Research article

Haematological parameters in systemic lupus erythematosus patients at Kenyatta National Hospital, Nairobi

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Abstract

Background: Haematological abnormalities are the most common manifestations of Systemic Lupus Erythematosus (SLE). Anaemia of Chronic Disease (ACD) has been associated with significantly higher disease activity. Thrombocytopenia early in the course of disease is indicative of more severe active disease and if severe it is an independent predictor of damage accrual and mortality. Leucopenia usually reflects disease activity.
Objectives: To determine the prevalence of haematological abnormalities, among SLE patients on follow up at Rheumatology and Renal Outpatient clinics at Kenyatta National Hospital. Specifically, the study aimed to describe the prevalence of anaemia, leucopenia, and thrombocytopenia and identify patient factors associated with these abnormalities.
Design: Cross-sectional hospital based descriptive study.
Setting: Rheumatology out-patient clinic and Renal out-patient clinic at KNH.
Subjects: Sixty five patients who fulfilled the 1997 American College of Rheumatology Classification Criteria for SLE.
Results: Sixty five eligible SLE patients were recruited into the study. The mean (SD) age was 36.5 (± 12) years. There were 3 (5%) males and 62 (95%) females. Forty nine (75%) patients had at least one abnormality. The abnormalities involved all the three cell lines. The prevalence of abnormalities were; anaemia 43%, leucopenia 26% and thrombocytopenia 20%.
Conclusion: Haematological abnormalities were the second most common manifestation of the disease after arthritis and arthralgia among SLE patients on follow up at Kenyatta National Hospital Rheumatology and Renal clinic. Though majority of these abnormalities were mild to moderate and clinically asymptomatic, the proportions of anaemia, leucopenia and thrombocytopenia were substantially high.

Key words: Haematological parameters, Systemic Lupus Erythematosus, Kenyatta National Hospital

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disorder that results in multi-systemic inflammatory damage. It's often severe and can affect virtually all organs including the haematologic system.

Haematological abnormalities have been noted to be among the commonest in SLE patients in several studies[1,2]. This is attributed to blood and blood vessels together containing 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. Haemolytic anaemia, leucopenia, lymphopenia, and thrombocytopenia are part of the diagnostic criteria for SLE according to American College of Rheumatology criteria (ACR) 1997[3] and the more recently validated Systemic Lupus International Collaborating Clinics Classification Criteria (SLICC) 2012 for Systemic Lupus Erythematosus[4].

SLE patients with Anaemia of Chronic Disease (ACD) have been shown to have significantly higher disease activity[5]. Thrombocytopenia early in the course of SLE is indicative of more severe active disease, if severe it is an independent predictor of damage accrual and mortality[6,7]. Leucopenia is also common in SLE and usually reflects disease activity[7,8].

Different studies report different prevalence rates. Agrawal *et al*[9] in Central India in 2012 reported haematologic manifestation in SLE in 72.4% of patients while Houman *et al*[10] in Tunisia reported a prevalence rate of 81%.

Materials and Methods

A cross sectional descriptive hospital based study conducted between March 2015 to June 2015 at Rheumatology and Renal outpatient clinics of Kenyatta National Hospital (KNH). The study was commenced after obtaining all the necessary ethical approvals from the KNH research and ethics committee and from the Department of Clinical Medicine and Therapeutics, University of Nairobi. All

patients aged above 18 years seen at KNH Rheumatology and Renal clinics fulfilling the 1997 ACR classification criteria for diagnosis for SLE were eligible. 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 KNH Department of Human Pathology, Unit of Haematology and Blood Transfusion 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 haematologist.

Statistical analysis was done using SPSS version 21. Analysis included descriptive statistics such as means, medians and standard deviation for continuous variables and frequency distributions for categorical variables, with their corresponding 95% Confidence Intervals (CI). Comparisons for continuous data was made using the t-test, and of categorical data using the chi-square test. Prevalence of study variables, (e.g. anaemia, leukopenia and thrombocytopenia) was calculated as the proportion of subjects having the variable divided by the total number of subjects. Precision was indicated by 95% Confidence Interval (CI) limits. A p value ≤ 0.05 was considered significant. The final results were presented in tables, charts and graphs.

