DOI: https://doi.org/10.54393/pjhs.v6i2.1999

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 02 (February 2025)

Original Article

OPEN ACCESS

Analysis of Hematological and Biochemical Parameters in Rheumatoid Arthritis Patients from Faisalabad, Punjab

Syed Kashif Raza[1*], Rizwan Ahmad[2], Faisal Murtaza Wahla[2], Usama Bin Majid[2], Muhammad Areeb[2] and Abdul Rahman[2]

[1]Department of Allied Health Sciences, Superior University, Faisalabad, Pakistan
[2]Faculty of Rehabilitation Sciences, Riphah International University, Faisalabad, Pakistan

ARTICLE INFO

Keywords:
Rheumatoid Arthritis, Potential Markers, White Blood Cells, Erythrocyte Sedimentation Rate

How to Cite:
Raza, S. K., Ahmad, R., Wahla, F. M., Majid, U. B., Areeb, M., & Rehman, A. (2025). Analysis of Hematological and Biochemical Parameters in Rheumatoid Arthritis Patients from Faisalabad, Punjab: Hematological and Biochemical Parameters in Rheumatoid Arthritis Patients. Pakistan Journal of Health Sciences, 6(2), 74-79. https://doi.org/10.54393/ pjhs.v6i2.1999

***Corresponding Author:**
Syed Kashif Raza
Department of Allied Health Sciences, Superior University, Faisalabad, Pakistan
kashif.raza.fsd@superior.edu.pk

Received date: 27th September, 2024
Acceptance date: 17th February, 2025
Published date: 28th February, 2025

ABSTRACT

Rheumatoid Arthritis (RA) is a long-term autoimmune disease that causes inflammation and joint degeneration. It can lead to significant impairment and a loss in quality of life for millions of people worldwide. When diagnosing and treating RA, hematological and biochemical indicators are frequently assessed. These data are essential for monitoring the disease's progression, identifying organ involvement, and making treatment decisions. **Objectives:** To come up with some significant differences in hematological and biochemical indicators between patients with RA and healthy controls for the diagnosis of RA. **Methods:** Three hundred blood samples were taken in total from the population of Faisalabad City; 150 blood samples were drawn from people who have been confirmed diagnosed with RA, and 150 blood samples were collected from healthy people without any disease. The significant levels between the two groups were ascertained by calculating descriptive statistics and statistical comparisons using independent t-tests for continuous variables. **Results:** Among assessed parameters, erythrocyte sedimentation rate (ESR) and white blood cells (WBCs) were hematological parameters found to be highly elevated in RA patients, whereas hemoglobin (Hb) and alkaline phosphatase (ALP) are biochemical parameters that have been demonstrated significantly low in RA patients as compared to healthy. **Conclusions:** Deferentially expressed parameters ESR, WBCs, Hb, and ALP can be used for the diagnosis of RA.

INTRODUCTION

Rheumatoid Arthritis (RA) is a systemic autoimmune disease that damages joint and is characterized by a persistent, symmetrical inflammation of the afflicted joints, which leads to osteoporosis and other impairments. Even though just a small number of joints are impacted at first, extra-articular symptoms are frequently seen as more joints become affected [1, 2]. Joint cartilage and bone are both severely damaged by RA, resulting in severe synovitis [3]. RA is classified as non-inflammatory joint (osteoarthritis) and inflammatory due to crystal formation (pseudogout and the basic calcium phosphate disease, Gout), or by bacteria or viruses (Staphylococcus aureus Neisseria Gonorrhea, Parvovirus and Enterovirus), or due to auto-immune processes. It can also cause damage to other organs, such as the kidney, heart and lungs, the eye, the digestive system, the nervous system, and skin [4]. Rheumatoid factor and antibodies against post-translational modified proteins such as citrullination (ACPA) and carbamylation (anti-CarP antibodies) are among the autoantibodies that are indicative of the condition. Immune cells may be drawn to the joint as a result of these autoantibodies forming immune complexes. Patients with RA can be classified as either autoantibody-positive or autoantibody-negative based on the presence of these autoantibodies [5]. The effects of RA include significant morbidity, a rise in mortality, and annual

