

Study Of Hematological Profile In Rheumatoid Arthritis Patients

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Abstract

Introduction

Of the systemic lesions caused by rheumatoid arthritis, anemia and a focal subcutaneous granuloma are the most characteristic. Our aim is to study the hematological status in patients with rheumatoid arthritis and 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).

Methods: It is a cross-sectional prospective study using convenient simple random sampling of 44 patients attending the rheumatology clinic in Coimbatore medical college hospital over a period of one year.

Results: Sex ratio of females to males in this study is 4:1. The risk of developing disease 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 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 52.3%, severe 45.5% and mild 4.5%. Anemia is very well correlated with rheumatoid factor positivity, disease activity (DAS 28 score), duration of disease and ESR. Microcytic hypochromic anemia (iron deficiency anemia) is present in 25% of anemic patients and anemia of chronic disease (normocytic normochromic) anemia is present in 60% of anemic patients and dimorphic anemia in 15% anemic patients. Patients with anemia of chronic disease have higher disease activity (DAS 28 score) than iron deficiency anemia patients in rheumatoid arthritis. 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.

Conclusion: The clinical and hematological profile of the patients with rheumatoid arthritis is studied. In this study, attempt has been made to analyze the risk factors and outcome of anaemia on the severity of rheumatoid arthritis based on the DAS28 score.

I. Introduction

Rheumatoid Arthritis (RA) is the most common form of chronic inflammatory joint disease. It is a symmetrical, non-supportive polyarticular disease unique to modern man.¹ Rheumatoid arthritis affects the synovial joints, but it is not confined to them and the many visceral manifestations have led to the classification of RA as a systemic disorder of the immunological mechanism. Of the systemic lesions, anemia and a focal subcutaneous granuloma are the most characteristic. Some cases of RA, particularly those that are seropositive, are fulminating and rapidly progress to severe deformity.¹ Our aim is to study the hematological status in patients with rheumatoid arthritis and 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).

II. Materials And Methods

It is a cross-sectional prospective study using convenient simple random sampling of 44 patients attending the rheumatology clinic in Coimbatore medical college hospital over a period of one year. Ethical committee clearance was obtained from the hospital.

Inclusion criteria:

- 1) Patients who satisfied the American Rheumatologic association criteria 1987, irrespective of hematological signs present or not.
- 2) Age group 20 to 60 years irrespective of sex.
- 3) duration of disease upto 5 years.

Exclusion criteria:

- 1) Previously diagnosed anemia and treated
- 2) Previously have any other bleeding disorder not related to Rheumatoid arthritis.

- 3) Those who have mixed disorder like SLE and RA ;SS& RA and MCTD and overlap syndrome.
- 4) Previously known malignancies, renal failure, hemolytic anemia any other chronic blood loss like hemorrhoids

Data analysis was done using epidemiological information statistical software. Using the software the frequencies, mean, standard deviation and p values calculated with yate's test for qualitative variables and kruskal wallis chi square test for quantitative variables. p value <0.05 is taken as significant.

DAS 28 score

Disease activity score is a composite score using tender and swollen joints count , ESR and patients global assessment activity using a 100 mm visual analogue scale.

Classification

Mild <3.1

Moderate 3.2-5.1

Severe >5.1 (Minimum score: 0; Maximum score : 9)

III. Results

In this study out of 44 cases, 35 were female and 9 were male. The age distribution is shown in Table-1.

Table 1: Age distribution

Age group	Cases	
	No.	%
20-29 years	5	11.4
30-39 years	12	27.3
40-49 years	16	36.4
50-59 years	11	25
Total	44	100
Mean	40.98 years	
S.D.	9.73 years	

The table-2 shows that 2 people out of 44 (4.5%) had mild disease and 23 people (52.3%) has moderate disease. 20 people (45.5%) 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)	2	4.5
Moderate (3.2-5.1)	23	52.3
Severe (> 5.1)	20	45.5
Total	44	100
Score		
Range	2.75 -5.81	
Mean	4.8	
S.D.	0.78	

Rheumatoid factor is positive in 35 cases (79.5%) and negative in 9 cases (20.5%). Serum proteins were normal. There was no reversal of albumin / globulin ratio and there was no hyperglobulinemia noticed in the study .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. Concomitant usage of NSAIDS 80% and corticosteroids 40% and methotrexate 4% was present.

