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A STUDY OF HAEMATOLOGICAL MANIFESTATIONS OF SLE WITH SPECIAL REFERENCE TO DISEASE ACTIVITY

Medicine

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ABSTRACT

Background: Our understanding of Systemic Lupus Erythematosus (SLE) has been evolved very significantly over the period of last few decades. The hematological abnormalities though more commonly seen are not properly evaluated or estimated and are not given enough representation . In some of these cases presenting with Anaemia, Thrombocytopenia, Pancytopenia or Thrombotic episodes, especially so in young females, the diagnosis may be delayed or initially missed if the index of suspicion is low or if there is improper and inadequate follow up. Thus keeping this in mind this study as be carried out.

Aim and Objectives :(1) To study Haematological manifestations of SLE and (2) To study its correlation with the disease severity.

Materials and Methods: This study is an Observational Cross Sectional Study done in Assam Medical College for a period of one year. All cases who fulfilled the ACR criteria 1997 who came to Rheumatology opd and those who admitted in Medicine ward taken up for the study.

Results: Totally 106 patients were taken up for the study. The most common constitutional symptom was Fatigue which present among 57 (53.7%). Raynaud 's phenomenon was present among 15(14.15%) patients. Anaemia was present in 99 patients (93%) of the study group with most common type being Anaemia of chronic disease. Neutropenia was present among 8 (7.5%), Thrombocytopenia among 8(7.55%) in the study group. Severity of anaemia and Serum Ferritin Level were in correlation with the Disease severity (SLEDAI).

Conclusion: Haematological Manifestations is one of the most common manifestation presents very early in the disease process and in many cases as the only presentation. This Study demonstrated similarities with most of other studies, revelling at the same time much Higher incidence of Haemotological manifestations compared to other studies.

KEYWORDS

Anaemia, Disease, Hematological, Severity.

1. Introduction

Systemic lupus erythematosus is a remarkable and challenging disorder. Its diversity of clinical features is matched by the complexity of the factors (genetic, hormonal, and environmental) that cause it, and the array of autoantibodies with which it is associated(1).

Systemic lupus Erythematosus (SLE) is a prototype autoimmune disease characterized by a wide variety of clinical manifestations and presence of numerous autoantibodies resulting in organ and tissue damage(2). It mostly affecting young women with several manifestations on the human body including skin, joints, kidneys, nervous system, and serous membranes(3).

Hematological abnormalities are common in SLE. Worldwide studies have shown varied incidence of hematological manifestations in SLE patients. The Major manifestations of SLE are anemia, leucopenia, thrombocytopenia, and antiphospholipid syndrome (APS). Hematological abnormalities in SLE patients require early diagnosis, careful monitoring and prompt therapeutic intervention(2).

Since blood and blood vessels together contain more diverse number of antigens than any other organ in the body, it is only natural to expect hematological manifestations more common than others(4)(5). In one study done in South India done by SaidharanPK shown prevalence of 82% of anemia in hisStudy. Intersting part is that in 35% of the cases Haematological manifestations are the only manifestations. This led to the formulation of a new criteria for the SLE with special emphasis given for Hematological manifestations known as Kozhikode criteria(6).

