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ORIGINAL ARTICLE

Relation between Red Blood Cells and Platelets Related Indices and Disease Activity in Patients with Juvenile Idiopathic Arthritis

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ABSTRACT

Background: Red blood cells (RBCs) and platelets have been linked to inflammation in various rheumatological illnesses. As a result, the present research sought to assess the association between each of the RBC- and platelet-related parameters and disease activity in JIA patients, as well as to compare these indices between JIA patients and normal children. **Methods**: A case-control study included 88 subjects, 44 in each group (JIA & control). The variations in platelet indices between normal and JIA children were documented. The associations between CBC-related parameters and disease activity, disease subtype, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were determined. **Results:** JIA patients had significantly higher hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), plateletcrit (PCT), HB to platelets (HPR), mean corpuscular hemoglobin (MCH) platelets count, platelets to lymphocytes ratio (PLR) & WBC count and lower mean platelet volume (MPV), RBCs to platelet ratio (RPR), and compared to healthy children ($P < 0.05$).
Active JIA patients had considerably less MPV, Hb, MCH, RPR, and HPR, but significantly more platelets than inactive JIA patients' children ($P < 0.05$). Both CRP & ESR levels showed significant negative correlations with MCHC, hemoglobin levels, MCH, RPR, and HPR in JIA patients ($P<0.05$). Meanwhile, ESR values displayed a significant positive correlation with platelet count and PCT, and CRP values showed only a strong positive correlation with platelet count. **Conclusion:** In JIA patients, HB, MCV, and MCHC levels were considerably lower. Active JIA patients had considerably lower HB, MCH, RPR, and HPR levels than inactive group. Polyarticular subtype had the lowest HPR.
Keywords: JIA, RBCs, HB, platelets, MPV, CBC indices, biomarkers.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a highly frequent chronic rheumatic disease in children [1]. Juvenile idiopathic arthritis (JIA) is a diverse type of idiopathic inflammatory arthritis that impacts those below the age of 16 for six weeks or more. The key criteria for the condition include disease commencing before the age of 16 and arthritis in a minimum of one joint that lasts for six weeks or more after any other reasonable cause of joint inflammation has been ruled out [2]. Although the origin and pathogenesis of JIA are uncertain, it is established that autoimmunity contributes a vital part to the progression of the disease [3]. Megakaryocyte activation in the liver is a particular effect of pro-inflammatory cytokines released in reaction to the systemic inflammation induced by this autoimmune disease , which causes an increase in platelet number. It leads to the formation of bigger and highly reactive platelets [4],[5]. In another explanation, however, inflammatory molecules encourage bone marrow cells in the course of autoimmune illnesses to create greater numbers of platelets by speeding up the development time, so smaller platelets reach the bloodstream, whereas active platelets are

removed at the area of inflammation [6]. Recent results suggest that anemia may happen in the context of autoimmune disorders, as bone marrow performance and iron metabolism may be altered by inflammation [7]. Inflammatory cytokines have been shown to inhibit red blood cell (RBC) development [8].

Therefore, RBC-related parameters, like red blood cell distribution width (RDW) and hemoglobin (Hb) contents, were utilized as inflammatory clues to predict the severity of several autoimmune diseases, such as systemic lupus erythematosus, primary Sjögren's syndrome, and autoimmune hepatitis [9]. Yet, few studies have examined link between RBC, Hb, red blood cells-platelet ratio (RPR), and hemoglobin-platelet ratio (HPR) and JIA disease activity. Although various projects have been carried out on variations in platelet indices in adult rheumatological diseases, far fewer studies have been performed on JIA patients' platelet changes. A collection of platelet metrics seen in routine CBC analyses are (MPV, PDW, and PCT); their values vary with platelet shape and multiplication velocity, which helps quantify the activity of platelets [10]. Platelet indices are gaining popularity as prospective markers of platelet activation due to their ease of measurement in epidemiological research and the broad accessibility of dependable automated blood cell counts. These instruments offer platelet count as part of the overall blood count, as well as associated indices that affect platelet size, such as PCT, MPV, and PDW, which directly assess platelet size variability and increases in the presence of platelet anisocytosis [11].

Some studies imply a decrease in MPV in other rheumatological illness, for example, patients with active SLE [12] and, RA [13]. An additional investigation examined the association between MPV and clinical activity indices of RA and ankylosing spondylitis, and the findings revealed that MPV was decreased in the active phase of RA and AS than in the placebo group, but considerably rose in the patient group after therapy. In a 2023 study, platelet indices had an inverse correlation with JIA activity [14]. However, another study on JIA patients found increased MPV during the active phase of JIA [15]. Furthermore, little is established about the utility of CBC-related indices in identifying active from inactive JIA. This work sought to investigate the link between JIA disease activity and CBC indices such as Hb, MCH, MCV, MCHC, platelet count, MPV, PDW, RPR, HPR, etc. We further assessed the diagnostic value of these indicators in distinguishing between JIA patients with varying disease activity.

METHODS

A case-control study involved 88 participants, 44 of whom had JIA attended the Rheumatology and Rehabilitation Department (inpatient and outpatient clinics), Faculty of Medicine, Zagazig University Hospitals, between September 2022 and April 2023.

