ORIGINAL ARTICLE

RBC Parameters in Patients of Systemic Lupus Erythematosus Report of 75 Cases from Lahore, Pakistan

ASMA MUNIR, MONA AZIZ, MANAAL AFZAAL, MUHAMMAD USMAN, ATIYA MAHBOOB
1Consultant haematologist, 2Associate professor of Hematology Shaikh Zayed FPGMI Lahore, 3Senior registrar of Dermatology, Shaikh Zayed FPGMI Lahore, 4Trainee Registrar, Dept of Nephrology, Shaikh Zayed FPGMI Lahore, 5Professor of Dermatology, Shaikh Zayed FPGMI Lahore.
For correspondence: Dr. Asma Munir, 200-D, DHA-EME, Lahore. Pakistan. Email: gemini_twinz01@hotmail.com

ABSTRACT
Background: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease that may virtually affect every organ in the body. It is characterized by the production of a variety of autoantibodies. Haematological manifestations of SLE are diverse. Anemia is the major haematologic manifestations of SLE .
Objectives: To determine the various RBC parameters in patients of Systemic Lupus Erythematosus .
Design: Prospective, cross sectional.
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 fulfilling the inclusion criteria presenting to the medical in- and out-patient departments of Shaikh Zayed Medical complex Lahore, were included in the study. Written informed consent was taken. Patients were investigated in Haematology Laboratory, 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 age 29.49±11.7 years). Anemia was seen in 74 patients (98.67%). Mean Hb was 8.45±1.95 g/dl (range 4.2-13.0 g/dl). Mean RBC count was $3.45x10^{12}$±0.93/l (range 1.15-$5.52x10^{12}$/l. Mean Hematocrit was 26.92±7.17% (range 12.19-43.27%).Value of MCV ranged from 51-115fl (mean MCV 78.5±9.98 fl). Similarly mean MCH was 25.19±4.19pg (range 14.7-44.7 pg), while mean MCHC came out to be 31.6±2.53g/dl (range 26-42g/dl) .
Conclusion: All RBC parameters were disturbed to a variable range in patients with SLE in the study cases. Complete haematological examination should be carried out in every patient of SLE in early course of the disease for proper management and prevention of morbidity associated with anemia.

Key Words: Systemic Lupus Erythematosus,Anemia, RBC parameters.

INTRODUCTION
SLE is an inflammatory autoimmune disorder characterized by auto antibodies to nuclear antigens. Multiple organ systems can be affected. Many of its clinical manifestations are secondary to the trapping of antigen-antibody complexes in capillaries of visceral structures or to autoantibody-mediated destruction of host cells (e.g., thrombocytopenia). The main clinical features include fever, rashes and arthritis, but renal, pulmonary, cardiac and neurological and haematological involvement may occur, with increased mortality.[1] Haematological complications are frequently seen in SLE. [2] For any individual patient, the ARA (American Rheumatology Association) criteria may be used as an aid to diagnosis.

The term lupus (Latin for wolf) is attributed to the thirteenth century physician Rogerius who used it to describe erosive facial lesions that were reminiscent of a wolf's bite.[3,4] The history of lupus can be divided into three periods: the classical period which saw the description of the cutaneous disorder, the neoclassical period which saw the description of the systemic or disseminated manifestations of lupus, and the modern period which was heralded by the discovery of the LE cell in 1948.[5]

The condition is universal, but is three times more common in black people than in white

people. 90% of patients with lupus are females. The condition tends to occur in early adult life and the peak age of onset of the first symptom or sign in females is approximately 38 years (35.5 in black women, and 40.7 in white women); it is 44.2 in men. [6]

Haematological complications are frequently seen in SLE. Anemia, leucopenias and thrombocytopenia may result from bone marrow failure or excessive peripheral cell destruction, both of which may be immune mediated, drugs and infection. [2,7] Anaemia, of some degree, is found in approximately 75% of patients and is brought about by deficiency of iron, haemolysis or renal failure. SLE can present with hematological manifestations alone or along with features of other system involvement. With a low index of clinical suspicion or inadequate follow up the diagnosis may be delayed or missed at the time of presentation, in those with hematological abnormalities as the initial manifestation.[8]

