



Prevalence of Hematological Manifestations in Seropositive Rheumatoid Arthritis in a Tertiary Care Centre in South Kerala

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ABSTRACT

Rheumatoid arthritis is a systemic inflammatory disease, affecting 1-2% of the population worldwide. Most chronic inflammatory rheumatic diseases are complicated by hematologic abnormalities. Patients with rheumatoid arthritis (RA) may suffer from a variety of hematologic disorders, particularly anemia, leukopenia, and thrombocytosis.

Aim: To study the prevalence of hematological manifestations in patients with seropositive Rheumatoid Arthritis in a tertiary care centre in South Kerala.

Materials and Methods: A cross sectional study was conducted among 50-60 seropositive Rheumatoid arthritis patients who have visited the Medicine OP of the institution over a period of 1 year. After detailed clinical examination, a complete haemogram, ESR, Peripheral smear, Serum Ferritin, TIBC and Stool Occult Blood were done in these patients. Data was analyzed using SPSS version 16.

Results: Among the 50 patients enrolled in the study most common hematological manifestation was anaemia which was seen in 60% of the patients. Iron deficiency anemia was more prevalent than anemia of chronic disease which was found in 33% of the patients with seropositive Rheumatoid arthritis. Anaemia was common in patients with disease duration more than 5 years. 2% of the patients had thrombocytosis. Another finding was the high prevalence of stool occult positivity in Iron deficiency anemia indicating that chronic GI blood loss due to drug induced gastritis may be the cause for iron deficiency anemia.

Conclusion: The most common type of hematological abnormality in Rheumatoid arthritis is anemia and most common type is Iron deficiency anemia. So early screening, diagnosis and appropriate treatment will reduce the incidence and thus reduce the mortality associated with hematological manifestations with rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Hematological manifestations, Anemia.

BACKGROUND

Rheumatoid arthritis (RA) is the most common inflammatory joint disease, affecting 1-2% of the population worldwide, with women affected two to three times more commonly than men¹. Rheumatoid arthritis is a systemic inflammatory disease that can involve other tissues and organs as well as synovial joints. Rheumatoid arthritis can also affect non-articular muscular structures such as tendons, ligaments, and fascia.

Extra-articular manifestations are all the conditions and symptoms which are not directly related to the locomotor system²⁻⁵. Recent epidemiologic studies of extra-articular RA manifestations have emphasized their major role as predictors of premature mortality in patients with RA^{3,4}. Extra-articular RA is a serious condition, and rheumatoid arthritis patients with extra-articular manifestations should be aggressively treated and monitored⁶. Extra-articular manifestations of RA occur in about 40% of patients, either in the beginning or during the course of their disease⁷.

Systemic features in RA are frequent, mostly related to vasculitis, and often a reflection of longstanding inflammation. Most organs can be involved^{8,9}. These manifestations occur as frequent in men as in women, and may appear at any age. Many of these manifestations are related to the more active and severe RA, so early and more aggressive RA drug therapies are being employed and, although evidence from randomized studies is not available, this approach would seem appropriate in view of the adverse effect of extra-articular manifestations on RA outcomes^{3,4,10,11}.

Patients with RA, who have high titers of rheumatoid factor i.e., auto antibodies to the Fc component of immunoglobulin G are most likely to have extra-articular manifestations of their disease, including rheumatoid nodules, rheumatoid vasculitis, and pleuropulmonary, neurologic, digestive, cardiovascular, cutaneous, hematologic, and ocular complications^{12,13,14}. The prevalence of extraarticular manifestations of RA

has declined in recent years, with the timing and pattern of the decline indicating that disease-modifying RA treatments maybe changing the natural history of the disease.

HAEMATOLOGIC MANIFESTATIONS

Patients with RA may present with haematological abnormalities either at the time of diagnosis, or during the course of their illness. Haematological manifestations in RA can be broadly categorized into areas of anaemia, neutropenia, thrombocytopenia, thrombocytosis, eosinophilia, and haematological malignancies¹⁵. Anaemia is, by far, one of the most common extra-articular symptoms of RA. The cause of anaemia in RA is multifactorial-disease activity, drug-induced, nutritional, gastrointestinal bleed, bone marrow suppression, and ineffective erythropoiesis¹⁶. Anaemia of chronic disease is observed in RA, where it usually correlates with the disease activity, particular the degree of articular inflammation. It is normochromic and normocytic. Eosinophilia in RA reflects active disease or hypersensitivity to drugs¹⁷. Thrombocytosis is a frequent finding in active RA and is correlated with the number of active inflamed joints¹⁸.

The extraarticular manifestations in rheumatoid arthritis are associated with a high mortality rate. So early identification and appropriate treatment can significantly decrease mortality rate associated with extrarticular manifestations of RA. So knowing about its prevalence is important so as to suspect and diagnose these conditions early with minimum investigations. The present study is for finding the prevalence of hematological manifestations in seropositive rheumatoid arthritis and thus identifies the burden of it in our society.

OBJECTIVES OF THE STUDY

PRIMARY OBJECTIVE

To study the prevalence of hematological manifestations in patients with seropositive Rheumatoid arthritis.

SECONDARY OBJECTIVE

To study its relation with the duration of illness

Study design: Cross sectional study

Study period: 1 Year from date of ethical clearance

Sample size: All patients coming to Govt. TD medical college, Alappuzha during one year period. Expected patients during this study time are 50-60.