The Institutional Review Board (IRB) at Zagazig University in Egypt issued the research protocol permission code ZU-IRP#10319, following the World Medical Association's Code of Ethics for Human Studies (Declaration of Helsinki 1964).

Patients meeting the LIAR criteria for JIA were included [16]. Forty-four healthy individuals were chosen from the same hospitals' health assessment centers and age- and gender-matched to our JIA patients. Most of the studied patients received disease-modifying anti-rheumatic drugs (DMARDs) only or with biological therapies, depending on their symptoms severity and disease category.

Patients with persistent infections (e.g., osteomyelitis, endocarditis), other autoimmune inflammatory disorders, cancer, or a history of other chronic diseases such as cardiovascular, respiratory, or gastrointestinal problems were excluded.

Using Epi software version 6 at a confidence interval (CI) of 95%, our patients will be selected by a simple random sample. Assuming the mean PLT was 215.61+_60.95. Vs. 257+_76.27, in cases vs control, at 80% power and 95% CI, the estimated sample was calculated to be 88 subjects, 44 subjects in each group. Each child included in the study gave provided verbal consent as well as their parents' written informed consent.

Assessment of Disease Activity:

The patients with oligo-articular and poly-articular JIA subtypes were assessed by the juvenile arthritis disease activity score (JADAS-27 CRP). While the Systemic JIA subtype and enthesitis-related arthritis (ERA) were assessed by the Systemic Juvenile Arthritis Disease Activity Score (sJADAS) and the Juvenile Spondylarthritis Disease Activity Index (JSpADA) respectively [17].

Using the Childhood Health Assessment Questionnaire (CHAQ), provided us with a score in the 0 to 3.0 range with the score category of (0) = no disability, (>0 and≤ 0.5) = mild disability, (>0.5 and ≤ 1.5) = moderate disability and (>1.5) = severe disability [18]. The CHAQ form that was used in this study was in Arabic [19].

Clinical and Laboratory Parameters:

Patients' personal and medical information, including their chronological age, gender, medical history, symptoms and signs, therapy, and laboratory test values, were obtained from their current medical files. The laboratory tests revealed RBC count, RDW, Hb, MCV, MCH, ESR, CRP, RF, and anti-nuclear antibodies (ANA). The RPR and HPR results were determined.

STATISTICAL ANALYSIS

The data gathered was coded, logged in, and analyzed on a computer via IBM SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA) and the jamovi project (2022) (Version 2.3). Continuous variables with normal distribution were shown as mean values ± standard deviation (SD). Non-normally distributed data were reported as the median (interquartile range). Categorical variables were reported as frequencies or percentages. Continuous variable differences were compared using the Student's t-test or the Mann-Whitney U-test, while categorical variable differences were compared using the chi-square test. Spearman correlation analysis was used to determine the relationship between variables.

Receiver operating characteristic (ROC) curves were used to discriminate active JIA from the inactive group. The area under the curve (AUC) and 95% CI were used to assess the diagnostic value of each index. The appropriate cut-off value, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (AC) of the indices were determined.

RESULTS

This work included 88 participants split into two categories. The first (Group I) included 44 patients diagnosed with JIA. The second (Group II) included 44 subjects, who were apparently healthy volunteers. The most common subtype among our JIA patients was the poly-articular subtype (50%), followed by systemic JIA (22.7%) and oligo-articular (15.9%) respectively. Most of our JIA patients were in active disease states (77.3%) with moderate activity (Table 1).

In JIA patients, hemoglobin, HPR, and MCV levels were highly significantly lower, whereas plateletcrit (PCT) was highly significantly higher than healthy participants (P <0.001). Also, MCH, MCHC, MPV, and RPR levels were significantly lower in patients with JIA, additionally, there were significantly higher platelet, PLR, and WBC counts in healthy participants (P-value < 0.05), as demonstrated in (Table 2).

A comparison between active and inactive JIA patients, when it comes to CBC indices is shown in (Table 3). Both Hb & MCH were significantly lower in active patients. Also, platelet count was significantly higher among active JIA patients. Moreover, MPV, RPR & HPR were significantly lower among active JIA patients. As demonstrated in (figure 1), at cut-off ≤ 10.7 (gm/dl), Hb in JIA patients had 25% sensitivity and 85.7% specificity. At cut-off ≥ 9.2 units, MPV in JIA patients had 93.75% sensitivity and 85.71% specificity. Also, at a cut-off ≥ 112.91, PLT in JIA patients had 81.25% sensitivity and 71.43% specificity. Therefore, both were benefit tests for the detection of JIA activity patients.

The cut-off points for RPR & HPR of 0.013 & 0.041 respectively had sensitivities of 56.2% & 62.5% respectively & specificities of 84.71% & 85.7% respectively. So similar to Hb, they were good positive tests for JIA activity. As shown in (figure 2, 3) there were significant negative correlations between of hemoglobin levels, MCH, MCHC, MPV, RPR, and HPR with ESR & CRP levels (P <0.05). There were also significant positive correlations between platelet count and each of ESR & CRP, While PCT had demonstrated a significant positive correlation with ESR only (P <0.05).