The course of SLE is very variable. SLE is an episodic disease. Survival is related to organ involvement and to frequency of exacerbations .[6,9] There is no cure for SLE, and complete sustained remissions are rare. The mainstay of treatment for any inflammatory life-threatening or organ-threatening manifestations of SLE is systemic glucocorticoids.[9]

Cytoxic /immunosuppressive agents added to glucocorticoids are recommended to treat serious SLE.[10]

The present study was conducted to document RBC parameters in SLE in our population. This study may provide direction for further research to determine prognostic role of RBC parameters.

MATERIALS AND METHODS

Seventy five diagnosed cases of SLE fulfilling the inclusion criteria presenting to Medical in- and out-patient departments of Shaikh Zayed Medical complex Lahore, 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. Name, age and address were recorded in a specially designed proforma. Patients were investigated in Haematology laboratory, Shaikh Zayed medical complex, Lahore for Complete blood count (CBC) including Haemoglobin (Hb), RBC count, Hematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH) and Mean Corpuscular Haemoglobin concentration (MCHC) [using Abacus+ hematological autoanalyzer]. All collected information was entered into SPSS version 17.0 and analyzed using its statistical package. RBC parameters were expressed as Mean ± SD.

RESULTS

Seventy five diagnosed cases of SLE presenting to medical in- and out-patient departments of Shaikh Zayed Medical complex Lahore, were included in the study, out of which, 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 for the case series was 29.49±11.7 years. Mean age for females was 29.06±11.88 years and for males was 32.30±11.02 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 while most of the male patients were in age group 26-35 (Table -1).

Table 1: Age and gender distribution in study population (n=75)

Age group (years)	Males	Females	Total	Percentage %
15-25	3	34	37	49.33
26-35	4	17	21	28.0
36-45	1	7	8	10.66
46-55	2	5	7	9.33
56-65	0	2	2	2.66
Total	10	65	75	100

Table 2: 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)	-	-	

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

Table 3: RBC count according to age and gender (n=75)

Age groups	Gender	RBC count (x10^{12}/l)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	1.15-5.52	3.35±0.78	0.748
	Male (n=3)	3.05-3.48	3.20±0.24	
26-35	Female (n=17)	1.33-4.50	3.16±0.85	0.693
	Male (n=4)	1.30-4.89	3.39±1.65	
36-45	Female (n=7)	2.87-4.91	4.27±0.71	0.375
	Male (n=1)	5.00	5.00	
46-55	Female (n=5)	2.00-4.30	3.77±0.99	0.679
	Male (n=2)	3.32-4.97	4.15±1.17	
56-65	Female (n=2)	1.37-4.56	2.96±2.26	--
	Male (n=0)	--	--	

[12] Normal range: RBC count : Males 4.5-5.5x10^{12}/l Females 3.8-5.8x10^{12}/l

Table 4: Haematocrit according to age and gender (n=75)

Age groups	Gender	Haematocrit (%)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	12.19-43.27	26.25±6.44	0.648
	Male (n=3)	23.28-26.06	24.51±1.42	
26-35	Female (n=17)	12.70- 43.00	25.43±7.47	0.672
	Male (n=4)	12.50-36.06	27.39±11.17	
36-45	Female (n=7)	21.30-37.19	32.00±5.42	0.216
	Male (n=1)	40.00	40.00	
46-55	Female (n=5)	15.00-36.04	29.95±8.60	0.512
	Male (n=2)	25.40-25.41	25.41±0.01	
56-65	Female (n=2)	13.36-33.56	23.46±14.28	--
	Male (n=0)	--	--	

[12]Normal range Haematocrit: Males- 40-50% Females- 36-46%

Table 5: MCV according to age and gender (n=75)

