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Relationship between Different Hematological Parameters and Disease Activity in Patients with Rheumatoid Arthritis

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Abstract

Background and objectives: Rheumatoid arthritis is a type of immune disorder that has an impact on the entire body. The objective was to measure and compare various hematological parameter values between chronic and new cases also in new patients who exhibited varying degrees of disease activity.

Methods: This study was a cross-sectional survey, conducted in Rizgary Hospital and private clinics in Erbil city/ Kurdistan Region of Iraq. Two groups each of 30 patients; with newly diagnosed the 2010 ACR/EULAR criteria are divided into four groups, each of which has a point score: joint symptoms, serology (including Rheumatoid factor and/or Anti-Citrullinated Peptide Antibody), duration of symptoms (less than or more than 6 weeks), and acute-phase reactants (c-reactive protein and/or erythrocyte sedimentation rate) and chronic Rheumatoid Arthritis cases enrolled in this study from October 2021 till September 2022. Hematological parameter and disease activity monitored and compared between both groups, in addition to comparison between cases in the same group.

Results: The majority (81.7%) of patients were female and (18.3%) of them were male, mean age ± std. deviation of respondents was 48.80 ± 9.13 years. There was significant statistical association between study groups and joint swelling, multiple or single joint and disease activity (DAS 28), also, the difference between both groups was statistically significant regarding mean pain score, white blood cells, serum folate, and rheumatoid factor. Likewise; the association was significant between study groups and multiple or single joint. There was significant statistical association between study groups and DAS 28, the majority (86.7%) of newly diagnosed patients had low – moderate level of DAS 28 while 40% of chronic subjects measured high level of DAS 28.
Conclusion: Hematological markers including disease activity score, white blood cells, serum folate, C-reactive protein and rheumatoid factor were good indicators for measurement of rheumatoid arthritis severity and activity in the selected sample of patients.

Keywords: Chronic cases, Disease activity score, Hematological parameters, Rheumatoid arthritis.

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Introduction

Rheumatoid arthritis (RA) is a form of immune disorder that has an impact on the entire body. Rheumatoid arthritis is characterized by enhanced synovial inflammation, neovascularization, and osteoclast formation. It is responsible for inflammatory arthritis as well as accelerated joint destruction, which ultimately results in a decline in life satisfaction and an enhance in impairment. During the past twenty years, there was significant improvement in the understanding of the illness pathogenic mechanism that have led to significant shifts in RA therapy.[1-4]

This illness has a complicated and multifaceted origin, most probably including an oligogenic predisposition and an "environmental trigger". The immune system is responsible for the regulation and limitation of inflammatory conditions in a healthy person. However, in RA, some immune system problems promote inflammation and result in a wide range of pathologic and clinical symptoms. The presence of many clinical manifestations at the same time, the variety on both the immunological and clinical characteristics, and the absence of a specialized checkup exam make it tough to identify and evaluate the status of a rheumatic disease accurately and in a timely manner[5].

Multiple composite measures have been established to evaluate clinical illness activity, such as SDAI (Simplified Disease Activity Index), CDAI (Clinical Disease Activity Index), DAS 28 and DAS 28-3 score (Modified Disease Activity Score).[6-8] The DAS 28-3 score method (tender joint count, swollen joint count, and ESR) is the most commonly used factor to evaluate illness impact because it has been demonstrated accurate and can be clinically interpreted. The DAS 28-3 scoring system is the most commonly used parameter. However, Research for simpler and more useful measures of therapy response or sickness activity is ongoing [9].

Liver impairment was also discovered in arthritic individuals with primarily elevated alkaline phosphatase levels. New research suggests that hematological factors, such as hemoglobin (Hb) and platelets, as well as white blood cells (WBCs), are related to inflammatory process.[10-12] Patients with active disease suffer from lower Hb and mean platelet volume (MPV) levels this found by researchers[13] but people with active disease have greater neutrophil-to-lymphocyte ratios (NLRs) and platelet counts. [14,15] Considering the fact that the complete blood count (CBC) is an easy and informative blood test in inflammatory diseases and cheap diagnostic procedure in the laboratory, CBC parameters may be a valuable supplement for monitoring the disease activity of rheumatoid arthritis RA.[16-18] This research was conducted with objective of measuring hematological parameter values, include hemoglobin (Hb), red blood cells (RBC), white blood cells (WBC), and platelet components, in RA patients who exhibited varying degrees of disease activity. It was also established how well combined hematological measures perform as a tool for anticipating the RA remission phase.[18]

