

## Comparison of Some Clinical Criteria and Features in Iraqi Patients with Rheumatoid Arthritis and *Salmonella Typhi*

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### Abstract:

The current study was conducted on a sample of Iraqi patients with rheumatoid arthritis and *Salmonella typhi*, as blood samples were collected from 60 patients with rheumatoid arthritis and infected with *Salmonella typhi* bacteria with ages ranging between 21-70 years, the number of females was more than the number of males with a significant difference of  $P < 0.001$  where the number of females was 55 and by 91.7% while the number of males was 5 and by 8.3%. For the purpose of comparison, another 28 blood samples were collected from healthy people (healthy control) ranging from Between 21-60 years, the number of males was 5, by 17.9%, and the number of females was 23, by 82.1%. The numbers and rates of rheumatoid arthritis and people with *Salmonella typhi* were studied for the study groups by age groups, as the results indicated that the highest incidence rate was in the age group 41-60 years and 51.7% for rheumatoid arthritis patients and those with *Salmonella typhi* with a significant difference ( $P < 0.001$ ) and that the lowest incidence rate was within the age group ( $\leq 20$ ) years and an average of (3.3%) among the two study groups. The results indicated a statistically significant difference ( $P < 0.01$ ) between the incidence of the disease among married people and was the largest compared to the incidence of unmarried people in a sample of 60 patients with rheumatoid arthritis and *Salmonella typhi*. The number of married persons with the disease reached 48 patients (80.0%) compared to 12 patients (20.0%) who are unmarried. The results indicated that there was no significant difference between the body mass index (BMI) for each of the sample of rheumatoid arthritis patients, *Salmonella typhi* patients and the healthy control sample, which indicates that body mass is not affected by the disease. There was a statistically significant difference ( $P < 0.001$ ) between the incidence of the disease in non-smokers and was the largest compared to the incidence of smoking people in a sample of 60 patients with rheumatoid arthritis and those with *Salmonella typhi*. The number of non-smokers with the disease reached 54 patients (90.0%) compared to 6 patients (10.0%) who were smokers. The results indicated that the percentage of patients who underwent biological therapy constituted (50.0%), which is the highest percentage, while the percentage of patients who underwent chemotherapy constituted (15.0%), which is the lowest percentage, and the percentage of patients who underwent mixed treatment (35.0%) with very high significant differences ( $p < 0.001$ ). The study dealt with the periods of injury (years) among patients with rheumatoid arthritis and those with *Salmonella typhi*, where it was found that there are significant differences ( $p < 0.001$ ) in the duration of the disease, where the percentage of (16) patients for the duration of their illness (1-5) years reached 26.7%, and the highest percentage of (23) patients for the duration of their illness (6-10) years was 38.3%, and the lowest percentage for (5) patients for the duration of their illness (11-15) years was 8.3%, and the percentage of (8) patients for the duration of their illness (16-20) years was (13.3%) and reached The same ratio for the same number of patients whose period exceeded (20) years. Studies indicated that there were significant differences between the levels of education among patients, where the highest percentage of rheumatoid arthritis and those with *Salmonella typhi* were among those with primary education, which numbered 27 patients, by 45%, while the lowest percentage was among patients with secondary and university education, which numbered 7 patients per level, by 11.7%.

Rheumatoid arthritis was studied in patients infected with and without Covid-19, where the results showed that the number of people infected with the virus was (13) by 21.7%, while the number of non-infected was (47) by 78.3% and a high difference of  $p < 0.001$ .

**Keywords: Rheumatoid arthritis, Age, Gender, Smoking, Iraqi**

### **Introduction:**

Rheumatoid arthritis (RA) is a chronic and most prevalent autoimmune disease, primarily affecting the joints and this disease can manifest itself Serious injuries in many joints (foot, knee, hip, spine, shoulders) and extra-articular injuries (rheumatic ganglia, muscle weakness, eye injuries, heart disease and vasculitis, pneumonia) has a significant impact on morbidity and mortality rates in patients (Mitsuhiro et al. 2022). Because it is difficult to diagnose because it has many clinical and phenotypic characteristics and periods of stability and exacerbation, the American Society of Rheumatology has developed criteria for its classification (Chang et al., 2016). Rheumatoid arthritis disease attacks many joints of the body and various cell types stimulating the immune system to activate the autoimmune response as well as worsening tissue inflammatory events (Ruda and Bungau, 2021). Rheumatoid arthritis is characterized by persistent synovitis, systemic inflammation and the appearance of autoantibodies (especially rheumatoid factor and citrulline peptide). The risk of rheumatoid arthritis is attributed to genetic factors, environmental factors and many risk factors such as smoking, which is the main environmental hazard, microbial infections, bacterial infections such as salmonella bacteria, as well as the influence of age, sex and obesity on the disease (Littlejohn and Monrad, 2018) . Rheumatoid arthritis is the most common in women and the elderly as uncontrolled active rheumatoid arthritis causes joint damage, disability, joint deformities that hinder normal life, and cardiovascular and other comorbidities (Scott et al., 2021).

