Pediatric Systemic Lupus Erythematosus in Siriraj Hospital

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A descriptive study of one hundred and one pediatric patients with systemic lupus erythematosus treated between July 1985 and March 2003 in Department of Pediatrics, Faculty of Medicine Siriraj Hospital was conducted. According to existing database, there were a total of 181 patients, 101 of them (55.8%) had available data for review. The female to male ratio was 6.2:1. The mean and median ages of onset were 9.7 $\pm$ 2.8 and 10 $\pm$ 2.2 years, respectively (range 4-14 years). The clinical presentations were renal involvement in 87 patients (86.2%), skin and mucocutaneous involvement 77 patients (76.3%), hematological abnormalities 74 patients (73.4%), musculoskeletal involvement 32 patients (31.7%), prolonged fever 24 patients (23.8%), neuropsychiatric symptoms 21 patients (20.8%), gastrointestinal involvement 20 patients (19.8%), cardiac involvement 14 patients (13.9%), lymphadenopathy 13 patients (12.9%), and pulmonary involvement 7 patients (6.9%). The most common renal, skin and mucocutaneous, and hematological manifestations were proteinuria, malar rash, and anemia, respectively. Lupus nephritis with WHO class IV was the most common histopathological finding of the initial renal biopsies. The most common neuropsychiatric, gastrointestinal, cardiac, and pulmonary involvements were seizure, hepatomegaly, pericarditis, and pleuritis, respectively. Ninety-two percent of patients reported as having significant ANA positive results using rat liver tissue as a substrate. Sixty-six out of 94 patients (70.2%) had positive test result of Anti-dsDNA.

In conclusion, the age at onset, clinical manifestations and laboratory investigation results of SLE in children at Siriraj Hospital are comparable to other studies in the Country and also to other Asian and Western studies.

Keywords: *Childhood, SLE, Lupus nephritis, Epidemiology*

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Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by highly diverse clinical manifestations involves mainly skin, joints, kidneys, lungs, heart, nervous system, and hematological system with the presence of autoantibodies reacting to cell nuclei components. The etiology of this disease remains unknown but direct binding of autoantibodies to self-antigen or deposition of immune-complexes in vessels or tissues leading to organ injury. Most children with SLE are diagnosed during adolescence and often more severe than in adults with multiple system involvement[1]. Incidence and prevalence of SLE depends on age, sex, and ethic group. The incidence of SLE in children is approximately 0.36, 0.47, and 0.6 per 100,000 population per year in Canada, Japan, and America [2-4]. Asian, Hispanic and Black populations had higher relative risk of SLE compared with white populations [5]. Onset of SLE is rare before 5 years of age. The female to male ratio increases with advance age from 4.5:1 in prepubertal to 4.79:1 in post-

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pubertal children and 8:1 in adults[6]. In Thailand, at King Chulalongkorn Memorial Hospital the average age at onset of SLE in children was approximately 11 years[7].

The aim of this study is to identify epidemiological data, incidence, presenting signs and symptoms, and laboratory and immunological findings of 101 Thai children with SLE.

Material and Method

A retrospective study of 181 patients diagnosed with SLE following American College of Rheumatology (ACR) criteria 1982 in the Department of Pediatrics, Faculty of Medicine Siriraj Hospital from July 1985 through March 2003 was undertaken. One hundred and one patients had data available for study. Eighty seven patients received renal biopsy.

Data on the following items were analyzed: age, sex, date of birth, date of diagnosis, weight and height at diagnosis, presenting symptoms, clinical manifestations, and laboratory findings i.e., urinalysis, Complete blood count (CBC), Coombs' test, Erythrocyte sedimentation rate (ESR), and immune profiles [antinuclear antibodies (ANA), antibodies to double-stranded DNA (anti-dsDNA), anti-smith antibodies (anti-Sm), anti-Ro antibodies (anti-Ro), anti-La antibodies (anti-La), antibodies to ribonucleoprotein (anti-RNP), Anticardiolipin antibodies (ACA), lupus anticoagulants (LA), complement component 3 (C3), complement component 4 (C4)]. Abnormal urinalysis was considered when there were > 5 red blood cells or white blood cells per high-power field, urine protein at least 1+ if urine specific gravity < 1.015 or urine protein at least 2+ if urine specific gravity > 1.015, and/or cellular casts. Nephrotic appearance was defined as clinical edema or nephrotic range of proteinuria (protein > 50 mg/kg/day or 40 mg/m^2/hr in 24 hour urine).

