EJR European Journal of Rheumatology

DOI: 10.5152/eurjrheum.2017.16117

Original Article

Childhood lupus nephritis: 12 years of experience from a developing country's perspective

Moumita Samanta[1], Madhumita Nandi[1], Rakesh Mondal[2], Avijit Hazra[3], Sumatra Sarkar[4], Tapas Sabui[5], Chanchal Kumar Kundu[6], Arnab Biswas[1]

Abstract

Objective: To assess the long-term outcome of lupus nephritis in children with systemic lupus erythematosus followed up over 12 years at a tertiary care teaching hospital in Eastern India.

Material and Methods: This is a retrospective observational study of the clinicopathological presentation, management, and outcome in 46 children with lupus nephritis over a period of 12 years at a tertiary teaching hospital in Eastern India. Mortality was compared between different lupus classes and therapy groups with Kaplan-Meier analysis and log-rank test

Results: The incidence of lupus nephritis was 58.97% [95% confidence interval (CI) 48.06%–59.89%] with the mean age at presentation being 10.2±2.43 years (range 5.5–14.5) years. Majority belonged to class IV (30.43%), followed by class II (26.91%), class III (23.91), and class V (8.70%). Outcome analysis of children with lupus nephritis over 12 years revealed that 24 (52.17%) achieved complete remission of disease activity, 5 attained partial remission, 4 continued to have active disease, 5 developed end-stage renal disease (ESRD), and 8 died. Overall mortality thus observed was 17.39% with septicemia in the background of ESRD being the commonest cause. No significant difference in mortality was observed between different lupus nephritis classes or therapy arm groups.

Conclusion: The study throws light on various aspects of lupus nephritis and their long-term outcome patterns in children from developing countries such as India.

Keywords: Childhood lupus nephritis, developing country, outcome, end-stage renal disease

Cite this article as: Samanta M, Nandi M, Mondal R, Hazra A, Sarkar S, Sabui T. Childhood lupus nephritis: 12 years of experience from a developing country's perspective. Eur J Rheumatol 2017; 4: 178-83.

[1] Department of Pediatrics, NRS Medical College, Kolkata, India
[2] Department of Pediatrics, Medical College and Hospital, Kolkata, India
[3] Department of Pharmacology, IPGME&R SSKM Hospital, Kolkata, India
[4] Department of Pediatrics, IPGME&R SSKM Hospital, Kolkata, India
[5] Department of Pediatrics, RGKAR Medical College, Kolkata, India
[6] Department of Pediatrics, Chittaranjan Sishu Sadan Hospital, Kolkata, India

Address for Correspondence: Rakesh Mondal, Department of Pediatrics, Medical College and Hospital, Kolkata, India

E-mail: ivanrakesh2001@gmail.com

Submitted: 13 December 2016
Accepted: 12 April 2017

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder that manifests as a chronic inflammatory disorder with multisystem involvement. The presentation is highly variable, the disease follows a relapsing and remitting course, and although standardized treatment has improved the short- and medium-term outlook, long-term prognosis remains poor in children with lupus with major organ involvement (1). Lupus has a higher incidence of renal involvement in children than in adults (2-4). Lupus nephritis is seen in nearly 50% patients with pediatric-onset SLE (pSLE), which may manifest as asymptomatic urinary findings, acute kidney injury, and even chronic renal disease (5). Renal involvement remains one of the important factors influencing management and long-term prognosis of pSLE (6-9). There is some evidence that the prognosis of lupus nephritis in developing countries is worse than that in developed countries (10). Some studies from other parts of India have highlighted the long-term outcome in children with lupus nephritis (11, 12), but there has been no detailed report from Eastern India.

This study aimed to evaluate the long-term outcome of lupus nephritis in pSLE followed up over 12 years at a tertiary care teaching hospital in Eastern India. The outcome of half these children with 8 years of follow-up has been previously reported (13).

Material and Methods

Patient selection

A retrospective observational study was conducted with follow-up data on pSLE from the pediatric rheumatology clinic collected over the past 12 years from in the institute concerned. The study was conducted in accordance to the guidelines of the Institutional Ethics Committee for human research. As it was a retrospective study, requirement for informed consent was waived. Children with SLE, defined according to the American College of Rheumatology (ACR) 1997 revised criteria, who developed lupus nephritis in due course or presented with lupus nephritis within 12 years of age were included (14-16). Data on disease onset, biopsy findings (expressed in terms of World Health Organization classification), therapy received,

and outcome were collected. For the analysis of short-term outcomes, children were classified into those with complete (CR) remission, partial remission (PR), active disease or no response, and progression to ESRD (those requiring renal replacement therapy). For survival analysis, time till death (actuarial survival) and time till ESRD (renal survival) were assessed. In cases of death, the cause of death was noted.