Age groups	Gender	MCV (fl)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	56-115	80.06±11.56	0.689
	Male (n=3)	76-79	77.33±1.52	
26-35	Female (n=17)	68-96	78.74±8.12	0.642
	Male (n=4)	73-81	76.75±3.30	
36-45	Female (n=7)	59-81	73.42±6.90	0.645
	Male (n=1)	77	77.00	
46-55	Female (n=5)	74-88	78.80±5.89	0.193
	Male (n=2)	51-80	65.50±20.51	
56-65	Female (n=2)	74-98	86.00±16.97	--
	Male (n=0)	--	--	

[12] Normal range MCV: 83-101 fl

Table 6: MCH according to age and gender (n=75)

Age groups	Gender	MCH (pg)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	20.00-44.70	25.80±4.73	0.866
	Male (n=3)	24.60-26.40	25.33±0.94	
26-35	Female (n=17)	19.50-37.00	25.10±3.81	0.600
	Male (n=4)	23.10-30.00	26.20±2.93	
36-45	Female (n=7)	18.00-25.80	22.35±2.53	0.402
	Male (n=1)	24.80	24.80	
46-55	Female (n=5)	24.20-29.00	26.08±2.03	0.087
	Male (n=2)	14.70-24.60	19.65±7.00	
56-65	Female (n=2)	21.30-31.80	26.55±7.42	--
	Male (n=0)			

[12] Normal range MCH : 27-32 pg

Table 7: MCHC according to age and gender (n=75)

Age groups	Gender	MCHC (g/dl)		p value
		Range	Mean ± SD	
15-25	Female (n=34)	26.00-42.00	31.66±2.79	0.394
	Male (n=3)	32.90-33.30	33.07±0.21	
26-35	Female (n=17)	28.00-38.80	31.42±2.53	0.382
	Male (n=4)	31.50-35.00	32.62±1.60	
36-45	Female (n=7)	27.40-33.90	30.54±2.53	0.587
	Male (n=1)	32.10	32.10	
46-55	Female (n=5)	29.00-35.90	32.80±2.48	0.188
	Male (n=2)	28.80-30.90	29.85±1.48	
56-65	Female (n=2)	29.00-31.40	30.20±1.69	--
	Male (n=0)			

[12] Normal range MCHC 32.5-34.5g/dl

On analysis of the haematological parameters anemia was seen in 74 patients. Mean Hb was 8.45±1.95 g/dl (range 4.2-13.0 g/dl). Mean Hb in males was 9.05±2.67 g/dl and in females was 8.36±1.82g/dl. Mean Hb of the age group 15-25 years, with maximum number of females, was 8.218±1.72g/dl while mean Hb for the age group having maximum number of males (26-35 yrs) was 8.575±3.29g/dl. There was no significant difference between males and females (Table 2).

Mean RBC count was $3.45x10^{12}$±0.93/l (range $1.15\text{-}5.52x10^{12}$/l). Mean RBC count of the females of age group 15-25 years was $3.34x10^{12}$±0.77 /l while that of males belonging to age group 26-35 yrs was $3.39x10^{12}$±1.64/l with no significant difference (Table 3)

Mean Hematocrit was 26.92±7.17% (range 12.19-43.27%). Mean haematocrit of the age group 15-25 years, of female patients, was 26.249±6.43% (range 12.19-43.27%) while mean Hct for the age group 26-35 yrs of male patients was 27.39±11.17% (range 12.5-36.06%). There was no significant difference. (Table 4)

On analyzing the RBC indices mean MCV was 78.5±9.98 fl (range 51-115fl). Mean MCV of females of age group 15-25 was 80.06±11.56fl (56-115fl) and for males aged 26-35 was 76.75±3.30fl (range73-81fl). The difference between males and females was not significant. (Table 5).

Mean MCH was 25.19±4.19pg (range 14.7-44.7 pg), while mean MCHC came out to be 31.6±2.53g/dl (range 26-42g/dl) . The mean values of these indices for females age 15-25 years were 25.80±4.73pg (range 20-44.7pg) and 31.66 ±2.79g/dl (range 26-42g/dl) respectively. The mean values of these indices for males age 26-35 years were 26.2±2.92 pg (range 23.10-30.00pg) and 32.62±1.60g/dl (range 31.5-35.0g/dl) respectively with no significant difference. (Table-6, 7).

