PATTERN OF ANAEMIA IN SYSTEMIC LUPUS ERYTHEMETOSUS (SLE) PATIENTS

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Abstract

Background: Anaemia of Chronic Disease (ACD) is the most common form of anaemia in patients with Systemic Lupus Erythemetosus (SLE) Autoimmune Hemolytic Anaemia (AIHA), Iron Deficiency Anemia (IDA) drug-induced myelotoxicity, and anaemia due to chronic renal failure are also often detected. Distinctly different therapeutic approaches are required for the multiple causes of anaemia in these patients. However, the pattern of anaemia among the SLE patient of this geographical area is less studied. Aim of this study was to investigate the pattern of anaemia in patients with SLE. **Materials and methods:** This study was carried out on the patients who had been admitted in the Departments of Medicine, Nephrology and also from outpatient Department of Chittagong Medical College Hospital (CMCH) Chittagong. SLE patients were selected consecutively as per inclusion and exclusion criteria. Detailed history and physical examinations were performed in every patient. Necessary investigations were carried out. Hematological manifestations with regards to anaemia were scrutinized and statistically analyzed. **Results:** A total of 42 patients (97.62% females, mean age 27.02 ±8.63 years) were studied. All the study population was anaemic (Mean±SD of Hb was 9.14±1.84 mg/dl).ACD was most prevalent (52.4%) types of anaemia 22(52.4%), followed by IDA10(23.8%), AIHA6 (14.3%) and 4(9.5%) of total patient is undetermined cause of anemia. No significant association was found between anaemia and Disease Activity Index (SLEDAI) score, fatigue and Coombs' positivity. No association was found between the degrees of anaemia with urine protein loss. **Conclusion:** Anaemia is frequently encountered in SLE. A sound conception about the relative frequency of different types associated with systemic lupus erythematosus will help the clinician to take necessary measures for the wellbeing of the patient.

Key words

SLE; Anaemia; IDA; AIHA; Anaemia of chronic diseases.

Introduction

Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease that predominantly affects women of child bearing age. It is also a major cause of mortality and morbidity in the young populations[1,2]. The prevalence of SLE varies throughout the world. In the western world, it is about 40 per 100000 populations. There appear to be a higher incidence in Blacks and Hispanics than in other population. Over 80 percent of cases occur in women during their child bearing age[3, 4]. Hematological abnormalities are frequently encountered in patients with SLE and are part of American Rheumatological Association Criteria for classifying the disease. But there is a relative paucity of information on the significance of these abnormalities in the course of the condition[5-6]. Anaemia is the most common hematological abnormality seen in SLE[2]. Among the different types iron deficiency anaemia, anaemia of chronic disease and autoimmune haemolytic anaemias are commonest. Autoimmune haemolytic anaemia occurs in approximately 5-10% of SLE patients and it responds well to corticosteroid treatments[7]. Neutropenia is relatively common and has been related to an increased risk of infection in patients with SLE. Although thrombocytopenia caused by peripheral immune destruction is common in SLE (20-40%) severe thrombocytopenia is comparatively rare (~5%). It is now recognized that lymphopenia is one of the most common hematological findings in SLE[8, 9].

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Though the hematological abnormalities encountered in SLE have been well documented in literature, there are very few studies done in Bangladesh addressing pattern of anaemia, hence this study is undertaken to establish the frequency and severity and types of anaemia in patients of SLE in our geographical area.

Materials and method

This was a hospital based cross sectional descriptive study carried in the indoor and outpatient Department of Medicine and Nephrology unit of Chittagong Medical College Hospital (CMCH). After obtaining approval from CMC (Chittagong Medical College) Ethical Review Committee, the study was conducted from January to December 2015.

Patients of SLE as diagnosed according to American College of Rheumatology (ACR) criteria were included in the study and patients with hematological problems for due to other diseases were excluded. A structured questionnaire and necessary investigations were used as research instrument. Detailed history was collected in the structured questionnaire which includes demographic variables and co-morbidity. The form also included different physical signs found on examination ranging from general examination to systemic examinations.

