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ASSESSMENT OF CRP AND RF LEVEL IN RHEUMATOID ARTHRITIS PATIENTS IN DIYALA GOVERNORATE

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ABSTRACT

Rheumatoid arthritis (RA) is a severe autoimmune disease that causes chronic joint inflammation. The study aimed to comparison of levels of RF, CRP in the serum of patients and healthy controls, and study the influence of age and gender on the prevalence of RA. This study was conducted from the beginning of February to the end of April 2023. The samples were diagnosed by the specialist consulting physician at Baquba Teaching Hospital. Seventy blood samples were collected from patients with periodontal diseases, and 40 apparently healthy individuals who were considered as a control group. The current study showed that the prevalence of the disease was higher in females (n=49) than in males (n=21), (70 %, 30 %), respectively. This study looked at patients between the ages of (16-83) years and the rate of infection with rheumatoid arthritis was (43.43 ± 1.85) compared with healthy people aged (19-75) was (41.68 ± 2.23), there is no significant difference ($P > 0.05$). It was found that the number of arthritis patients who were positive for RF was (5), while the number of negative ones was (65), at a rate of (7.1%, 92.9%), there is a significant difference ($P < 0.001$). It was found that the number of rheumatoid arthritis patients who were positive for CRP was (32), at a rate of (45.7%), while the number of negative ones was 38, at a rate of (45.7%, 54.3%), respectively. There is a significant difference ($P < 0.001$). Samples were investigated by the latex agglutination test was used to examine CRP and RF.

KEYWORDS: Rheumatoid arthritis, Rheumatoid factor, C-reactive protein.

INTRODUCTION

Rheumatoid arthritis is a prevalent immune-mediated illness. Its main symptom is inflammatory arthritis, which is typified by symmetric, polyarticular pain and swelling, usually in the hands and feet's tiny joints, but rheumatoid arthritis is a systemic illness with extraarticular symptoms and a number of concomitant illnesses. Specific environmental exposures combined with genetic variables cause the onset of inflammatory synovitis. Before the condition may be labeled as rheumatoid arthritis, the disease process starts years before clinically evident arthritis and presents as a continuum that starts with asymptomatic immune dysfunction and advances through many phases (Gravallese & Firestein, 2023). Rheumatoid arthritis affects between 0.5% and 1.0% of people globally, with certain populations—like Indigenous North Americans—having a greater frequency than others. Although rheumatoid arthritis can strike anybody at any age, it is most prevalent in the third and fifth decades of life, and it affects women two to three times more frequently than it does males. The condition is more common in women, which is likely due in part to the effects of estrogen on immunological function (Cutolo & Straub, 2020). Patients with RA experience higher morbidity and mortality, mostly from cardiovascular disease (CVD), in addition to chronic discomfort, fatigue, and potential disability (Symmons et al., 2011). Synovitis is the most common symptom of rheumatoid arthritis with a 1 in 150 chance of developing it, women in their 30s and 50s are the most affected. It is accompanied by multi-organ issues, edema, pain, and stiffness in numerous joints. Joint deterioration happens fast after it starts, resulting in physical dysfunction and irreversible joint deformity. As a result, in the early stages of the disease, thorough diagnosis and therapy are essential (Tanaka & Yoshiya, 2020). This increase in immune system defense Mechanisms may exist in the body before synovitis in the joints becomes clinically evident. The spread of autoimmunity may be detected prior to an inflammatory-based RA diagnosis, therefore the genetic and environmental risk factors for RA may also be having an impact on the body and its systems long before the distal joints swell. The familial genome may account for 50% of the risk of developing RA in seropositive patients (Deane et al., 2017). A number of immune response components, including neutrophils, mast cells, lymphocytes, synovial tissue cells, and platelet microparticles, are essential to the inflammatory process in synovial fluid. (Boilard et al., 2010). A genetic family history contributes to a three- to five-fold increased risk of developing the disease, and in 2016 the genes

responsible for the disease were studied and found 40-65% of cases of serous rheumatoid arthritis (Firestein & McInnes, 2017). RA is strongly associated with MHC type I genes. HLA-DR4 is the main genetic factor. It varies relatively between ethnic groups. Mutations that affect common response immune pathways, for example (CD28, CD40) and increased activation of the innate immune pathway appear to be its effect is less than that of HLA mutations (Firestein & McInnes, 2017). A number of variables can raise your chances of developing arthritis, including: The elderly: since their joints are used for a longer period of time. Women are more prone than males to develop osteoporosis, particularly after the age of fifty. Having a history of osteoarthritis in your family. Obesity or being overweight: Being overweight or obese can aggravate arthritis in the weight-bearing joints (eg: knees, hips, and spine). People who work in jobs that involve repetitive movement are more vulnerable (Hema & Aswathy, 2007). Symptoms of arthritis: Arthritis symptoms appear gradually and usually start with one joint. They include: when using the joint, there is pain that may improve with rest. The discomfort may be severe at night for some people with it, especially in the later stages of the condition. In the morning or after resting for a while, joint stiffness that lasts less than 30 minutes. Swelling around and around the joint, particularly after a lot of movement. Weakness in the joint's capacity to move. Feeling as if the joint is shaky. When moving the joint, a sound is heard. Some tasks may become difficult to conduct as symptoms intensify (eg: climbing stairs) (van de Sande & Baeten, 2016).

