

# Plateletcrit is a Useful Marker in the Quality of Life Assessment of Patients with Rheumatoid Arthritis: A Cross-Sectional Study from Erbil, Iraq

Sheelan Faroz Aref, Aryan Mohamadfatih Jalal, Zhala Kakamin Mawlood, Marwan Salih Al-Nimer<sup>1,2</sup>

Department of Rheumatology, Rizgari Teaching Hospital, Kurdistan Board for Medical Specialties, Erbil, <sup>1</sup>Department of Clinical Pharmacology, College of Medicine, University of Diyala, Baqubah, <sup>2</sup>Department of Pharmacy, Al-Kut University College, Wasit, Iraq

## Abstract

**Background:** In patients with rheumatoid arthritis (RA), hematological indices and ratios have been reported to be related to the severity of illness, and thus could potentially be useful determinants of quality of life (QoL).

**Objective:** To evaluate the association between hematological indices or ratios, which serve as biomarkers of disease activity, and the QoL of RA patients.

**Materials and Methods:** This study was carried out in the Rizgary Teaching Hospital in the Kurdistan region of Iraq between December 01, 2021, and March 31, 2022. All female patients with a confirmed diagnosis of RA and aged  $\geq 18$  years were included. Data relating to the disease activity score (DAS-28), biochemical measurements of the profile, and hematological indices and ratios were assessed. The QoL of each patient was assessed using the Quality of Life-Rheumatoid Arthritis II (QoL-RA II) and the World Health Organization-Quality of Life (WHOQOL-BREF) scales.

**Results:** A total of 81 participants were included, with a median disease duration of 9 years. The median values of the hematological indices were as follows: mean corpuscular volume, 80 fL; platelet count  $282 \times 10^3/\text{mm}^3$ ; mean platelet volume, 9.7 fL; neutrophil-to-lymphocyte ratio, 2.76; and platelet-to-lymphocyte ratio, 170.5. In six of the eight domains of the QoL-RA II scale, the median score was  $\leq 5$ , indicating poor QoL. The transformed scores of WHOQOL-BREF domains were  $< 50$ . Multivariate regression analysis showed significant inverse correlations between plateletcrit and the health domains. The area under the curve of the physical, psychological, and environmental domains was  $< 0.5$  at a cutoff value of plateletcrit of 0.25.

**Conclusions:** In RA patients, hematological indices and ratios could serve as a QoL assessment tool, particularly plateletcrit, as higher plateletcrit ( $\geq 0.25$ ) were found to negatively impact the physical health, psychological, and environmental domains.

**Keywords:** Disease activity, hematological index, Iraq, plateletcrit, quality of life, rheumatoid arthritis

**Address for correspondence:** Prof. Marwan Salih Al-Nimer, Department of Clinical Pharmacology, College of Medicine, University of Diyala, Baqubah 32001, Iraq.

E-mail: alnimermarwan@gmail.com

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## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease affecting 1% of the population at any age, and women are more commonly affected than men by a ratio of 2:1.<sup>[1]</sup> The chronic course of articular and systemic manifestations of the disease leads to disabilities and reduces daily activity with impairment of the quality of life (QoL).<sup>[2]</sup>

Most studies use the score of the QoL as an indicator of the assessment of pharmacological and non-pharmacological interventions in the management of RA.<sup>[3-6]</sup> The relationships between RA severity, as measured by Disease Activity Score-28 (DAS-28) for Rheumatoid Arthritis with C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), and QoL have been thoroughly investigated, and it has been discovered that a higher DAS-28 is associated with QoL impairment.<sup>[7,8]</sup> Several studies have assessed the hematological indices and ratios in RA patients and found a nonsignificant relationship between mean platelet volume (MPV) and disease severity in treated RA patients,<sup>[9]</sup> no association between red cell distribution width (RDW) with complications of RA,<sup>[10]</sup> association between platelet-to-lymphocyte ratio (PLR) and the chronicity of the disease,<sup>[11]</sup> and significantly higher neutrophil-to-lymphocyte ratio (NLR) in patients with active RA than those in remission.<sup>[12]</sup> In a systematic review and meta-analysis that included 13 studies that assessed NLR and 8 studies that assessed PLR in RA patients, it was found that these hematological ratios were significantly higher in RA compared with healthy subjects.<sup>[13]</sup>

