Correlation of Serum IL-1β Level in Rheumatoid Arthritis Patients with Disease Severity Parameters

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KEYWORDS

Rheumatoid arthritis , IL-1β, A-CCP, Disease activity, Activity index.

ABSTRACT

Rheumatoid arthritis (RA) is a systemic inflammatory, chronic disorder, characterized by prolonged inflammation of the synovial joints, with ultimate destruction of joints, high concentrations of IL-1β in the synovial fluid and serum RA patients correlated with RA incidence. This study was conducted to compare IL-1β concentration in serum from patients with RA and healthy controls with the correlation parameter being related to markers indicating disease severity. A case-control study enrolled 71 patients with RA and 46 healthy controls from an Iraqi Arab population. In the present study, the level of serum IL-1β was detected using a quantitative sandwich enzyme immunoassay method of Enzyme-Linked Immunosorbent Assay (ELISA). This study found a correlation between the serum level of IL-1β and DAS28-CRP severity among RA patients (p=0.065). Furthermore, the serum level of IL-1β was significantly increased in RA patients compared to the level noted in the healthy group (p=0.039). Moreover, the results demonstrated a very weak correlation between the IL-1β level with CRP, ESR, and ACCP (r=0.079, r=0.059, r=0.080), respectively. In conclusion, the current study showed a correlation between the serum level of IL-1β and RA disease severity (DAS28) among the Iraqi Arab population, additionally, the study noted a very weak correlation between the IL-1β level with CRP, ESR, and ACCP.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder causing symmetrical inflammation of peripheral joints with ensuing synovial hyperplasia, vascular changes, destruction of cartilage and bone, ligaments, and tendons, leading to deformity of joints, and systemic effects. [1]. The pathophysiology of RA entails the interaction of numerous genetic, environmental, and immunological variables interplaying with each other in a very complex way, wherein cytokines form an important link in the mediation of processes related to inflammation. Among these cytokines, IL-1β has turned out to be a major pro-inflammatory inducer for the development and aggravation of RA [2].The Disease Activity Score (DAS28) is a very well-established clinical tool for the measurement of severity of disease activity in RA, based on the general health assessment of the patient, sore and swollen joint count, and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) values. ESR and CRP are acute-phase reactants that read systemic inflammation; their relation to each other and to IL-1β levels explains the inflammatory burden in RA patients [3]. In terms of therapeutic monitoring, however, none of the biomarkers in current use in RA seem to represent the gold standard. Work on more accurate biomarkers is consequently in hand [4]. Cytokines are small protein molecules secreted by different cells and, therefore, may also represent potential biomarkers for their involvement in interactions between cells. A deregulation of cytokine networks produced by peripheral blood mononuclear cells may lead to states of inflammation and tissue damage, which set a stage for the development and perpetuation of RA [4]. Associations between RA disease activity and serum levels of cytokines have been repeatedly investigated [5,6]. According to Meyer et al., (2010), IL-1β was significantly associated with the degree of disease activity in patients with high disease activity, DAS28 > 5.1 [7]. The current study investigated the possible correlation between IL-1β with disease activity scores, and also with laboratory parameters (ESR, CRP, RF, and ACCP) among Iraqi Arab patients.

2. Methodology

The current study had a total of 117 participants: 71 RA patients and 46 controls. This study included Iraqi Arab patients diagnosed with RA illness at Al-Sader Medical Teaching, Najaf City, admitted to the Rheumatology department. Serological tests, such as ESR, CRP, RF, and ACCP, are done by a

specialized rheumatologist, and the determination is based on the 2010 Criteria set by the American College of Rheumatology/European League Against Rheumatism. 52 female patients and 19 male patients between the ages of 21-70 years were involved in this study. In contrast, the control group consisted of approximately 31 girls and 15 males whose ages ranged from 21 to 68 years. According to clinical definitions, DAS28 ≥ 5.1 (n = 31) indicated high disease activity, whereas DAS28 ≥ 3.2 – < 5.1 indicated moderate disease activity, with n = 35. On the other hand, there were (n = 42) high clinical disease activity index (CDAI > 22), and (n = 19) moderate CDAI > 10-22 [8].

Immunological examination

In this study, the amount of serum IL-1β will be determined using a noninvasive Enzyme-Linked Immunosorbent Assay kit that involves a quantitative sandwich enzyme immunoassay technique. The microplate was pre-coated with a monoclonal antibody specific to IL-1β. Standards and samples were pipetted into the wells, and the coated antibody binds to any IL-1β present. After extensive washing, a biotin-conjugated antibody was added for the detection of captured IL-1β protein. This was followed by the addition of the horseradish peroxidase-conjugated streptavidin and tetramethylbenzidine (TMB) reagent to obtain a signal. After that, the wells were washed, the unbound reagents washed away, and an enzyme conjugate was added. Color development was stopped with the help of a stop solution (sulfuric acid); the absorbance was measured at 450 nm against the blank, and the color intensity was directly proportional to the amount of bound IL-1β.

3. Result and Discussion

Comparison of serological parameters (ESR, CRP, RF, and ACCP) between RA patients and controls.

A comparison of serological tests revealed a significant increase in serum levels of ESR, CRP, and ACCP among individuals who suffer from RA compared with a control group (p=0.001). At the same time, the results showed no significant difference in RF in patients with RA compared to controls, as demonstrated in table (1).