STUDY VARIABLES

Cases were diagnosed according to 2010 Revised ACR-EULAR criteria for diagnosis of rheumatoid arthritis

Classification criteria for RA (score-based algorithm: add score of categories A-D ;)

A score of >6/10 is needed for classification of a patient as having definite RA

A. Joint involvement

Score

1 large joint.	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)	5

B. Serology (at least 1 test result is needed for classification)

Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3

C. Acute-phase reactants (at least 1 test result is needed for classification)

Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1

D. Duration of symptoms

<6 weeks	0
>6 weeks	1

METHOD OF COLLECTION OF DATA

Patients coming to medicine OP and admitted in TD Medical College, Alappuzha who satisfy inclusion criteria is taken as study subjects. Written consent will be obtained from all patients

participating in the study. Patients included in the study will be evaluated with detailed history, clinical examination, investigations as per the Proforma

STATISTICAL ANALYSIS

Data will be entered into Excel sheet and analysis by using SPSS version 16. All numerical variables will be compared using independent samples t test or ANOVA. Categorical variables will be compared using Chi square test.

INCLUSION CRITERIA

- 1) Subjects with RA factor serology positive.
- 2) Subjects consenting to take part in study.
- 3) Clinically stable with vital signs within normal limits.

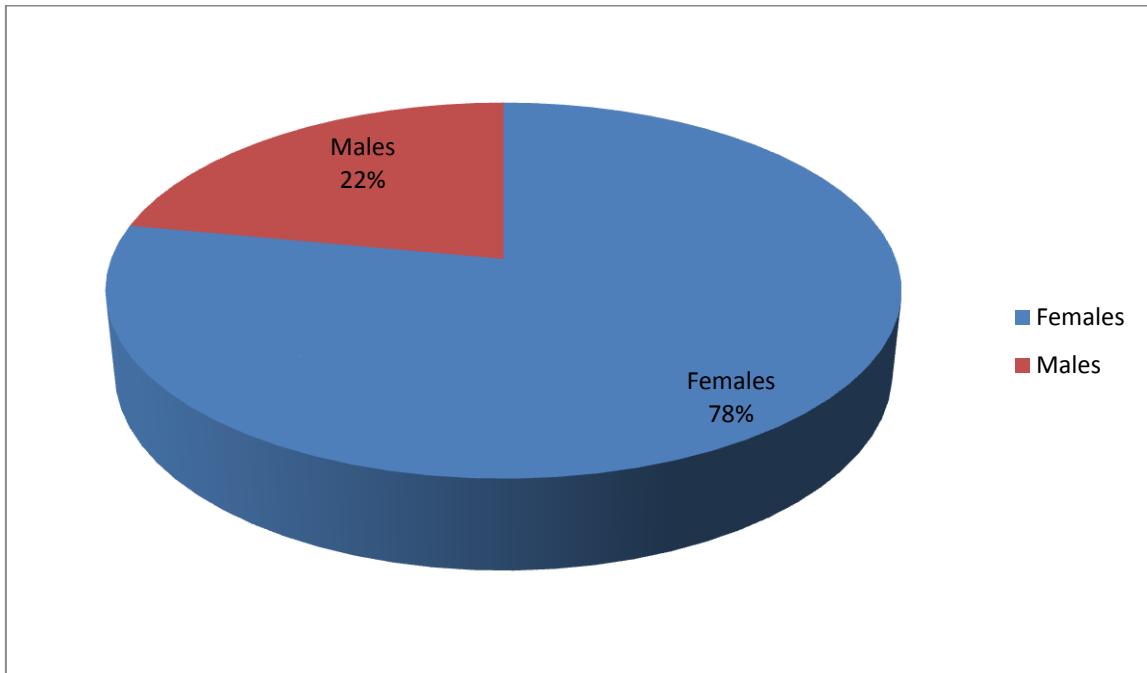
EXCLUSION CRITERIA

1. History of any hematological abnormality before diagnosis of rheumatoid arthritis

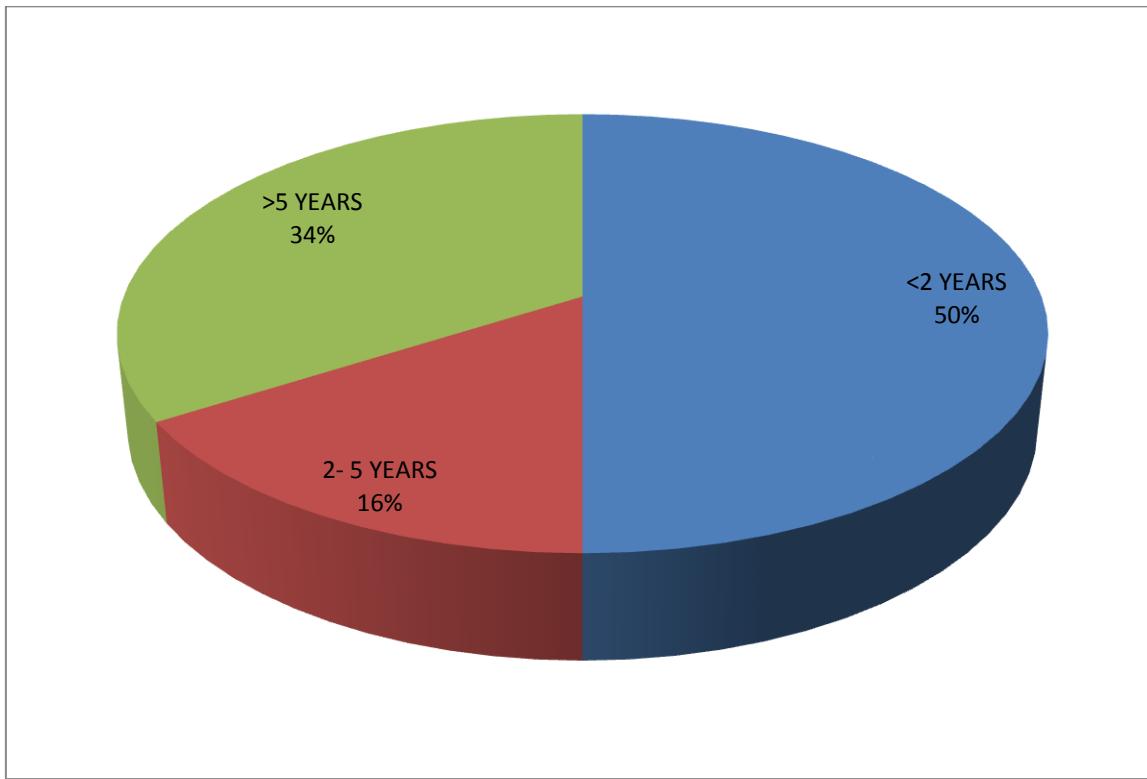
INVESTIGATION REQUIRED FOR STUDY

- i. Complete hemogram
- ii. Peripheral smear
- iii. ESR
- iv. Serum ferritin
- v. TIBC
- vi. Stool occult blood.

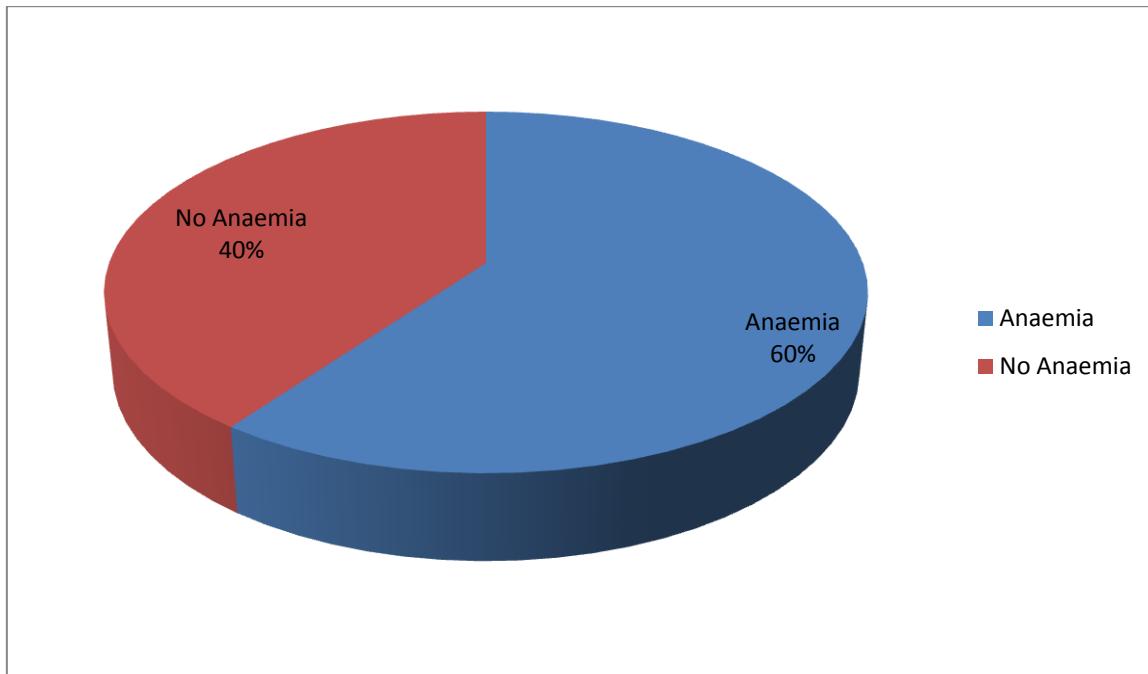
All routine investigations such as Hb%, Total RBC count, Total Leucocyte Count, Differential Count, Platelet Count are done using Fully Automated Hematology Analyzer (SYSMEX KX-21) in the Central lab. The technique used is any abnormal reports will be rechecked manually by expert laboratory staffs.

OBSERVATIONS**Figure 1:** Sex distribution of cases

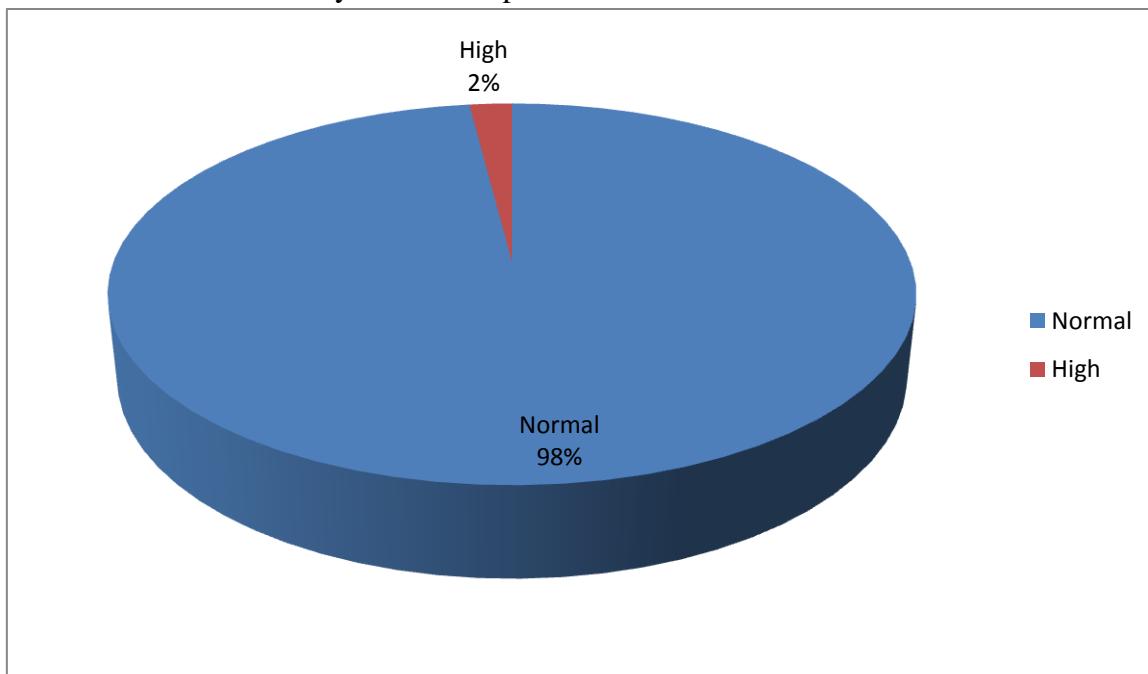
In the present study prevalence of Rheumatoid arthritis is higher in females.