Patients and methods

This study was a cross-sectional survey; the research was designed and performed in Rizgary Teaching Hospital and private clinic, Erbil, Kurdistan region. In total 60 participants enrolled then we divided the patients over two different groups. The first group consisted of 30 patients of newly diagnosed with RA according ACR/EULAR 2010 classifications criteria. The second group was those patients diagnosed before six months and they were under treatment. After receiving verbal

agreement, patients were questioned and examined; clinical information were recorded in a comprehensive questionnaire form. The present study included information on age, gender, type of treatment and duration, sign and symptoms, joint swelling, joint site, single or multiple joint, pain score and DAS28. The research duration was for one year from October 2021 till September 2022.

Venous blood was drawn from each patient into tubes with and without anticoagulant. Standard laboratory workup included: WBC, RBC, Hb HCT, MCV, MCH, MCHC, RDW, PLT, MPV, PDW, PCT, ESR, Blood urea, S. creatinine, serum folate, CRP, anticyclic citrullinated peptide) antibodies-Anti CCP and RF.

The collection of samples had been done after taking informed consent of a participant, blood specimens had been withdrawn from the antecubital vein by using a dry sterile disposable syringe and needle. 2 ml of blood was dispensed into the anticoagulant tube. Specimens were labelled with the subject's name, age, sex, and then sent to a laboratory for hematological and serological investigations.

All patients who had RA who accepted to participate in the study were enrolled in our study. One group is newly diagnostic and they don't undergo treatment yet, the second group who were under treatment for six months. The patients were between 21 to 60 years. Patients who had malignancy, arterial or venous thrombosis and any other systemic or connective tissue disorders were excluded from the study.

We gained the approval to conduct this study from Ethics committee of the Kurdistan Higher Council of Medical Specialties. The information will thereafter be kept private and would not be utilized in any way.

The Statistical Package for Social Sciences was employed to investigate the data (SPSS, version 25). Microsoft Excel (version 2013) was used for making the pie chart. Chi square test of association was employed to compare proportions. Fisher's exact test was unemployed when the predicted frequency (value) < 5 or > 20% of the cells of the table. A p-value of ≤ 0.05 was regarded as statistically significant.

Results

We enrolled 60 participants in the current study that divided into two groups, newly diagnosed and chronic disease, the majority (81.7%) of patients were female and (18.3%) of them were male, mean age ± std. deviation of respondents was 48.80 ± 9.13 years.

One third (33.3%) of participants took methotrexate (MTX), folic acid, Hydroxy chloroquine (HCQ), followed by 30% of them took MTX, folic acid treatment, 16.7% of patients took HCQ, prednisolone (PRD), only 3.3% for each of them took sulfasalazine, PRD and MTX, methylprednisolone, meloxicam.

Findings of Table (1) reveal that there was significant statistical association between study groups and joint swelling, the majority (80%) of newly diagnosed group had joint swelling while only 43.3% of chronic cases diagnosed with joint swelling. There was significant statistical association between study groups and multiple or single joint, most (66.7%) of newly diagnosed cases had single join involvement while most of chronic cases had negative joint involvement (56.7%). There was significant statistical association between study groups and DAS 28, the majority (86.7%) of newly diagnosed patients had low – moderate level of DAS 28 while 40% of chronic subjects measured high level of DAS 28. Chi square test was done and p-value was <0.05.

