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Assessing the connection between rheumatoid arthritis and the interleukin IL36 level in tonsillitis patients in the Diyala Governorate

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ABSTRACT

This study investigated the relationship of IL-36 with tonsillitis and rheumatoid arthritis patients. Using Enzyme Linked Immunosorbent Assay (ELIZA) technique. This study conducted in Diyala Governorate from beginning of October 2023 to end of May 2024. 88 samples collected and divided into four groups, their ages ranged between) 80-10) years, the first group included 22 blood samples with rheumatoid arthritis, and second group included 22 samples with acute and chronic tonsillitis. And third group, included 22 samples with tonsillitis and rheumatoid arthritis. Fourth group, controls included 22 samples from healthy people Clinically. Their aged from (21-60) years. The statistical results among study groups showed that infection rate among females 18 (82.0%) higher than males 4 (18.0%) among patients with rheumatoid arthritis, infection rate among females 16 (% 73.0) higher than males 6 (%27.0) among tonsillitis patients, infection rate for females 17 (77.0%) more than males 5 (23.0%) among patients with tonsillitis and rheumatoid arthritis. Results also showed that infection rate among females 8 (36.0%) less than males 14 (% 64.0) among controls. The current study results revealed increased level IL-36 with rheumatoid arthritis (551.83 ± 65.86) Pg/ML, patients with tonsillitis (271.15 ± 64.40) Pg/ML, and patients with tonsillitis and rheumatoid arthritis (279.53 ± 50.79) Pg/ML compared to controls (193.14 ± 21.04) Pg/ML. These results suggest IL36 increases with tonsillitis or rheumatoid arthritis, so it may have an anti-inflammatory effect.

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1. INTRODUCTION

Tonsillitis causes irritation and inflammation of the membranes lining the pharynx due to exposure to a bacterial infection. Streptococcus pyogenes affects all age groups, and the infection is usually active in late fall and early spring . The tonsils are the first line of defense against pathogens and are also the site of recurrent chronic inflammatory processes, as acute recurrent tonsillitis is a common chronic inflammation of the palatine tonsils that often requires surgical removal [1]. Rheumatoid arthritis (RA) is one of the most widespread diseases in the world resulting from tonsillitis resulting from infection with the bacterium *S. pyogenes*. It is an inflammatory disorder resulting from an autoimmune response that develops into a chronic condition that affects different joint parts of the body. Rheumatoid arthritis is characterized by persistent synovitis, which leads to the appearance of autoantibodies (especially to rheumatoid factor) [2]. The pathogenesis of rheumatoid arthritis involves a complex network of different cytokines and cells that lead to the proliferation of synovial cells and cause damage to both cartilage and bone, the most important of which is the cytokinetic interleukin 1 family, which consists of seven ligands with pro-inflammatory activity (IL-1α،IL-1β،IL-18،IL-33،IL-36α،IL-36β،IL-36γ).

These cytokines are known to play a critical role in modulating both innate andadaptive immune response, with their dysregulation associated with a variety of autoimmune and inflammatory diseases and the pathogenesis of rheumatoid arthritis [3]. Interleukin-36 alpha plays a prominent role in inflammatory diseases, such as inflammatory bowel diseases, rheumatoid and psoriatic arthritis, and many skin diseases, and the expression of IL-36 increases by microbial stimuli [4]. The IL-36 family is thought to play a main role in maintaining homeostasis and first-line defense mechanisms [5].IL-36R is expressed by DCs, CD4+ T cells, and macrophages. Binding of agonists to membrane-bound IL-1RrP2 results in recruitment of the co-receptor IL-1RAcP. This stimulates an intracellular signaling cascade via JNK, ERK1/2, and NF-kB resulting in the production of pro-inflammatory mediators. Conversely, binding of the natural inhibitors IL-36Ra and IL-38 inhibits signaling. During recent years, the cytokine IL-36 has aroused increasing interest, as it has been found to have a role in various diseases, including rheumatoid arthritis [6].

2. METHODS

This study was conducted in Diyala Governorate for the duration from the beginning of October 2023 to the May 2024. 88 blood samples were collected and divided into four groups, their ages ranged between (80-10) years, where the first group included 22 samples from patients with rheumatoid arthritis, and the second group included 22 samples from patients with acute and chronic tonsillitis. As for the third group, it included 22 samples from patients with tonsillitis and rheumatoid arthritis. The samples were taken after the clinical diagnosis of the disease cases by the specialist doctor from the ear, nose and throat division as well as the joint diseases division in the consulting clinic at Baquba Teaching Hospital in Diyala Governorate. The fourth group, the control group, included 22 samples from apparently healthy people Clinically. Their ages from (21-60) years.

