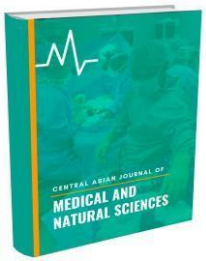


CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 06 Issue: 01 | January 2025 ISSN: 2660-4159

Article

Hematological Parameters and Their Relationship to Interleukin-6 in Rheumatoid Arthritis Men

Zainab Qasim Muhammad Al-Yasiri [1]

1. Dept. of Biology, College of Education for Women, University of Shatrah, Iraq
* Correspondence: Zainab-alyasiri@shu.edu.iq

Abstract: This study was intended to look at the relationship between Hematological parameters and IL-6 in men with rheumatoid arthritis in Thi Qar province/Iraq, as well as to study the effect of age, body mass index and blood groups on blood parameters. The study included 100 men, 60 of whom were RA patients and 40 healthy men as a group in control. Their ages were in the range of 45-75 years. Blood samples were used to examine ABO blood groups and complete blood count (CBC), while serum was used to measure IL-6. The samples were divided into two groups according to age group, three groups according to BMI and eight groups according to blood groups.
According to the findings, IL-6 was considerably elevated (P<0.05) in RA patients compared to the control group. In contrast, the Hematological parameters examination indicated that the total WBC was greatly raised (P<0.05) in patients, while differential count of WBC was significantly increased in neutrophils and eosinophils, while the lymphocytes were dramatically reduced (P<0.05) in patients with RA as opposed to the control group .On other hand, the red blood cell count indicated that RBC, HGB, HCT and HGB, MCV, MCH, MCHC and HGB/HCT were substantially lower in patients (P<0.05). In contrast, platelet parameters PLT, PDW and PCT were much higher (P<0.05) in patients, except for MPV, which was significantly decreased in RA patients compared to the control group.When comparing the Hematological parameters of RA patients according to age group, MPV and PDW were considerably higher (P<0.05) in the second category of age GII (60-75) years as opposed to the first age category GI (45-60) years. On the other hand, the comparison between patients according to BMI indicated that the same two parameters above were significantly increased (P<0.05) in the third group GIII (Class I obesity) compared to the first group GI (Normal weight). In contrast, the comparison between RA patients according to blood groups showed no significant differences (P>0.05) in all Hematological parameters. Blood group O recorded the highest incidence of RA while group AB recorded the lowest incidence.

The results of the correlation analysis indicated a significant positive correlation between IL-6 and each of Neu, PLT, PDW, PCT and PLT/Lym ratio while IL-6 recorded a significant negative correlation with HGB, HCT, MCV, MCHC and HGB/HCT ratio.

Keywords: Rhematoid arthritis, interleukin-6, hematological parameters.

Citation: Alameen, I. M. A., Salman, H. K., Aoda, F. A., & Sulaiman, A. K.. Does every diabetic patient have obesity? Or does every obese necessarily have diabetes? Central Asian Journal of Medical and Natural Sciences, 6(1) (2025), 337–342

Received: 15th Dec 2024
Revised: 26th Dec 2024
Accepted: 8th Jan 2025
Published: 17th Jan 2025

1. Introduction

The chronic systemic inflammatory autoimmune disease known as rheumatoid arthritis (RA) mainly affects the peripheral joints in a symmetrical pattern. It is typified by persistent, long-term inflammation of the synovial joints, which gradually erodes bone and cartilage. If left untreated, RA can lead to joint deformities and may impact various organ systems (Fraenkel et al., 2021; Scherer et al., 2022).

Up to 90% of patients can prevent or reduce joint injury with early diagnosis and therapy. Monitoring the progression of RA is based on specific symptoms and laboratory findings, including increased levels of C-reactive protein, positive rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPAs), and erythrocyte sedimentation rate, as well as early alterations in radiology. Therefore, it is crucial to monitor the disease according to the criteria of the American College of Rheumatology (Kristyanto et al.,2020; Alivernini et al., 2022).

Spontaneous activation of T cells occurs either locally by activated antigen-presenting cells (APC) or in the lymph nodes (LN), which present self-antigen-derived peptides. Auto-activated T cells subsequently induce macrophages and fibroblasts in the affected joint to release the pro-inflammatory mediators TNF-, IL-17, IFN-, and receptor activator of nuclear factor kappa B ligand (RANK-L) (Singh et al.,2021; Scherer et al., 2022).

After a triggering event, which may be autoimmune or infectious, synovial macrophages and fibroblasts proliferate, causing the first signs of joint destruction in rheumatoid arthritis. Endothelial cell proliferation in the perivascular regions is caused by lymphocyte infiltration. Angiogenesis follows that. Inflamed cells or tiny clots block the blood arteries in the afflicted joint. (Coutant and Miossec, 2020). Inflamed synovial tissue eventually starts to develop an invasive tissue called Pannus that invades and breaks down bone and cartilage over time. The subsequent release of several cytokines, interleukins, proteins, and growth factors causes the degeneration of the joints to accelerate and the emergence of systemic problems (Conforti et al.,2021; Yoo et al.,2022).

Reducing inflammation and achieving remission are the major goals of RA treatment in order to stop or slow down erosions of the bones and joints. To achieve this, a variety of disease-modifying anti-rheumatic drugs (DMARDs) were used. The use of conventional-synthetic disease-modifying anti-rheumatic drugs (cs-DMARDs), including methotrexate, steroids, and hydroxychloroquine, is the cornerstone of the therapy of RA (Warjukar et al., 2024). These medications can decrease inflammation, but they don't always work to bring on remission. Targeted by the biological treatment, which includes anti-TNF medications, have specific soluble or cell-surface molecules (Guo et al., 2021; Blanter et al., 2021).

Previous research suggests that Patients with RA have a better chance of recovering if they receive early detection and therapy by reducing the risk of joint deformities and decreased bone density associated with the disease. Therefore, early diagnosis and treatment are essential to improve the situation and prevent the progression of RA (Kristyanto et al., 2020; Scherer et al., 2022).

Aim of study:

This study was designed to investigate the relationship of hematological parameters with interleukin-6 and to know the effect of age, body mass index and blood groups on hematological parameters in rheumatoid arthritis sufferers.

