STUDY OF HAEMATOLOGICAL ABNORMALITIES AMONG PAEDIATRIC LUPUS CASES ATTENDING A TERTIARY CARE HOSPITAL IN INDIA

Paediatrics

Md Rakibul Hassan

Department of Pediatrics, IPGME&R and SSKM Hospital, Kolkata.

Ashik Hossain*

Department of Pediatrics, IPGME&R and SSKM Hospital, Kolkata. *Corresponding Author

Tamana Parvin

Department of Pharmacology, NRSMCH, Kolkata

Prof. Supratim Datta

Department of Pediatrics, IPGME&R and SSKM Hospital, Kolkata.

Debarshi Jana

IPGME&R and SSKM Hospital, Kolkata.

ABSTRACT

Systemic lupus erythematosus or SLE is a chronic autoimmune disorder of multiple systems that affects blood vessels and connective tissues. Children with SLE generally have a more severe and aggressive disease course than patients with adult-onset disease.

Assess the hematological manifestations of systemic lupus erythematosus (SLE), namely leucopenia, thrombocytopenia, anemia-with special reference to autoimmune haemolytic anemia (AIHA). Co-relation among different antibodies and clinical and hematological findings

In-patients and Out-patients Department (OPD) of Paediatric Medicine, and out-patient Department (OPD) of Dept. of Rheumatology IPGME&R and SSKM Hospital, Kolkata 700020, a tertiary care center in West Bengal. Period of study-1.5 years (February 2018-July 2019). Inpatient Department and Out patient Department(OPD) of Department of Paediatric Medicine, IPGME&R and SSKM Hospital. Depending upon the previous records, available patients eligible for the study, 30 patients were taken as study population. Definition of population- Children upto 12 years of age, attending the Department of Paediatric Medicine of IPGME&R and SSKM Hospital, who were diagnosed cases of Systemic Lupus Erythematosus satisfying inclusion and exclusion criteria for this study.

Lupus nephritis was seen in more than half of the pediatric SLE cases. Larger number of study population needed to find statistically significant association between different parameters in this study

KEYWORDS

Haematological Abnormalities, Paediatric, Lupus

INTRODUCTION

Systemic lupus erythematosus or SLE is a chronic autoimmune disorder of multiple systems that affects blood vessels and connective tissues. Children with SLE generally have a more severe and aggressive disease course than patients with adult-onset disease¹.

Prevalence of SLE in child and adolescent age groups is 1-6/1,00,000², approximately 20% of all SLE patients are detected in the pediatric age group¹. Increased incidence of SLE is seen among black, Hispanic, and Asian patients compared with white patients. The median age at the onset of childhood SLE is 12 years, and 80% of the patients are girls¹. Due to availability of newer improved diagnostic tests more cases of childhood SLE are now being diagnosed³. SLE predominantly affects females, with reported 2-5:1 ratio before puberty, 9:1 ratio during reproductive years, and return to near prepubertal ratios in the postmenopausal period. Childhood SLE is usually diagnosed in adolescence, with a median age at diagnosis of 11-12 yr. Around 20% of all individuals with SLE are diagnosed before age 16 yr. Some define pediatric-onset lupus as onset of symptoms before age 16, and others as onset before age 18². Some authors also defined pediatric SLE as cases diagnosed before 21 years of age¹.

Classification criteria for SLE was given in 1971 by American College of Rheumatology (ACR), it was modified in 1982 and 1997^{3,4}.

1. To assess the hematological manifestations of systemic lupus erythematosus (SLE), namely leucopenia, thrombocytopenia, anaemia-with special reference to autoimmune haemolytic naemia (AIHA)
2. To assess co-relation among different antibodies and clinical and hematological findings

MATERIALS AND METHODS

Study design- Hospital based, prospective, observational study, cross-sectional.

Study setting- In-patients and Out-patients Department (OPD) of Paediatric Medicine, and out-patient Department (OPD) of Dept. of Rheumatology IPGME&R and SSKM Hospital, Kolkata 700020, a tertiary care center in West Bengal. Period of study-1.5 years (February 2018-July 2019).

Place of study- Inpatient Department and Out patient Department (OPD) of Department of Paediatric Medicine, IPGME&R and SSKM Hospital.

