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HAEMATOLOGICAL PARAMETERS IN AUTOIMMUNE DISEASES

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ABSTRACT

Aim: Autoimmune diseases are increasingly being found to be a significant cause of morbidity in the general population**.** And it has been observed that hematological parameters are altered in these conditions. This study was done to investigate the changes in routine hematological parameters in cases of autoimmune diseases presenting at a tertiary care center.

Methodology: This was a hospital based retrospective study done over a 2-month period. The demographic data and clinical diagnosis of the patients were accessed from the hospital medical records division and the records in the haematology laboratory.

Results: There was a total of 84 cases of which females were predominant. There were 54 cases of Rheumatoid arthritis (RA), followed by 15 cases of SLE. The remaining were of other autoimmune diseases. Anemia was seen to be the commonest hematological manifestation, followed by eosinopenia, leukocytosis and neutrophilia. Other findings included lymphocytosis, thrombocytosis, thrombocytopenia and eosinophilia. Anemia was seen in most of the RA cases followed closely by leukocytosis and thrombocytosis. Leukocytosis was more evident in the female RA patients.70% of the systemic lupus erythematosus (SLE) cases also had anemia, followed by leukocytosis in 40%.

Conclusion: Hematological abnormalities are commonly seen in autoimmune diseases. The most common abnormality can be an anemia presenting as the earliest manifestations of an underlying autoimmune disorder. This study attempts to re-establish the importance of reviewing the basic hematological parameters carefully and considering the presence of an autoimmune etiology in patients with hematological changes.

Keywords: Autoimmune diseases, Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE)

1.INTRODUCTION

Autoimmune diseases are characterized by a loss of self-tolerance causing immune mediated tissue destruction [1]. Approximately 5-6% of the world population is affected by autoimmune diseases that affect the body systemically. Globally, there is increasing evidence for a steady rise in the frequency of autoimmune diseases (AD), in the last few decades [2]. Autoimmune diseases are multifactorial and are caused by an interaction of both genetic and environmental factors. Many autoimmune diseases display a striking imbalance between the sexes, with females representing the majority of cases [3].

Routine blood count examination is one of the most common tests run in a hospital setup and has immense importance in showing up abnormalities which are to be investigated further. Haematological parameters are tightly regulated traits with high clinical relevance and present as informative biomarkers for many disorders, such as autoimmune diseases, cardiovascular diseases, cancers and also in infectious states. They provide

information regarding erythrocytes, leukocytes and platelets, which are sensitive to disease development and progression. [4,5].

Simple haematological tests such as the differential count especially the neutrophils, mean platelet volume (MPV) and haemoglobin can reflect the systemic inflammatory burden in various autoimmune diseases like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis and primary Sjögren's syndrome [5,6,7].

The aim of this study is to investigate the common haematological changes in various autoimmune diseases encountered in the day-to-day rheumatology clinical practice at our institute.

2. MATERIAL AND METHODS

This retrospective study was done at Saveetha Medical College & Hospital, Chennai during a 2-month period from January to February 2021. The demographic data and clinical status of patients were accessed from hospital records and the haematological parameters were retrieved from the database of the Sysmex XN1000 Automated 6-part haematology analyser in the haematology laboratory. When a patient had multiple blood samples, the hematologic parameters of the first sample taken after the disease diagnosis and before starting treatment was used for evaluation. The haematological parameters measured are Hb, RBC count, MCV, MCHC, MCH, PCV, RDW, Total leucocyte Count, Differential count, Platelet count. Statistical analysis was carried out using the SPSS software version 23.
Inclusion criteria: Haematological parameters of patients of common autoimmune diseases presenting with arthritis at a rheumatology clinic.
Exclusion criteria: All arthritis due to non-autoimmune causes that presented at the rheumatology clinic were excluded.
The reference values for the haematological parameters were obtained from a standard haematology textbook. [9] (Table 1)

3. RESULTS AND DISCUSSION

The autoimmune cases included in the study were split predominantly between 54 cases of rheumatoid arthritis (67.5%) and 15 cases of systemic lupus erythematosus (SLE) with the remaining divided between Mixed connective tissue disease (MCTD) 4 cases (5.5%), Systemic sclerosis (SS) 3 cases (4%), Juvenile idiopathic arthritis (JIA) (2%) and one case each of dermatomyositis and Sjogren's syndrome (Figure 1).

