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Original research

RED BLOOD CELL - PLATELET RATIO (RPR) AND HEMOGLOBIN - PLATELET RATIO (HPR) IN PATIENTS WITH RHEUMATOID ARTHRITIS: A STUDY AT HUE UNIVERSITY OF MEDICINE AND PHARMACY HOSPITAL

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ABSTRACT

Background: *Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic inflammation of the joints, resulting in destruction and deformation of bones and cartilage. In addition to causing joint damage, up to 30 - 70% of RA patients have chronic anemia that reduces quality of life. The inflammatory process affects some red blood cell and platelet indices such as increased platelet count, anemia and hypochromic microcytic cells. Red blood cell - platelet ratio (RPR) and hemoglobin - platelet ratio (HPR) are considered as indicators to help assess inflammation and activity level in patients with RA. This study describes hematological characteristics and the relationship of RPR and HPR indices with inflammation in patients with RA.*

Methods: *The study was conducted on 30 patients with RA at the Department of General Internal Medicine - Endocrinology - Musculoskeletal and a control group of 30 healthy people who came to hospital of Hue University of Medicine and Pharmacy from April 2023 to August 2023.*

Results: *Both RPR and HPR indices in the disease group were statistically significant lower than the control group ($p < 0.001$). The predictive value of rheumatoid arthritis of RPR and HPR with cutoff points of 0.016 and 0.455 respectively ($p < 0.05$). The RPR index was strongly positively correlated with HPR ($p < 0.001$). PLT was strongly negatively correlated with RPR ($p < 0.001$) and HPR ($p < 0.001$).*

Conclusion: *The RPR and HPR indices in RA patients were lower than those in controls, and could be one of the indicators to help assess inflammation in patients.*

Key words: *Red blood cell - platelet ratio (RPR), hemoglobion - platelet ratio (HPR), rheumatoid arthritis.*

I. INTRODUCTION

Rheumatoid arthritis is a chronic disease with a wide variety of systemic manifestations including persistent inflammatory synovitis, usually involving peripheral joints in a symmetric manner. Synovitis leads to cartilage damage and bone erosions and subsequently leads to changes in joint integrity. Clinical presentation varies from mild oligoarticular illness to relentless progressive polyarthritis with significant functional impairment [1]. RA affects 0.5-1% of adult population, this disease affects women three times more than men [2]. The inflammatory process affects the differentiation and development of erythroid precursors in the bone marrow, and the cytokines produced during this process stimulate the bone marrow to increase platelet production. There are few studies that have systematically assessed the association of PLT, RBC, Hb, red blood cells-platelet ratio (RPR) and hemoglobin-platelet ratio (HPR) with the disease activity of RA patients. And little is known about the diagnostic value of the peripheral blood PLT and RBC related indices in distinguishing

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between active RA and inactive RA. Therefore, this study aimed to describe hematological characteristics and the relationship of RPR and HPR indices with inflammation in patients with RA.

II. MATERIALS AND METHODS

2.1. Subjects

Patients fulfilled the 2010 ACR/EULAR criteria for RA [3] and agreed to participate in the study at the Department of General Internal Medicine - Endocrinology - Musculoskeletal at hospital of Hue University of Medicine and Pharmacy from April 2023 to August 2023.

Exclusion criteria: Patients who had hematologic diseases, other autoimmune inflammatory diseases, infections, malignancies, or had any history of other chronic diseases such as diabetes mellitus, dyslipidemia, thyroid dysfunction, severe liver or kidney impairment, those receiving treatment with corticosteroids within the last 3 months as well as not agreeing to join in the study.

Healthy individuals were recruited from the health examination center of the same hospital, and matched with RA patients for age and gender. At the end of the study, we selected 30 per group to participate in the study.

2.2. Methods

We conducted a described, cross-sectional study with convenience sampling. After being selected into each group, the study subjects will have blood drawn for testing. Complete blood cell (CBC) was performed on a Sysmex XN550 machine at the Department of Hematology. The study variables included gender, age, red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), white blood cell (RBC), neutrophils (Neu), lymphocytes (Lym), platelets (PLT), RPR, HPR.

Processed by SPSS 26.0 software, calculate mean, percentage and compare between groups with statistical significance when $p < 0.05$, predictive value of a variable is evaluated based on analysis Receiver Operating Characteristic (ROC) curve.

