# Clinical and Immunological Spectrum of Systemic Lupus Erythematosus in Children

**Sandesh Kini, Ramesh Bhat Y, Chennakeshava Thunga, Sowmya Shashidhara and Akshatha Anand**

Department of Paediatrics, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India

**Correspondence**:
Ramesh Bhat Y
Department of Paediatrics,
Kasturba Medical College, Manipal,
Manipal Academy of Higher Education,
Manipal, Karnataka, India.
Email: ramesh.bhaty@manipal.eduu

**DOI:** 10.3126/jnps.v40i1.28460

**Submitted on:** 2020-04-13

**Accepted on:** 2020-05-30

**Acknowledgements:** None

**Funding:** None

**Conflict of Interest:** None declared

**Permission from IRB:** Yes

**To cite this article:** Kini S, Bhat RY, Thunga C, Shashidhara S, Anand A. Clinical and immunological spectrum of systemic lupus erythematosus in children. J Nepal Paediatr Soc. 2020;40(1):14-20.

## ABSTRACT

**Introduction:** Systemic Lupus Erythematosus (SLE) is an auto immune disorder affecting mainly adolescent females and young women of reproductive age. The disease is characterised by widespread inflammation of blood vessels and connective tissues due to the presence of anti-nuclear antibodies (ANA). There are limited number of studies from South India on paediatric lupus. Our objectives were to study the clinical and immunological features of childhood SLE along with treatment modalities and its outcome at the end of one year follow up. The correlation between various auto-antibodies and systemic involvement was also assessed.

**Methods:** This was a retrospective observational study carried out in paediatric unit at a tertiary care centre in South India. Data was obtained through patient's medical records. From April 2003 to April 2019, 32 children were diagnosed to have SLE as per the American college of Rheumatology 1997 criteria.

**Results:** The study population included 32 children fulfilling the criteria. Female to male ratio was 4.3:1. The mean age at diagnosis was 11.52 years. The most common clinical manifestations were renal (87.5%) followed by haematological (81.3%), musculoskeletal (59.4%), mucocutaneous (53.1%) and nervous system (31.3%) involvement. All patients were positive for anti-nuclear antibodies. Anti-double stranded DNA (78.1%) was the most common auto-antibody profile followed by anti-ribosomal p protein (37.5%) and anti-nucleosome antibody (37.5%). During the follow up, 13 (40.6%) children attained complete remission, 10 (31.2%) went into partial remission and nine (28.1%) had persisting active disease.

**Conclusion:** The clinical spectrum and outcome of paediatric SLE depends upon the age of presentation and number of organ systems involved at the time of diagnosis. Our study throws light on various aspects of SLE in children from developing countries like India.

**Key words**: auto-immune; children; lupus; nephritis; outcome

## INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a multi-system disorder characterised by auto antibody production. The presentation is highly variable marked by periods of flare and remission with significant morbidity and mortality.[1] The peak incidence is around 10-14 years with a male to female ratio of 3:4 before puberty and 1:4 after puberty. SLE is rare in children under five years and the disease has a higher risk of mortality and morbidity compared to adults.[2] Rates of organ involvement are higher in children compared to adults as children tend to have more severe symptoms at onset.[2] The clinical manifestations and severity of SLE vary between different geographic regions which is probably related to genetic and environmental factors.[3] Studies have shown that the prognosis of SLE is worse in developing countries compared to the developed.[4] Our objectives were to study the clinical and immunological features of SLE along with treatment modalities and outcome at the end of one year follow up. We also assessed the relationship between various auto-antibody types and probability of systemic involvement.

## METHODS

After obtaining approval from the institutional ethics committee (IEC:396/2019), we conducted a retrospective observational study in a paediatric unit at a tertiary care centre in South India. The study population included children between one month to 18 years of age, diagnosed with SLE during April 2003 to April 2019. Children who fulfilled at least four of the criteria for SLE by American College of Rheumatology - 1997, including one clinical and one immunological criterion or in the presence of biopsy proven lupus nephritis with positive ANA profile were recruited into the study. Children who were lost to follow up within one year following diagnosis were excluded from the study. Patient data including demographic, clinical, laboratory findings, treatment received and follow up details were obtained from patient's medical records.

