ORIGINAL ARTICLE

Patterns of Anemia in patients of Systemic Lupus Erythematosus Study of 75 cases from Lahore, Pakistan

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ABSTRACT
Objectives: To determine the frequency and types of anaemia in patients of Systemic Lupus Erythematosus (SLE).
Design: Cross sectional survey.
Place and duration of study: Department of Haematology, PGMI/Shaikh Zayed Hospital, Lahore from May 2011 to April 2012.
Patients and Methods: Seventy five diagnosed cases of SLE presenting to the in- and out-patient departments of Shaikh Zayed Medical Complex Lahore, fulfilling the inclusion criteria were included in the study. Written informed consent was taken. Patients were investigated in Haematology and Biochemistry Laboratories, Shaikh Zayed Medical Complex, Lahore. All collected information was entered into SPSS version 17.0 and analyzed using its statistical package.
Results: There were 65 (86.7%) females and 10 (13.3%) male patients. Female to male ratio was 6.5**:**1. Age ranged from 15 to 65 years, mean 29.49±11.7 years. Most of the patients were in the age group of 15-25years. Anemia was seen in 74 patients (98.67%). Anaemia of chronic disorder (ACD) was the most common type of anemia (52.7%) followed by iron deficiency anaemia (IDA) (32.4%).
Conclusion: All common types of anemia associated with SLE were recorded in the study. Complete haematological examination should be carried out in every patient of SLE for proper management and prevention of morbidity associated with anemia.

Key Words: Systemic Lupus Erythematosus, Anemia: chronic disease, Iron deficiency.

INTRODUCTION
SLE is a systemic, inflammatory autoimmune disorder characterized by autoantibodies to nuclear antigens. At least 50 antigen targets for autoantibody production are described in SLE.[1,2] The main clinical features include fever, rashes and arthritis, but renal, pulmonary, cardiac, haematological and neurological involvement may occur, with increased mortality.[3] For any individual patient, the ARA(American Rheumatology Association) criteria may be used as an aid to diagnosis.

SLE is an uncommon disease, with incidence estimated 1–12.5 in 100,000 per year at Leeds General Infirmary.[4] The prevalence of SLE is influenced by many factors, including gender, race, and genetic inheritance. 90% of patients with lupus are females, an important role for female hormones seems likely, but a protective role for male hormones or an effect of genes on the X chromosome is also possible.[5] Evidence of a genetic component includes familial clustering, and higher concordance rates between monozygotic twins (>20%) relative to dizygotic twins and other siblings (2-5%).[6]

White people with SLE have increased frequencies of HLA-B8, -DR3, -A1 and -DR2 [7,8]. HLA-DQ antigens may be even more closely related to the risk of developing the disease [9]. There is evidence of linkage disequilibrium between B8-DR3 and alleles at the DQ locus [10].

A range of pathogenic autoantibodies may be present in the disease.[11] An association with environmental factors such as ultraviolet B light, infectious agents such as retroviruses or bacterial lipopolysaccharides, certain drugs and dietary factors has also been reported.[12]

The disease may affect many systems of the body, and the presentation and course are by no means uniform. Haematological complications are frequently seen in SLE. Anemia, leucopenia and thrombocytopenia may result from bone marrow

failure or excessive peripheral cell destruction, both of which may be immune, drugs or infection mediated. [13]

Anemia is present in between 50-66% patients and may be multifactorial.[14] The frequency of various types of anemia known to complicate SLE are IDA 44%, ACD 34% and autoimmune hemolytic anemia (AIHA) 12% .[15] In addition, anemia in SLE may be accompanied by various syndromes of hematopoietic failure, such as aplastic anemia (AA), hemophagocytic syndrome and rarely pure red cell aplasia (PRCA).[16,17,18]

The course of SLE is very variable.[19]There is no cure for SLE, and complete sustained remissions are rare. The aim of treatment is to maintain optimal function with minimum therapy.[20] The mainstay of treatment of SLE is systemic glucocorticoids. [21] Minor joint symptoms can be alleviated by rest and NSAIDs. Antimalarials (hydroxychloroquine) may be helpful in treating lupus rashes or joint symptoms refractory to NSAIDs. [22]

This study was conducted to find the patterns of anemia in patients with SLE and improve quality of life in them by early diagnosis and management of anemia.