Significantly, RA activity is linked to inflammation. There are several ways to quantify this activity, such as using the Disease Activity Score-28 for Rheumatoid Arthritis with C-reactive protein (DAS28-CRP). (Batista et al., 2023). Even though RF and ACPA are strongly associated with RA, no research has looked at the relationship between a person's age at RA diagnosis or the corresponding relationship with sex and specific RA autoantibodies (Pertsinidou et al., 2021).

MATERIALS AND WORKING METHODS

From the start of February to the end of April 2023, this study was carried out. (70) blood samples were taken from arthritis patients in the consulting clinic following their diagnosis by the specialist physician.at Baqubah Teaching Hospital in Diyala Governorate. Within the age range of (16–83) years, there were (21) males and (49) females. Blood samples were taken from healthy individuals of both sexes and utilized as a control group. There were (12) female participants and (28) male participants, ages ranging from (19 to 75). They didn't have any acute or chronic illnesses. Samples were obtained through venous blood collection. Five milliliters were drawn. Blood was drawn using plastic medical syringes filled with wine. The blood was then allowed to coagulate for thirty minutes at room temperature in test tubes. The serums were then separated using a centrifuge Central for five minutes at a rate of three thousand cycles per minute. Latex agglutination test was used to examine CRP and RF.

Statistical analysis

The software used is IBM SPSS version 27.0, and the tests used are: Frequency and percentage data for sex, RF, and CRP, and significant differences were calculated using the chi-square test. As for the age data, the mean ± SE was calculated, and the significant differences in the age data for the study groups were determined by using the independent T-test.

RESULTS

This study looked at patients between the ages of (16-83) years and the rate of infection with was rheumatoid arthritis between (43.43 ± 1.85) compared with healthy people aged (19-75) was (41.68 ± 2.23), there is no significant difference (P > 0.05).

Table 1: Rheumatoid arthritis Disease and Age.

Age mean ± SE (Years)		Probability
Patients group	Control group	
43.43 ± 1.85	41.68 ± 2.23	P > 0.05

The current study included 110 individuals, including 70 patients with RA. Males made up 21, at a rate of (30%), while females made up 49, at a rate of (70%). control group, which included 40 people, was made up of 28, or 70% of the male population, and 12, or the 30 percent of the female population.

Table 2: Rheumatoid arthritis Disease and Gender.

Sexes	Patients group No. (%)	Control group No. (%)	Probability
Males	21 (30.0)	28 (70.0)	P < 0.001
Females	49 (70.0)	12 (30.0)	
Total	70 (100.0)	40 (100.0)	

The results of the current study showed that the number of males with RA was 21, with a rate of (30%), while the number of infected females was 49, with an infection rate of (70%). It was found that the incidence of females is higher than that of males, and this difference is significant, as ($p < 0.001$) as shown in Table 2.

Table (3) shows rheumatoid factor positivity in Rheumatoid arthritis patients and the control group. It

was found that the number of arthritis patients who were positive for Rheumatoid factor was (5), at a rate of (7.1%), while the number of negative ones was 65, at a rate of (92.9%), while in the healthy group Positive the number was (0), at a rate of (0.0%), and for those who were negative, the number was (40), at a rate of (100.0%). There is a significant difference (P < 0.001).

Table 3: Number and Percentage of Rheumatoid factor test positivity for study groups.

RF status	Patients group No. (%)	Control group No. (%)	Probability
Positive	5 (7.1)	0 (0.0)	P < 0.001
Negative	65 (92.9)	40 (100.0)	
Total	70 (100.0)	40 (100.0)	

Table (4) shows C-reactive protein positivity in arthritis patients and the control group It was found that the number of Rheumatoid arthritis patients who were positive for C-reactive protein was 32, at a rate of (45.7%), while the number of negative ones was 38, at a rate of (54.3%), while in the healthy group Positive the number was (3), at a rate of (7.5%), and for those who were negative, the number was (37), at a rate of (92.5%). There is a significant difference (P < 0.001).

Table 4: Number and Percentage of CRP test positivity for study groups.

CRP status	Patients group No. (%)	Control group No. (%)	Probability
Positive	32 (45.7)	3 (7.5)	P < 0.001
Negative	38 (54.3)	37 (92.5)	
Total	70 (100.0)	40 (100.0)	

DISCUSSION

Rheumatoid arthritis is a long-term autoimmune inflammatory disease that damages joints. (McInnes and Schett, 2017). If left untreated, it causes deformities in the bones and joints. (Dai et al., 2020). This study showed that most RA patients (n=70) were female (49/70) (70%) while males were (21/70) (30%). So, the female to male ratio among RA patients in this study was closed compared with the previous study recorded in Iraq which showed that the ratio of female: male is (5.6.1). RA is higher in women than in men due to the changes in hormone levels and genetic factors which may affect the level of proteins in the blood that contribute to inflammation. The estrogen hormone plays a role in affecting the B and T cells which are involved in the immune response and environmental factor could explain the reverse in the trend for women (Al-kefaee et al., 2022; Favalli et al., 2019).