For different blood tests 5cc venous blood was collected by a trained laboratory technologist and peripheral blood film also was produced in the spot to avoid technical error. Investigations were recorded are blood complete picture, absolute values, peripheral smear, and reticulocyte count in all patients of anaemia. These investigations are necessary to analyze the causes of anaemia in SLE. Patients with hypochromic microcytic anaemia was advised to have serum iron and ferritin levels, patients with macrocytic anaemia was advised to have direct and indirect coombs' test, LFTs, serum LDH, serum B_{12} and folate levels. Patients with normochromic and normocytic anaemia are considered to have anaemia of chronic disease. Bone marrow aspiration and Hb electrophoresis was done in special cases. Forty two adult patients were included in this study. Severity and various types of anaemias were recorded. Anaemia was graded according to severity, as mild (Hb 10-12 gm/dl), Moderate (Hb 8-10 gm/dl) and severe (Hb < 8 gm/dl)[10].

All the collected data were checked and compiled in a master sheet first. Then statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 19 for Windows. Continuous variables were reported as the means ± SD, and categorical variables were reported as frequencies and percentages. Continuous variables were compared by paired sample t-test between baseline and follow up findings. Statistical significance was defined as $p < 0.05$ and confidence interval set at 95% level.

Results

Table I : Age & sex distribution of the study population (n=42)

Characteristics	
Age in years	
< 20 years	11 (26.19%)
20-29Years	15 (35.71%)
30-39Yeras	12 (28.57%)
≥40 years	4 (9.52%)
Mean ± SD	27.02 (±8.63)
Sex	
Female	41 (97.62%)
Male	1 (2.38%)

*Data are presented either in number (Percentage) or in mean(± SD)

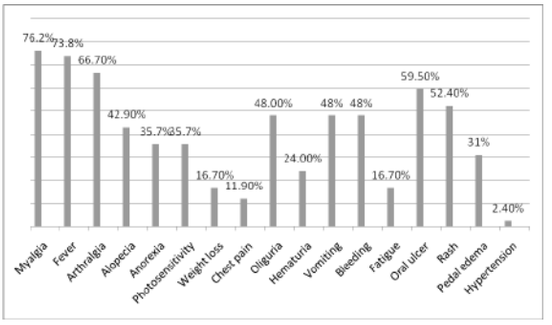

Fig 1 : Clinical features of the study population

Table II : Drugs taken by the study population (n=42)

Drug	Frequency (n)	Percentage (%)
NSAID	28	66.7
Steroid	21	50.0
Cyclophosphamide	3	7.1
Azathioprine	5	11.9
Methotrexate	3	7.1
OCP	2	4.8

Table III : Etiological types of anaemia (n=42)

Pattern of anaemia	Frequency (n)	Percentage (%)
Anaemia of chronic disease	22	52.4
Autoimmune hemolytic anaemia	6	14.3
Iron deficiency anaemia	10	23.8
Undefined	4	9.5

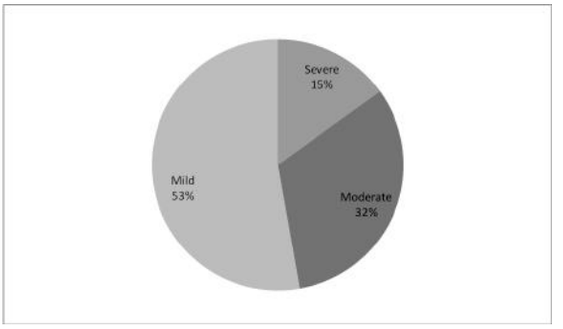

Figure 2 : Degrees of anaemia

Table IV : Distribution of haematological parameter in different types of anaemia (n=42)

Parameters	ACD (n=22)	AIHA (n=6)	IDA (n=10)
Age (Years)	26.50±8.60	32.30±7.29	21.30±4.42
SLEDAI	7.55±2.85	9.00±3.1	6.70±2.66
Hemoglobin(gm/dl)	9.41±1.593	8.50±1.97	9.50±1.43
MCV(fl)	83.27±7,27	81.17±8.30	71.80±7.1
MCH(pcgm)	27,32±2.62	26.83±2.13	23.20±4.36
MCHC(gm/dl)	31.91±2.56	27.83±11.75	31.40±3.20
Serum iron(mcg/dl)	40.27±6.46	83.80±38.01	41.70±3.94
Serum ferritin(ngm/ml)	713.09±1711.86	455.40±516.42	23.10±37.65
TIBC(mcg/dl)	229.86±27.87	307.00±84.55	463.30±56.13

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, MCV: Mean Corpuscular Volume, MCHC: Mean Corpuscular Hemoglobin Concentration, TIBC: Total Iron Binding Capacity. ACD: Anaemia of Chronic Disease, AIHA: Autoimmune Hemolytic Anaemia, IDA: Iron Deficiency Anaemia, Data are presented as mean±SD.