2. Material and Methods

This is a Observational Cross Sectional Study done in the Assam Medical College during a period of one year (2016 – 2017). All the patients who fulfilled with criteria of American college of Rheumatology criteria (1997), were taken up for the study after taking a proper consent. Exclusion criteria were Age less than 13 years, Infection, Recent Blood Transfusion, Haemoglobinopathies. Totally 106 patients fulfilled the above mentioned criteria. Disease activity was accessed using the SLEDAI scale. . Change in SLEDAI>3 points is called mild to moderate flare and change in score >12 is severe flare. Detailed history was taken for every patient and Disease activity was calculated using SLEDAI for everyone. Haemoglobin- by standard acid haematin method in Hellige'shaemoglobinometer,RED CELL INDICES(MCV, MCH, MCHC)and PCV,RED CELL WIDTH, WBC count: by using improved Neuber ruling slide after proper dilution under low power objective, DLC count -peripheral blood film stained with Leishman's stain, examined under oil immersion lens, Platelet count, ESR : by Westergrens method more than 30 mm/ hr is taken as significant in accordance with previous studies done by Stojan et al (7), Serum Ferritin by ELISA, Serum Iron and Serum TIBC were done using Coral systems in a Semi autoanalyser, Hb typing by HPLC, APLA, Coombs Test (direct and indirect),C-reactive protein, Urine R/E- Physical, Chemical, Cytological analysis, Renal function test :- Blood Urea &Creatinine, 24 hour urinary protein: to look for evidence of lupus nephritis and .A level more than0.5g/24h was taken as positive for proteinurea (as per SLEDAI index), Antinuclear antibody assay - assessment by Immunofluorescence, dsDNA assay- Assessment by Immunofluorescence were done for every patients.

Statistical Analysis

Statistical analysis was performed with IBM SPSS Statistics version 21 Software. Pearson correlation coefficient was used to assess the correlation between variables. The independent-samples t-test is used to compares the means between two unrelated groups on the same continuous, dependent variable. The Kruskal-Wallis H test is used for the comparison of more than two independent groups.

3. Results:

Out of the 106 patients in our study there was only 1 male. The reason for this is the other male patients in this study were excluded because of the Haemoglobinopathy. It was observed that the maximum age incidence was in between 20—<29 years (38.63%) followed by 30—<39 years (31.13%). Mean duration of illness was 2.92 years. With majority of the patients presented within 1 year of onset of disease. Among the clinical manifestations most common was Mucocutaneous manifestations (90.5%) followed by Renal Involvement (76.4%). Among the Mucocutaneous Manifestations most common was Hair loss (54.15%) followed by Photosensitivity (51.9%) of patients. Musculoskeletal Manifestations were seen in 42.4% of the patients while Neuropsychiatric Manifestations were seen in 32.7% of the patients. Lupus Head ache were present in 24.53% of the patients. Hepatomegaly was present in 14.14% and Splenomegaly was present in 2.83% of the patients.

Among the Haemotological manifestations Anemia(Haemoglobin <12 mg/dl) was seen in 99 patients (93.4%) of the patients. Leucopenia(Total leucocyte count <4000) was observed in 8 patients (7.55%). Thrombocytoepnia (Platlet count < 1,00,000) was observed in 7 patients (6.6%). Anemia of Chronic Diseases was the most common type of Anemia with (79.2%) followed by Iron deficiency Anemia (14.1%). Autoimmune Haemolytic Anemia was absorbed in 6.6% of the patients.

