogeneity of disease presentation and course. Rheumatoid Factor (RF) is the autoantibody mostly relevant in rheumatoid arthritis against the Fc portion of IgG. RF and IgG join to form immune complexes that contribute to the disease process. There is an association between rheumatoid factor and more persistently active synovitis, more joint damage and greater eventual disability [7]. Antibodies against cyclic citrullinated peptide (anti-CCP) are highly specific marker for RA. Anti-CCP antibodies are now considered as an important serological marker for the diagnosis of RA and as a possible prognostic marker for the development of erosive disease [8]. The links between chronic inflammation and joint damage has been widely established, especially the relevance of inflammatory markers such as erythrocyte sedimentation

rate (ESR) and C reactive protein (CRP). However, the damage may progress in spite of decreased inflammatory activity and erosions may develop in patients without clinical signs of significant inflammation. Therefore, an identification of reliable predictor's and markers of joint damage is necessary [9].

To meet the need for improved diagnostic and prognostic tests and algorithms, various serum biomarkers are being assessed for the improved diagnosis and prognosis of RA, including a wide range of autoantibody. However, only RF and anti-CCP have gained wide acceptance.

Patients and methods

A sample of hospital patients were attends to the bones and joints department were studied. 10-patients with RA: 4-men and 6-women and 10 other control were chosen randomly in different ages. Clinically evaluated disease activity was performed on the bases of recommendation and diagnosis of seniors and doctors of Al-Nassyria hospital in the period from first of February to first of April 2013. The patients have had suffering of morning stiffness, pain of joints. The acute cases have had radiographic X-ray diagnosis of the main joints. From each patient and control member 5 ml of venous blood was collected, the sera were stored in refrigerator (-20 C) until the assays had been performed.

The Scanning fast test were used for RF determination, Latex agglutination tests were performed by a Singer and Plotz technique, a titer of $> 1/80$ being considered positive. For the positive cases the Enzyme linked immunosorbent assay (ELISA) was performed [10,11]

The serum levels of anti-CCP were measured by using CCP IgG ELISA kit (Sigma, USA) following manufacturer's instructions and the titer of 20 U/ml being considered positive.

For acute phase of inflammation, C - reactive protein measurement were used as it's firstly mentioned by Tillet and Francis, the normal being defined as < 10 mg/L [9]. CRP was measured by latex turbidimetric immunoassay. Westergren method had been used to measure the ESR [11]. The statistics had been performed by using t-test for comparison the positivity and negativity.

The results and discussion

Early diagnosis and prevention of joint disease is an important role in treatment. In the present study, the diagnostic utility of RA diagnosis had been compared. Which are anti-CCP antibodies and other parameters such as RF and onset acute protein of inflammation represented by C-reactive protein (CRP), in addition to the common inflammation marker ESR. The mean age of the patients was 52.7 ± 12 years. Sixty percent of the all patients were RF positive and 40% were negative. The values of Anti-CCP antibody was more sensitive than the other tests, 50% of all patients were positive, and 50% negative. CRP measures were fluctuated around 37% positive and 63% were negative. ESR values showed a significant increase 90% were positive, whereas 10% were negative. The values of patients with RA according to Anti-CCP or RF positivity are shown in table 1. The disease of RA involves abnormal B cell-T cell interaction, with producing antigen via HLA-DR eliciting T cell help and consequent production of RF and Anti-CCP. The abnormal immune by lymphocytes and

Immunoglobins, IgG and IgM mainly activates macrophages which seems to play an important role in the inflammatory response that present in RA [12].

Recent study showed that in patients with synovitis, a combination of anti-CCP antibodies and RF had confirmed [13]. Furthermore, anti-CCP have been incorporated into proposed diagnostic criteria for rheumatoid arthritis as in Tab.1 The positivity and negativity of RF, Anti-CCP, CRP and ESR of the patient sera had been shown in Fig.1. Where the clear similarity in change between the RF and Anti-CCP, more than CRP and ESR. Our data also illustrated the combination of Anti-CCP and RF factors, more than other factors. Ellitsgaard et al., conducted a study on 140 elderly patients with hip fractures that measured CRP and ESR during weak after operation. Eighty two fractures were reduced with a dynamic compression screw, 20 with cancellous screw only, and 38 received hemiarthroplasty. The ESR and CRP did not differ with the type of fixation used. Indicate that CRP measurements were more reliable than ESR in postoperative infection after hip fracture surgery [14,15]. In conclusion, our data showed no single variable can assure correct diagnosis and prediction in an individual case; hence combined scores have been sought.

