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Evaluation of Some Interleukins Levels of Rheumatoid Arthritis (RA) in Baghdad province / Iraq

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Abstract
Autoantibodies damage and weaken joints in rheumatoid arthritis (RA), an autoimmune condition. Leukocyte (Monocyte, Lymphocyte, Mast Cell, etc.) infiltrations into the synovial compartment that cause inflammation in the synovial membrane are characteristics of RA.
This study's objectives were to measure the levels of IL-6 and IL-17 in the serum in a sample of RA patients and to examine the relationship between those levels and a variety of clinical outcomes. It included fifty (50) rheumatoid arthritis patients of both sexes. They are taken from hospitals and clinics, and their ages range from (31 to) 79. The control group consists of (40) people who appear normal. The concentration of IL-6 in serum has been determined using the ELISA enzyme-linked immuno-sorbent test. The findings indicated that men have a higher prevalence of sickness than women. 30% for females against 70% for males. Regarding the age distribution of the patients, they were between the ages of 31 and 79, with a median age of 55. Compared to healthy individuals, who had an interleukin-6 concentration of 139.8–165.88 pg/ml, the concentration in the study participants was 217.1–152.6 pg/ml. Interleukin 17 was present in patients at an average concentration of 129.19 36.88 pg/ml as opposed to 61.62 16.75 pg/ml in healthy individuals.

Key word; Rheumatoid arthritis, RA, IL-6, IL-17

Introduction

Inflammation of the synovium and structural damage to the joints are two features of the chronic inflammatory disease rheumatoid arthritis (Robert and Miossec 2019). Although the exact cause of rheumatoid arthritis (RA) is unknown, intra-articular macrophages play a crucial pathogenic role in the onset and development of the disease by producing excessive amounts of proinflammatory cytokines like tumour necrosis factor- (TNF-), interferon gamma, interleukin-6 (IL-6), interleukin-1 (IL-1), and others (Chen *et al.*, 2019). Few studies have particularly looked at the relationship between renal problems and RA patients receiving biological therapy (anti-TNF -) (Elshabrawy *et al.*, 2015). Several studies have revealed that RA significantly increases the risk of renal injury, which can manifest as diminished tubular and glomerular function (GFR) (Elhewala *et al*., 2015). Its difficulty could be somewhere between 5% and 50%. Clinically, complications in RA patients are frequent because they both restrict how the underlying disease is managed every visit and raise the mortality rate (Al-quraishi, 2015).
The role of IL-15 and IL-18 in the production and maintenance of chronic inflammation during experimental and clinical rheumatoid synovitis was highlighted by recent findings, mostly from laboratories (Zhair *et al.*, 2016). These findings imply that inhibitors of these cytokines may be useful in treating organ-specific autoimmune disorders (Akchurin and Kaskel, 2015). In vitro systems and animal models have amply

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demonstrated that the pro-inflammatory cytokine IL-1 can promote joint erosion, erosive inflammation, and the inhibition of tissue repair mechanisms (Ting-yan et al., 2014).
Biological therapy, which targets inflammatory mediators to treat autoimmune disorders like RA, has gradually advanced the treatment of autoimmune rheumatic diseases (Zhair *et al.,* 2016).). This type of medicine, known as biological therapy, is an antagonist of tumor necrosis factor-alpha (anti TNF-) (Schulz *et al.,* 2014). These drugs work by preventing the production of the pro-inflammatory cytokine TNF-, such as infliximab and the IL-6 receptor inhibitor (tocilizumab), which targets the IL-6 protein (Wang, 2015).
The goal of this study was to compare the serum levels of a few specific cytokines in a group of Iraqi RA patients to those of controls who appeared to be in good health.

Materials and Methods

50 RA patients with a range of ages between 31 and 79 years (15 female, 35 male) who visited the outpatient clinic of the department of rheumatology at Al-Yarmook Teaching Hospital and private clinics in Baghdad City were included in this study. The American College of Rheumatology's categorization criteria were used to determine the diagnosis of RA (Kany *et al.,* 2019).
Participants in the study had healthy liver function tests and blood workups.

Sample Collection

At the time of the clinical examination, three milliliters (ml) of venous blood were drawn from each participant under strictly sterile conditions, after which the serum was separated and stored at -20°C for IL-6 and IL-17 level determination.

measurement of IL-6 and IL-17

Using an enzyme-linked immuno-sorbent assay (ELISA), serum IL-6 levels were measured in both RA patients and healthy controls in accordance with the manufacturer's recommendations (Abcam-UK).
the ELISA approach is used to test IL-17 in serum in accordance with the manufacturer's instructions (IL-17 kit, Diaclone/France);

Results and discussion

1- Demographic study

Our most recent survey of arthritis patients revealed that men are more likely than women to get the disease. 30% for females against 70% for males.
Table 1 displays the age distribution of the patients, who ranged in age from 31 to 79, with an average age of 55.