The clinical evidence of lupus nephritis comprised abnormal urinalysis, hypertension, and/or abnormal serum creatinine level, and pathological results of renal biopsies. Renal biopsies were classified according to the World Health Organization (WHO) classification criteria for lupus nephritis [8]. All results are expressed as mean $\pm$ SD.

Table 1. Age at Onset of Disease and the Ratio of Females and Males

Age (year)	Male (n=14)		Female (n=87)		Total (n=101)		F : M
	No.	%	No.	%	No.	%	
0-4.9	1	7.1	2	2.3	3	3.0	2 : 1
5-9.9	6	42.9	30	34.5	36	35.6	5 : 1
10-14.9	7	50.0	55	63.2	62	61.4	7.9 : 1
Total	14	100.0	87	100.0	101	100.0	6.2 : 1

Table 2. Signs and Symptoms at Diagnosis

Signs & symptoms	Male (n=14)		Female (n=87)		Total (n=101)	
°	No.	%	No.	%	No	%
Renal	11	78.6	76	87.4	87	86.2
Skin & Mucocutaneous	10	71.4	67	77	77	76.3
Hematological	10	71.4	64	73.6	74	73.4
Musculoskeletal	5	35.7	27	31	32	31.7
Prolonged fever	7	50	17	19.5	24	23.8
Neuropsychiatry	3	21.4	18	20.7	21	20.8
Gastrointestinal	3	21.4	17	19.5	20	19.8
Cardiac	2	14.3	12	13.8	14	13.9
Lymphadenopathy	2	14.3	11	12.6	13	12.9
Pulmonary	0	0	7	8	7	6.9

Results

Clinical Profiles

One hundred and one (55.8%) out of 181 patients with a diagnosis of SLE from July 1985 through March 2003 had data available for study. From 1997, all patients diagnosed with SLE were included in this study. There were 87 females and 14 males. Ratio of female and male was 6.2:1. Sixty-two (61.4%) patients were in the age group 10-14.9 years, which was the majority of patients in both female and male (Table 1). The mean age of patients was 9.7 ± 2.8 years with the range 4-14 year of age. The median age of patients was 10 ± 2.2 years.

The major clinical manifestations at diagnosis of the 101 patients are shown in Table 2. Renal, skin and mucocutaneous, and hematological involvement were the major manifestations at the diagnosis of pediatric SLE in 87 (86.2%), 77 (76.3%), and 74 (73.4%) patients, respectively.

Abnormal urine finding is indicative of renal involvement in SLE. Urine findings in SLE patients included normal finding, mild to heavy proteinuria, nephritis appearance, and cellular cast. Normal urine findings were presented in one-third of patients. Nephritis appearance and mild proteinuria were the major manifestations at the time of diagnosis (Table 3). Eighty-seven (86.2%) patients received renal biopsies and classified according to WHO classification of lupus nephritis[8]. The majority of renal biopsy results were in WHO Class IV and II (Table 4).

Skin and mucocutaneous involvements presented as malar rash in 54 patients (53.5%), oral ulcer in 32 patients (31.7%) and photosensitivity in 22 patients (21.8%). Other skin and mucocutaneous manifestations were alopecia in 14 patients (13.9%), dermal vasculitis in 8 patients (7.9%), discoid rash in 2 patients (2%) and palpable purpura in 2 patients (2%).

There were hematological abnormalities in 74 patients (73.4%). Anemia (Hb <10 g/dl, Hct <30%) was present in 53 patients (52.5%). Of these patients, there were positive direct Coombs' tests in 35 patients (66%). Leukocytopenia (WBC < 4000 cell/mm^3), lymphopenia (lymphocyte < 1500 cell/mm^3) and thrombocytopenia (platelet < 100,000 cell/mm^3) were found in 21 patients (20.8%), 34 patients (33.7%) and 14 patients (13.9%), respectively.