2. Materials and Methods

Subjects

A study was carried out on 100 men, including 60 suffering from rheumatoid arthritis, and 40 men in good health as a reference group, they were between the ages of 45-75 years, between June and December 2024, samples were collected in specialized outpatient clinics in the Thi Qar Governorate, Iraq. Rheumatoid arthritis cases were identified by a specialized physician, while the control group consisted of people who appeared to be in good condition. Both the control group and the rheumatoid arthritis patients had a venous blood sample of approximately 5 ml, which was separated into two sections: 2 ml were put into an anticoagulant (EDTA) tube, which was used to analyze the complete blood count (CBC) and ABO blood group test. To determine Interleukin-6, 3 ml

were put in a tube without an anticoagulant to coagulate in order to separate the serum, which was then centrifuged for 10 minutes at 3000 rpm. Patients were split evenly into two age groups GI (45–60) years and GII (60–75) years, based on their ages. The same applied to healthy controls. Conversely, patients and healthy individuals were split into three groups based on their body mass index (BMI): GI for normal weight, GII for overweight, and GIII for class I obesity. While, the patients were divided into eight groups according to ABO blood groups.

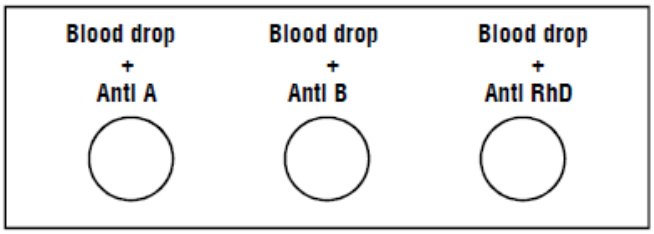
Hematological parameters determination:

Complete Blood Count (CBC) Analysis.

Both patients and controls had a complete blood count that included the quantity of red blood cells (RBCs) and their markers, white blood cells (WBCs), total and differential counts, and platelet characteristics. CBC was performed utilizing Automated haematology analyzer (Sysmex corporation XP-300, japan).

Blood groups (ABO system).

The ABO and Rh blood typing system is depending upon agglutination reaction (Brecher, 2002).



Interleukin-6 (IL-6) determination:

It was measured as inflammatory parameter using enzyme-linked immunosorbent assay (ELISA) (Bakker and Mucke, 2007).

Statistical Analysis:

Version 23 of the Statistical Package for the Social Sciences (SPSS) for Windows was used to statistically analyze the data. utilizing the t-test and analysis of variance (ANOVA). LSD (least significant differences), means, and standard deviations (SD) were discovered. to ascertain if the differences are significant at a level of significance ($P<0.05$). Pearson's correlation coefficient was also used to study correlation.

3. Results

Hematological parameters

Complete Blood Count (CBC)

The current study's findings in Table 3-1 indicated that total white blood cell count increased significantly ($P<0.05$) in patients compared with the healthy group. In contrast, the differential white blood cell count showed that the numbers of neutrophils and eosinophils increased significantly ($P<0.05$), while the numbers of lymphocytes decreased significantly ($P<0.05$) in rheumatoid arthritis-affected men as opposed to the control group, while the basophils showed no discernible change ($P>0.05$) between the two groups.

However, the findings indicated that parameters of red blood cells (RBC), HGB, HCT, MCV, MCH, MCHC and HGB/HCT decreased significantly in patients as opposed to a control group. Regarding platelet parameters, PLT, PDW and PCT were significantly increased in patients, except for MPV, which was significantly decreased when contrasting with the control group.

Table 3-1: Levels of Hematological parameters in Rheumatoid arthritis patients and control

Hematological parameters Mean ± SD	Groups		P- value
	Patients	Control	
WBC (10^9/L)	8.527[a] ± 2.119	7.123[b] ± 1.455	0.038
Neu %	60.519[a] ± 6.678	53.428[b] ± 4.622	0.012
Lym %	30.296[b] ± 6.459	38.215[a] ± 3.842	0.022
Mon %	6.029[a] ± 1.782	5.770[a] ± 1.539	0.435
Eos %	2.420[a] ± 1.379	1.823[b] ± 0.753	0.012
Bas %	0.724[a] ± 0.302	0.760[a] ± 0.254	0.516
Neu/Lym Ratio	2.162[a] ± 0.826	1.426[b] ± 0.289	0.021
RBC (10^{12}/L)	4.269[b] ± 0.356	4.882[a] ± 0.330	0.015
HGB (g/dl)	11.589[b] ± 1.418	13.863[a] ± 0.941	0.012
HCT %	36.148[b] ± 3.683	39.982[a] ± 2.6133	0.014
MCV (fL)	82.225[b] ± 9.702	86.195[a] ± 2.6296	0.013
MCH (pg)	27.396[b] ± 3.509	28.630[a] ± 1.0735	0.032
MCHC (g/L)	325.34[b] ± 12.815	331.90[a] ± 7.203	0.015
HGB/HCT Ratio	0.325[b] ± 0.048	0.346[a] ± 0.013	0.016
PLT (10^9/L)	263.76[a] ± 67.460	236.20[b] ± 43.561	0.021
MPV (fL)	8.569[b] ± 0.818	10.338[a] ± 0.657	0.011
PDW (fL)	16.138[a] ± 0.749	14.670[b] ± 0.700	0.007
PCT (ml/L)	2.761[a] ± 0.522	2.208[b] ± 0.481	0.013
PLT/Lym ratio	9.236[a] ± 3.476	6.258[b] ± 1.399	0.032

There are no significant differences between similar letters (a,a), and significant differences between distinct letters (a,b) at ($P < 0.05$), (SD): the standard deviation.

On the other hand, the results in Table 2-3 showed that when comparing the two groups of patients according to age group, There were no notable variations ($P>0.05$) in Hematological parameters except for MPV and PDW, which considerably ($P<0.05$) increased in the second age group, G II (60-75) years compared to the first age group G I (45-60) years.

Table 3-2 : Hematological parameters in Rheumatoid arthritis patients and control subjects according to age.