Therapy

Depending on renal biopsy findings, therapy was decided according to the ACR guidelines (14). Various activity and chronicity indices were considered while selecting the available therapy options. Oral hydroxychloroquine (5-10 mg/kg/day) were administered to all pSLE patients, unless contraindicated, since 2008 as per recommendations (17). Angiotensin-converting enzyme inhibitors were the preferred first line antihypertensive, wherein renal function was preserved. For comparative analysis, treatment modalities were categorized into four groups, arm 1 being prednisolone only, arm 2 being prednisolone and cyclophosphamide, arm 3 being prednisolone and azathioprine, and arm 4 being prednisolone and mycophenolate mofetil.

Response to therapy, as guided by ACR criteria, was defined as CR, PR, nonresponse or progression of active disease (NR/P), and ESRD. Indications of renal biopsy were also in accordance to the ACR guidelines.

Analysis

Statistica version 6 (StatSoft Inc.; Tulsa, OK, USA) and MedCalc version 11.6 (MedCalc Software; Mariakerke, Belgium) were used for statistical analysis. Normally distributed numerical variables were expressed as mean and standard deviation (SD), whereas numerical variables when skewed were expressed as median and interquartile range (IQR). Numerical variables were tested for normal distribution by Kolmogorov–Smirnov Goodness-of-Fit test. Mortality was compared among the different lupus classes and therapy groups with Kaplan–Meier analysis and log-rank test. Two-tailed $p<0.05$ was considered statistically significant.

Results

Over 12 years, a total of 78 children were diagnosed with pSLE, of which 46 developed lupus nephritis, giving an incidence of 58.97% (95% CI 48.06%–59.89%). The age at onset of lupus nephritis was 10.2±2.43 years (mean±SD) with the range of 5.5–14.5 years. The median duration of the follow-up (n=46) was 90 months (IQR 70.5–108 months). The basic demographic and clinical profile of the subjects is shown in Table 1.

Majority of children presented with lupus nephritis at onset (82.61%), whereas the rest developed at a later date. Of the children who underwent renal biopsy, majority belonged to class IV (30.43%) followed by class II and then class III.

The commonest presenting feature of lupus nephritis was oliguria with anasarca (13/46; 28.26%), and the commonest laboratory abnormality was proteinuria with hematuria (14/46; 30.43%) as depicted in Table 2.

Among extrarenal manifestations, hematological abnormalities were the commonest, followed by serosal and neurological manifestations. Of the hematological manifestations, autoimmune hemolytic anemia was the commonest followed by immune thrombocytopenic purpura and antiphospholipid antibodies (APLA). The latter presented as recurrent thrombosis, cerebrovascular accidents, and acute renal failure, which were fatal. Incidence of neuropsychiatry SLE (NPSLE) in boys was significantly higher than that in girls (p=0.005). Headache was the commonest manifestation of NPSLE, followed by seizures and behavioral abnormalities. Regarding serosal involvement, joints followed by pleura and peritoneum were affected. Among cardiovascular involvement, three newborns had second degree heart block, one had pericardial effusion as a part of the flare-up of disease activity, and one developed congestive heart failure secondary to SLE myocarditis.

Of the four treatment options, 11 children received arm 1 therapy, 21 arm 2, 8 arm 3, and

Table 1. Basic demographic and clinical profile of 46 children with lupus nephritis