2.1 Collection of Blood Samples

Samples were collected by venous blood draw. (5 ml) of blood using a disposable syringe and placed in test tubes and left for (30) minutes at room temperature for coagulation. Then the sera were separated by centrifuge for 5 minutes at a rate of 3000 rpm. The serum was divided into equal amounts (250 µl) in Eppendorf tubes and stored at a temperature of (-20) until use. Each section of the conserved serum used once to avoid repeated thawing. For the purpose of measuring the concentration level of IL-36 by using the sandwich ELISA assay [3].

2.2 ASSAY PROCEDURE

1-prepared standard solutions and samples according to the instructions and opened the measuring plate for the purpose of starting work.

2- After adding 100 µl of the standard and samples to the appropriate holes, the plate was sealed with an adhesive cover that included the diagnostic kit. It was then incubated for two hours at 37°C in an incubator.

3- All liquids were removed from the holes without washing.

4- Each hole was filled with 100 µl of (1x) Biotin antibody. The plate was then sealed with a fresh adhesive cover and incubated for an hour at 37°C.

5- The plate was washed three times for two minutes each time.

6- After adding 100 µl of HRP-Avidin (1x) to each hole and covering the plate with a fresh adhesive cover, the plate was incubated for an hour at 37°C.

7- The plate was washed five times for two minutes each time.

8- The plate was incubated at 37°C for 15–30 minutes and kept out of direct sunlight after 90 µl of the base material (TMB) (tetramethylbenzidine) was applied to each hole.

9- 50 µL of 2M Sulfuric acid stopping solution was added to all the holes, and the color changed from blue to yellow.

10- The absorbance of the samples was read at a wavelength of (450) nanometers five minutes after adding the stop solution. As shown in figure (1)

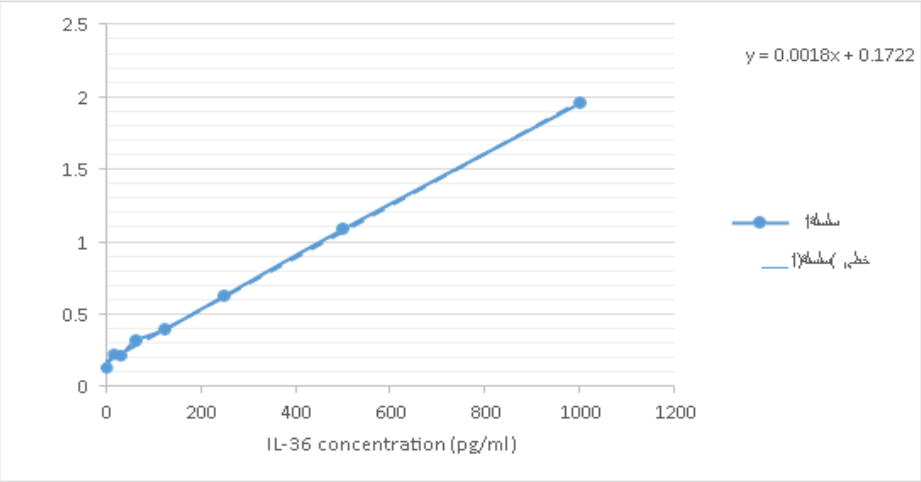

Figure 1. Standard curve for IL36 concentration.

2.3 Statistical analysis:

The program: IBM SPSS computer program versionV27.0. The used tests: mean, SE, ANOVA table (Duncan test), independent t-test, frequency and percentage, and chi square test.

3. RESULTS AND DISCUSSION

Table (1) shows the results of the study groups that the infection rate among females was 18 (82.0%) higher than that of males 4 (18.0%) among patients with Rheumatoid Arthritis, where mean of age for females was (48.24 ± 1.32)years and for males (48.78 ± 2.92) years, As shown in Table (2) and the infection rate among females 16 (%73.0) is higher than that of males 6 (%27.0) among tonsillitis As shown in Table (1) and mean of age for females is (37.79± 1.59) years and for males (38.81 ± 3.25) years. As shown in Table (2)The infection rate among females 17 (77.0%) is higher than that in males 5 (23.0%) among patients with tonsillitis and rheumatoid arthritis due to mean of age for females (44.65 ± 3.22) years and males (43.75 ± 5.22) years, compared to control, as the infection rate in Females 8(% 36.0) are less than males 14 (%64.0) among healthy people, and mean of age for females is (32.35 ± 2.30) years and for males (31.32 ± 1.95) years. As shown in Table (2). The results of the current study showed that the age of females infected with the disease is greater than the age of males infected with the disease, and there was no statistically significant difference between the study groups, as the p-value was (p > 0.05), as shown in the two tables below.

