

STUDY OF HAEMATOLOGICAL PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS

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ABSTRACT :

INTRODUCTION: Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder of unknown aetiology that may affect many tissues and organs In the previous years, various authors have studied the association between disease activity of RA and these haematological parameters separately. The current study intended to find out the association of DAS 28-score of RA with platelet count, MPV and Hb level so that an assessment of disease activity of RA can be done by these haematological parameters in addition to conventional serological markers so that a better management of the patients of RA can be done.

MATERIAL AND METHODS; patients of rheumatoid arthritis attending rheumatology opd were randomly selected and detail history and examination done. Lab investigation like CBC, ESR, CRP, S.ferritin done.

RESULT: rheumatoid arthritis was more common in female with rheumatoid factor positivity in 80% and prevalence of anemia was 73.3%. Anemia is very well correlated with rheumatoid factor positivity, disease activity (das 28 score),duration of disease and ESR.

CONCLUSION: The anemia is the one of the indicator of disease severity and anemia incidence is more in our Population. It was also observed that thrombocytosis and eosinophilia also the indicators of disease severity which positively correlated with DAS 28 score.

KEY WORDS: RHEUMATOID ARTHRITIS(RA), DAS SCORING ,ANEMIA

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder of unknown aetiology that may affect many tissues and organs but principally attacks the joints symmetrically producing a non-suppurative proliferative and inflammatory synovitis. Regarding clinical course of the disease, vast majority of the patients exhibit a pattern of persistent and progressive disease activity that wax and wane in intensity over time. In clinical practice, there is general agreement that rheumatoid inflammation should be controlled as soon as possible, as completely as

possible, and that control should be maintained for as long as possible consistent with patient safety.[1]

As the goal of treatment is to control rheumatoid inflammation, it is clear that the management of RA should include systematic and regular quantitative evaluation of disease activity. So an accurate, valid and reliable method for assessment of disease activity is one of the most important issues for guiding the treatment protocol during management of the RA patients.

Several composite indices have been developed to assess clinical disease activity like SDAI (Simplified Disease Activity Index), CDAI (Clinical Disease Activity Index), DAS 28 and DAS 28-3 score (Modified Disease Activity Score). Among these DAS 28-3 (using three variables-tender joint count, swollen joint count and ESR) score system is the most commonly used parameter now-a-days to measure the disease activity as it is extensively validated and clinically interpretable[2] but it is mainly dependent on clinical findings. In this era of evidence based clinical practice, addition of laboratory based investigations like some haematological parameters including Haemoglobin (Hb) level, Platelet count and Mean Platelet Volume (MPV) which are found to be altered in this chronic inflammatory disease can further improve the assessment status of disease activity.

In the previous years, various authors have studied the association between disease activity of RA and these haematological parameters separately. Most of them found inverse relationship between disease activity and Hb level and thrombocytosis with high disease activity. But data regarding MPV is not conclusive. However, evidences have shown an important role of MPV as a marker of inflammation and disease activity. But there is hardly any study which provided the association between these three haematological parameters altogether and markers of disease activity in RA on the basis of reliable index like DAS 28-3 score specially in Eastern region of India.

The current study intended to find out the association of DAS 28-score of RA with platelet count, MPV and Hb level so that an assessment of disease activity of RA can be done by these haematological parameters in addition to conventional serological markers so that a better management of the patients of RA can be done.

AIMS AND OBJECTIVES

1. To study the hematological status in patients with rheumatoid arthritis.
2. To find out the prevalence of anemia in these patients and its correlation with seropositivity and disease activity which is measured by DAS 28 score (Disease activity score).
3. To know the prevalence of iron deficiency anemia and anemia of chronic disease among anemic patients of rheumatoid arthritis and its correlation with disease activity i.e DAS 28 score.
4. To analyse other hematological parameters and its correlation with DAS 28 score.

MATERIALS AND METHODS

STUDY LOCATION: Department of Medicine, V.S. hospital, NHL Medical College, Ahmedabad from January 2017-August 2018

STUDY POPULATION: Patients attending Rheumatology OPD randomly selected after proper consent and explaining in detail about the study to be undertaken.

INCLUSION CRITERIA:

- Patients with rheumatoid arthritis satisfied the American Rheumatologic association criteria 1987,
- Age group 20 to 60 years .
- Duration of disease more than 1 year.