Table 4 shows that the WBC count was significantly the highest among systemic JIA patients. The JIA patients with the poly-articular subtype had the lowest MPV and HPR which was statistically significant (P <0.05). The differences in other CBC indices among all subtypes of the disease were insignificant.

Table (1): Demographic, socioeconomic & clinical data among studied groups.

Variables		Group I(n=44) (JIA group)	Group II(n=44) (Control group)	P-value*
Age (years)	mean±SD (range)	12.9±2.64 (7 - 16)	11.4±3.13 (7 - 16)	0.2[a] **(NS)**
Sex N. %	Female Male	22 (50%) 22 (50%)	20 (45.5%) 24 (54.5%)	0.67[b] **(NS)**

Variables		Group I(n=44) (JIA group)	Group II(n=44) (Control group)	P-value*
Residence N. %	Rural Urban	31 (70.5%) 13 (29.5%)	19 (43.2%) 25 (56.8%)	0.18[b] **(NS)**
Socioeconomic status N. %	Low Moderate High	20 (45.5%) 24 (54.5%) 0 (0%)	15 (34.1%) 29 (65.9%) 0 (0%)	0.28[b] **(NS)**
Weight (Kg)	mean±SD (range)	33.18 ± 12.44 (13 - 59)	42.22 ± 10.65 (15 - 60)	0.06[a] **(NS)**
Height (cm)	mean±SD (range)	122.13 ± 20.72 (75 - 153)	132.16 ± 18.43 (80 - 172)	0.42[a] **(NS)**
JIA subtypes N. (%) **Oligo-articular** **Poly-articular** **Systemic onset** **ERA**		 7 (15.9%) 22 (50%) 10 (22.7%) 5 (11.4%)		
Activity indices among different JIA subgroups:				
Oligo-articular by JADAS-27 CRP (n=7) Median (IQR) (range)		 14.7 (6.3) (3 – 20)		
Poly-articular by JADAS-27 CRP (n=22) Median (IQR) (range)		 21 (19.15) (6 – 40)		
Systemic JIA by sJADAS (n=10) Median (IQR) (range)		 14.5 (10.43) (4 – 21)		
ERA by JSpADA (n=5) Median (IQR) (range)		 4.25 (2) (3.5 – 6)		
Disease activity Inactive N. (%) Active N. (%)		 10 (22.7%) 34 (77.3%)		
CHAQ Median (IQR) (range)		 0.7 (1.21) (0 - 2.5)		
CHAQ grades **None** N. (%) **Mild** N. (%) **Moderate** N. (%) **Severe** N. (%)		 5 (11.4%) 14 (31.8%) 16 (36.4%) 9 (20.5%)		
Physician global assessment Median (IQR) (range)		 6 (5) (0 – 8)		
Parent assessment Median (IQR) (range)		 6 (3) (0 – 9)		

[a]: Independent sample t-test, [b]: Chi-square test, *: Significant: P <0.05, Non-Significant: P >0.05.
CHAQ: Childhood Health Assessment Questionnaire**, Cm:** Centimeters**, ERA**: Enthesis Related Arthritis, **IQR**: Interquartile Range**, JADAS:** Juvenile Arthritis Disease Activity Score **JIA:** Juvenile Rheumatoid Arthritis, **JSpADA:** Juvenile Spondyloarthritis Disease Activity **Kg:** Kilograms**, SD:** Standard Deviation**, sJADAS:** systemic Juvenile Arthritis Disease Activity Score, **NS:** Non- Significant,

Table (2): Comparison of CBC Indices between JIA Patients and Controls.

	Group I (JIA group) mean±SD (range)	**Group II (Control)** mean±SD (range)	**P-value***
RBCs	4.5±0.36 (4 – 5.66)	4.68±0.35 (4.29 – 5.59)	0.079 **(NS)**
Hb	11.23±1.15 (8.1 – 13.8)	12.2±0.5 (11.4 – 13.2)	**<0.001 (HS)**
MCV	71±8.3 (51.7 – 88.2)	78.6±3.8 (68.4 – 82.7)	**<0.001 (HS)**
MCH	24.7±2.9 (19 – 30)	26±2.8 (22.1 – 28.1)	**0.014 (S)**
MCHC	30±4.3 (15.3 – 39.2)	32.3±2.34 (31 – 39.5)	**0.001 (S)**
RDW%	13.4±4.8 (8.1 – 37.1)	12.7±0.3 (12.4 – 13.4)	0.159 **(NS)**
PLTs	339.8±122.5 (167 – 656)	277.2±79.1 (155 – 455)	**0.04 (S)**
PCT	0.26±0.06 (0.16 – 0.45)	0.23±0.01 (0.21 – 0.24)	**<0.001 (HS)**
PDW%	12.2±4.7 (7.9 – 39.4)	11.2±1.61 (10.2 – 16)	0.199 **(NS)**
MPV	8.5±0.7 (7.5 – 9.3)	9.4±1.5 (7.1 – 12.5)	**0.009 (S)**
RPR	0.015±0.005 (0.006 – 0.026)	0.019±0.007 (0.009 – 0.032)	**0.003 (S)**
HPR	0.037±0.013 (0.012 – 0.067)	0.049±0.017 (0.03 – 0.08)	**<0.001(HS)**
PLR	119.86±52.8 (52.9 – 298.18)	97±40.18 (37.04 – 206.8)	**0.025 (S)**
WBCs	7.9±3 (4.1 – 22.9)	6.64±1.76 (4.6 – 10.4)	**0.008 (S)**