Lupus nephritis (LN) was considered if child had hypertension (systolic or diastolic blood pressure more than 95$^{th}$ centile for age and sex), abnormalities in urine analysis, elevated serum creatinine or hypo-complementemia as per age specific limits.[5] Details of renal biopsy from children with lupus nephritis were noted and classified as per world health organisation (WHO) criteria.[5] Outcome at the end of one year follow up was classified into four categories as complete remission, partial remission, presence of active disease and expired. Clinical remission was defined as at least six months absence of disease activity clinically, either on or off treatment.[6] Laboratory remission was defined as the time taken for indicators of active disease like C3 complement, proteinuria and hypertension to normalise either on or off treatment.[6] Complete remission was considered when proteinuria was < 4 mg/m$^2$/hr, urine analysis showed 1+/nil protein, there were less than five red blood cells (RBCs) and or less than five white blood cells (WBCs), no cellular casts, no evidence of extra-renal manifestations with normal complement levels.[6] Partial remission was considered when proteinuria was four to 40 mg/m$^2$/hr or was reduced by at least 50% from baseline and there were < 5 RBCs, < 5 WBCs and no cellular casts.[6] Active disease was said to persist when proteinuria was > 40 mg/m$^2$/hr or between four to 40 mg/m$^2$/hr with a reduction of less than 50% from baseline or presence of active sediment or extra-renal manifestations.[6] Measurable worsening of disease activity in the form of new or worse disease related symptoms or signs in at least one organ system requiring change or increase in immunosuppressive treatment was considered as a disease flare.[6]

Data was analysed using SPSS version 21. Mean and standard deviation were used to describe data following normal distribution. Median and interquartile range was used to describe skewed data. Chi-square test was used for categorical variables. Mann-Whitney test was used to analyse continuous variables.

## RESULTS

Over 16 years, there were 32 children diagnosed with SLE. The study population included 26 females and six males, with a female to male ratio of 4.3:1. Mean age at diagnosis was 11.52 (SD ± 3.66) years with the earliest presentation at 1.02 years. Children over 10 years (75%) in their second

**Table 1.** Demographic data of the study population

| Parameter | Result |
|---|---|
| **Age at diagnosis in years:** mean (range) | 11.52 (1.02-16.15) |
| **Age category** | |
| < 5 years: n (%) | 2 (6.25) |
| 5-10 years: n (%) | 6 (18.75) |
| 10-18 years: n (%) | 24 (75) |
| **Sex** | |
| Male: n (%) | 6 (18.8) |
| Female: n (%) | 26 (81.3) |
| **BMI** < 3rd centile: n (%) | 12 (37.5) |
| **Duration of illness at diagnosis:** median (range) in months | 2 (1-24) |

decade were the most commonly affected. The median duration of illness at the time of diagnosis was two months (IQR: 1-3). The demographic characteristics of SLE has been summarised in table 1.

The clinical characteristics of SLE has been summarised in table 2, with renal involvement (87.5%) being the most common followed by haematological (81.3%) and musculoskeletal (59.4%). Proteinuria (> 4 mg/m$^2$/hr) was observed in 20 (62.5%) children. Of the 28 children with renal involvement, in whom 24-hour urine protein quantification was done, two children had nephrotic range proteinuria (> 40 mg/m$^2$/hr), 18 had non-nephrotic range proteinuria (4 - 40 mg/m$^2$/hr) and eight had proteinuria < 4 mg/m$^2$/hr. The median value of timed urine protein was 8 mg/m$^2$/hr (range: 1.2 - 190). The laboratory parameters at presentation has been summarised in table 3.

All the children in our study were positive for ANA. Anti-ds DNA (78.1%) was the most commonly observed auto antibody profile followed by anti-ribosomal P protein (37.5%) and anti-nucleosome antibodies (37.5%). However, we found no significant association between the auto-antibody profile and systemic involvement as depicted in table 4.