Hematological parameters Mean ±SD	Age Groups				LSD
	GI (45-60) years		**GII** (60-75) years		
	Patients	Control	Patients	Control	
WBC (10^9/L)	8.385[a] ± 1.849	7.081[b] ± 1.047	8.429[a] ± 2.379	7.165[b] ± 1.797	1.016

Neu %	60.067[a] ± 6.696	54.225[b] ± 5.164	60.970[a] ± 6.715	52.630[b] ± 3.980	3.918
Lym %	30.320[b] ± 6.709	37.655[a] ± 4.462	30.273[b] ± 6.286	38.775[a] ± 3.118	3.706
Mon %	6.288 [a] ± 1.949	5.255 [a] ± 1.505	5.770[a] ± 1.579	6.285 [a] ± 1.428	1.079
Eos %	2.489[a] ± 1.407	1.711[b] ± 0.629	2.358[a] ± 1.366	1.570[b] ± 0.809	0.777
Bas %	0.758[a] ± 0.319	0.800[a] ± 0.213	0.690[a] ± 0.285	0.720[a] ± 0.289	0.185
Neu/Lym Ratio	2.145[a] ± 0.793	1.478[b] ± 0.341	2.179[a] ± 0.868	1.374[b] ± 0.224	0.451
RBC (10^12/L)	4.339[b] ± 0.343	4.855[a] ± 0.243	4.199[b] ± 0.359	4.911[a] ± 0.404	0.221
HGB (g/dl)	11.420[b] ±1.555	13.070[a] ±0.825	11.357[b] ±1.284	12.655[a] ±1.058	0.828
HCT %	36.363[b] ±3.639	39.585[a] ±2.312	35.932[b] ±3.759	40.380[a] ±2.888	2.173
MCV (fL)	79.550[b] ±11.872	86.155[a] ±2.318	82.100[b] ±5.919	87.895[a] ±2.811	5.032
MCH (pg)	26.503[b] ± 4.029	28.380[a] ±1.039	27.085[b] ±2.665	28.990[a] ±1.027	1.839
MCHC (g/L)	325.01[b] ±15.970	332.89[a] ±9.311	322.75[b] ±7.993	331.97[a] ±4.255	7.166
HGB/HCT Ratio	0.322[b] ± 0.065	0.348[a] ± 0.014	0.324[b] ± 0.021	0.346[a] ± 0.012	0.022
PLT (10^9/L)	269.80[a] ±69.979	230.77[b] ±39.977	260.93[a] ±65.482	221.60[b] ±42.989	38.83
MPV (fL)	7.993[c] ±0.535	10.280[a] ±0.706	9.145[b] ±0.625	10.395[a] ±0.617	0.391
PDW (fL)	15.900[b] ±0.726	14.725[c] ±0.603	16.375[a] ±0.704	14.615[c] ±0.799	0.457
PCT (ml/L)	2.829[a] ±0.509	2.346[b] ±0.329	2.693[a] ±0.531	2.072[b] ±0.572	0.323
PLT/Lym Ratio	9.331[a] ±3.313	6.751[b] ±1.339	9.142[a] ±3.672	5.766[b] ±1.309	1.905

Similar letters (a,a): no notable distinctions, (LSD) stands for least significant difference, (SD) for standard deviation, and (a,b) for significant differences.

In contrast, the results in Table 3.3 showed that when comparing the three groups of patients according to the body mass index BMI (GI normal weight, GII overweight and GIII obesity class I) there were no significant differences (P>0.05) in the patients' hematological parameters. Despite the difference in BMI, all differences were insignificant, except for MPV and PDW which were significantly increased (P<0.05) in Group III compared to Group I for BMI. While the differences were significant when comparing each category with its control group.

Table 3-3: Hematological parameters in Rheumatoid arthritis patients and control subjects according to BMI.

Hematological parameters Mean ±SD	**BMI Groups**						**LSD**
	(GI) Normal weight		**(GII)** Over weight		**(GIII)** Class I obesity		
	Patients	Control	Patients	Control	Patients	Control	

WBC (10^9/L)	8.190[a] ± 1.875	7.093[b] ± 1.438	8.279[a] ± 2.802	7.154[b] ± 1.244	8.320[a] ± 1.526	7.165[b] ± 1.886	1.012
Neu %	60.131[a] ± 8.562	52.369[b] ± 3.922	60.610[a] ± 6.493	53.740[b] ± 4.980	60.581[a] ± 6.276	51.456[b] ± 3.902	6.197
Lym %	30.800[b] ± 6.925	38.994[a] ± 3.030	29.320[b] ± 6.390	36.673[a] ± 4.906	30.911[b] ± 6.434	39.400[a] ± 2.314	5.856
Mon %	6.369[a] ± 2.056	5.938[a] ± 1.810	6.353[a] ± 1.845	5.013[a] ± 0.964	6.733[a] ± 1.266	5.646[a] ± 1.591	1.695
Eos %	2.785[a] ± 1.123	1.715[b] ± 0.775	2.873[a] ± 1.715	1.773[b] ± 0.792	2.742[a] ± 1.035	1.722[b] ± 0.710	1.019
Bas %	0.759[a] ± 0.284	0.763[a] ± 0.282	0.770[a] ± 0.344	0.800[a] ± 0.220	0.654[a] ± 0.262	0.689[a] ± 0.266	0.291
Neu/Lym Ratio	2.132[a] ± 0.909	1.357[b] ± 0.214	2.236[a] ± 0.852	1.564[b] ± 0.362	2.112[a] ± 0.794	1.315[b] ± 0.185	0.717
RBC (10^12/L)	4.481[b] ± 0.308	4.926[a] ± 0.338	4.185[b] ± 0.326	4.796[a] ± 0.198	4.265[b] ± 0.329	4.881[a] ± 0.275	0.345
HGB (g/dl)	11.434[b] ± 1.538	13.091[a] ± 1.094	11.123[b] ± 1.333	12.826[a] ± 0.786	11.301[b] ± 1.972	12.977[a] ± 0.593	1.642
HCT %	36.915[b] ± 1.246	39.781[a] ± 2.017	36.496[b] ± 2.005	39.413[a] ± 1.648	37.821[b] ± 2.014	40.656[a] ± 1.573	2.025
MCV (fL)	79.623[b] ± 3.769	85.962[a] ± 2.837	81.073[b] ± 3.333	85.693[a] ± 1.859	80.459[b] ± 2.594	86.278[a] ± 3.038	4.033
MCH (pg)	26.623[b] ± 2.769	29.325[a] ± 1.033	27.046[b] ± 1.666	29.560[a] ± 3.025	25.338[b] ± 2.096	28.100[a] ± 2.044	2.410
MCHC (g/L)	322.741[b] ± 4.285	330.938[a] ± 5.195	325.566[b] ± 6.667	334.067[a] ± 8.159	321.432[b] ± 4.324	330.100[a] ± 2.645	7.214
HGB/HCT Ratio	0.308[b] ± 0.018	0.328[a] ± 0.015	0.303[b] ± 0.016	0.324[a] ± 0.014	0.297[b] ± 0.018	0.318[a] ± 0.017	0.020
PLT (10^9/L)	276.92[a] ± 69.433	242.63[b] ± 52.261	271.03[a] ± 75.853	237.27[b] ± 43.663	263.24[a] ± 59.368	228.00[b] ± 17.521	33.436
MPV (fL)	7.654[c] ± 0.592	10.413[a] ± 0.737	8.563[b] ± 0.760	10.307[a] ± 0.626	8.908[b] ± 0.851	10.589[a] ± 0.464	1.128
PDW (fL)	16.003[b] ± 0.471	14.344[c] ± 0.722	16.237[a] ± 0.910	14.680[c] ± 0.612	16.446[a] ± 0.690	14.800[c] ± 0.634	0.339
PCT (ml/L)	2.990[a] ± 0.509	2.245[b] ± 0.633	2.817[a] ± 0.593	2.230[b] ± 0.373	2.635[a] ± 0.436	2.106[b] ± 0.344	0.514
PLT/Lym Ratio	9.471[a] ± 2.501	6.252[b] ± 1.392	8.743[a] ± 2.349	5.554[b] ± 0.594	9.326[a] ± 2.476	6.241[b] ± 1.399	3.026

