

A Study of Haematological Profile in Systemic Lupus Erythematosus

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1. Introduction

Systemic lupus erythematosus (SLE) is a prototypic systemic autoimmune disease with variable multisystem involvement and heterogeneous clinical features, ranging from mild to life threatening manifestations. SLE affects mainly female gender especially during child bearing age group.

The prevalence rate has been reported to be 52/100,000 populations in United States [1] and Asia has prevalence rate of disease from 30 to 50/100,000 population. (1,2)

The first case of SLE in India was reported in 1955.[3]. Subsequently, many studies have been conducted in different parts of the country reporting prevalence and varied manifestations of SLE. One prevalence study conducted from rural India has shown very low prevalence rate (3.2/100,000 population).[4] In another study conducted in Eastern India found that 3.9% of the children in the rheumatology department had SLE.[5]

There is no gold standard test to diagnose SLE, hence the determination of the presence of this disease, in addition to being a diagnosis of exclusion, ultimately rests with the judgement of a clinician. The first classification criteria for SLE were developed by the American Rheumatological Association (predecessor of the American College of Rheumatology (ACR)) in 1971(6) The criteria were revised first in 1982 (incorporating Immunological tests) and in 1997 (included advancing knowledge about the association of antiphospholipid (aPL) antibodies with SLE) (7,8) The Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria , proposed in 2012, comprise 11 clinical and 6 immunological criteria.(9) In contrast to the ACR criteria, the SLICC criteria require at least one clinical and one immunological criteria for the classification of SLE.

Haematological manifestation form a major part of all criterion for SLE. There are very few studies however about the hematological manifestation of SLE in North-eastern India.

2. Objectives of the Study

- 1) To estimate the proportion of patients with hematological abnormalities as the manifestation of SLE
- 2) To study the nature of hematological presentation

3. Methods and Study Material

A cross sectional descriptive hospital based study conducted between August 2016 to Nov 2017 at Department of Medicine , Silchar Medical College and Hospital , Assam. The study was commenced after obtaining all the necessary ethical approvals from SMCH research and ethics committee.

The study included a total of 20 patients aged above 12 years seen at Silchar Medical College OPD and those admitted in Dept of Medicine and fulfilling the 2012 SLICC classification criteria for diagnosis for SLE .Exclusion Criteria: Female patients with any disease that may affect the hematological parameters under study such as thalassemia or iron deficiency anemia.

All patients gave an informed written consent. Consecutive sampling method was applied. Targeted clinical history and physical examination was done. Approximately 4ml of venous blood was drawn aseptically, following standard guidelines from each patient for measurement of a complete blood count, reticulocyte count, erythrocyte sedimentation rate and peripheral blood film examination. The tests were undertaken at the SMCH using a CELL-DYN 3700 automated blood counter. ESR interpretation was undertaken at the same laboratory by the Wintrobe method and a PBF was reported after staining with maygrunwald / giemsa stain by direct visualization on a microscope at various powers of magnification by a pathologist.

4. Results

Hematological manifestation (80%cases) was the second most common mode of presentation after Arthritis.

Table 1: Baseline Characteristics Of Study Group

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Sex	Male	1(5%)
	Female	19(95%)
Age Distribution	<24 Yrs	07 (35%)
	24-40 Yrs	10(50%)
	>40yrs	03(15%)
Age	Mean	25.6 YRS
	Range	16-46 YRS
	Median	27 YRS
Duration Of Disease	(Mean)	36 MONTHS
Residence	Urban	08(40%)
	Rural	12(60%)