DOI: https://doi.org/10.54393/pjhs.v6i2.1999

expenses in the billions [6]. Women are more likely than males in the same age group to get RA, and the condition's incidence increases with age [7]. The systemic character of RA leads to a significantly shorter life expectancy than the general population, worse quality of life, and decreased social and occupational functioning [8]. Between 0.1% to 2.0% of persons globally are thought to have RA. Self-reported data from the National Health Survey (NHS) for the years 2014–2015 indicates that, in terms of RA prevalence (2%), Australia has the largest population worldwide [9]. Pakistani patients are 44 years old on average [10]. Globally, the prevalence of RA varies, with industrialized nations typically having a greater prevalence. This can be attributed to a variety of variables, including genetics, demographic differences, and underreporting in other regions of the world, as well as exposure to environmental risk factors [2]. There are no established diagnostic criteria for RA. To be diagnosed with RA, a patient must have at least one clinically swollen joint and receive at least six out of ten points on an evaluation test [11]. The primary diagnostic tools are the findings from imaging and blood testing. The rheumatoid factor test is one of the many blood tests used to identify RA [12].

The aim aimed to potential biomarkers associated with RA, so the CBC and biochemical chemistry of RA patients were compared to those of a control group in this study.

METHODS

This study was a prospective, cross-sectional study. The formula for comparing two independent means was used to get the study's sample size, taking into account important statistical factors, such as research power (0.84 for 80% power) and the standard normal variate for the significance level (1.96 for a 95% confidence interval). It was calculated that in order to guarantee sufficient statistical power, each group needed at least 150 participants. As a result, the study involved 300 people in total—150 RA sufferers and 150 healthy controls. The Safi Teaching Hospital of Riphah International University in Faisalabad, Pakistan, analyzed the samples from April to August 2023. The hematological and biochemical parameters were compared. Simple random sampling technique was used to enroll the participants. Rheumatoid arthritis patients and healthy controls from the Faisalabad area made up the study population. The American College of Rheumatology's diagnostic and clinical standards were met by the patients. Rheumatoid arthritis and other inflammatory or autoimmune disorders were not present in the participants in the healthy control group, nor had they ever been. Those who had recently undergone major surgery or blood transfusions were nursing or pregnant, had a history of medication use, or had co-occurring medical disorders were among the exclusion criteria. Written, informed consent was taken by each participant. The research protocol was approved by the Research Ethical Committee, Riphah International University, Faisalabad, Pakistan. Reference No. Res/RcRAHS/23/126 to ensure adherence to accepted ethical guidelines. Together with the complete blood count (CBC), the following parameters were measured: erythrocyte sedimentation rate (ESR), rheumatoid factor (RA factor), and c-reactive protein (CRP). In addition, aspartate transaminase (AST), alanine transaminase (ALT), blood urea, creatinine, total bilirubin, direct bilirubin, indirect bilirubin, alkaline phosphatase (ALP), gamma GT (gGT), and anti-CCP tests were performed to assess organ function. Red vacutainers without anticoagulants were used to collect serum samples from fasting subjects while EDTA-containing vacutainers were used for CBC samples. The equipment underwent quality control testing and was calibrated following the manufacturer's instructions. For serum collection For the collection of serum The blood was collected in a sterile test tube, and the serum was separated by centrifuging 5 ml of each sample for 5 minutes at 3500 rpm. Tests were carried out 24 hours after the collection. A hematology analyzer was used to perform a CBC to evaluate several parameters, such as the RBC, WBC, platelet, Hb level, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), and DLC. SLECTRA MINI and ROCHE COBAS c 311, were used to measure the levels of RA factor and CRP in plasma or serum. Enzyme-linked immunosorbent assay (ELISA) was utilized to identify the existence of antibodies directed against CCP in blood samples. SPSS version 23.0 was used to analyze the data. For every variable, descriptive statistics (mean ± standard deviation) were computed. The means of the RA group and the healthy control group were compared using the independent t-test. Relationships between independent predictors (such as hemoglobin, WBC count, and ESR) and dependent variables (such as CRP and anti-CCP) were investigated using regression analysis. Boxplots were used to depict only statistically significant parameters for better interpretability, and all statistical tests were set at a significance level of $p<0.05$.

