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Research Article

Serum IL-22 In Patients with Rheumatoid Arthritis

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Abstract- :
Background Rheumatoid arthritis (RA), a chronic inflammatory autoimmune illness that affects multiple systems, has an unknown cause. This disease mostly affects synovial joints, causing chronic inflammation and consequent degeneration of both cartilaginous and osseous tissues. These organs Furthermore, when cytokines stimulate synoviocytes, they release matrix metalloproteinase (MMP) into the synovial fluid. These digestive enzymes digest and break down cartilage. consist of sialadenitis, interstitial pneumonia, and kerato-conjunctivitis sicca. It was formerly thought to be a T-helper (Th-17) cytokine because it was seen to be created in cells that also make IL-17, but further research showed that it may also be produced separately from IL-17. In contrast to other cytokines, which target haematological cells, In organs as diverse as the lungs, liver, kidneys, thyroid, pancreas, breast, gut, skin, and synovial membrane, IL-22 significantly affects both epithelial cells and fibroblasts.
Objective: This study will highlighted role of IL-22 in rheumatoid arthritis.
Materials and methods: A period of December 2021 to March 2022 was chosen for this inquiry. Matching the ages for the patients involved in the study were 42 newly diagnosed patients with rheumatoid arthritis in the 30- to 50-year age range, and 42 healthy persons serving as controls. was to measure serum IL-22 level using an ELISA kit.
Results: In Rheumatoid arthritis patients median serum IL-22 level was (20.43pg/ml) and it is significantly higher than that healthy group (5.65pg/ml).
Conclusion: As a helpful biomarker for RA diagnosis and disease activity assessment, interleukin-22 can be evaluated.

Keywords: Rheumatoid arthritis, IL-22, ESR, CRP.

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Introduction: -

Rheumatoid arthritis (RA), a chronic inflammatory autoimmune illness that affects multiple systems, has an unknown cause. This disease mostly affects synovial joints, causing chronic inflammation and consequent degeneration of both cartilaginous and osseous tissues. In women between the ages of thirty and sixty, it happens 1 in 150 times. It causes inflammation in various tissues, oedema, stiffness, and troubles with several organs. Joint degeneration with rapid advancement leads to irreversible joint dysfunction and deformity. Consequently, it is essential to detect and treat diseases early [1, 2, 3, 4,5].

In synovitis lesions, lymphocytes and synoviocytes create significant amounts of inflammatory cytokines, including tumor necrosis factor (TNF) and interleukin-1 and interleukin-6, which cause synovitis. In addition to systemic symptoms, including low-grade fever and malaise, extra-articular organ involvement is frequently observed[6,7]. These organs Furthermore, when cytokines stimulate synoviocytes, they release matrix metalloproteinase (MMP) into the synovial fluid. These digestive enzymes digest and break down cartilage. consist of sialadenitis, interstitial pneumonia, and kerato-conjunctivitis sicca. Receptor activator of nuclear factor kappa B (RANKL) ligand, which promotes osteoclast activation and proliferation, is also produced by lymphocytes and synoviocytes. Inflammatory granulation tissue that is stratified, proliferative, and contains synoviocytes grows till it reaches the bones. Multinucleated osteoclasts mainly degrade joints where they come into contact by breaking down and absorbing bone [7, 8,9].

One of the interleukin-10 (IL-10) subunits with the most investigation is IL-22. Interleukin-22, or interleukin-10 associated T-cell derived factor Interleukin-Tumor necrosis factor (IL-TIF), has drawn much interest lately. The cytokine family also includes the cytokines lambda-interferons-28A, lambda-interferons-28B, and interleukin-29(IL-29), as well as the cytokines interleukin-10 (IL-10), interleukin-1,interleukin-20 , interleukin-24 and interleukin-26 [10]. It was formerly thought to be a T-helper (Th-17) cytokine because it was seen to be created in cells that also make IL-17, but further research showed that it may also be produced separately from IL-17. In contrast to other cytokines, which target haematological cells, In organs as diverse as the lungs, liver, kidneys, thyroid, pancreas, breast, gut, skin, and synovial membrane, IL-22 significantly affects both epithelial cells and fibroblasts [10,11]. On the other hand, four serological tests—rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)—are included in the revised ACR/EULAR 2010 criteria for the early diagnosis of RA [12]. Clinical evaluation continues to be the primary means of disease activity monitoring due to the absence of suitable biomarkers for this purpose. Furthermore, nonspecific acute-phase reactants like ESR and CRP might have increased levels for a variety of causes [13]. Patients with rheumatoid arthritis (RA) have been shown to have elevated serum levels of IL-22, which can be used as a marker of the severity of the condition [14]. In addition to examining their functions in inflammatory arthritis, this study sought to determine the diagnostic utility of interleukin-22 (IL-22) as an optimal biomarker for the diagnosis of RA and distinguish it from other forms of inflammatory arthritis.