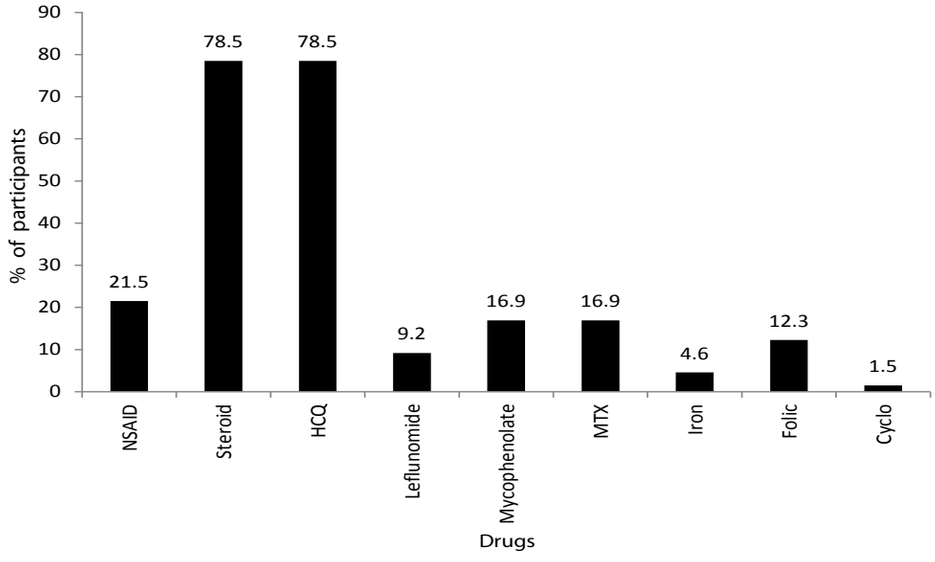
Results

In a period of 4 months (March 2015 to June 2015) 71 patients with SLE were identified, of these 66 met the ACR criteria for SLE and were recruited to the study. Three patients had SLE and Rheumatoid Arthritis (RA) while two had SLE with Mixed Connective Tissue Disease (MCTD) and were excluded. One patient was eligible but refused to give consent to have blood tests done. Final analysis included 65 patients.

Table 1: Baseline characteristics of the study population

Characteristic	Frequency(%)
Sex	
Male	3 (5%)
Female	62 (95%)
Age (years)	
Mean (SD)	36. 5 (± 12)
Range	18-62
Median	35
Age distribution (years)	
>20	7 (11%)
21-40	36 (55%)
>41	22 (34%)
Age at diagnosis	
Mean (SD)	33 (±12)
Duration of disease in months	
Median (IQR)	36 (12-60)
Level of education	
Primary	14 (21.5%)
Secondary	36 (55.4%)
Tertiary	15 (23.1%)
Occupation	
Employed	15(23.0%)
Self employed	25(38.5%)
None	25(38.5%)
Residence	
Urban	28(43.1%)
Rural	37(56.9%)

Figure 1: Medications taken by study participants



NSAID = Non Steroidal Anti-inflammatory drugs), HCQ = Hydroxychoroquine), MTX = Methotrexate, Cyclo = Cyclophosphomide

Table 2: Haematological parameters of study participants (n=65)

Parameter	Median (Range)	Mean±SD	Ref Range (Male)	Ref Range (female)
RBC (x10^{12}/L)	4.5 (1.9-5.9)	4.3 (0.8)	4-6	3.5-6.5
Haemoglobin (g/dl)	12.4 (5.4-17.9)	12 (2.6)	13.5-18	12-15
WBC (x 10^9 /L)	5 (1.1-17.1)	6.2 (3.3)	4-11	4-11
Neutrophil (x 10^9/L)	2.8 (0.1-14.8)	3.7 (2.7)	2.0-7.5	2.0-7.5
Lymphocytes (x 10^9/L)	1.6 (0.3-6.4)	1.8 (1.1)	1.5-4.0	1.5-4.0
Platelets (x 10^9/L)	266 (28-521)	263.8 (107)	150-400	150-400
ESR (mmhr)	30 (1-122)	38.2 (28)	0-9	0-20

