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Evaluation of ESR, CRP, RF and Anti-CCP levels as risk factors in Rheumatoid Arthritis

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Abstract: Rheumatoid Arthritis (RA) is a chronic inflammatory relapsing autoimmune disorder which often affects multiple systems. The aim of the present study was to investigate the relation of some biochemical parameters like Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (C-RP), Rheumatoid Factor (RF) and Anti-cyclic Citrullinated Peptide Antibody (ACCP) with Rheumatoid Arthritis patients and controls in North Coastal Andhra Pradesh. A total of 100 samples (50 RA patients and 50 controls) were included in the present study by using Enzyme Linked Immuno Sorbent Assay (ELISA) method. The biochemical data was analyzed by using Graph Pad Prism 7 software for association studies. From this study, it may be concluded that the statistical significance have been observed for age and gender of RA patients and controls. The frequency of females was more than males in both RA patients and controls. The mean values for age of onset and disease duration were more in females than males. The ESR mean value was slightly elevated in female RA patients whereas, the mean values of CRP, RF and Anti-CCP were almost equal in both male and females of RA patients. The biochemical parameters (ESR, CRP, RF, and Anti-CCP) were statistically insignificant, in RA patients.

Keywords: Rheumatoid Arthritis, Erythrocyte Sedimentation Rate, C-reactive protein, Rheumatoid Factor, Anti-Cyclic Citrullinated Peptide Antibody, Enzyme Linked Immuno Sorbent Assay.

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Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory relapsing autoimmune disorder which often affects multiple system. It is characterized by infiltration of inflammatory cells into the synovium and synovial hyperplasia ultimately leading to the destruction of bone as well as articular cartilage. The prevalence of RA is around 1-2% of the world population with women being affected 3 times more often than men. Although individuals of any age can be affected but the onset is more frequent in 40's or 50's .The exact etiology of RA is yet unknown but it is depends on the interaction of number of environmental and genetic factors (Klareskog *et al.,* 2006). So it is a multi-factorial Inheritance. X-rays and laboratory testing may support a diagnosis (Majithia and Geraci, 2007).When RA is clinically suspected, testing for the presence of rheumatoid factor (RF, a non- specific antibody) and anti-circulated

proteins antibodies (ACPAs) may be required (Westwood *et al*., 2006). Also, several other blood tests are usually done to allow for other causes of arthritis, such as lupus erythematosus. The erythrocyte sedimentation rate (ESR), C-reactive Protein (CRP), full blood count, kidney function, liver enzymes and other immunological tests (e.g., antinuclear antibody/ANA) are all performed at this stage (Westwood *et al*., 2006). Acute phase reactants (APRs), such as serum, C-reactive protein (CRP), plasma fibrinogen, and ESR are common biomarkers used to monitor the status of inflammatory disease. The acute- phase response to tissue injury and inflammation is accompanied by a dramatic increase in hepatic synthesis of acute phase reactants (APR). Therefore, characterization of APR responses in RA is essential to gain insights into the activity of this disease and to assess the degree of inflammation. Both CRP and ESR levels are used to monitor the disease activity and response of patients to treatment (Gabay and Kushner, 1999; Pedrazzi *et al.*, 1998).

Aim and Objectives

Based on the present knowledge our study was primarily aimed to investigate the relation of some biochemical parameters like Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Rheumatoid Factor (RF), and Anti-cyclic Citrullinated Peptide Antibody(Anti-CCP) with Rheumatoid Arthritis patients and controls in North Coastal Andhra Pradesh.

- To obtain the mean values of age and gender in Rheumatoid Arthritis patients and controls.
- To obtain the mean values of age of onset and disease duration in Rheumatoid Arthritis patients only.
- To evaluate mean values of ESR, CRP, RF, Anti-CCP and compared as students unpaired "t" -test between Rheumatoid Arthritis patients and controls.

Materials and Methods

The present case control study was carried out in the Department of Human Genetics, Andhra University, Visakhapatnam, India, during January 2017 to December 2017. The RA patients attending King George Hospital (KGH) OPD were selected for the study. 50 newly diagnosed RA Patients and 50 age and sex matched healthy individuals as controls were taken. The study was approved by Institutional Ethical Committee (IEC) and informed written consent was taken from all participants.

Biochemical Analysis

The biochemical parameters such as Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Rheumatoid Factor (RF) and Anti-cyclic Citrullinated Peptide Antibody (Anti-CCP) were evaluated by Enzyme Linked Immunosorbent Assay (ELISA) method.

Statistical Analysis

Data analysis was performed using Graph Pad Prism 7 software. The data was carefully evaluated to obtain the mean values and SD and compared as students unpaired "t" –test between RA patients and controls. P-value <0.05 was considered as statistically significant.

