



Levels of Alkaline Phosphatase, Erythrocyte Sedimentation Rate, and C-Reactive Protein in Rheumatoid Arthritis Individuals

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ABSTRACT

Rheumatoid Arthritis (RA) is a chronic autoimmune polyarticular disorder characterized by inflammation of joints leading to systemic complications. Early detection of rheumatoid arthritis is difficult to achieve due to a variety of reasons. The present study was conducted to estimate the level of alkaline phosphatase (ALP), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in individuals suffering from rheumatoid arthritis and compared them with individuals who were not experiencing this condition. The levels of all these markers rise in plasma following tissue damage or injury. This cross-sectional analytical study recruited 130 participants, 70 rheumatoid arthritis patients and 60 healthy individuals. The mean age were found to be 41.14 ± 9.93 years and 41.14 ± 9.93 years for individuals with rheumatoid arthritis and healthy controls, respectively. This condition was found to be more prevalent in female gender. RA afflicted patients had significantly elevated levels of ALP, ESR and CRP compared to healthy group. No significant co-relation was found between levels of ALP, ESR and CRP. It was inferred that each of the three markers has an independent role in predicting the progression of the disease and a combination of these markers can assist in the early and reliable identification of rheumatoid arthritis among patients. Thus, this would subsequently be helpful in early treatment and management of the disease so that the subjects can have a productive lifestyle.

KEY WORDS: Rheumatoid arthritis, Alkaline phosphatase, C-reactive protein, Erythrocyte sedimentation Rate, Autoimmune disorder

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by the inflammation of synovial membrane of the joints, leading to its destruction. This disease has extra-articular effects that may affect organs such as the skin, heart, lungs, and eyes. Hence, this disease is associated with higher incidence of co-morbidities that may prove to be fatal¹. Women are at a greater risk of being afflicted with rheumatoid arthritis compared to men². The age for the onset of the disease ranges from 35 years to 50 years³. RA is diagnosed based on physical examination and X-rays along with the results for complete blood cell count (CBC), rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP), C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR)^{4,5}.

As RA is an autoimmune disorder, the levels of directly the inflammatory biomarkers CRP and ESR are

associated with the disease progression and activity^{6,7}. Alkaline phosphatase (ALP) is extensively used as one of the biochemical markers for determining the status of the various diseases including RA and their subsequent management⁸. Hence the combination of CRP, ESR and ALP are considered to be a reliable prognostic biomarker for the progression of the joint damage and the disease outcome⁹. This study focused on to determine the levels of ALP, ESR and CRP among RA individuals and their comparison with health individuals.

MATERIALS AND METHODS

Sample collection

Patients suffering from RA were recruited from Arthritic Care Foundation Clinic, Behbood Center, Chamba House Lane, G.O.R., Lahore. An informed consent was taken and questionnaire regarding the

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demographics, clinical history and biochemical aspects was filled. Patients with liver diseases, cancer, AIDS, tuberculosis, bacterial endocarditis and other parasitic infections were excluded. Individuals, who did not suffer from RA and belonged to the same age group as that of the patients, were taken as controls.

Determination of RA, ESR, CRP and ALP

Fresh serum sample was used for the determination of rheumatoid factor using Atlas Rheumatoid Factor Latex kit (Atlas Medical, Cat. no. 8.00.04.0.0100). Serum CRP and ALP levels were measured with the Humatex CRP kit (Human Diagnostics, Germany, Cat. no. 40043) by) and Alkaline Phosphatase liquid color kit (Human Diagnostics, Germany, Cat. no. 40043), respectively. Levels of ESR were determined using standard protocol¹⁰.

Statistical analysis

Data was analyzed by using SPSS (version 21, IBM) software.

RESULTS

The study was undertaken to estimate the levels of biochemical markers i.e., ALP, ESR and CRP in RA afflicted individuals and were compared with the healthy controls. A total of 130 individuals participated in this study, out of which 70 individuals tested positive for rheumatoid factor while 60 were tested negative for it and were hence labeled as RA affected and healthy or control group, respectively.