Sample size - Depending upon the previous records, available patients eligible for the study, 30 patients were taken as study population. Definition of population- Children upto 12 years of age, attending the Department of Paediatric Medicine of IPGME&R and SSKM Hospital, who were diagnosed cases of Systemic Lupus Erythematosus satisfying inclusion and exclusion criteria for this study.

Sample design- All the children attending the study place in presence of the principal investigator (myself) satisfying the inclusion and exclusion criteria was included in the study.

Study tool:- Weighing machine, Sphygmomanometer, Measuring tape, Torch, Stethoscope, Hammer, Ophthalmoscope and Case proforma

INCLUSION CRITERIA-

1. Systemic Lupus patients diagnosed by clinical and different laboratory parameters.
2. Age upto 12 years.
3. Available adequate medical records supplemented with history from reliable source.
4. Parents have given informed consent and patients more than 7 years have given assent.

EXCLUSION CRITERIA

1. Other hematological diseases with SLE like presentation.
2. Other causes of similar hematological abnormalities.

RESULTS AND ANALYSIS

We found, out of 30 child studied 5 were 10 years and below and rest (25) were above 10 years. Out of 30 children studied 26 were girl and 4 were boy. Sex ratio is 6.5:1 in favour of female sex. The age of whole study population was within 6-12 years. Anemia in this age group is defined as hemoglobin level below 11.5 mg/dl⁴⁴. Total 24(80%) children had anemia for age and sex, Rest (20%) were non-anemic.

RBC indices were studied among the study population. PCV were low among 25 and normal among 5 patients. MCV values were found normal in 24, low in 4 and higher in 2 children. MCH values were normal in 22, low in 7 and high in 1 children. MCHC values were normal in 7, low in 22 and 1 cases.

Our study showed that 25 children had normocytic normochromic RBC morphology whereas 5 had microcytic hypochromic RBC. Low reticulocyte counts were noted in 2 cases (6.66%), while high reticulocyte counts were noted in 14 (46.67%) cases. Rest of the children had normal reticulocyte count. Leukopenia (TLC < 4000/cmm as per SLICC criteria) was seen in 7 cases (23.33%), while rest of the children had normal or increased total leucocyte counts. Neutropenia (ANC < 1000/cmm as per SLICC criteria) was noted in only one (3.33%) case. Lymphopenia (absolute lymphocyte count < 1000/cmm as per SLICC criteria) was noted in 7 (23.3%) cases. Thrombocytopenia (platelets count < 100000/cmm) was seen in 2 (6.7%) cases.

We found out of 30 children, 11 had positive direct Coomb's test. 4 children had hyperbilirubinemia. Elevated LDH levels are suggestive of hemolysis. Normal cut off level of LDH in the age group of our study population was 330 U/L. Anti ds-DNA antibody was seen positive in 25 cases, 5 cases were anti-dsDNA negative. Out of 30 children, 10 were positive for anti-RO-52 antibody. Anti-RNP antibody was found positive in 12 children, rest were anti-RNP negative. According to our laboratory reference C3 level below 90 mg/dl and C4 level below 10 mg/dl are defined as low C3 and low C4 levels respectively. Out of 30 pSLE children 27 had low C3 and 22 had low C4 levels.

In our study CRP is usually not raised (negative) in SLE, but may be raised (positive) in a few conditions like infection, serositis. 17 out of the 30 children had SLE nephritis. Mucocutaneous involvement were seen in 16 cases. Serositis were found in 4 (13.3%) cases out of 30. Central nervous system involvement (neuropsychiatric) were found in 3 (10%) cases. In anemia, 19 (79.2%) patients had DsDNA positive and 5 (20.8%) patients had DsDNA negative. Association between dsDNA vs Anaemia was not statistically significant (p-value 0.540).

We showed in thrombocytopenia, 7 (87.5%) patients had DsDNA positive and (12.5%) patients had DsDNA negative. Association between dsDNA vs THROMBOCYTOPENIA was not statistically significant (p-value: 0.853). In neutropenia, 1 (100.0%) patients had DsDNA positive and no patients had DsDNA negative. Association between dsDNA vs neutropenia was not statistically significant (p-value: 0.362).