DISCUSSION

Anaemia is a common clinical finding in patients with SLE. It is present in 1/2 to 2/3 patients and may be multifactorial[13]. It may be due to disease, hematopoietic failure, drugs, hypersplenism, marrow suppression or due to accompanying factors. [14,15,16] The various types of anaemia seen in SLE are iron deficiency , anemia of chronic disease or autoimmune hemolytic anemia .[17]

The aim of present study was to determine the frequency of RBC parameters in patients of SLE.

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. Shaikh MA et al, in their study group, found the mean age to be equal to 28±6.22 years.[18] Similarly in Khan AA et al study the mean age of patients was 29.92 years.[17] The mean age of patients in the current study is comparable with these studies. In a study by Chen JL mean age of patients was 33.4 years,[19] while a study conducted by Al Saleh J et al the mean age came out to be 35.5 years,[20] which was not close to mean age of our study.

SLE is more common in females. This fact is well established in present study also. There were 65(86.7%) females and 10 (13.3%) males. Male to female ratio was 6.5:1. In a study by Chen JL there were 207 (86.7%) females and 29 (13.3%) males. [19] Beyan E et al reported a series of 115 cases where 20 (17.4%) were males and 85 (73.9%) were females.[21] Shaikh MA et al reported a case series of 27 females (90%) and 3 (10%) males.[18] Khan AA et al reported a study of 47 (94%) females and 3 (6%) males. [17] In a study by Al Saleh J et al the male to female ratio came out to be 20.5:1. [20]

According to WHO criteria a person is said to be suffering from anemia when Hb 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% with mean Hb of 8.45 ± 1.94 g/dl in present study. Shaikh MA et al in their study from Hyderabad, Pakistan found 93.33% of their SLE patients to be anemic.[18] In a study by Khan AA et al in 2006 from Islamabad, Pakistan the frequency of anemia was 79.37%.[17] 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. [19, 22] Voulgarelis M et al in a study from Greece in 2000 came up with a figure of 38%. [22]

In our study mean RBC count was $3.45x10^{12}$±0.93/l and mean Hematocrit was 26.92±7.17%. On analyzing the RBC indices mean MCV was 78.5±9.98 fl , mean MCH was 25.19±4. 19pg while mean MCHC came out to be 31.6±2.53g/dl. No comparative studies showing analysis of RBC indices on medline and medscape could be found which addressed these findings. Therefore, more studies are needed to explore more extensively determine the prognostic role of RBC indices in patients with SLE.

CONCLUSION

Based on above findings it is concluded that in SLE patients values of Hb concentration and Hct may be markedly deranged, MCH moderately affected while RBC count, MCV and MCHC values can be normal to mildly deranged. Therefore RBC parameters may be employed not only for the diagnosis but also to find out the prognosis of the disease.