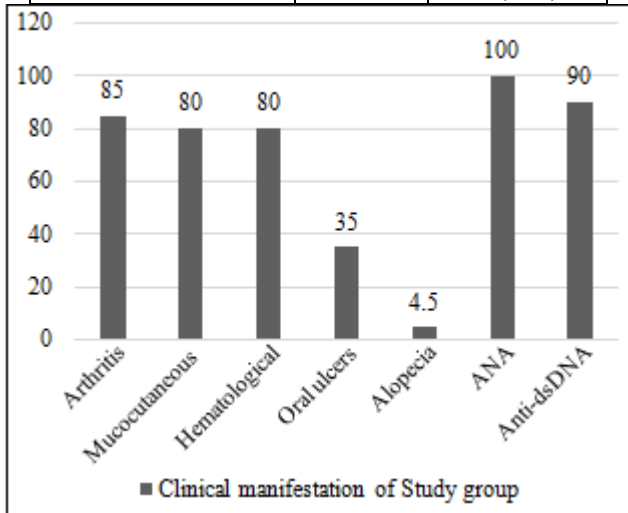


Figure 1: Clinical manifestation of Study population

Table 2: Haematological Parameters of Study Population

Parameter	Range	Median	Reference Range
RBC	2.8- 5.75	3.9	$4-6 \times 10^{12}/L$
Haemoglobin	6.3- 14.2	9.6	> 11 gm% Female >12 gm% Male
WBC	2.2- 19	5.5	$4-11 \times 10^9/L$
Neutrophils	0.9- 8.9	3.1	$2-7.5 \times 10^9/L$
Lymphocytes	1.1-3.9	1.9	$1.5-4 \times 10^9/L$
Platelets	1.7-5.6	236	$150-400 \times 10^9/L$

Table 3: Pattern of Haematological Abnormalities

	Frequency	Percentage
Anaemia	16	80
Leucopenia	5	25
Neutrophilia	2	10
Thrombocytosis	3	15

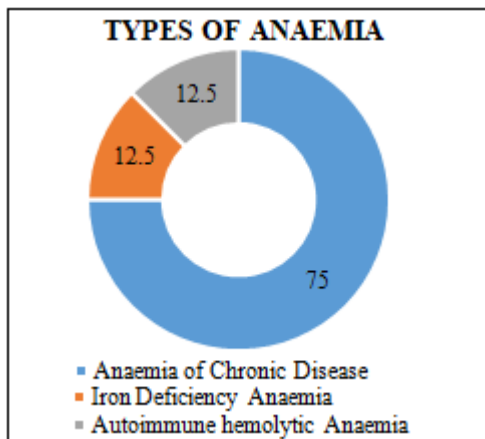


Figure 2: Types of Anaemia in SLE study group

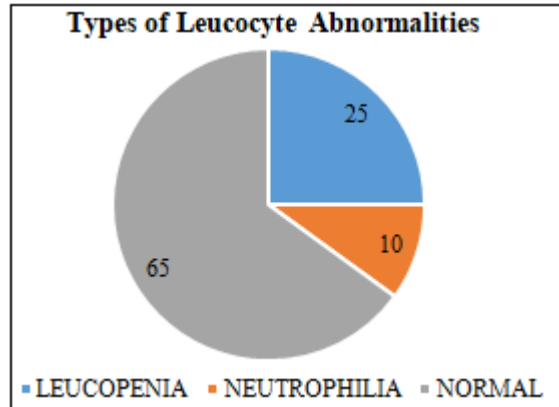


Figure 3: Leucocyte abnormalities in SLE study group

Table 4: Peripheral blood film

PBF finding	Frequency	Percentage
Normocytic Normochromic	13	65
Normocytic Hypochromic	04	20
Microcytic Hypochromic	03	15

5. Discussion

This cross sectional study was done to evaluate the hematological manifestations among 20 patients with SLE from Barak Valley.

We observed a female preponderance in the studied patients, females were 19 (95%) and males 1(5%).. Most of the studies show a similar results(10,11). Malviya et al reported similar finding in northern India analyzing 1366 patients (10) . Cameron et al has reported a male to female ratio of 1:8 to 1: 14 in a series of adult patients(11). SLE predominately affects young females, the causes are unknown but genetic, immunological , environmental and hormonal factors may contribute (12,13). Immunological factors could be major cause since fetal cells can persist in mothers circulation for decades after delivery which provide antigenic exposure that may be a source of immune reactions in women.

The mean age of the patients in our study was 25.6 years. SLE is a disease of child bearing age. The median age of onset of SLE is 24 years in a series reported by Malaviya (10). In another study, the mean age was 28 ± 6.2 years [11]. Being a reproductive age worsens the situation and put this target group at risk.

Various studies have been conducted from different part of the country regarding clinical and epidemiological of SLE . The most common manifestation was arthralgia(85%) followed by Mucocutaneous(especially malar rash) and haematological changes(80%) each . Similar results were observed by Malaviya et al(10) and Wallace et al(14). However, studies conducted by Binoy et al.[15] and Kosaraju et al.[16] from the south India have shown less prevalence of mucocutaneous manifestation, which might be because of dark complexion of the study population making it difficult to detect these features.