Results

Table 1. Age and Gender of Rheumatoid Arthritis Patients and Controls

Age and Gender	RA Patients (n=50) Mean ±SD	Controls (n=50) Mean ±SD	P-Value
Age	42 ±11.31	41 ± 12.72	0.0003**
Gender	47±4.24	46±5.65	0.0001**

Table 1 shows the age and gender of Rheumatoid Arthritis patients and controls. The mean age values of RA patients and controls were 42and 41. The mean gender values of Rheumatoid Arthritis patients and controls were 47 and 46. Though, there was no significant difference have been observed for mean values of age and gender of RA patients and controls, a statistical significance has been observed.

Table 2. Sex wise distribution of Rheumatoid Arthritis Patients and Controls

Gender	RA Patients (n=50) Frequency	Controls (n=50) Frequency
Male	6(12%)	5 (10%)
Female	44(88%)	45(90%)

Table 2 shows the sex wise distribution of Rheumatoid Arthritis patients and controls. The frequency of male RA patients and controls were 12% and10%. The frequency of female RA patients and controls were 88% and 90%. The gender frequency of females was higher than the males in RA patients and controls.

Table 3. Age of onset and Disease duration in Rheumatoid Arthritis Patients

Age of onset and Disease duration	Male(n=6) Mean ± SD	Female (n=44) Mean ± SD	Total RA Patients (n=50) Mean ±SD
Age of onset	29 ± 32.52	38±67.21	42.40±11.30
Disease duration	2.60 ± 18.42	17.02±8.27	12.92±1.56

Table 3 shows the age of onset and disease duration in RA patients. The mean age of onset values in male and female RA patients were 29 and 38respectively. The total mean value for age of onset was 42.40 in Rheumatoid Arthritis patients.

The mean disease duration values in male and female RA patients were 2.60 and17.02 respectively. The total mean value for disease duration was 12.92 in Rheumatoid Arthritis patients. The mean values for age of onset and disease duration were more in females than the males of RA patients.

Table 4. Biochemical Parameters in Rheumatoid Arthritis Patients

Biochemical Parameters	Male(n=6) Mean ± SD	Female (n=44) Mean ± SD	t	df	p-value
ESR(mm/hr)	31.60 ±16.30	35±0.35	0.3	48	0.70 NS
CRP(mg/dl)	1.60±0.54	1.60±0.49	-0-	48	1 NS
RF(U/ml)	1.24±0.00	1.00±0.43	1.24	48	0.21 NS
Anti-CCP(µ/ml)	1.40±0.44	1.2±0.49	0.84	48	0.39 NS

Table 4 exhibits the mean values of ESR, CRP, RF, and Anti-CCP in RA patients. The mean ESR value in male and female RA patients were 31.60 and 35respectively. The mean CRP value in male RA patients was 1.60 and female RA patients 1. 60. The mean RF value in male and female RA patients were 1.24 and 1.00 respectively. The mean Anti-CCP value in male RA patients was 1.40 and in female RA patients 1.2. The ESR mean value was slightly elevated in female Rheumatoid Arthritis patients. The remaining values were almost similar in both males and females of RA patients. All the biochemical parameters were statistically insignificant.

Table 5. Biochemical Parameters in Rheumatoid Arthritis Patients

Biochemical Parameters	Male(n=6) Mean ± SD
ESR(mm/hr)	49.5 ± 0.70
CRP(mg/dl)	31 ± 26.87
RF(U/ml)	43.5 ± 9.1
Anti-CCP(µ/ml)	36 ± 19.79

Table 5 shows the mean values of ESR, CRP, RF and Anti-CCP in Rheumatoid Arthritis patients. The mean ESR, CRP, RF and Anti-CCP values in RA patients were 49.5, 31, 43.5, and 36 respectively.

Discussion

The modern trend of RA treatment has been changed to start treatment as early as possible, based on the concept that early control of inflammation results in reduced joint damage (Emery, 1994). It therefore is important to differentiate between RA and other forms of arthritis early after the onset of symptoms (Lindovist *et al.*, 2005; Visser, 2005). Although the 1987 American College of Rheumatology classification criteria for RA (Amett *et al*., 1988) are often used in clinical practice as diagnostic tool for RA, they are not very well suited for the diagnosis of early RA (Kaarela *et al*., 1995; Sarauxet *al*., 2001; Van Venrooij *et al*., 2002). The ACR criteria rely heavily on the expression of clinical symptoms of RA, but in early RA these clinical parameters are often not (yet) manifest. Therefore, a specific and sensitive (serological) marker, which is present very early in the disease, is needed

The present study mean values of age in RA patients and controls were 42 and 41 respectively. According to the study of somaiyamateen *et al.,* 2016, the mean values for RA patients and controls were 40.02 and 43.11 respectively. In the study of Alirezasadeghi *et al*., 2017, the mean values of age in RA patients and controls were 44.89 and 34.89. The mean values of the other studies were almost similar to the present study.