Abbreviations: **JIA:** Juvenile Rheumatoid Arthritis **, SD:** Standard Deviation**, RBCs** : Red Blood Cells ; **Hb** : Hemoglobin ; **MCV** : Mean Corpuscular Volume ; **MCH** : Mean Corpuscular Hemoglobin ; **MCHC** : Mean Corpuscular Hemoglobin Concentration ; **RDW** : Red Blood Cell Volume Distribution Width; **PLT** : platelet count ; **PCT** : Plateletcrit ; **PDW** : platelet distribution width ; **MPV**: Mean platelet volume ; **RPR** : RBCs to platelets ratio ; **HPR**: Haemoglobin to Platelets ratio; **PLR** : Platelets to Lymphocytes ratio ; **WBCs**: White Blood Cells Count.
NS: Non- Significant, **S:** Significant, **HS:** Highly-Significant,
Significant: P <0.05, Non-Significant: P > 0.05.

Table (3): Comparison of CBC indices Between Active JIA Patients and Inactive JIA.

	Inactive JIA (n=10)	**Active JIA (n=34)**	**P-value***
RBC s	4.4±0.3 (4 - 4.94)	4.6±0.4 (4.06 – 5.66)	0.2 **(NS)**
Hemoglobin	11.7±0.83 (10.8 – 13)	10.4±1.4 (8.1 – 13.8)	**0.02 (S)**
MCV	72.9±7.6 (64.2 – 86.9)	70.5±8.5 (51.7 – 88.2)	0.4 **(NS)**
MCH	26.4±1.7 (24.4 – 30)	24.3±3 (19 – 30)	**0.03 (S)**

	Inactive JIA (n=10)	Active JIA (n=34)	P-value*
MCHC	26.4 ±1.76 (24.4 – 39.2)	33.8±4.5 (15.3 – 39)	0.06 **(NS)**
RDW%	10.4±2.1 (8.1 – 35.2)	12.3±5 (8.5 – 37.1)	0.3 **(NS)**
PLTs	276.1±68.8 (155 – 385)	316.8±130.2 (167 – 656)	**0.04 (S)**
PCT	0.25±0.05 (0.18 – 0.37)	0.27±0.07 (0.16 – 0.45)	0.3 **(NS)**
PDW	11.3±1.2 (9.2 – 12.7)	12.4±5.4 (7.9 – 39.4)	0.8 **(NS)**
MPV	9.92±1.21 (8.6 – 14.21)	8.12±1.31 (6.9 – 13.21)	**<0.001(HS)**
RPR	0.019±0.006 (0.01 – 0.032)	0.013±0.004 (0.006 – 0.025)	**0.02 (S)**
HPR	0.04±0.01 (0.029 – 0.08)	0.035±0.012 (0.012 – 0.067)	**0.04 (S)**
PLR	104±26.3 (75.2 – 158)	103±28.5 (57.1 – 173)	0.97 **(NS)**
WBCs	7.59±2.31 (4.1 – 22.9	8.23±4.22 (5.3 – 12.5)	0.6 **(NS)**

JIA: Juvenile Rheumatoid Arthritis, **RBCs**: Red Blood Cells; **Hb**: Hemoglobin; **MCV**: Mean Corpuscular Volume; **MCH**: Mean Corpuscular Hemoglobin; **MCHC**: Mean Corpuscular Hemoglobin Concentration; **RDW**: Red Blood Cell Volume Distribution Width; **PLT**: platelet count; **PCT**: Plateletcrit ; **PDW** : platelet distribution width ; **MPV**: Mean platelet volume ; **RPR** : RBCs to platelets ratio ; **HPR**: Haemoglobin to Platelets ratio; **PLR** : Platelets to Lymphocytes ratio ; **WBCs**: White Blood Cells Count.
NS: Non- Significant, **S:** Significant, **HS:** Highly-Significant,
Significant: P <0.05, Non-Significant: P >0.05.

Table (4): Comparison of Indices in Patients with Different Subtypes of JIA in Acute Phase of Disease.