Feature	Value or Count
Sex (male:female)	17:29
Age at onset of lupus nephritis (years) [Mean±SD]	10.2±2.43
Onset of SLE to nephritis duration (months) [Mean±SD]	8.5±10
Lupus nephritis at presentation n (%)	38 (82.61%)
Antinuclear antibody-positive n (%)	45 (97.83%)
Anti-dsDNA antibody at presentation n (%)	38 (82.61%)
Low C3 at presentation n (%)	35 (76.09%)
Renal biopsy performed n (%)	41 (89.13%)
Histological class on renal biopsy n (%)	
• Class II	12 (26.09)
• Class III	11 (23.91)
• Class IV	14 (30.43)
• Class V	4 (8.70)
Extrarenal features n (%)	
• Overlap syndrome	3 (6.52)
• Central nervous system symptoms	13 (28.26)
• Cardiac involvement	5 (10.87)
• Serositis	20 (43.48)
• Pulmonary involvement	10 (21.74)
• Hematological involvement	
• Autoimmune hemolytic anemia	18 (39.13)
• Antiphospholipid antibody	2 (4.35)
• Immune thrombocytopenic purpura	7 (15.22)
• Gastrointestinal (lupoid hepatitis)	2 (4.35)
• Skin and mucosa involvement	30 (65.22)

SD: standard deviation; SLE: systemic lupus erythematosus; Anti-dsDNA: anti-double stranded deoxyribose nucleic acid; C3: complement 3

6 arm 4. Children of either sex were equally distributed between these treatment groups (p=0.436). Cyclophosphamide and mycophenolate mofetil were used interchangeably in cases of poor therapeutic response to either one of these agents in four children. Of 46 children with nephritis, renal biopsy could not be performed in five children due to logistic or financial constraints. Indications for repeat biopsy were repeat renal manifestations after a period of remission or progression to chronic kidney disease. Though indicated repeat biopsy could be done only in two children because of financial constraint and parent refused consent in others. Disease flare-ups in these five children were managed by methyl prednisolone pulse therapy; three children responded and two required additional intravenous immunoglobulin. Of these, one responded and one required additional rituximab. Of the two children who underwent repeat biopsy, one died at 11.5 years post-diagnosis due to septicemia with ESRD.

Outcome analysis of children with lupus nephritis over 12 years revealed CR of disease activity in 24 (52.17%), PR in 5, continuation of active disease in 4, ESRD in 5, and death in 8 children. Mortality thus observed was 17.39% (95% CI 6.44%–28.34%) (Table 3), with 37.5% occurring within the first year of diagnosis. The commonest cause of death was septicemia (3/8; 37.5%), followed by ESRD with septicemia (also 3/8; 37.5%) and APLA (2/8; 25%) leading to cerebrovascular accident and acute renal failure. Among the children who died, two did not undergo renal biopsy for disease staging, two belonged to stage II, two to stage III, and one to stages IV and V each. With Kaplan–Meier analysis, the 5-year survival probability and 5-year ESRD-free survival was 91.3% and 97.5%, respectively. The 10-year survival probability was 76.2%.

Among the children who died, 11.4±3.01 years (range 6.5-14.5 years) was the mean age of onset of nephritis, and the duration of illness till death was 57.9±54.57 months (range 5-138 months). In cases of ESRD, the age of onset of nephritis was 10.5±2.26 years (range 9.0-14.5 years), and the mean duration of illness till the development of ESRD was 94.8±24.88 months (range 60–120 months). Statistically significant number of boys died compared with girls [p 0.038; RR 5.12 (95% CI 1.16 to 22.58)]. All five children with ESRD were boys.

Differences in mortality were not significant among the different lupus classes (Figure 1) and therapy groups (Figure 2) using survival analysis techniques (p=0.860 and 0.630, respectively). Because of limited numbers, median survival could be estimated only for lupus class II and therapy arm 2 (138 months). Comparison of ESRD between lupus classes and therapy groups showed a similar pattern (Table 3). Again, because of limited numbers, median time till ESRD development could not be estimated in individual subgroups.

Table 2. Frequency distribution of presenting features of lupus nephritis in 46 children

Feature	Value or Count
Clinical features	
• Oliguria alone	7 (15.22)
• Anasarca alone	4 (8.70)
• Hypertension alone	4 (8.70)
• Oliguria + Anasarca	13 (28.26)
• Oliguria + Hypertension	8 (17.39)
• Anasarca + Hypertension	7 (15.22)
• All three present	3 (6.52)
Laboratory features	
• Hematuria alone	5 (10.87)
• Proteinuria alone	4 (8.70)
• Raised urinary protein–creatinine ratio alone	1 (2.17)
• Hematuria + Proteinuria	14 (30.43)
• Hematuria + Raised urinary protein–creatinine ratio	14 (30.43)
• Proteinuria + Raised urinary protein–creatinine ratio	1 (2.17)
• All three present	7 (15.22)