Materials and Methods:

A period of December 2021 to March 2022 was chosen for this inquiry. Matching the ages for the patients involved in the study were 42 newly diagnosed patients with rheumatoid arthritis in the 30- to 50-year age range, and 42 healthy persons serving as controls. The Medical City, Baghdad Teaching Hospital is now accepting patients. Following their separation from the whole blood, serum samples were aliquoted and kept at -20ºC until needed. Enzyme-linked immunosorbent assay (ELISA) was the method they used to find human IL-22. IL-22 ELISA kit (CLOUD-CLONE CORP.(CCC).) human interleukin 22(catalog No. SEC032Ra). USA.

Statistical analysis: - The statistical package for the social sciences (SPSS), version 20.0 for Windows, Chicago, IL, USA, was utilized in the study. It was determined that the distribution of IL-22 was atypical through the application of the Kolmogorov-Smirnov test. For quantitative data with a normal distribution, the terms mean, standard deviation, and range are used; for non-normal data, the terms median, IQR (interquartile range), and range are used. The distribution of sexes in the IL-22 group was ascertained using the chi-square test. The age difference between the patient and control groups was investigated using the student's t-test. Using the Mann-Whitney U test, the levels of IL-22 in the patient and control groups were compared. For a P-value to be considered statistically significant, it has to be less than 0.05.

Results:-

The studied group consisted of 42 RA patients, 17 (40.5%) male and 25 (59.5%) female. Forty-two matched-sex, healthy volunteers were considered a control group; 16 (38.1%) were male and 26 (61.9%) were female. The distribution of sex of the studied groups is shown in **(Table 1).**

Table (1): Distribution of sex in patient and control groups

			Group		**Total**	**P- value**
			Patient	**Control**		
Sex	**Male**	Count	17	16	33	**0.823** ^{*NS}
		%	40.5%	38.1%	39.3%	
	Female	Count	25	26	51	
		%	59.5%	61.9%	60.7%	
Total		Count	42	42	84	
		%	100.0%	100.0%	100.0%	

*** NS=non -significant**

Table (2) shows that the mean age of patients was 40.00±50.0 years, whereas for healthy subjects it was 40.00±49.00 years with no significant differences (p > 0.05).

Table 2: Age distribution of two studied groups

Age	**Group**				**P -value**
	Patient		**Control**		
	Mean ±SD	Rang	Mean ±SD	Rang	
	40.00 ±50.0	30.00-50.00	40.00 ±49.00	30.00-50.00	**0.197*** ^{NS}

***NS=non -significant**

Table 3 and Figure 1 show the difference in serum IL-22 level in RA patients in comparison to the healthy group. It shows that the median serum IL-22 level was 20.43 (12.08%) pg/mL, and it is significantly higher than the healthy group's 5.65 (4.55%) pg/mL.

Table (3): Serum IL-22 levels in the groups of patients and controls

	Group						**P value**
	Patient			**Control**			
IL-22	Median	IQR	Rang	Median	IQR	Rang	**0.005** **S
	20.43	12.08	16.63-1000.0	5.65	4.55	1.50-15.63	