For the gender of RA patients, the present study shows statistical significance between RA patients and controls. It does not correlates with the study of Alirezasadeghi *et al.,* 2017, which shows statistical insignificance for gender.

The mean age of disease onset in the present study was 42.40 whereas, the mean values of the other studies Goertz *et al*., 2003 and Youssef et al., 2014 were 44 and 36 respectively. The mean values of disease onset were almost similar to the other studies.

The mean value for disease duration was 12.92in RA patients of present study whereas, the mean values of the other studies Anna kotulska *et al*., 2015; Kalpanapanati *et al.,* 2012; Munneversedaroglu*et al*., 2008 and Youssef *et al.,* 2004 were6.1 , 4.37, 6.8 and 10.33, respectively. The mean value for disease duration of RA patients correlates with the study of Youssef *et al*., 2004. Whereas the other three studies shows the lower mean values.

The erythrocyte sedimentation rate is a physical phenomenon related to plasma viscosity and the number of red cells. Plasma viscosity, or more precisely the albumin/globulin ratio, is altered in an acute phase reaction and is probably the most significant factor affecting ESR. An additional factor which influences ESR is serum fibrinogen level (Ablij and Meinders, 2002). The test is simple and very cheap. C-reactive protein is an acute-phase protein belonging to the highly conserved pentraxin family. C-reactive protein is synthesized in the hepatocyte and its transcription is mainly regulated by interleukin-6. Biological functions of

CRP are partially known and include activation of complement via the classical pathway and contribution to opsonization and phagocytosis of some microorganisms as well as clearance of necrotic cells (Siemons *et al.*, 2015).

The present study the mean values of ESR in male and female RA patients were 31.60 and 35 respectively. The mean value was slightly higher in female RA patients than males. It is concomitant with other studies of Shearn and Kang, 1986; Siomans *et al.*, 2015. The study of Anna Kotulska *et al.*, 2015 did not revels and differences between female and male RA patients. The total mean value for ESR was 49.5 in present study. The mean values of ESR for other studies Goertz *et al.*, 2003; Munevver Serdaroglu *et al*., 2008; Somaiya Mateen *et al.*, 2016, were 30.89, 29.2 and 13.47 respectively. The present study shows higher ESR mean value in RA patients than the other studies.

The present study mean CRP value in male RA patients was 1.60 and female RA patients 1.60.There is no generally accepted agreement on sex difference in serum CRP levels. It is concomitant with the finding of Anna Kotulska *et al*., 2015. The study of Lee *et al.*, 2009 shows higher mean values in men, while the study of pieroni *et al.*, 2003, shows higher mean value in women.

The mean value of Rheumatoid Factor in RA patients was 43.5, whereas the mean values of other studies Mohamed Babikir et *al.*,2008; Munnever Sedaroglu *et al*., 2008and Youssef *et al.*, 2014 were 35.52, 103.5 and 126.31 respectively. Our study correlates with the study of Mohamed Babikir et *al.*, 2017, with respected to the mean value of RF factor in RA patients. Higher mean values were found in the studies of Munnever Sedaroglu *et al*., 2008 and Youssef *et al.*, 2014.

With its high specificity, Anti-CCP plays an important role in the diagnosis of rheumatoid arthritis (Lee and Schur, 2003; Suzuki *et al.*, 2003; Dubucquoi *et al.*, 2004). The presence of anti-CCP is associated with radiographic erosion and damage in rheumatoid arthritis (Kroot *et al*., 2000; Jansen *et al*., 2003; Meyer *et al.*, 2003; Forslind *et al.*, 2004; Kastbom *et al*., 2004).

The mean value of Anti-CCP in RA patients was 36. The mean values of the other studies, Mohamed Babikir *et al*., 2017; MunevverSerdaroglu*et al*., 2008 and Youssef *et al*., 2014 were 14.76, 104.6 and 201.77 respectively. The mean values ranges from lower values to the higher values in different studies. The present study Anti-CCP mean value in RA patients was concomitant with the study of Mohamed Babikir *et al*., 2017. Our study not correlates with the other two studies regarding the Anti-CCP of RA patients.

The variation in ESR, CRP, RF and Anti-CCP mean values in different studies may be attributed to the geographical or sample size variations.

Conclusions

From this study, it may be concluded statistical significance have been observed for age and gender of study population. The frequency of females was more than males in both RA patients and controls. The mean values for age of onset and disease duration was more in females than males. The ESR mean value was slightly elevated in female RA patients, whereas the mean values of CRP, RF and Anti-CCP were almost equal in both male and females of RA patients. The biochemical parameters (ESR, CRP, RF, and Anti-CCP) were

statistically insignificant, in RA patients. Further study is required to determine underlying genetic association in patients with Rheumatoid Arthritis.

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