DISCUSSION

Pediatric SLE has been defined by different age limit by different authors. Some authors have defined pSLE as onset of SLE symptoms before 16 years of age, some has defined as onset before 18 years of age². Some authors have defined pSLE as onset of symptoms before 21 years of age¹. But in our setup pediatric age group is defined as age upto 12 years, the upper age limit my study population was 12 years. Previously diagnosed cases of pediatric SLE, who fulfilled the clinical and laboratory criteria of SLICC 2012⁵, were included in the study. Total 30 such children were included as study population.

Mean age of presentation was 11.15 years in our study population. Among 30 children under study female: male ratio was 6.5:1, it is almost equal (7:1) to the sex ratio mentioned in Textbook of Pediatric Care, American Academy of Pediatrics¹. Hematological involvements were found in 80% cases (n=30), it is also mentioned in several textbooks and journal, though an article by Thakur N et al³⁸ mentioned that 39% pSLE case develop hematological abnormalities³.

In our study, out of 30 children, anemia was noted in 25 (80%) cases, among them 83.3% had normocytic normochromic and 16.7% had microcytic hypochromic anemia. Most textbooks and studies showed anemia as commonest haematological abnormality. But, Levy D.M., Kamphuis S have mentioned that mild leukopenia as commonest finding. Anemia was the most common hematological manifestation in 36.3% cases in a study done in Eastern India by Mondal R et al¹⁶.

Auto immune haemolytic anemia is characterised by anemia, increased reticulocyte count, hyperbilirubinemia and elevated serum LDH. In our study, DCT was positive in 11 (36.7%) cases, DCT positive AIHA was noted in 4 cases (13.3%). Most studies showed Coomb's positive hemolytic anaemia around 20%, Gokce M. et al in

their study among 43 pSLE cases found 81% anemic and among them 76.6% had Coomb's positive haemolytic anemia⁷.

Thrombocytopenia was found in only 2 children (6.7%) in our study, which is almost near to the value mentioned in Textbook of Pediatric Rheumatology.

D.F. et. Al⁸. in their study in 1998 found thrombocytopenia in 12% pSLE cases¹⁵.

Leukopenia (TLC < 4000/cmm) was seen in 7 cases (23.33%) in our study. But, Zehra Serap Arıcı & Ezgi Deniz Batu & Seza Ozen in their article "Reviewing the Recommendations for Lupus in Children" mentioned that leukopenia occurs in two-third of the pSLE cases in any time of illness. A. Martini in their article "Paediatric-onset systemic lupus erythematosus" mentioned 46% to 64% incidence of leukopenia in pSLE cases.

In this study lymphopenia (absolute lymphocyte count < 1000/cmm) was noted in 7 (23.3%) cases (n=30). Mohamed D.F. et. Al⁸ in their study found lymphopenia in 36.25% children with SLE.

We found neutropenia in only one case (3.3%). But many authors have found neutropenia to be significant⁸. Hava Uskudar Teke, Dondu Uskudar Cansu, Cengiz Korkmaz in their study among 221 adult patients found neutropenia in 4.5% cases.

Anti-dsDNA antibody was found positive in 83.3% cases in my study population (n=30). Other auto antibodies like anti-RO-52 (33%), anti-RNP antibodies (40%) were also seen positive in significant percentage of my study population. Anti phospholipid antibody (APLA) was not found positive in any cases. Mohamed D.F. et al found anti-dsDNA positivity in 83.8%, anti-cardiolipin antibody positivity in 35% cases of juvenile SLE cases⁸.

Mondal R et. al found 70% anti-dsDNA positivity but didn't find any case positive for anti-Rnp and APLA⁶. Font J et. al in their study in 1998 found anti-dsDNA positivity in 85% pSLE cases and 29% positivity for IgG anticardiolipin antibodies which is an APLA⁹.

Low serum level complement factor 3 (C3) and complement factor 4 (C4) is one of the most important test for diagnosis of SLE as well as measurement of disease activity. Low serum C3 and C4 were found in 90% and 73.33% of the study population respectively. Mohamed D.F. et al found low C3 and low C4 levels in 61.25% and 38.8% of juvenile SLE cases respectively⁸.