A few studies have assessed the relationships between the circulating biomarkers and the QoL in RA patients. One study found that sarilumab and adalimumab improved the articular manifestations of RA, physical activity, and health-related QoL, by inhibiting interleukin-6 and tumor necrosis factor- $\alpha$ , respectively.<sup>[14,15]</sup> Kingsley *et al.* found that the impairment of QoL in RA patients is linked with the duration, severity, and suppression of inflammatory biomarkers with antirheumatic drugs.<sup>[16]</sup> Another study found significant associations between ESR and CRP and higher plateletcrit level.<sup>[17]</sup>

In diseases other than RA, hematological indices have been shown to be useful as biomarkers of disease severity.<sup>[18,19]</sup> However, few studies have assessed the relationship between hematological indices and QoL, despite the link between hematological indices and disease severity. Therefore, the current study was conducted with the objective of determining the relationship between the

hematological indices and ratios with the QoL in female patients with RA, taking into consideration the severity and chronicity of the disease.

## MATERIALS AND METHODS

This was a single-center cross-sectional study carried out in the Rizgary Teaching Hospital (Hawler Medical University) in the Kurdistan region of Iraq from December 1, 2021, to March 31, 2022. This study was approved by the High Council of Medical Specialties at the Kurdistan Board for Medical Specialties in Erbil, Iraq.

All participants provided a written consent before inclusion. The researchers interviewed each participant and explained to them the purpose of the study, that no medical interventions would be made, and that participation was voluntary and they could withdraw from the study at any time. The participants were also assured of anonymity and data confidentiality.

### Participants

Known cases of RA who attended the consultant clinic of rheumatology in the Rizgary Teaching Hospital were recruited for this study. The diagnosis of RA was based on the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 classification criteria.<sup>[20]</sup>

The criteria for inclusion were being female with a confirmed diagnosis of RA and being aged  $\geq 18$  years. Patients with overt extraarticular manifestations, iron deficiency anemia treated with iron supplementation, recent infections, cardiovascular illness, thyroid gland dysfunction, kidney and liver diseases, pregnancy, and terminal illnesses were excluded from the study. Males were excluded because RA is mostly prevalent in females, and thus their inclusion could have statistically skewed the results.

The demographic characteristics of each patient were obtained, and the data were then analyzed. DAS was assessed and calculated by three independent practicing clinicians in rheumatology. Disease activity of 28 joints was calculated and a score of  $>2.6$  indicated active disease. The researchers interviewed each patient and completed the Quality of Life-Rheumatoid Arthritis II (QoL-RA II)<sup>[21]</sup> and the World Health Organization-Quality of Life (WHOQOL-BREF)<sup>[22]</sup> questionnaires using the native Kurdish language to explain each item of the questionnaire. The QoL-RA II scale consists of eight questions, and for each positive answer, a score of +1 is reported. The WHOQOL-BREF questionnaire is composed of 26 items

and covers four domains, including physical health, psychological, social interaction, and environmental. The calculated raw scores of 26 items were transformed to 100 scores using the manual instructions of WHOQOL-BREF.

### Sample size

The sample size for the participants was estimated using the Gpower software version 3.1 (Heinrich-Heine-Universität Düsseldorf, Germany), with power (1-error) set at 0.95 and error set at 0.05. For tests using linear bivariate (one group) and linear multiple regression (fixed model, one regression coefficient), the sample size was computed, and it has been found of 60 participants.