III. RESULTS

3.1. General characteristics of subjects

Table 1: Distribution by sex of study subjects

Group / Gender	Disease group	Control group
Male	6 (20.0%)	14 (46.7%)
Female	24 (80.0%)	16 (53.3%)
Sum	30 (100.0%)	30 (100.0%)

The female/male ratio in the case group was 4/1 while that in the control group was about 1/1.

Table 2: Age characteristics of research subjects

	Disease group	Control group
Age, mean ± SD	59.8 ± 10.8	37.7 ± 9.6
p	< 0.001	

There was a statistically significant difference in gender between the two study groups ($p < 0.001$).

3.2. Biological characteristics of the study group

Table 3: Number of peripheral blood cell lines of the study sample

	Disease group (n = 30)	Control group (n = 30)	p
RBC (1012/L)	4.0 ± 0.5	5.0 ± 0.7	< 0.001
Hb (g/L)	117.4 ± 11.3	139.7 ± 16.0	< 0.001
Hct (%)	36.4 ± 3.4	42.2 ± 4.3	< 0.001

	Disease group (n = 30)	Control group (n = 30)	p
MCV (fL)	91.0 ± 6.7	85.2 ± 8.7	0.006
MCH (pg)	29.4 ± 2.2	28.3 ± 3.4	0.151
MCHC (g/L)	332.5 ± 7.5	330.8 ± 10.7	0.001
WBC (10^9/L)	8.7 ± 2.4	7.1 ± 1.8	0.005
Neu (10^9/L)	6.0 ± 2.3	3.9 ± 1.3	< 0.001
Lym (10^9/L)	2.2 ± 0.7	2.6 ± 0.6	0.022
PLT (10^9/L)	320.9 ± 90.5	273.3 ± 62.9	0.021

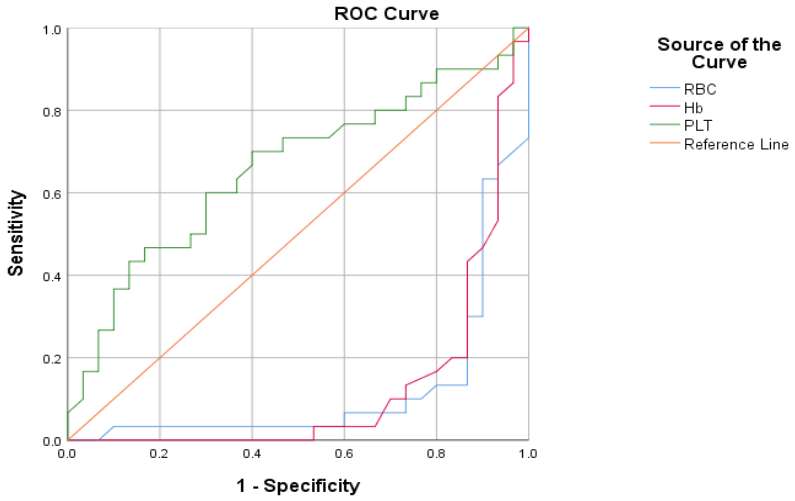
There was a statistically significant difference in the number of RBC, Hb, Hct, MCV, MCHC, WBC, Neu, Lym and PLT in the disease group and control group ($p < 0.05$). In contrast, MCH in the control group was not statistically different from the disease group ($p > 0.05$).

Table 4: RPR and HPR indices in the study group

	Disease group (n = 30)	Control group (n = 30)	p
RPR	0.014 ± 0.005	0.019 ± 0.006	< 0.001
HPR	0.400 ± 0.123	0.541 ± 0.147	< 0.001

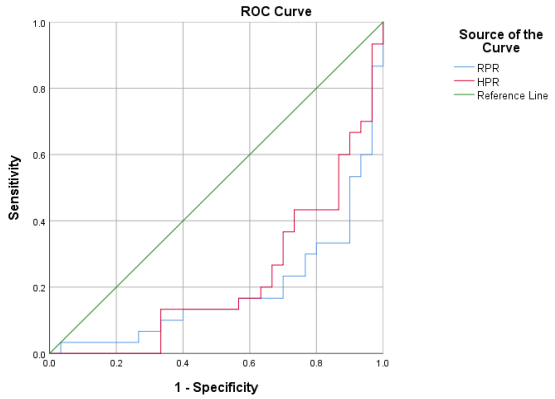
Both RPR and HPR indices in the disease group were statistically significant lower than the control group ($p < 0.001$).

