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HEMATOLOGICAL PROFILE IN PATIENTS OF RHEUMATOID ARTHRITIS AND CORRELATION WITH DISEASE ACTIVITY AND TREATMENT

General Medicine

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily affecting synovial joints and causing progressive disability. Apart from joint involvement, RA is associated with various hematological abnormalities, which often reflect systemic inflammation. Hematological markers, being easily accessible and cost-effective, may serve as reliable tools for disease activity assessment, particularly in resource-constrained settings. **Objectives:** To evaluate hematological profile in patients of rheumatoid arthritis and correlation with disease activity and treatment. **Methods:** A cross-sectional observational study was conducted at the Department of General Medicine, BRD Medical College, Gorakhpur. A total of 80 patients diagnosed with RA according to the ACR/EULAR 2019 classification criteria were enrolled. Hematological parameters including hemoglobin (Hb), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelet count, mean platelet volume (MPV), neutrophil and lymphocyte counts, and hematological ratios (neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), platelet-to-neutrophil ratio (PNR)) were assessed. Disease activity was evaluated using the Disease Activity Score-28 based on ESR (DAS-28 ESR). Statistical analysis was performed using SPSS version 23.0, with $p < 0.05$ considered significant. **Results:** The majority of patients were females (90.24%), with most belonging to the middle-aged group. Moderate disease activity was observed in 69.51% of patients. Significant increases in ESR, CRP, neutrophil counts, and NLR were observed with higher disease activity ($p < 0.05$). Hemoglobin levels declined significantly as disease severity increased. **Conclusion:** Hematological parameters, particularly ESR, CRP, Hb, and NLR, significantly correlate with disease activity in RA and can be useful adjuncts for disease monitoring.

KEYWORDS

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease predominantly affecting synovial joints, leading to progressive inflammation, joint destruction, and functional impairment. The disease exhibits a global prevalence of approximately 1%, with a notably higher occurrence in women, often affecting individuals between 40 and 60 years of age (1-3). In India, RA poses a significant health burden, with prevalence estimates ranging from 0.28 to 0.7% in the adult population (4).

Although RA primarily manifests as symmetrical polyarthritis of small joints, its systemic nature extends beyond the musculoskeletal system, with frequent hematological abnormalities. Anemia of chronic disease, thrombocytosis, leukocytosis, and alterations in red blood cell indices are well-documented hematological manifestations of RA and are closely linked to disease activity and inflammatory burden (5). Pro-inflammatory cytokines, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), play key roles in both disease pathogenesis and hematological alterations (6,7).

Assessment of disease activity is critical for guiding treatment and predicting prognosis in RA. While established indices like the Disease Activity Score-28 (DAS28) are widely used, they primarily rely on clinical and laboratory inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (8,9). However, complete blood count (CBC)-derived parameters, including hemoglobin concentration, platelet count, and mean platelet volume (MPV), have emerged as accessible, cost-effective indicators that may reflect systemic inflammation and disease activity (9-11).

Despite growing evidence supporting the association between hematological parameters and RA disease activity, their integrated use in routine clinical practice remains limited, particularly in resource-limited settings like Eastern India. This study aimed to systematically evaluate the hematological profile in patients with RA and examine its correlation with disease activity and treatment response, with the objective of enhancing disease monitoring and guiding individualized therapy.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of General Medicine, BRD Medical College, Gorakhpur, after obtaining approval from the Institutional Ethics Committee and Research Committee.

Sample Size and Study Duration

The sample size was calculated using the formula:

$n = Z^2P(1-P)/d^2$

where:

- Z = 1.96 (for 95% confidence level)
- P = expected prevalence of rheumatoid arthritis (5.5% or 0.055)
- d = precision (4% or 0.04) (6)

Based on the calculation, a total of 80 patients were included in the study, conducted over a period of 12 months or until the target sample size was achieved.

Inclusion Criteria

- Age between 20 to 70 years.
- Diagnosis of rheumatoid arthritis according to ACR/EULAR 2019 classification criteria.
- Patients providing written informed consent.

Exclusion Criteria

- Refusal to give consent.
- Presence of malignancy, arterial or venous thrombosis.
- Other systemic inflammatory diseases such as inflammatory bowel disease.