Out of the 80 cases, 66 were females and the remaining 14 were males with a M: F ratio of 1:5 (Figure 2).

Age ranged from 16 to 72 years with a mean age of 41.5 years. The most common age group of presentation of autoimmune diseases in this study, was between 30-40 years followed by 40 to 50 years. (Table 2) The second most common entity in our study was SLE, with average age of presentation being 32.4 years.

The number and type of autoimmune diseases noted in both sexes is given in Table 3. There was a total of 54 cases of RA, of which 43 were females. SLE and mixed connective tissue diseases (MCTD) comprised purely of female patients (15cases) and 4 cases respectively.

The number of cases with alterations in common haematological parameters and the mean values of these haematological parameters in the spectrum of our autoimmune disease cases are given in Table 4 and Table 5 respectively**.** 70% of the cases with autoimmune disease had anaemia. 73% of patients with SLE and 70% of patients with RA were anaemic.

36.6% (29) cases out of 80 had leukocytosis and only 6.25% (5) cases had leukopenia. 17 cases (31.84%) of RA had leukocytosis while 4 cases (7.40%) presented with leucopenia. Among the cases with SLE, leukocytosis was seen in 6 out of the 15 cases and only one case had leukopenia.

Out of the 80 cases, eosinopenia was present in 47 (58%), while eosinophilia was present in 9 cases (11.2%). 59% (32 cases) of RA presented with eosinopenia, while 8 RA cases had eosinophilia. 8 of the 15cases (53%) of SLE had eosinopenia and only one case had eosinophilia.

An equal number of cases presenting with autoimmune disease, had thrombocytosis and thrombocytopenia (12 each).

Almost all the MCTD patients had leucocytosis with a mean TC -10970($X10^3$g/dl). All other haematological parameters in these patients were normal.

A slight fall in Hb with a mean value of 10.33g/dl was seen in SS. Total count was also elevated in this condition with a mean value of 10370.0 (cells/cumm).

The JIA cases had relatively normal RBC and WBC parameters, except for a median TLC being in the upper limit of normal 9880cells/cumm.

3.1 DISCUSSION:

Epidemiological data provide evidence of a steady rise in autoimmune diseases throughout Westernized societies and in India over the last few decades [2]. It has been widely accepted that these conditions are more prevalent in women, and this has also been substantiated in the present study [3,7,8].

Variations in hematological parameters in autoimmune diseases have been studied in order to find indicators that can give clues for disease management and prognostication. Among the blood counts, it was found that there were changes predominantly in hemoglobin, total leucocyte count, absolute eosinophil count and platelet count.

Anemia was the predominant hematological finding observed in our study, being seen in 70% of cases. Anemia was common in both the SLE (73%) and RA cases (70.3%) cases. [7,16,17,18,19] The commonest cause of anemia in SLE and RA is suppressed erythropoiesis due to the chronic inflammatory state [10,11,12].

Overall,36.4% of our autoimmune disease patients (29 cases) presented with leukocytosis, while 6.2% of cases had leucopenia. Leukocytosis was evident in 17 cases (31.34%) of RA as in other studies by Tripathi et al and Isenberg DA et al. Gawali PS et al [18]in his study on 300 patients with RA, attributed leukocytosis to an ongoing infection and the pro inflammatory state associated with RA as the contributory cause. [7,16,17,18,19]. Most of our SLE cases, showed leukocytosis (40%) or normal TLC count, and has been said to be due to an underlying infection, use of high dose steroids or as an acute exacerbation of SLE. [10-15]

Studies by Xiaoxia Lao et, Sasidharan PK et al, Dias et al showed that leucopenia is common in SLE, reflecting the disease activity and they have postulated that it is mainly due to peripheral destruction from lymphotoxic or anti-neutrophil antibody effects, complement-mediated cell lysis, excessive neutrophil apoptosis as well as marrow suppression [10-15], In our study only one case of SLE had leucopenia. Out of the 43 cases of RA, 5 had leucopenia.

