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Research Article

Clinical and Biochemical Characteristics of Iraqi Patients with Rheumatoid Arthritis According to Treatment Status: A Comparative Study

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder characterized by persistent inflammation and potential alterations in biochemical and inflammatory parameters. Disease-modifying antirheumatic drugs (DMARDs) are used to control disease activity and limit disease progression; however, treatment-related changes in laboratory parameters require continued evaluation. **Objective:** To compare selected inflammatory and biochemical parameters among Iraqi patients with RA according to treatment status and with apparently healthy controls. **Methods:** This observational study, which is comparative in nature, encompassed 84 individuals diagnosed with RA who visited Al-Sadder Hospital, Al-Najaf, Iraq, from November and December 2024. Subject were divided into a treated cohort (n = 30) and an untreated cohort (n = 54), and have been compared with 20 presumably healthy controls. The participant's ages were from 17 to 80 years. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), Erythrocyte sedimentation rate (ESR), and serum urea were assessed. The characteristics of the group and laboratory measures were compared using statistical techniques outlines in the study protocol. **Results:** Females represented 78.6% of the rheumatoid arthritis patients (66/84). The 38 to 58- year- age cohort represented the most significant age group within the RA patient's population (32/84, 38.1%). The mean ESR readings were 36.7 mm/h among patients receiving treatment, 62 mm/h among those not receiving treatment, and 13.5 mm/h in the control group. The mean values of ALT were 14, 18.4, and 26.5 U/L, respectively, whereas the mean value for AST values were 18, 19, and 23.4 U/L. The finding suggests variations in these characteristics across the research cohort. **Conclusion:** The results reveal disparities in certain inflammatory and biochemical markers between rheumatoid arthritis patients and healthy controls, along with noticeable differences between treated and untreated patients. Additional researches with well-defined treatment protocol, suitable adjustment for confounders variables, and extended follow-up is required to determine the relationship between particular therapies and laboratory results.

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1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic immune-mediated inflammatory condition distinguish by progressive joint damage, continual synovitis, functional disability, and other systemic symptoms. RA affects around 0.5–1% of the adult population in industrialized nations and is reported two to three times more often in females. The prevalence increases with advancing age, with peak disease onset typically observed in those over 40 years old [1]. In spite of significant developments in treatment strategies, RA remains a progressive illness for many patients and continues to be a leading cause of reduced life quality and long-term disability around the world [2].

RA is a biologically divers immune-mediated disease marked by significant differences in the treatment efficacy. Despite the availability of multiple conventional synthetic, biologic, and targeted synthetic disease-modifying antirheumatic drugs (DMARDs), many patients fail to achieve adequate disease control or experience secondary loss of efficacy, underscoring the need for predictive biomarkers that can guide treatment selection [3].

Disease-modifying antirheumatic drugs (DMARDs) are a class of immunomodulatory agents indicated for the treatment of inflammatory arthritis's such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, as well as connective tissue diseases and select malignancies [4].

Assessment of disease activity is an important component of the clinical evaluation of patients with rheumatoid arthritis (RA). The Disease Activity Score in 28 joints based on erythrocyte sedimentation rate (DAS28-ESR) is a validated composite index used to assess RA disease activity. It incorporates the number of tender and swollen joints, the erythrocyte sedimentation rate (ESR), and the patient's global assessment of health. The DAS28-ESR provides a quantitative measure of disease activity, with higher scores reflecting greater inflammatory activity. It is widely used in clinical assessment and monitoring of treatment response. Despite this, the comparisons of DAS28-ESR scores between treated and untreated patients in observational studies must be interpreted with caution, as disparities may potentially indicate differences in baseline disease activity and other clinical feature [5, 6].

Although disease-modifying antirheumatic drugs (DMARDs) have significantly improved the management of rheumatoid arthritis (RA), differences in clinical and biochemical profiles between treated and untreated patients remain important to investigate, particularly in regional populations where treatment patterns and patient characteristics may vary. Therefore, the present study aimed to compare disease activity, inflammatory markers, and selected hepatic and renal biochemical parameters among Iraqi patients with RA according to their treatment status, alongside apparently healthy controls.

2. Research Methodology

2.1. Study Design and Setting

Comparative observational research was performed at Al-Sadder Hospital in Al-Najaf Governorate, Iraq, from November to December 2024.

2.2. Study Population and Groups

The study comprised 84 Iraqi patients diagnosed with rheumatoid arthritis (RA), with ages ranging from 17 to 80 years, in addition to 20 presumably healthy persons who served as a control group.

The RA patients were dividing according to their treatment status into two groups:

- The treated cohort consisted of 30 individuals with RA who were undergoing therapy at the sample collection period.
- Untreated group: 54 patients with RA who were not receiving treatment at the sample collection period.