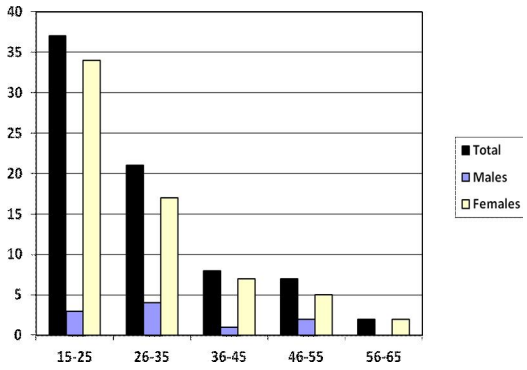
PATIENTS AND METHODS

Newly diagnosed 75 patients of SLE (aged 15yrs and above) of both genders presenting in- and outpatient departments of Shaikh Zayed Medical Complex, Lahore, diagnosed on the basis of ARA criteria were included in the study. Patients with other diseases like Rheumatoid arthritis, systemic sclerosis, dermatomyositis and chronic infections like tuberculosis, chronic Hepatitis B and C were excluded from the study. Written informed consent was taken and name, age and address recorded. Patients were investigated in Haematology Laboratory, Shaikh Zayed Medical Complex, Lahore for Complete blood count (CBC), retic count, peripheral smear and bone marrow examination (where indicated) . These investigations were necessary to analyze anaemia in SLE. Male patients with Hb less than 13 g/dl and females with Hb less than 12 g/dl were considered anemic (WHO criteria).[23] Patients with microcytic hypochromic anemia were advised to have serum iron and TIBC levels while those with macrocytic anemia were investigated for direct and indirect coomb's test, serum LDH, B12 and folate levels. Patients with normocytic and normochromic anemia were considered to have anemia of chronic disease. Aplastic anemia and pure red cell aplasia were diagnosed on bone marrow examination. All this information was entered in a specially designed proforma and entered into SPSS version 17.0 for statistical analysis. Age was presented in terms of mean and standard deviation, gender in terms of frequency and percentages. Presence or absence of anemia and its types were expressed as frequency and percentages.

RESULTS

The study was carried out over a period of six months. Out of 75 patients, 65 (86.7%) were females and 10 (13.3%) were males. Female to male ratio was 6.5:1. Age ranged from 15 to 65 years. Mean age was 29.49 ±11.7 years. Mean age for females was 29.06 ±11.88 years (range= 15-65 years) and for males 32.30 ±11.02 years (range 17-50 years). Most of the patients were in the age group of 15-25 years. Maximum number of females was in the age group 15-25 years while most of the male patients were in age group 26-35 years (Figure 1).

Figure 1: Age and gender distribution in study Population



(n=75)

On analysis of the haematological parameters, anemia was seen in 74 patients (98.67%). Mean Hb was 8.45 ± 1.95g/dl (range 4.2-13.0 g/dl). Mean Hb in male patients was 9.05 ± 2.67g/dl (range 4.2- 13.0 g/dl) and in females was 8.36±1.82g/dl (range 4.9-11.6g/dl). Mean haemoglobin concentration of the age group 15-25 years, with maximum number of female patients, was 8.22 ±1.72g/dl (range 5.1-11.6g/dl) while mean Hb for the age group having maximum number of male patients (26-35 yrs) was 8.56±3.29g/dl (range 4.2-11.3 g/dl).The difference was not statistically significant (Table 1).

Table 1: Hb concentration according to Age and gender (n=75)

Age groups	Gender	Hb conc (g/dl)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	5.1-11.6	8.22±1.72	0.331
	Male (n=3)	7.7-12.0	9.26±2.37	
26-35	Female (n=17)	4.9-11.6	7.84±1.85	0.542
	Male (n=4)	4.2-11.3	8.58±3.29	
36-45	Female (n=7)	7.6-11.2	9.83±1.27	0.058
	Male (n=1)	13.0	13.0	
46-55	Female (n=5)	5.6-10.6	9.32±2.09	0.353
	Male (n=2)	7.3-8.1	7.70±0.57	
56-65	Female (n=2)	5.8-9.7	7.75±2.76	-
	Male (n=0)	-	-	

Normal Hb: Males 13.0-17.0 g/dl Females- 12-15.0 g/dl [23]

Table 2: Types of Anemia and their frequency (n=74)