Neuropsychiatric involvements were observed in 21 patients (20.8%). Seizure was the most common manifestations in both sexes (15 patients, 14.9%). Two female patients had psychosis. There were 6 other neuropsychiatric manifestations, which included 2 alteration of consciousness and one each

Table 3. Urine Findings at Diagnosis

Urine findings	Male (n=14)		Female (n=87)		Total (n=101)	
	No.	%	No.	%	No.	%
Normal urine	6	42.9	27	31	33	32.7
Urine protein (1+) — (2+)	3	21.4	37	42.5	40	39.6
Nephrotic appearance	6	42.9	21	24.1	27	26.7
Nephritis appearance	7	50	45	51.7	52	51.5
Cellular casts	4	28.6	26	29.9	30	29.7
Urine protein 24 hr. >0.5 g/day	4/7	57.1	24/27	88.9	28/34	82.4

Table 4. Renal Biopsy Findings

Lupus Nephritis Classification	Male (n=12)		Female (n=75)		Total (n=87)	
	No.	%	No.	%	No.	%
WHO I	1	8.3	4	5.3	5	5.7
WHO II	0	0	19	25.3	19	21.8
WHO III	3	25	4	5.3	7	8
WHO IV	8	66.7	41	54.7	49	56.3
WHO V	0	0	7	9.3	7	8

with aseptic meningitis, CNS vasculitis, personality change, and anxiety with adjustment disorder.

Gastrointestinal abnormalities were documented in 20 patients (19.8%); hepatomegaly in 11 patients (10.9%), splenomegaly in 5 patients (5%), peritonitis in 4 patients (4%) and hepatitis in 4 patients (4%). Hepatitis was defined as having blood SGOT and SGPT higher than 3 folds of normal level (~120 IU/L). Other gastrointestinal manifestations were pancreatitis in 2 patients (2%), diarrhea in 2 patients (2%), gut obstruction in 1 patient (1%) and autoimmune hepatitis in 1 patient.

There were cardiac manifestations in 14 patients (13.9%). Pericarditis was the major finding in both sexes existed in 13 patients (12.9%) representing 92.9% of cardiac problems. Other cardiac problems were myocarditis in 3 patients (3%) and pericardial effusion in 3 patients (3%). All patients with cardiac manifestations were females.

There were pulmonary manifestations in 7 female patients (6.9%). 6 of them (85.7%) had pleuritis and one had pleural effusion.

Laboratory Data

Abnormal immune profiles in 101 patients were demonstrated. One hundred patients had ANA determined; 83% of them were reported as significant ANA titer > 1:80 by using rat liver tissue as a substrate. Nine percent were reported as having positive test results without titer number, 4% as negative test results and 4% as ANA titer = 1:40. ANA titer e ≥ 1:2,560 were present in 59 patients (59%). The characteristic of ANA was described as speckles pattern in 55 patients (55%), homogenous pattern in 31 patients (31%) and no data available in 14 patients (14%).

Anti-dsDNA test were determined in 94 patients. Sixty-six patients (70.2%) had positive Anti-dsDNA test. There were no differences of test results in both sexes. Anti-extractable nuclear antigen including anti-Sm and anti-RNP were also determined. Eleven of 47 patients (23.4%) had positive anti-Sm whereas 11 of 30 patients (36.7%) had positive anti-RNP. In 21 patients, significant titers of anti-Ro and anti-La were reported in 6 and 3 patients (28.6%, 14.3%), respectively. Seventeen patients had ACA determined. Three of them (18.8%) had significant of ACA titer which was > 14 GPL (1 GPL unit = cardiolipin binding activity of purified IgG anticardiolipin (at 1 mcg/ml) from an international reference standard). LA was performed in 3 patients with positive results in 2 patients.

Seventy-seven patients had C3 measured with 17 patients had C4 measured. Sixty-two patients (80.5%) had low C3 titers (< 77 mg/dl) and 8 patients (47.1%) showed low C4 results (< 7 mg/dl). There were no

Table 5. Comparison of Clinical Manifestations of SLE (in %)

	Our study N =101	Chula-longkorn[7] N =41	Rama-thibodi[12] N =78	Tucker[1] N = 39	Cassidy[9] N = 58	Cameron[11] N = 672	Saudi[18] N = 60	Chiang Mai (adult)[33] N = 349
Mucocutaneous	76.3			83			73	
Malar rash	53.5	13	59		51	68	40	47
Discoid rash	2	0	15			ND		28
Photosensitivity	21.8	5	22		16	ND	15	29
Oral ulcer	31.7	42	24		12	ND	16	26
Renal	86.2	68	79	27	84	82	62	66
Hematological	73.4			38			67	76
Anemia	52.5	35	78		43	56		
Thrombocytopenia	13.9	10	14		22	25		
Cardiac	13.9			19	40	40	33	
Pulmonary	6.9	7			31	ND	13	
Gastrointestinal	19.8							
Hepatomegaly	10.9		35		43			
Splenomegaly	5				20			
Neuropsychiatry	20.8	18	10	19	9	30	27	19
Musculoskeletal	31.7		36	78	72		92	
Prolonged fever	23.8	41.5				78		