RESULTS

The mean ± SD of each parameter for both groups and the p-value. Only the statistically significant parameters are shown in boxplot graphs. The Hb level is 13.2 ± 0.86 g/dL in healthy individuals but is significantly lower in patients (12.10 ± 1.16 g/dL) due to a statistically significant difference ($p=0.000$). The red blood cell count in healthy individuals is 4.22 ± 0.40 million/µL, whereas in patients, it is somewhat higher at 4.43 ± 0.33. The statistically significant difference in RBC counts between the two groups ($p=0.000$) suggests a potential alteration in RBC turnover or patient generation.

DOI: https://doi.org/10.54393/pjhs.v6i2.1999

In healthy persons, the mean WBC count is 7860.93 ± 1486.73/µL, while in patients, it is 8595.86 ± 2592.07/µL. The variation in WBC counts is statistically significant (p=0.003), indicating a sickness or immune response. With a p-value of less than 0.0001, it was discovered that there was a significant difference in the mean number of eosinophils between the two groups: 3.49 ± 1.98 in the RA patients and 2.61 ± 1.99 in the control group. The mean platelet count in patients is somewhat lower, at 247086.66 ± 74730.74/µL with a p-value of 0.055, than the platelet counts in healthy individuals, which is 264646.66 ± 82754.51/µL. The ESR is considerably greater in patients at 39.66 ± 12.55 mm/hr than in healthy individuals at 12.30 ± 3.11 mm/hr. A significant difference between the two groups (p=0.000). Between healthy individuals and patients, there are no appreciable variations in the neutrophil, lymphocyte, monocyte, and basophil parameters (Table 1).

Table 1: Descriptive Statistics of Biochemical Parameters

Parameter	Healthy	Patients	p-value
Hb	13.2 ± 0.86	12.10 ± 1.16	0.000
RBCs	4.22 ± 0.40	4.43 ± 0.33	0.000
WBCs	7860.93 ± 1486.73	8595.86 ± 2592.07	0.003
Neutrophils	60.74 ± 8.49	60.41 ±10.52	0.767
Lymphocytes	29.18 ± 7.99	30.28 ± 9.79	0.287
Monocytes	6.46 ±1.52	6.20 ± 1.42	0.129
Eosinophils	3.49 ±1.98	2.61 ± 1.99	0.000
Basophils	0.29 ± 0.17	0.31 ± 0.19	0.625
Platelets	264646.66 ± 82754.51	247086.66 ± 74730.74	0.055
ESR	12.30 ± 3.11	39.66 ± 12.55	0.000

A descriptive statistical analysis of the biochemical parameters, p=0.139 shows that the difference in urea levels between patients (25.75 ± 6.79 mg/dL) and healthy people (26.93 ± 6.97 mg/dL) is not statistically significant. The mean creatinine levels of patients are significantly higher (0.73 ± 0.22 mg/dL) than those of healthy individuals (0.64 ± 0.19 mg/dL), with a p-value of 0.001, suggesting a potential kidney malfunction in the patient group. The p-value 0.000 indicates that patients' mean uric acid levels are significantly higher (6.57 ± 2.41 mg/dL) than those of healthy people (5.66 ± 0.92 mg/dL). The RA factor levels in patients were found to differ significantly from those in healthy individuals (8.01 ± 1.72 IU/ml) by 83.83 ± 166.92 IU/ml, with a highly significant p-value of 0.000. Patients' CRP levels are significantly higher than those of healthy individuals (7.21 ± 1.51 mg/L) at 22.33 ± 72.31 mg/L, with a p-value of 0.011, indicating higher inflammatory activity in the patient group. The mean uric acid levels of patients are significantly higher (6.57 ± 2.41 mg/dL) than those of healthy individuals (5.66 ± 0.92 mg/dL), as indicated by p=0.000. With a highly significant p-value of 0.000, it was discovered that the RA factor levels in patients differed significantly (8.01 ± 1.72 IU/ml) from those in healthy individuals by 83.83 ± 166.92 IU/ml. With a p-value of 0.011, the CRP levels of patients are significantly higher at 22.33 ± 72.31 mg/L than those of healthy individuals (7.21 ± 1.51 mg/L), suggesting higher inflammatory activity in the patient group. The mean ALP (90.39 ± 37.56 IU/L) and gGT (40.66 ± 26.21 IU/L) of the patients are significantly different from the healthy individuals' (ALT: 57.73 ± 87.52 IU/L; gGT: 33.36 ± 24.31 IU/L) values (p-values of 0.000 and 0.013, respectively). However, there are no significant differences between the ALT (p=0.896) and AST (p=0.658) values of the two groups. Patients with rheumatoid arthritis exhibit a substantial relationship with their mean Anti-CCP level of 221.60 ± 143.24 U/ml, which is significantly higher than that of healthy individuals. The relationship is highly significant, with a p-value of 0.000 (Table 2).