### Measurements of rheumatic profiles and hematological indices

Each patient provided a total of 10 mL of blood, which was divided in half before being included in the trial. To determine the total blood count (using an electronic Coulter machine) and ESR (using the Westergren method), the first 5 mL of the blood was drawn into an anticoagulant tube. The sera were separated by centrifuging the second batch of blood samples at 3000 rpm for 15 min. The levels of CRP, anti-cyclic citrullinated peptide (ACCP), and rheumatoid factor (RF) were measured in the sera. The Rizgary Teaching Hospital performed all hematological and rheumatic profile tests. The reference normal ranged values of rheumatic and hematological indices are as follows: ESR: 1–20 mm/hour; CRP: 3 mg/L; ACCP: 0.2–5.0 U/mL; RF: 1–19 U/mL; hemoglobin (Hb): 11.6–15 g/dL; platelet: 150,000–450,000 cells/ $\mu$ L; packed cell volume (PCV): 0.36–0.48; mean corpuscular volume (MCV): 80–100 fL; white blood cell count: 4500–11,000/mm<sup>3</sup>; neutrophil: 50%. The NLR and PLR were calculated by dividing the absolute number of neutrophils or platelets (as numerator) and the lymphocyte number (as denominator). Plateletcrit was calculated using the following formula: platelet count  $\times$  MPV/10,000

### Statistical analysis

Continuous data are presented in the following formats: median, interquartile range, 95% confidence interval (CI), and mean (SD). Categorical variables are presented as absolute numbers and percentages. Linear regression analysis was used to assess the association between each domain of QoL (as dependent variables) and the hematological indices (as independent variables). Multivariate regression analysis and analysis of variance were carried out for the calculation of the probability. A significant value indicates a strength in the association between each hematological index and the QoL domains and is predictive of the QoL. By using the cutoff values of each QoL domain of <50%,

logistic regression was used to determine the odds ratio and 95% CI of the deterioration of QoL, at a higher plateletcrit value. A receiver operating characteristic curve analysis with a 95% CI of QoL-domains was performed using the optimal cut-off value of plateletcrit for QoL prediction. *P* value  $\leq$  0.05 was considered significant. All statistical analysis was carried out using SPSS version 20 (IBM Corp., Chicago, USA).

## RESULTS

The study included a total of 81 participants. Table 1 shows the characteristic features of the participants. The majority of the patients (67.5%) lived in urban areas, were nonsmokers (80.2%), had a negative family history of RA (59.3%), and had a DAS-28 score of  $\geq$ 2.6 (90.1%). The rheumatoid profile showed that most of the participants were in a relapsed state, with inter-quartile levels of the ESR and ACCP as 18–49.5 mm/hour and 1.8–76.8 U/mL, respectively [Table 2].

The hematological indices showed that the participants had lower limits of Hb, PCV, and MCV compared with the normal ranges [Table 3]. The interquartile range of RDW

**Table 1: Characteristics of the patients (N=81)**

Characteristic	n (%)
Age (years) (mean $\pm$ SD)	48.8 $\pm$ 12.0
Residence	
Rural	19 (23.5)
Urban	62 (76.5)
Smoking	
No	65 (80.2)
Ex-smoker	9 (11.1)
Current	7 (8.6)
Occupation	
Student	1 (1.2)
Unemployed	1 (1.2)
Employee	13 (16.0)
Retired	2 (2.5)
Housewife	64 (79.0)
Family history of RA	
Negative	48 (59.3)
Positive	33 (40.7)
Duration of disease (years) (mean $\pm$ SD)	10.8 $\pm$ 8.4
1–5	30 (37.0)
6–10	19 (23.5)
10–15	12 (14.8)
>15	20 (24.7)
Status of the disease	
Relapse	72 (88.9)
Suicidal ideation	6 (7.4)
DAS-28 score (mean $\pm$ SD)	5.29 $\pm$ 1.82
Remission (<2.6)	8 (9.9)
Active	73 (90.1)
Low (2.6–<3.2)	4 (5.5)
Moderate (3.2– $\leq$ 5.1)	24 (32.9)
High >5.1	45 (61.6)

The results are expressed as n (%) and mean $\pm$ SD. SD – Standard deviation; RA – Rheumatoid arthritis; DAS – Disease activity score

was 12.7–14.3%, which was within the normal range of reference values in adult females (12.2–16.1%). The white blood cell count and the percentages of lymphocytes and neutrophils were within the normal reference ranges. The mean  $\pm$  SD of the platelet count, plateletcrit, and MPV was within the normal reference values, while 9.9% (8 of 81) of the participants had blood platelet counts  $>450,000/\text{mm}^3$ . The mean  $\pm$  SD of the NLR is higher than the expected reference ratio in healthy subjects, and 46.9% (38 out of 81) had an NLR ratio of  $>3.0$ . The median value of PLR was 170.5, which was higher than the reference values in healthy adults [Table 3].