Among the 44 cases of rheumatoid arthritis 33 cases are anemic (75%) and not anemic in 11 case (25%) Mean hemoglobin level in patients was 10.67+1.83

Table 3: Anemia and rheumatoid factor positivity:

Anemic	26/33
Not anemic	6/11
P value	0.0305 significant

In patients who are anemic, number of rheumatoid factor positivity was 87% and in not anemic patients 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.

Anemic and non-anemic patients were comparatively studied with their erythrocyte sedimentation rate levels and seropositivity for rheumatoid factor. Out of 33 patients 32 patients have elevated ESR out of which rheumatoid factor positive in 29 patients (90.6%) whereas in 11 non anemic patients 10 had elevated ESR of which only 6 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	2.0	-
Moderate	2.83	1.17
Severe	3.5	1.16
'p'	0.0471 Significant	

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

Table 5: Anemia and DAS 28 Score

Anemia	DAS 28 Score	
	Mean	S.D.
Absent	4.32	0.91
Present	5.04	0.58
'p'	0.0060 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	8	18.2	8	100
Normocytic normochromic	20	45.5	17	85
Dimorphic	5	11.4	4	80
normal	11	25	6	54

When analyzing the above data 8 patients (18.2%) patients show microcytic hypochromic anemia. Out of 8 patients all shows rheumatoid factor positivity. 20 patients (45.5%) shows normocytic normochromic anemia.

Table 7: DAS 28 Score and Peripheral Smear Study

Peripheral Smear Study	DAS 28 Score	
	Mean	S.D.
Microcytic hypochromic anaemia	4.77	0.35
Normocytic normochromic anaemia	5.38	0.46
Dimorphic anemia	4.71	0.48
Normal	3.8	0.51
'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 (5.38) than iron deficient patients (4.77) p value is significant 0.001.

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

	Anemic patients		Not anemic patients		P value
	Mean	S.D	Mean	S.D	
Tender joint count,	10.4	5.45	5.27	3.85	0.004 significant
Swollen joint count	6.5	3.78	3.28	4.82	0.006 significant
Visual analogue scale	66.10	53.1	31.2	43.3	0.005 Significant
Hemoglobin	9.72	1.43	12.49	0.75	0.0001 significant
Mean corpuscular volume	78.27	8.87	86.42	5.3	0.0036 significant
Mean corpuscular hemoglobin	24.51	3.63	27.92	2.2	0.0033

					significant
Mean corpuscular hemoglobin concentration	31.08	1.73	32.27	0.81	0.0071 Significant

In this study MCV, Hb, MCH and MCHC have higher values in anemic patients than non-anemic patients. p value was significant . In DAS 28 score we are using the variables like swollen joints, tender joints, visual analogue scale and ESR. ESR already shows the highly significant correlation with anemia and rheumatoid factor positivity and disease activity. Swollen joints and tender joints and visual analogue scale with anemia correlation were highly significant. P value was <0.05.

Out of 44 patients 13 patients have leukocytosis (29.5%). No patient had leucopenia. Neutrophilia is present in 36 patients. Lymphopenia is present in 23% of patients.12 patients (27%) have eosinophils >6%. All 12 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.

IV. Discussion

In our study we selected 44 cases of rheumatoid arthritis on random basis as per the American rheumatism association guidelines 1987. The sex distribution in this study, is predominantly affects females in a ratio of 4:1. Mean age is 58.5 years. In our study is 40.98 years. Navarocarogregioet al⁽³⁷⁾ and Abach, R.R. Buchanan et al⁽³⁸⁾ 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.

B.Fleeb, L.Andel, J.Sautner et al⁽³⁹⁾ in their study the mean DAS 28 score was 4.23+1.2 .In this study mean DAS 28 score was 4.8+0.78. In this study patients with mild DAS 28 was around 4.5% and moderate score was 52.3% and severe 45.5%. This states that most of the patients are in moderate severity. Card Richard et al⁽⁴¹⁾ in his study rheumatoid factor positivity was 80% and negativity 20%. In this study RF positivity was 79.5% and while 20.5% RF was negative . The ratio of rheumatoid factor positivity to negativity is 4:1. Tracey Houston et al⁽⁴²⁾ in their study ,mean hemoglobin in rheumatoid arthritis patients was 9.57 gm% and in this study mean Hb is 10.6gm%.