No notable differences exist between the similar letters (a,a). The letters (a, b) stand for significant differences, (LSD) for least significant difference, and (SD) for standard deviation.

On the other hand, the results in Table 3.4 when comparing the Hematological parameters between patients according to blood groups indicated that there were no significant differences (P> 0.05). All the differences were insignificant in the eight blood groups, meaning that the blood group and the type of Rh factor did not have a significant effect on the values of the Hematological parameters.

Table 3-4: Hematological parameters in Rheumatoid arthritis patients according to Blood groups.

Hematological parameters Mean ±SD	**patients' Blood groups**								**LSD**
	A		B		AB		O		
	+	-	+	-	+	-	+	-	

WBC (10^9/L)	8.415[a] ± 2.730	8.077[a] ± 1.227	8.059[a] ± 1.736	7.210[a] ± 0.906	8.713[a] ± 1.593	7.833[a] ± 1.064	8.075[a] ± 1.806	8.942[a] ± 3.187	2.803
Neu %	59.876[a] ± 8.226	58.243[a] ± 6.115	61.245[a] ± 5.834	57.840[a] ± 3.755	59.317[a] ± 6.215	58.333[a] ± 5.234	61.227[a] ± 5.559	63.011[a] ± 8.274	9.809
Lym %	30.729[a] ± 8.504	32.871[a] ± 5.860	30.091[a] ± 5.468	33.120[a] ± 5.420	30.033[a] ± 6.191	32.033[a] ± 7.552	29.664[a] ± 5.357	27.300[a] ± 7.234	8.731
Mon %	6.076[a] ± 1.896	5.614[a] ± 1.923	5.573[a] ± 1.187	6.640[a] ± 2.398	7.117[a] ± 1.419	5.800[a] ± 2.260	6.050[a] ± 1.975	5.778[a] ± 1.518	3.243
Eos %	2.600[a] ± 1.319	2.443[a] ± 1.016	2.400[a] ± 1.475	2.860[a] ± 1.571	2.517[a] ± 1.059	2.133[a] ± 0.896	2.400[a] ± 1.474	1.589[a] ± 0.847	2.498
Bas %	0.794[a] ± 0.352	0.829[a] ± 0.228	0.700[a] ± 0.275	0.900[a] ± 0.316	0.750[a] ± 0.207	0.633[a] ± 0.365	0.623[a] ± 0.256	0.644[a] ± 0.229	0.529
Neu/Lym Ratio	2.222[a] ± 1.082	1.857[a] ± 0.570	2.140[a] ± 0.648	1.726[a] ± 0.322	2.074[a] ± 0.589	1.911[a] ± 0.581	2.182[a] ± 0.739	2.648[a] ± 1.156	1.486
RBC (10^12/L)	4.200[a] ± 0.357	4.400[a] ± 0.317	4.165[a] ± 0.387	4.288[a] ± 0.394	4.373[a] ± 0.269	4.506[a] ± 0.450	4.271[a] ± 0.309	4.258[a] ± 0.483	0.646
HGB (g/dl)	11.594[a] ± 1.538	11.293[a] ± 0.639	11.445[a] ± 1.983	11.800[a] ± 1.106	11.873[a] ± 1.121	10.933[a] ± 0.378	11.400[a] ± 1.521	11.433[a] ± 1.112	2.574
HCT %	35.688[a] ± 3.691	38.614[a] ± 1.380	34.727[a] ± 5.468	36.780[a] ± 1.388	36.633[a] ± 1.899	34.133[a] ± 2.200	35.841[a] ± 4.076	37.578[a] ± 2.606	6.545
MCV (fL)	83.371[a] ± 9.626	86.271[a] ± 2.776	80.709[a] ±11.196	84.580[a] ± 6.975	76.850[a] ±13.832	78.433[a] ± 3.817	83.091[a] ± 7.297	82.856[a] ± 7.249	11.246
MCH (pg)	27.406[a] ± 4.285	28.700[a] ± 1.968	27.045[a] ± 4.608	27.740[a] ± 3.138	27.833[a] ± 2.178	25.800[a] ± 1.905	27.505[a] ± 3.309	27.244[a] ± 3.336	5.379
MCHC (g/L)	325.00[a] ±16.128	328.29[a] ±10.579	325.82[a] ±14.777	326.00[a] ± 8.093	329.00[a] ±11.628	321.33[a] ±10.017	324.91[a] ±14.034	323.67[a] ± 5.315	13.546
HGB/HCT Ratio	0.323[a] ± 0.017	0.319[a] ± 0.009	0.328[a] ± 0.017	0.321[a] ± 0.040	0.330[a] ± 0.024	0.314[a] ± 0.010	0.334[a] ± 0.085	0.303[a] ± 0.021	0.079
PLT (10^9/L)	241.65[a] ±53.870	259.57[a] ±31.994	277.55[a] ±54.147	240.80[a] ±31.164	267.67[a] ±51.628	281.00[a] ±143.698	277.36[a] ±80.475	256.00[a] ±81.626	65.845
MPV (fL)	8.612[a] ± 0.759	8.429[a] ± 0.813	8.982[a] ± 0.744	8.380[a] ± 0.875	8.617[a] ± 0.988	8.833[a] ± 0.230	8.400[a] ± 0.884	8.389[a] ± 0.840	1.271
PDW (fL)	16.065[a] ± 0.704	16.171[a] ± 0.782	15.936[a] ± 0.366	15.640[a] ± 0.503	16.117[a] ± 0.711	16.467[a] ± 1.159	16.227[a] ± 0.984	16.356[a] ± 0.500	1.356
PCT (ml/L)	2.588[a] ± 0.602	2.681[a] ± 0.279	2.870[a] ± 0.462	2.752[a] ± 0.157	2.756[a] ± 0.527	2.833[a] ± 0.800	2.871[a] ± 0.566	2.730[a] ± 0.574	0.753
PLT/Lym Ratio	8.812[a] ± 4.289	8.249[a] ± 2.549	9.160[a] ± 2.277	8.440[a] ± 1.584	9.202[a] ± 2.420	9.764[a] ± 6.982	9.612[a] ± 3.063	9.993[a] ± 4.783	6.321

There are no notable distinctions between the identical letters (a,a). The different letters stand for significant differences (a, b), least significant difference (LSD), and standard deviation (SD).