	Oligo-art. JIA (n=7)	Poly-art. JIA (n=22)	Systemic JIA (n=10)	ERA (n=5)	P-value
RBCs	4.54±0.4 (4.06 – 5.20)	4.61 ± 0.4 (4.12 -5.66)	4.29 ± 0.2 (4 – 4 .5)	4.76 ± 0.3 (4.40 –5 .1)	0.4 **(NS)**
HB	11.5 ± 0.5 (8.1 –12 .2)	10.9 ± 1.1 (9.2 –13 .8)	10.4 ± 1.3 (8.1 –12)	11.4 ± 1.25 (9.5 –12 .7)	0.2 **(NS)**
MCV	72.1 ± 8.7 (63.2 –86 .9)	73.5 ± 4.3 (64.1 –81 .9)	65.5 ± 11.47 (51.7 –88 .2)	69.5 ± 10.7 (51.8 –77 .5)	0.3 **(NS)**
MCH	25.5 ± 2.8 (21.8 –28 .6)	25 ± 2.5 (21 –30)	24 ± 3.8 (19.2 –30)	24.9 ± 3.1 (9 –27 .4)	0.8 **(NS)**
MCHC	35.5 ± 3.1 (31.2 –39)	33.2 ± 5 (15.3 –38 .9)	33 ± 3.3 (30.2 –39 .2)	34.9 ± 2.7 (30.9 –37 .1)	0.09 **(NS)**
RDW%	12 ± 3.4 (8.1 –16 .4)	13.4 ± 3.4 (8.3 –19 .8)	11.8 ± 2.3 (8.7 –16 .3)	18.8 ± 10.4 (10.8 –37 .1)	0.2 **(NS)**
PLTs	301.6 ± 76.6 (210 –400)	332 ± 92.7 (167 –548)	338 ± 155.9 (173 –656)	325.8 ± 100 (181 –402)	0.5 **(NS)**
PCT	0.25 ± 0.03 (0.2 –0 .3)	0.26 ± 0.06 (0.16 –0 .41)	0.27 ± 0.08 (0.18 –0 .45)	0.27 ± 0.09 (0.16 –0 .41)	0.9 **(NS)**
PDW	13.1 ± 2.3 (10.2 –15 .5)	10.8 ± 2.1 (7.9 –15 .8)	14.2 ± 8.9 (9.9 –39 .4)	12.9 ± 3.2 (8.5 –17)	0.1 **(NS)**

	Oligo-art. JIA (n=7)	Poly-art. JIA (n=22)	Systemic JIA (n=10)	ERA (n=5)	P-value
MPV	9.2 ± 2.1 (7 – 9)	8.9 ± 1.8 (8.2 – 9.5)	9.2 ± 1.8 (7 – 12)	10.4 ± 0.4 (8.2 – 12.5)	**0.03 (S)**
RPR	0.02 ± 0.003 (0.01 –0 .02)	0.02 ± 0.005 (0.007 –0 .02)	0.02 ± 0.006 (0.001–0.03)	0.02 ± 0.005 (0.01 –0 .02)	0.8 **(NS)**
HPR	0.04 ± 0.01 (0.03 –0 .05)	0.023 ± 0.02 (0.01 – 0.05)	0.04 ± 0.02 (0.01 –0 .07)	0.04 ± 0.02 (0.02 –0 .06)	**0.03 (S)**
PLR	92.1 ± 29.7 (52.9 – 145.5)	125.2 ± 47.2 (73.9 – 298.2)	122.8 ± 67.2 (62.1 – 289)	129.3 ± 72.2 (57.1-232.1)	0.8 **(NS)**
WBCs	6.4 ± 2.2 (4.1 –9 .5)	8.1 ± 1.8 (4.5 –10 .9)	10.2 ± 5.3 (4.6 –22 .9)	7.7 ± 1.1 (6.4 –9 .3)	**0.04 (S)**

PLT: platelet count; **PCT**: Plateletcrit; **PDW:** platelet distribution width; **MPV:** Mean platelet volume; **RPR:** RBCs to platelets ratio; **HPR:** Haemoglobin to Platelets ratio; **PLR**: Platelets to Lymphocytes ratio; **WBCs**: White Blood Cells Count.
NS: Non- Significant, **S:** Significant
[a] Significant ($P < 0.05$).

