

# Impact of Gender and Age on Clinical and Medical Features of Rheumatoid Arthritis in Tripoli, Libya

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## Abstract

Rheumatic disorders, which exhibit notable age- and gender-related demographic trends, are characterized by inflammation and discomfort in the joints and connective tissues. This study aimed to evaluate the demographic characteristics and inflammatory biomarker profiles of patients with rheumatic illnesses and to examine the relationship between these characteristics and age and gender. Between September and November of 2025, 70 patients with rheumatic diagnoses from various clinics in Tripoli, Libya, participated in the study. Every patient underwent laboratory testing. The Alshark Laboratories was the site of this investigation. All participants were asked to complete the questionnaire in order to gather information on their age, sex, and health. Females constituted the majority of the study population (61.4%), while males accounted for 38.6%. Adults (>16 years) represented 60.0% of participants, and children (≤16 years) accounted for 40.0%. A statistically significant association was observed between age group and gender distribution ( $P=0.009$ ), with males predominating among children and females predominating among adults. Female patients exhibited significantly higher Antistreptolysin O titer (ASO) levels compared with males (median: 316.0 vs. 189.0 IU/mL;  $P=0.047$ ). Erythrocyte Sedimentation Rate (ESR) values also differed significantly between genders ( $P=0.048$ ), whereas no significant gender-based differences were observed in C-Reactive Protein (CRP) and Rheumatoid Factor (RhF). When comparing age groups, children showed higher ASO levels than adults; however, this difference was not statistically significant ( $P=0.060$ ). No significant differences were found between children and adults for CRP, ESR, and RhF. Spearman's correlation analysis revealed a significant negative correlation between age and ASO levels (IQR = -0.244,  $P=0.042$ ) and a weak but significant positive correlation between age and ESR (IQR = 0.264,  $P=0.027$ ). No significant correlations were observed between age and CRP and RhF. The results show significant variations in the distribution of rheumatic illness patients by age and gender, as well as in several inflammatory biomarkers, including ASO and ESR. These findings demonstrate how crucial it is to take demographics into account when analyzing inflammatory marker profiles in rheumatic illness patients.

**Keywords.** Rheumatic Diseases, Anti-streptolysin O (ASO), Inflammatory Biomarkers, Age, Gender.

## Introduction

A diverse range of long-term inflammatory and immune-mediated conditions that impact people of all ages, including children and adults, make up rheumatic illnesses [1]. These diseases, which include juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA), are marked by systemic inflammation, persistent immune dysregulation, and possible multisystem involvement. They frequently result in substantial morbidity and a lower quality of life [2]. The prevalence of this disease is 0.1% in North Africa and 0.5% and 1%, respectively, in populations in Europe and North America [3]. It is four times more prevalent in women than in men due to sex hormones and genetic predisposition [4]. Compared to men, women typically have stronger innate and adaptive immune responses, which increases their vulnerability to rheumatic and autoimmune disorders [5,6].

Inflammatory biomarkers continue to be essential tools for rheumatic disease diagnosis and clinical monitoring. Antistreptolysin O titer (ASO), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and rheumatoid factor (RhF) are examples of laboratory markers that are frequently used to indicate inflammatory load and immunological activation [7,8]. Another significant factor influencing the levels of inflammatory markers is age. Age-related changes in plasma protein composition and erythrocyte properties are known to cause ESR to physiologically rise [9]. On the other hand, ASO titers are more often enhanced in pediatric populations, which is indicative of children's stronger humoral immune response and increased exposure to streptococcal infections [10,11]. Since age at RA onset may be interpreted as a criterion of poor diagnosis that is frequently observed in the literature, studies, and research on the impact of age at onset on RA development are essential [12]. While late-onset RA (LORA) usually begins after the ages of 50 to 65, young-onset RA (YORA) is generally recognized to occur between the ages of 30 and 45. Furthermore, YORA has a greater rate of remission, a lower frequency of radiographic progression and functional score, and a higher rate of anti-CCP and RF than LORA [13].