Anemia type	Males (n=9)	Percentage %	Females (n=65)	Percentage %	Total (n=74)	Percentage %
ACD	4	10.25	35	89.74	39	52.7
IDA	4	16.67	20	83.33	24	32.4
AIHA	0	--	5	100	5	6.7
AA	1	33.33	2	66.67	3	4.0
PRCA	0	--	2	100	2	2.7
MA	0	--	1	100	1	1.3

ACD= Anemia Of Chronic Disease
IDA=Iron Deficiency Anemia
AIHA= Autoimmune Hemolytic Anemia
AA=Aplastic Anemia
PRCA=Pure Red Cell Aplasia
MA= Megaloblastic Anemia

Table 3: Types of anemia according to age and gender (n=74)

Gender	Age group (yrs)	Anemia type	Frequency	Percent %
Female (n=65)	15-25 (n=34)	ACD	20	58.8
		IDA	8	23.5
		AIHA	3	8.8
		AA	2	5.9
		MA	1	2.9
	26-35 (n=17)	ACD	6	35.3
		IDA	9	52.9
		AIHA	1	5.9
		PRCA	1	5.9
	36-45 (n=17)	ACD	6	85.7
		IDA	1	14.3
	46-55 (n=5)	ACD	3	60.0
		IDA	1	20.0
		PRCA	1	20.0
	56-65 (n=2)	IDA	1	50.0
		AIHA	1	50.0
Male (n=9)	15-25 (n=3)	ACD	2	66.7
		IDA	1	33.3
	26-35 (n=4)	ACD	1	25.0
		IDA	2	50.0
		AA	1	25.0
	46-55 (n=2)	ACD	1	50.0
		IDA	1	50.0

Table 4: Hb levels in various types of anemia according to age and gender (n=74)

Anemia type	Age groups	Gender	Hb conc (g/dl)		p value
			Range	Mean ± SD	
ACD (n=39)	15-25	Female (n=20)	5.8-11.6	8.45±1.78	0.324
		Male (n=2)	7.7-12.0	9.85±3.04	
	26-35	Female (n=6)	5.2-11.6	8.07±2.44	0.201
		Male (n=1)	4.2	4.2	
	36-45	Female (n=6)	7.6-11.2	10.00±1.29	-
		Male (n=0)	-	-	
	46-55	Female (n=3)	10.0-10.6	10.33±0.3	0.024
		Male (n=1)	8.1	8.1	
IDA (n=24)	15-25	Female (n=8)	6.3-10.5	7.75±1.40	0.821
		Male (n=1)	8.1	8.1	
	26-35	Female (n=9)	6.4-10.0	8.13±1.33	0.015
		Male (n=2)	10.9-11.3	11.1±0.28	
	36-45	Female (n=1)	8.8	8.8	-
		Male (n=0)	-	-	
	46-55	Female (n=1)	10.0	10.0	-
		Male (n=1)	7.3	7.3	
	56-65	Female (n=1)	9.7	9.7	-
		Male (n=0)	-	-	
AIHA(n=5)	15-25	Female (n=3)	5.1-10.6	7.67± 2.75	-
		Male (n=0)	-	-	
	26-35	Female (n=1)	4.9	4.9	-
		Male (n=0)	-	-	
	56-65	Female (n=1)	5.8	5.8	-
		Male (n=0)	-	-	
AA (n=3)	15-25	Female (n=2)	7.3-10.2	8.75±2.05	-
		Male (n=0)	-	-	
	26-35	Female (n=1)	7.9	7.9	-
		Male (n=0)	-	-	
PRCA (n=2)	26-35	Female (n=1)	6.7	6.7	-
		Male (n=0)			
	46-55	Female (n=1)	5.6	5.6	-
		Male (n=0)	-	-	
MA (n=1)	15-25	Female (n=1)	7.6	7.6	-
		Male (n=0)	-	-	

Normal Hb: Males 13.0-17.0 g/dl Females- 12-15.0 g/dl[23]

ACD was seen in 39 patients (52.7%), IDA in 24 patients (32.4%), AIHA in 5 patients (6.7%), AA in 3 patients (4.0%), PRCA in 2 patients (2.7%) and megaloblastic anaemia (MA) in 1 patient (1.3%) (Table 2).

Maximum number of female patients (20 patients) having ACD belonged to age group 15-25 years (Table 3).