EXCLUSION CRITERIA:

- Previously diagnosed anemia and treated
- Previously have any other bleeding disorder not related to Rheumatoid arthritis
- Those who have mixed disorder like SLE and RA; SS & RA and MCTD and overlap syndrome.
- Previously known malignancies, renal failure, hemolytic anemia
- Any other chronic blood loss like hemorrhoids.

SAMPLE SIZE: 75 patients of rheumatoid arthritis were selected on random basis for the study from rheumatology clinic, V.S. hospital, Ahmedabad

METHOD OF DATA COLLECTION:

The selected patients were evaluated with following parameters:

1. History of the patient
2. General examination
3. Systemic examination
4. Laboratory parameters
5. Who grading for anemia and DAS28 score
- 6.

METHODOLOGY:

History:

- Demographic details
- Duration of disease
- history of drug intake
- time of onset of symptoms noted.

Presence of joint swelling, tenderness and deformities and number of tender joints and number of joint swelling noted. Rheumatological functional class was assigned clinically.

General examination:

- Pallor
- Rheumatoid nodule
- lymphadenopathy was undertaken.

Systemic examination:

All systems were examined carefully and visual analogue pain score was carefully assessed.

LABORATORY PARAMETERS:

Hemoglobin, Red blood cell count, White blood cell count , Hematocrit, Differential count, MCV, MCH, MCHC, Platelet count, RDW, MPV, Serum ferritin, Total iron binding capacity, Serum iron, Peripheral smear, Bleeding time, Clotting time, ESR, Rheumatoid factor, anti CCP, C reactive protein, random blood Sugar ,S.urea, S.creatinine, serum protein, albumin and globulin were done in laboratory.

GRADING SYSTEM:

WHO grading of severity of anemia:

Non anemic: more than or equal to 11 gm/dl

Mild: 9.0-10.9 gm/dl

Moderate: 7-9.0 gm/dl

Severe: less than 7 gm/dl

DAS 28 score

Disease activity score is a composite score using tender and swollen joints count, ESR and patient's global assessment activity using 0 (no pain) to 100 (worst pain) mm (line) visual analogue scale.

$DAS28 = 0.56\sqrt{(\text{no of tender joints})} + 0.28\sqrt{(\text{no. of swollen joints})} + 0.70 \log(ESR) + 0.014(\text{global assessment in mm}).$

Classification:

- Mild < 3.1
- Moderate 3.2-5.1
- Severe > 5.1 (Minimum score : 0; Maximum score : 9)

Parameters used in Disease activity score:

- Total 28 joint count for tenderness
- Total 28 joint for swelling
- ESR in mm in first hours
- Patient assessment of global health using a 100mm visual analogue scale ranging from 0(very good) to 100 (very poor)

28 joint counts:

- Shoulders (2)
- Elbows (2)
- Wrists (2)
- MCP for 4 fingers (8)
- MCP thumb (2)
- PIP for 4 fingers and thumb (10)
- Knees (2)

Data analysis was done using epidemiological software.

Results:**Table 1: age wise distribution of patients with rheumatoid arthritis**

Age group	No of Patients
20-29	9 (12%)
30-39	20 (26.6%)
40-49	27 (36%)
50-59	19 (25.4%)
Total	75 (100%)

In this study of 75 patients ,the age of the patients was from 20-60 years with an average of 40 years and more cases from 40- 49 years of age group (27%) with 60(80%) are females and 15(20%) are males. The Female : male ratio was 4:1.

Table 2: das 28 score wise distribution of patients with rheumatoid arthritis

DAS score 28	No of Patients
Mild	03 (04%)

Moderate	39 (52%)
Severe	33 (44%)
Means DAS Score	4.64 ± 0.88
Total	75 (100%)

This table shows that 3 people out of 75 (4%) had mild disease and 39 people (52%) has moderate disease, While 33 people (44%) had severe disease. DAS 28 score ranges from 2.75 to 5.81 with a mean value of 4.64 ± 0.88 .

Table 3: duration of illness and patients with anemia

Duration of years	No of Patients with anemia
1 year	10 (13.3%)
2 years	23 (30.6 %)
3 years	19 (25.3%)
4 years	20 (26.6%)
5 years	3 (4%)
Mean years	2.77 ± 1.10

In the present study, among the rheumatoid arthritis patients 30.60% of patients were diagnosed with anemia within 2 years of illness. The maximum number of patients was having duration of illness of rheumatoid arthritis between 2 to 4 years in patients with anemia. The duration of illness ranged from 1 year to 5 years with an average of 2.77 ± 1.10 years.