Table 6. The Results of Renal Biopsies

References	Number of patients	WHO I (%)	WHO II (%)	WHO III (%)	WHO IV (%)	WHO V (%)
Our study	87	5.7	21.8	8	56.3	8
Chulalongkorn[7]	25	0	24	4	72	0
Ramathibodi[12]	71	3	24	1	55	17
Cameron[11]	79	0	11	29	49	10
Bogdanovic[14]	53	7.5	20.8	1.9	64.1	57
King[24]	66	0	27	18	52	3
Okawa[34]	18	11	5.5	11	61	11
Garin[35]	25	0	0	20	60	20
Schaller[36]	33	3	6	9	67	15

Table 7. Immune Profiles

	Our study		Chulalongorn[7]		Ramathibodi[12]		Tucker[1]	
	N =101	%	N = 41	%	N = 78	%	N = 39	%
ANA (> 1:40)	96/100	96		97	75/75	100		97.4
Anti-dsDNA (positive)	66/94	70.2		75	58/68	85		84.6
Anti-Sm (positive)	10/46	21.7		ND	10/37	27		23
C3 (Low)	62/77	80.5		73	61/71	86		ND
C4 (Low)	8/17	47.1		70	ND	ND		ND
ESR ($\geq$ 20)	36/37	97.3		94	66/66	100		ND
LE preparation (positive)	34/41	82.9		84	29/67	43		ND

differences of test results in both sexes. ESR was determined in 37 patients. Twenty-nine patients (78.4%) and 7 patients (18.9%) had ESR result in the range of 21-100 mm/hr and $\geq$100 mm/hr, respectively whereas one patient (2.7%) had normal ESR.

Discussion

In our study, the ratio of female to male was 6.2:1. The mean and median ages at onset were 9.7 $\pm$ 2.8 and 10 $\pm$ 2.2 years, respectively. Almost two-third of our patients had symptoms at 10-14.9 years of age and only 3 patients were less than 5 years old. The result of our report was slightly different from that of King Chulalongkorn Memorial Hospital [7] which shows ratio of female to male of 4.5:1 and the average age at onset of 11 years. The mean age at onset in our study would have increased if we had studied SLE in children up to 18 years old. Lehman et al.[5] described SLE in children up to 19 years old with the ratio of female to male 6.5:1 and the average age at onset of 11 years old. Cassidy et al.[9] reported the ratio of female to male with SLE (in the age range 0-9 years old) was 4:3; in the age range 10-14 years old, 4:1 and in the age range 15-18 years old, 5:1. The incidence of SLE in children in our hospital was 1:6,940 in 2001 and 1:6,475 in 2002. Clinical manifestations of our patients with reports from other hospitals are shown in Table 5.

Renal involvement is more often a presenting clinical manifestation of SLE in children than in adults[10]. Renal manifestations were the most presenting signs and symptoms in 86.2% of our patients, which was comparable to other studies [9,11,12]. Class IV nephritis, observed in 49 out of 87 patients (56.3%), was the most frequent histopathology on initial renal biopsy. This was not different from several studies reported in the range of 50-70% (Table 6). Emre et al.[13] reported that patients with class IV lupus nephritis had a tendency to develop nephrotic syndrome, heavy proteinuria, increased creatinine levels and persistent hypertension. Adverse outcome (i.e., end stage renal failure or death) was significantly associated with the persistent hypertension, anemia, high serum creatinine level, heavy proteinuria, nephrotic syndrome, and class IV lupus nephritis at presentation. However Bogdanovic et al.[14] reported only nephrotic

syndrome and class IV nephritis at initial biopsy to be associated with adverse outcome. On the contrary a study from Korbet et al.[15] demonstrated the factors which were predictive of remission were stable renal function after 4 weeks on therapy, lupus nephritis class IV, lower chronicity index, white race, lower urine protein excretion level at baseline, and lower baseline serum creatinine level. SLE patients with nephritis have higher mortality rate than those without renal involvement. Ten to 60% of SLE patients with severe nephritis eventually develop end-stage renal disease. A previous study in our hospital by Pattaragarn et al.[16] demonstrated initial presence of hypertension, hematuria, proteinuria, and renal insufficiency in SLE to be associated with worse outcome. Moroni et al.[17] defined renal flare-ups either as a rapid increase in plasma creatinine or by an increase in proteinuria. The study found that SLE patients with renal flares of any type had more probabilities of reaching end point than patients who never had flares. Our patients were treated with corticosteroids alone or combined with azathioprine or intravenous methylprednisolone with or without intravenous cyclophosphamide.