3.3. Indices in predicting rheumatoid arthritis



	AUC*	Cut-off	Sensitivity (Se)	Specificity (Sp)	95% CI	p
RBC	0.120	4.39	0.133	0.133	0.026 - 0.214	< 0.001
Hb	0.125	129.5	0.133	0.267	0.030 - 0.220	< 0.001
PLT	0.659	292.5	0.600	0.633	0.519 - 0.799	0.034

Figure 1: ROC curves of RBC, Hb and PLT in predicting RA



	AUC	Cut-off	Sensitivity (Se)	Specificity (Sp)	95% CI	p
RPR	0.189	0.016	0.233	0.233	0.077 - 0.301	< 0.001
HPR	0.224	0.455	0.3	0.3	0.107 - 0.342	< 0.001

Figure 2: ROC curves of RPR and HPR in predicting RA

The predictive value of rheumatoid arthritis of RBC, Hb, PLT, RPR and HPR with cutoff points of 4.39, 129.5, 292.5, 0.016 and 0.455 respectively ($p < 0.05$).

3.4. Correlation between hematological indices in patients with RA

Table 5: Correlation between hematological indices in disease group

Hematological indices	RPR		HPR		PLT		WBC	
	r	p	r	p	r	p	r	p
RPR	-		0.930	< 0.001	-0.894	< 0.001	0.084	0.800
HPR	0.930	< 0.001	-		-0.930	< 0.001	0.064	0.735
PLT	-0.894	< 0.001	-0.930	< 0.001	-		0.001	0.998
WBC	0.084	0.800	0.064	0.735	0.001	0.998	-	

The RPR index was strongly positively correlated with HPR. PLT was strongly negatively correlated with RPR and HPR.

IV. DISCUSSION

4.1. General characteristics of subjects

In the results presented in table 1, our study has a female/male ratio of 4/1 while the control group was about 1/1. This result is epidemiologically consistent in that the disease affects women three times more than men [2]. Research of Essam T, et al. (2022) study on 60 RA patients showed that the female/male ratio was 6.5/1, quite similar to our study [4]. Uttam Biswas and colleagues (2020) showed that the female/male ratio was 4/1 when studying on 50 RA patients [5]. It can be explained by the fact that RA is an autoimmune disease, so it appears more in women than men.

The mean age of the patient group and the control group in our study was 59.8 ± 10.8 and 37.7 ± 9.6 years old, respectively, there was a difference in age between the control group and the patient group ($p < 0.05$) (table 2). The authors Essam T (2022), Li Xue (2022), Smyrnova Ganna (2014) also showed that the average age of the group of patients with RA was respectively 50.6 ± 8.8 [4], 57.11 ± 14.17 [6], 51.7 ± 10.3 [7], respectively.

4.2. Biological characteristics of the study group

In table 3, there was a statistically significant difference in the number of RBC, Hb, Hct, MCV, MCHC, WBC, Neu, Lym and PLT in the disease group and control group ($p < 0.05$). In contrast, MCH in the control group was not statistically different from the disease group ($p > 0.05$). The RBC, Hb, Hct and Lym indices in the disease group were lower than the control group, but the MCV, MCHC, WBC, Neu, PLT indices in the disease group were higher than the control group. In patients with RA, the chronic inflammatory process increases the production of inflammatory cytokines such as IL6, IL1β, IL-10, and IFNγ, which cause iron restriction, inflammation suppression of erythropoietic activity and decreased erythrocyte survival [8], finally causes anemia and reduces RBC, Hb and Hct. Chronic inflammation also stimulates the bone marrow to increase WBC, especially neutrophils (neu). At the same time, IL6 is a cytokine that stimulates the liver to increase thrombopoietin, thus increasing platelet production. Research by Li Xue et al (2022) on 178 RA patients including 88 inactive diseases (DAS 28 - CRP ≤ 2.7) and 90 active diseases (DAS 28 - CRP > 2.7); 164 patients as a control group showed that the group of RA patients had a higher PLT while the number of RBC, Hct and Hb were statistically significantly lower than the group control ($p < 0.001$). In addition, patients with active RA had higher PLT and lower RBC, Hct, and Hb with statistical significance compared to the group of patients with inactive RA ($p < 0.001$ or $p < 0.01$) [6]. A cross - sectional study by Manas Talukdar et al (2017) of 80 newly diagnosed RA patients presented significantly lower Hb and higher PLT, MPV in the highly active RA group compared to moderately active or inactive RA group ($p < 0.001$) [9]. A study by Aditi Patel et al (2022) on 20 newly diagnosed RA patients showed that 55% of chronic anemia, 27.5% iron - deficiency anemia; Patients with strong disease activity had lower Hb while PLT and MPV were statistically significantly higher than patients with moderate and low disease activity [10].