The control group consisted of 20 apparently healthy individuals.

The diagnosis of RA was determined by the physicians in accordance with the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) classification criteria.

2.3. Eligibility Criteria

Patients with a confirmed diagnosis of RA were eligible for inclusion. Patients with concurrent infections, malignancies, recent blood transfusions, or hematological disorders unrelated to RA were excluded.

2.4. Blood Sample Collection and Processing

Approximately 5 mL of venous blood was collected from each participant under aseptic conditions. The collected blood was divided into two portions: 2 mL was transferred into an EDTA tube for hematological investigations, while 3 mL was transferred into a gel-separator tube. The blood collected in the gel-separator tube was allowed to clot for approximately 30 minutes and subsequently centrifuged at 3000 rpm for 15 minutes to obtain serum. Serum samples were maintained at 4°C and processed within two hours of collection.

2.5. Laboratory Investigations

2.5.1. Erythrocyte Sedimentation Rate (ESR)

ESR was measured using an ESR Fast Detector system. Whole blood collected in the appropriate ESR tube was used for the determination of the erythrocyte sedimentation rate.

2.5.2. C-Reactive Protein (CRP)

Serum CRP concentrations were determined using the AFIAS-10 immunoassay analyzer with the corresponding CRP assay kit, according to the manufacturer's instructions.

2.5.3. Biochemical Investigations

Biochemical parameters were measured using the Mindray BS-230 automated chemistry analyzer. The investigated parameters included:

- Liver-related parameters: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP).
- Renal-related parameters: Urea and creatinine.
- Lipid profile: Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

All analyses were performed according to the manufacturers' instructions and laboratory procedures.

2.6. Assessment of Disease Activity Using DAS28-ESR

Disease activity was evaluated using the 28-joint Disease Activity Score based on erythrocyte sedimentation rate (DAS28-ESR), a validated composite measure of rheumatoid arthritis (RA) disease activity. The score incorporates the number of tender and swollen joints among 28 assessed joints, erythrocyte sedimentation rate (ESR), and the patient's global assessment of health (GH) on a visual analogue scale (0–100 mm). DAS28-ESR scores were calculated using the WebDAS online calculator (Version 5.00; [7]). The calculated scores were subsequently used to compare disease activity between treated and untreated RA patients. Higher scores indicate greater disease activity, whereas lower scores indicate better disease control [5, 6].

2.7. Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 20. Descriptive statistics were used to summarize demographic and laboratory data. Continuous variables were expressed as mean and standard deviation or median and interquartile range, as appropriate, while categorical variables were presented as frequencies and percentages. Comparisons among the study groups were performed using appropriate statistical tests according to data distribution and study design. A *p-value* of less than 0.05 was considered statistically significant.

Ethical Considerations approved by the Medical Ethics Committee of the Ministry of Health in Iraq as well as agreement were obtained from all patients with filling questionnaire from each patient.

3. Results

3.1. Demographic Characteristics of the Study Population

A total of 104 participants were included in the study, comprising 84 patients diagnosed with rheumatoid arthritis (RA) and 20 apparently healthy controls. The RA patients were divided according to treatment status into a treated group (n = 30) and an untreated group (n = 54). Females constituted the predominant percentage of participants across all groups, accounting for 80.0% of the treated group, 77.8% of the untreated group, and 70.0% of the control group. The demographic parameters and age distribution of the study cohort are illustrated in Table 1.

Table 1: Demographic characteristics of the study population

Characteristic	Treated RA (n=30)	Untreated RA (n=54)	Controls (n=20)	Total (n=104)
Male, n (%)	6 (20.0)	12 (22.2)	6 (30.0)	24 (23.1)
Female, n (%)	24 (80.0)	42 (77.8)	14 (70.0)	80 (76.9)
Age distribution, years				
17–37, n (%)	4 (13.3)	10 (18.5)	6 (30.0)	20 (19.2)
38–58, n (%)	12 (40.0)	20 (37.0)	8 (40.0)	40 (38.5)
59–79, n (%)	10 (33.3)	22 (40.7)	6 (30.0)	38 (36.5)
≥80, n (%)	4 (13.3)	2 (3.7)	0 (0.0)	6 (5.8)

3.2. Disease Activity Assessment Using DAS28

The evaluation of disease activity was conducted with the Disease Activity Score in 28 joints (DAS28). The average DAS28 score was elevated in untreated patients (4.1) compared to those receiving treatment (3.3). Signifying increased disease activity in the untreated cohort. The difference was reported as statistically significant ($p < 0.001$) Table 2.

