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Original Research Article

A HOSPITAL BASED PROSPECTIVE STUDY TO FIND OUT THE CORRELATION OF HEMATOLOGICAL STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS AT NEWLY ESTABLISHED TERTIARY CARE CENTER

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Abstract

Background: Inflammatory reactions play a crucial role in rheumatological diseases and encompass alterations in peripheral blood cells' number, shapes, and sizes. Our aim of this present study is to assess the hematological parameters in rheumatoid arthritis (RA) and identify their relationship with disease activity. **Materials and Methods:** This is a cross-sectional prospective study using convenient simple random sampling of 50 patients attending the department of general medicine, Government Bangur Hospital & Medical college, Pali, Rajasthan, India over a period of one year. Complete blood picture showing red blood cells (RBCs) count and indices, white blood cells (WBCs); both total and differential counts, and platelets parameters was done to all patients. A full medical history, general and musculoskeletal examination and assessment of the disease activity using the DAS 28 score-ESR were done. **Result:** The mean age of RA patients was 46.458± 11.98 years. 78% of them were females and 22% were males. 32 patients were active while 18 patients (36%) were inactive. There was statistically significant positive correlation between ESR and RDW%, PLT count, PLR while it was significantly negatively correlated with HG levels, Hb/PLT ratio, RDW%/PLT ratio, RBCs/PLT ratio, Hb/RDW% ratio. Both RF and Anti CCP titres were positively correlated to RDW%, PLT count and PLR, but they were negatively correlated with HG levels, Hb/PLT, RDW%/PLT, RBCs/PLT and Hb/RDW% ratios. **Conclusion:** Alterations in haematological parameters are significantly associated with disease activity in RA patients and these changes go hand in hand with inflammatory markers. CBC and haematological parameters are simple, available and cheap laboratory investigation that could be used in future to assess and follow up RA patients.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic immune-mediated systemic inflammatory disease characterized by chronic synovitis with pannus formation, leading to joint destruction and disability. In clinical practice, there is general agreement that rheumatoid inflammation should be controlled as soon as possible, as completely as possible, and that control should be maintained for as long as possible consistent with patient safety.[1] Rheumatoid arthritis affects the synovial joints, but it is not confined to them and the many visceral manifestations have led to the classification of RA as a systemic disorder of the immunological mechanism. Of the systemic lesions, anemia and a focal subcutaneous granuloma are the most characteristic. Some cases of RA, particularly those that are seropositive, are fulminating and rapidly progress to severe deformity.[2] Inflammatory reactions play a crucial role in rheumatological diseases and encompass alterations in peripheral blood cells' number, shapes, and sizes. Complete blood cell parameters could act as indicators of inflammation and disease activity.[3]

As the goal of treatment is to control of rheumatoid inflammation, it is clear that the management of RA should include systematic and regular quantitative evaluation of disease activity. So an accurate, valid

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International Journal of Academic Medicine and Pharmacy (www.academicmed.org)
ISSN (O): 2687-5365; ISSN (P): 2753-6556

and reliable method for assessment of disease activity is one of the most important issues for guiding the treatment protocol during management of the RA patients. Several composite indices have been developed to assess clinical disease activity like SDAI (Simplified Disease Activity Index), CDAI (Clinical Disease Activity Index), DAS 28 and DAS 28-3 score (Modified Disease Activity Score). Among these DAS 28-3 (using three variables- tender joint count, swollen joint count and ESR) score system is the most commonly used parameter now-a-days to measure the disease activity as it is extensively validated and clinically interpretable4 but it is mainly dependent on clinical findings. In this era of evidence based clinical practice, addition of laboratory-based investigations like some haematological parameters including Haemoglobin (Hb) level, Platelet count and Mean Platelet Volume (MPV) which are found to be altered in this chronic inflammatory disease can further improve the assessment status of disease activity.[4]