With age, the prevalence and incidence of rheumatoid arthritis increases. In the vast majority of the world, the maximum incidence of rheumatoid arthritis is between 55 and 64 years in women and between 65 and 75 years in men. Age continues to increase (Littlejohn and Monrad, 2018). Rheumatoid arthritis can occur at any age, with its peak incidence usually between the ages of 40 and 60. Furthermore, age at the onset of the disease is an indicator of disease activity, disease severity, comorbidity and effective drug therapy The risk increases with age (Innala et al., 2014).

Women are two to three times more likely to develop rheumatoid arthritis than men, and hormones are thought to play a role. This is partly evidenced by research showing that women often develop the disease after major shifts in their hormones (Alpizar-Rodríguez et al., 2017) and factors that have been associated with an increased risk of rheumatoid arthritis include menopause (Bengtsson et al., 2017).

Family history of rheumatoid arthritis increases risk by about three to five times, and genes are likely to account for 40 to 65 percent of rheumatoid arthritis cases, but only about 20 percent of serous positive rheumatoid arthritis cases (Deane et al., 2017).

Smoking is one of the main environmental risk factors for rheumatoid arthritis. Smoking can cause rheumatoid-specific immune reactions to citrulline-containing proteins as portable exposure to air by inhalation, especially among individuals genetically susceptible to rheumatoid (Jiang and Alfredsson, 2020). According to several studies, exposure to smoking accounts for 20-30% of the environmental risk of rheumatoid The strongest of these factors is tobacco exposure. Multiple studies have found that the odds ratios of the association between smoking and rheumatoid increase, and it is estimated that exposure to smoking accounts for approximately 20% to 30% of environmental risks (Doherty et al., 2006).

The current study aimed to compare some clinical parameters and features in Iraqi patients with rheumatoid arthritis and Salmonella typhi.

### **Materials and methods of work:**

#### **StudySubjects**

The current study was conducted on a group of Iraqi patients visiting the consultation clinics for joint diseases at the Baghdad Teaching Hospital of the Medical City in Baghdad Governorate and all governorates of Iraq who are visiting the consulting clinic for the period between December 20 2021. Patients with rheumatoid arthritis and Salmonella typhi by specialist doctors and those undergoing treatment (biological, chemical, mixed). The clinical diagnosis in all cases was made according to the standards approved by the American College of Rheumatology (1997) Yu et al., 2014).

All information about patients who are reviewing and undergoing periodic treatments for patients was recorded according to the questionnaire form, which included health and social indicators such as name, gender, age, housing, academic achievement, occupation, marital status, family genetic history, height, weight and period of illness, type of treatment (biological or chemical), corona infection, infection with other diseases, typhoid infection.

The study also included a group of apparently healthy people (control samples) who do not suffer from any disease and do not have any history of any autoimmune disease, and this group included 28 healthy people.

**Measuring Disease Activity**

The effectiveness of the disease was measured according to the disease effectiveness guide approved by the American College of Rheumatology, where the clinical results of each patient were evaluated according to the disease activity indicators form and in the light of the clinical tests shown, which included many questions about specific indicators, each indicator determines the effectiveness of the disease and Four levels according to Table (1).

**Table 1: Evidence of the effectiveness of rheumatoid arthritis**

Disease effectiveness	Disease activity	Score
Remission	Remission	less or equal to 2.6
Low efficacy of the disease	Low disease activity	Greater than 2.6-3.2
Mild	Moderate disease activity	Greater than 3.2-5.1
High efficacy of the disease	High disease activity	Greater than 5.1

On this basis, disease efficacy among patient groups was calculated and compared with the remaining clinical analysis results as described by Kuper et al. (1997).

**Calculation of Body mass index**

The body mass index (BMI) was calculated for each sample of the study according to the following equation:

$$BMI = \frac{\text{Weight (kg)}}{\text{Length (cm)}}$$

**Statistical analysis**

Immunomodulatory and hematological parameters were first tested for the normal state (Kolmogorov-Smirnov and Shapiro-Wilk test). All parameters that fit both tests (no significant difference) were given as mean ± standard deviation (SD). The differences between the means were calculated by the test T and F (ANOVA). Other parameters were given as a percentage of frequencies, and statistically significant differences between frequencies were evaluated by Pearson-Chi-square testing. Pearson's binary correlation was used to understand the correlation between certain parameters. A receiver running property (ROC) curve was created for each parameter, thus estimating the area under the curve (AUC), sensitivity and specificity. SPSS v25.0 and

Dashboard Prism v6 were used to perform these analyses. The distribution of genotypes and allele frequency was calculated according to the Hardy & Wienberg law.