Table V : Immunological findings (n=42)

Test	Frequency (n)	Percentage (%)
Positive ANA	42	100.0
Positive anti Ds DNA	39	92.9
Positive Coombs' test(Direct)	6	14.3

Among the 42 enrolled patients 41 (97.62%) were female and 1 (2.38%) were male. Highest number of patients (35.71%) was from the 20 to 29 years age group. Mean age (±SD) was 27.02±8.63 years (Table I).

The most common presenting complaints were myalgia (76.20%), followed by fever (73.8%), arthralgia (66.7%) oral ulcer (59.5%) and malar rash (52.4%) (Figure 1).

Drugs play an important role in causing cytopenia. Most commonly taken drugs by the patients were NSAID, steroid and DMRDs. (Table II).

Anemia was detected in 42 (100%) patients (Table IV). ACD was the most prevalent (52.4%) followed by IDA (23.8%) and AIHA (14.3%) (Table III). Most of the patient (53%) had mild anaemia (Figure 2).

Hematological profiles in different types of anaemia among the patients are showed in Table IV. Patients with ADA were comparatively younger and had less disease activity index in comparison to other two types.

All the patients satisfied immunological criteria with positive for ANA . 92.9% patients were anti-ds-DNA positive and a positive direct Coomb's test was found in 14.3% of the patients (Table V).

Association of SLEDAI with severity or types of anaemia, positivity of Coombs' test could not be established in this study. No relation was found with the degree of anaemia with urine protein loss but change of renal function in the form of raised serum creatinine was associated with severity of anaemia (Not shown in the result).

Discussions

Although it was initially suspected that anaemia in SLE was mainly a result of antibody induced damage of erythrocytes, evidence to date indicates that the causes of anaemia in SLE vary and that the pathogenesis may be immune or non-immune. Anaemia of Chronic Disease (ACD) Iron Deficiency Anaemia (IDA) Autoimmune Haemolytic Anaemia (AHA) anaemia of chronic renal insufficiency, and cyclophosphamide-induced myelotoxicity are the most common causes. It is noteworthy that ACD often coexists with anaemia caused by other mechanisms. Iron deficiency is common in patients with SLE as a

result of menorrhagia and increased gastrointestinal blood loss, caused by the use of nonsteroidal anti-inflammatory drugs, aspirin, and oral anticoagulants[11-14]. This cross-sectional study was conducted in Department of Medicine and Nephrology of Chittagong Medical College Hospital to evaluate the pattern of anaemia among 42 patients with SLE.

There was a female preponderance in the studied patients; females were 97.62% and males 2.38%. Male female ratio was 1:44. This is consistent with most of the studies[15].

Cameron et al has reported a male to female ratio of 1:8 to 1: 14 in a series of adult patients[16]. Mean (±SD) age of the patients in this study was 24.86 (±5.88) years. Highest number of patients (31.5%) was in 21 to 25 years age group followed by 15 to 20 years of age (25.8%). SLE is a disease of child bearing age. The median age of onset of SLE is 24 years in a series reported by Malaviya AN[17].

The most common presenting complaints were myalgia (76.20%) followed by fever (73.8%) arthralgia (66.7%). Oral ulcer (59.5%) malar rash (52.4%) pedal edema (31%) were also common presenting symptoms. This is similar to some study done in India with a large sample size (321), where the presenting problems were the arthralgia (76%) and then the fever (61.9%) [18]. In another study conducted at Chittagong Medical College Hospital by Md. Abdur Rauf et al the most common presenting complaints were photosensitivity (84.2%) followed by fatigue (50%) and rash (45%)[19]. Fever (44%) was also a common presenting symptom with arthralgia (41%). Oral ulcer was found in 47.8% in our patients consistent with Malviya et al[17]. In a series of studies done by Wallace18 oral ulcers were present in 7-36% of cases[20]. 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. Malar rash was found in 74% of our patients. Overall the relative frequency of each of the major clinical features at presentations was similar to what has been documented in literature, except from those which were conducted with small sample size.