Figure 2: Duration of Rheumatoid Arthritis among the study population:

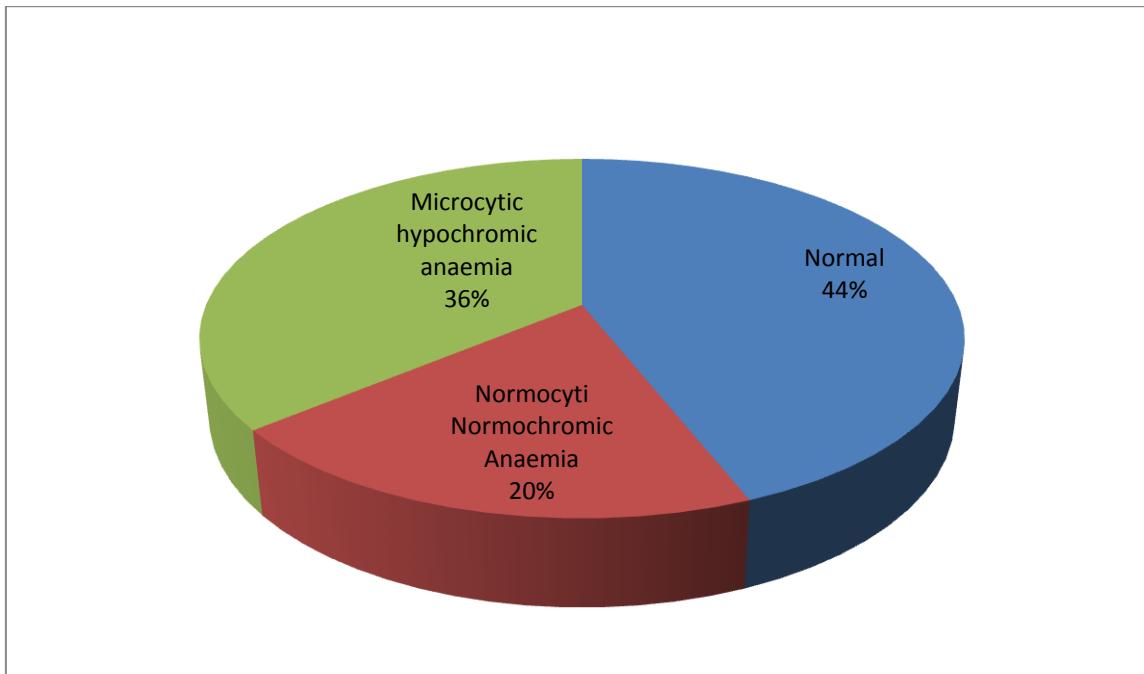
Majority of the RA patients belonged to the group with disease duration less than 2 years.

Figure 3: Prevalence of anemia among RA patients:

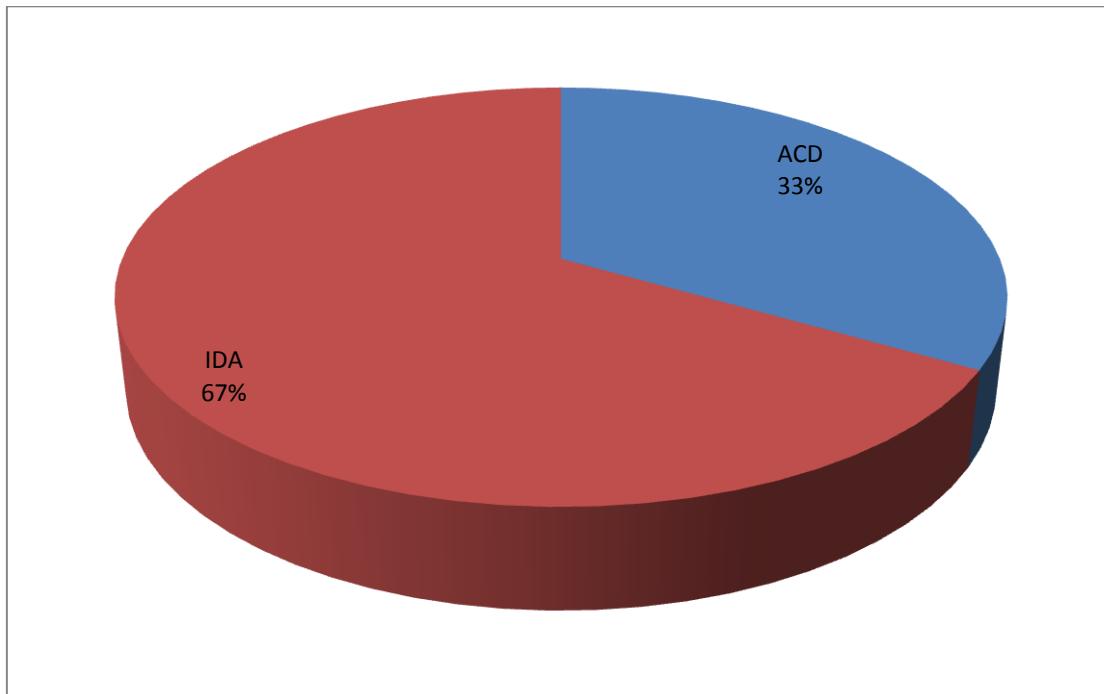
Anaemia was present in 60% of the patients with RA.