****S=significant**

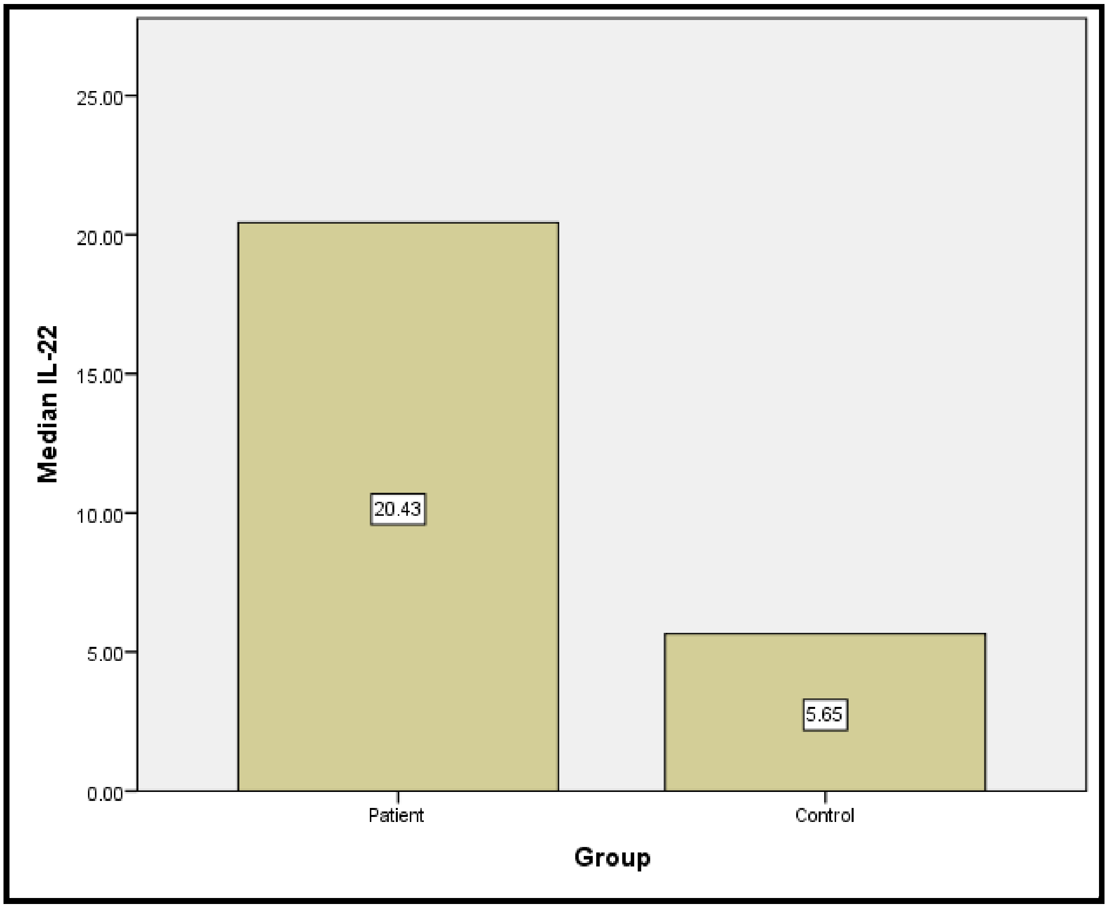

Figure (1): Serum IL-22 levels in the groups of patients and controls

There was a statistically significant correlation of IL-22 value with ESR level (P = 0.001), but there was no significant correlation between IL-22 level and the CRP titer (P = 0.098) as shown in **Table (4)**

Table(4):Correlations between IL-22 level and levels of ESR,CRP in the RA patients.

Parameters	**IL-22 (pg/ml)**		**ESR (mm/h)**	**CRP titer (mg/L)**
IL-22 (pg/ml)	**r**	**1**		
	p			
ESR (mm/h)	**r**	**0.240**	**1**	
	p	**0.001****		**1**
CRP titer (mg/L)	**r**	**0.147**	**0.45**	
	p	**0.098**	**0.001**	

Linear regression, r: regression coefficient, **=highly statistical significance at P <0.001.

Discussion: -

Adults can develop rheumatoid arthritis, an autoimmune and inflammatory condition, with a percentage of 0.5 to 1% [15]. The study involved 42 participants with rheumatoid arthritis. A mean patient age of 40 years was found among 42 RA patients, with 17 (40.5%) male and 25 (59.5%) female ranging in age from 30 to 50. The difference in age and sex between trematoid arthritis patients and the control group was not statistically different; the corresponding P-values were 0.197 and 0.823, according to Moeez et al. [16]. Rheumatoid arthritis is three times more common in women than in men, and individuals between the ages of 30 and 60 are the most commonly affected. Almoallim et al. [14, 17].

According to the current study, individuals with RA have higher serum levels of IL-22 compared to controls, consistent with previous researchers' findings [18, 19, 20]. Zhao and colleagues discovered that major IL-22-producing CD4+Th-cells may function by excessively generating IL-22 to accelerate the pathogenesis in rheumatoid arthritis. According to the current study's findings, an elevated level of IL-22 is thought to be a significant indicator of heightened disease activity in RA patients. Moreover, the IL-22 level can be utilized to track the progression of the disease and how well treatment is working. As a result, since this biomarker offers crucial information regarding disease activity, keeping an eye on it can help treat RA [5,21].Rheumatoid arthritis patients had considerably higher serum IL-22 levels and percentages of Th-22, IL-22+Th-1, and IL-22+Th-17 cells than healthy controls [21,22]. IL-22 contributes significantly to the production of inflammatory components by inhibiting Th-1 plasticity and increasing Th-17 maintenance and survival. This indicates the potential treatment advantages of IL-22 suppression for RA patients, including decreased production of immune complexes and joint deterioration [23,24]. IL-22 may contribute to the development of RA, according to specific research [25,26,27,28,29,30]. In RA synovial tissues, elevated amounts of IL-22 have been found, and the lining and sub-lining layers of rheumatoid synovium expressed more significant levels of IL-22R1 [31,32]. The results of this study showed a strong relationship between the ESR and IL-22 levels. The present outcome is consistent with Yousef et al.'s findings. This implies that either these autoantibodies may affect the production or activity of IL-22, or IL-22 may play a role in the synthesis of RF and ACPA [21,33,34,35].

Conclusion: As a helpful biomarker for RA diagnosis and disease activity assessment, interleukin-22 can be evaluated.

Conflict of Interest: There are no conflicts of interests

Funding: Self

Ethical clearance: is not required

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