SD: standard deviation; SLE: systemic lupus erythematosus; Anti-dsDNA: anti-double stranded deoxyribose nucleic acid; C3: complement 3

Discussion

The incidence of lupus nephritis found to be 58.8% in our study is comparable with those of other recent Indian and western studies (8-10, 12, 19). A small increase in incidence of nephritis is noted from 54.7% as reported from our institution in 2012 to the current 58.8%. There has also been an increase in the proportion of children with lupus nephritis who underwent biopsy (13/23 in the 2012 report against 41/46 in the current report) (13). This might be attributed to the growing awareness of lupus nephritis among doctors who aggressively look for evidence of nephritis by clinical and laboratory evaluation. Although greater proportion of girls was affected by lupus nephritis, boys were found to have a poorer prognosis. A similar observation was made by Hari et al. (19) that more boys were found to be affected with stage IV nephritis.

Table 3. Mortality and ESRD experience by lupus class and therapy type

	Lupus class II	Lupus class III	Lupus class IV	Lupus class V	Therapy arm 1	Therapy arm 2	Therapy arm 3	Therapy arm 4
N	12	11	14	4	11	21	8	6
Mortality (%)	2 (16.67)	2 (18.18)	1 (7.14)	1 (25.00)	–	6 (28.57)	1 (12.50)	1 (16.67)
p value by log-rank test	0.860				0.184			
ESRD (%)	1 (8.33)	1 (9.09)	1 (7.14)	1 (25.00)	–	3 (14.29)	2 (25.00)	–
p value by log-rank test	0.630				0.269			

ESRD: end-stage renal disease

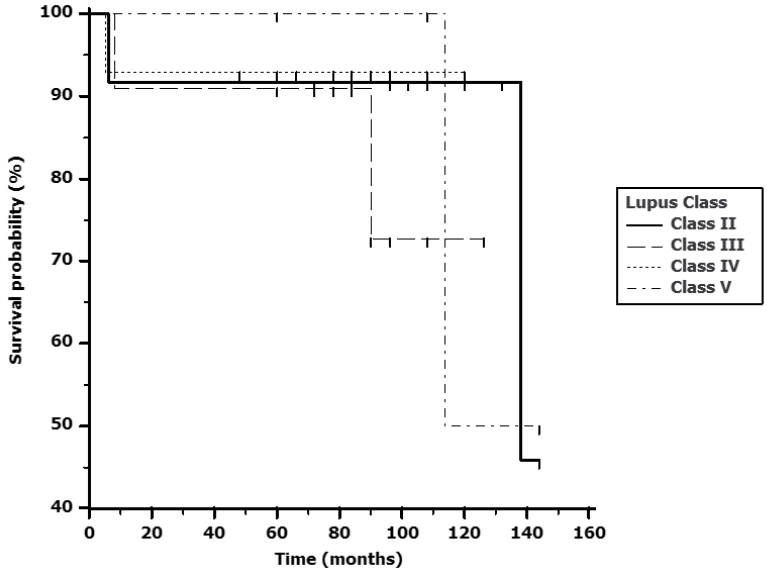

Figure 1. Kaplan-Meier plot showing mortality over time in 41 children (excluding five who did not undergo renal biopsy) by lupus class. Differences were not statistically significant (p=0.860 by log-rank test)

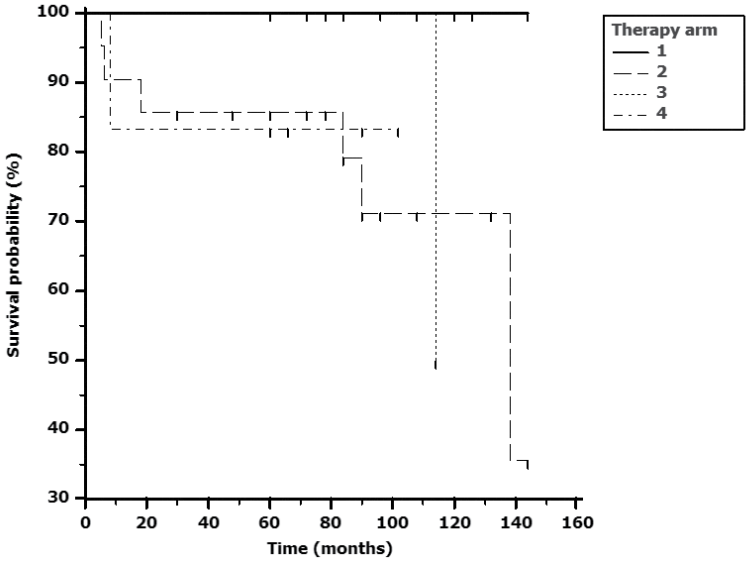

Figure 2. Kaplan-Meier plot showing mortality over time in 46 children by treatment class. Differences were not statistically significant (p=0.184 by log-rank test)