Renal biopsy was done in 18 children with lupus nephritis (LN) as per clinical and laboratory indications. Class II (28.1%) was the most common

**Table 2.** Clinical features and organ involvement at presentation (n = 32)

| Organ involvement | Number (%) |
|---|---|
| **Constitutional symptoms** | 23 (71.9) |
| Fever | 23 (71.9) |
| Weight loss | 3 (9.4) |
| Headache | 5 (15.6) |
| **Muco-cutaneous** | 17 (53.1) |
| Malar rash | 15 (46.9) |
| Alopecia | 4 (12.5) |
| Photosensitivity | 2 (6.3) |
| Oral ulcer | 7 (21.9) |
| Raynaud's phenomenon | 4 (12.5) |
| **Musculoskeletal** | 19 (59.4) |
| Arthralgia | 17 (53.1) |
| Arthritis | 8 (25) |
| Myalgia | 4 (12.5) |
| **Serositis** | 6 (18.8) |
| Pleural effusion | 2 (6.3) |
| Ascites | 6 (18.8) |
| **Nervous system involvement** | 10 (31.3) |
| Seizure | 4 (12.5) |
| Paraparesis | 2 (6.3) |
| Peripheral neuropathy | 4 (12.5) |
| Depression | 1 (3.1) |
| **Vasculitis** | 2 (6.3) |
| **Renal involvement** | 28 (87.5) |
| Periorbital puffiness | 6 (18.8) |
| Hypertension | 6 (18.8) |
| Proteinuria | 20 (62.5) |
| Microscopic haematuria | 10 (31.3) |
| **Hypocomplementemia** | 23 (71.9) |
| Low C3 | 23 (71.9) |
| Low C4 | 23 (71.9) |
| **Haematological abnormalities** | 26 (81.3) |
| Anaemia | 23 (71.9) |
| Leukopenia | 2 (6.3) |
| Thrombocytopenia | 6 (18.8) |
| AIHA | 4 (12.5) |
| Elevated ESR | 24 (75) |
| **Others** | |
| Hepatosplenomegaly | 20 (62.5) |
| Lymphadenopathy | 3 (9.4) |
| Hematemesis | 1 (3.1) |
| Delayed puberty | 1 (3.1) |

*AIHA: auto-immune haemolytic anaemia, ESR: erythrocyte sedimentation rate*

histopathological category in renal biopsy as depicted in table 5.

Among the treatment modalities steroids were the mainstay of treatment as depicted in table 6. Of the

**Table 3.** Laboratory parameters at presentation

| Parameters | Result: median (range) | Normal values |
|---|---|---|
| Haemoglobin (g/dL) | 9.9 (6.1 - 14.8) | 11 - 14 |
| Total WBC count (cells/µL) | 7400 (2500 - 15900) | 4500 - 13000 |
| Platelet count (cells/µL) | 239000 (50000 - 560000) | 150000 - 350000 |
| ESR (mm/hour) | 47 (4 - 140) | 0 - 20 |
| Serum creatinine (mg/dL) | 0.6 (0.2 - 1.2) | 0.5 - 1 |
| C3 levels (ng/dL) | 45 (10 - 213) | 90 - 150 |
| C4 levels (mg/dL) | 8 (1 - 70) | 15 - 50 |

32 patients, 30 received prednisolone, or the equivalent, in the initial dose of 2 mg/kg/day (maximum 60 mg/day). These were then gradually tapered to a dosage adequate to control the disease clinically. Two patients received pulse methyl prednisolone (30 mg/kg/day) for renal disease. Cyclophosphamide was used at a dose of 2-2.5 mg/kg/day in 14 patients with renal disease. Hydroxychloroquine (HCQ) at the dose of 6 mg/kg/day was used in 23 children mainly to treat musculoskeletal symptoms. Other commonly used immunosuppressive agents were azathioprine (2 mg/kg/day) and methotrexate (10-20 mg/m$^2$/week).

The decision to optimise the dose of steroids or addition of immunosuppressive drugs during follow up was based on clinical symptomatology and laboratory investigations especially ESR and C3 levels.