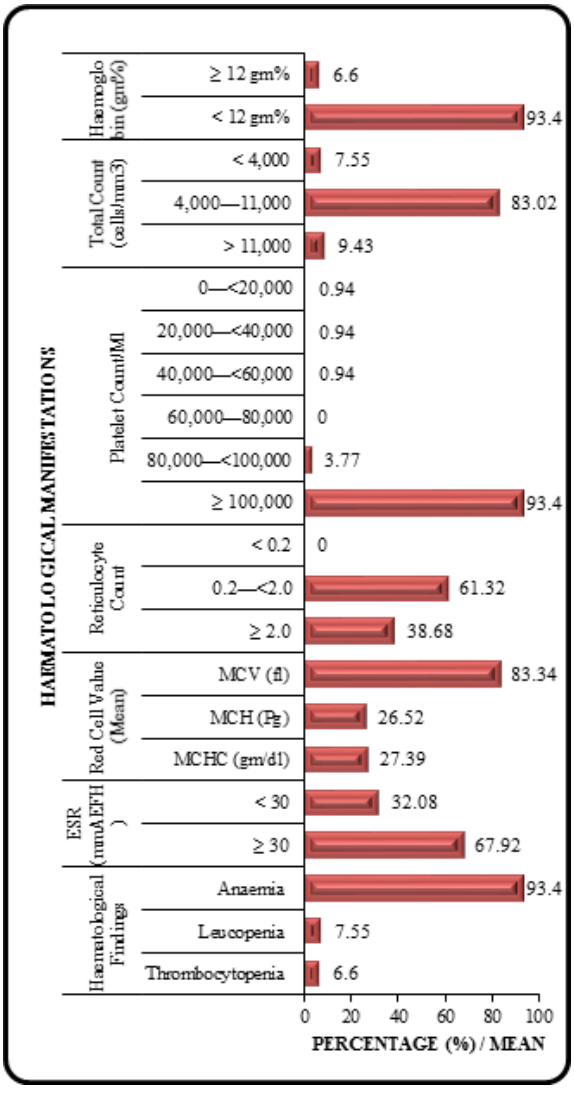

Figure 1: Haematological Manifestations

There was a statistically signification negative correlation seen between SLEDAI and the Haemoglobin (r=-.330,p=0.001) (Figure2), Total Leucocyte count (r= -.228, p= .0019) . There was also a significant Positive correlation seen between the SLEDAI and Serum ESR (r=.266, p=.006), Serum Ferritin (r=0.209 p = 0.032). There was correlation seen between the SLEDAI and Serum CRP. There was a steady decrease in both Haemoglobin and Total Leucocyte count as the SLEDAI increase with a statistically significant Mean difference between the three Groups of SLEDAI (ie No flare, Mild Flare and Severe Flare) and Haemoglobin(p=0.002),Total Leucocyte count (p = 0.018). There is also a Statistically significant Mean difference between SLEDAI and Serum Ferritin (Fig 3) and ESR with P value of 0.035 and 0.025 respectively. There was no statistically significant Mean difference between SLEDAI and the Serum CRP. Also Serum Ferritin was positively correlated with the ESR (r =0.197 p =0.043) (Fig :4) and there was no correlation between Serum Ferritin and CRP (r = 0.085 p =0.388) .ANA positivity was present in 95.2% of patients dsDNA positivity was present in 28.3% of the patients. we also observed that Significant correlation seen between Anaemia and dsDNA (p=0.007),anti nucleosome (p= 0.004), Anti Histone (p = 0.0024), Anti Pm Scl (p= 0.012), Anti ku (p= 0.012).