SLE nephropathy was seen in 56.7% (n=30) of pSLE cases in my study. Serositis in 13.3%, neurological involvement in 10% and haematological involvement in 80% cases. Font J et al found nephropathy in 50%, serositis in 32% and neurological involvements in 26% cases⁹. Mohamed D.F. et al found 72.5%, serositis in 12.5% and neuropsychiatric manifestations in 22.5% of juvenile SLE cases⁸. Mondal R et. al found renal involvement, hematological involvement and neurological involvement in 54%, 54% and 25% respectively in pSLE cases⁷. Textbook of Pediatric Rheumatology by Pattey et al¹⁰ mentioned incidence of nephropathy and neuropsychiatric involvement as 20%-75% and 20%-95% respectively.

Co-relation studies between auto-anti body positivity (anti-dsDNA, anti-RO-52 and anti-RNP) and different hematological parameters (anemia, leukopenia, thrombocytopenias) were done, but statistically significant association was not noted.

CONCLUSION

For the pediatric SLE patients in Eastern India following points can be concluded from our study:

- Hematological abnormalities occur in around 4/5th pediatric SLE patients
- All types of cytopenias can occur.
- Anemia is the most common haematological presentation (80%).
- Leukopenia seen in significant population (23.3%).
- Thrombocytopenia also seen in significant percentage (6.7%)
- Low C3 and low C4 are quite common (90% and 73.3% respectively).
- Anti-dsDNA was most prevalent autoantibody
- Lupus nephritis was seen in more than half of the pediatric SLE cases.
- Larger number of study population needed to find statistically

significant association between different parameters in this study.

Table: Distribution of Sex, Distribution of Leukopenia, Distribution of DCT, Distribution of dsDNA and Distribution of CRP positivity

		Frequency	Percent
Sex	FEMALE	26	86.7%
	MALE	4	13.3%
	Total	30	100.0%
Leukopenia	No	23	76.67%
	Yes	7	23.33%
	Total	30	100.0%
DCT	NO	19	63.3%
	Yes	11	36.7%
	Total	30	100.0%
dsDNA	No	5	16.7%
	Yes	25	83.3%
	Total	30	100.0%
CRP	No	24	80.0%
	Yes	6	20.0%
	Total	30	100.0%

REFERENCE

1. David M.Siegel,Harry L.Gewanter,Shashi Sahai. Rheumatologic diseases in: Textbook of Pediatric Care,American Academy of Pediatrics-2nd edition,Chapter-324,p.2586-92
2. Rebecca E, Sadun, Stacy P.Ardoin, Laura E Schanberg. systemic lupus erythematosus. In: Kleigman, Stanton, StGeme et.al editor. Nelson Textbook of Pediatrics. 21st edition. Elsevier; p. 1274–80.
3. E.M. Tan, A.S. Cohen, J.F. Fries, et al., The 1982 revised criteria for the classification of systemic lupus erythematosus, Arthritis Rheum. 25 (1982) 1271–1277.
4. M.C. Hochberg, Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus, Arthritis Rheum. 40 (1997) 1725.
5. Neha Thakur, Jagdish Chandra, Bhavna Dhingra, V. Singh: Pediatric Lupus: Varied Haematological Picture and Presentation: Indian J Hematol Blood Transfus (Jan-Mar 2015) 31(1):68–70 DOI 10.1007/s12288-014-0357-5
6. Mondal R et. Al, Childhood Lupus: Experience from Eastern India Indian J Pediatr 2010; 77(8): 889-891
7. M. Gokce, Y. Bilginer, N. Besbas, et al., Hematological features of pediatric systemic lupus erythematosus: suggesting management strategies in children, Lupus 21 (2012) 878–884.
8. D.F. Mohamed et al. Juvenile lupus: Different clinical and serological presentations compared to adult lupus in Egypt; The Egyptian Rheumatologist 40 (2018) 55–58
9. Font J, Cervera R, Espinosa G, Pallarés L, Ramos-Casals M, Jiménez S, et al. Systemic lupus erythematosus (SLE) in childhood: analysis of clinical and immunological findings in 34 patients and comparison with SLE characteristics in adults. Ann Rheum Dis. 1998 Aug 1;57(8):456–9.
10. Klein-Gitelman M, Lane J C in Textbook of Pediatric rheumatology, 7th e, editors: Pattey, Laxer, Lindsley, Wedderburn; chapter-23, p 285-315