### **Results and discussion:**

#### **Study samples**

The study sample included a group of patients with rheumatoid arthritis and *Salmonella typhi* with a total of 60 patients, the group was compared with the control group apparently healthy, which was a total of 28 people, the study groups were distributed according to percentages for sex, age group, marital status, body mass index as they were distributed in relation to the genetic aspect as follows:

#### **Distribution of study groups by percentages for sex:**

The current study included 60 patients with rheumatoid arthritis and *Salmonella typhi* with ages ranging from 21-70 years, the number of males was five by 8.3% and the number of females was 55 by 91.7%, while the second group was the apparently healthy control group, which included 28 people with ages ranging between 21-60 years, and the number of males was 5, by 17.9%, and the number of females was 23, by 82.1%, as shown in Table (2).

These results indicate that the number of females infected with the disease is more than the number of males with a statistically significant difference ( $P < 0.001$ ). These results are identical to many studies that indicated that the incidence of the disease is greater in females compared to males, and there are many possible reasons for the tendency of females to develop the disease, including hormonal differences along with genetic and environmental factors may play a complex role in enhancing immunity, which is confirmed by the emergence of autoimmune disease and the fluctuations associated with the disease. When hormonal changes occur, as observed during puberty, pregnancy, hormone replacement therapy (HRT) and menopause, males and females have been shown to deal differently with their chronic diseases (Favalli et al. 2018). Certain genes can affect the Y and X chromosomes responsible for differentiation of gonads and gonadotropin hormonal products. Estrogen has shown a dichotomous effect on immune system function by both increasing the regulation of immunoglobulin production and deregulating inflammatory immune responses. On the other hand, decreased levels of androgens such as testosterone, dihydrotestosterone (DHT) and dihydroepiandrosterone have been observed . (DHEA) in both men and women with rheumatoid arthritis. Besides the direct pathogenic effect of sex hormones on the immune system, sex may indirectly contribute to increased susceptibility to rheumatoid arthritis by influencing environmental/behavioral factors affecting an individual's apparent sex, which together with societal and behavioral factors contributes to the process known as sexual differentiation and provides a framework for considering how an individual's sex is involved in a pathological process such as rheumatoid arthritis (Baggio et al. 2013). ). On the other hand, the results were consistent with those conducted by Ghosh et al. (2017) in a study of a group of rheumatoid arthritis patients, and they showed that most of those affected were women, who were two to three times more likely to develop the disease than men.

#### **Distribution of Study Groups by Age Groups**

Table (2) shows the numbers and rates of rheumatoid arthritis and people with *Salmonella typhi* for the study groups by age groups, as the results indicated that the highest incidence rate in the age group 41-60 years and 51.7% for rheumatoid arthritis patients and those with *Salmonella typhi* with a significant difference ( $P < 0.001$ ) and that the lowest rate of infection within the age group ( $\leq 20$ ) years and a rate of (3.3%) ) between the two study groups.

The results of the current study are consistent with those of (Littlejohn and Monrad, 2018 ) as their study conducted on a group of patients with rheumatoid arthritis who confirmed that the disease increases at the age of 55-64 years in women and between 65-75 years Our study was also consistent with (Innala et al., 2014). ) Their study also showed the possibility of contracting the disease at any age.

#### **Marital status**

Rheumatoid arthritis disease was studied among married and unmarried people in a sample of Iraqi patients, and the results shown in Table (2) indicated a statistically significant difference ( $P < 0.01$ ) between the incidence of the disease among married people and was the largest compared to the incidence of unmarried people in a sample that included 60 patients with rheumatoid arthritis and those with *Salmonella typhi*. The number of married people with the disease reached 48 patients (80.0 %) compared to 12 patients (20.0%) who are unmarried. These results indicate that married couples are more likely to develop the disease compared to unmarried couples, and this may be due to female or male hormonal disorders that are a risk factor for the disease, and as found (Jennifer et al., 2010) that the disease increases in married people more due to rheumatoid arthritis strains the marital relationship due to increased restrictions on activities, changes in responsibilities, and emotional stress while Ward and Leigh were found. , 1993) in their study that single patients with rheumatoid arthritis show greater disease progression and disability than their married counterparts.