Blood groups (ABO system):

The results of the current study showed in Figure (3-1) that the incidence of rheumatoid arthritis peaked in blood type O, followed by blood group B, then blood group A, while the lowest rate of disease was in blood type AB. On the other hand, the results indicate that, for all blood groups, the rate of rheumatoid arthritis with Rh+ was higher than in the case of Rh-.

Figure (3-1): Percentage distribution of rheumatoid arthritis according to blood groups.

Interleukin-6 (IL-6)

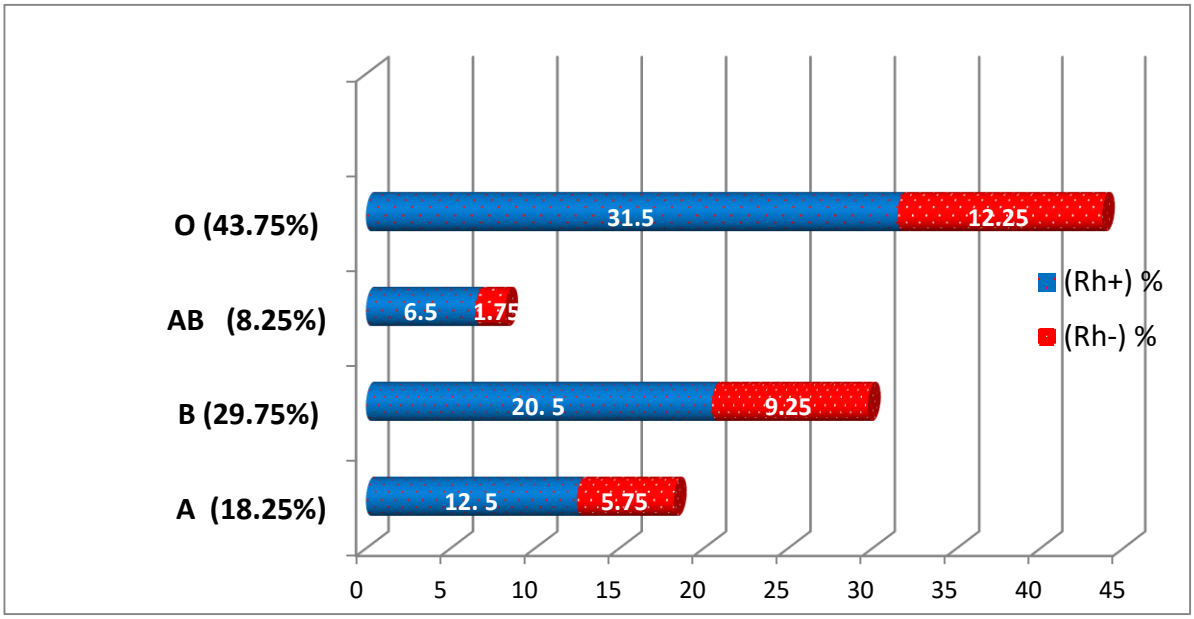


Table 3-5 showed that Interleukin-6 as inflammatory parameter increased significantly (P<0.05) in men with Rheumatoid arthritis opposed to those in the control group.

Table 3-5: Level of Interleukin-6 as inflammatory parameter in Rheumatoid arthritis patients and control

Parameter Mean ± SD	**Groups**		
	Patients	Control	P- value
IL-6 (ng/L)	68.736[a] ±17.125	25.862[b] ±7.015	0.002

different letters (a,b): there are significant differences at (P < 0.05) , (SD): standard deviation.

Correlation analysis of IL-6 and Hematological parameters in rheumatoid arthritis patients.

The results in Table 3-6 indicate that IL-6 showed a significant positive correlation (P<0.05) with Neu, PLT, PDW, PCT and PLT/Lym ratio, while it showed a non-significant positive association (P> 0.05) with WBC, Mon, Eos, Bas and Neu/Lym ratio. However, IL-6 showed a notable negative correlation (P<0.05) with HGB, HCT, MCV, MCHC and HGB/HCT ratio, while it recorded a non-significant negative correlation (P> 0.05) with Lym, RBC and MPV.

Table 3-6: correlation between hematological parameters and Interleukin-6 in Rheumatoid arthritis patients.

Hematological parameters Mean ± SD	IL-6 (ng/L)		
	Positive Correlation R	Negative Correlation r	P- value
WBC (10^9/L)	0.162	-	0.176
Neu %	0.205	-	0.05*
Lym %	-	-0.064	0.531
Mon %	0.003	-	0.914
Eos %	0.073	-	0.068
Bas %	0.002	-	0.823
Neu/Lym Ratio	0.097	-	0.072
RBC (10^{12}/L)	-	-0.163	0.121
HGB (g/dl)	-	-0.318	0.024*
HCT %	-	-0.187	0.05*
MCV (fL)	-	-0.192	0.048*
MCH (pg)	-	-0.073	0.064
MCHC (g/L)	-	-0.302	0.043*
HGB/HCT Ratio	-	-0.171	0.031*
PLT (10^9/L)	0.584	-	0.026*
MPV (fL)	-	-0.103	0.152
PDW (fL)	0.196	-	0.034*
PCT (ml/L)	0.201	-	0.049*
PLT/Lym Ratio	0.425	-	0.037*

0.25 < R < 0.75 = moderate extreme, 0.75 < R < 1 = strong extreme, R=1 = perfect, negative value = inversely, 0.00< R < 0.25 means weak extreme, and R=0 = no correlation.

* . Correlation is significant at the 0.05 level.

4. Discussion

Hematological parameters

Complete Blood Count (CBC)

The current study indicated in Table 3-1 that the total WBC was significantly increased in rheumatoid arthritis patients compared to the control group. This may be due to the fact that it is a chronic inflammatory disease. Since white blood cells are the first line of defense against infections, it is natural for their numbers to increase in patients to resist the infection, this result is consistent with (Pereckova et al., 2022; Muhammed et al., 2024).