Study Procedure

Eligible patients from the outpatient and inpatient departments were enrolled after obtaining written consent. A detailed clinical history and relevant examination were performed.

Laboratory Investigations

Blood samples were collected aseptically using a 23G needle and distributed into three vials:

1. EDTA vial for Hb, ESR, platelet count, and MPV.
2. Fluoride-oxalate vial for fasting blood sugar.
3. Plain vial for urea, creatinine, CRP, RF, and anti-CCP antibody tests.

Samples were analyzed within 1 to 3 hours. Hematological parameters were assessed using an automated cell counter, while platelet morphology was examined on Leishman-stained smears. ESR was measured by the conventional method. Anti-CCP was estimated using INOVA QUANTA Lite® CCP3 IgG ELISA kit, and CRP was analyzed accordingly.

Statistical Analysis

Data were compiled in Microsoft Excel and analyzed with SPSS version 23.0. The Chi-square test, independent t-test, and Pearson's correlation coefficient were applied. A p-value < 0.05 was considered statistically significant.

RESULTS

In our study, the age and gender distribution reveals that the majority of RA patients belonged to the 41–50 years age group (26.83%), followed by 51–60 years (23.17%), with a female predominance (90.24%). This highlights that RA predominantly affects middle-aged females, consistent with established epidemiological trends (Table 1).

Table 1: Age and Gender Distribution of RA Patients (N = 82)

Category	Sub-Category	N	%
Age Group (Years)	≤ 20 years	8	9.76
	21 – 30 years	8	9.76
	31 – 40 years	11	13.41
	41 – 50 years	22	26.83
	51 – 60 years	19	23.17
	> 60 years	14	17.07
Gender	Female	74	90.24
	Male	8	9.76

The descriptive statistics indicate elevated inflammatory markers (mean ESR: 29.10 mm/hr, CRP: 32.15 mg/l, Anti-CCP: 82.97 U/ml, RA Factor: 66.35 IU/ml) and significant hematological variations, including elevated TLC (mean: 11,595 cells/mm³), neutrophils, and platelet counts. The mean DAS-28 score of 4.05 suggests moderate disease activity in the cohort. These findings reflect the inflammatory and hematological burden of RA (Table 2).

Table 2: Descriptive Statistics of Inflammatory Markers, Haematological Markers, and Disease Activity Score (DAS-28 ESR) and Joint Count

Category	Sub-Category	Mean	Median	Std. Deviation	Minimum	Maximum	25th Percentile	75th Percentile
Inflammatory Markers	ESR (mm/hr)	29.10	28.00	12.47	5.00	86.00	22.00	34.00
	CRP (mg/l)	32.15	30.65	20.61	1.30	86.00	16.90	49.68
	Anti-CCP (U/ml)	82.97	34.15	91.30	0.50	403.90	4.90	195.60
	RA Factor (IU/ml)	66.35	29.50	70.78	1.20	216.00	4.65	146.63
Haematological Markers	TLC (cells/mm³)	11595.00	10100.00	7116.85	3300.00	59000.00	7600.00	13925.00
	Neutrophils (cells/mm³)	8.40	6.80	5.37	1.60	33.50	5.30	9.35
	Lymphocytes (cells/mm³)	1.83	1.70	1.02	0.10	5.40	1.00	2.30
	Platelets (cells/mm³)	238400.00	235500.00	100643.00	76000.00	533000.00	154250.00	284750.00
	MPV (%)	10.95	10.80	2.25	0.00	16.50	9.68	12.30
	MCV (fl)	79.75	81.75	12.79	10.80	103.30	76.98	85.63
	RDW (%)	16.41	15.40	5.23	11.20	53.80	14.08	17.30
	PCV (%)	32.33	32.60	7.39	10.80	48.40	28.20	37.50
	RBC Count (million cells/mm³)	3.85	3.91	0.79	1.01	5.71	3.52	4.29
	Hemoglobin (gm/dl)	11.05	11.40	2.45	3.30	15.80	9.68	12.53
	MCH (pg)	29.08	28.15	9.02	22.00	106.90	26.80	29.93
	Platelet/Lymphocyte Ratio (PLR)	191130.00	133060.00	194725.00	19814.80	1460000.00	93997.00	223880.00
	Platelet/Neutrophil Ratio (PNR)	37230.00	32021.00	26541.30	5104.47	158571.40	20974.00	48567.00
Disease Activity Score (DAS-28 ESR) and Joint Count	DAS-28 (ESR)	4.05	3.80	1.00	2.20	6.90	3.30	4.53
	Tender Joint Count	4.46	4.00	2.69	2.00	10.00	2.00	6.00
	Swollen Joint Count	0.50	0.00	0.92	0.00	4.00	0.00	0.25