Rates of skin and mucocutaneous manifestations was relative comparable to result from other countries [1,18]. However the study from Wananukul et al.[19] in Thai children had higher mucocutaneous manifestations. This could be due to the fact that patients who presented with skin involvement were usually seen by dermatologists.

Anemia in our patients (52.5%) did not differ from manifestation in other studies [9,20], but leucopenia was less observed (13.9% vs. 30-60%). In studies from King Chulalongkorn Memorial Hospital [7] and Ramathibodi Hospital [12], anemia was reported in 35% and 78% of their patients respectively. Thrombocytopenia in the range 10-15% was similar in all three studies. Tucker et al.[1] examined the difference which might distinguish SLE presentation in adult or childhood. He found that major hematological manifestations were more frequent in the childhood-onset group whereas cardiopulmonary disease was more common in adult onset group.

SLE patients with neuropsychiatric manifestations can present with diffuse and/ or focal symptoms involving the brain, spinal cord, or peripheral nervous system [21]. Although the clinical manifestations of neuropsychiatric lupus erythematosus are extremely diverse, ranging from mild cognitive dysfunction to severe life-threatening presentations, only seizure and psychosis were included in the revised ACR criteria for SLE. We found neuropsychiatric involvement in 20.8% of patients which was comparable to other studies [1,7,12]. Male and female were equally affected in our study. Seizure was the most frequent symptoms (14.9%). The incidence increased to 19.8% during follow up period. We also reported 2 psychotic patients (2%). Parikh et al.[22] recorded 108 patients with childhood lupus. Twenty-five of them (23.1%) had neurological findings. There were 4 patients with neurological symptoms preceding the diagnosis. Four patients had coincident neurological symptoms at the time of diagnosis of lupus erythematosus. In those patients with symptoms after the diagnosis, the average elapsed time until symptoms appeared was 33 months. Headache was the most frequent finding (16/25). This finding agrees with data from Yancey et al.[20]. This probably reflected underreporting of headache in our study. All patients were treated with corticosteroids and azathioprine. Resolution occurred from days to months. There were much higher incidence in seizure and psychosis reported by Haji et al.[23] who studied childhood cerebral lupus in Malaysia. Eighteen out of 24 (75%) patients had clinical and neurophysiologic evidence of cerebral lupus. Seizure was the most common manifestation represented in 11 patients (45.8%), followed by psychosis, encephalopathy and headache in five each (20.8%). He found that EEG results had poor correlation with the clinical presentation.

Gastrointestinal manifestations in our study were lower than data from other studies[24,25]. Hepatosplenomegaly was noted in 28-43% and up to two thirds of patients but usually had mild degree [9,24,25]. Two patients with pancreatitis could be due to active SLE, corticosteroid therapy, or both.

There was no report of cardiac manifestations from 2 previous papers in Thailand [7,12]. Cardiac involvement in 14 of our 101 (13.9%) patients is similar to data by King et al.[24]. Pericarditis was the most common cardiac manifestation representing in 12.9% of our patients. Other studies recorded cardiac manifestation to be as high as 38-40% of patients [9,25]. Pericardial effusion and myocarditis were the subsequent common cardiac manifestations.

The most common pulmonary manifestations of SLE in childhood were pleurisy and pleural effusions [9,24]. Although pulmonary hemorrhage and pneumothorax were less frequent, they could be life threatening. Pneumonia was the most common fatal pulmonary complication of SLE in children and adolescents [26].

Pulmonary manifestations in our study did not differ from other studies in Asian countries [7,18,27]. However in Western countries the incidence of pulmonary findings was 20-30% [9,20,24].

Arthritis and myositis are the prominent musculoskeletal abnormalities of SLE in children and adolescent. We reported musculoskeletal involvement in 31.7% of our patients. This is similar data from Ramathibodi Hospital [12] but was much lower than from United States and Saudi Arabia [1,9,18]. Incidence of musculoskeletal involvement in White, Black and Asian adults were higher than in children [1].