Outcomes of Table (2) indicate that that there was a non-significant statistical difference between chronic disease and newly diagnosed RA groups regarding to RBC, Hb, PLT, ESR, blood urea, S. creatinine and CRP. Chi square test was done and p-value was >0.05. There was a significant statistical difference between study groups and mean pain score, mean pain score of newly diagnosed cases was 6.33 while mean pain score of chronic cases was 4.7. There was a significant statistical difference between study groups and DAS-28, mean DAS-28 of newly diagnosed group was 5.009 while mean DAS 28 of chronic disease cases was 3.781. There was a significant statistical difference between study groups and WBC, mean WBC of chronic disease cases was 8.6240 µL while newly diagnosed had the mean of 6.3527 µL. There was a significant statistical difference between study groups and serum folate, newly diagnosed cases had serum folate level of 13.97 ng/ml while in the chronic group the level was 10.00 ng/ml. There was a significant statistical difference between study groups and anti-CCP, the test considered high level 220.234 u/ml in chronic disease cases in reverse newly diagnosed group had lower level 58.509 u/ml of anti CCP. There was a significant statistical difference between study groups and mean RF for newly diagnosed was 62.14 while mean RF for chronic patients was35.34. Chi square test was done and p-value was significant (<0.05). Results of Table (3) reveal that there was a non-significant statistical difference between DAS 28 and some of hematological parameters among newly diagnosed RA patients, Chi square was done and p-values were more than 0.05, except for HB, ESR, CRP and RF for which the associations were significant. Findings of Table (4) show that there was a non-significant statistical difference between DAS 28 and hematological or serological parameters

except for WBC and CRP. Chi square test was done and p-values were >0.05.

Table (1): Association between study groups and joint swelling, site, number and DAS 28.

Variable	Categories	study groups		p-value
		chronic disease	newly diagnosed	
joint swelling	yes	13 (43.3%)	24 (80%)	0.003
	no	17 (56.7%)	6 (20%)	
multiple or single joint	negative	17 (56.7%)	4 (13.3%)	<0.001
	multiple joint	6 (20%)	6 (20%)	
	single joint	7 (23.3%)	20 (66.7%)	
DAS 28	low - moderate	26 (86.7%)	18 (60%)	0.017
	high	4 (13.3%)	12 (40%)	
Total		30 (100%)	30 (100%)	

Table (2): The difference between chronic disease and newly diagnosed RA cases in disease activity, serology and hematology parameters.

	study groups	N	Mean	Std. Deviation	p-value
pain score	chronic disease	30	4.70	1.31	<0.001
	newly diagnosed	30	6.33	0.60	
DAS-28	chronic disease	30	3.78	1.16	<0.001
	newly diagnosed	30	5	0.57	
WBC	chronic disease	30	8.62	2.73	<0.001
	newly diagnosed	30	6.35	1.72	
HGB	chronic disease	30	12.09	1.68	0.918
	newly diagnosed	30	12.05	1.50	
PLT	chronic disease	30	296.37	61.81	0.072
	newly diagnosed	30	266.93	62.63	
ESR (mm/hr)	chronic disease	30	30.87	21.75	0.162
	newly diagnosed	28	38.29	17.73	
Blood urea (mg/dl)	chronic disease	30	26.98	9.48	0.171
	newly diagnosed	30	32.14	18.04	
Serum creatinine (mg/dl)	chronic disease	30	0.74	0.15	0.276
	newly diagnosed	30	0.84	0.46	
Serum folate (ng/ml)	chronic disease	30	10	3.804	0.002
	newly diagnosed	30	13.97	5.307	
CRP (mg/dl)	chronic disease	30	14.79	12.18	0.466
	newly diagnosed	30	12.34	13.68	
Anti-CCP (U/ml)	chronic disease	30	220.23	235.61	0.001
	newly diagnosed	30	58.50	109.57	
RF	chronic disease	30	35.34	36.70	0.013
	newly diagnosed	30	62.14	43.85	

Table (3): Difference between DAS-28 and hematological and serological parameters of newly diagnosed cases.