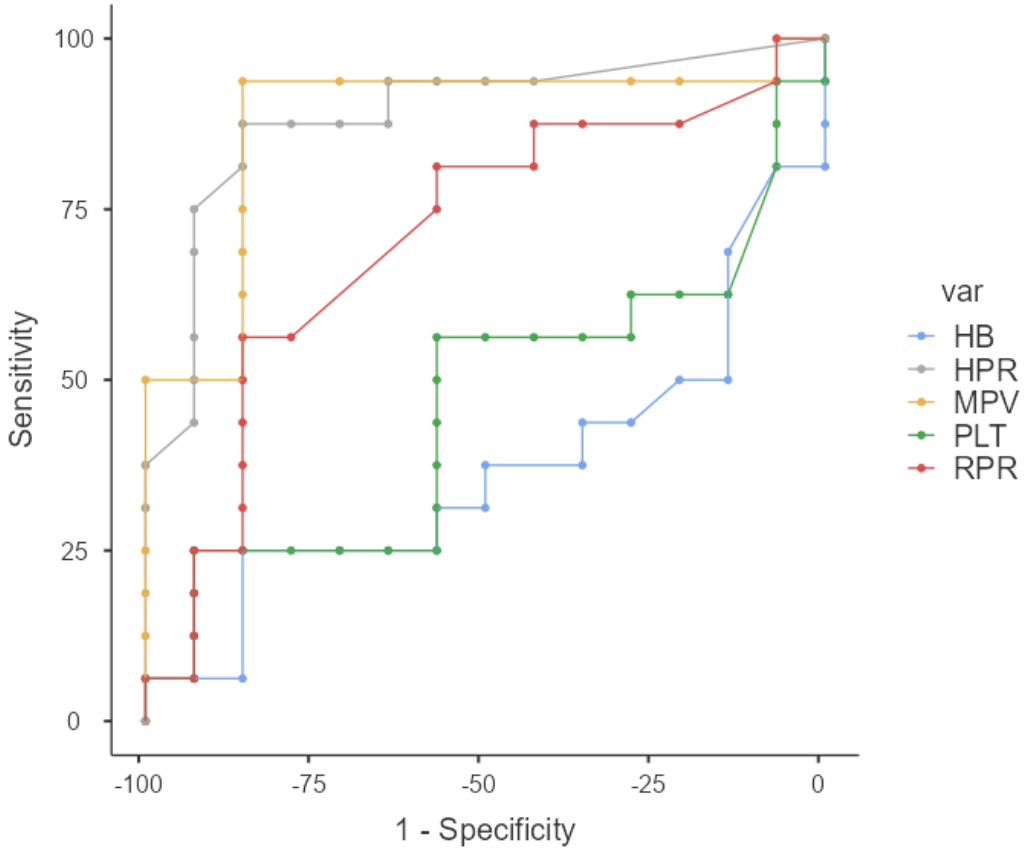

Figure (1): ROC curve analysis for discriminating active from Inactive JIA patients.

	Cut-off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (%)
HB	10.7	25%	85.71%	66.7%	50%	0.368
MPV	9.2	93.75%	85.71%	88.24%	92.31%	0.879
RPR	0.013	56.2%	84.71%	81.82%	63.16%	0.708
HPR	0.041	62.5%	85.7%	83.3%	66.67%	0.788
PLT	112.91	81.25%	71.43%	76.47%	76.92%	0.781

Abbreviations: **PPV:** Predictive Value for Positive**, NPV:** Negative Predictive Value, **AUC:** Area Under the Curve**, Hb**: Hemoglobin; **PLT**: platelet count; **MPV**: Mean platelet volume; **RPR**: RBCs to platelets ratio; **HPR**: Haemoglobin to Platelets ratio.

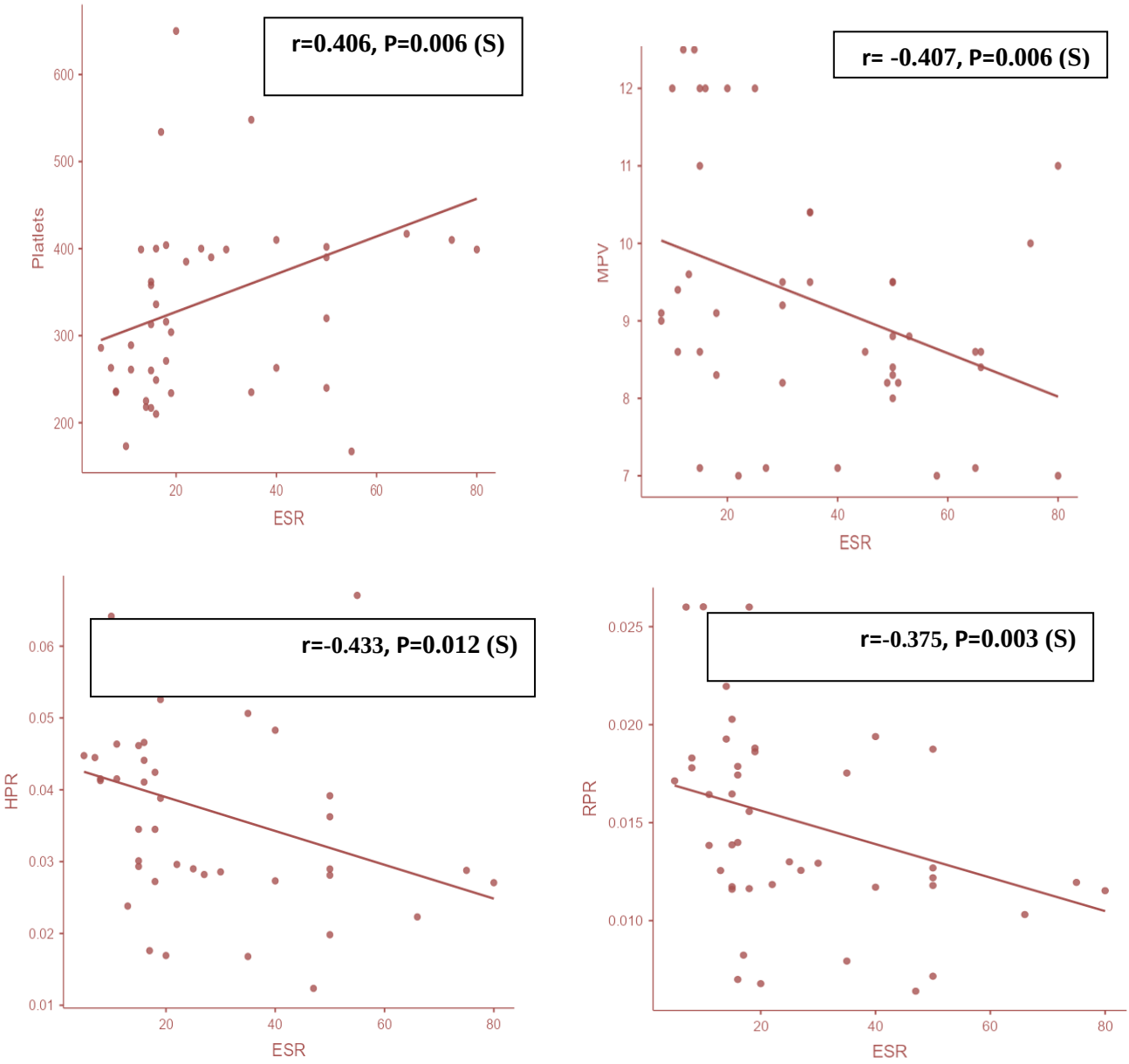

Figure (2): Scatter plot shows a significant positive correlation between ESR with PLT and a significant negative correlation with MPV, RPR & HPR.