Figure 4: Prevalence of Thrombocytosis in RA patients

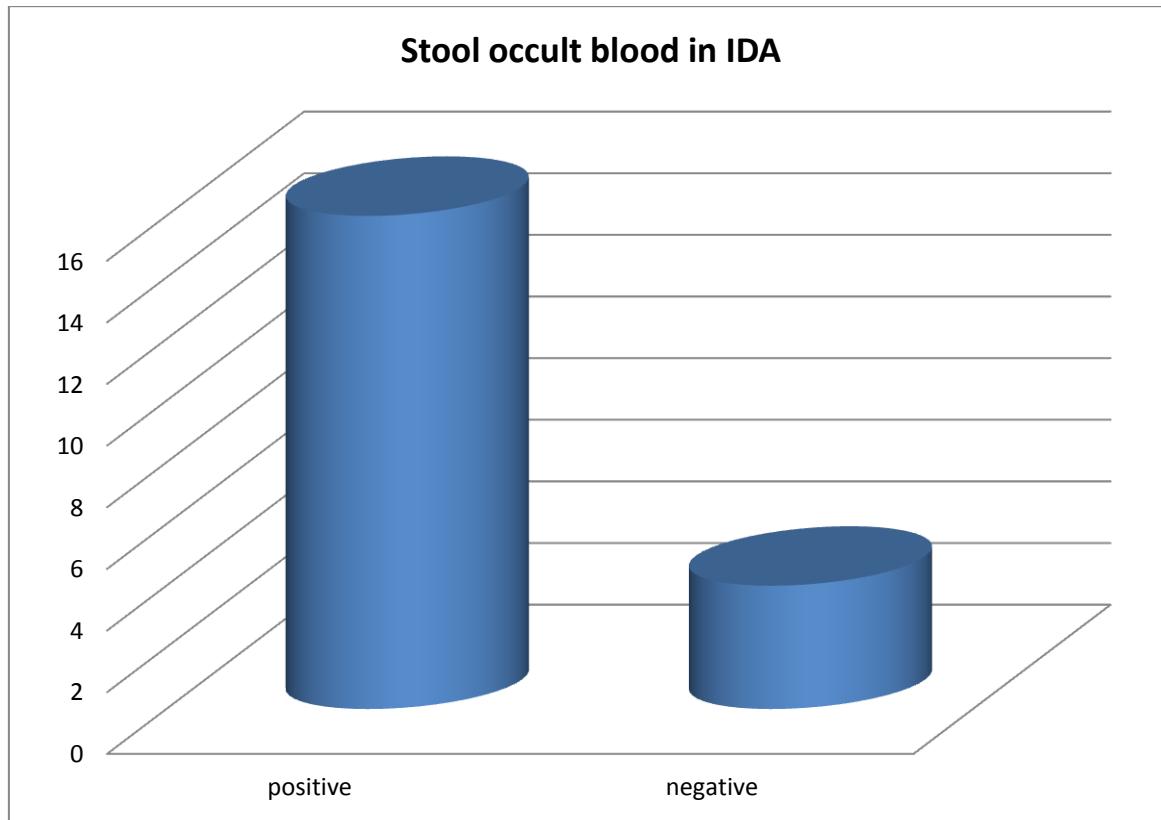
Showing prevalence of thrombocytosis. Only 1 patient (2%) out of the whole study subjects was found to have thrombocytosis.

Figure 5: Peripheral smear abnormalities in RA patients.

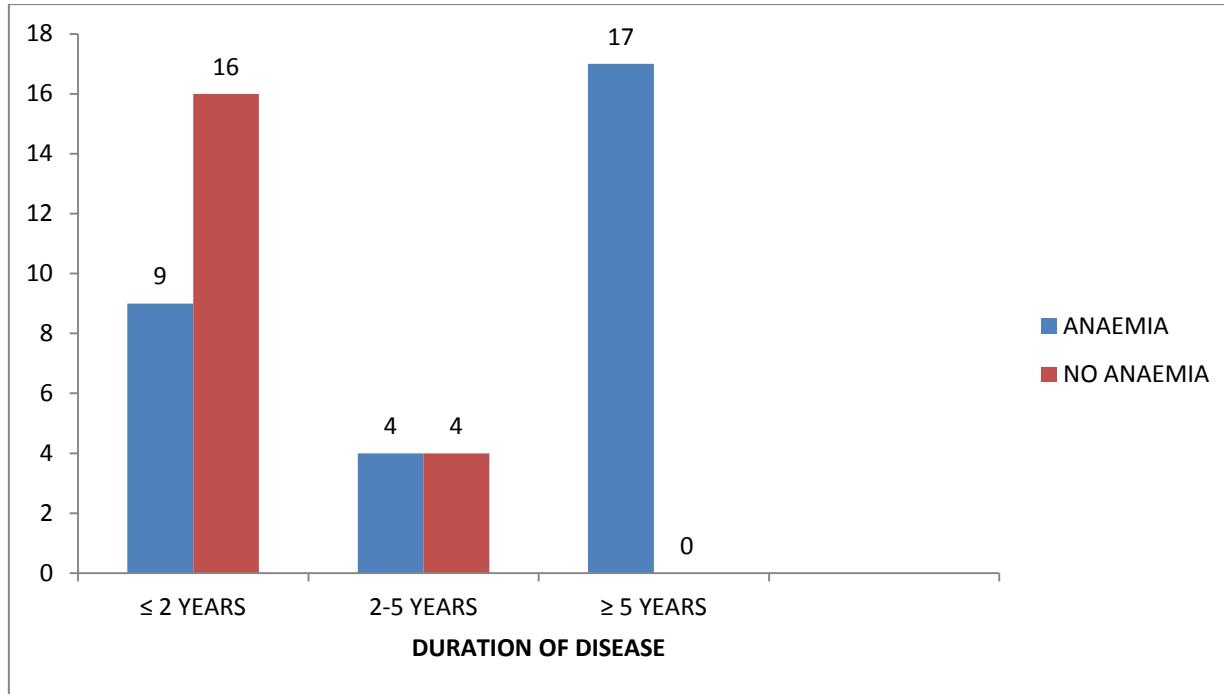
The present study showed higher prevalence of microcytic hypochromic anaemia when compared to normocytic normochromic anaemia in patients with RA.