Oral ulcers were reported in 35% cases in our study. . Our study has documented a higher incidence of oral ulcers compared with western studies but the incidence is similar to

that documented in the study from India .Malaviya[10] reports a 50% incidence of oral ulcers in his patients from eastern India. In a series of studies done by Wallace[10], oral ulcer were present in 7-36% of cases(14).

The commonest criteria satisfied was ANA positivity. It was seen in all of our patients. This is an expected finding as ANA negative lupus is a rare clinical entity in our setting. ANA is the most sensitive indicator of the presence of SLE. Changes in hematological profile of SLE patients found in our study are described In table 2 and table 3.

Anemia was frequent among SLE patients which is evident by significant decrease in Hb level, RBC count and PCV. Anaemia was found in 80% cases with Anaemia of Chronic Disease(ACD) being predominant followed by Iron deficiency anaemia(IDA) and Autoimmune hemolytic anaemia(AIHA) . The mean hemoglobin value was 8.5mg/dL. (hemoglobin level <11gm/dL in females and <12gm/dL in males was taken as anemia).

The pathogenesis of anaemia include inflammation, renal insufficiency, blood loss, infection.

A frequent cause of anemia in SLE is suppressed erythropoiesis from chronic inflammation (anemia of chronic disease or anemia of chronic inflammation), being the most common form . This type of anemia is normocytic normochromic. Many studies found stated that ACD and IDA are the most frequent types of anemia among SLE patients [12, 17, 18] postulating the cause to be inflammation, EPO impairment and disturbance in iron hemostasis. Cytokines and cells of reticuloendothelial system induce changes in iron hemostasis, the proliferation of erythroid progenitor cells, the production of erythropoietin, and the life span of red cells leading to disturbance of iron hemostasis, which increased up and retention of iron within cells of reticuloendothelial system(12).IDA may have been due to menorrhagia as most of our participants were young females in the reproductive age group, gastrointestinal blood loss due to the frequent use of NSAIDS and steroids, nutritional and possibly due to hookworm infestationsprevalant in this part of the country . The findings is similar to that documented by Voulgarelis et al(19).

Autoimmune Hemolytic anaemia(AIHA) was found in 12.5% of patients having SLE. This result was similar to that observed by Budman et al (20). . AIHA was diagnosed on basis of positive coombs test and reticulocytosis. Patients with SLE with AIHA can have other concomitant autoimmune haematological manifestations. For example, patients with SLE canpresent with AIHA and idiopathic thrombocytopenic purpuraconcomitantly or sequentially, which is known as Evans syndrome.

Leucopenia in this study was defined using the haematology laboratory reference range as WBC count < 4 x 10⁹/L. The prevalence of leucopenia was 25%, especially neutropenia. The causes may include Immune destruction of antibody coated WBC, active disease and steroid therapy . Several studies have shown leucopenia is associated with active disease and steroid therapy (21). Neutropenia in our

population was largely multifactorial; it may have been due to immune mediated mechanism by anti-neutrophil antibodies, medications (e.g.azathioprine), bone marrow dysfunction, or hypersplenism. (21)

Our study had a higher prevalence of leucopenia as compared to other Indian study by Sasidharan et al(22). Sasidharan's study found a leucopenia prevalence of 15.7% while Agrawal et al(23) found a prevalence of 18.4%. This difference in leucopenia could be attributable to the racial differences between the two populations. Leucopenia observed in in the study participants could be due to both active disease and steroid therapy.

Leucocytosis: Neutrophilia was also present in 10% of study population. It could be due to the high proportion of patients who were on steroids or any active infection.

Thrombocytosis was seen in 15% of the cases. Such high prevalence of thrombocytosis in our study could be secondary to microcytic hypochromic anaemia We observed a higher prevalence of thrombocytosis as compared to other studies. Castellino et al(24) found a prevalence of 3.7% in Caucasians with SLE. These low prevalences may be attributed to racial differences.

Hematological manifestations are common since blood and blood vessels together contain more diverse number of antigens than any other organ in the body and in SLE auto antibodies are known to develop against any antigen or tissue.

6. Conclusion

Hematological manifestation is the second most common presenting manifestation of SLE in people of Barak valley, India. The study concludes that treatment of hematological abnormalities is challenging because the treatment itself can cause undue complication such as Leucopenia due the use of high doses of steroids or granulocytosis due to infections .It is important to take these factors into consideration for disease therapy and management. Also evaluation of SLE need to be done in cases of anaemia not responding to conventional treatment.

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