Regarding the differential white blood cell count, the significant increase in neutrophil numbers may be due to the increase in IL-6 levels according to the current study, as it is a multifunctional factor that regulates the immune response, acute phase reactions, and hematopoiesis (Guo et al., 2021; Blanter et al., 2021) . In the acute phase response, IL-6 regulates neutrophil activity by stimulating the production of neutrophils by the bone marrow and causing the release of neutrophils into the bloodstream. IL-6 also

stimulates the production of hepatic proteins that participate in the systemic response to infection (Lajqi et al., 2021).

However, there has been a notable rise in eosinophils was observed in patients, which is consistent with (Klion et al., 2020), they confirmed that eosinophilia, an increase in the number of eosinophils in the peripheral blood, is present in patients with arthritis, especially when they have concomitant drug reactions or allergies. Peripheral and tissue eosinophilia can be a prominent feature of many unique rheumatic and vascular diseases (Ni et al., 2021).

Eosinophilia is often directly associated with rheumatoid disease and has been considered a marker of disease activity, the risk of developing eosinophilia appears to be significantly associated with the presence of autoantibodies to rheumatoid factor (Xiao et al., 2021).

In contrast, the number of lymphocytes decreased significantly in patients, which is consistent with Mahmoud et al., (2022) who confirmed that rheumatoid arthritis is a chronic inflammation of the synovial tissues and is characterized by low lymphocytes and high levels of inflammatory cytokines that attract macrophages to the joint site. As a result of this need to recruit these nearby cells for reconstruction and phagocytosis, there is a need to prevent them from leaving. Therefore, the number of lymphocytes decreases, perhaps as a result of a lack of signals, including CD69, sphingosine-1-phosphate, and CXCR4 signals (Michalaki et al.,2022).

On the other hand, red blood cell parameters decreased significantly in RA patients, while platelet count increased significantly, which is in agreement with Muhammed et al., (2024). It has been proven that the use of RBC and PLT indices, in addition to related measures, is used to diagnose RA patients. In addition, low hemoglobin may be due to liver dysfunction. People with arthritis who have elevated alkaline phosphatase levels have been shown to have liver dysfunction. According to recent studies, white blood cells (WBCs), hemoglobin (Hb) and platelets may be associated with the inflammatory process; some studies have evaluated the relationship between RA disease severity and PLT, RBC, Hb, hemoglobin-to-platelet ratio (HPR), and the ratio of red blood cells to platelets (RPR). There is growing evidence that MPV is a valid and trustworthy inflammatory biomarker in autoimmune illnesses, along with the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR) and others. (Shakil et al., 2021; Xue et al., 2022)

Recent studies have also shown the crucial role of platelets (PLT) in inflammatory reactions, noted that patients with active disease had higher neutrophil-to-lymphocyte ratios (NLRs) and platelet counts, but lower hemoglobin and mean platelet volume (MPV) values (Pereckova et al., 2022 ; Muhammed et al., 2024).

The results in Table 2-3 showed that when comparing the blood parameters of patients according to age group, no notable variations were observed. ($P>0.05$) except for MPV and PDW, which rose considerably ($P<0.05$) in the second age group, G II (60-75) years compared to the first age group G I (45-60) years. The reason for the increase in MPV may be due to a deficiency in vitamin D or due to metabolic disorders, which are often common in the elderly, as they have been proven to be among the reasons leading to an increase in MPV. As for the reason for the increase in PDW, it may be attributed to the increase in inflammatory indicators and the increase in vascular diseases with increasing age (Khaled et al., 2020; Sierra et al., 2023).

In contrast, Table 3.3 indicated that when comparing patients based on body mass index, there were no significant differences in blood parameters except for MPV and PDW, which increased significantly in the third group (GIII obesity class I) in contrast to the first group (GI normal weight). This may be due to the effect of obesity in increasing the inflammatory state, in addition to high cholesterol and insulin resistance, which are complications associated with obesity and increased body mass index. As for the increase in PDW, it may be attributed to increased disease activity and increased inflammation resulting from it, as it is a chronic inflammatory disease. It is known that the increase in

adipose tissue in the case of obesity increases the cytokines that cause inflammation, and thus PDW increases (Nikiphorou et al., 2020; Atwa et al., 2022). On the other hand, Table 3.4 indicated that there were no significant differences (P>0.05) in blood parameters when comparing patients based on blood groups and Rhesus factor.

Blood groups (ABO system).

Since blood type O constitutes the largest proportion of this data, it is possible that most Iraqis are of blood type O, and therefore the results indicated that this group has the highest incidence of rheumatoid arthritis. This outcome is in line with the investigation of Baughman et al., (2020) which indicated that the highest proportion of people with rheumatoid arthritis belong to blood type O.

Interleukin-6 (IL-6)

Table 3-5 indicated that IL-6 was significantly increased in RA patients, which is consistent with several studies have reported elevated levels of IL-6 in the serum of RA patients, and its levels increase with increasing disease activity, and it would be useful as a marker of the current disease stage. Its elevation indicates ongoing local inflammation, even if the results of the remaining laboratory tests reflecting the systemic inflammatory response are within normal levels (Favalli, 2020; Sebba, 2021).

One of the most significant mediators of the inflammatory response, interleukin 6 (IL-6), is generated locally in response to an inflammatory stimulus and can result in systemic symptoms distant from the site of inflammation, as demonstrated by Witeska et al., (2022). The number of cell types that react to IL-6 has significantly increased due to its distinct signaling strategy, which includes both classical and transient signaling pathways (Aliyu et al., 2022). This cytokine plays a significant role in the pathophysiology of rheumatoid arthritis (RA) and is implicated in numerous extra-articular symptoms that accompany the condition (Kondo et al., 2021; Li et al., 2024).

Immunity and systemic inflammation are significantly influenced by IL-6. In reaction to several danger signals and cytokines like TNF-α and IL-1, myeloid cells create and release it quickly. IL-6 can travel through the bloodstream from the site of local inflammation to key organs and trigger systemic reactions (Favalli, 2020; Warjukar et al., 2024).

Correlation analysis of IL-6 and Hematological parameters in men with rheumatoid arthritis.