Table 2: Descriptive Statistics of Biochemical Parameters

Parameter	Healthy	Patients	p-value
Urea	26.93 ± 6.97	25.75 ± 6.79	0.139
Creatinine	0.64 ± 0.19	0.73 ± 0.22	0.001
Uric Acid	5.66 ± 0.92	6.57 ± 2.41	0.000
RA Factor	8.01 ± 1.72	83.83 ± 166.92	0.000
CRP	7.21 ±1.51	22.33 ± 72.31	0.011
Total Bilirubin	0.39 ± 0.13	0.46 ± 0.51	0.069
Direct Bilirubin	0.34 ± 0.57	0.22 ± 0.40	0.032
Indirect Bilirubin	0.30 ± 0.19	0.26 ± 0.17	0.100
ALT	57.73 ± 87.52	58.88 ± 63.68	0.896
ALP	125.96 ± 56.84	90.39 ± 37.56	0.000
gGT	33.36 ± 24.31	40.66 ± 26.21	0.013
AST	35.69 ± 30.84	34.31 ± 22.65	0.658
Anti-CCP	7.63 ± 1.46	221.60 ± 143.24	0.000

The relationships between hematological and biochemical variables and specific RA-specific biomarkers like anti-CCP, CRP, uric acid, and RA factor was also conducted. There is a statistically significant positive association based on regression coefficients between uric acid levels and ESR based on the p-value of 0.012 and the coefficient of 0.023. The association between urea levels and uric acid is statistically significant, as indicated by the regression coefficient of 0.081 and p-value of 0.000. Lower hemoglobin levels and higher levels of RA Factor are associated, as indicated by the p-value of 0.034 and regression coefficient of -15.146. Additionally, platelets showed a significant positive association with increased levels of RA Factor and decreased platelet counts, with a p-value of 0.022 and a regression coefficient of 0.000. ESR also showed a significant positive association, with a regression coefficient of 1.987 and a p-value of 0.001. WBCs demonstrated a positive association with a p-value of 0.001 and a regression coefficient of 0.005, suggesting a relationship between elevated WBC counts and elevated CRP levels. Notably, a substantial negative association with a p-value of 0.000 and a coefficient of -30.916 was discovered between anti-CCP levels and Hb. This implies a relationship between elevated anti-CCP levels and

DOI: https://doi.org/10.54393/pjhs.v6i2.1999

decreased Hb levels. Furthermore, a noteworthy positive association with a p-value of 0.002 was observed between the WBC and anti-CCP levels. The regression coefficient of this connection was 0.011. This implies an association between elevated WBC counts and elevated anti-CCP levels. With a regression coefficient of 4.649 and a p-value of 0.000, ESR also showed a significant positive link, suggesting a potential association between elevated ESR levels and elevated anti-CCP levels. Additionally, a statistically significant negative association between the levels of anti-CCP and urea was discovered, with a regression coefficient of -2.815 and a p-value of 0.015. This suggests a connection between reduced urea levels and elevated anti-CCP levels. ALP's regression coefficient is -0.323. This means that Anti CCP should drop by 0.323 units for every unit increase in ALP. ALP and Anti-CCP levels may be inversely associated, based on the negative regression coefficient (Table 3).

