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Research Article

A Study of Hematological Profile in Rheumatoid Arthritis Patients

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Abstract: Background: Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily characterized by inflammation of the joints. It affects millions of individuals globally, leading to pain, swelling, stiffness, and potential joint destruction if left untreated. The pathophysiology of RA involves the immune system attacking the synovial tissues of the joints, resulting in the release of inflammatory mediators and the activation of various immune cells. Materials and methods: The present study was a cross sectional study was conducted on patients who fulfilled the American Rheumatologic association criteria, in Department of General Medicine. The data was collected from patients who fulfilled the criteria and have undergone the hematological tests. A total of 88 subjects were enrolled for the study, who were divided into 2 groups-cases group and control group with 44 subjects in each group based duration of rheumatoid arthritis up to 5 years. Result: Sex ratio of females to males is this study is 4:1. The risk of developing disease is greatest between 40 to 49 years. Rheumatoid factor positivity is 79% and rheumatoid factor negativity is 21%. The prevalence of anemia in rheumatoid arthritis patients is 75%. In rheumatoid factor positive patients mean Hb values is less (9.11gm %) compared to rheumatoid factor negative patients (10.23gm%). Iron deficiency anemia patients mean Hb is lower(8.6gm%) than in anemia of chronic disease is (10.9gm%). The prevalence of rheumatoid arthritis according to DAS 28 score categories in decreasing order are moderate 45.4% , severe 48.9% and mild 5.7%. Anemia is very well correlated with rheumatoid factor positivity, disease activity (DAS 28 score), duration of disease and ESR. Conclusion The hematological profile of RA patients is influenced by the underlying disease, the level of inflammation, and the treatment regimen. Anemia, leukocytosis, thrombocytosis, and coagulation abnormalities are common findings, with significant clinical implications. Understanding these changes helps clinicians assess disease activity, predict potential complications, and make informed decisions about treatment. Regular monitoring of hematological parameters is crucial to managing RA effectively, minimizing complications, and improving patient outcomes.

Keywords: Rheumatoid arthritis, Disease activity, Hematologic parameters.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily characterized by inflammation of the joints. It affects millions of individuals globally, leading to pain, swelling, stiffness, and potential joint destruction if left untreated. [1] The pathophysiology of RA involves the immune system attacking the synovial tissues of the joints, resulting in the release of inflammatory mediators and the activation of various immune cells. [2]

While RA is primarily a musculoskeletal disorder, it has significant systemic implications, affecting various organs and systems, including the hematological system. Hematological abnormalities are common in patients with RA, and changes in blood cell counts, composition, and function are frequently observed. [3] These abnormalities not only reflect the inflammatory burden of the disease but also contribute to disease progression and the patient's overall clinical status. [4]

Key hematological manifestations in RA include anemia, thrombocytosis (elevated platelet count), and leukocytosis (elevated white blood cell count), along with changes in the red blood cell morphology. [5] The mechanisms behind these abnormalities are multifactorial, involving inflammation, cytokine release, autoantibody production, and medication effects. Inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other mediators can lead to bone marrow suppression, altered erythropoiesis, and increased destruction of blood cells, contributing to anemia and other blood-related complications. [6]

This study is important not only for clinicians to evaluate disease severity and progression but also for predicting patient outcomes and tailoring individualized treatment regimens. In this context, understanding the hematological changes in RA can provide valuable insights into the systemic nature of the disease and its broader impact on health.

METHODOLOGY & MATERIALS

The present study was a cross sectional study was conducted on patients who fulfilled the American Rheumatologic association criteria, in Department of General Medicine.

Source Of Data:

The data was collected from patients who fulfilled the criteria and have undergone the hematological tests.

Sampling Method:
A total of 88 subjects were enrolled for the study, who were divided into 2 groups-cases group and control group with 44 subjects in each group-based duration of rheumatoid arthritis up to 5 years.

Inclusion Criteria:
Patients meeting the following criteria were enrolled in the study. 1. Patients who satisfied the American Rheumatologic association criteria 1987, irrespective of hematological signs present or not. 2. Patients of age group 20 to 60 years, both male and female. 3. Patients who have the duration of disease up to 5 years.

Exclusion Criteria:
The patients meeting the following criteria were excluded from the study. 1. Patients who were previously diagnosed with anaemia and treated. 2. Patients who previously have any other bleeding disorder not related to Rheumatoid arthritis. 3. Patients who have mixed disorder like SLE and RA, SS & RA and MCTD and overlap syndrome. 4. Patients with previously known malignancies, renal failure and haemolytic anaemia. 5. Patients having any other chronic blood loss like haemorrhoids.