Table 3-6 revealed that there was a substantial positive connection between IL-6 and (P<0.05) with Neu, PLT, PDW, PCT and PLT/Lym ratio. While IL-6 showed an insufficient positive association (P>0.05) with WBC, Mon, Eos, Bas and Neu/Lym ratio. This can be logically explained by the role of IL6 in stimulating neu production as explained above. In addition to being a strong indicator of the presence of an inflammatory state, it is natural for its increase to be accompanied by an increase in platelets (Holers et al.,2022). On the other hand, PDW increases in an inflammatory state. Also, PLT/Lym ratio is a strong inflammatory indicator. All of these criteria are accompanied by an increase in IL6, the first inflammatory indicator in RA patients (Pereckova et al., 2022 ; Muhammed et al., 2024).

On the other hand, IL-6 recorded a significant negative correlation (P<0.05) with HGB, HCT, MCV, MCHC and HGB/HCT ratio. While it recorded a non-significant negative correlation (P>0.05) with Lym, RBC and MPV (Koster et al., 2021). It has been scientifically proven that hemoglobin decreases with increasing severity of RA disease this may be due to the fact that people with arthritis who have elevated alkaline phosphatase levels primarily have liver dysfunction and thus less stimulation of red blood cell and hemoglobin production, which are associated with the inflammatory process (Khaled et al., 2020; Sierra et al., 2023).

According to other studies, increased white blood cells (WBCs) and platelets may be due to the increased neutrophil-to-lymphocyte ratio (NLRs) and platelet counts (Aliyu et al., 2022). Researchers have observed that patients with active disease have higher

neutrophil-to-lymphocyte ratios (NLRs) and platelet counts, but also lower hemoglobin and mean platelet volume (MPV) (Nikiphorou et al., 2020; Atwa et al., 2022)..

Other studies have evaluated the relationship between RA severity and platelet count, red blood cell count, hemoglobin, hemoglobin-to-platelet ratio (HPR), and red blood cell-to-platelet ratio (RPR). There is growing evidence that MPV, along with platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and others, are accurate and reliable biomarkers of inflammation in autoimmune diseases (Muhammed et al., 2024), this was demonstrated by testing the relationship of these parameters with IL-6 in our current study (Pereckova et al., 2022; Xue et al., 2022).

5. Conclusion

There is a positive correlation between IL-6 and each of Neu, PLT, PDW, PCT and PLT/Lym ratio.

There is a negative correlation between IL-6 and HGB, HCT, MCV, MCHC and HGB/HCT ratio.

Some ratios, specifically PLT/Lym ratio and HGB/HCT ratio, can be adopted as effective inflammatory indicators in the early detection of RA disease due to their significant correlation with IL-6.

MPV and PDW values increase with increasing age and body mass index in RA patients, while blood parameters are not affected by differences in blood groups.

Study of the relationship between hematological parameters and other types of cytokines in RA patients.

Study of the association between IL-6 and kidney function in RA patients.

Study of the relationship between IL-6 and thyroid function and metabolic rate in RA patients.

Study of the association between IL-6 and hematological parameters of other inflammatory diseases..

REFERENCES

1. Alivernini, S., Firestein, G. S., & McInnes, I. B. (2022). The pathogenesis of rheumatoid arthritis. Immunity. sciencedirect.com.
2. Aliyu, M., Zohora, F. T., Anka, A. U., Ali, K., Maleknia, S., Saffarioun, M., & Azizi, G. (2022). Interleukin-6 cytokine: An overview of the immune regulation, immune dysregulation, and therapeutic approach. International immunopharmacology, 111, 109130. [HTML]
3. Atwa E.T., Omar H.M., Amin A., Hammad M. Red Cell Distribution Width and Mean Platelet Volume in Rheumatoid Arthritis Patients: Its Association with Disease Activity. Reumatol. Clínica (Engl. Ed.) 2022;18:399–405. doi: 10.1016/J.REUMAE.2021.04.011. [DOI] [PubMed] [Google Scholar]
4. Available from: https://www.ncbi.nlm.nih.gov/pubmed/35046715.
5. Bakker AJ, Mücke M.(2007). Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.
6. Baughman, R.P.; Cremers, J.P; Harmon, M.; Lower, E.E; Drent, M. Methotrexate in sarcoidosis: hematologic and hepatic toxicity encountered in a large cohort over a six year period. Sarcoidosis, Vasculitis, and Diffuse Lung Diseases 2020, 37(3), e2020001. DOI: https://doi.org/10.36141/svdld.v37i3.9362.
7. Blanter, M., Gouwy, M., & Struyf, S. (2021). Studying neutrophil function in vitro: cell models and environmental factors. Journal of inflammation research. tandfonline.com.
8. Brecher M. (2002) Technical Manual. (ed) 14th ed. Bethesda, MD: American Association of Blood Banks, 2002.