The commonest criteria satisfied were anti ANA (Immunological) as evidenced by positivity in 100% cases. 92.9% patient showed ds-DNA positivity. ANA positivity is reported to in about 90-95% of cases[18].

Most common hematological abnormality was anemia (100%). Various studies have shown anaemia is highly prevalent in SLE patients[21]. In a series of studies reviewed by BudMan anemia occurred in 57- 78% of patients with SLE[11]. Aleem et al concluded of hematological abnormalities, anemia was the most common disorder present in 63% of patients[22]. Iron deficiency anemia, anemia of chronic disease and autoimmune hemolytic anemia are the common cause of anemia in SLE. Iron deficiency has been diagnosed on the basis of hypochromicity on the peripheral smear mainly, along with some clinical features like pica, nail changes, glossitis and chelitis. Anemia of chronic disease on the basis of a normocytic and normochromic blood picture in the presence of negative Coomb's test and AIHA on the basis of positive Coomb's test and reticulocytosis. Further investigations to evaluate anemia such as iron studies, serum folate levels and bone marrow examinations has not been done due to financial constraints.

Anaemia of chronic disease has been found in 52.4% cases, autoimmune hemolytic anaemia in 14.3% cases and iron deficiency anaemia in 23.28% patients. The finding is similar to that documented by Voulgarelis et al[23]. A positive Coomb's test was observed in 37.1% of our patients but AIHA was documented in only 10.1%. Budman et al in a review of a series of studies has found 18 to 65% of Coomb's positivity in patients with SLE. However the incidence of AIHA in his study was less than 10%[11]. Aleem et al found a positive Coombs' test was found in 80 (35.9%) of the 223 patients tested, and 29/624 (4.6%) patients developed Autoimmune Hemolytic Anemia (AIHA)[22]. Three of our patients developed Evans syndrome (3%) which was higher than that of Aleem et al [3 (0.5%)][22]. Reticulocytosis was one of the diagnostic criteria for the diagnosis of AIHA. The bone marrow response to hemolysis in the form of reticulocytosis may be depressed if associated or folate deficiency is present or associated bone marrow suppression of chronic disease is present. This could be responsible for the gross discrepancy seen between the incidence of Coomb's positivity and the incidence of AIHA. More sophisticated test would perhaps have documented hemolysis in a greater number of patients.

Study patients were taking Disease Modifying Anti Rheumatic Agents (DMARDs) and steroids that might play a role in causing cytopenia. 50% of patients were taking steroids and 26% were taking DMRDs. Aleem et al found that most common causes of cytopenias during the course of SLE include drugs, infections and immune mediated. Drugs like cyclophosphamide and azathioprine were considered to be the cause of cytopenias in a substantial number of cases in this study[22].

The mean of SLE disease activity index has been noticed 7.49, in our study. Association of SLEDAI with severity or types of anaemia, positivity of Coombs' test could not be established in this study. No relation was found with the degree of anaemia with urine protein loss but change of renal function in the form of raised serum creatinine was associated with severity of anaemia. To establish whether or not any association between those, large scale study is needed.

Conclusion

In conclusion, anaemia is common findings inpatients with SLE.In our study anemia of chronic disease is most common followed by iron deficiency anaemia. Myalgia, fever , arthralgia and oral ulcer are the commonest symptom. It is important to distinguishanaemia as either manifestation of SLE,consequence of SLE treatment or as a part of another blooddyscrasia.This study has some potential limitations like small sample size, it was a single center study with absences of long term follow up findings and some relevent investigations could not be done like soluble transferrin receptor and hemoglobin elecetropheresis. Similar surveys shouldbe conducted to delineate the actual intensity of the problemwith modern lab facilities, bigger sample size, withelimination of confounding variables. Moreover cohortstudies should be undertaken to find natural history of theanaemia and to evaluate the effect oftherapeutic interventions upon it.

Disclosure

All authors declare no competing interest.

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