The clinical and laboratory features of lupus nephritis encountered in our study are broadly in conformity with other reports (20-23). It has been the classical textbook teaching that SLE results in non-erosive arthritis; however, we found two children with deforming arthritis satisfying the rhupus syndrome designation and one with SLE and cutaneous scleroderma overlap syndrome (24, 25). Neuropsychiatric involvement in SLE can be severe and troubling, greatly influencing the quality of life and disease outcome. The expressions can be complex with central, peripheral, and autonomous nervous systems affected (26). Central nervous system symptoms were encountered in 28.26% cases in our series. Relevant immunological markers were encountered in the majority of cases, with nearly 98% positive for antinuclear antibodies. Previous studies revealed that those who present at a younger age with severe nephritis and nervous system affections have poorer prognosis (2, 27).

At 17.39%, mortality in our study was between what has been observed in various other studies and higher than the 8.2% observed in a large Indian series with a 25-year follow-up (4, 11, 28-31). However, no significant difference in mortality was observed in different lupus nephritis classes or therapy arm groups. Septicemia occurring on a background of ESRD or otherwise was the commonest cause of death (75%). Other previous Indian studies and studies from other developing countries (Table 4) have also reported a similar trend wherein most children with lupus nephritis succumbed to serious infections (11, 18, 31-34).

Of the five children who developed ESRD, three succumbed to serious sepsis, and among them, one was on continuous ambulatory peritoneal dialysis and had undergone a change in the therapy arm for severe disease. The other two children however could not afford renal replacement therapy and were lost to follow-up. This poor outcome in children with ESRD highlights the constraints faced by caregivers and merits the establishment of support groups for children with lupus in developing countries such as ours.

The institution in which the study was performed serves as an apex referral center in the government sector, and patients from all over the state and neighboring states are referred to our pediatric rheumatology clinic with provisional diagnosis or suspicion of SLE for further work-up, management, and follow-up. We therefore had the advantage of a large catchment area. However, this study also has its share of limitations. Maintenance of patient records and follow-up data was a tedious procedure in the absence of fully computerized medical records, but this could largely be overcome with diligence and cooperation among treating physicians. Renal biopsy could not be performed in all nephritis patients owing to financial constraints in some and lack of consent in others. Use of biologicals, although indicated, was seldom encountered in our series due to the lack of affordability.

In conclusion, this study enlightens us about various aspects of lupus nephritis and their outcome patterns in children from developing countries such as India. Further studies are required to assess the effectiveness of existing and new treatment options and their impact on long-term disease outcome in these resource-poor setting.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Institute of Post Graduate Medical Education & Research, Kolkata.

Informed Consent: Written informed consent was not obtained due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - T.S., R.M.; Design - R.M., M.N.; Supervision - M.N., S.S.; Resources - T.S., S.S.;

Table 4. Comparison of series of lupus nephritis from various countries

Country	Author	Year of publication	Sample size; female:male	Follow-up period (years)	Age of onset Mean±SD (years)	Survival rates	Outcome observations
India	Singh et al. (18)	2015	72; 3:1	24	Onset of lupus 9.3±2.4 years and time from onset-to-nephritis 9.4±12.6 months	67% at 5 years	30% mortality, infection and ESRD important causes of death
	Dhir et al. (31)	2012	188 (47≤16 years); 173:15	20	23.6±10.5	84% at 5 years	16 died, majority secondary to infection.
	Srivastava et al. (11)	2016	134; 121:14	25	13.7±3.5	91.1% at 5 years	8.2%, infection being major cause
	Hari et al. (19)	2009	54; 30:14	10	9.6±2.6	88% at 3 years	9 died, majority secondary to infection or ESRD
China	Lee et al. (29)	2013	189; 164:25	20	12.62±2.77	93.4% at 5 years	15 died, infection being the major cause
	Wong et al. (32)	2006	128; 120:8	16	11.9±2.8	91.5% at 5 years	3.9%, Lupus flare, infection and ESRD being the commonest causes
Poland	Szymanik-Grzelak et al. (4)	2016	18; 8:1	10	14.4±1.81	100%	None
Africa	Flower et al. (33)	2012	22; 21:1	10	-	68% at 5 years	17 deaths in the whole cohort, ESRD and sepsis being the commonest causes
	Elmougy et al. (28)	2015	136; 109:27	16	12.5±2.9	88% at 5 years	11%, infection being the major cause
South-east Asia	Tan et al. (34)	2015	64; 5:1	5	11.9 (range 2.6–18.0)	98.4% at 5 years	1.6%, Infection is the main cause
India	Present study	-	46; 29:17	12	10.2±2.43	91.3% at 5 years	17.39%, Infection and ESRD being the major causes