ESR: Erythrocyte Sedimentation Rate **PLT**: platelet count**, MPV**: Mean platelet volume; **RPR**: RBCs to platelets ratio; **HPR**: Haemoglobin to Platelets ratio; **PLR**: Platelets to Lymphocytes ratio.

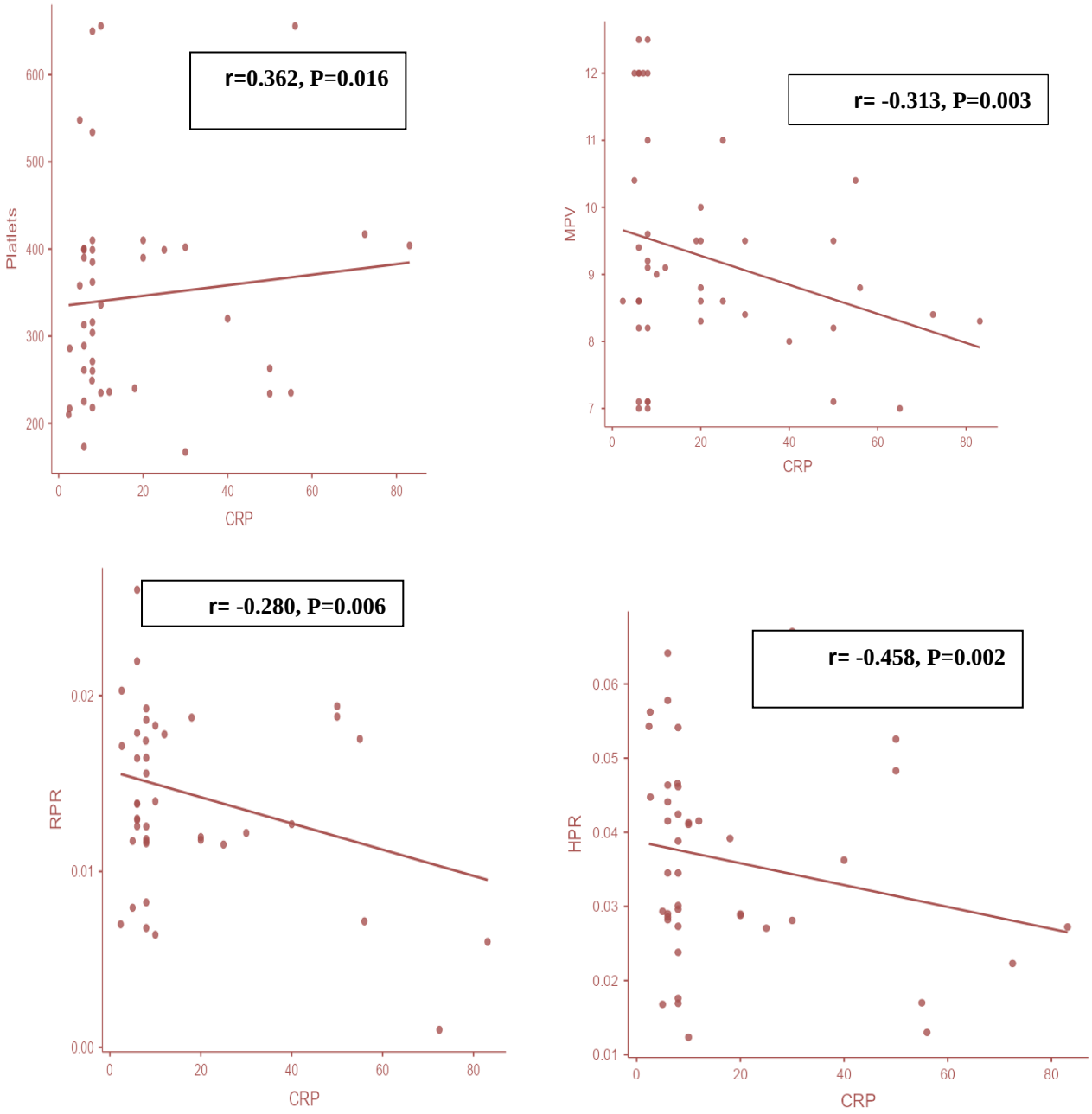

Figure (3): Scatter plot shows a significant positive correlation between CRP with platelets and a significant negative correlation with MPV, RPR, and HPR.
CRP: C- Reactive Protein; **PLT**: platelet count; **MPV**: Mean platelet volume; **RPR**: RBCs to platelets ratio; **HPR**: Haemoglobin to Platelets ratio.