Immune profile in our study did not differ from other studies. Significant ANA described as positive or titer > 1:40 was found in more than 95% of lupus patients [1,7,12,27]. ESR $\geq$ 20 mm/hr was reported in more than 94%. Positive anti-dsDNA and low C3 were found in 70-85% and 67-86% of patients, respectively [1,7,12] (Table 7). Anti-Sm, specific marker for SLE, was found in 20-30% of patients [1,7,28]. Serologically, anti-dsDNA, anti-Sm, and anti-RNP antibodies and a low C3 were all found more frequently in the childhood-onset group [1]. Ter Borg et al.[29] reported serial measurement of anti-dsDNA levels which was more sensitive than serial measurement of C3 and/or C4 levels in predicting exacerbation in SLE. Significant increase in anti-dsDNA levels precedes exacerbation by 8-10 weeks. A variety of antiphospholipid (APL) antibodies such as LA and ACA, have been noted in patients with renal disorders. In an analysis of 29 published studies comprising more than 1,000 SLE patients, 34% were positive for LA and 44% for ACA [30]. The clinical manifestations of APL antibodies syndrome are related to thrombotic events and consequent ischemia such as superficial and deep vein thrombosis, arterial thrombosis, pulmonary hypertension, stroke, memory impairment, and fetal loss (caused by placental thrombosis) [31]. However, many SLE patients with APL antibodies do not have thrombotic events. Farrugia et al.[32] reported occlusive glomerular, arteriolar, and arterial fibrin thrombi, along with varying degrees of renal thrombotic microangiopathy in five of 33 SLE patients with LA, but none of 32 SLE patients without LA. Even though, three patients with ACA and two patients with LA in our study did not show evidence of APL antibodies syndrome. They were treated with daily aspirin therapy.

Conclusion

The age at onset, clinical manifestations and laboratory investigation results of SLE in children at Siriraj Hospital were comparable with other reports from Thailand and from other Asian and Western countries. Incidences of cardiac, pulmonary, gastrointestinal and musculoskeletal manifestations in our country were lower than those from other countries. These differences possibly reflected by several factors, including referral patterns and ethnic diversity.

Prospective study is needed for more complete data of clinical manifestations and laboratory results to associate with prognosis and outcome of disease.

References

1. Tucker LB, Menon S, Schaller JG, Isenberg DA. Adult-and childhood-onset systemic lupus erythematosus: a comparison of onset, clinical features, serology, and outcome. Br J Rheumatol 1995;34: 866-72.
2. Malleson PN, Fung MY, Rosenberg AM. The incidence of pediatric rheumatic diseases: result from the Canadian Pediatric Rheumatology Association Disease Registry. J Rheumatol 1996; 23:1981-7.
3. Fujikawa S, Okuni M. A nationwide surveillance study of rheumatic diseases among Japanese children. Acta Pediatrica Japonica 1997;39: 242-4.
4. Siegel M, Lee SL. The epidemiology of systemic lupus erythematosus. Semin Arthritis Rheum 1973; 3: 1-54.
5. Lehman TJA, McCurdy DK, Bernstein BH, King KK, Hanson V. Systemic lupus erythematosus in the first decade of life. Pediatrics 1989;83:235-9.
6. Cameron JS. Lupus nephritis in childhood and adolescence. Pediatr Nephrol 1994;8:230-49.
7. Ngamsil K. Systemic lupus erythematosus and lupus nephritis in children at King Chulalongkorn Memorial Hospital. (Dissertation, Bangkok, Thailand, Chulalongkorn University;2536).
8. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
9. Cassidy JT, Sullian DB, Petty RE, Ragsdale C. Lupus nephritis and encephalopathy, prognosis in 58 children. Arthritis Rheum 1977;20:315-21.
10. Petty RE, Cassidy JT. Systemic lupus erythematosus. In: Cassidy JT, Petty RE, eds. Text book of Pediatrics Rheumatology. W.B.Saunder Company, Philadelphia 2001;396-449.