Cyclophosphamide and HCQ were used mainly in class II and class III lupus, while azathioprine, cyclophosphamide and methotrexate were used in class IV and class V lupus. None of these children with LN progressed to end stage renal disease (ESRD) during the entire follow up period. The median duration of follow up from the time of diagnosis was 49 months (range: 12-173 months). At the end of one year follow up, 13 (40.6%) children attained complete remission, 10 (31.3%) attained partial remission while nine (28.1%) children had persistent active disease. On long term follow up, 19 (59.4%) children were noticed to have flares after achieving remission. The median duration of clinical and laboratory remission were 11 months (IQR:4.5-24) and 21 months (IQR: 3-28) respectively. Among the study subjects, mortality was recorded in one girl aged 15.4 years at diagnosis, with class III lupus nephritis, who expired 5.4 years post diagnosis due to septic shock.

**Table 4.** Spectrum of systemic involvement in relation to immunological profile

| Antibody type detected | Lupus nephritis (n = 28) (p value) | Neuro psychiatric lupus (n = 10) (p value) | Serositis (n = 6) (p value) | Haematological involvement (n = 26) (p value) |
|---|---|---|---|---|
| Anti-ds DNA (n = 25) | 23 (0.20) | 8 (1.00) | 5 (1.00) | 22 (0.10) |
| Anti-RNP (n = 7) | 7 (0.55) | 3 (0.64) | 0 (0.29) | 6 (1.00) |
| Anti-Smith (n = 7) | 7 (0.55) | 3 (0.64) | 0 (0.29) | 6 (1.00) |
| Anti-Rib P (n = 12) | 12 (0.27) | 4 (1.00) | 2 (1.00) | 12 (0.06) |
| Anti-Nucleosome (n = 12) | 12 (0.27) | 3 (0.70) | 2 (1.00) | 12 (0.06) |
| Anti-Histone (n = 9) | 9 (0.30) | 2 (0.68) | 2 (1.00) | 9 (0.15) |
| Anti-AMA (n = 6) | 6 (0.56) | 1 (0.63) | 0 (0.56) | 6 (0.56) |
| Anti-SSA/Ro (n = 7) | 7 (0.55) | 3 (0.64) | 0 (0.29) | 7 (0.29) |
| Anti-Jo 1 (n = 1) | 1 (1.00) | 0 (1.00) | 0 (1.00) | 1 (1.00) |

*Ds-DNA: double stranded deoxy ribonucleic acid, RNP- ribo-nucleo proteins, Rib P: ribosomal phosphorylated protein, AMA: anti-mitochondrial antibodies, SSA aka Ro: Sjogren's syndrome related antigen A, Jo: named after John, a patient with polymyositis.*

**Table 5.** Lupus nephritis class and outcome at 1 year

| WHO Class | Number (n = 18) | Outcome |
|---|---|---|
| II | 9 | CR-4, PR-4, AD-1 |
| III | 1 | AD |
| IV | 7 | CR-5, PR-1, AD-1 |
| V | 1 | AD |

*CR- Complete Remission, PR- Partial Remission, AD- Active Disease*

## DISCUSSION

In our study we have described in detail about the clinical, immunological, laboratory and treatment aspects of SLE in children from a developing country like India. We also studied the association of various auto antibody types and systemic involvement. The mean age at diagnosis in our study was 11.52 years with 75% of the patients above 10 years of age. Our findings were consistent with a similar study from Israel in which the mean age at diagnosis was 13.3 years.[7] The youngest child in our study was one year old, who presented with generalised anasarca, nephrotic range proteinuria, hypocomplementemia with ANA profile positive for Ro-52 antibodies. Lupus has been described even in newborn babies with a spectrum of cutaneous, cardiac and systemic abnormalities.[8] Female to male ratio in our study was 4.3:1. Studies from United Kingdom (UK) have reported female to male ratio as high as 5.6:1.[9]