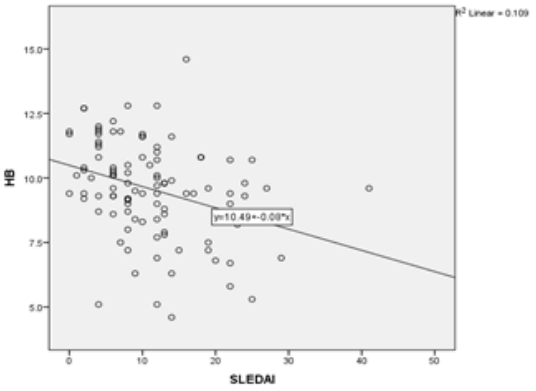

Figure 2: Correlation of Haemoglobulin and SLEDAI in SLE Patients

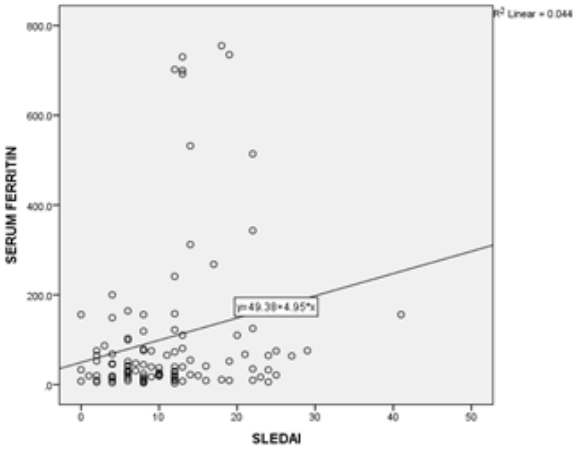

Figure 3: Correlation of Ferritn and SLEDAI in SLE Patients

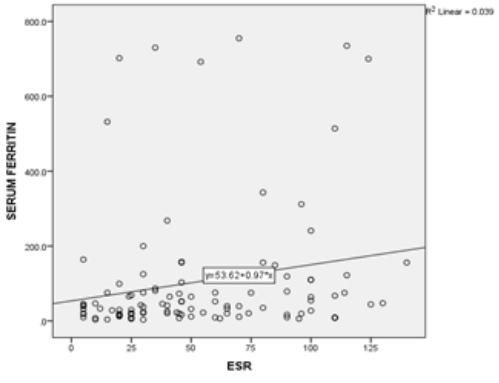

Fig 4: Correlation of Serum Ferritin with ESR

4.Discussion

Hematological abnormalities are very common in systemic lupus erythematosus. Anaemia is found in approximately 50% of patients, with anaemia of chronic disease being the most common form. Impaired erythropoietin response and presence of antibodies against erythropoietin may contribute to the pathogenesis of this type of anaemia. Patients with autoimmune haemolytic anaemia usually belong to a distinct category, which is associated with anticardiolipin antibodies, thrombosis, thrombocytopenia and renal involvement, often in the context of secondary antiphospholipid syndrome. Finally, as recently suggested, auto antibodies, T lymphocytes and deregulation of the cytokines network can affect bone marrow erythopoiesis leading to anaemia (8).

It was observed that the maximum age incidence was in between 20—<29 years (38.68%) in our Study which is in accordance with studies done by Agarwal et al (9), Santhanam et al (10), Saigal et al (11), Kishore et al (12) which showed the maximum prevalence was between 21 – 40 yrs.

Table 1: Over all Comparison of various Clinical Manifestations with Other Studies

ClinicalManifestations	Our Study	HavaEt al (13)	MalaviyaEt al (14)	MadhavanEt al (15)	AgarwalEt al (9)	PaudyaEt al (16)	MiahEt al (17)	BinoyEt al (18)	KosarajuEt al (19)	SanthanamEt al (10)
Muccocutaneous	92.5	30.8	-	-	83.9	70	75	-	-	-
Constitutional	61.3		-	-	-	72	91	-	-	81
Musculo Skeletal	42.4	83.2	-	-	-	-	81	-	-	-
Renal	76.4	55	-	-	69	44	36	33.3	20.8	-
Cardiac	17.9	-	1	5.2	-	-		5.3	-	-
Pulmoanry	11.3	-	-	-	-	-		6	6	
Neuro Psychiatry	32.7	-	12	35		6		13.3	-	-

All variables are expressed in percentage.

In our study the prevalence of Mucocutaneous manifestations , Renal and Neuropsychiatric manifestations were similar to the study done by Agarwal et al(9).The prevalence of anaemia in our study was 99.34% comparable with the study done by sheikh in South India which showed a prevalence of 93.3%(122) but however the prevalence is very high compared to the other studies probably because of our cut off for Anaemia is 12mg/dl compared to most other studies who had a cut off of 10mg/dl. Thrombocytopenia prevalence in our study was 6.6% which is comparable to the studies done by Malaviya et al(14) and Madhavan et al(15) their studies showed a prevalence of 10%. While other studies had a prevalence high than our study. Leucopenia prevelance was 7.55% comparable to study done by Madhavan et al(14) with showed 12.5 but other studies showed an Higher prevalence (Table 2).

Table 2:Comparison of Haemotological manifestations between various studies to our present study

	Havaet al (13)	Sasidharan et al (6)	Malaviyaet al (14)	MadhavanEt al (15)	SaigalEt al (11)	BinoyEt al (18)	KishoreEt al (12)	ShaikhEt al (20)	Our Study
Anaemia	66.5	63	38	52	53.3	56	55	93.3	99.34
Leucopenia	48	16	16	12.5	43.3	-	15	-	7.55
Thrombocytopenia	34	40	10	10	33.3	-	48	-	6.6

All variables are expressed in percentage.