Figure 6: Types of anemia in RA patients.

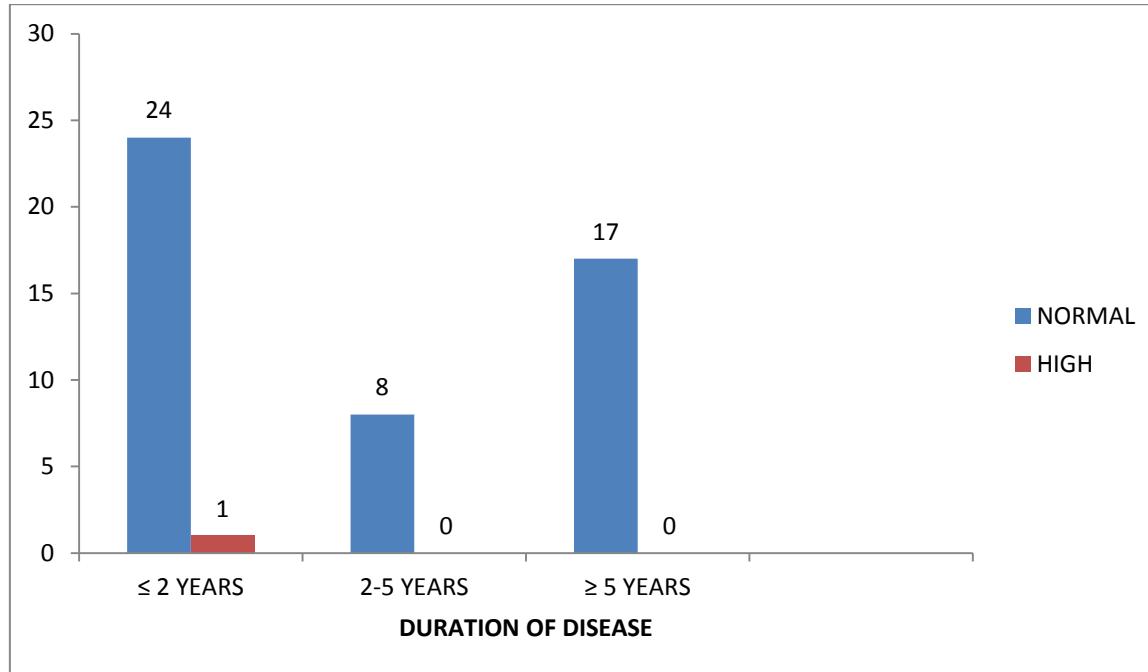
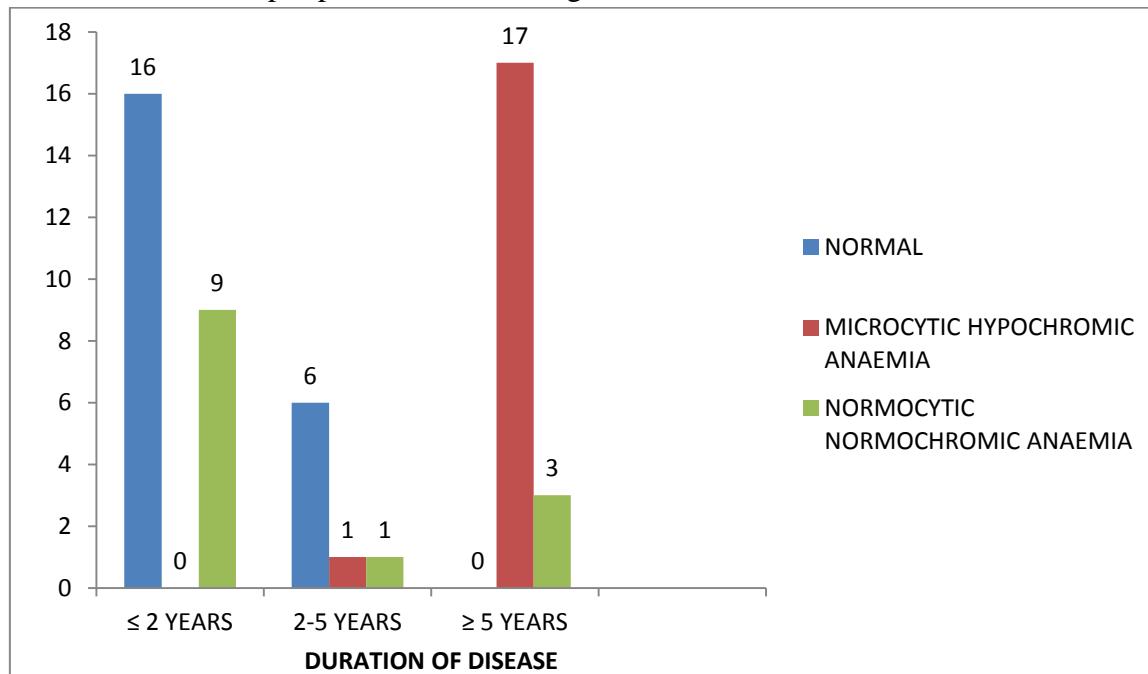
The present study showed higher prevalence of Iron deficiency anemia among the subjects when compared to anemia of chronic disease.