The median values of six of the eight domains of the QoL-RA scale were 4–5, indicating a poor QoL, while the median values of the interaction and help domains were 7. In the WHOQOL-BREF, the median scores for physical health, psychological, and environmental domains were  $<50$ , while for the social domain, it was 50 [Table 4]. The odds ratios and CI for the impairment of the physical, psychological, social, and environmental domains were 1.189 (0.752–1.626), 1.613 (1.165–2.061), 0.884 (0.447–1.321), and 1.382 (0.941–1.823), respectively.

Multivariate regression analysis showed a significant correlation between the physical health domain of the WHOQOL-BREF and hematological indices/ratios ( $r = 0.483$ , F-value = 2.402,  $P = 0.019$ ) with a

prediction rate of 23.3%. Significant inverse correlations were observed with plateletcrit and NLR [Table 5]. For the psychological health domain, hematological indices or ratios were not significant predictors ( $r = 0.352$ , F-value = 1.113,  $P = 0.365$ ), with a 12.4% prediction rate. A high plateletcrit value was the only significant predictor of a low psychological health score ( $P = 0.019$ ) [Table 5]. For the social interaction and environmental domains, hematological indices and ratios were nonsignificant predictors ( $r = 0.217$ , F-value = 0.388,  $P = 0.937$ ; and  $r = 0.397$ , F-value = 1.476,  $P = 0.174$ , respectively), with prediction rates of 4.7% and 15.8%, respectively. High plateletcrit and lymphocytes (%) values were found to be significant predictors of low environmental domain scores ( $P = 0.019$ ) [Table 5].

Further analysis revealed that the sensitivity and specificity at a cutoff value of 0.25 plateletcrit for the health domain were 61.2% and 43.8%; for the psychological domain, they were 64% and 48.4%; and for the environmental domain, they were 70.2% and 55.9%, respectively. Figure 1 shows the area under the curve with 95% CIs of the physical, psychological, and environmental health were  $<0.5$  with a cutoff plateletcrit value of 0.25.

## DISCUSSION

The results of this study showed that plateletcrit value is a critical determinant of QoL in RA patients. It is correlated inversely with scores of WHOQOL-BREF domains, and a cutoff value of  $\geq 0.25$  differentiates patients with a poor QoL in terms of physical, psychological, and environmental health. Most patients were in the relapsed phase and had active disease, and thus their physical activity and psychological health were impaired, as shown by the low scores in QoL domains. Therefore, changes in the hematological indices and ratios represented active RA.

**Table 2: Rheumatic profile of the patients**

Rheumatic profile	Mean $\pm$ SD	Median (IQR)	95% CI
CRP (mg/L)	1.2 $\pm$ 2.5	0.44 (0.195–1.09)	0.639–1.759
ESR (mm/h)	34.2 $\pm$ 21.2	33.0 (18.0–49.5)	29.5–38.9
RF (IU/mL)	67.1 $\pm$ 127.7	12.0 (8.0–60.0)	38.9–95.4
Anti-cyclic citrullinated protein (U/mL)	75.7 $\pm$ 122.5	11.9 (1.8–76.79)	48.6–102.8

CRP – C-reactive protein; ESR – Erythrocyte sedimentation rate; RF – Rheumatoid factor; IQR – Interquartile range; CI – Confidence interval; SD – Standard deviation

**Table 3: Hematological indices and ratios**

Hematological indices	Mean $\pm$ SD	Median (IQR)	95% CI
Hb (g/dL)	11.8 $\pm$ 1.2	12.0 (11.1–12.7)	11.5–12.1
PCV (%)	35.7 $\pm$ 3.4	36 (33.6–38.4)	34.9–36.4
Mean cell volume (fL)	79.2 $\pm$ 6.5	80 (76.5–84.0)	77.8–80.6
RDW (%)	13.73 $\pm$ 1.52	13.3 (12.7–14.3)	13.4–14.1
White blood cell (count/ $\text{mm}^3$ )	7903 $\pm$ 2764	7340 (5785–9,210)	7292–8514
Neutrophil (%)	67.9 $\pm$ 10.6	68.0 (60.0–75.0)	67.9–86.0
Lymphocyte (%)	24.5 $\pm$ 10.3	24.0 (15.5–32.0)	22.3–26.8
Platelet (count/ $\text{mm}^3$ )	291,185 $\pm$ 108,428	282,000 (221,500–336,000)	271,688–317,393
PCT (%)	0.283 $\pm$ 0.092	0.270 (0.210–0.330)	0.263–0.303
MPV (fL)	9.75 $\pm$ 1.32	9.7 (8.8–10.3)	9.46–10.04
NLR	3.72 $\pm$ 2.81	2.76 (1.90–4.78)	3.10–4.35
PLR	188.2 $\pm$ 97.1	170.5 (127.5–220.2)	166.7–209.6