TABLE 4: RHEUMATOID FACTOR POSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Rheumatoid factor	No of Patients	% of Patients
Positive	60	80%
Negative	15	20%
Total	75	100%

TABLE 5: ANEMIA AND RHEUMATOID ARTHRITIS

	No of Patients	% of Patients
Anaemic	55	73.3%
Not-Anaemic	19	26.6%

Anemia is defined as <11gm/dl as per WHO guidelines of anemia. Among the 75 cases of rheumatoid arthritis 55 cases are anemic (73.3%) and not anemic is 19 case (26.6%). Mean haemoglobin level in anemic patients was 9.49 ± 2.25 .

TABLE 6: ANEMIA AND RHEUMATOID FACTOR POSITIVITY WITH DAS 28 SCORE

	Anemic (n=55)	Not-Anemic (n=19)	P value
Rheumatoid factor (+)	48	12	0.0092
Rheumatoid factor (-)	7	8	
Mean Hb	8.64 ± 22.47	12.94 ± 2.45	<0.0001
TC	11148 ± 3293.1	10110 ± 3226.1	0.2377
Eosinophils	4.80 ± 4.57	3.88 ± 4.71	0.4553
Neutrophils	67.10 ± 7.87	67.32 ± 9.76	0.9217
DAS 28 Score	4.97 ± 0.88	4.42 ± 0.84	0.0283

In patients who are anemic, number of rheumatoid factor positivity was 87.2% and in not anemic patient's rheumatoid factor positivity was only 60%.

Mean Hb level in rheumatoid factor positivity was 9.59 ± 2.20 and rheumatoid factor negativity was 11.06 ± 2.45 . There was no significant co-relation found between neutropenia and anemia. But it was found that patients with high disease activity score and on multiple drugs had neutropenia, making drug induced neutropenia a likely explanation for the same. When analysing the above values, anemia is one of the indicator of disease activity and severity of rheumatoid arthritis. When analysing the data incidence of anemia correlated with activity of disease and anemia, patients had higher DAS 28 score than non-anemic patients ($p < 0.05$).

TABLE 7: PERIPHERAL SMEAR STUDY**TYPES OF ANEMIA AND RHEUMATOID FACTOR POSITIVITY**

Type of Anemia	No of Patients	Rheumatoid positivity
Microcytic hypochromic	13 (17.3%)	13 (100%)
Normocytic normochromic	34 (45.3%)	29 (85.2%)
Dimorphic	9 (12%)	8 (88%)
Normal	19 (25.3%)	10 (52.6%)
Total	75 (100%)	60

When analysing the above data 13 patients (17.3%) show microcytic hypochromic anemia. Out of 13 patients all shows rheumatoid factor positivity. 34 patients (45.3%) shows normocytic normochromic anemia. Out of 34 patients 29 patients (85.2%) were rheumatoid factor positive. 9 patient's showed dimorphic anemia. Out of 9 patients 8 patients shows (88%) rheumatoid factor positive. But p value is >0.05 not significant. That means the type of anemia doesn't correlate with rheumatoid factor positivity.

TABLE 8 : DAS 28 SCORE AND PERIPHERAL SMEAR STUDY

Peripheral Smear Study	Avg DAS 28 Score	P Value
Microcytic hypochromic anemia	4.64 ± 0.59	<0.0001
Normocytic normochromic anemia	5.29 ± 0.61	
Dimorphic anemia	4.52 ± 0.93	
Normal(non anemic)	3.67 ± 0.64	

When analysing the above data anemia patients has more DAS 28 score than non anemic patients(3.67). Patients with normocytic anemia that means anemia of chronic disease has high DAS 28 score (5.29) than iron deficient patients (4.67) where p value is significant 0.001.

TABLE 9: DAS 28 SCORE AND RHEUMATOID FACTOR

Rheumatoid Factor	DAS 28 Score
Positive	4.84 ± 0.87
Negative	3.82 ± 0.62

When analysing the above data rheumatoid factor positive patients have higher DAS 28 score than rheumatoid factor negative patients.