Table 1. The infection rate for the study groups and its comparison with the control group by gender

Groups	*Male*	*Female*	*Total*
R.Arthritis	4 (18.0)	18 (82.0)	22 (100.0)
Tonsilitis	6 (27.0)	16 (73.0)	22 (100.0)
R.Arthritis& Tonsilitis	5 (23.0)	17 (77.0)	22 (100.0)
Control	*14 (64.0)*	*8 (36.0)*	*22 (100.0)*

***Rheumatoid Arthritis group**

Table 2. Distribution of study groups and comparison with healthy controls according to gender and age

Groups	Male	Female	Total	
R.Arthritis	48.78 ± 2.92	48.24 ± 1.32	48.39 ± 1.24A	P > 0.05
Tonsilitis	38.81 ± 3.25	37.79 ± 1.59	38.17 ± 1.56B	P > 0.05
R.Arthritis& Tonsilitis	43.75 ± 5.22	44.65 ± 3.22	44.48 ± 2.74AB	P > 0.05
Control	31.32 ± 1.95	32.35 ± 2.30	31.78 ± 1.48C	

Similar letters indicate no significant differences

Table 3. The level of IL-36 in the study group and its comparison with the control group.

Group	Male	Female	Probability	Total
R.Arthritis	636.40±181.47	536.46±71.93	P > 0.05	551.83±65.86A
Tonsilitis	391.05±130.70	202.63±65.41	P > 0.05	271.15 ± 64.40B
R.Arthritis& Tonsilitis	275.13±175.97	280.57± 51.15	P > 0.05	279.53 ± 50.79B
Control	216.78±27.40	154.74± 29.79	P > 0.05	193.14±21.04B
Similar letters indicate no significant differences				

***Rheumatoid Arthritis group**

The results of the current study found that the incidence rate with tonsillitis and rheumatoid arthritis in females, the infection rate increased more than in males. This can be due to several reasons, including hormonal influence in the case of infection in women, which is more than in men, genetic predisposition, type of life, environmental factors, and lack of interest in health care. It has been observed that there is an interaction between endogenous sex hormones and the occurrence of inflammation, with an increased risk of contracting the disease. The results of this study indicated a higher incidence of chronic tonsillitis in females than in males. The results of the current study were consistent with the results of the study [7].

The study agreed with a study conducted by [8]. In addition to this, lack of health awareness, lack of regular exercise, and following an unbalanced diet, as the disease is associated with being overweight in females more than males due to eating unhealthy food and lack of movement, which increases the chance of contracting chronic diseases that weaken the efficiency of the immune system, in addition to genetic factors. And the environment plays a complexrole in enhancing immunity, which is confirmed by the emergence of autoimmune diseases and the fluctuations accompanying the disease when hormonal changes occur. In addition, males and females deal differently with their chronic diseases [9]. Chronic tonsillitis is a trigger for the occurrence of autoimmune diseases and is one of their causes as a result of the induction of helper T cells, which has a role in the development of inflammation. In addition to the presence of other factors that have a significant impact on the weak efficiency of the immune system, such as aging and a family history of tonsillitis and rheumatoid arthritis [1]. The results of Table (3) for the current study groups showed a high level of interleukin IL- 36 in patients with rheumatoid arthritis (551.83 ± 65.86) Pg/ML, patients with tonsillitis (271.15± 64.40) Pg/ML, and patients with tonsillitis and rheumatoid arthritis (279.53 ± 50.79) Pg/ ML compared to healthy group (193.14 ± 21.04) Pg/ML. These results agreed with the findings of [11], who found increased levels of IL-36 in the serum of patients with rheumatoid arthritis, which is regulated in the synovial tissue of the patients. In a study by [12].on the effect of IL-36 on a group of systemic inflammatory diseases, including rheumatoid arthritis, IL-36 alpha and its receptors were discovered in patients with rheumatoid arthritis, the expression of IL-36 in synovial tissue was higher than in patients with osteoarthritis. In a study, it was found that the increase in the production of interleukin 36 accompanying synovial cells increases the production of IL-6 and IL-8. It is believed that the presence of synovial plasma cells is the main source of expression of interleukin 36 in rheumatoid arthritis, as well as for cell-specific markers. Due; Because IL-36α positive cells were closely associated with leukocyte infiltration While it is also found with plasma cells in the synovial membrane [13]. Note that all previous studies dealt with rheumatoid arthritis without tonsillitis, which makes the current study the first of its kind that combined patients with rheumatoid arthritis and those with tonsillitis and IL-36 according to the limits of the researcher's knowledge.

4. CONCLUSIONS

A high level of interleukin IL-36 in patients with rheumatoid arthritis and tonsillitis and patients with tonsillitis and rheumatoid arthritis. These results suggest that IL36 may have a role in disease pathogenesis.

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