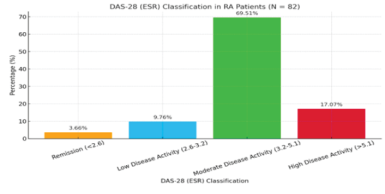

Figure 1: DAS-28 (ESR) Classification in RA Patients

Comparison across disease activity categories demonstrates a statistically significant increase in inflammatory markers (ESR, CRP, Anti-CCP, RA Factor) and neutrophil counts with worsening disease activity. TLC also increases significantly, while lymphocyte count shows a declining trend, though not statistically significant. Platelet counts did not significantly differ.

This confirms that inflammatory burden correlates with disease severity in RA patients (Table 3).

Table 3: Comparison of Inflammatory and Serological Parameters, Neutrophil Counts (cells/mm³), Total Leukocyte Count (TLC in cells/mm³), Lymphocyte Counts (cells/mm³), Platelet Counts (cells/mm³) Across Different Categories of Disease Activity in Patients with Rheumatoid Arthritis, as Measured by DAS-28 (ESR)

Category	Sub-Category	Remission (Mean ± SD)	Low Disease Activity (Mean ± SD)	Moderate Disease Activity (Mean ± SD)	High Disease Activity (Mean ± SD)	F	p-Value
Inflammatory and Serological Parameters	ESR (mm/hr)	7.00 ± 1.73	17.25 ± 2.60	28.51 ± 8.62	43.00 ± 15.35	18.98	<0.001
	CRP (mg/l)	12.47 ± 10.39	22.43 ± 14.81	30.02 ± 18.73	50.59 ± 21.64	6.56	0.001
	Anti-CCP (U/ml)	3.57 ± 4.71	30.90 ± 69.14	82.24 ± 93.48	132.71 ± 76.99	3.26	0.026
	RA Factor (IU/ml)	9.87 ± 11.50	14.29 ± 20.66	55.69 ± 65.25	151.61 ± 43.50	13.62	<0.001
Neutrophil Counts (cells/mm³)	Neutrophils (cells/mm³)	3.83 ± 1.95	5.99 ± 1.45	8.52 ± 4.13	11.56 ± 2.18	6.14	0.001
Total Leukocyte Count (TLC in cells/mm³)	TLC (cells/mm³)	6833.33 ± 1965.54	7462.50 ± 1922.01	10247.37 ± 6910.92	14107.14 ± 1965.65	2.83	0.044
Lymphocyte Counts (cells/mm³)	Lymphocytes (cells/mm³)	1.90 ± 1.15	3.94 ± 6.91	1.89 ± 1.01	1.31 ± 0.49	2.45	0.069
Platelet Counts (cells/mm³)	Platelets (cells/mm³)	231666.67 ± 57552.87	187250.00 ± 58073.23	227736.84 ± 96098.82	201785.71 ± 55114.12	0.75	0.523

Hematological parameters such as Hemoglobin show a significant declining trend with worsening disease activity ($p = 0.016$), suggesting anemia of chronic disease. However, other indices like MCV, RDW, RBC count, and hematological ratios (PLR, PNR) showed no significant differences, except for PNR, which declined significantly with increasing disease activity ($p < 0.001$), indicating its potential role as a marker of disease severity. These hematological alterations reflect the systemic impact of RA (Table 4).