Autoimmune haemolytic anaemia in our study was 6.6% comparable with study done by Kosaraju et al (19) which showed 7.5%. However the percentage of Haemolytic Anaemia prevalence is high in other studies done by Volgarelis et al (21)and Shaikh et al(20)which showed 14.4% and 23.3% respectively. While Anaemia of Chronic disease in our study was 79.2% which was high compared to the studies done by Volgarelis et al (21) and Shaikh et al(20)which showed 37.1% and 40% respectively.

While studying the correlation between the Serum Ferritin and the Disease activity in our study we found theSerum Ferritin is Positvely correlated with the SLEDAI which is similar to the studies done by Vandhana et al (22), Seyhan et al (23), Tripathi et al (24) Lim MK et al (25).

There was also positive correlation is seen between the SLEDAI and the ESR value is seen in our study which is in accordance with the studies done by Stojan G et al (7).

In our study we also found that there is no significant correlation was found between SLEDAI and the Serum CRP which is in accordance with studies done by Williams RC jr et al (26)Enocsson et al (27)Cengic M (28).

We found that there is a positive correlation between the Serum Ferritin and Serum ESR while there is no significant correlation between the Serum Ferritin and Serum CRP. The above correlation signifies that in a case of in a case of SLE flare the serum Ferritin will in increase with a normal or near normal Serum CRP that may help to differentiate between the flare and infection.

We also found that there is a significant statistical difference between the three Groups of SLEDAI(ie No flare, Mild Flare and Severe Flare) and Haemoglobulin, Total Leucocyte count, Serum ESR and Serum Ferritin.

Also there is a significant negative correlation Between the Haemoglobulin, Total Leucocyte count and SLEDAI (considering SLEDAI as single variable).