In the previous years, various authors have studied the association between disease activity of RA and these haematological parameters separately. They investigated the association between the activity of RA and the haematological parameters.[5] Some studies assessed the correlation between platelets (PLT), red blood cells (RBC), red blood cells-platelet ratio (RPR) and haemoglobin-platelet ratio (HPR) as regards the disease activity. Little is known about the significance of the PLT and parameters of RBC in differentiating active from inactive disease.6 Studies found negative correlation between disease activity and haemoglobin (Hb) level and thrombocytosis with high disease activity, but results were not conclusive as regard the mean platelet volume (MPV).5 Most of them found inverse relationship between disease activity and Hb level and thrombocytosis with high disease activity.[7-10] But data regarding MPV is not conclusive. However, evidence have shown an important role of MPV as a marker of inflammation and disease activity.[11] But there is hardly any study which provided the association between these three haematological parameters altogether and markers of disease activity in RA on the basis of reliable index like DAS 28-3 score specially in Eastern region of India. Our aim of this present study is to assess the hematological parameters in rheumatoid arthritis (RA) and identify their relationship with disease activity.[12]

MATERIALS AND METHODS

This is a cross-sectional prospective study using convenient simple random sampling of 50 patients attending the department of general medicine, Government Bangur Hospital & Medical college, Pali, Rajasthan, India over a period of one year.

Inclusion Criteria
- Rheumatoid arthritis patients diagnosed according to 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria for RA.12
- Age group 20 to 60 years irrespective of sex.
- Duration of disease upto 5 years.

Exclusion Criteria
- Previously diagnosed anemia and treated
- Previously have any other bleeding disorder not related to Rheumatoid arthritis.
- Patients with blood diseases, malignancies, advanced kidney disease, advanced liver disease and other autoimmune diseases.
- Those who have mixed disorder like SLE and RA; SS & RA and MCTD and overlap syndrome.

Methods: A full medical history, general and musculoskeletal examination and assessment of the disease activity using the DAS 28 score-ESR were done. DAS 28 score 13

According to DAS 28 score; a score <2.6 was considered inactive, 2.6-3.2 was considered low disease activity, >3.2-5.1 was considered moderate disease activity and >5.1was considered high disease activity. Patients with active disease were those having low, moderate and severe activity.

Complete blood picture showing red blood cells (RBCs) count and indices, white blood cells (WBCs); both total and differential counts, and platelets parameters was done to all patients. Markers of disease activity including Erythrocyte sedimentation rate (ESR) (Westergren method) was done, C reactive protein (CRP) titre [performed on Modular P auto analyzer], RF titre and anti-CCP titre (determination by a COBAS Autoanalyzer were also done.

Statistical Analysis: Data analysis was done using epidemiological information statistical software. Using the software the frequencies, mean, standard deviation and p values calculated with yate's test for qualitative variables and kruskol walls chi square test for quantitative variables. p value <0.05 is taken as significant.

RESULTS

The mean age of RA patients was 46.458± 11.98 years. 78% (N=39) of them were females and 22% (N=11) were males. 32 (64%) patients were active while 18 patients (36%) were inactive. WBCs, neutrophil, RDW%, PLT, NLR and PLR were significantly higher in active RA patients while HCT, Hb, Hb/PLT, RDW%/PLT, Hb/RDW% and RBCs/PLT ratios were significantly lower compared to the inactive patients [Table 1].

There was statistically significant positive correlation between ESR and RDW%, PLT count, PLR while it was significantly negatively correlated with HG levels, Hb/PLT ratio, RDW%/PLT ratio, RBCs/PLT ratio, Hb/RDW% ratio. Both RF and Anti CCP titres were positively correlated to RDW%, PLT count and PLR, but they were negatively correlated with HG levels, Hb/PLT, RDW%/PLT, RBCs/PLT and

Hb/RDW% ratios. However, anti CCP titre was positively correlated with NLR [Table 2].

Table 1: Comparison between active and inactive RA patients as regards WBCs, RBCs and platelet parameters.

RA	DAS 28 Activity		P-value
	Inactive	Active	
WBCS (10^9/L)	6.572±2.012	7.450±2.526	<0.05*
NEUT (10^9/L)	3.78±1.72	4.587±2.582	<0.05*
Lympho (10^9/L)	2.32±0.58	2.285±0.753	>0.05
HCT (%)	36.71±2.46	35.862±2.289	<0.05*
RBCs(10^{12}/L)	4.86±0.52	4.765±0.542	>0.05
Hb(g/L)	12.263±0.772	11.841±0.793	<0.05*
MCV (fL)	78.45±8.02	79.109±6.99	>0.05
MCH (pg)	25.95±3.131	26.752±2.94	>0.05
RDW%	11.572±1.191	14.987±1.652	<0.001*
PLT (10^9/L)	238.76±98.62	492.87±138.4	<0.001*
MPV/fl	9.148±0.873	9.19±1.083	>0.05
PDW%	10.246±1.64	10.562±1.672	>0.05
Hb/PLT ratio	0.056±0.017	0.025±0.013	<0.001*
RDW%/PLT ratio	0.054±0.015	0.034±0.010	<0.001*
RBCs/PLT ratio	0.024±0.008	0.012±0.005	<0.001*
Hb/RDW% ratio	1.073±0.124	0.809±0.123	<0.001*
NLR ratio	1.71±0.765	2.312±1.76	<0.05*
PLR ratio	110.274±53.948	249.35±147.75	<0.001*