Cases with ACD had a mean Hb of 8.73 ±2.01g/dl as compared with 8.47 ±1.53g/dl for AA, 8.38 ±1.51g/dl for IDA, 7.6 g/dl for MA, 6.8±2.38g/dl for AIHA and 6.15± 0.78g/dl for PRCA. Females of age group 15-25 years with maximum number of ACD cases had Hb of 8.45 g/dl. The difference was significant in Hb levels of both genders of 46-55 age group of patients with ACD and 26-35 age group of IDA patients (Table 4).

DISCUSSION

Anaemia is a common clinical finding in patients with SLE. The most common form of anaemia in

these patients is anaemia of chronic disorder, however autoimmune haemolytic anaemia, iron deficiency anaemia, drug induced myelotoxicity and anaemia of chronic renal failure are not uncommon. The aim of present study was to determine the frequency and types of anemia in SLE.

Anemia was seen in a considerable percentage of patients i.e. 98.67%. In the present study, the mean age of the patients was 29.49±11.75 years. Majority of our patients were in the 3rd decade. In a study by Chen JL mean age of patients was 33.4 years.[24] Shaikh MA et al, in their study group, found the mean age to be equal to 28±6.22 years.[5] Al Saleh J et al conducted a study where the mean age came out to be 35.5 years.[25] Khan AA et al found a mean age of 29.92 years of the SLE patients included in their study. [15] The mean age of patients in the current study is comparable with all these studies.

The fact that SLE is more common in females is well established in this study. There were 65(86.7%) females and 10 (13.3%) males. Female to male ratio was 6.5:1. In a study by Chen JL there were 207 (86.7%) females and 29 (13.3%) males. [24] Shaikh MA et al reported a case series of 27 females (90%) and 3 (10%) males.[5] Beyan E et al reported a series of 115 cases where 20 (17.4%) were males and 85 (73.9%) were females. [26] In a study by Al Saleh J et al the female to male ratio came out to be 20.5:1. [25] Khan AA et al reported a study of 47 (94%) females and 3 (6%) males. [15]

A pathological deficiency in the oxygen-carrying component of the blood, measured in unit volume concentrations of hemoglobin, red blood cell volume, or red blood cell number is called anemia. According to WHO criteria a person is said to be suffering from anemia when haemoglobin concentration is below 13 g/dl for males and 12 g/dl for females. Keeping these values as standard, frequency of anemia came out to be 98.67% in our study. Shaikh MA et al in their study from Hyderabad, Pakistan found 93.33% of their SLE patients to be anemic.[5] From China Chen JL et al in 2007 and Xiongyan L et al in 2010 reported the frequency to be 52.1% and 37.2% respectively. [24, 28] In a study by Khan AA et al in 2006 from Islamabad, Pakistan the frequency of anemia came out to be 79.37%.[15] Voulgarelis M et al in a study from Greece in 2000 came up with a figure of 38%. [27]

In the present study ACD was seen in 52.7%, IDA in 32.4%, AIHA in 6.7%, AA in 4.0%, PRCA in 2.7% and MA in 1.3%. Shaikh MA found IDA in 30%, ACD in 40% and 23.33% had AIHA.[5] In their study Chen JL et al observed that 66.7% patients had ACD, 14.6% had AIHA, 6.6% had hematopoietic abnormalities and 12% had anemia caused by unknown reasons.[24] Identified causes in 89 anemic patients in a series of 239 cases, reported by Xiongyan L, were ACD in 39.3%, IDA in 36%, AIHA in 23.6% and 10.1% had anemia due to other causes. [28] Khan AA found IDA in 44%, ACD in 34%, AIHA in 12%, combination of AIHA and IDA in 6%. [15] In a study by Voulgarelis M ACD was seen in 37.1% of cases, IDA in 35.6%, AIHA in 14.4% and other causes 12.9%.[27]

Mean Hb for ACD cases was 8.85±2.04g/dl, for IDA was 8.42±1.65g/dl, AIHA 6.8± 2.38g/dl, AA 8.47±1.53g/dl, PRCA 6.15 ±0.78 g/dl, MA 7.6g/dl. In their study Voulgarelis M et al found that ACD cases had mean Hb 9.94 ±1.31g/dl, IDA 10.87± 0.91g/dl, 8.99± 1.51 g/dl for AIHA and 9.64 ± 1.80 g/dl for the group of other causes.[27]

CONCLUSION

All common types of anemia associated with SLE were recorded in the study. Complete haematological examination should be carried out in every patient of SLE for proper management and prevention of morbidity associated with anemia.

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