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REFERENCES

1. Larissa L, Grainne M, PDavid I. Systemic Lupus Erythematosus. The Lancet. 2014 November; 384: p. 1878–1888.
2. Zandman-Goddard G, Orbach H, Armon-Levin N, Boaz H, Amital Z, Szekanecz G. Hyperferritinemia is associated with serological anti-phospholipid syndrome in SLE patients. Clin Rev Allergy Immunol. 2013; 44: p. 23-30.
3. Petri M, Perez-Gutthann S, Longenecker J, Hochberg M. Morbidity of systemic lupus erythematosus:role of race and socioeconomic status. Am J Med. 1991; 91: p. 345-53.
4. Sasidharan P, Bindiya M, SajeethKumar K. Hematological Manifestations of SLE at Initial Presentation,Is It Underestimated? ISRN Haemotology. 2012.
5. PK S. SLE as a hematological disease. In MB A, editor. Hematology Today. India: Vikas Publications p. 953-966.
6. Sasidharan P, Bindiya M, Sajeeth KK. Systemic Lupus Erythematosus- A Hematological Problem. Journal of Blood disorders and Transfusion. 2013; 4(6).
7. Stojan G, Fang H, Magder L, Petri M. Erythrocyte sedimentation rate is a predictor of renal and overall SLE disease activity. Lupus. 2013 July; 22(8): p. 827-34.
8. Stavroula G, Voulgarelis M, Panayiotis DZ, Athanasios GT. BMJ Group. [Online].; 2005 [cited 2017 August 30. Available from: http://ard.bmj.com/.
9. Sachin RA, Iadarilang T, Atulsingh R, Ajitprasad J. A cross Sectional Hospital Based Study of Clinical and Immunological profile of Systemic Lupus Erythematosus in central rural India. Indian Journal of Allerfy, Asthma and Immunology. 2013 January-June; 27(1): p. 33-37.
10. Sham S, Madeshwaran M, Tamilselvam T, Rajeswari S. Clinical and immunological profile of SLE patients: Experience from a Chennai-based tertiary care centre. Internet journal of Rheumatology and Immunology. 2016 January ; 4(1).
11. Saigal R, Kansal A, Mittal M, Singh Y, Maharia H, Juneja M. Clinical profile of systemic lupus erythematosus patients at atertiary care centre in Western India. J Indian Acad Clin Med. 2011; 13: p. 27-32.
12. Neethu K, Rekha B, T KS. A cross Sectional Study of clinico Immunological profile of Systemic Lupus Erythematosus in aTertiary care centre in Mangalore. Indian Journal of Allergy, Asthma, Immunology. 2016; 30: p. 91-4.
13. Hava ÜT, Döndü ÜC, Cengiz K. Detailed features of hematological involvement and medication-induced cytopenia in systemic lupus erythematosus patients: single center results of 221 patients. Eur J Rheumatol. 2017 June; 4(2): p. 87–92..
14. Malaviya A, Singh R, De A, Kumar A, Aradhye S. Systemic lupus erythematosus in northern India: A review of 329 cases. J Assoc Physicians India. 1988 36;: p. 476-480.
15. Madhavan R, Porkodi R, Ramakrishnan S. Systemic lupus erythematosus- the Madras experience. J Assoc Physicians India. 1988; 36: p. 473-75.
16. Paudyal B, Gyawalee M. Clinical profile of patients with systemic lupus erythematosus. JNMA J Nepal Med Assoc. 2012 July - September; 52(187): p. 111-7.
17. Miah T, Haque M, Mahmood T, Tarafder B. Clinical profile, management and outcome of lupus. Mymensingh Med J. 2008 July; 17(2): p. 6-11.
18. Binoy, J, Paul; Muhammed, Fassaludeen; Nandakumar; M, V, Razia. J Indian Rheumatol Assoc. 2003; 11: p. 94-97.
19. K Kosaraju SSUS. A cross-sectional hospital-based study of autoantibody profile and clinical manifestations of systemic lupus erythematosus. Indian Journal of medical Microbiology. 2010; 28(3): p. 245-247.
20. Mumtaz AS, Iqbal M, Rafi AG. Frequency of anaemia in patients with systemic lupus erythematosus at tertiary care hospitals. JAPMA. 2010 October; 60(10).
21. Michalis Voulgarelis SIGKJPAIAGTKHMMKHMMKHMM. Anaemia in systemic lupus erythematosus:aetiological profile and the role of erythropoietin. Ann Rheum Dis. 2009; 59: p. 217–222.
22. Vandana P, Pallavi P, Anjali R, Manisha P, Prathamesh S, Pradnya K, et al. Association of

Serum Ferritin Levels with Hematological Manifestations in Systemic Lupus Erythematosus Patients from Western India. Journal of The Association of Physicians of India. 2016 May; 64: p. 14-18.
23. Seyhan S, Pamuk O, Pamuk G, Cakir N. The correlation between ferritin level and acute phase parameters in rheumatoid arthritis and systemic lupus erythematosus. Eur J Rhuematol. 2014; 1: p. 92-5.
24. Tripathy R, Panda A, Das B. Serum ferritin level correlates with SLEDAI scores and renal involvement in SLE. LUPUS. 2015; 24: p. 82-9.
25. Lim M, Lee C, Ju Y, Cho Y, Lee M, B Y, et al. Serum ferritin as a serologic marker of activity in systemic lupus erythematosus. Rheumatol Int. 2001 April; 20(3): p. 89-93.
26. Williams RJ, Harmon M, Burlingame R, Du CT. Studies of serum C-reactive protein in systemic lupus erythematosus. J Rheumatol. 2005 March; 32(3): p. 454-61.
27. Enocsson H, Sjöwall C, Kastbom A, Skogh T, Eloranta M, Rönnblom L, et al. Association of serum C-reactive protein levels with lupus disease activity in the absence of measurable interferon-α and a C-reactive protein gene variant. Arthritis Rheumatol. 2014 June; 66(6): p. 1568-73.
28. Cengić M, Heljić B, Rasić S, Dilić M. Role of C-reactive protein in systemic lupus erythematosus. Med Arh. 2002; 56(3): p. 147-9.