To minimize diagnostic ambiguity, prevent misunderstanding of laboratory results, and maximize tailored patient care. A better understanding of these demographic factors is crucial. Thus, the purpose of this study is to examine how age and gender affect important inflammatory biomarkers in rheumatic illness patients, including ASO, CRP, ESR, and RhF, to improve clinical interpretation and facilitate more precise and individualized assessment of inflammatory activity in rheumatology practice by clarifying demographic-related changes in these markers. This study was conducted to analyze Inflammatory Biomarkers:

Determine and contrast the levels of ASO, CRP, ESR, and RH in patients with rheumatic disease across various age groups (adults and children) and genders (males and females). To Determine Gender Differences: Look at the differences in inflammatory biomarker levels between males and females in the population with rheumatic disease. To Assess Age Impact: Find out how inflammatory indicators differ in rheumatic illness patients who are children and adults.

## Methods

### Study Design

From September to November 2025, specimens were gathered from several clinics in Tripoli, Libya, for this investigation, which was carried out at Alshark Laboratories. The study received ethical approval from the ethical research committee. This research uses a cross-sectional design. The questionnaire was submitted to all patients to collect information such as age, gender, and health condition.

### Eligibility Criteria

The study included adults and children with a confirmed diagnosis of rheumatic diseases, specifically rheumatoid arthritis and juvenile idiopathic arthritis, who were attending outpatient clinics. Patients with concurrent infections, malignancies, or other inflammatory conditions unrelated to rheumatic disease were excluded.

### Study population

A study was conducted on 70 participants, 43 of whom were females and 27 of whom were males. The participants were divided into two age groups: adults (>16 years old) and children (7– ≤16 years old). Statistical analysis: The relationship between age group and gender was evaluated using the chi-square test. The Mann-Whitney U test was used to compare groups, and Spearman's correlation was used to evaluate the association between inflammatory markers and age. It was employed to evaluate the degree of correlation between variables within and between subgroups.  $P \leq 0.05$  was deemed statistically significant, and analyses were conducted using JASP 0.95.2.

## Results

A total of 70 patients diagnosed with rheumatic diseases were included in this study. Table 1 illustrates the demographic distribution of the participants. In regard to gender distribution, females represented the majority of the study population, accounting for 61.4%, while males comprised 38.6%. Regarding age distribution, 60.0% of participants were considered adults (>16 Years), while the remaining 40.0% of participants were children, aged ≤16 years.

**Table 1. Gender and Age Group Distribution Among Patients with Rheumatic Disease.**

Variable	N	%
<b>Gender</b>		
Male	27	38.6%
Female	43	61.4%
<b>Age Group</b>		
Children (≤16 Years)	28	40.0%
Adults (>16 Years)	42	60.0%

The association between gender and age group among patients was examined using the Chi-square test, as shown in Table 2. Among the children, males were more prevalent, accounting for 57.1%, while females made up 42.9%. In contrast, among the adult group, the gender distribution differed significantly, with females representing 73.8% and males only 26.2%. The difference in gender distribution across age groups was found to be statistically significant ( $P = 0.009$ ).

**Table 2. Cross-tabulation of Age Group and Gender.**

Age Group	Gender				Total		C <sup>2</sup>	p-value
	Male		Female					
	N	%	N	%	N	%		
Children (≤16 Years)	16	57.1%	12	42.9%	28	100.0%	6.793	0.009
Adults (>16 Years)	11	26.2%	31	73.8%	42	100.0%		
Total	27	38.6%	43	61.4%	70	100.0%		

Table 3 presents a comparison of inflammatory biomarkers between male and female patients. As the data were not normally distributed, comparisons were conducted using the Mann-Whitney U test, and results were reported as medians with interquartile ranges (IQRs). Female patients showed significantly higher ASO levels, with a median of 316.0 IU/mL, compared to males at 189 IU/mL, with a p-value of 0.047. Similarly,

the distribution of ESR values differed significantly between genders ( $P = 0.048$ ), despite observing identical medians (26.5 mm/hr), but a wider IQR in males (23.0) than females (10.0). No statistically significant differences were observed in CRP and RhF levels ( $P = 0.411$  and  $P = 0.797$ , respectively).

**Table 3. Comparison of Inflammatory Marker Levels by Gender.**

Marker	Male (N=27)		Female (N=43)		Mann-Whitney U	p-value
	Median	IQR	Median	IQR		
ASO (IU/mL)	189.0	228	316.0	389	416.000	0.047
CRP (mg/L)	5.85	10.1	5.85	14.6	512.500	0.411
ESR (mm/hr)	26.5	23.0	26.5	10.0	418.000	0.048
RhF (IU/mL)	9.0	0.0	9.0	0.0	562.500	0.797

Furthermore, inflammatory marker levels were compared between age groups in Table 4. ASO levels were notably higher among children, with a median of 308.00 IU/mL compared to adults (224.00 IU/mL). However, this difference did not reach statistical significance ( $p = 0.060$ ). Similarly, no significant differences were observed between the two age groups in CR, ESR, and RhF levels ( $P > 0.05$ ).