Figure 7: Stool occult blood positivity in patients with iron deficiency anemia:

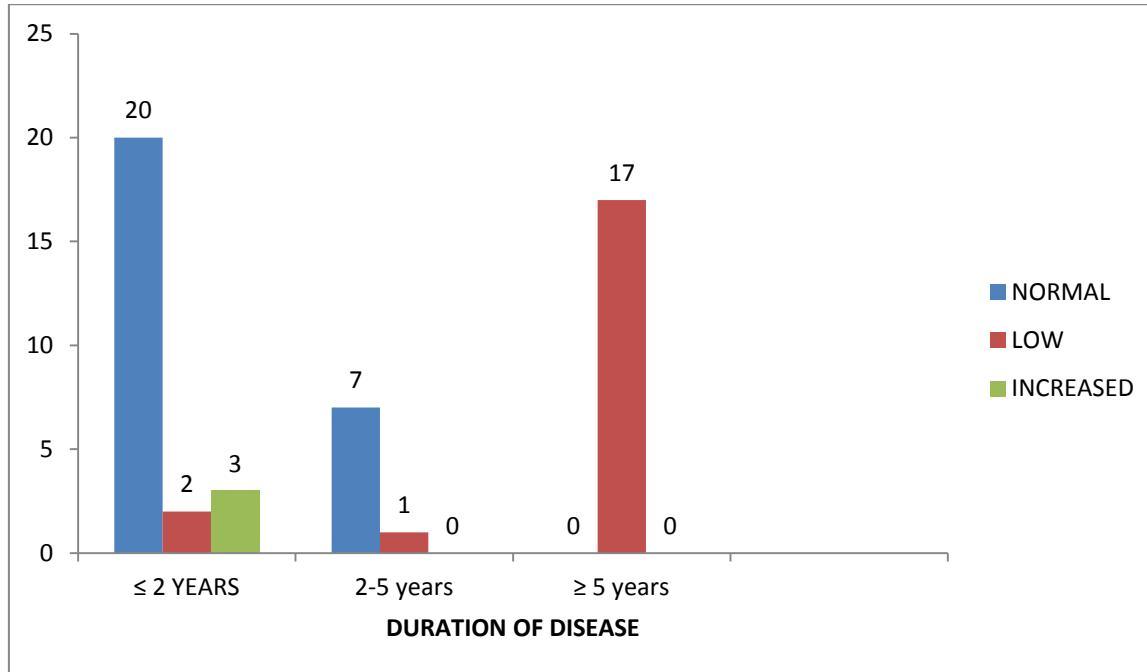
Stool occult positivity was higher among patients with Iron deficiency anemia.

Figure 8: Relation of hematological manifestations with the duration of RA

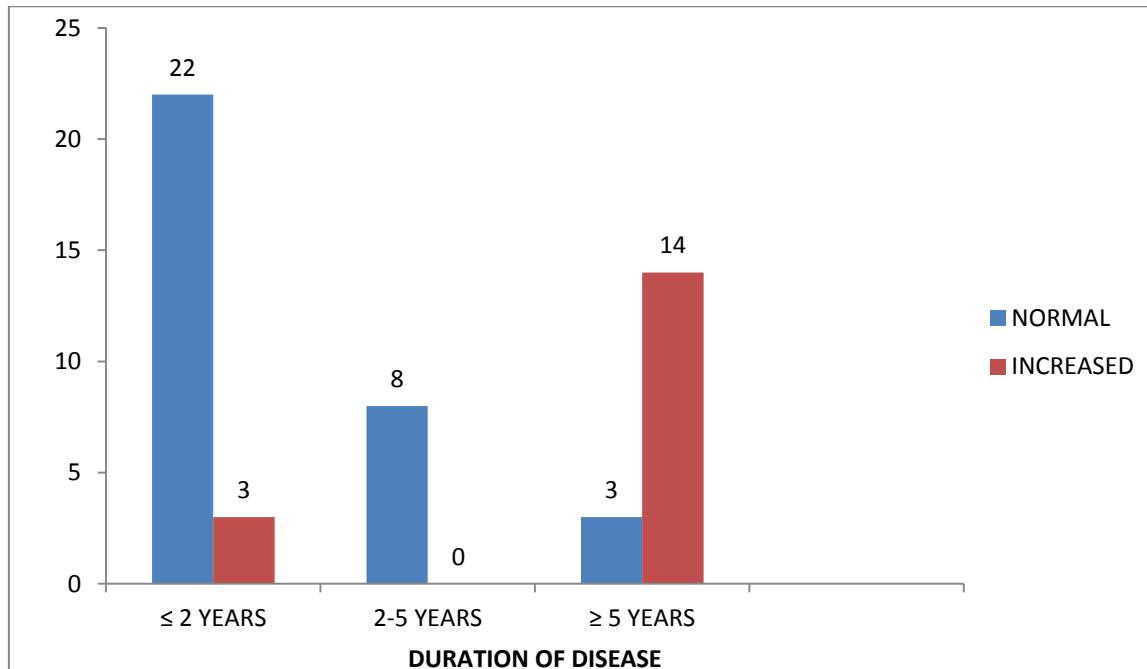
Prevalence of anemia was higher in group with disease duration more than 5 years when compared to the other groups.(p value <0.01)