**Body Mass Index (BMI)**

Obesity is a risk factor for many diseases, including autoimmune diseases. The results shown in Table (2) indicate that there is no statistically significant difference between the body mass rate (BMI) of rheumatoid arthritis compared to the healthy control group, indicating that there is no effect of the body mass of people on the incidence and severity of the disease. These results are contrary to those of Moroni et al. (20-20) who showed that the increase in BMI is one of the Obesity and overweight are among the main risk factors for chronic low back pain and osteoporosis. But in a study by Rodriguez et al., (2009) showing that obesity does not increase the odds of being diagnosed with rheumatoid arthritis and therefore this study is identical to our findings, if most of the evidence so far points to an increased risk of rheumatoid arthritis in obese individuals, the exact causative role of this co-disease still needs to be clarified.

**Smoking**

Rheumatoid arthritis disease was studied in smokers and non-smokers in a sample of Iraqi patients, and the results shown in Table (2) indicated a statistically significant difference ( $P < 0.001$ ) between the incidence of the disease in non-smokers and was the largest compared to the incidence of infection among people who smoked in a sample that included 60 patients with rheumatoid arthritis and people with *Salmonella typhi*. The number of non-smokers with the disease was 54 patients (90.0%) compared to 6 patients (10.0%) who were smokers. These results indicate that non-smokers are more likely to develop the disease compared to smokers, these results were contrary to the findings of (Vittecoq et al., 2017) where their study showed that smoking is a risk factor for worsening the symptoms of rheumatoid arthritis, while (Bergman et al., 2013) found that passive smoking and previous use of tobacco do not seem to have an effect on rheumatoid arthritis activity and this is in accordance with our study.

**Table 2): The use of the Kay Square test in comparing some of the studied criteria among Iraqi patients with rheumatoid arthritis and *Salmonella typhi* .**

			Groups		Total	Statistics
			patients (N=60)	healthy (N=28)		
Gender	Female	N	55	23	78	$p > 0.05$ 0.89 (0.44-1.28)
		%	91.7%	82.1%	88.6%	
	Male	N	5	5	10	$p > 0.05$ 2.21 (1.29-5.22)
		%	8.3%	17.9%	11.4%	
P value			$P < 0.001^{***}$	$P < 0.001^{***}$	$P < 0.001^{***}$	
Age groups (years)	≤20	N	2	0	2	$p > 0.05$ 0.42 (0.12-1.11)
		%	3.3%	0.0%	2.3%	



	21-40	N	18	6	24	p>0.05 0.71 (0.23-1.43)
		%	30.0%	21.4%	27.3%	
	41-60	N	31	22	53	p>0.05 1.52 (0.89-2.81)
		%	51.7%	78.6%	60.2%	
	>60	N	9	0	9	<b>P&lt;0.05*</b> <b>0.11 (0.09-0.81)</b>
		%	15.0%	0.0%	10.2%	
P value			P<0.001***	P<0.01**	P<0.01**	
Smoking	No	N	54	23	77	p>0.05 0.91 (0.44-2.01)
		%	90.0%	82.1%	87.5%	
	Yes	N	6	5	11	p>0.05 1.78 (1.23-3.29)
		%	10.0%	17.9%	12.5%	
P value			P<0.001***	P<0.001***	P<0.001***	
BMI	Normal weight	N	17	5	22	p>0.05 0.63 (0.22-1.91)
		%	28.3%	17.9%	25.0%	
	Over weight	N	18	3	21	p>0.05 0.35 (0.21-1.21)
		%	30.0%	10.7%	23.9%	
	Obese	N	25	20	45	p>0.05 1.71 (1.21-4.21)
		%	41.7%	71.4%	51.1%	
P value			p>0.05	P<0.001***	P<0.01**	
Social status	Married	N	48	20	68	p>0.05 0.89 (0.21-1.92)
		%	80.0%	71.4%	77.3%	
	Single	N	12	8	20	p>0.05 1.42 (1.21-4.24)
		%	20.0%	28.6%	22.7%	
P value			P<0.001***	P<0.001***	P<0.001***	

### Type of treatment

Patients with rheumatoid arthritis take types of treatments, either biological therapy, chemotherapy, or combination therapy (biological and chemotherapy) together. The results shown in Table (3) showed that there are very high significant differences ( $p < 0.001$ ) as it was found that patients who underwent biological therapy constituted (50.0%), which is the highest percentage, while the percentage of patients who underwent chemotherapy constituted (15.0%), which is the lowest percentage, and the percentage of patients who underwent mixed treatment (35.0%), these results were consistent with the findings of (Abbasi et al., 2019). ) They showed that the frequent use of the new generation of biological therapies leads to a reduction in the overactivity of the immune system and the reduction of inflammatory manifestations. The results were also identical to the findings of (Smolen and Aletaha, 2015) where their research confirmed that for most patients with confirmed disease, the cessation of biological therapy will be followed by an outbreak of the disease, and this is also found that reducing the dose or increasing the interval between doses allows maintaining the success of treatment. While (Singh et al., 2016) confirmed that this type of treatment contributes quickly to pain relief and improvement of swelling in rheumatoid arthritis patients, while the disease-modifying drugs are mostly methotrexate, sulfasalazine, lflunomide, hydroxychloroquine.