**Table 4. Comparison of Inflammatory Marker Levels by Age Group.**

Marker	Children (N=28)		Adults (N=42)		Mann-Whitney U	p-value
	Median	IQR	Median	IQR		
ASO (IU/mL)	308.00	451	224.00	352	431.000	0.060
CRP (mg/L)	5.92	21.08	5.85	9.2	513.000	0.367
ESR (mm/hr)	26.50	25.8	26.50	17.0	451.000	0.098
RhF (IU/mL)	9.00	0.0	9.00	9.0	581.500	0.927

Table 5 presents the Spearman correlation between age and inflammatory biomarker levels. A statistically significant negative correlation was observed between age and ASO levels ( $r = -0.244$ ,  $p = 0.042$ ), indicating that ASO levels tend to decrease with increasing age. Conversely, ESR showed a weak but significant positive correlation with age ( $R = 0.264$ ,  $P = 0.027$ ), indicating higher ESR values in older patients. No significant associations were found between age and CRP and RhF levels ( $P > 0.05$ ).

**Table 5. Spearman's Correlation Between Age and Inflammatory Biomarkers.**

Marker	Correlation with age	
	Spearman's r	p-value
ASO	-0.244	0.042
CRP	-0.048	0.692
ESR	0.264	0.027
RhF	-0.031	0.797

## Discussion

In this study, in patients with rheumatic disorders, the effects of age and gender on specific inflammatory biomarkers (ASO, CRP, ESR, and rheumatoid factor) were investigated. The results show that specific inflammatory indicators are strongly influenced by demographic factors. According to recent research, sex-related variations in immunological responses are mostly caused by hormonal and genetic variables, which together contribute to females' higher immune reactivity and vulnerability to immune-mediated illnesses [15,16]. In terms of inflammatory biomarkers, ASO and ESR levels were considerably greater in female patients than in male individuals. Stronger humoral immune responses may be indicated by elevated ASO titers in females. According to recent immunological research, females typically have longer-lasting immunity than males [17]. Similarly, research showing that sex-specific physiological and hematological variables, such as differences in plasma protein composition and erythrocyte properties, affect ESR is compatible with the reported gender difference in ESR [18].

On the other hand, neither CRP nor rheumatoid factor levels showed any discernible gender-based variations. Recent research has shown that sex-related biological variations have less of an impact on CRP, a sensitive acute-phase reactant that predominantly reflects current inflammatory activity rather than demographic variables [19]. Similarly, rheumatoid factor is more strongly linked to immunopathological processes, disease duration, and disease phenotype than it is to age or gender alone [20]. Children had greater median ASO levels than adults, according to age-related comparisons, although the difference was not statistically significant. Given that youngsters are more likely to contract streptococcal infections and usually show stronger antibody responses, this trend makes biological sense. Higher streptococcal antibody titers in pediatric populations, especially in school-aged children, have been routinely observed in recent investigations [21].

The idea that streptococcal antibody titers decrease with age was supported by correlation analysis, which showed a strong inverse relationship between age and ASO levels. This discovery is in line with current research on immune function changes associated with aging, such as immunosenescence, which eventually reduces the production of antibodies [22]. On the other hand, there was a small but significant positive connection between ESR and age, meaning that older patients had higher ESR levels. This finding is consistent with current clinical findings demonstrating that age-related changes in fibrinogen levels and erythrocyte aggregation cause ESR to physiologically rise with aging, regardless of inflammatory illness [23]. Overall, the study's findings highlight how crucial it is to take gender and age into account when interpreting inflammatory biomarkers in rheumatic disease patients. Ignoring these demographic factors could result in poor clinical decision-making and erroneous disease activity assessment. In rheumatology, a more customized, demographic-adjusted approach to laboratory examination may improve patient care and diagnostic precision.