ESRD: end-stage renal disease

Materials - R.M., M.S.; Data Collection and/or Processing - M.S., C.K.; Analysis and/or Interpretation - A.H., C.K.; Literature Search - A.H., A.B.; Writing Manuscript - M.S., A.B.; Critical Review - T.S., M.N.; Other - R.M., M.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Doria A, Iaccarino L, Ghirardello A, Zampieri S, Arienti S, Sarzi-Puttini P, et al. Long-term prognosis and causes of death in systemic lupus erythematosus. Am J Med 2006; 119: 700-6. [CrossRef]
2. Lech M, Anders HJ. The pathogenesis of lupus nephritis. J Am Soc Nephrol 24: 1357-66. [CrossRef]
3. Ambrose N, Morgan TA, Galloway J, Ionnoau Y, Beresford MW, Isenberg DA, et al. Differences in disease phenotype and severity in SLE across age groups. Lupus 2016; 25: 1542-50. [CrossRef]
4. Szymanik-Grzelak H, Kuźma-Mroczkowska E, Małdyk J, Pańczyk-Tomaszewska. Lupus nephritis in children - 10 years' experience. Cent Eur J Immunol 2016; 41: 248-54. [CrossRef]
5. Malattia C, Martini A. Paediatric-onset systemic lupus erythematosus. Best Pract Res Clin Rheumatol 2013; 27: 351-62. [CrossRef]
6. Mina R, Brunner H. Update on differences between childhood-onset and adult-onset systemic lupus erythematosus. Arthritis Res Ther 2013; 15: 218. [CrossRef]
7. Feng X, Zou Y, Pan W, Wang X, Wu M, Zhang M, et al. Associations of clinical features and prognosis with age at disease onset in patients with systemic lupus erythematosus. Lupus 2013; 23: 327–34. [CrossRef]
8. Amaral B, Murphy G, Ioannou Y, Isenberg DA. A comparison of the outcome of adolescent and adult onset systemic lupus erythematosus. Rheumatology (Oxford) 2014; 53: 1130-5. [CrossRef]
9. Hiraki LT, Benseler SM, Tyrrell PN, Hebert D, Harvey E, Silverman ED. Clinical and laboratory characteristics and long-term outcome of pediatric systemic lupus erythematosus: a longitudinal study. J Pediatr 2008; 152: 550-6. [CrossRef]
10. Tektonidou MG, Dasgupta A, Ward MM. Risk of end-stage renal disease in patients with lupus nephritis, 1971-2015: a systematic review and Bayesian meta-analysis. Arthritis Rheumatol 2016; 68: 1432-41. [CrossRef]
11. Srivastava P, Abujam B, Misra R, Lawrence A, Agarwal V, Aggarwal A. Outcome of lupus nephritis in childhood onset SLE in North and Central India: single-centre experience over 25 years. Lupus 2015; 25: 547-57. [CrossRef]
12. Pradhan V, Patwardhan M, Rajadhyaksha A, Ghosh K. Clinical and immunological profile of systemic lupus erythematosus. Indian Pediatr 2013; 50: 405-7. [CrossRef]
13. Nandi M, Mondal R. Renal involvement in childhood lupus: a study from Kolkata, India. Saudi J Kidney Dis Transpl 2012; 23: 871-5. [CrossRef]
14. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for classification of systemic lupus erythematosus. Arthritis Rheum 1982; 25: 1271-7. [CrossRef]
15. Smith EL, R H Shmerling RH. The American College of Rheumatology criteria for the classification of systemic lupus erythematosus: Strengths, weaknesses, and opportunities for improvement. Lupus 1999; 8: 586-95. [CrossRef]
16. Yu C, Gershwin ME, Chang C. Diagnostic criteria for systemic lupus erythematosus: a critical review. J Autoimmun 2014; 48-49: 10-3. [CrossRef]
17. Hahn BH, MacMahon MA, Wilkinson A, Wallace WD, Daikh DI, Fitzgerald JD, et al. American College of Rheumatology guidelines for screening,

