STUDY OF ERYTHROCYTE SEDIMENTATION RATE AND ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN RHEUMATOID ARTHRITIS

Sabeen Khalid, Javad Yousaf, Amir Rashid

Army Medical College/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To study the erythrocyte sedimentation rate (ESR) and anti-cyclic citrullinated peptide (anti-CCP) antibodies in rheumatoid arthritis patients on disease modifying anti-rheumatic drug therapy.

Study Design: Cross sectional comparative study.

Place and Duration of Study: Centre for Research in Experimental and Applied Medicine (CREAM-I), Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi in collaboration with Rheumatology Department, Military Hospital Rawalpindi, from Jan 2016 to Jun 2016.

Material and Methods: Study sample was seventy in number and was divided into two groups. Group I consisted of thirty five patients suffering from rheumatoid arthritis, while group II consisted of thirty five healthy individuals who were not suffering from any chronic illness. Non probability purposive sampling was done. ESR was measured using Westergren method, while anti-CCP was estimated by enzyme-linked immune sorbent assay (ELISA).

Results: Data were analyzed using SPSS 22 version. Mean age of patients of rheumatoid arthritis was 49.69 ± 11.5 years and that of control group was 47.4 ± 10.4 years. Among the study population 30 (43%) individuals were males and 40 (57%) were females. In patient category, there were 10 (29%) males and 25 (71%) females. In control group 20 (57%) males and 15 (43%) females were present. Independent t-test was applied between the two variables i.e. ESR and anti-CCP, with showed significant *p*-value of less than 0.001.

Conclusion: There was significant increase in both ESR and anti-CCP levels in rheumatoid arthritis patients on disease modifying anti-rheumatic drugs as compared with control group.

Keywords: Anti-cyclic citrullinated peptide antibodies, Disease modifying anti-rheumatic drugs, Erythrocyte sedimentation rate, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a persistent autoimmune, poly articular inflammatory disease affecting nearly 1% of world population[1,2]. Rheumatoid arthritis is a prevailing disease in Pakistan as well[3]. The prevalence of rheumatoid arthritis in southern Pakistan is found to be 0.142% while in northern Pakistan it is about 0.55%[3]. Although the prevalence is small but due to its crippling affect it has been a major devastating disease of today´s world.

It is categorized by inflammation and hypertrophy of synovial membranes leading to progressive joint destruction. It may occur at any age but it mostly occurs between 40-70 years and usually advances with age[4]. Inflammatory response occurs due to several chemokines, cytokines and growth factors released from different cells of synovium[5]. Macrophages and monocytes play a role in pathogenesis of RA by releasing different pro-inflammatory cytokines[6]. Studies have shown that RA is associated with multiple genetic and environmental factors like cigarette smoking, exposure to environmental hazards for example silica dust[7-9]. Human leukocyte antigen (HLA)-DRB1 and (HLA-SE) shared alleles possess strongest genetic risk factors for development of RA. Studies also showed that HLA-SE and anti-cyclic citrullinated peptide (anti-CCP) together have greater risk for development of RA than either one alone[10].

Correspondence: Dr Sabeen Khalid, Dept of Biochemistry, Army Medical College Rawalpindi Pakistan
Email: sabeen88@hotmail.com
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Patients are being clinically diagnosed with the help of American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) classification criteria for RA[11]. This criteria is based upon four variables i.e. small joint involvement, at least 6 months disease duration, positive serology for rheumatoid factor (RF) or anti-cyclic citrullinated peptide (anti-CCP) and presence of any one of the acute phase inflammatory markers i.e. erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). As early as patient is diagnosed with RA, therapy with disease modifying anti rheumatic drugs (DMARDs) should be started[12]. Disease modifying anti-rheumatic drugs have been the treatment of choice for their ability to lessen the disability of patients[13]. The current recommended DMARD therapy includes both conventional and biological agents. They can either be used alone or in combination with each other. Commonly used conventional agents are methotrexate, leflunomide, hydroxy chloroquine, sulfasalazine[14]. Biological agents include tumor necrosis factor alpha inhibitors like infliximab, rituximab, etanercept and adalimumab[12].

ESR reveals the degree of inflammation in human body. ESR is a non-specific inflammatory marker, raised in various inflammatory disorders. It is used for diagnosis and for monitoring the disease outcome of RA patients[15]. High ESR level usually depicts active RA. Anti-CCP is helpful in early detection of rheumatoid arthritis[16]. Citrullination means post translational modification of arginine to citrulline residue with the help of enzyme peptidyle arginine deaminase (PAD)[17]. Anti-CCP has more important role in early diagnosis of RA, but it is more specific biological marker for prediction of erosive joint damage in both seropositive as well as seronegative RA patients[18]. This study aims to see significance of parameters i.e. ESR and anti-CCP in RA progression and monitoring.

Table: Comparison between two groups.

Parameters	Group 1 (n=35) Mean ± SD	Group 2 (n=35) Mean ± SD	*p*-value
ESR	31.60 ± 10.63	19.51 ± 6.71	<0.001
Anti-CCP	70.94 ± 46.81	3.46 ± 1.85	<0.001

MATERIAL AND METHODS

This cross sectional comparative study was conducted at Centre for Research in Experimental and Applied Medicine (CREAM-I), Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi in collaboration with Rheumatology Department, Military Hospital Rawalpindi. Formal approval from ethical review committee of Army Medical College was taken. Non probability purposive sampling was done. The duration of study was six months starting from January 2016 to June 2016.