Figure 2: Prevalence of haematological abnormalities in SLE

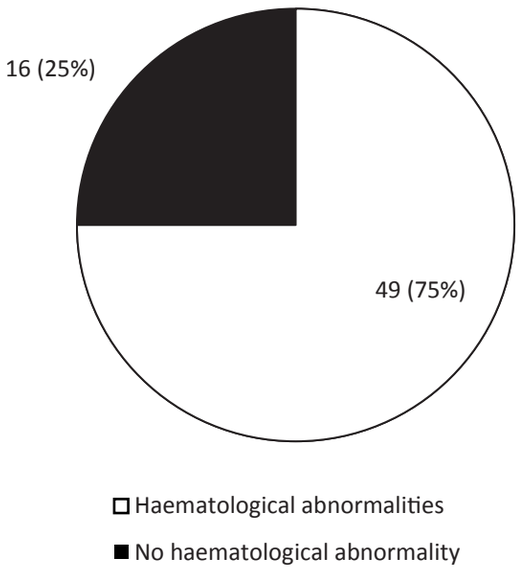


Table 3: Prevalence of various haematological abnormalities amongst study participants (n=65)

Abnormality	Frequency	(%)	95% CI
Anaemia	28	43.1	30.7-55.4
Leucopenia	17	26.2	15.2-37.1
Neutropenia	18	27.7	17.3-40.2
Lymphocytopenia	29	44.6	32.2-57.5
Leucocytosis	6	9.2	2-16.5
Neutrophilia	6	9.2	2-16.5
Lymphocytosis	3	4.6	112.9
Thrombocytopenia	13	20	10-30
Thrombocytosis	8	12.3	4.1-20.5

Figure 3: Type of anaemia in study participants

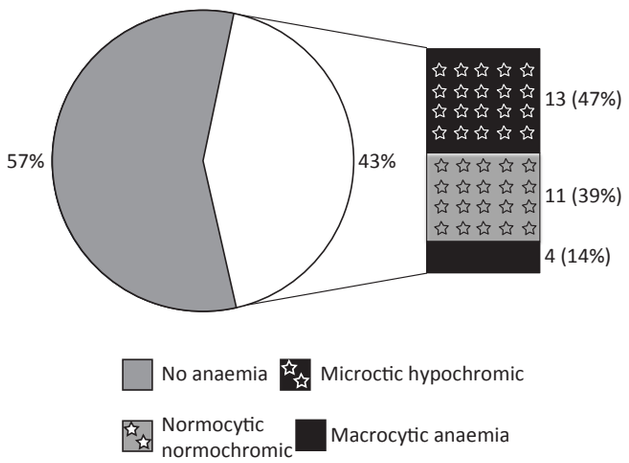
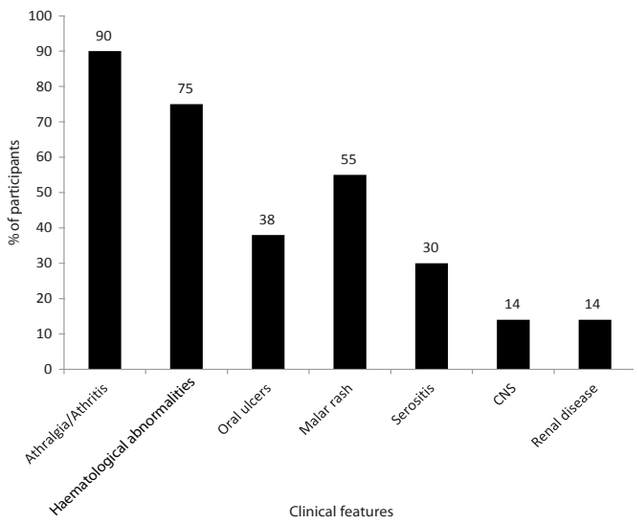