14% of our RA cases showed raised AEC levels (>$500x10^9$/L). In a study by Emmanuel D et al, out of 1092 RA cases, 191 patients (17.5%) had eosinophilia among which majority were due to secondary causes; the patients had either proven intestinal helminthic infection or response to empirical anti-helminthics. [24] Another study from Kashmir in northern India also reported a similarly high prevalence of eosinophilia in RA patients [25]. SLE is said to be associated with hyper eosinophilic syndrome but there are no systematic studies on the incidence and severity of eosinophilia in SLE and eosinophilia does not form one of the diagnostic criteria for the condition [Petri et al, 2012].

In the present study, there was, however, a marked preponderance of eosinopenia (58.7%) over eosinophilia (12.5%). An extensive search of literature did not report any similar finding and hence this could probably be explained by any drug intake by the patients, especially steroids, prior to their initial reporting to this center.

An equal incidence of thrombocytosis and thrombocytopenia was noted in majority of the cases. In SLE, thrombocytosis is an unusual finding, and it may suggest auto splenectomy [29], Similar to the study by Castellino G et al, in our study, 20% of SLE cases had thrombocytosis but we couldn't find any association with auto-splenectomy. Though 74% cases of RA cases had normal platelet counts, 12.94% of cases had thrombocytosis, Farr et al [31]in his study on platelets and RA, claims that the presence of an underlying inflammation is the cause of thrombocytosis in rheumatoid arthritis (RA).

Despite previously normal platelet counts, patients may have thrombocytopenia as a manifestation of an acute severe SLE flare. Immunologically mediated platelet destruction is reported to be a contributing factor for SLE associated thrombocytopenia, occurring in 7 to 26% of patients. These findings were consistent with our study (13.3%) and in studies by Miller MH et al [30]

4. CONCLUSION

Hematological abnormalities are commonly seen in autoimmune diseases. They may present as the earliest manifestations, thus warranting the clinician to have a high degree of suspicion in order to identify and treat these conditions as early as possible. This hospital-based study attempts to re-establish the importance of reviewing basic hematological parameters in autoimmune diseases especially the common ones.

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COMPETING INTERESTS

No competing interests exist.

AUTHORS' CONTRIBUTIONS

DR. Danita G S Edwin[1] - Wrote the protocol, performed the statistical analysis, wrote the first draft of the manuscript.

DR. Neha Agarwal[2] and E.Kshitij [3] – Data collection and literature search

DR. Ganthimathy Sekhar[4] - Designed the study, correction and approval of the final manuscript

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Tables

Table 1: Reference values

Reference values	Male	Female
Hb(g/dl)	13-17	12-15
RBC Count(x10^6/µL)	4.5-5.5	3.8-4.8
PCV(l/l)	40-50	36-46
MCV (fl)	83-101	
MCH (Pg)	27-32	
MCHC (g/dl)	31.5-34.5	
TC(x10^3/µL)	4-10	
DC-N(%)	40-80	
DC-L(%)	20-40	
DC-E(%)	1-6	
DC-M(%)	2-10	
DC-B(%)	<1-2	
Platelet(x10^3/µL)	150-410	
ANC(x10^9/L)	2-7	
AEC(x10^9/L)	0.02-0.5	

Table 2: Age wise distribution of autoimmune disease

Age in years	Female	Male	Total
0-10	-	-	-
11-20	3	2	5
21-30	12	1	13
31-40	19	4	23
41-50	18	2	20
51-60	11	2	13
61-70	2	2	4
71-80	1	-	1
Total	**70**	**14**	**80**

Table 3: Gender wise distribution of individual autoimmune diseases

Autoimmune disease	Female	Male	Total
RA	43	11	54
SLE	15	-	15
MCTD	1	-	4
SS	3	-	3
JIA	-	2	2
Sjogren's	1	-	1
Dermatomyositis	-	1	1
Total	**70**	**14**	**80**

Table 4: Number of cases with alterations in common haematological parameters

Autoimmune diseases	↓Hb(n)	↑TC(n)	↓TC(n)	↑AEC(n)	↓AEC(n)	↑Platelet(n)	↓Platelet(n)
RA	38	17	4	8	32	7	7
SLE	11	6	1	8	1	2	3
MCTD	2	3	-	-	2	1	1
SS	3	2	-	-	2	-	1
Sjogren's	-	-	-	-	1	-	-
JIA	1	-	-	-	2	-	-
Dermatomyositis	-	1	-	-	1	1	-