treatment and management of lupus nephritis. Arthritis Care Res 2012; 64: 797-808. [CrossRef]
18. Singh S, Abujam B, Gupta A, Suri D, Rawat A, Saikia B, et al. Childhood lupus nephritis in a developing country-24 years' single-center experience from North India. Lupus 2015; 24: 641-7. [CrossRef]
19. Hari P, Bagga A, Mahajan P, Dinda A. Outcome of lupus nephritis in Indian children. Lupus 2008; 18: 348-54. [CrossRef]
20. Silva CA. Childhood-onset systemic lupus erythematosus: early disease manifestations that the paediatrician must know. Expert Rev Clin Immunol 2016; 12: 907-10. [CrossRef]
21. Barsalou J, Levy DM, Silverman ED. An update on childhood-onset systemic lupus erythematosus. CurrOpin Rheumatol 2013; 25: 616-22. [CrossRef]
22. Malattia C, Martini A. Paediatric-onset systemic lupus erythematosus. Best Pract Res Clin Rheumatol 2013; 27: 351-62. [CrossRef]
23. Boneparth A, Wenderfer SE, Moorthy LN, Radhakrishna SM, Sagcal-Gironella AC, von Scheven E. Clinical characteristics of children with membranous lupus nephritis: the Childhood Arthritis and Rheumatology Research Alliance Legacy Registry. Lupus 2017; 26: 299-306. [CrossRef]
24. Mitra S, Mondal R. Childhood 'rhupus' syndrome. Indian Pediatr 2015; 52: 346.
25. Mondal R, Sarkar S, Nandi M, Hazra A, Pal P, Banerjee I, et al. Overlap syndrome - a child cohort. Indian J of Pediatr 2013; 80: 434-5. [CrossRef]
26. Govoni M, Bortoluzzi A, Padovan M, Silvagni E, Borrelli M, Donelli F, et al. The diagnosis and clinical management of the neuropsychiatric manifestations of lupus. J Autoimmun 2016; 74: 41-72. [CrossRef]
27. Schwartz N, Goilav B. The pathogenesis, diagnosis and treatment of lupus nephritis. Curr Opin Rheumatol 2014; 26: 502-9. [CrossRef]
28. Elmougy A, Sarhan A, Hammad A, El-Refaey A, Zedan M, Eid R, et al. Lupus nephritis in Egyptian children: a 16-year experience. J Nephrol 2015; 28: 557-62. [CrossRef]
29. Lee PY, Yeh KW, Yao TC, Lee WI, Lin YJ, Huang JL. The outcome of patients with renal involvement in pediatric-onset systemic lupus erythematosus – a 20-year experience in Asia. Lupus 2013; 22: 1534-40. [CrossRef]
30. Singh S, Devidayal, Minz R, Nada R, Joshi K. Childhood lupus nephritis: 12 years experience from North India. Rheumatol Int 2006; 26: 604-7. [CrossRef]
31. Dhir V, Aggarwal A, Lawrence A, Agarwal V, Misra R. Long-term outcome of lupus nephritis in Asian Indians. Arthritis Care Res 2012; 64: 713-20. [CrossRef]
32. Wong SN, Tse KC, Lee TL, Lee KW, Chim S, Lee KP, et al. Lupus nephritis in Chinese children--a territory-wide cohort study in Hong Kong. Pediatric Nephrology 2006; 21: 1104-12. [CrossRef]
33. Flower C, Hennis A, Hambleton I, Nicholson G, Liang M. Systemic Lupus Erythematosus in an African Caribbean population: Incidence, clinical manifestations, and survival in the Barbados National Lupus Registry. Arthritis Care Res 2012; 64: 1151-58.
34. Tan JHT, Hoh SF, Win MTM, Chan YH, Das L, Arkachaisri T. Childhood-onset systemic lupus erythematosus in Singapore: clinical phenotypes, disease activity, damage, and autoantibody profiles. Lupus 2015; 24: 998-1005. [CrossRef]