REFRENCES

1. Askanase A, Shum K, Mitnick H. Systemic lupus erythematosus: an overview. Soc Work Health Care. 2012 Aug;51(7):576-86.
2. Hepburn AL, Narat S, Mason JC. The management of peripheral blood cytopenias in systemic lupus erythematosus. Rheumatology (Oxford). 2010 Dec;49(12):2243-54.
3. Lahita RG. Introduction. In: Lahita RG, ed. Systemic Lupus Erythematosus. New York: John Wiley and Sons. 1987; 1-3. (Fourth edition published 2004).
4. Boltzer JW. Systemic lupus erythematosus. I. Historical aspects. MD State Med J 1983; 37:439.
5. Hochberg MC. The History of Lupus Erythematosus. The Lupus Foundation Of America Newsletter. 2003: 93-102.
6. Goodfield MJD, Jones SK, Veale DJ. The Connective Tissue Diseases. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Textbook of Dermatology. 8th ed. UK. Blackwell Publishing; 2010: 51.1-51.138.
7. Mehta AB, Hoffbrand AV. Haematological aspects of systemic disease. In: Hoffbrand AV, Catovsky D, Tuddenham EGD, Green AR editors. Postgraduate Haematology. 6th edition. Oxford: Wiley-Blackwell; 2011:p940-955.
8. Kontos AP, Jirsari M, Jacobsen G, Fivenson DP. Immunoglobulin M predominance in cutaneous lupus erythematosus. J Cutan Pathol. 2005 May;32(5):352-5.
9. Swaak AJG, Nossent JC, Bronsveld W, Rooyen AV, Nieuwenhuys EJ, Theuns L,et al. Systemic lupus erythematosus. I. Outcome and survival: Dutch experience with 110 patients studied prospectively. Ann Rheum Dis 1989; 48: 447–54.
10. Hahn BH. Systemic Lupus Erythematosus. In: Fauci AS, Kasper DL, Longo DL, Braunwald E, Hauser SL, Jameson JL, et al editors. Harrison's Principles of Internal Medicine. 17th ed.USA, McGraw Hill's; 2008:2075-83.
11. Robak E, Robak T. Novel and emerging drugs for systemic lupus erythematosus: mechanism of action and therapeutic activity. Curr Med Chem. 2012;19(3):438-53.
12. Lewis SM. Reference ranges and normal values. In: Lewis SM, Bain BJ, Bates I editors. Dacie and Lewis Practical Haematology. 10th ed. 2006:11-25.
13. Giannouli S, Voulgarelis M, Ziakas P D, Tzioufas A G. Anaemia in systemic lupus erythematosus: from pathophysiology to clinical assessment. Ann Rheum Dis. 2006; 65(2): 144–148.
14. Minami R, Izutsu K, Miyamura T, Yamamoto M, Suematsu E.A case of systemic lupus erythematosus accompanied with pure red cell aplasia. Nihon Rinsho Meneki Gakkai Kaishi. 2006; 29(3):148-53.
15. Tagoe C, Shah A, Yee H, Belmont HM. Aplastic anemia in systemic lupus erythematosus a distinct presentation of acquired aplastic anemia? J Clin Rheumatol. 2001;7(6):377-83.
16. Baumann P, Völkl A, Bäuerle M, Schmidmaier R, Oduncu FS.Aplastic crisis as primary manifestation of systemic lupus erythematosus. Onkologie. 2011;34(8-9):452-4.
17. Khan AA, Mahmood Q, Khan BA, Bilal N. Frequency and types of anemia in systemic lupus erythematosus. Ann Pak Inst Med Sci 2006;2(4):272-6.
18. Shaikh MA, Memon I, Ghori RA. Frequency of anaemia in patients with systemic lupus erythematosus at tertiary care hospitals. J Pak Med Assoc. 2010; 60(10):822-5.
19. Chen JL, Huang XM, Zeng XJ, Wang Y, Zhou MX, Ma YH, et al. Hematological abnormalities in systemic lupus erythematosus and clinical significance thereof: comparative analysis of 236 cases. Zhonghua Yi Xue Za Zhi. 2007;87(19):1330-3.
20. AlSaleh J, Jassim V, ElSayed M, Saleh N, Harb D. Clinical and immunological manifestations in 151 SLE patients living in Dubai. Lupus 2008;17(1):62-6.
21. Beyan E, Beyan C, Turan M. Hematological presentation in systemic lupus erythematosus and its relationship with disease activity. Hematology 2007;12(3):257-61.
22. Xiong-yan L, Feng-xia WU, Zhong T, Ning-tao L, Xiao-yun S, Jiang KB, et al. Chinese Journal of Clinicians 2010; 4(10).
23. Voulgarelis M, Kokori SI, Ioannidis JP, Tzioufas AG, Kyriaki D, Moutsopoulos HM. Anaemia in systemic lupus erythematosus: aetiological profile and the role of erythropoietin. Ann Rheum Dis. 2000;59(3):217-22.