DISCUSSION

JIA's clinical manifestations vary greatly, ranging from mild self-limiting arthritis to severe damaging arthritis. Yet, few particular and sensitive markers for assessing JIA activity rate have been established. These patients can be evaluated by measuring acute phase reactants like platelet indices. whilst few projects have been undertaken on CBC indices in rheumatologic illnesses, there are far fewer studies on these parameters in JIA[3]. Many results suggest that anemia might happen in the context of autoimmune conditions in which bone marrow function and iron metabolism may be altered by inflammation [20]. As a result, it has been proposed that RBC-related metrics, such as RDW and Hb levels, could be utilized as

inflammatory markers to predict the activity of numerous autoimmune illnesses [21]. In JIA patients, persistent disease activity may lead to serious morbidity, such as articular injury and deformities. As a result, following JIA patients' disease activity is critical [14].

Reactive thrombocytosis is a marker of inflammation in JIA [22]. In the present work, mean platelet count increased during the acute phase of the disease. However, unlike Vakili *et al* 's study, where this increase was more pronounced in systemic and polyarticular subtypes, this research showed no significant difference in platelet count between different subtypes [1]. A platelet index MPV is linked to platelet function and activity and is influenced by inflammatory reactions. MPV was significantly lower in JIA patients than in normal children and active JIA than inactive JIA patients. JIA patients with poly-articular subtype had the lowest MPV in the current research results. Other studies showed that MPV of all the cases was within the normal range during the acute JIA phase. The oligoarticular subtype had the highest MPV, followed by the systemic and polyarticular subtypes [4]. A study demonstrated that the MPV levels are lower in severe inflammatory disorders but higher in moderate inflammatory diseases [23].

Mounting evidence that RDW and other parameters are illustrated as reliable, accurate bio-inflammatory markers in various autoimmune diseases monitoring**.** So, it has been proposed that RBC-related metrics like RDW and Hb levels may be employed as inflammatory markers to anticipate the activity of numerous autoimmune disorders [21]. Although CBC-based parameters are not completely specific and sensitive to rheumatic disorders, based on the results of previous studies, these parameters are inflammatory biomarkers with a prognostic role in rheumatic disorders that can also assess the activity of the disease [24]. A majority (67.1%) of JIA patients had microcytic hypochromic anemia according to studies [25]. According to Al-Hemairi *et al*, anemia was the commonest abnormal test result (59.75%), and it was identified in 80% of systemic JIA patients [26].

Albokhari and Muzaffer stated that anemia is common in JIA and other rheumatologic disorders; it affects about 50% of patients and is mostly caused by inflammation. In their patients, oligoarthritic JIA had a substantially greater frequency of anemia (71.4%) than the other JIA subtypes [27], in contrast, in this work there was no significant difference in anemia occurrence between the different JIA subtypes. In another study, children with systemic JIA tended to have lower hemoglobin concentrations than non-systemic JIA [28].

PDW is another platelet volume indicator, that measures platelet dispersion by analyzing the top 20% of the distribution curve [29]. Our findings revealed no significant difference in PDW% between JIA patients & normal children, between active & inactive JIA children, and between different JIA subtypes of patients. Some studies found that PDW decreased in all subtypes during the acute phase of the disease, with the systemic subtype experiencing the greatest decline, followed by the polyarticular and oligoarticular subtypes [3]. Isık *et al*, found that PDW, like MPV, has an inverse association with inflammatory disease severity and is reduced in severe inflammatory disorders, such as the active phase of rheumatoid arthritis [30]. Plateletcrit (PCT) is the volume filled by platelets in the blood as a percentage and is determined using the formula PCT = platelet count x MPV / 10,000 [31]. Our study showed that PCT is significantly higher in JIA children when compared to normal children (p-value <0.001). Yet, no significant difference was found between the PCT of active patients & that of inactive patients. Also, no significant difference in PCT was found between different subtypes.

RPR & HPR were both significantly lower in JIA children than healthy controls (P- value = 0.003, < 0.001 respectively). PLR was significantly higher in JIA children (P- value = 0.0025). Comparing active & inactive JIA patients, RPR & HPR were both significantly lower in active JIA (P- value = 0.0.02, 0.04 respectively). However, no significant difference was found in PLR. In addition, JIA patients with poly-articular subtype had the lowest HPR which was statistically significant (P =0.03). whilst, no significant difference was found in PLR or RPR between different JIA subtypes. To our knowledge, this is one of the very first studies considering these parameters with such wide scope.

Limitations:

There were some limitations in this study. The comparison group didn't involve patients with other autoimmune disorders that had clinical symptoms like JIA. Also, the current research was limited to patients with JIA in a single area. As a result, a large sample size still is needed to corroborate the veracity of the findings. Furthermore, considering the influence of DMARDs on disease activity in JIA patients, we plan to evaluate the connection of these RBC-related indices with disease activity in newly diagnosed JIA patients who did not get therapy in subsequent work.

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CONCLUSION

In JIA patients, HB, MCV, and MCHC levels were considerably lower. Active JIA patients had considerably lower HB, MCH, RPR, and HPR levels than inactive group. Polyarticular subtype had the lowest HPR.

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