Renal system was the most common organ involvement in our study seen in 87.5% of the subjects followed by haematological (81.3%) and musculoskeletal system (59.4%). Study done by Watson et al from UK found higher rates of involvement of haematological system (91%) followed by musculoskeletal (82%), renal (80%) and neurologic system (26%).[9] Another study from Eastern India by Mondal et al. found renal involvement in 54%, haematologic abnormalities in 54% and neuropsychiatric features in 25%.[10] Proteinuria was the most common renal abnormality in our study seen in 62.5% of the children. A study from Turkey by Bastug F et al. has reported renal involvement in 56% of the children, of which 43.3% had proteinuria.[11] The definitive diagnosis of LN is based on immunofluorescence pattern on renal biopsy. In our study Class II (n = 9) was the most common histopathological type on renal biopsy followed by class IV (n = 7). In a study done by Srivastava et al. from North India, among 92 children who underwent renal biopsy for lupus nephritis, 13 (14.2%) had class II, 24 (26%) had class III, 43 (46.7%) had class IV and 12 (13.1%) had class V type.[12] The study by Srivastava et al. showed that patients with class III and IV lupus nephritis had worse outcome (ESRD/death) compared to those with class II and V.[12] Another study from South India by Andy SK et al. showed proteinuria (> 0.5 g/day) in 40% of the study subjects and the most common histopathological type found on renal biopsy was class IV (42.8%) followed by class III (21.4%) and class V (21.4%).[13] Among children with SLE, 20-75% will develop LN, with 18-50% progressing to ESRD.[14] However, in our study none of the children with renal involvement progressed to ESRD.

**Table 6.** Treatment modalities in children with SLE (n = 32)

| Treatment | Number (%) |
|---|---|
| Steroid | 30 (93.8) |
| Hydroxychloroquine | 23 (71.9) |
| NSAID | 19 (59.4) |
| Azathioprine | 16 (50) |
| Cyclophosphamide | 14 (43.8) |
| Methotrexate | 7 (21.9) |
| Cyclosporine | 2 (6.3) |
| Rituximab | 1 (3.1) |

*NSAID: Non-steroidal anti-inflammatory drugs*

Study by Watson et al from UK reported haematological abnormalities in 91% of the study subjects consisting of haemolytic anaemia in 27%, leukopenia in 32%, and thrombocytopenia in 20%.[9] Bastug F et al. from Turkey has reported haematological abnormalities in 70% of the study subjects, with anaemia in 60%, leukopenia in 53% and thrombocytopenia in 33%.[11] In our study 81.3% of the children had haematological abnormalities, with anaemia (71.9%) being the

most common, with a median value of 9.9 g/dl. We also found elevated ESR (median: 47 mm/hr) in 75% of children indicating high disease activity. Bastug F et al. also reported elevated ESR in 93.3% of the study subjects with a mean value of 76 ± 35.6 mm/hr.[11] Neuropsychiatric manifestations in paediatric SLE has a prevalence ranging from 20 to 50.9% and the most common clinical features are headache, cognitive dysfunction, mood disorders, anxiety disorders, movement disorders, seizures, psychosis, cerebrovascular disease and peripheral neuropathy.[15] In our study 31.3% of the children had neurological involvement mainly in the form of seizures and peripheral neuropathy.

All children in our study had ANA positivity. ANA as a diagnostic tool for SLE has a sensitivity greater than 95% but lacks specificity.[16] Recognising the subtype of autoantibodies by ANA profile is important as various studies have shown correlation between autoantibodies and characteristic organ involvement.[16] Study by Jurencak R et al. showed significant association of LN with anti-ds DNA, haemolytic anaemia with anti-Ro and anti-ribosomal P antibodies.[16] Study by Hiraki LT et al. showed significant association of LN with anti-La, anti-smith, anti-RNP and anti-cardiolipin antibodies.[17] Hiraki LT et al. also found significant association of central nervous system disease with anti-La and lupus anticoagulant antibodies.[17] Anti-ds DNA is also observed to have strong association with SLE disease flare especially in renal aspect.[14] However, in our study we found no significant association between the autoantibody types and the characteristic organ involvement.

Our patients showed good response to different treatment modalities that were used in different combinations according to disease presentation and organ involvement. We were able to achieve complete remission in 40.6% and partial remission in 31.3% of the children at the end of one year follow up. Despite effective immunosuppressive treatment, 59.4% of our patients had disease flares during long term follow up. The incidence of lupus flares in different studies range from 27% to 66%.[12] The prognosis in our series reflects the improved care for children with SLE and longer life expectancy for these patients. The limitations of our study are small sample size, drop outs during long term follow up and non-availability of renal biopsy for all children with renal involvement.

## CONCLUSIONS

We conclude that the clinical presentation and course of progression of the disease varies depending on the age of onset and organ system involved. Renal involvement is an important cause of morbidity and mortality in paediatric SLE. Early diagnosis with good treatment protocols and timely follow up for early detection of organ damage are the key to long term survival with better outcome.