RF is highly prevalent in RA patients. This autoantibody provides not only the insights of how immune system is deregulated but also the clues for clinical diagnosis and managements. Cohort studies reveal that about 60–80% of RA patients are sero-positive (Firestein and McInnes, 2017). The most current RA classification criteria include RF status and level as significant factors. In at-risk individuals, the presence of RF is predictive of the development of RA, indicates a more severe course of the disease in RA patients, and may have implications for treatment choices. Here, we demonstrate how measured levels can differ between individual samples (Falkenburg et al., 2018). The statistical result of this study refers to the high frequency of positive serum RF patients 7.1% compared with 0.0% in control group. This result was nearly compatible with Motta, et al. (2023), and Pope et al. (2018) and Hwang et al., (2019). In order to improve immune complex clearance, support B cell uptake for antigen presentation, and ease complement fixation, RF is physiologically significant. (Wu et al., 2021). A theory has been proposed to account for the potential pivotal role of RF in RA, encompassing their ability to enhance macrophage clearance of immune complexes. Additionally, it has been proposed that RFs enhance the presentation of antigens to T cells through the uptake of immune complexes containing exogenous antigens by dendritic cells and through RF B cells, which appear to be more effective APCs than other types of B cells. (Ingegnoli et al., 2013). Through a reaction with IgG, autoantibodies such as IgM-RF+ are highly effective complement activators. (Okroj et al., 2007). This activation causes synovial cells to produce inflammatory cytokines, which can cause inflammation, damage to cartilage, and erosion of bone. (Firestein and McInnes, 2017). Previous research on RA synovium revealed that IgM-RF+ and IgG3—both of which activate complement—were more complement-dependent when it comes to inflammation. Arntz et al reported finding IgG on exosomes made from B-cells. (Arntz et al., 2018). An additional hypothesis is that auto-reactive B-cells are the source of IgM-RF+, and since B-cells are crucial in RA. (Marston et al., 2010), In this subgroup of RA patients with a more active disease, there may be modifications to the BCR repertoire or increased B-cell activation. If so, circulating levels of "free" IgM-RF, which represents plasma activity, may not reflect changes in pre-B-cell immunity and disease activity as quickly as IgM-RF+ pEVs. (Takahashi et al., 2013).

In this investigation, the CRP level was assessed and used to gauge the patients' state of disease activity. Prior research validated the use of C-reactive protein to assess disease activity. (Roodenrijs et al., 2018). C-reactive protein measurement is used to assess the state of disease

activity in patients with RA, despite its non-specific nature. (Dessie et al., 2021). Positive CRP was elevated in RA patients by a statistically significant margin (45.7%) compared to controls (7.5%). This study's outcome is in line with the earlier studies Bagdi et al. (2022) and Dessie et al. (2020). Prior research has demonstrated the critical role CRP plays in the inflammatory response and host defense mechanisms against infectious agents. (Popea and Choy, 2021). An amplification loop of inflammation results from CRP binding to immunoglobulin Fc gamma receptors (FcgR), which stimulates the synthesis of proinflammatory cytokines. Hepatocytes are the main source of CRP production in response to IL-6 stimulation; smooth muscle cells, macrophages, endothelial cells, lymphocytes, and adipocytes have also been shown to express CRP.(Sproston and Ashworth, 2018). Study Wang et al. (2013), demonstrated a significant relationship between tissue inflammation scores from knee synovium biopsy samples and serum CRP levels in RA patients. CRP is not only a sign of infection or inflammation, but also an immune regulator. (Popea and Choy, 2021). Although the precise role of CRP in inflammation and infection has been disputed, the discovery of CRP isoforms with various biological characteristics has offered a possible explanation for contradictory findings. Hepatocytes produce CRP, which is then released into the bloodstream as pentameric CRP (pCRP), sometimes referred to as native CRP. It is believed that pCRP regulates the immune system. When pCRP binds to cell membranes or liposomes, it can irreversibly dissociate into monomeric CRP (mCRP), a proinflammatory isoform that can bind complement component 1q to activate complement and activate platelets, leucocytes, and endothelial cells. (Thiele et al., 2015). According to earlier research, CRP interacts with a range of leucocytes and endothelial cells, promoting the release of proinflammatory cytokines such as TNF-a, IL-1b, and IL-6, upregulating adhesion molecules, increasing the release of monocyte chemo attractant protein-1 to attract monocytes, preventing the production of nitric oxide, and activating platelets, all of which contribute to the proinflammatory effects. (McFadyen et al., 2018).

CONCLUSIONS

The rates of Rheumatoid arthritis among females compared to males have increased significantly. Higher levels of CRP and RF are also found in patients compared to healthy people.

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