Table 1: Laboratory parameters in RA patients and controls

Serological Parameters		N	Mean	±SD	P. Value
CRP	RA	71	16.63	10.07	0.001*
	Control	46	3.58	1.88	
ESR	RA	71	30.67	19.58	0.001*
	Control	46	8.78	4.88	
ACCP	RA	71	62.13	22.31	0.001*
	Control	46	0.53	0.9	
RF	Positive	60	21.45	13.35	0.581
	Negative	11	19.09	10.71	

SD: Standard deviation

*: Significant difference

The present study showed in serological parameters (CRP, ESR, and ACCP) a significant elevation in Iraqi Arab patients who suffer from RA disease (P = 0.001) and these results agreed with Ibrahim *et al*., (2023) who demonstrated an increase in the CRP, ESR, and ACCP levels (P= <0.001) [3]. Multiple studies have shown agreement with these results [9,10,11]. On the other hand, the study noted no significant increase in RA patients compared to controls (p=0.581), which is compatible with Sokka & Pincus, (2009) [12]. However, Yu *et al*., (2024) revealed conflicting results and found a significant increase in RF among RA patients compared to controls (P= <0.05) [13]. Although RF is not

particularly specific to RA, it can be seen in people who have a variety of rheumatic illnesses and is also highly noticeable in healthy individuals [14]. Compared with RF, ACPA has a low frequency in healthy subjects and is very specific for RA. Besides, ACPA plays a diagnostic role in the prediction of the course of the disease and the likelihood of RA patients experiencing bone erosions [15].

1.2 The Association of IL-1β with RA Disease Activity

There was a no significant difference between the IL-1β concentration level and DAS-CRP severe grade (21.65 ± 13.72) compared with moderate and mild grade (22.65 ± 12.40, 9.44 ± 2.96)(p=0.065), respectively, as noted in table (2). This result agreed with Su *et al*., (2024) who demonstrated a significant correlation between IL-1β levels and DAS28-CRP (p=0.05) [15]. On the other hand, the current study didn't found a correlation in the serum level of IL-1β with DAS-ESR severity, and CDAI severity (P>0.05).

Table 2: Serum IL1β level in RA patients and severity parameters

Severity Parameters		N	Mean	±SD	P. Value
DAS28-ESR Severity	Mild	6	13.78	6.53	0.228
	Moderate	34	20.20	14.30	
	Severe	31	23.18	13.90	
	Total	71	13.78	6.53	
DAS28-CRP Severity	Mild	6	9.44	2.96	0.065
	Moderate	33	22.65	12.40	
	Severe	32	21.65	13.72	
	Total	71	21.08	12.93	
CDAI Severity	Mild	10	14.62	12.07	0.171
	Moderate	19	20.17	14.64	
	Severe	42	23.04	12.04	
	Total	71	21.08	12.93	

SD: Standard deviation

The increased IL-1β levels may be associated with more severe DAS28-CRP in RA patients because CRP responds very fast to inflammation, and its levels are closely related to cytokines such as IL-1β. The straight relationship makes CRP a sensitive marker for the immediate activity of inflammation driven by IL-1β. On the other hand, ESR is modified by a series of factors other than inflammation that may weaken its correlation with specific cytokines like IL-1β, for example, anemia and age [16]. CDAI, by contrast, is more based on subjective assessments, and joint counts and may poorly represent the cytokine-driven inflammation reflected by IL-1β levels. The strong association of IL-1β with DAS-CRP but not with DAS-ESR or CDAI clearly shows the complexity of interpreting RA disease activity across a considerable number of markers. Maybe what happens is that IL-1β is much more immediately reflected by CRP and then ESR, and certainly by CDAI, which is influenced by so many factors that the correlation was not seen to be as high [17].

3.3 Correlation of IL-1β with CRP, ESR, and ACCP in RA patients

The results demonstrated very weak correlations between IL-1β and CRP (r=0.079), ESR (r=0.059), and ACCP (r=0.080) among Iraqi Arab patients, as shown in table (3).

Table 3: Correlation of IL-1β with CRP, ESR, and ACCP in RA patients

		IL-1β	CRP	ESR	ACCP
IL-1β	Pearson Correlation (r)	1	0.079	0.059	0.080
	Sig. (2-tailed)	-	0.399	0.526	0.392

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

The correlation of IL-1β with ESR, ACCP, and CRP in this study was in agreement with Meyer *et al*., (2010) who revealed a correlation among ACCP (p= 0.0207) [7]. Furthermore, there was a study that noted a significant correlation of IL-1β with CRP and ESR [18]. On the other hand, Youssef *et al*., (2015) demonstrated a correlation between ESR and CRP with disease activity [19]. Moreover, the current study demonstrated a significant increase in serum levels of IL-1β in RA patients compared with controls (p=0.039).

The correlations between IL-1β and CRP, ESR, and ACCP in patients with RA underline the multilevel role of IL-1β in the induction of inflammation and autoimmunity. Increased levels of IL-1β are accompanied by increased levels of CRP and ESR, reflecting their contribution to systemic inflammation. Although this relationship with ACCP antibodies is more complex, indirectly, via promotion of the inflammatory environment, IL-1β might influence the production of autoantibodies. These correlations can thus be used in assessing disease activity and in the development of targeted therapies in RA [20].

4. Conclusion and future scope

Generally, there was a clear and prominent relationship between serum IL-1β levels and disease activity (DAS28-CRP) among the Iraqi Arab population. Also, there was a correlated IL-1β with CRP, ESR, and ACCP in RA patients.

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Reference

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