TABLE 10 : CLINICAL AND LABORATORY FEATURES OF ANEMIC AND NON-ANEMIC PATIENTS

	Anemic patients	Non Anemic patients	P value
Tender joint count,	10.84 ± 3.21	5.18 ± 1.27	<0.0001
Swollen joint count	6.30 ± 2.21	2.13 ± 0.71	<0.0001
Hemoglobin	8.51 ± 1.28	13.06 ± 1.11	<0.0001
Mean corpuscular volume	77.84 ± 10.76	84.8 ± 7.88	0.0187
Mean corpuscular hemoglobin	24.91 ± 4.14	28.53 ± 2.75	0.0166
Mean corpuscular hemoglobin Concentration	30.89 ± 1.99	30.94 ± 2.10	0.9300

In this study MCV and MCH have higher values in non-anemic patients than anemic patients (P<0.01). In DAS 28 score by using the variables like swollen joints and tender joints and ESR. ESR already shows the highly significant correlation with anemia and rheumatoid factor positivity and disease activity. Swollen joints and tender joints correlation with anemia was highly significant. P value was <0.05.

TABLE 11: RELATIONSHIP BETWEEN DAS 28 SCORE AND HEMATOLOGICAL PARAMETERS

Parameter	Value for cases with DAS 28 Score			P value
	Mild	Moderate	Severe	
PLT	3.20 ± 0.30	3.69 ± 0.97	3.93 ± 0.94	<0.0001
Eosinophil	0.33 ± 0.57	3.33 ± 3.61	6.24 ± 5.21	<0.0001
CRP	27 ± 41.74	28.2 ± 27.1	46.97 ± 25.73	<0.0001
Ferritin	46.33 ± 28.02	50.39 ± 47.81	119.33 ± 77.76	<0.0001
ESR	30 ± 13.12	46.84 ± 13.09	63.03 ± 22.51	<0.0001

When analyzing the above data ESR, CRP, platelet count, eosinophil count and ferritin are well correlated with disease activity. It was found that if ESR, CRP and platelet count and eosinophil and ferritin was high, disease activity and DAS28 score was also high. All the other parameters did not correlate with DAS 28 score.

DISCUSSION

Rheumatoid arthritis is a chronic, systemic, inflammatory disorder of unknown etiology that has a pattern of diarthrodial joint involvement. Its primary site of pathology is the synovium of joints. The rheumatoid factor positivity and extra articular manifestations commonly accompany the joint disease, but arthritis is the major manifestation.

In our study we selected 75 cases of rheumatoid arthritis on random basis as per the American rheumatism association guidelines 2015.

TABLE 12 : SEX WISE DISTRIBUTION OF RA IN DIFFERENT STUDIES

Study	Male	Female
Premkumar et al	22.67%	73.1%
Our Study	20%	80%

The sex distribution in this study, is predominantly affects females in a ratio of 4:1. In our study males are 20% and females are 80% with mean age of 42.52 years. **PremKumaret al[3]** in his study males are 22.67% and females are 73.1%. Mean age is 48.1 years. Moreover, in his study the risk of developing disease is greatest between 40 and 50 years. In our study the risk also is between 40 to 49 years around 36%.

TABLE 13 : DURATION OF RA & DAS 28 SCORE

Study	DAS 28 Score	Duration
R. Arul et al	4.8 + 0.8	> 3 Years
Present Study	4.64 + 0.8	> 3 Year

R Arul[4] et al in their study the severity of disease is in positive correlation with duration of disease. In this study patients who had disease more than 3 year have more DAS 28 score. The p value is significant and this shows that duration of disease is directly proportional to the severity

of disease. In their study the mean DAS28 score was 4.8 ± 0.8 . In this study mean DAS 28 score was 4.64 ± 0.88 .

R Arul[4] et al in their study reported 4.5% patients had mild DAS 28 score and 52.3% has moderate DAS 28 score and 45.5% patients had severe DAS 28 score. In this study patients with mild DAS28 was around 4% and moderate score was 52% and severe 44%. This states that most of the patients are in moderate severity. In his study rheumatoid factor positivity was 80% and negativity 20%. In this study RF positivity was 80% while 20 % RF was negative. The ratio of rheumatoid factor positivity to negativity is 4:1

TABLE 14 : MEAN Hb LEVEL IN PATEINTS OF RA IN DIFFERENT STUDIES

IL Okoroiwu et al	9.6 gm%
Present Study	10.06 gm%

IL Okoroiwu et al in their study, mean hemoglobin in rheumatoid arthritis patients was 9.6 gm% and in this study mean Hb is 10.06 gm%.