	DAS 28	N	Mean	Std. Deviation	p-value
WBC	low - moderate	26	8.50	2.72	0.538
	high	4	9.42	3.07	
HB	low - moderate	26	12.37	1.54	0.017
	high	4	10.27	1.56	
PLT	low - moderate	26	293.35	64.07	0.505
	high	4	316	46.15	
ESR (mm/hr)	low - moderate	26	26.15	18.29	0.001
	high	4	61.50	18.52	
Blood urea (mg/dl)	low - moderate	26	26.25	9.45	0.288
	high	4	31.75	9.53	
S.Creatinine (mg/dl)	low - moderate	26	0.75	0.15	0.238
	high	4	0.65	0.10	
Serum folate (ng/ml)	low - moderate	26	9.83	3.50	0.542
	high	4	11.11	5.96	
C.R Protein (mg/dl)	low - moderate	26	12.71	11.41	0.014
	high	4	28.34	8.14	
Anti-CCP (U/ml)	low - moderate	26	207.01	230.41	0.443
	high	4	306.19	287.79	
RF	low - moderate	26	30.20	30.85	0.049
	high	4	68.76	58.05	

Table (4): Difference between DAS 28 and hematological and serological parameters of chronic RA cases.

	DAS 28	N	Mean	Std. Deviation	p-value
WBC	low - moderate	18	6.97	1.80	0.013
	high	12	5.41	1.12	
HGB	low - moderate	18	11.98	1.47	0.759
	high	12	12.16	1.60	
PLT	low - moderate	18	280.22	54.64	0.158
	high	12	247	70.73	
ESR (mm/hr)	low - moderate	18	32.94	13.47	0.073
	high	12	44.50	20.62	
Blood urea (mg/dl)	low - moderate	18	30.62	13	0.582
	high	12	34.41	24.24	
S. creatinine (mg/dl)	low - moderate	18	0.77	0.38	0.312
	high	12	0.94	0.56	
Serum folate (ng/ml)	low - moderate	18	12.80	4.72	0.142
	high	12	15.73	5.84	

C.R Protin (mg/dl)	low - moderate	18	5.61	6.16	<0.001
	high	12	22.42	15.82	
Anti-CCP (U/ml)	low - moderate	18	83.47	136.85	0.129
	high	12	21.05	12.66	
RF	low - moderate	18	50.27	31.69	0.069
	high	12	79.94	54.23	

Discussion

The primary objective of this research was to identify any associations that may exist between various hematological and serological parameters in order to put these evidence-based and cost-effective parameters to use in assessing disease activity and, as a result, improve clinical management of rheumatoid arthritis.[13] The study clearly proved that patients newly diagnosis RA had swollen joint two times more than what was found for chronic patient group. The results were also substantial for newly diagnosed cases of both single and multiple joint and DAS -28. The findings were important for newly diagnosed cases of both single and multiple joint and DAS-28. [19] Han et al reported that anemia independently contributes to physical disability in patients with RA. 40% of studied RA patients in newly diagnosis group had high DAS-28 activity. This result is near with that mentioned by Ganna study,[20] which mention that 30% of RA patients had high DAS-28 activity and for chronic group there is large difference we found only 13.3 of patient had high DAS28 activity.[21]

Some of the sign and symptoms are observed clearly in Chronic disease group in different percentage while other signs like swelling joint, multiple joint pain, morning stiffness and neck pain noted in patients with newly diagnoses which was in line with data found by Marrium et al.[22]

The results were greatly significant between them. This study shows a non-significant statistical correlation between DAS-28 and hematological parameters according to WBC, PLT, blood urea, S. creatinine, folate and anti-CCP. There is significant correlation between DAS 28 and chronic disease patients. Other study shows significant effect between DAS-28 with PLT.[23] Newly diagnosed groups with high DAS-28 shows significant result in case of HGB. High DAS-28 patients was suffering from lower HGB. This result completely agrees with what found by Padjen et al[24]. Other studies confirmed that patients suffering from high DAS-28 their ESR and CRP were higher than patients with low-moderate cases.[25] The result in this investigation supports significant effects when we compared RF of highly DAS-28 to low- and moderate disease activity in newly diagnosed group. This result shows disagreement with data obtained by Hisham et al. [21]

Conclusions

It was clear when we compared newly diagnosed to chronic cases parameters like main pain score, average DAS-28, WBC, serum folate, anti-CCP, CRP and RF were proved to be good markers and parameters. In newly diagnosed group the difference between high, low and moderate DAS-28 was in hematological parameters like Hb, ESR, CCP and RF.

Conflict of interest

The researchers declare that there is no any conflict of interest.

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