Table 2: Comparison of DAS28 scores between treated and untreated RA patients

Group	Number of patients (n)	Mean DAS28
Treated RA patients	30	3.3
Untreated RA patients	54	4.1

3.3. Erythrocyte Sedimentation Rate (ESR)

The mean ESR was diminished in treated RA patients (36.7 mm/h) compared to untreated patients (62.0 mm/h). The control group had a mean ESR of 13.5 mm/h. The overall difference between the study groups was reported as statistically significant ($p < 0.001$) Table 3.

Table 3: Comparison of ESR among the study groups

Group	Number of participants (n)	Mean ESR (mm/h)
Treated RA patients	30	36.7
Untreated RA patients	54	62.0
Healthy controls	20	13.5

3.4. Biochemical Parameters

The biochemical evaluation encompassed serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and urea. The mean ALT levels were 14.0, 18.4, and 26.5 U/L in the treated, untreated, and control cohorts, respectively. The associated average AST values were 18.0, 19.0, and 23.4 U/L. Mean serum urea values were 31.0, 35.0, and 17.0 mg/dL, respectively Table 4.

Table 4: Comparison of selected biochemical parameters among the study groups

Parameter	Treated RA (n=30)	Untreated RA (n=54)	Controls (n=20)
ALT (U/L)	14.0	18.4	26.5
AST (U/L)	18.0	19.0	23.4
Urea (mg/dL)	31.0	35.0	17.0

4. Discussion

The current research indicated that female group with RA represented a higher percentage than the male group in both treated and untreated cohort, with almost 80% of patients being female. this is consistent with previously reported results [8] and with the worldwide data indicating a female-to-male ratio of approximately 3:1. The higher incidence in females may be attributed to genetic, hormonal and immunological factors, especially the role the role of estrogen in controlling immune responses [9]. A study conducted in Iraq with 470 patients indicated a female incidence of 81.9% [10]. Genetic susceptibility, comprising HLA-DR4 and HLA-DR1 alleles, may also contribute to this prevalence.

The majority of patients were between the ages of 38 and 58 years, which may indicate that RA is more common in this demographic. According to Mousavi et al. [11] the highest incidence of RA was observed in males aged 50-54 and females aged 45-49, and the most prevalent age group for RA diagnosis is 40 - 60 years. Environmental variables, including infections, smoking, and hormonal changes, in addition to genetic factors play significant role in the development of [12]. An other study conducted in Iraqi found that RA patients tended to be middle-aged, with an average age of 49.9 years [10].

Regarding inflammatory activity, the mean erythrocyte sedimentation rate (ESR) was considerably lower in treated patients (36.7 mm/h) than in untreated patients (62.0 mm/h), while the control group exhibited a mean value of 13.5 mm/h. The lower ESR observed in treated patients may reflect a comparatively reduced inflammatory burden. ESR is an important laboratory marker used in the assessment and monitoring of inflammatory activity in RA. Previous studies have demonstrated that targeted therapies, particularly tumor necrosis factor (TNF) inhibitors and interleukin-6 (IL-6) pathway inhibitors, can reduce inflammatory markers and improve clinical disease activity [13]. Nevertheless, the present study did not classify patients according to specific conventional or biological therapies; therefore, the observed differences cannot be attributed to any particular therapeutic agent. Moreover, persistent inflammatory activity may occur in some patients despite treatment, emphasizing the multifactorial nature of disease control.

The inflammatory activity was measured by significantly decreased mean erythrocyte sedimentation rate (ESR) in the treated patients (36.7 mm/h) compared to the untreated patients (62.0 mm/h), with a control group exhibited a mean value of 13.5 mm/h. A potentially reduced inflammatory burden may explain treated patients show a lower ESR. ESR serves as a crucial indicator for evaluating and tracking inflammatory activity in RA. Previous investigations have established that the targeted therapies, particularly tumor necrosis factor (TNF) inhibitors and interleukin-6 (IL-6) pathway blockers, may diminish the inflammatory indicators and enhance clinical disease activity [14]. however, the current study did not categorized patients according to specific conventional or biological treatment; so, the observed disparities cannot be attributed to any distinct therapeutic agent. Additionally, chronic inflammatory response may persist in certain individuals regardless of treatment, highlighting the diverse factors influencing disease control.