Table 3: Regression Analysis Results

Dependent Variable	Independent Variable	Coefficient (B)	Standard Error	Significance
Uric Acid	ESR	0.023	0.009	0.012
Uric Acid	Urea	0.081	0.018	0.000
RA Factor	Hb	-15.146	7.113	0.034
RA Factor	Platelets	0.000	0.000	0.022
RA Factor	ESR	1.987	0.607	0.001
CRP	WBCs	0.005	0.002	0.001
Anti-CCP	HB	-30.916	6.339	0.000
Anti-CCP	WBCs	0.011	0.003	0.002
Anti-CCP	ESR	4.649	0.497	0.000
Anti-CCP	Urea	-2.815	1.155	0.015
Anti-CCP	ALP	-0.323	0.147	0.028

DISCUSSION

It is thought that the most significant improvement index is early diagnosis. Yet early diagnosis is still challenging since it relies entirely on clinical data from the patient's health record, physical examination, and blood and imaging examinations [13]. Many autoimmune rheumatic diseases can present as hematologic disorders, such as anemia, coagulopathy, WBC and platelet abnormalities, and hematologic malignancies [14]. This study indicated the systemic characteristics of Rheumatoid and its effect on hematopoiesis by identifying substantial variations in several hematological markers between RA patients and healthy controls. Anemia, a common consequence linked with chronic inflammatory disorders like RA, was seen in RA patients' significantly lower HB levels; similarly, low levels have previously been observed in previous investigations [15, 16]. RA patients showed a considerably higher mean RBC, which was unexpected. According to reports, inflammatory cytokines may inhibit RBC maturation [17]. Consequently, we propose that aberrant red cell indices could be the reason for low HB even in cases where the RBC count is larger. It is essential to carry out additional studies into the underlying mechanisms triggering RBC changes in RA. The WBC counts of RA patients were considerably higher, suggesting increased immune-mediated activity or a possible infection [18]. Moreover, leukocytes might be drawn to inflammatory synovial tissues as a result of systemic inflammation in RA, which would further raise WBC levels [19]. The systemic inflammatory burden associated with RA is further emphasized by the noticeably higher ESR levels seen in these patients [20]. ESR is a non-specific inflammatory marker that is influenced by red cell aggregation and plasma protein concentration. It assesses how quickly erythrocytes settle in an anticoagulated blood vertical column [21]. Elevated ESR levels in RA are indicative of increased production of acute phase reactants in response to cytokine-mediated inflammation [21]. Elevated ESR readings in RA patients correlate with disease activity, making them a helpful tool for monitoring treatment response and disease progression [22]. Patients with RA had lower platelet counts, however not to a statistically significant degree. All these results point to a considerable difference between the hematological features of RA patients and healthy individuals. This is in line with the systemic inflammatory aspect of the illness and how blood cell counts are affected by it. Notably, RA patients had higher uric acid levels, which may indicate a metabolic disease [23]. Elevated amounts of uric acid can be caused by medication adverse effects or increased purine breakdown in patients with RA. Since raised uric acid levels are associated with an increased risk of gout, a common comorbidity in persons with RA, monitoring uric acid levels and treating hyperuricemia is essential to preventing complications from the condition. Serum uric acid elevation is more common in RA patients and may serve as an inflammatory marker for the degree of joint inflammation. Furthermore, there is mounting evidence that suggests larger steroid doses might result in hyperuricemia. Therefore, it is important to implement suitable preventative measures for these individuals [24]. The autoimmune origin of RA was confirmed by the significantly higher levels of RA factor in RA patients as compared to healthy controls. Most RA patients' serum contains RA factor, an autoantibody that targets the Fc region of immunoglobulin G (IgG) and is a crucial diagnostic sign for the condition. RA factor contributes to synovial inflammation, cartilage deterioration, and joint degeneration in RA by promoting immune complex formation and complement activation [25]. Patients with RA have elevated CRP values, which are indicative of both the disease activity and systemic inflammatory burden. Elevated CRP is correlated with extra-articular symptoms, joint destruction, and synovial inflammation in RA, making

DOI: https://doi.org/10.54393/pjhs.v6i2.1999

it a useful biomarker for monitoring disease activity and directing treatment approaches. In contrast to earlier research, increased bilirubin levels were also noted in RA patients [26, 27]. These findings indicate notable variations in several biochemical indicators, pointing to possible anomalies in renal function, inflammation, and autoimmune activity in individuals with RA.