Figure 4: Distribution of clinical features of SLE in the study population



CNS = Central Nervous System

Discussion

Haematological abnormalities: In this study haematological abnormalities were the second most common manifestations (75%) of SLE after athralgia and arthritis. Anaemia was the commonest abnormality present in 43% of patients followed by leucopenia (26%) and thrombocytopenia (20%). Severe haematological involvement has been associated with significant CNS and renal disease[11] and this raises a concern of possible severe disease in our SLE population.

The prevalence of haematological abnormalities in this study was comparable to what has been found in other studies conducted in other parts of the world. In Nigeria, Houman *et al*[10] found a prevalence rate of 81%. Several studies done in India among them Agrawal *et al*[9] found a prevalence 72.4% and Sasidharan *et al*[12] found prevalence of 82%. Western literature also indicates haematological abnormalities are a common presentation of SLE[13]. These findings support our observation and emphasizes that haematological abnormalities are a common manifestation of SLE patients.

Anaemia: Anaemia was present in 43.1% of the patients. Although the mean haemoglobin was 12g/dl, and the median was 12.4g/dl, the haemoglobin range was 5.4 - 17.9g/d. The aetiology of anaemia in SLE is usually heterogeneous and may result from immune and non immune mechanisms. Some of the possible causes of anaemia in our population are Iron Deficiency Anaemia (IDA), Anaemia of Chronic Disease (ACD), Autoimmune Haemolytic Anaemia (AIHA), and drug induced myelotoxicity. Other rare causes eg aplastic anaemia and myelofibrosis may also have contributed to anaemia in our SLE population. ACD in our population may have been due to chronic inflammation and renal disease while IDA may have been due to menorrhagia as most of our participants were young females in the reproductive age group, gastrointestinal bleeding due to the frequent use of NSAIDS and steroids, nutritional and possibly due to hookworm infestations.

The prevalence of anaemia in this study is lower than that found by Sasidharan *et al* [12] in India. They found an anaemia prevalence of 62%. This could be attributed to co-existing high prevalence of anaemia in India (approximately 50%) in the rural areas as compared to Kenya's prevalence of 38%, (WHO global data base on anaemia burden[14]). The reason given for the high anaemia burden among Indians are nutritional related being predominantly vegetarian society with limited nutritional iron sources and chronic blood loss from hookworm infestations in rural areas. This study population was predominantly urban. Additionally the study focussed on a highly preselected population which was being followed up in a tertiary setting with improved care and ability to access quality health care.

Anaemia in SLE is largely multifactorial but morphologically most of the study population had microcytic hypochromic anaemia. Microcytic anaemia is usually due to either IDA or less commonly ACD. These findings differ with other studies in other centers where normocytic normochronic anaemia has been found to be most common[12]. The high prevalence of microcytic anaemia can be explained by increased number of patients on steroids, NSAIDS and antimalarials. Other possible cause could be due to our study population consisting of predominantly young females in the reproductive age group.

Despite the high prevalence of moderate anaemia (20%) in our study population only a small proportion of patients were on treatment with hematinics, such as iron (4.3%) and folic acid (12.2%) indicating that anaemia in this group was largely untreated. Folic acid was co-prescribed with methotrexate. None of the patients was on erythropoesis stimulating agents.

White cell abnormalities: The mean white cell count in the study population was 6.2 x 10^9/L a median of 5 x 10^9/L and a range 1.1-17.7 x 10^9/l. However in Africans a lower limit of normal WBC of 2.6 X 10^9/ L has been described[15].

Leucopenia: Leucopenia in this study was defined using the haematology laboratory reference range as WBC count < 4 x 10^9/L. The prevalence of leucopenia was 26.2%, mainly due to lymphopenia and neutropenia. Immune destruction of antibody coated WBC, active disease and steroid therapy may have contributed to leucopenia in our population. Several studies have shown leucopenia is associated with active disease and steroid therapy[16]. 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. Several studies have demonstrated these possible mechanisms[16].