Values	Anti-CCP			RF		
	Positive	Negative	P value	Positive	Negative	P value
Age	51±13	53±11	NS	52±12	50±10	NS
CRP(mg/l)	30±3	46±13	<0.05	41±5	27±8	<0.05
ESR(mm/l)	42.85±1	36±62	NS	48±2	16±44	<0.05

Table 1.

The values of patients with RA according to anti-CCP or RF positivity show that the presence of anti-CCP antibodies in patients with RA has a better diagnostic performance if combine with RF, rather

than RF parameter alone, and analyze the effect of each marker on the positivity and negativity of Anti-CCP and RF. Abbreviation: CRP- C-reaction.

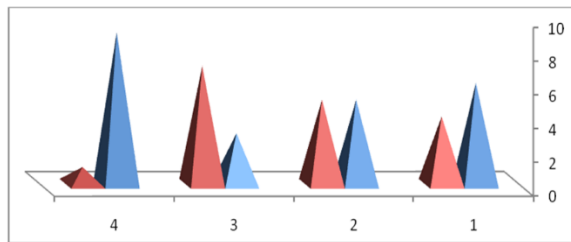


Figure 1.

Shown the positive and negative values for the RA parameters where the clear similarity in change between the RF and Anti-CCP, more than CRP and ESR. Abbreviation: RF, 2- Anti-CCP, 3- CRP, 4- ESR.

Competing interests

The author declare that they have no competing interests.

References

1. Lee DM, Weinblatt ME. Rheumatoid arthritis. *Lancet* 2001; 358: 903-11.
2. Plenge Robert M, Seielstad P. TARF1-C5 as a risk factor for rheumatoid Arthritis—A genome wide study. *The New England Journal of Medicine* 2007; 357(12):1199-209.
3. Wen H, Baker JF. Vitamin D, immunoregulation and rheumatoid arthritis. *Journal of Clinical rheumatoid arthritis* 2011;17(2):102-7.
4. Waaler Erik. On the occurrence of a factor in human serum activating the specific agglutination of Sheep Blood Corpuscles. *Acta pathologica Microbiologica Scandinavica* 2009;17(2):172.
5. Riedeman JP, Munoz S, Kavanaugh A. The use of second generation anti CCP antibody (anti-CCP) testing in RA- a systemic review. *Clin. Exp. Rheumatol* 2005; 23: 569-576.
6. Combe B, Landewe R, Lukas C. EULAR recommendations for the management of early arthritis: report of task force of the European Standing Committee for international clinical studies including therapeutics (ESCISIT). *Annals of the rheumatic diseases* 2007;66(1): 4-45.
7. Mierau R, Genth E. Diagnosis and prognosis of early rheumatoid arthritis, with special emphasis on laboratory analysis. *Clinical chemistry and laboratory medicine* 2006;44(2):138-143.
8. Hassan TM, Kim D. C-reactive protein and Erythrocyte Sedimentation rate in orthopedics. *The University of Pennsylvania Orthopedics Journal, Orthopedics Journal* 2002;15:13-16.
9. Gioud-Paquet M, Auvent M, Raffin T, et al. IgM rheumatoid factor (RF), IgA RF, IgE RF and IgG RF detected by ELISA in rheumatoid arthritis. *Annals of the Rheumatoid Disease* 1987; 46: 65-71.
10. Carson DA, Lawrance S, Catalano MA, Vaughan JH, Abraham G. Radio-immunoassay of IgG and IgM rheumatoid factors reacting with human IgG. *J Immunol* 1977;119:285-300.
11. Ng T. Erythrocyte sedimentation rate, plasma viscosity and C-reactive protein levels in clinical practice. *Br. J. Hosp. Med* 1998;58(10):512-523.
12. Boldt AB, Goeldner I, de Messias-Reason II. Relevance of the lectin pathway of complement in rheumatic diseases. *Adv Clin Chem* 2012;56:105-53.
13. Goeldner I, Skare TL, de Messias Reason LT, et al. Anti-cyclic citrullinated peptide antibodies and rheumatoid factor in rheumatoid arthritis patients and relatives from Brazil. *Rheumatology*, 2010.
14. Mustard RA, Bohnen JMA, Haseeb S. C-reactive protein (CRP) levels predict postoperative septic complication. *Arch Surg* 1987;122:69-73.
15. Kragstbjerg P, holmberg H. Serum concentrations of interleukin-6, tumor necrosis factor- α , and C-reactive protein in patient undergoing major operations. *Eur J. Surg* 1995;161:17-22.