11. Cameron JS, Chantier C, Haycock G, Hicks J. The nephritis of systemic lupus erythematosus in childhood and adolescence. In Brodehl J, Ehrich JW, eds. Pediatric nephrology. Springer, New York Berlin Heidelberg 1984;230-6.
12. Tapaneya-Olarn W, Tapaneya-Olarn C, Boonpucknavig V, Boonpucknavig S. Lupus nephritis in children at Ramathibodi hospital. Rama Med J 1989;12:4:203-6.
13. Emre S, Bilge I, Sirin A, Kilicaslan I, Nayir A, Oktem F, Uysal V. Lupus nephritis in children: prognostic significance of clinicopathological findings. Nephron 2001;87:118-26.
14. Bogdanovic R, Nikolic V, Pasic S, Dimitrijevic J, Markovic JL, Marinkovic JE, et al. Lupus nephritis in childhood: a review of 53 patients followed at a single center. Pediatr Nephrol 2004;19:36-44.
15. Korbet SM, Lewis EJ, Schwartz MM, Reichlin M, Evans J, Rohde RD. Factors predictive of outcome in severe lupus nephritis: for the lupus nephritis collaborative study group. Am J Kidney Dis 2000;35:904-14.
16. Pattaragarn A, Sumboonnanonda A, Supavekin S, Suntornpoch V. Systemic lupus erythematosus in Thai children: clinicopathological findings and outcome. J Med Assoc Thai. 2005 (in press)
17. Moroni G, Quaglini S, Maccario M, Banfi G, Ponticelli C. Nephritis flares are predictors of bad long-term renal outcome in lupus nephritis. Kidney Int 1996;50:2047-53.
18. Bahabri S, Al Sabban E, Al Rashed A, Al-Moyouf S, Al Mazyed A, Abdulrazik A, et al. Juvenile systemic lupus erythematosus in 60 Saudi children. Ann Saudi Med 1997;17:612—5
19. Wananukul S, Watana D, Pongprasit P. Cutaneous manifestation of childhood systemic lupus erythematosus. Pediatr Dermatol 1998;15:342-6.
20. Yancey CL, Doughty RA, Athreya BH. Central nervous system involvement in childhood systemic lupus erythematosus. Arthritis Rheum 1981;24:1389-95.
21. West SG. Neuropsychiatric lupus. Rheum Dis Clin North Am 1994;20:129-58.
22. Parikh S, Swaiman KF, Kim Y. Neurologic characteristics of childhood lupus erythematosus. Pediatric Neurology 1995;13:198-201.
23. Haji Muhammad Ismail Hussain I, Loh WF, Sofiah A. Childhood cerebral lupus in an Oriental population. Brain Dev 1999;21:229-35.
24. King KK, Kornreich HK, Berbstein BH, Singsen BH, Hanson V. The clinical spectrum of systemic lupus erythematosus in children. Arthritis Rheum 1977;20(suppl):287-93.
25. Meislin AG, Rothfield N. Systemic lupus erythematosus in childhood: analysis of 42 cases, with comparative data on 200 adult cases followed concurrently. Pediatrics 1968;42:37-49.
26. Nadorra RL, Landing BH. Pulmonary lesions in childhood onset systemic lupus erythematosus. Analysis of 26 cases, and summary of literature. Pediatr Pathol 1987;7:1-18.
27. Bakr A. Epidemiology treatment and outcome of childhood systemic lupus erythematosis in Egypt. Pediatr Nephrol 2005;20:1081-6.
28. Barada F, Andrews BS, David JS, Taylor RP. Antidodies to Sm in patients with systemic lupus erythematosis. Correlation of Sm antibody titers with disease activity and other laboratory parameters. Arthritis Rheum 1981;24:1236-44.
29. Ter Borg EJ, Horst G, Hummel EJ, Limburg PC, Kallenberg CGM. Measurement of increases in anti-double-stranded DNA antibody levels as a predictor of disease exacerbation in systemic lupus erythematosus: a long-term, prospective study. Arthritis Rheum 1990;33:634-43.
30. Love PE, Santoro SA. Antiphospholipid antibodies: anticardiolipin and lupus anticoagulant in SLE and in SLE disorders. Ann Intern Med 1990; 112: 682-98.
31. Asherson RA, Khamashta MA, Ordi-Ros J, Derksen RH, Machin SJ, Barquinero J, et al. The "primary" antiphospholipid syndrome: major clinical and serological features. Medicine (Baltimore) 1989;68:366-74.
32. Farrugia E, Torres VE, Gastineau D, Michet CJ, Holley KE. Lupus anticoagulant in systemic lupus erythematosus: a clinical and renal pathological study. Am J Kidney Dis 1992;20:463-71.
33. Kasitanon N, Louthrenoo W, Sukitawut W, Vichainun R. Causes of death and prognostic factors in Thai patients with systemic lupus erythematosus. Asian Pac J Allergy and Immunol 2002;20:85-91.
34. Okawa KI, Wada H, Kobayashi O: Systemic lupus erythematosus in children. Acta Med Biol 1976;23:147-7.
35. Garin Eh, Donnely WH, Fennell RS, Richard GA. Nephritis in systemic lupus erythematosus in children. J Pediatr 1976;89:366-71.
36. Schaller J: Lupus in childhood. Clin Rheum Dis 1982;8:219-28.