Leucopenia in this study was more pronounced than in the Indian study by Sasidharan *et al*[12]. Sasidharan's study found a leucopenia prevalence of 15.7% while Agrawal *et al*[9] found a prevalence of 18.4%. This difference in leucopenia could be attributable to the racial differences between the two populations. Black Africans have been found to have a slightly lower WBC count than other races[15]. Several studies have shown leucopenia is associated with active disease and steroid therapy[16]. Leucopenia in the study participants could be due to both active disease and steroid therapy.

Leucocytosis: Leucocytosis was present in 9.2% of study population, majorly driven by neutrophilia. We attributed this to the high proportion of patients who were on steroids. Other possible explanation is the patients may have had active infection.

Platelet abnormalities: The mean platelet cell count in the study population was 263.8 x 10^9/L, a median of 266 x 10^9/L and a range 28-521 x 10^9/ L.

Thrombocytopenia: Thrombocytopenia was defined using the haematology laboratory reference range as platelet count < 150 x 10^9/L.

Several mechanism may have contributed to thrombocytopenia in our population among them immune destruction, drugs, infections and possibly bone marrow suppression. Thrombocytopenia in our study population was most of the time mild and benign and not associated with any overt bleeding. These patients did not require any specific treatment. Nevertheless since thrombocytopenia is an independent risk factor for mortality[16], the sub-group of patients with thrombocytopenia will require more aggressive management and more frequent follow up.

In their Indian study, Sasidharan *et al*[12] found a thrombocytopenia prevalence of 39.8% in SLE patients. The prevalence of thrombocytopenia in this study was 20% which was significantly lower. This difference could be partly due to the fact that their study looked at thrombocytopenia as an initial presentation of SLE while in this study platelets counts were measured among participating patients at different times in the course of their illness. In addition majority of our patients were already on treatment and had achieved some control of the disease. Agrawal *et al*[9] in their study found a lower prevalence of thrombocytopenia of 14.9%. However it is notable that in Agrawal's study, thrombocytopenia was defined as a platelet count below 100 x10^9/ L as opposed to this study where we defined thrombocytopenia as a platelet count below 150 x 10^9/ L.

Thrombocytosis: There were 8 cases (12.3%) of thrombocytosis of which 3 cases had confirmed APLAS. The other 5 cases had not been investigated for APLAS. A plausible explanation for this is a possible reactive thrombocytosis in our study population due to the high prevalence of microcytic hypochromic anaemia.

Our prevalence of 12.3% was significantly higher than that reported in other studies. Castellino *et al*[17] found a prevalence of 3.7% in Caucasians with SLE. These differences may be attributed to racial differences.

Erythrocyte Sedimentation Rate: The mean ESR 38.2mm/ hr with a median of 30mm/hr and range of 1-122mm/hr. Majority of the patients (66%) had an elevated ESR. This may be explained by the high prevalence of anaemia at 43.1%. Other possible causes are the patients may have had active disease as several studies have shown that elevated levels of ESR may be associated with disease activity and accumulated damage[18].

Conclusion

Haematological abnormalities were the second most common manifestation of the disease after arthritis and arthralgia among SLE patients on follow up at Kenyatta National Hospital Rheumatology and Renal clinic. Though majority of these abnormalities were mild to moderate and clinically asymptomatic, the proportions of anaemia, leucopenia and thrombocytopenia were substantially high.

Study limitations

Our analysis did not scrutinize the causes of haematological abnormalities and correlate our findings with disease activity due to financial constraints.

Recommendations

A study to further scrutinize the causes of these haematological abnormalities needs to be done. A bigger multicenter study to correlate these haematological abnormalities with disease activity in patients with SLE, which may be useful as surrogate markers of disease activity in resource constrained settings. Long term follow up of subgroup of patients who had thrombocytopenia to determine outcome.

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