DATA COLLECTION:

- All the data was collected from the patients admitted in the department of general medicine and those patients who attended in-patients and outpatient department with detailed history & thorough physical examinations.
- It included age, sex, nationality, complaints, and duration of symptoms.
- Telephone contact numbers and detailed address were collected for follow up.
- The data from the patient's hematological tests was recorded, documented and analyzed.

Statistical Analysis:
The collected data was entered into Microsoft Excel Worksheet-2010 and data was taken into IBM SPSS Statistic for windows, version 29 (IBM Corp., Armonk, N.Y., USA) software for calculation of frequency, percentage, mean, standard deviation and Probability value. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi Square test with continuity correction for 2 x 2 tables and Fisher's exact test for all 2 x 2 tables, where P value of chi square test was not valid due to small counts. Quantitative data was represented using mean & Standard deviation. Analysis of quantitative data within the groups was done using paired t test if data passes 'Normality test'. One Way Analysis (ANOVA) was used to compare more than two groups. A 'P' value of <0.05 was considered statistically significant.

RESULT

In this study out of 88 cases, 69 were female and 19 were male. The age distribution is shown in Table-1.

Table 1: Age distribution

Age group	Cases	
	No.	%
20-29 years	9	10.2
30-39 years	27	30.7
40-49 years	31	35.2
50-59 years	21	23.9
Total	88	100
Mean S.D.	40.98 years 9.73 years	

The table-2 shows that 2 people out of 88 (5.7%) had mild disease and 43 people (48.9%) has moderate disease. 40 people (45.4%) had severe disease. DAS 28 score ranges from 2.75 to 5.81 with a mean value of 4.8 with standard deviation 0.78.

Table 2: DAS Score 28

DAS Score 28	Cases	
Mild (< 3.1)	5	5.7
Moderate (3.2-5.1)	43	48.9
Severe (> 5.1)	40	45.4
Total	88	100
ScoreRange Mean S.D.	2.75 -5.81 4.8	

	0.78

Rheumatoid factor is positive in 69 cases (78.4%) and negative in 19 cases (21.6%). Serum calcium and uric acid were normal in all patients. 27 patients showed radiological evidence of rheumatoid arthritis. No patients had splenomegaly or significant generalized lymphadenopathy. Among the 44 cases of rheumatoid arthritis 66 cases are anemic (75%) and not anemic in 22 case (25%)Mean hemoglobin level in patients was 10.67+1.83

Table 3: Anemia and rheumatoid factor positivity:

Anemic	46/66
Not anemic	16/22
P value	0.0305 significant

In patients who are anemic, number of rheumatoid factor positivity was 87% and in not anemic patient's rheumatoid factor positivity was only 54%. Mean Hb level in rheumatoid factor positivity was 9.11 gms+2.05 SD. Mean Hb level in rheumatoid factor negativity was 10.23+1.19 SD. On analyzing the above values, anemia is one of the indicator of disease activity and severity of rheumatoid arthritis.

Out of 66 patients 62 patients have elevated ESR out of which rheumatoid factor positive in 60 patients (96.8%) whereas in 22 non anemic patients 20 had elevated ESR of which only 12 are rheumatoid factor positive (60%). The values suggest that the anemic patients have more elevation of ESR and percentage of rheumatoid factor positivity is also more in this group.

Table 4: DAS 28 Score and duration of disease

DAS 28 Score	**Duration of disease (in years)**	
	Mean	**S.D.**
Mild	4.0	-
Moderate	4.88	1.23
Severe	5.7	1.20
'p'	**0.0475 Significant**	

When analyzing the above charts DAS 28 score was correlatedvery well with duration of disease.

Table5: Anemia and DAS 28 Score

Anemia	**DAS 28 Score**	
	Mean	**S.D.**
Absent	6.38	0.95
Present	7.08	0.64
'p'	**0.0065 Significant**	

When analyzing the data, incidence of anemia correlated with activity of disease and anemic patients had higher DAS 28 score than non-anemic patients. P value is significant.

Table 6: Peripheral smear study, Types of anemia and rheumatoid factor positivity

	No.of pts	**Percentage**	**Rheumatoid positivity**	**percentage**
Microcytic hypochromic	18	20.4	18	100
Normocytic normochromic	32	36.4	28	87.5
Dimorphic	15	17.1	12	80
normal	23	26.1	15	65.2

When analyzing the above data 8 patients (20.4%) patients show microcytic hypochromic anemia. Out of 18 patients all shows rheumatoid factor positivity. 32 patients (36.4%) shows normocytic normochromic anemia.

Table 7: DAS 28 Score and Peripheral Smear Study

Peripheral Smear Study	**DAS 28 Score**	
	Mean	**S.D.**
	6.82	**0.41**

	7.44	**0.50**
	6.75	**0.54**
	5.9	**0.55**
'p'	**0.0001 Significant**	

When analyzing the above data, anemic patients have more DAS 28 score than non- anemic patients. Patients with normocytic anemia that means anemia of chronic disease has high DAS 28 score (7.44) than iron deficient patients (6.82) p value is significant 0.001.