ผู้ป่วยเด็กโรคลูปัสในโรงพยาบาลศิริราช

สุโรจน์ ศุภเวคิน, วนิดา ฉัตรชมชื่น, อนิรุธ ภัทรากาญจน์, วิบูล สุนทรพจน์, อัจฉรา สัมบุณณานนท์

การศึกษาครั้งนี้เป็นการศึกษาผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่าเป็นโรค SLE ครั้งแรกที่มารับการรักษาที่ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ตั้งแต่ ก.ค. พ.ศ. 2528 ถึง มี.ค. พ.ศ. 2546 เป็นระยะเวลา 18 ปี โดยศึกษาถึงระบาดวิทยา อาการและอาการแสดงผลการตรวจทางห้องปฏิบัติการ ครั้งแรกที่ได้รับการวินิจฉัย โดยมีวัตถุประสงค์เพื่อหาอุบัติการณ์ ระบาดวิทยา และอาการแสดงที่พบบ่อยในผู้ป่วยกลุ่มนี้เพื่อนำไปสู่แนวทางในการวินิจฉัยผู้ป่วย เด็กที่เหมาะสมต่อไป ผลการศึกษา พบว่ามีผู้ป่วย 181 ราย แต่มีข้อมูลให้ศึกษาได้ 101 ราย (ร้อยละ 55.8) โดยมีอัตราส่วน หญิง:ชาย เท่ากับ 6.2:1 อายุเฉลี่ยและอายุเฉลี่ยมัธยฐานเมื่อแรกวินิจฉัย 9.7 $\pm$ 2.8 ปี และ 10 $\pm$ 2.2 ปี (4 - 14 ปี) อาการแสดงที่นำผู้ป่วยมารักษาได้แก่ อาการทางไต 87 ราย (ร้อยละ 86.2) อาการทางผิวหนังและเยื่อบุ 77 ราย (ร้อยละ 76.3) อาการทางระบบโลหิต 74 ราย (ร้อยละ 73.4) อาการทางระบบกล้ามเนื้อและกระดูก 32 ราย (ร้อยละ 31.7) ไข้เรื้อรัง 24 ราย (ร้อยละ 23.8) อาการทางระบบประสาทและจิตเวช 21 ราย (ร้อยละ 20.8) อาการทางระบบทางเดินอาหาร 20 ราย (ร้อยละ 19.8) อาการทางหัวใจ 14 ราย (ร้อยละ 13.9) อาการทางต่อมน้ำเหลือง 13 ราย (ร้อยละ 12.9) และอาการทางระบบทางเดินหายใจ 7 ราย (ร้อยละ 6.9) อาการทางไต ผิวหนังและเยื่อบุ และระบบโลหิตที่พบบ่อยที่สุดคือ โปรตีนในปัสสาวะ ผื่น malar และภาวะซีด โดยลำดับ ลูปัสที่ไตขั้น 4 ตามการแบ่งขององค์การอนามัยโลกเป็นพยาธิสภาพที่พบได้บ่อย ที่สุดจากการตรวจชิ้นเนื้อไต อาการทางระบบประสาทและจิตเวช ระบบทางเดินอาหาร หัวใจ และระบบทางเดินหายใจที่พบบ่อยที่สุดคือ อาการชัก ตับโต เยื่อหุ้มหัวใจ อักเสบ และเยื่อหุ้มปอดอักเสบ โดยลำดับ ผู้ป่วยร้อยละ 92 มีค่าผลบวกของ ANA และผู้ป่วย 66 คนในจำนวนที่ส่งตรวจ 94 คน (ร้อยละ 70.2) มีค่าผลบวกของ Anti-dsDNA. โดยสรุปผลการศึกษาครั้งนี้พบว่าผู้ป่วยลูปัสของศิริราชมีอายุที่เริ่มเป็นลักษณะทางคลินิก และผลการตรวจทางห้องปฏิบัติการใกล้เคียงกับรายงานอื่นๆ ทั้งในประเทศไทย ประเทศอื่นๆ ในเอเชีย และประเทศตะวันตก