Figure 9: Relation between platelet count and duration of RA**Figure 10:** Relation between peripheral smear findings and duration of RA

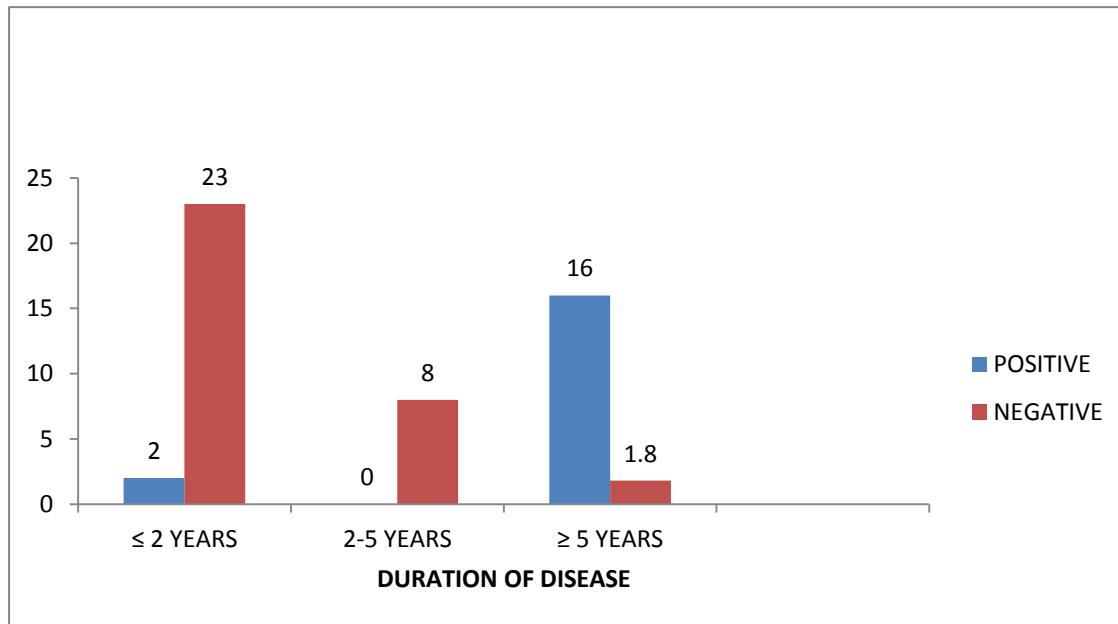
Normocytic normochromic anemia was more prevalent in disease duration less than 2 years (p value < 0.01). Microcytic hypochromic anemia was more prevalent in disease duration more than 5 years (p value <0.01)

Figure 11: Relation between serum ferritin and duration of RA.

Low serum Ferritin was more prevalent in Rheumatoid arthritis patients with disease duration more than 5 years when compared to other groups.(p value <0.01)

Figure 12: Relation of TIBC with duration of RA

Increased TIBC was seen in disease duration more than 5 years.82% was seen in disease duration more than 5 years.(p value<0.01)

Figure 12: relation between the duration of illness and stool occult blood

SUMMARY AND CONCLUSIONS

The present study was undertaken to find out the prevalence of hematological manifestations in seropositive Rheumatoid arthritis and find its relation with duration of the illness. 50 patients were included in the study. A Complete hemogram, peripheral smear, serum ferritin, TIBC, stool occult blood was done in all patients. The findings obtained in this study are as follows;

- Anemia was the most common hematological manifestation found in patients with rheumatoid arthritis seen in 60% of patients.
- Most common type of anemia was Iron deficiency anemia
- Other hematological abnormality found was thrombocytosis.
- Anemia was more prevalent in patients with rheumatoid arthritis disease duration more than 5 years.
- Stool occult blood was positive in 80% of patients with iron deficiency anemia.

According to the findings obtained anemia is the most common hematological manifestation. Iron deficiency anemia was more prevalent than anemia of chronic disease. Anemia was more prevalent in disease duration more than 5 years showing the relation of anemia with the duration

of the illness. Another finding was the high prevalence of stool occult positivity in Iron deficiency anemia indicating that chronic GI blood loss due to drug induced gastritis may be the cause for iron deficiency anemia.

In summary, the most common type of hematological abnormality in Rheumatoid arthritis is anemia and most common type is Iron deficiency anemia. The cause for iron deficiency is thought to be due to drug induced GI blood loss. So early screening, diagnosis and appropriate treatment will reduce the incidence and thus reduce the mortality associated with hematological manifestations with rheumatoid arthritis. Another important point is to control the use of NSAIDs and corticosteroids to reduce the risk of GI blood loss.

ACKNOWLEDGEMENT

We thank the Almighty for His unfailing love and bountiful blessings during this research endeavor. We owe a great deal of thanks to the Government TD medical college, Alappuzha for providing us the opportunity to conduct this study. We express the most sincere thanks to all the teaching and non teaching staff of the departments of medicine and gastroenterology of our institution. Last but not the least we great fully remember all the patients who gave consent and participated in this study

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ABBREVIATIONS

- RA – Rheumatoid Arthritis
 ACD – Anemia of chronic disease
 IDA – Iron deficiency anemia
 ACPA – Anti citrullinated peptide antibody
 TIBC – Total iron binding capacity