Table 8: Clinical and laboratory features of anemic and non-anemic patients:

	Anemic patients		**Not anemic patients**		
	Mean	**S.D**	**Mean**	**S.D**	**P value**
Tender joint count,	12.8	7.50	7.33	5.89	**0.004 significant**
Swollen joint count	8.7	5.82	5.32	6.88	**0.oo6 significant**
Visual analogue scale	68.15	55.2	33.5	45.5	**0.005 Significant**
Hemoglobin	11.75	2.49	14.55	0.79	**0.0001 significant**
Mean corpuscular volume	80.33	10.92	88.44	7.5	**0.0036 significant**
Mean corpuscular hemoglobin	26.55	5.69	29.98	4.4	**0.0033**
					significant
Mean corpuscular hemoglobin concentration	33.09	2.78	34.33	0.85	**0.0071 Significant**

Out of 88 patients 25 patients have leukocytosis (28.4%). No patient had leucopenia. Neutrophilia is present in 56 patients. Lymphopenia is present in 23% of patients.22 patients (25%) have eosinophils >6%. All 22 patients are rheumatoid factor positive. No patients had immature cells or large granular lymphocytes.Clotting time was normal in all patients. No patients had features of hyper viscosity syndrome and no patient had a features of Felty syndrome and no patient had a feature of pure red cell aplasia and no lymphoma and leukemia.

DISCUSSION

Rheumatoid arthritis (RA) is a systemic autoimmune disease primarily affecting the synovial joints but also influencing various extra-articular systems, including the hematological system. [11] Hematological abnormalities in RA patients are common and often correlate with the disease activity, severity, and response to treatment. Understanding the hematological profile in these patients is crucial for diagnosis, monitoring disease progression, and managing complications. [12] Below is a detailed discussion of the key hematological changes observed in RA patients. [13]

Anemia is one of the most common hematological abnormalities in RA, affecting up to 40-60% of patients. Anemia in RA is often multifactorial, with both chronic disease-related mechanisms and medication-induced effects contributing to its development. [14] Anemia of Chronic Disease (ACD): The most common form of anemia in RA is ACD, which results from persistent

inflammation. [15] Pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) induce the production of hepcidin, a liver-derived peptide that reduces iron absorption in the gut and sequesters iron in macrophages. This leads to functional iron deficiency, despite normal or elevated iron stores, impairing red blood cell production in the bone marrow.
[16]

Anemia in RA patients is often associated with fatigue, weakness, and reduced quality of life. It also correlates with more severe disease and poorer treatment outcomes. It is essential to differentiate between anemia of chronic disease and other types of anemia (e.g., iron-deficiency anemia or vitamin B12 deficiency) in order to guide appropriate. [17] RA patients are also at an increased risk for coagulation abnormalities, including a heightened risk of thrombosis. This is partly due to inflammation, which increases the levels of procoagulant factors and decreases anticoagulant proteins. [18]

The hypercoagulable state in RA patients warrants careful management, particularly in those with

additional cardiovascular risk factors. Prophylactic anticoagulation may be considered in high-risk patients, especially in those undergoing surgery, with a history of VTE, or with severe disease activity. [19]

RA therapies, especially disease-modifying antirheumatic drugs (DMARDs), can contribute to bone marrow suppression. Medications like methotrexate, cyclophosphamide, and leflunomide are known to affect hematopoiesis, leading to leukopenia, thrombocytopenia, or even aplastic anemia in rare cases. [20] Monitoring blood counts regularly is crucial to detect these potentially serious side effects early. [21]

The advent of biologic therapies has transformed the treatment landscape for RA. Biologic agents, particularly TNF inhibitors, IL-6 inhibitors, and Janus kinase (JAK) inhibitors, have improved disease control but also carry potential risks for hematological abnormalities. [22] These therapies can impact immune cell function and influence blood counts, sometimes resulting in neutropenia, thrombocytopenia, or an increased susceptibility to infections. [23]

Close monitoring of hematological parameters is necessary for patients receiving biologic therapy, as they may be more prone to developing infections or hematologic complications. Early detection of abnormalities allows for timely intervention and adjustment of treatment. [24]

CONCLUSION

The hematological profile of RA patients is influenced by the underlying disease, the level of inflammation, and the treatment regimen. Anemia, leukocytosis, thrombocytosis, and coagulation abnormalities are common findings, with significant clinical implications. Understanding these changes helps clinicians assess disease activity, predict potential complications, and make informed decisions about treatment. Regular monitoring of hematological parameters is crucial to managing RA effectively, minimizing complications, and improving patient outcomes.

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