CONCLUSIONS

Raised ESR, WBCs, and low HB were the patients' differential hematological markers; correlation studies also showed a relationship between these parameters and particular diagnostic tests. Biochemical tests revealed elevated creatinine and gGT, low direct bilirubin and ALP. Regression analysis revealed a link between ALP and anti-CCP as well. Thus, high WBCs, low HB, low ALP, and elevated ESR can all be utilized as indicators of rheumatoid arthritis. The study's overall findings emphasize how crucial thorough hematological and biochemical profiling is for comprehending the pathogenesis of RA and formulating effective clinical care plans. The study's shortcomings, including its cross-sectional methodology and comparatively small sample size, must be acknowledged. Future research will consider this strategy in the hopes of finding unique markers linked to every stage of RA. To sum up, the intricate relationship between hematological and biochemical indicators in RA highlights the disease's systemic character and diverse pathogenesis. To improve patient outcomes, advance our understanding of the disease, and improve diagnostic accuracy and treatment options, more study is needed into the complex interactions between hematological and biochemical parameters in RA.

Authors Contribution

Conceptualization: SKR
Methodology: RA, FMW, UBM, MA, AR
Formal analysis: RA, FMW, UBM, MA, AR
Writing review and editing: SKR
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Lin YJ, Anzaghe M, Schülke S. Update on the pathomechanism, diagnosis, and treatment options for rheumatoid arthritis.Cells. 2020 Apr; 9(4): 880. doi: 10.3390/cells9040880.

[2] Finckh A, Gilbert B, Hodkinson B, Bae SC, Thomas R, Deane KD *et al.* Global epidemiology of rheumatoid arthritis. Nature Reviews Rheumatology.2022 Oct; 18(10): 591-602. doi: 10.1038/s41584-022-00827-y.

[3] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. The Lancet 2016;388:2023-38. 10.1016/S0140-6736(16)30173-8:10.1016/S0140-6736(16)30173-8

[4] Radu AF and Bungau SG. Management of rheumatoid arthritis: an overview. Cells. 2021 Oct; 10(11): 2857. doi: 10.3390/cells10112857.

[5] van Delft MA and Huizinga TW. An overview of autoantibodies in rheumatoid arthritis. Journal of Autoimmunity.2020Jun;110:102392.doi:10.1016/j.jaut .2019.102392.

[6] Deane KD and Holers VM. Rheumatoid arthritis pathogenesis, prediction, and prevention:an emerging paradigm shift. Arthritis & Rheumatology. 2021 Feb; 73(2): 181-93. doi: 10.1002/art.41417.

[7] Liu D, Zhang F, Cao H, Wang X. Can sexual dimorphism in rheumatoid arthritis be attributed to the different abundance of Gardnerella?. Annals of the Rheumatic Diseases.2022 Mar;81(3):e36-.doi:10.1136/ annrheumdis-2020-217214.

[8] Krajewska-Włodarczyk M, Szeląg M, Batko B, Żuber Z, Orleański M, Podwójcic K *et al.* Rheumatoid arthritis epidemiology: a nationwide study in Poland. Rheumatology International. 2024 Jun; 44(6): 1155-63. doi: 10.1007/s00296-024-05591-8.

[9] Almutairi K, Nossent J, Preen D, Keen H, Inderjeeth C. The global prevalence of rheumatoid arthritis: a meta-analysis based on a systematic review. Rheumatology International.2021 May; 41(5): 863-77.doi: 10.1007/s 00 296-020-04731-0.

[10] Naqvi AA, Hassali MA, Naqvi SB, Kachela B, Khan I. Estimation of direct cost of managing rheumatoid arthritis treatment to Pakistani patients using real-world follow-up data. International Journal of Rheumatic Diseases.2020Mar;23(3):325-33.doi:10 .1111/1756-185X.13776.

[11] Aletaha D and Smolen JS. Diagnosis and management of rheumatoid arthritis: a review.Jama.2018 Oct; 320(13): 1360-72. doi: 10.1001/jama.2018.13103.