Table 4: Comparison of Several Hematological Parameters, Hemoglobin (Hb) and Mean Corpuscular Hemoglobin (MCH), Hematological Ratios Across Patients with Varying Disease Activity Levels

Category	Sub-Category	Remission (Mean ± SD)	Low Disease Activity (Mean ± SD)	Moderate Disease Activity (Mean ± SD)	High Disease Activity (Mean ± SD)	F	p-Value
Hematological Parameters	MPV (%)	12.00 ± 2.95	10.81 ± 0.15	10.83 ± 2.36	11.28 ± 1.79	0.37	0.773
	MCV (fl)	81.17 ± 6.91	77.39 ± 5.49	78.45 ± 14.55	83.21 ± 7.00	0.60	0.618
	RDW (%)	14.23 ± 1.17	14.74 ± 2.63	17.17 ± 5.99	14.73 ± 1.92	1.34	0.267
	PCV (%)	36.63 ± 10.34	33.45 ± 7.66	31.57 ± 7.31	33.84 ± 7.24	0.79	0.504
	RBC Count (million cells/mm³)	4.18 ± 0.86	3.80 ± 0.82	3.82 ± 0.83	3.93 ± 0.60	0.25	0.863
Hemoglobin (Hb) and Mean Corpuscular Hemoglobin (MCH)	Hemoglobin (gm/dl)	13.07 ± 3.81	12.13 ± 1.21	10.93 ± 2.50	9.36 ± 1.47	3.67	0.016
	MCH (pg)	29.43 ± 3.25	27.65 ± 2.65	29.38 ± 10.72	28.61 ± 2.15	0.10	0.960
Hematological Ratios	Platelet/Lymphocyte Ratio (PLR)	162463.77 ± 101856.43	131628.32 ± 93778.94	177287.64 ± 206037.12	180318.89 ± 112948.39	0.16	0.925
	Platelet/Neutrophil Ratio (PNR)	70466.45 ± 29913.92	33799.82 ± 14020.82	31006.53 ± 16430.92	18100.43 ± 6274.98	9.75	<0.001

DISCUSSION

In our study, the majority of rheumatoid arthritis (RA) patients were middle-aged, with the highest prevalence in the 41–50 years age group (26.83%), followed by 51–60 years (23.17%). This pattern is consistent with the findings of Masoumi et al. (2024), Asra et al. (2024), and Farouk et al. (2023), all of whom reported peak RA occurrence in middle-aged adults (12-14). A strong female predominance (90.24%) was observed, aligning with reports from Masoumi et al. (2024), Pan et al. (2023), and Elnemr et al. (2024), reinforcing the well-established gender disparity in RA (12,15,16).
Inflammatory markers in our cohort were significantly elevated. The mean ESR was 29.10 mm/hr, and CRP was 32.15 mg/L, reflecting active systemic inflammation. These results align with Masoumi et al. (2024), Farouk et al. (2023), and Pan et al. (2023) who highlighted ESR and CRP as reliable indicators of disease activity (12,14,15).

Serological markers also demonstrated their relevance. We observed higher Anti-CCP and RA factor levels in patients with greater disease activity, similar to the findings of Asra et al. (2024), Farouk et al. (2023), and Raza et al. (2025), who reported their association with more severe, erosive disease (13,14,17).

Anemia was common, with hemoglobin levels showing a significant decline as disease activity increased. This observation is consistent with studies by Asra et al. (2024), and Elnemr et al. (2024) who emphasized anemia as a marker of systemic inflammation in RA (13,16).

Although platelet count and RDW variations across groups were not statistically significant, their trends mirrored those reported by Masoumi et al. (2024) and Farouk et al. (2023), supporting their role as supportive inflammatory markers (12,14).

Neutrophil counts and NLR were significantly higher in patients with more active disease, consistent with the results of Farouk et al. (2023), Mercan et al. (2016), and Uslu et al. (2015), highlighting NLR as an accessible inflammatory marker in RA (14,18,19).

DAS-28 (ESR) scores demonstrated that most patients (69.51%) had moderate disease activity, with significant correlations observed between hematological markers and disease activity. These findings are in agreement with Masoumi et al. (2024), Farouk et al. (2023), and Pan et al. (2023 (12,14,15).

Limitations: The limitations of the study include a relatively small, single-center sample size and the cross-sectional design, which limits the ability to assess causal relationships or track changes in hematological markers over time.

Strengths: The strengths of the study include a comprehensive evaluation of hematological markers alongside clinical and serological parameters, providing a cost-effective approach to assess disease activity in RA patients in a real-world, resource-constrained environment.

CONCLUSION

We concluded that Integration of hematological and serological parameters with clinical assessment tools like DAS-28 significantly correlate with disease activity and treatment.Early identification of high-risk patients through these markers may facilitate timely therapeutic interventions, ultimately improving long-term outcomes in RA management.

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