D.J. Borah et al [5] in their study, out of 20 anemic patients 18 patients were rheumatoid factor positive (90%) and in non-anemic patients out of 11 patients 6 patients (54%) were rheumatoid factor positive. In this study, out of 48 anemic patients 55 patients are rheumatoid factor positive (87.2%) and in non-anemic 8 patients patients, 7 (60%) are rheumatoid factor positive. This states that anemia is very well correlated with rheumatoid factor positivity and disease activity.

TABLE 15 : MEAN DAS 28 SCORE & ANEMIA IN RA PATIENTS

Study	Anemia	DAS 28 Score
S. Agarwal et al	Anemic	5.13
Present Study	Anemic	4.97

S Agarwal et al[6] in their study, mean DAS 28 score in non-anemic patients was 3.83 compared to anemic patients which was 5.13. In this study in non-anemic patients mean DAS 28 score is 4.42 and in anemic patients 4.97.

Anemia was defined as hemoglobin level of less than 11 g/dl. The prevalence reported in RA patients from Western countries which varies from 33.3 to 59.1% although the cutoff hemoglobin value used to define anemia in these studies was higher than our study. This is possibly related to high background prevalence of anemia in general adult Indian population as well as poor access to medical care leading to poor disease control of RA.

Serum ferritin is a reliable parameter to predict bone-marrow iron stores in uncomplicated anemic states. However, in chronic inflammation, ferritin is increased as a part of acute-phase reaction and hence determining a cutoff level to differentiate between iron-replete and depleted state becomes difficult. The value of serum ferritin indicative of iron-deficient state in various studies range from 30 to 70 µg/l. Bone-marrow iron staining is considered as the gold-standard in such conditions. However, the procedure is invasive, time-consuming and expensive.

In this study iron deficiency anemia patients are less (24.5%) because iron deficient anemia with inflammation (Dimorphic anemia) is included separately (12%) and there is a probable folic acid and/or VitB12 deficiency .

K Yildirim, et al in his study, mean ESR was 36.6 ± 23.5 .In their study ferritin was 121.3 ± 34.2 , ESR ,CRP and ferritin showed significant correlation with disease activity as well as DAS 28 score .The p value was significant <0.001 . In this study mean ESR is 53.29 ± 22.3 and ferritin is 100.56 ± 49.93 .

S Agarwal et al[6] This study well correlated with disease activity and the p value was 0.006 for ESR and 0.0001 for CRP and ferritin respectively .

J. Borah et al[5] and **S Agarwal et al[6]** in their study, the variables used in calculating DAS 28 score like tender joint count, swollen joint count, ESR and visual analogue scale was correlated significantly. The p value was more significant in anemic patients than non-anemic patients.

SUMMARY AND CONCLUSION

- Sex ratio of females to males in this study is 4:1
- The risk of developing rheumatoid arthritis is greatest between 40 to 49 years.
- Rheumatoid factor positivity is 80% and rheumatoid factor negativity is 20%
- The prevalence of anemia in rheumatoid arthritis patients is 73.3%.
- Duration of disease more than 3 years increases the chances of anemia.
- In rheumatoid factor positive patients mean Hb values is less ($9.59\text{gm}\%$) compared to rheumatoid factor negative patients ($11.06\text{gm}\%$).
- The prevalence of rheumatoid arthritis according to DAS 28 score categories in decreasing order are moderate 52% , severe 44% and mild 4%.
- Anemia is very well correlated with rheumatoid factor positivity, disease activity (DAS 28 score), duration of disease and ESR.
- Rheumatoid factor, ESR, CRP and ferritin positively correlates with DAS 28 score significantly.
- Thrombocytosis is present in 31% of patients and eosinophilia is present in 27% of patients and very well correlated with DAS 28 score.
- 29.5% have leukocytosis while leucopenia is present in 20% of RA patients.
- Bleeding time and clotting time are normal among all patients.

The anemia is the one of the indicator of disease severity and anemia incidence is more in our Population. Anemia of chronic diseases is more common than iron deficiency and dimorphic anemia among rheumatoid arthritis patients. It was also observed that thrombocytosis and eosinophilia also the indicators of disease severity which positively correlated with DAS 28 score; like ESR, CRP, rheumatoid factor and ferritin.

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