M. Kar, S. Roy et al⁽⁴³⁾ in their study, mean hemoglobin level in rheumatoid positivity patients was 9.57gm% and 10.45gm%. Among rheumatoid negative patients. In this study mean Hb level in rheumatoid factor positive patients is 9.11+2.05 and mean Hb among rheumatoid factor negative is 10.23+1.19 gm%. This states that anemia is very well correlated with rheumatoid factor positivity and disease activity.

Agarwal Sumeet et al⁽⁴⁵⁾ 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 4.32 and in anemic patients 5.04. D J Borah ,Farhis Iqbal et al⁽⁴⁴⁾ in their study, in non-anemic patients mean DAS 28 score was 4.76 while anemic patients it was 6.85.This states that anemic patients have more DAS score and disease activity than non anemic patients.

Agarwal Sumeet et al⁽⁴⁵⁾ in their study, of rheumatoid arthritis patients with iron deficiency anemia DAS 28 score was 4.7 and in patients with anemia of chronic disease DAS 28 score was 5.69 . In this study patients with iron deficiency DAS 28 score was 4.77 and in anemia of chronic disease was 5.38. The p value is significant(0.001) .This states that DAS 28 score is higher in ACD than in IDA.

In this study iron deficiency anemia patients are less (24.5%) because iron deficient anemia with inflammation(Dimorphic anemia)is included separately(15%) and there is a probable folic acid and/or Vit B12 deficiency. Microcytosis (<80 femtolitre) in this study is 27% patients among rheumatoid arthritis patients .Alexander et al⁽⁸⁾ in their study showed 30% prevalence of microcytosis.

Hypochromia (less than 26pg) is present in 38% of rheumatoid arthritis patients in this study. Caris J Bastley et al⁽⁵⁵⁾ reported 50% hypochromia in their study.

Sumeet Agarwal et al⁽⁴⁵⁾ and D J Borah , Fahler Iqbalet al⁽⁴⁴⁾ 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 .In this study also all the 4 variables shows high significance in anemic patients compared to non anemic patients. Agarwal et al⁽⁴⁵⁾ in their study; tender joint count , swollen joint count , ESR and visual analogue scale in patients with anemia of chronic disease showed higher value than iron deficiency anemic patients. Similar results were obtained in all the variables showing higher significance in patients with anemia of chronic disease than iron deficiency anemic patients in this study. The p value is significant.

Hutchuson et al⁽⁵⁷⁾ and Dulaguistet al⁽⁵⁸⁾ in their study thrombocytosis in rheumatoid arthritis was 52% and 60% respectively AtofSelross et al⁽⁵⁹⁾ in their study ;thrombocytosis was present in 33% of patients and it correlated with disease activity. In our study thrombocytosis is present in 31%. Patients with thombocytosis have higher DAS 28 score with significant p value.

Agarwal Sachdevet *al*⁽⁶³⁾ reported pure red cell aplasia and immune thrombocytopenia. In this study no patients had thrombocytopenia and pure red cell aplasia. No patient had decreased red cell distribution width. Abach,R,R,Buchnanet *al*⁽³⁸⁾ reported a hyperviscosity syndrome in rheumatoid arthritis. In this study no patient had symptoms suggestive of hyperviscosity syndrome.

Paraiaz ,Fayazetal⁽³³⁾ study none of the patient of rheumatoid arthritis had evidence of bleeding and DIC. An only isolated abnormality of coagulation was present. Protein C and protein S was low in 1case each while decreased factor VIII level was detected in 5 cases. Hypofibrinogenemia was demonstrated in 1 case. All patients had normal factor IX level. In this study no patient had evidence of bleeding and abnormal bleeding time as well as clotting time.

V. Conclusion

Sex ratio of females to males in this study is 4:1. The risk of developing disease 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 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 52.3% , severe 45.5% and mild 4.5%. Anemia is very well correlated with rheumatoid factor positivity, disease activity (DAS 28 score) ,duration of disease and ESR.

Microcytic hypochromic anemia (iron deficiency anemia) is present in 25% of anemic patients and anemia of chronic disease (normocytic normochromic) anemia is present in 60% of anemic patients and dimorphic anemia in 15% anemic patients. Patients with anemia of chronic disease have higher disease activity (DAS 28 score) than iron deficiency anemia patients in rheumatoid arthritis. 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 none of the patients have leucopenia. Lymphopenia is present in 20% of RA patients. Bleeding time and clotting time are normal among all patients .

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