Table 2: Correlation between WBCs, RBCs and platelet parameters with laboratory parameters of the disease activity.

RA	ESR		CRP		RF		ANTI CCP	
	r	P-value	r	P-value	r	P-value	r	P-value
WBCS (10^9/L)	0.124	>0.05	0.267	0.001*	-0.037	>0.05	0.060	>0.05
NEUT (10^9/L)	0.142	>0.05	0.296	<0.001*	0.020	>0.05	0.106	>0.05
Lympho (10^9/L)	-0.003	>0.05	-0.022	>0.05	-0.213	>0.05	-0.198	>0.05
HCT (%)	-0.098	>0.05	-0.087	>0.05	-0.099	>0.05	-0.067	>0.05
RBCs(10^{12}/L)	-0.121	>0.05	-0.057	>0.05	-0.140	>0.05	-0.119	>0.05
Hb (g/L)	-0.377	<0.001*	-0.186	<0.05*	-0.238	0.005*	-0.187	<0.05*
MCV (fL)	-0.022	>0.05	0.078	>0.05	-0.118	>0.05	0.000	>0.05
MCH (pg)	0.063	>0.05	-0.075	>0.05	0.077	>0.05	0.149	>0.05
RDW%	0.578	<0.001*	0.399	<0.001*	0.285	0.001*	0.299	<0.001*
PLT (10^9/L)	0.554	<0.001*	0.328	<0.001*	0.276	0.001*	0.357	<0.001*
MPV/fl	-0.016	>0.05	0.018	>0.05	-0.040	>0.05	-0.012	>0.05
PDW%	0.148	>0.05	0.109	>0.05	-0.003	>0.05	-0.070	>0.05
Hb/PLT ratio	-0.477	<0.001*	-0.313	<0.001*	-0.269	0.001*	-0.329	<0.001*
RDW%/PLT ratio	-0.410	<0.001*	-0.255	0.003*	-0.225	0.007*	-0.230	<0.001*
RBCs/PLT ratio	-0.427	<0.001*	-0.309	<0.001*	-0.301	<0.001*	-0.310	<0.001*
Hb/RDW% ratio	-0.595	<0.001*	-0.378	<0.001*	-0.328	<0.001*	-0.315	<0.001*
NLR ratio	0.160	>0.05	0.297	<0.001*	0.113	>0.05	0.189	<0.05*
PLR ratio	0.389	<0.001*	0.223	0.009*	0.343	<0.001*	0.395	<0.001*

DISCUSSION

The concept of disease activity is essential in rheumatology, for guiding the treatment and influencing the outcome in RA. This study was focused on finding an association between different haematological parameters (Hb, Platelet count and MPV) and DAS 28-3 score (Modified Disease Activity Score) so that these evidence-based and cost-effective parameters can be used to assess disease activity and thus, can improve clinical management of RA.[13,14]

Inflammatory process in rheumatic diseases causes changes in the peripheral blood cell counts, morphology and sizes. Therefore, blood cell indices were considered as indicators of inflammation and markers of disease activity.[15] Studies proved a significant role of platelets in the inflammatory response.[16] In addition, RBC-related parameters can be used as inflammatory markers in autoimmune diseases.[17] Ratios among haematological indices have shown to be useful tools for evaluation of inflammatory activity in various autoimmune diseases including ulcerative colitis and Familial Mediterranean Fever.[15] Few studies investigated the relationship between the parameters of PLT, RBC, WBCs parameters and disease activity; especially their importance in differentiating active from inactive RA.

In our study we selected 50 cases of rheumatoid arthritis on random basis as per the American rheumatism association guidelines 2010. The sex distribution in this study is predominantly affects females in a ratio of 3.54:1. Mean age is 46.458± 11.98 years. Compatible our results with Dr. R. Arul et al,[18] found sex ratio of females to males is this study is 4:1. The risk of developing disease is greatest between 40 to 49 years.