DMARDs are slow-acting agents that are useful in improving symptoms and radial progression, so they are used less often than biological drugs, and this is consistent with our findings.

#### **Infection period**

The research dealt with the study of injury periods (years) among patients with rheumatoid arthritis and those with Salmonella typhi, where it was found in Table (3) that there are significant differences ( $p < 0.001$ ) in the duration of the disease, where the percentage of (16) patients for the duration of their illness (1-5) years was 26.7% and the highest percentage of (23) patients for the duration of their illness (6-10) years was 38.3%. The lowest percentage of (5) patients with a period of illness (11-15) years was 8.3%, and the percentage of (8) patients with a period of illness (16-20) years was (13.3%), and the same percentage was for the same number of patients whose period exceeded (20) years. These differences in proportions are identical to their findings ( Zhou et al., 2019), partly due to biological factors with good therapeutic successes; and because response to biological therapy depends on treatment history, especially the duration of the disease. In general, the more experienced patients are with drugs, the lower the response rates, although this limitation can be overcome by immediately modifying or switching treatment in the treatment approach to the goal. And the duration during which treatment should continue once the treatment goal is reached, which should be in a state of dormancy or at least a state of disease activity is low. The available data indicate that in most patients with confirmed disease, the cessation of biological therapy will be followed by an outbreak of the disease, while reducing the dose or increasing the interval between doses makes it possible to maintain the success of the treatment .

#### **Level of education**

The research dealt with the study of the level of education among rheumatoid arthritis patients, where the results in Table (3) showed that there are high moral differences between the levels of education among patients, where the highest percentage of rheumatoid arthritis and those with Salmonella typhi were 27 patients with primary education, by 45%, while the lowest percentage was among patients with secondary and university education, which numbered 7 patients for each level, by 11.7%. The results showed the effect of educational level on The spread of the disease, where the spread of the disease increases and worsens among the uneducated class and decreases among educated students, and this indicates the importance of education and culture in early awareness of the disease and its control, and there was no previous study that studied the impact of education levels on the disease, so our first study was in that, but there is agreement between our study and the findings of Jing and others 2021 in terms of their study of the impact of nursing education for patients has a great impact on controlling the disease.

#### **Infection with Covid-19**

Rheumatoid arthritis was studied in patients infected with and without Covid 19, where the results in Table (3) showed that the number of people infected with the virus was (13) and by 21.7%, while the number of those without it was (47) by 78.3% and with a high difference of significance  $p < 0.001$  and this indicates that the disease does not worsen with infection with the virus, this study was consistent with the findings of (Ennio Giulio et al. 2020) where their study showed that the use of drugs that suppress the immune system leads to a reduced risk of infection, such as drugs, while their findings (Arleevskaya et al., 2017) were contrary to the findings of our study, where few studies investigated a possible link between respiratory viral infections and the development of rheumatoid arthritis, and in particular a Korean study by Joo reported et al. 2019, reported that influenza and coronavirus are linked to the number of rheumatoid arthritis virus cases. In addition, in patients with inflammatory arthritis infection is a major concern because it can contribute to the outbreak of the disease. On the other hand, rheumatoid arthritis patients carry an increased documented risk of infection compared to the general population.

**Table 3: Use of Kay Square Test in Measuring the Frequency and Ratio of Some Clinical Features of Iraqi Patients with Rheumatoid Arthritis and Salmonella Typhi**

	Value	Count	Percent	P value
Treatment type	Biotherapy	30	50.0%	p<0.001***
	Chemotherapy	9	15.0%	
	Mix	21	35.0%	
Infection time (years)	1-5	16	26.7%	p<0.001***
	6-10	23	38.3%	
	11-15	5	8.3%	
	16-20	8	13.3%	
	>20	8	13.3%	
Education level	un educated	15	25.0%	p<0.001***
	primary	27	45.0%	
	modere	4	6.7%	
	secondary	7	11.7%	
	Bchleorios	7	11.7%	
Covid-19	no infected	47	78.3%	p<0.001***

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