## Conclusion

This study shows that in patients with rheumatic disorders, age and gender have a substantial impact on inflammatory biomarkers. Age was favorably connected with ESR and negatively correlated with ASO, whereas females had greater ASO and ESR levels. These results highlight how crucial it is to take demographics into account when interpreting inflammatory indicators to accurately diagnose disease activity and provide the best possible care for patients.

**Conflict of interest.** Nil

## References

- Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Nat Rev Dis Primers*. 2018;4:18001.
- Tsokos GC, Lo MS, Reis PC, Sullivan KE. Systemic lupus erythematosus. *N Engl J Med*. 2011;365(22):2110–21.
- Aurrecoechea E, Llorca Diaz J, Diez Lizuain ML, McGwin G Jr, Calvo-Alen J. Gender-associated comorbidities in rheumatoid arthritis and their impact on outcome: data from GENIRA. *Rheumatol Int*. 2017;37(4):479–85.
- Barragan-Martinez C, Amaya-Amaya J, Pineda-Tamayo R, Mantilla RD, Castellanos-de la Hoz J, Bernal-Macias S, et al. Gender differences in Latin-American patients with rheumatoid arthritis. *Rheumatol Int*. 2021;41(3):521–30.
- Nigrovic PA, White PH. Juvenile idiopathic arthritis. *Lancet*. 2021;398(10314):1707–20.
- Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol*. 2016;16(10):626–38.
- Fairweather D, Rose NR. Sex and gender differences in autoimmune disease. *Nat Rev Immunol*. 2014;14(10):593–608.
- Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis. *JAMA*. 2018;320(13):1360–72.
- McInnes IB, Schett G. Pathogenetic insights from the treatment of rheumatoid arthritis. *Lancet*. 2017;389(10086):2328–37.
- Brigden ML. The erythrocyte sedimentation rate. *Am Fam Physician*. 2013;88(11):755–60.
- Martin JM, Green M, Barbadora KA, Wald ER. Erythrocyte sedimentation rate and antistreptolysin O titers in children. *Pediatrics*. 2010;126(2):303–9.
- Oliver J, Malliya Wadu E, Pierse N, Baker MG, Williamson DA, Moreland NJ. Group A streptococcus pharyngitis and immune responses in children. *Clin Infect Dis*. 2018;67(6):885–92.
- Arnold MB, Bykerk VP, Boire G, Haraoui B, Hitchon C, Thorne C, et al. Are there differences between young- and older-onset early inflammatory arthritis and do these impact outcomes? An analysis from the CATCH cohort. *Rheumatology (Oxford)*. 2014;53(6):1075–86.
- Krams T, Ruysen-Witrand A, Nigon D, Degboe Y, Tobon G, Fautrel B, et al. Effect of age at rheumatoid arthritis onset on clinical, radiographic, and functional outcomes: the ESPOIR cohort. *Joint Bone Spine*. 2016;83(5):511–5.
- Rubtsova K, Marrack P, Rubtsov AV. Sexual dimorphism in autoimmunity. *J Clin Invest*. 2015;125(6):2187–93.
- Furman D, Hejblum BP, Simon N, Jovic V, Dekker CL, Thiébaud R, et al. Systems analysis of sex differences reveals an immunosuppressive role for testosterone in the response to influenza vaccination. *Proc Natl Acad Sci U S A*. 2014;111(2):869–74.
- Brigden M, Heathcote JC. The erythrocyte sedimentation rate: still a helpful test when used judiciously. *Postgrad Med*. 2017;129(2):147–55.
- Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. *Front Immunol*. 2018;9:754.
- Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: a review. *Lancet*. 2018;391(10123):2338–51.
- Carapetis JR, Beaton A, Cunningham MW, Guilherme L, Karthikeyan G, Mayosi BM, et al. Acute rheumatic fever and rheumatic heart disease. *Nat Rev Dis Primers*. 2016;2:15084.
- Fulop T, Larbi A, Dupuis G, Le Page A, Frost EH, Cohen AA, et al. Immunosenescence and inflamm-aging as two sides of the same coin: friends or foes? *Front Immunol*. 2018;8:1960.
- Brigden ML, Graydon C. Problems in interpreting laboratory tests in elderly patients. *Clin Geriatr Med*. 2019;35(3):387–99.
- Kotulska A, Kopeć-Mędrek M, Grosicka A, Kubicka M, Kucharz EJ. Correlation between erythrocyte sedimentation rate and C-reactive protein level in patients with rheumatic diseases. *Reumatologia*. 2015;53(5):243–6.