The evaluation of hepatic biochemical markers indicated reduced mean ALT and AST levels in treated patients (14.0 and 18.0 U/L, respectively) in contrast to the untreated patients (18.4 and 19.0 U/L, respectively). furthermore, the corresponding values in the control group were elevated (26.5 U/L for ALT and 23.4 U/L for AST). These results reveal variations in liver enzyme profiles amongst the study cohorts; yet, they do not necessarily signify enhanced hepatic function related to treatment. Rheumatoid arthritis itself may be associated with hepatic abnormalities, while some medications used in its management, particularly methotrexate (MTX) and certain nonsteroidal anti-inflammatory drugs (NSAIDs), may produce adverse hepatic effects. Although MTX remains an important disease-modifying antirheumatic drug, its use requires appropriate monitoring because of potential adverse effects, including hepatotoxicity and hematological abnormalities [15]. Thus, the evaluation of liver enzyme levels should be analyzed in the context of treatment duration, medication exposure, and other clinical variables.

With respect to renal-related biochemical parameters, mean serum urea levels were 31.0 mg/dL in treated patients, 35.0 mg/dL in untreated patients, and 17.0 mg/dL in healthy controls. The treated group had a reduced mean urea concentration in comparison to the

untreated group; both RA groups maintained elevated values relative to the control group. These results warrant cautious interpretation, given that serum urea alone is inadequate to establish renal impairment. Kidney function may be impacted by several factors, including aging, hydration status, dietary protein intake, the use of medication, and disease-related inflammation. Certain drugs used in RA management, particularly NSAIDs, may adversely affect renal function, while impaired renal clearance can increase the systemic exposure to renally eliminated medications, including MTX [16, 17]. Accordingly, the interpretation of renal status requires consideration of additional parameters, particularly serum creatinine and estimated glomerular filtration rate (eGFR).

Disease activity assessment using DAS28-ESR provides an important clinical measure for evaluating RA severity and monitoring treatment response. In the present study, the mean DAS28-ESR score was 3.3 in treated patients compared with 4.1 in untreated patients, indicating lower mean disease activity in the treated group. According to standard DAS28-ESR classification thresholds, both group means fall within the moderate disease activity category, while the treated group mean is near to the threshold for low disease activity. Among treated patients, these results indicate a more advantageous disease activity profile; yet, the observational design of the study fails to confirm a causal link between treatment and diminished disease activity. Achieving remission or low disease activity is a significant treatment target in RA management since prolonged inflammatory control is critical for reducing joint damage and long-term impairment [14]. However, DAS28 should be analyzed together with clinical evaluation and, when appropriate, imaging data.

Various factors could impact the measurements of DAS28 and their interpretation. For instance, concurrent fibromyalgia may elevate tender joint counts and patient global evaluation scores, which could lead to higher DAS28 values without a corresponding measurable inflammatory activity. Moreover, variations in DAS28 have been linked with clinical and laboratory parameters, including hematological, inflammatory, and serological markers [18]. Previous studies have also highlighted the significance of interpreting disease activity scores together with treatment status and the particular characteristics of patient [19]. Consequently, the difference noted between treated and untreated patients in this study should be considered within the broader clinical context.

Study Limitations

The present study has significant limitations. First, its observational and cross-sectional design restrict the ability to determine causal relationships between treatment status and the noted clinical or biochemical variations. Second, the absence of comprehensive data regarding treatment duration, medication type, dosage, and adherence prevented additional assessment of the impact of individual therapeutic agents. Third, the analysis of renal and hepatic biochemical profiles had limitations imposed by the available markers and the absence of comprehensive clinical evaluation. Finally, the study was performed within a particular regional demographic, which may limit the generalizability of the results to other groups. It suggested that additional investigations with bigger group of patients, thorough treatment classifications, longitudinal follow-up should be performed.

5. Conclusion

The current research revealed variation in clinical and biochemical traits between the treated and the untreated Iraqi patients with rheumatoid arthritis. The treated cohort showed decreased mean DAS28-ESR and ESR values relative to the untreated group, implying a more beneficial disease activity and inflammatory profile. Variations were noted in ALT, AST, and serum urea concentrations; yet, these results must be interpreted with caution and do not independently establish enhanced hepatic or renal performance. Overall, the results underscore the importance of assessing disease activity and selected biochemical markers in patients with RA while considering treatment status and unique clinical traits. Further studies incorporating detailed medication data and longitudinal assessment are needed to clarify the relationship between treatment and clinical and biochemical outcomes.

Article Information

Ethical Approval: This study was reviewed and approved by the Institutional Ethics Committee of the Faculty of Medicine, University of Kufa, Najaf, Iraq, No.113 dated 22/08/2024.

Informed Consent: Written informed consent was obtained from all participants before their inclusion in the study.

Data Availability: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Author Contributions: E.S.A. - Conceptualization, Methodology, Formal Analysis, Resources, Writing – Original Draft, Supervision; L.A.H. - Investigation, Data Curation, Writing – Review & Editing, Project Administration.

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