The results presented in table 4 showed that the RPR and HPR index in the disease group are 0.014 ± 0.005 and 0.400 ± 0.123, respectively, both statistically significantly lower than the control group (0.019 ± 0.006 and 0.541 ± 0.147) ($p < 0.001$). In the world, there are some studies that showed that the RPR and HPR in RA were lower than that of the control group, specifically, the author Li Xue's group reported the results of these two indices in the patient group as 0.019 ± 0.0065 and 0.55 ± 0.21, respectively, while the control group was 0.024 ± 0.0072 and 0.727 ± 0.23 ($p < 0.001$) [6]. As explained above, anemia and thrombocytosis are the result of chronic inflammation, so in patients with rheumatoid arthritis, the RPR and HPR values will be lower than normal.

4.3. RPR and HPR indices in predicting rheumatoid arthritis

In the research results, figure 1 and 2 both showed the predictive value of rheumatoid arthritis of RBC, Hb, PLT, RPR and HPR with cutoff points of 4.39, 129.5, 292.5, 0.016 and 0.455 respectively ($p < 0.05$). However, the AUC of the RBC, Hb, RPR and HPR indices is quite low so it is difficult to use to predict this disease. In contrast, the AUC of PLT has a higher value, so it will predict the disease better than the other indicators. It is possible that because of the small sample size of the study, the analysis has not yet covered the entire population. ROC curve analysis in the study by Li Xue and colleagues (2022) showed that PLT, RBC, Hb, RPR, HPR were able to predict severe disease activity with a cutoff point of 243 G/L (Se = 56.19%, Sp = 73.91%, AUC = 0.666, 95% CI = 0.591 – 0.736); 4.22 T/L (Se = 83.96%, Sp = 68.12%, AUC = 0.780, 95% CI = 0.711 – 0.839); 121 g/L (Se = 81.13%, Sp = 68.12%, AUC = 0.786, 95% CI = 0.717 – 0.844); 0.017 (Se = 74.29%, Sp = 68.12%, AUC = 0.744, 95% CI = 0.673 – 0.807); 0.48 (Se = 56.19%, Sp = 81.16%, AUC = 0.727, 95% CI = 0.654 – 0.791) [6].

4.4. Correlation between hematological indices in patients with RA

In our research, the RPR index was strongly positively correlated with HPR ($r = 0.930$, $p < 0.001$). PLT was strongly negatively correlated with RPR ($r = - 0.894$, $p < 0.001$) and HPR ($r = - 0.93$, $p < 0.001$) (table 5). Research by Li Xue (2022) also showed that PLT was positively correlated with DAS index 28 - CRP ($r = 0.327$, $p < 0.001$), CRP ($r = 0.284$, $p < 0.001$), ESR ($r = 0.331$, $p < 0.001$); RBC was negatively correlated with DAS 28 - CRP

index (r = - 0.428, p < 0.001), CRP (r = - 0.289, p < 0.001), ESR (r = - 0.481, p < 0.001); Hb was negatively correlated with DAS 28-CRP index (r = - 0.489, p < 0.001), CRP (r = - 0.341, p < 0.001), ESR (r = - 0.569, p < 0.001). RPR was negatively correlated with DAS 28-CRP index (r = - 0.31, p < 0.001), CRP (r = - 0.397, p < 0.001), ESR (r = - 0.329, p < 0.001). HPR was negatively correlated with DAS 28-CRP index (r = - 0.293, p < 0.001), CRP (r = - 0.402, p < 0.001), ESR (r = - 0.362, p < 0.001) [6].

V. CONCLUSION

Through research, we found that rheumatoid arthritis patients have lower RPR and HPR index than control group, the cutoff points of RPR and HPR index in predicting rheumatoid arthritis are 0.016 and 0.455, respectively. There is a strong positive correlation between these two indices and a negative correlation between platelets and RPR and HPR.

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