[12] Visser H, Le Cessie S, Vos K, Breedveld FC, Hazes JMJA, Rheumatism. How to diagnose rheumatoid arthritis early: a prediction model for persistent (erosive)arthritis.2002;46:357-65.

[13] Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies.Bone Research. 2018 Apr; 6(1): 15. doi: 10.1038/s41413-018-0016-9.

[14] Stepanov A, Radocha J, Matuskova V. Blood Diseases. Ocular Manifestations of Systemic Diseases: Springer.

DOI: https://doi.org/10.54393/pjhs.v6i2.1999

2024; 23-77. doi: 10.1007/978-3-031-58592-0_2.
[15] Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies.Bone Research. 2018 Apr; 6(1): 15. doi: 10.1038/s41413-018-0016-9.
[16] Patel A, Bhatt V, Edara M. A Study of Haematological Profile in Newly Diagnosed Rheumatoid Arthritis and its Correlation with Disease Activity. The Journal of the Association of Physicians of India. 2022 Apr; 70(4): 11-2.
[17] Nikolaisen C, Figenschau Y, Nossent JCJTJor. Anemia in early rheumatoid arthritis is associated with interleukin 6-mediated bone marrow suppression, but has no effect on disease course or mortality. 2008;35:380-6.
[18] Farouk AM, Abdel Rahman SM, Abou Elwafa MA, Aboud FM. Hematological parameters in rheumatoid arthritis and their relationship with disease activity. Ain Shams Medical Journal.2023Jun;74(2):493-503.doi:10.21608/asmj.2023.307126.
[19] Li Y, Wu Y, Huang J, Cao X, An Q, Peng Y *et al.* A variety of death modes of neutrophils and their role in the etiology of autoimmune diseases. Immunological Reviews.2024Jan;321(1):280-99.doi:10.1111/imr.13284.
[20] Wu D, Luo Y, Li T, Zhao X, Lv T, Fang G *et al.* Systemic complications of rheumatoid arthritis: Focus on pathogenesis and treatment.Frontiers in Immunology.2022Dec;13:1051082.doi:10.3389/fimmu.2022.1051082.
[21] Lapić I, Padoan A, Bozzato D, Plebani M. Erythrocyte sedimentation rate and C-reactive protein in acute inflammation: meta-analysis of diagnostic accuracy studies. American Journal of Clinical Pathology.2020 Jan; 153(1): 14-29. doi: 10.1093/ajcp/aqz142.
[22] Alende-Castro V, Alonso-Sampedro M, Vazquez-Temprano N, Tuñez C, Rey D, García-Iglesias C *et al.* Factors influencing erythrocyte sedimentation rate in adults: new evidence for an old test. Medicine.2019 Aug;98(34):e16816.doi:10.1097/MD.0000000000016816.
[23] El Ridi R and Tallima H. Physiological functions and pathogenic potential of uric acid: A review. Journal of Advanced Research.2017 Sep; 8(5): 487-93. doi: 10.1016/j.jare.2017.03.003.
[24] Nada D, Gaber R, Mahmoud AS, Elkhouly R, Alashkar D. Hyperuricemia among Egyptian rheumatoid arthritis patients.Is it an association or an inflammatory marker? A cross-sectional observational study. Open Access Rheumatology: Research and Reviews.2021 Oct: 305-14. doi: 10.2147/OARRR.S331488.
[25] Sokolova MV, Schett G, Steffen U. Autoantibodies in rheumatoid arthritis: historical background and novel findings.Clinical reviews in allergy & immunology.2022 Oct; 63(2): 138-51. doi: 10.1007/s12016-021-08890-1.
[26] Zhang H, Yang G, Jiang R, Feng D, Li Y, Chen Y *et al.* Correlation between total bilirubin, total bilirubin/albumin ratio with disease activity in patients with rheumatoid arthritis. International Journal of General Medicine.2023Dec:273-80.doi:10.2147/IJGM.S393273.
[27] Juping D, Yuan Y, Shiyong C, Jun L, Xiuxiu Z, Haijian Y *et al*. Serum bilirubin and the risk of rheumatoid arthritis. Journal of Clinical Laboratory Analysis.2017 Nov; 31(6): e22118. doi: 10.1002/jcla.22118.