Table 5: Mean values of haematological parameters in cases of autoimmune disease

Autoimmune diseases	Hb(g/dl)	TC(x10^3/µL)	AEC (x10^3/µL)	Platelet(x10^3/µL)
RA	10.83	9208.00	199.64	2.86
SLE	10.67	9824.00	207.19	2.78
MCTD	11.95	10747.00	178.49	2.84
SS	10.33	10370.00	130.41	2.09
Sjogren's	13.00	8050.00	56.35	2.89
JIA	11.95	9015.00	13.00	3.04
Dermatomyositis	11.50	11500.00	120.00	5.32

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Figures

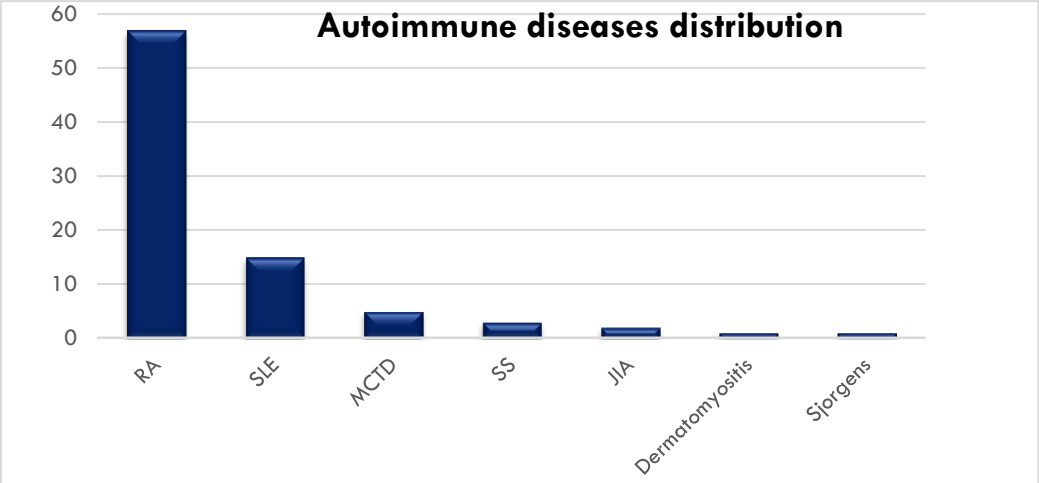

Figure 1: Distribution of autoimmune diseases

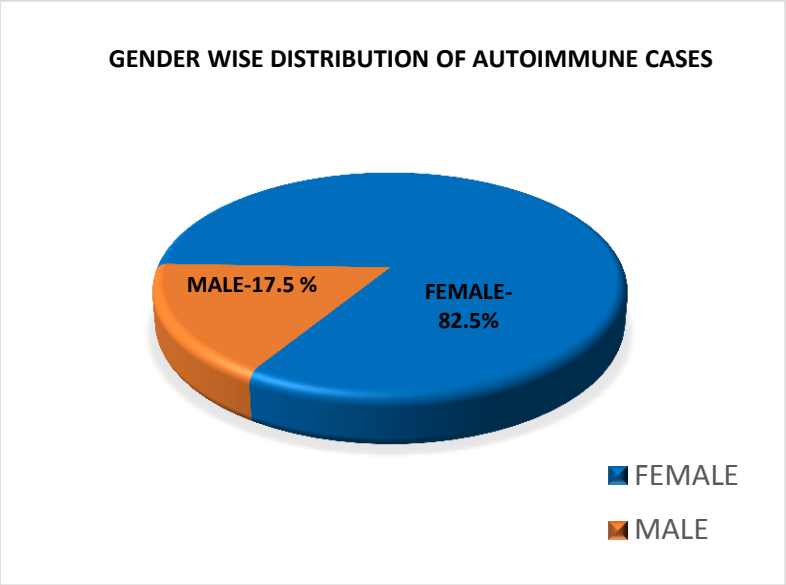

Figure 2: Gender wise distribution of autoimmune diseases