Hb – Hemoglobin; PCV – Packed cell volume; RDW – Red cell distribution width; MPV – Mean platelet volume; NLR – Neutrophil-to-lymphocyte ratio; PLR – Platelet-to-lymphocyte ratio; PCT – Plateletcrit; SD – Standard deviation; IQR – Interquartile range; CI – Confidence interval

There was evidence of anemia, as the median values of Hb and MCV were 12 g/dL and 80 fL, respectively, indicating iron deficiency anemia that is commonly reported in patients with RA.<sup>[23]</sup> The results showed that Hb is not a predictor of QoL. Previous studies have shown a significant inverse relationship between mental health but not physical or emotional health and Hb using the Short Form (SF)-36 questionnaire.<sup>[24]</sup>

RDW is reported as a biomarker of disease activity, and a cutoff value of 14.8% has been reported to be associated with higher disease activity.<sup>[25]</sup> The findings of our study substantiated those results, as the values of RDW ranged between 11.9% and 19.2%, and 14 of 81 patients had an RDW of >14.8%. The current study also found that RDW is a nonsignificant predictor of QoL. Recently, Ke *et al.*<sup>[26]</sup> reported that a higher RDW value is an indicator of a poor prognostic marker of RA disability when the onset of RA is presented later in life.

**Table 4: Domain scores of the quality of life-rheumatoid arthritis and World Health Organization-quality of life-BREF Scales**

Variables	Mean±SD (median)	
<b>QoL-RA (domains)</b>		
Physical ability	4.9±2.2	(5)
Help	6.9±2.1	(7)
Arthritis	4.6±2.1	(4)
Tension	5.2±2.1	(5)
Health	4.8±1.8	(5)
Arthritis (only)	4.7±2.0	(4)
Interaction	6.4±2.1	(7)
Mood	5.0±2.2	(5)
<b>Variables</b>		
<b>WHOQOL-BREF (domains)</b>		
	Mean±SD (median)	
	Raw score	Transformed score
Physical health	19.9±3.1 (20)	46.1±11.3 (44)
Psychological	16.5±2.9 (16)	43.7±12.1 (44)
Social interaction	8.7±2.1 (9)	48.0±17.6 (50)
Environmental	21.6±4.5 (21)	44.1±13.9 (44)

QoL – Quality of life; WHOQOL – World Health Organization QoL; RA – Rheumatoid arthritis; SD – Standard deviation

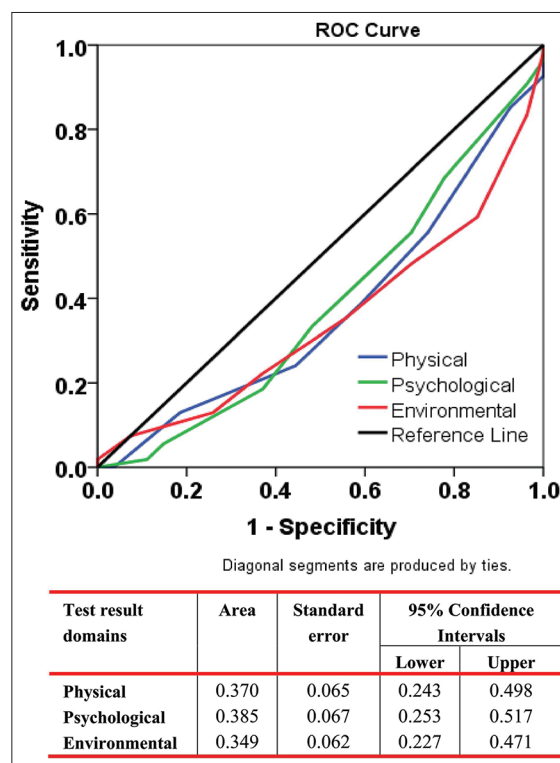
**Table 5: Multivariate regression analysis between hematological indices (as predictors) with each domain of the World Health Organization-Quality of Life-BREF (as responses)**