## REFERENCES

1. Samanta M, Nandi M, Mondal R, Hazra A, Sarkar S, Sabui T, et al. Childhood lupus nephritis : 12 years of experience from a developing country's perspective. Eur J Rheumatol. 2017;4:178-83. DOI: 10.5152/eurjrheum.2017.16117.
2. Pluchinotta FR, Schiavo B, Vittadello F, Martini G, Perilongo G, Zulian F. Distinctive clinical features of pediatric systemic lupus erythematosus in three different age classes. Lupus. 2007;16:550–5. DOI: 10.1177/0961203307080636.
3. Gedalia A, Molina JF, Molina J, Uribe O, Malagon C, Espinoza LR. Childhood-onset systemic lupus erythematosus: a comparitive study of African Americans and Latin Americans. J Natl Med Assoc. 1999;91:497-501. PMID:10517068.
4. Tektonidou MG, Ward MM. Methodological Quality of Studies of End-stage Renal Disease in Lupus Nephritis, 1970 to 2015. J Rheumatol. 2017;44(5):626–30. DOI:10.3899/jrheum.160546.

5. Levy DM, Kamphuis S. Systemic Lupus Erythematosus in Children and Adolescents. Pediatr Clin North Am. 2012;59(2): 345–64. doi:10.1016/j.pcl.2012.03.007.
6. Mina R, Klein-Gitelman MS, Ravelli A, Beresford MW, Avcin T, Espada G, et al. Inactive Disease and Remission in Childhood-onset Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2012;64(5):683–93. doi: 10.1002/acr.21612.
7. Uziel Y, Gorodnitski N, Mukamel M, Padeh S, Brik R, Barash J, et al. Outcome of a national Israeli cohort of pediatric systemic lupus erythematosus. Lupus. 2007;16:142–6. DOI: 10.1177/0961203306075385.
8. Hon KL, Leung AKC. Neonatal Lupus Erythematosus. Autoimmune Dis. Volume 2012, Article ID 301274. doi: 10.1155/2012/301274.
9. Watson L, Leone V, Pilkington C, Tullus K, Rangaraj S, Mcdonagh JE, et al. Disease Activity, Severity, and Damage in the UK Juvenile-Onset Systemic Lupus Erythematosus Cohort. Arthritis Rheum. 2012;64(7):2356–65. DOI 10.1002/art.34410.
10. Mondal R, Nandi M, Ganguli S, Ghosh A, Hazra A. Childhood Lupus : Experience from Eastern India. Indian J Pediatr. 2010;77:889–91. DOI-10.1007/s12098-010-0126-x.
11. Bastug F, Poyrazoglu H, Gunduz Z, Tulpar S, Dusunsel R. Juvenile Lupus Erythematosus : Fourteen Years of Experience. Turk J Rheumatol. 2011;26(4):308–15. doi:10.5606/tjr.2011.049.
12. 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;1:1–11. DOI: 10.1177/0961203315619031.
13. Andy SK, Kandasamy E. Clinical profile of systemic lupus erythematosus among children less than 12 years. Int J Contemp Pediatr. 2018;5(2):343–9. DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20180458
14. Mohamed DF, Aziz ABEA, Aziz EA, Hassan SA, Shedid NH, El-owaidy RH, et al. Juvenile lupus : Different clinical and serological presentations compared to adult lupus in Egypt. Egypt Rheumatol. 2018;40(1):55–8. doi: https://doi.org/10.1016/j.ejr.2017.04.004.
15. Fernandes H, Brito I. Juvenile Systemic Lupus Erythematosus : neuropsychiatric manifestations. Acta Reumatol Port. 2012; 37: 117–25. PMID:23149633.
16. Jurencák R, Fritzler M, Tyrrell P, Hiraki L, Benseler S, Silverman E, et al. Autoantibodies in Pediatric Systemic Lupus Erythematosus : Ethnic Grouping, Cluster Analysis, and Clinical Correlations. J Rheumatol. 2009;36:416-21. doi:10.3899/jrheum.080588.
17. 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. DOI: 10.1016/j.jpeds.2007.09.019.