Patients of RA taking DMARD therapy were enrolled from Rheumatology OPD, Military Hospital, Rawalpindi, after taking their written informed consent. Patients suffering from any kind of malignant disease, and other type of arthritis for example osteoarthritis were excluded.

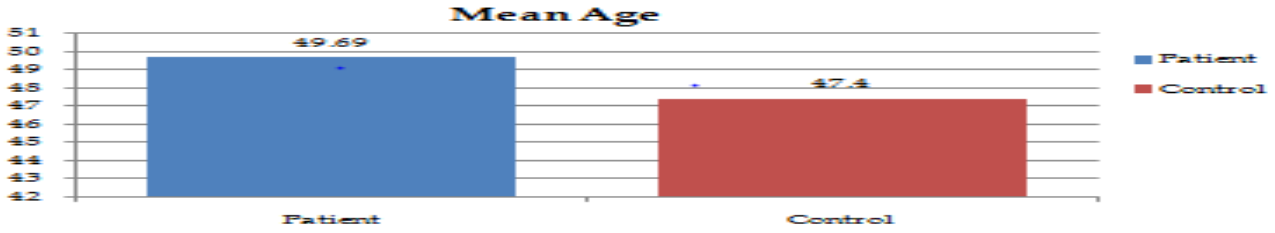

Figure-1: Figure showing mean age in control & disease groups.

Two groups were formed. Group one consists of thirty five patients of RA on DMARD therapy. While group two consist of thirty five healthy individuals, who are not suffering from any chronic illness.

Anti-CCP was analyzed using enzyme-linked immune sorbent assay (ELISA) following the standard protocols of the kit. ESR was determined using Westergren method following standard protocols.

Statistical Analysis

Data were analyzed on SPSS 22 version. Numerical variables were expressed as mean ± standard deviation. Qualitative data were expressed as frequency and percentages. Independent t-test was applied between ESR and Anti-CCP values to see the statistical significance among the groups. A *p*-value of less than 0.05 was considered significant.

RESULTS

Study sample was seventy in number and was divided into two groups. Group I consisted of thirty five patients of RA, while group II consisted of thirty five healthy individuals. Mean age of patients of RA was 49.69 ± 11.5 years and that of control group was 47.4 ± 10.4 years (fig-1). Among the study population 30 (42%) individuals were males and 40 (57%) were females. In patient category, there were 10 (29%) males and 25 (71%) females. In control group 20 (57%) males and 15 (43%) females were present. Mean ESR level of patients was 31.6 ± 10.6 Hg after 1 hr, that of control group was 19.5 ± 6.7 mm after 1 hour (fig-2). Independent t test was applied, which shows significant increase in both ESR and anti-CCP levels in RA patients on DMARD therapy as compared with control group, having *p*-value of less than 0.001 as shown in table.

DISCUSSION

The aim of this study was to find the significance of ESR and anti-CCP in RA disease progression and monitoring. Our study showed significant increase in ESR and anti-CCP levels in RA patients on DMARD therapy as compared with control group. ESR values were raised in all anti-CCP positive patients which was consistent with the previous study[19]. Shakiba et al also reported that raised ESR and increased anti-CCP are associated with active disease[20]. Our study also showed 100% specificity for RA patients as compared to control group, which was similar to a study conducted in Turkey[4].

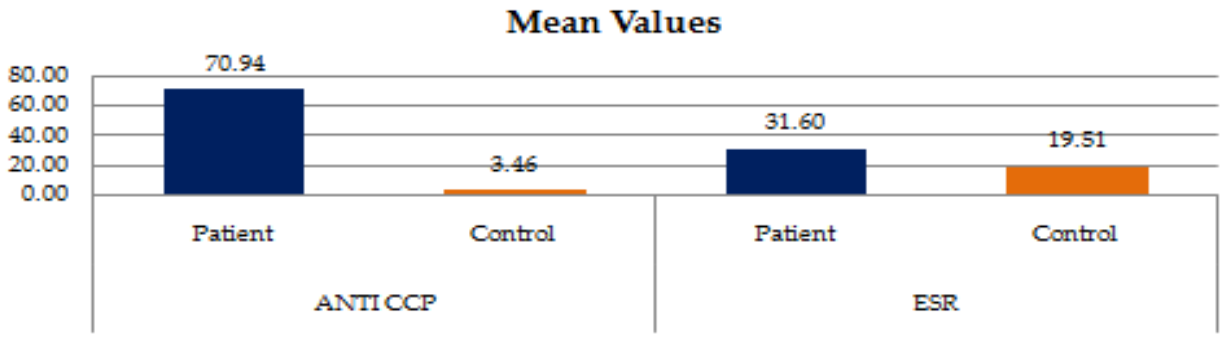

Figure-2: Figure showing mean values of Anti-CCP & ESR in both groups.

Earlier in 20th century RA was being diagnosed with rheumatoid factor along with history and clinical features, later on anti-CCP shown to be better marker for diagnosis and prognosis of RA patients. Study of anti-CCP in world proved that it is a better marker for early detection RA and for progression of disease as well[21].

Our study showed that anti-CCP value was found to be normal in control group, which consist of healthy individuals. That result was contrary with the study previously conducted in world showing that presence of anti-CCP in

normal individuals[22]. This fact supports that apparently healthy anti-CCP positive individuals might be at risk of developing RA in future. This study also showed that almost all of study population was on conventional DMARD therapy. This provides suggestion about switching patients to biological DMARD therapy for better disease outcomes and improving health and quality of life of patient[23].

CONCLUSION

There was significant increase in both ESR and anti-CCP levels in rheumatoid arthritis patients on disease modifying anti-rheumatic drugs as compared with control group.

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CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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