Domains	Hb	MCV	RDW	L (%)	PCT	MPV	NLR	PLR	ESR
Physical health									
β	0.582	-0.205	-0.671	-0.354	<b>-40.8</b>	0.886	<b>-2.558</b>	0.055	-0.053
P	0.643	0.520	0.629	0.108	<b>0.012</b>	0.352	<b>0.008</b>	0.027	0.406
Psychological									
β	0.320	-0.063	0.763	-0.207	<b>-43.5</b>	-0.516	-1.939	0.034	0.081
P	0.823	0.863	0.630	0.406	<b>0.019</b>	0.634	0.073	0.225	0.266
Social interaction									
β	1.968	-0.189	0.674	-0.112	-33.9	-0.154	-1.414	0.037	-0.002
P	0.365	0.731	0.778	0.766	0.218	0.925	0.383	0.378	0.983
Environmental									
β	1.831	-0.342	0.306	<b>-0.574</b>	<b>-50.0</b>	-0.052	-2.357	0.024	0.054
P	0.259	0.405	0.864	<b>0.043</b>	<b>0.016</b>	0.966	0.053	0.441	0.505

Bold indicates statistical significance at P<0.05. The results are expressed as β regression coefficient and probability (P). Hb – Hemoglobin; MCV – Mean corpuscular volume; RDW – Red cell distribution width; L (%) – Lymphocytes percentage; PCT – Plateletcrit; MPV – Mean platelet volume; NLR – Neutrophil-to-lymphocyte ratio; PLR – Platelet-to-lymphocyte ratio; ESR – Erythrocyte sedimentation rate

A recent meta-analysis study showed that a cutoff NLR value of 2.13 is a useful diagnostic marker of RA, which is similar to the findings of the current study.<sup>[27]</sup> In addition, we found that NLR was inversely related to physical health, that is, a higher NLR value was associated with more disabilities. PLR value has been reported to be significantly correlated with the disease activity of RA, with the mean PLR value in RA patients with active disease being 195.3; this was similar to the mean PLR value reported in the current study (188.2).<sup>[28]</sup>

Platelet indices are thoroughly investigated in RA patients, and the authors found that the values of MPV and platelet



**Figure 1:** The area under the curve of the domain scores at a cutoff ≥0.25 value of plateletcrit (%)

distribution width are higher in RA than in healthy subjects and are positively correlated with disease activity.<sup>[29]</sup> The results showed that plateletcrit, among the other platelet indices, is inversely correlated with the QoL domains, and a cutoff value of  $\geq 0.25$  differentiates patients with low scores in physical, psychological, and environmental domains.

### Strength and limitations

The strength of this study is the novelty and reproducibility of the relationship between the plateletcrit and QoL. One of the limitations of the study is that it used only two types of health assessment surveys, and thus future studies may utilize additional health-related questionnaires to cover all aspects of health. In addition, the current study had a sample size that was smaller than those in similar previous studies, and all the patients were from only a single center, which may limit the generalizability of the findings. Prospective studies that sequentially determine the hematological indices along with the evaluation of QoL over a longer period of time would substantiate the findings of this study.

### CONCLUSION

The findings of this study showed that hematological indices and ratios provide an indication of disease activity and QoL and that plateletcrit is a potentially useful and reproducible hematological marker for assessing the QoL in RA.

### Ethical considerations

This study was approved by the High Council of Medical Specialties at the Kurdistan Board for Medical Specialties in Erbil, Iraq (Research Protocol Ethics Committee No. 1451, Date: August 22, 2022). All participants provided a written consent before inclusion. The study adhered to the principles of Declaration of Helsinki, 2013.

### Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available but can be obtained from the corresponding author on reasonable request.

### Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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