Table 1: Demographic data of the RA patients

Characteristic group	RA group	%	comparison
Number (M / F)	50 (35/15)	70% /30%	40 (27/13)
Age (yr)	55		53

in comparison to other studies A large cohort of Arab patients were included in this study to assess the epidemiology and treatment patterns of RA. Throughout the study period, 87% of patients were female overall, which was roughly the same as the study conducted in 2018. (Mirlekar and Pylayeva-Gupta, 2021). The age of the patients in our study was younger than that of the patients in North America and Europe, but was equivalent to that of patients in neighboring countries; this may not only be connected to the lower average age of our population but also to genetic or environmental variables (Xin *et al.,* 2021). This is also observed with other diseases that are connected to genetic abnormalities, such as endocrine disorders or oncology disorders; in these conditions, the age of diagnosis was lower, averaging roughly 20 years less than in western nations (Ecoeur *et al.,* 2020).

2- Result of interleukin-6 and interleukin-17

According to the findings of our recent study, interleukin-6 levels in patients with arthritis were on average 217.1 152.6 pg/ml higher than those in healthy subjects, who were 139.8 165.88 pg/ml higher.

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As shown in Table 2, the average concentration of interleukin 17 was 129.19 36.88 pg/ml in patients as opposed to 61.62 16.75 pg/ml in healthy individuals.

Table 2: Mean of Concentration of IL-6 and IL-17 in RA patients and control.

IL	Patients	controls	P value
Concentration of IL-6 [pg/ml]	217.1 ± 152.6	139.8 ± 165.88	< 0.01
Concentration of IL-17 [pg/ml]	129.19 ± 36.88	61.62±16.75	< 0.01

The results of the present investigation showed a strong association between RF and IL-6, which clarifies the function of RF in the creation of ICs, complement activation, and ultimately cellular infiltration leading to the production of cytokines (Mirlekar and Pylayeva-Gupta, 2021). According to this study and other research, it was discovered that the disease worsens in the presence of RF, HLA-DR4 molecules [evidence of high disease activity], especially when they are coupled with an increase in IL-6 (Xin *et al.*, 2021). Patients with sporadic RA do not have a family history of the disease; yet, 42 out of 75 RA patients had a higher frequency of HLA-DR4 than those who appeared to be in good condition.

This study showed that (IL-6) is a protein that is overproduced in rheumatoid arthritis patients' sera and is thought to be the cause of swelling and joint destruction. In persons with rheumatoid arthritis, interleukin-6 may also contribute to fever and an overabundance of blood platelets (thrombocytosis). Researchers are hoping that inhibiting IL6 will lessen the harm it causes (Mirlekar and Pylayeva-Gupta, 2021).

Patients with RA have higher levels of IL-6 in their serum, plasma, and synovial fluid (Xin *et al.*, 2021). In RA patients, serum and plasma IL-6 levels are associated with clinical assessments of disease activity and radiographic development of joint damage (Wang *et al.*, 2018). Several investigations have demonstrated that the treatment target for RA is IL-6 suppression (Luo *et al.*, 2017). In phase I and II clinical studies with RA patients, a humanized anti-IL-6Ra monoclonal IgG1 antibody (tocilizumab) shown efficacy by preventing disease activity and joint damage (Yang *et al.*, 2020). High quantities of IL-6 have been found in the synovial fluid of RA patients, and blood levels of this cytokine strongly correspond with indicators of the disease's activity, like acute phase proteins (Bridgewood *et al.*, 2019).

According to the current study, RA patients had considerably greater levels of IL-15 and IL-17 than the control group. This finding is in line with a number of research (Xiao *et al.*, 2021). On the other hand, there was no discernible difference between RA patients and controls in the frequency of peripheral blood Th17 cells (Chen *et al.*, 2019). According to earlier research, IL-15 was found in the synovial membrane of RA patients, and up to 40% of them had modest amounts of it in their sera (Li *et al.*, 2021). The disparity between earlier studies and the current one could be explained by patient selection, therapy received, and assay conditions used to measure cytokine levels.

Regarding the length of the disease, there was no discernible variation in the mean serum IL-17 levels of our patients. Metawi et al. also came to the same conclusion (Li *et al.*, 2019). In contrast to our findings, Guan *et al.*, (2017). found a strong inverse relationship between RA patients' synovial IL-17 levels and the length of their disease. These disparities in the IL-15 and IL-17 trials can be explained by the fact that patients with early active RA (12 months) rather than patients with established RA were included in the research.

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