9. Conforti, A., Di Cola, I., Pavlych, V., Ruscitti, P., Berardicurti, O., Ursini, F., ... & Cipriani, P. (2021). Beyond the joints, the extra-articular manifestations in rheumatoid arthritis. Autoimmunity reviews, 20(2), 102735. [HTML]
10. Coutant F, and Miossec P. (2020) Evolving concepts of the pathogenesis of rheumatoid arthritis with focus on the early and late stages. Curr. Opin. Rheumatol., 32, 57–63.
11. Favalli, E. G. (2020). Understanding the role of interleukin-6 (IL-6) in the joint and beyond: a comprehensive review of IL-6 inhibition for the management of rheumatoid arthritis. Rheumatology and therapy. springer.com
12. Fraenkel, L., Bathon, J. M., England, B. R., St. Clair, E. W., Arayssi, T., Carandang, K., ... & Akl, E. A. (2021). 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis & Rheumatology, 73(7), 1108-1123. nih.gov.
13. Guo, F., He, Y., Fan, Y., Du, Z., Sun, H., Feng, Z., ... & Xiong, T. (2021). G-CSF and IL-6 may be involved in formation of endometriosis lesions by increasing the expression of angiogenic factors in neutrophils. Molecular human reproduction, 27(11), gaab064. researchgate.net.
14. Holers, V. M., Kuhn, K. A., Demoruelle, M. K., Norris, J. M., Firestein, G. S., James, E. A., & Deane, K. D. (2022). Mechanism-driven strategies for prevention of rheumatoid arthritis. Rheumatology & autoimmunity, 2(03), 109-119. mednexus.org
15. Khaled S. A, Eldin E. N, Makarem Y S and Mahmoud H. F (2020).Value of Platelet Distribution Width and Mean Platelet Volume in Disease Activity Score of Rheumatoid Arthritis. Journal of Inflammation Research. September 2020 13: 595-606. DOI:10.2147/JIR.S265811, Dovepress open access to scientific and medical research.
16. Klion AD, Ackerman SJ, Bochner BS. Contributions of Eosinophils to Human Health and Disease. Annu Rev Pathol (2020) 15:179–209. doi: 10.1146/annurev-pathmechdis-012419-032756 [DOI] [PMC free article] [PubMed] [Google Scholar]
17. Kondo, N., Kuroda, T., & Kobayashi, D. (2021). Cytokine networks in the pathogenesis of rheumatoid arthritis. International journal of molecular sciences, 22(20), 10922. mdpi.com
18. Koster, D., Egedal, J. H., Lomholt, S., Hvid, M., Jakobsen, M. R., Müller-Ladner, U., & Nielsen, M. A. (2021). Phenotypic and functional characterization of synovial fluid-derived fibroblast-like synoviocytes in rheumatoid arthritis. Scientific Reports, 11(1), 22168. nature.com.
19. Kristyanto, H., Blomberg, N. J., Slot, L. M., van der Voort, E. I., Kerkman, P. F., Bakker, A., & Scherer, H. U. (2020). Persistently activated, proliferative memory autoreactive B cells promote inflammation in rheumatoid arthritis. Science translational medicine, 12(570), eaaz5327. nih.gov.
20. Lajqi, T., Braun, M., Kranig, S. A., Frommhold, D., Pöschl, J., & Hudalla, H. (2021). LPS induces opposing memory-like inflammatory responses in mouse bone marrow neutrophils. International journal of molecular sciences, 22(18), 9803. mdpi.com.
21. Li, R., Ye, J. J., Gan, L., Zhang, M., Sun, D., Li, Y., ... & Chang, P. (2024). Traumatic inflammatory response: pathophysiological role and clinical value of cytokines. European Journal of Trauma and Emergency Surgery, 50(4), 1313-1330. springer.com.
22. Mahmoud, D. E., Kaabachi, W., Sassi, N., Tarhouni, L., Rekik, S., Jemmali, S., & Laadhar, L. (2022). The synovial fluid fibroblast-like synoviocyte: A long-neglected piece in the puzzle of rheumatoid arthritis pathogenesis. Frontiers in Immunology, 13, 942417. frontiersin.org.
23. Michalaki, E., Nepiyushchikh, Z., Rudd, J. M., Bernard, F. C., Mukherjee, A., McKinney, J. M., & Dixon, J. B. (2022). Effect of human synovial fluid from osteoarthritis patients and healthy individuals on lymphatic contractile activity. Journal of biomechanical engineering, 144(7), 071012. asme.org.
24. Muhammed, D.S., Polus,R.K. and Mohammed, N.S. (2024). Relationship between Different Hematological Parameters and Disease Activity in Patients with Rheumatoid Arthritis. Advanced Medical Journal, Vol.9, No.1, P.46-55, 2024 .DOI: https://doi.org/10.56056/amj.2024.236.
25. Ni, C., Gao, S., Zheng, Y., Liu, P., & Zhai…, Y. (2021). Annexin A1 attenuates neutrophil migration and IL-6 expression through Fpr2 in a mouse model of Streptococcus suis-induced meningitis. Infection and asm.org.

26. Nikiphorou E., De Lusignan S., Mallen C., Khavandi K., Roberts J., Buckley C.D., Galloway J., Raza K. Haematological Abnormalities in New-Onset Rheumatoid Arthritis and Risk of Common Infections: A Population-Based Study. Rheumatology. 2020;59:997–1005. doi: 10.1093/rheumatology/kez344. [DOI] [PMC free article] [PubMed] [Google Scholar].
27. Pereckova J, Martiniakova S, Payer J et al., (2022): Analysis of hematological parameters in rheumatoid arthritis patients receiving biological therapy: contribution to prevention of avoidable hematological complications. EXCLI Journal, 21:580-594.
28. Scherer, H. U., van der Woude, D., & Toes, R. E. (2022). From risk to chronicity: evolution of autoreactive B cell and antibody responses in rheumatoid arthritis. Nature Reviews Rheumatology, 18(7), 371-383. [HTML].
29. Scherer, H. U., van der Woude, D., & Toes, R. E. (2022). From risk to chronicity: evolution of autoreactive B cell and antibody responses in rheumatoid arthritis. Nature Reviews Rheumatology, 18(7), 371-383. [HTML].
30. Sebba, A. (2021). Pain: a review of interleukin-6 and its roles in the pain of rheumatoid arthritis. Open access rheumatology: research and reviews. tandfonline.com.
31. Shakil M, Saleem DM, Zafar A, Ali A, Raziq M, Shams S. Clinical and hematological parameters in patients of Rheumatoid arthritis in a tertiary care hospital. Rawal Med. J. 2021; 46(1):45. Available from: https://www.rmj.org.pk/fulltext/27-1588711248.pdf.
32. Sierra M G, Romo-Cordero A, Quevedo-Abeledo J C, et al., (2023). Mean Platelet Volume in a Series of 315 Patients with Rheumatoid Arthritis: Relationship with Disease Characteristics, including Subclinical Atherosclerosis and Cardiovascular Comorbidity. Diagnostics 2023, 13(20), 3208; https://doi.org/10.3390/diagnostics13203208.
33. Singh, A., Behl, T., Sehgal, A., Singh, S., Sharma, N., Naved, T., & Bungau, S. (2021). Mechanistic insights into the role of B cells in rheumatoid arthritis. International Immunopharmacology, 99, 108078. [HTML].
34. Warjukar, P. R., Mohabey, A. V., Jain, P. B., & Bandre, G. R. (2024). Decoding the correlation between inflammatory response marker interleukin-6 (IL-6) and C-reactive protein (CRP) with disease activity in rheumatoid arthritis. Cureus. nih.gov.
35. Xiao, Y., Cong, M., Li, J., He, D., Wu, Q., Tian, P., & Hu, G. (2021). Cathepsin C promotes breast cancer lung metastasis by modulating neutrophil infiltration and neutrophil extracellular trap formation. Cancer cell, 39(3), 423-437. cell.com.
36. Xue L, Tao L, Sun H, et al., Association Between Blood PLT and RBC Related Indices and Disease Activity in Patients with Rheumatoid Arthritis. Int J Gen Med. 2022; 15:573-81.
37. Yoo, B. W., Song, J. J., Park, Y. B., & Lee, S. W. (2022). 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease by Wallace et al., Annals of the Rheumatic Diseases, 81(9), e179-e179. bmj.com.