Association of RA with parameters related to demographics, clinical history and biochemical aspects were determined (Table I). Average age of RA afflicted patients included in the study was calculated to be 41.14 ± 9.93 years, while the healthy individuals had an average age of 41.9 ± 11.23 years (Table I). As per results, no significant difference between the mean ages of the two groups was observed. The sample population comprised of 20% males and 80% females of which the RA affected males constituted 13.84%, while the RA affected females constituted 56.15% of the total population. The higher frequency of females in the RA affected individuals indicated that there was greater incidence of rheumatoid arthritis among the female gender. Majority of the individuals having rheumatoid arthritis belonged to low-income groups. However, a small percentage, i.e., 6% and 9% RA affected individuals hailed from upper middle- and high-income class, respectively.

The estimation of ALP levels among the participants in the study showed that the RA affected individuals had significantly elevated ALP levels with a mean of 240.51 ± 66.81 U/I as compared with the mean ALP levels (135.40 ± 22.69 U/I) in healthy individuals (Table I).

The CRP levels in RA affected individuals were considerably higher in comparison to controls (Table I). The CRP levels were considerably raised in some (96 mg/l) while noticeably dropped in others (6mg/l) owing to the inflammation reducing and disease modifying effect of the drugs being utilized by them.

Table I. Demographic, clinical, and biochemical characteristics of healthy vs. RA individuals.

Demographic/clinical parameters	Healthy individuals (n=60)	RA affected individuals (n=70)
Age (years $\pm$ SD)		
	41.9 ± 11.23	41.14 ± 9.93
Gender 'n' (%)		
Males	8 (6.15%)	18 (13.84%)
Females	31 (23.84%)	73 (56.15%)
Age groups (%)		
Below 30	4	7
30-39	9	22
40-49	8	26
50-59	6	11
Above 60	3	4
Socio economic status (%)		
High income class	7	9
Upper middle class	8	6
Lower middle class	7	28
Low-income class	8	25
Family history of RA (%)		
Yes	0	32
No	60	38
Individuals taking prescribed drugs (%)		
Yes	0	68
No	30	2
Individuals with co-morbidities (%)		
No co-morbidity	30	29
Disease related co-morbidities	0	17
Drug induced co-morbidities	0	11
Disease and drug related co-morbidities	0	13
Smoking profile (%)		
Smokers	1	6
Non-smokers	29	64
ALP (U/I $\pm$ SD)	135.40 ± 22.69	$240.51 \pm 66.81^{**}$
CRP levels (mg/l $\pm$ SD)	0.4 ± 2.19	$27.09 \pm 21.73^{**}$
ESR levels (mm/h $\pm$ SD)	12.03 ± 3.44	$44.31 \pm 16.75^{**}$

^{**} p < 0.001

ALP, alkaline phosphatase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate

The evaluation of ESR in the sample population was carried out to estimate the degree of inflammation which is indicated by the rise in ESR levels. RA afflicted individuals had significantly elevated average ESR levels (44.31 ± 16.75 mm/h) in contrast to the mean ESR levels of healthy individuals which was calculated be 12.03 ± 3.44 mm/h (Table I). From the results, it was inferred that elevated average ESR levels in the diseased group illustrated high grade tissue inflammation associated with RA as compared to the controls.

The co-relational analysis of ALP, ESR and CRP was carried out to evaluate if any co-relation existed between the levels of these biochemical markers in the participants. No significant co-relations were found between ALP, ESR and CRP levels among different age groups of participants. Absence of co-relation between the measured biochemical markers suggested that each of these markers contributed independently to the disease process.

DISCUSSION

RA is an autoimmune disease, chronic in nature and is characterized by persistent inflammation of the synovial membrane leading to the erosion of the articular surface of bones and cartilage locally, and atrophy of the other organs principally lungs, eyes, heart and skin, systemically¹¹.

The present study was comprised of 130 individuals among whom 54% were diagnosed clinically positive for RA and constituted the diseased group whereas 46% represented the control or healthy group without RA. The mean ages of RA affected, and healthy individuals did not differ significantly and were almost same as 41.14 ± 9.93 years and 41.9 ± 11.23 years, respectively. However, when the participants of the study were segregated into various age groups, predominance by RA patients (26%) was exhibited in the age group ranging from 40-49 years of age. These results co-relate with an earlier study carried in Karachi, Pakistan in which the average age of incidence of RA in the patients was observed to be between 40-55 years. The outcome of another study undertaken¹² on RA patients visiting a rheumatology clinic in Karachi showed that the mean age of RA affected females was 38.5 ± 12.4 years, while males had an average age of 44.8 ± 13.12 years. According to a study conducted in India¹³, in which individuals aged between 20 to 65 years were recruited, the average age of participants came out to be 43 years.