In order to identify the relationship between different haematological parameters and DAS score and disease activity parameters, the patients with RA were divided into active RA [32 patients (64%)] and inactive RA [18 patients (36%)] groups. Then comparison between both groups as regards haematological parameters and correlation of haematological indices with parameters of disease activity were done.

Regarding WBCs parameters, there was significantly higher WBCs count, neutrophil count, and NLR in active patients. Also, WBCs and neutrophil counts correlated positively with both DAS score and CRP titre. NLR ratio correlated significantly positively with the DAS score, number of tender joints, CRP and Anti CCP titres. Fu et al,[19] and Mercan et al,[20] reported a positive correlation between the DAS28 score and WBCs count, neutrophil count and NLR in RA patients as in this study. Helal et al,[21] and Uslu et al,[22] detected significantly higher NLR in active disease and reported a significant relationship between NLR and PLR with the DAS-28. Another study by Mercan et al,[20] found that the NLR was positively correlated with ESR and CRP and NLR increased with increasing the DAS28 score.

Abd -Elazeem et al,[23] and Koiwa et al,[24] found that the DAS28 positively correlated with the NLR and PLR. These studies support the present study and may reflect the importance of WBCs indices as a marker of inflammation and disease activity in patients with RA.

Current results showed that the RBCs parameters may give an idea about the inflammatory status and activity status in RA patients, and that the alterations in these parameters go hand in hand with alterations in the inflammatory markers. Our study found that active patients had significantly higher RDW%, while HCT value, Hb levels, Hb/PLT ratio, RDW%/PLT ratio, Hb/RDW% ratio and RBCs/PLT ratio were significantly lower than the inactive patients. Current results showed that the RBCs parameters may give an idea about the inflammatory status and activity status in RA patients, and that the alterations in these parameters go hand in hand with alterations in the inflammatory markers. Our study found that active patients had significantly higher RDW%, while HCT value, Hb levels, Hb/PLT ratio, RDW%/PLT ratio, Hb/RDW% ratio and RBCs/PLT ratio were significantly lower than the inactive patients.

The current results are in line with Talukdar et al,[6] who observed that Patients with high disease activity had a significantly lower Hb values. Also, Xue et al,[25] illustrated that active RA patients showed significantly lower levels of RBC counts, Hb, Red blood cell /platelets ratio and haemoglobin-platelet ratio compared to inactive RA and that Hb, RPR and HPR were negatively related with DAS28-CRP.

On the other hand, Al-Rawi et al,[26] showed that there was no significant correlation between DAS28-ESR, RF, and ACPA with RDW. Also, Rodríguez-Carrio et al,[27] did not find correlation between RDW and DAS-28.

Platelet parameters in RA patients revealed that it could be a reflection of the inflammatory and activity status. The present study found that active patients had significantly higher platelets count and PLR. Moreover, Platelet count and PLR were positively correlated with DAS score and all other clinical and laboratory activity parameters. These results are in accordance with other results,[25] who showed that active RA patients had higher PLT counts, and that PLT count was positively correlated with DAS28 score. Similarly, Yildirim et al.28 observed a relationship between platelet indices and disease activity in RA.

Results of Talukdar et al,[6] agree with our results as they found significantly higher platelet count and MPV in high disease activity patients. Although the higher MPV in active patients did not reach statistical significance in the present results.

MPV showed significant importance as a marker of inflammation and disease activity.[11] In one study by Tekeoglu et al.[14] MPV was significantly associated with RA disease activity. Although the current results found higher MPV in active patients than in inactive patients, it did not reach statistical significance.

Gürol et al,[29] also supported this study and concluded that parameters of the blood cells may be used in evaluation of disease activity in autoimmune inflammatory disorders generally.

CONCLUSION

Alterations in haematological parameters are significantly associated with disease activity in RA patients and these changes go hand in hand with inflammatory markers. RDW%, platelets count, and PLR are the most affected hematologic parameters in relation to DAS score and parameters of disease activity. CBC and haematological parameters are simple, available and cheap laboratory investigation that could be used in the future to assess and follow up RA patients.

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International Journal of Academic Medicine and Pharmacy (www.academicmed.org)
ISSN (O): 2687-5365; ISSN (P): 2753-6556