In this study, a vast majority (53%) of the RA afflicted individuals belonged to poor and lower middle classes. These results co-relate with the earlier studies that indicated a strong association of lower occupational class and its associated psychological and lifestyle factors with the increased risk of developing RA¹⁴. It has been reported by various studies that the RA sufferers from lower income class experience more RA associated co-morbidities and

rate of mortalities as compared to patients from upper socioeconomic classes¹⁵⁻²⁰. According to a study conducted in Sweden²¹, the incidence of RA was higher among the individuals having lower socioeconomic status in contrast to those belonging to upper socioeconomic class.

In the current study, ALP, ESR and CRP levels were assessed in patients who were tested positive for RA factor and compared with their corresponding levels in healthy individuals. Significant increase in mean levels of ALP in RA individuals (240.51 ± 66.81 U/l) was estimated compared to the healthy controls (135.40 ± 22.69 U/l). Raised levels of serum ALP in rheumatoid patients have been reported by various studies²²⁻²⁸. Nanke *et al.*²⁸ suggested that elevated levels of ALP may be attributed to the action of inflammatory cytokines like Interleukin-1 (IL-1)^{27,28}. Our results have been supported by similar studies as demonstrated by Wasti *et al.*²⁹ who reported a significant elevation of the ALP levels in RA patients (386.47 ± 18.86 U/l) whereas the ALP levels of healthy participants were reported to be 204.65 ± 12.21 U/l.

The results of the present study demonstrate a significant elevation in the mean levels of CRP in RA afflicted individuals (27.09 ± 21.73 mg/l) when compared with controls (0.4 ± 2.19 mg/l). Similar results have been reported by other studies³⁰⁻³³. It has been proposed that the CRP levels can predict the future probability of cardiovascular disease linked mortality in rheumatoid arthritis, regardless of the presence of vascular risk factors like myocardial infarction, stroke, and elevated levels of LDL etc.³⁴. The mean ESR levels of the RA patients (44.31 ± 16.75 mm/h) were significantly elevated in contrast to the mean ESR levels of the healthy participants (12.03 ± 3.44 mm/h). These results are in accordance with the previous findings^{30, 33, 35}.

Previously it had been proposed that there exists a positive co-relation between the serum levels of ALP and the disease activity markers i.e. ESR and CRP^{28,33,35}. However, in our study no significant co-relation was found between any of these biochemical markers, perhaps owing to the small sample size taken. However, taking our results into consideration, it is suggested that each of these markers contributed to the disease process in an independent manner. Hence a combination of all these markers is expected to be a better and more effective choice for the early diagnosis and management of rheumatoid arthritis. This conclusion has been supported by the study conducted³⁰ in Rawalpindi, who demonstrated that there exists a direct relationship between each of these individual biochemical markers and the severity of the disease³⁰.

CONCLUSION

This study, which is based on 130 participants,

highlights that while all three biomarkers are markedly elevated in RA patients, there is no direct correlation between them, indicating their independent roles in disease progression. These findings provide valuable information about the combined diagnostic potential of these markers and their applicability in early diagnosis, disease progression and clinical treatment.

DECLARATIONS

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Authors' contribution

RT: Study conception and design; HS: Investigation; HS, IB, NA: Analysis and interpretation of results; HS, RT, FF: Draft manuscript. All authors reviewed the results and approved the final version of the manuscript.

Ethical statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and/or research committee and with the 1975 Declaration of Helsinki, as revised in 2013.

IRB approval

The study was approved by the Ethical Review Committee of Kinnaird College for Women, Lahore

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Generative AI and AI-assisted technology statement

The authors declare that no generative AI and AI assisted technology was used in the creation of this manuscript.

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Data availability statement

Data and supporting information would be available from the authors on request

Statement of conflict of interest

The authors have declared no conflict of interest.

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