

Clinical Manifestations of Systemic Lupus Erythematosus in Children at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

Reni Ghrahani,¹ Priya Darshani Ganesan,² Reni Farenia Soedjana Ningrat³

¹Department of Child Health Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital Bandung, Indonesia, ²Faculty of Medicine Universitas Padjadjaran, Indonesia

³Department of Biomedical Sciences Faculty of Medicine Universitas Padjadjaran, Indonesia

Abstract

Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease, characterized by production of autoantibodies, leading to damage caused by inflammation, directed toward multiple organs in the body. It is difficult to diagnose due to its mimicry with other diseases. The differential diagnosis of SLE is broad, including infection, malignancy and other inflammatory disorders. It is important to recognize the clinical manifestation of SLE from other possible diseases.

Methods: A descriptive study was conducted on 56 SLE patients from the Department of Child Health in Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, in which the medical records were collected from 2010 to 2014. A total sampling method was used and incomplete records were excluded.

Results: Out of the 56 subjects, 82.1% were female, with female to male ratio was 4.6:1. Most of the subjects (52%) was in the age category of 11 to 15 years old. Hematologic involvement was the most common clinical manifestation based on the diagnostic criteria (83.9%), and fever was the most common chief complaint (41.1%).

Conclusions: From this study, fever, rash, and joint pain are the common chief complaints among SLE patients in children with hematologic and renal disorders are also found to occur.

Keywords: Children, clinical manifestations, Systemic Lupus Erythematosus

Introduction

Systemic Lupus Erythematosus (SLE) is a systemic autoimmune disease that affects multiple organs such as kidneys and the central nervous system. Pediatric SLE occurs at a rate of 1-6/100,000 and occurs in children.^{1,2} Types of manifestations most commonly found in pediatric SLE differ slightly from adult SLE. Systemic Lupus Erythematosus is very difficult to diagnose as it presents as a mimicry of multiple diseases.^{3,4} Systemic Lupus Erythematosus is a disease that is extremely chronic in nature, which can severely lower the patients' quality of life. Due to a delayed diagnosis, patients may be admitted with severe organ damage and complications, which results in a worse prognosis. Systemic Lupus Erythematosus in children is more severe than in adults as the progressivity of the disease in children is much faster than in adults.^{1,4} Therefore, due to the difficulty in

diagnosis and its chronicity, it is essential to elaborate clinical manifestations of childhood lupus to gain better detection and diagnosis.

The objective of this study was to describe the various clinical manifestations of SLE. The clinical manifestations may differ between ethnicities and countries and there is a need to explore the variations that apply to Indonesia, specifically to those in Bandung.^{5,6} The difference of clinical manifestation based on ethnicity and countries were not established. This would allow for better diagnosis and a better prognosis.

Methods

A retrospective, descriptive study was conducted in 2015 and it involved the description of clinical manifestations in patients with SLE in the Department of Child Health at Dr. Hasan Sadikin General Hospital from the period of 2010 to 2014. This study

Correspondence: Reni Ghrahani, Department of Child Health, Faculty of Medicine, Universitas Padjadjaran, Jalan Raya Bandung-Sumedang KM 21, Indonesia, Email: renighrahani@yahoo.com

involved a total sampling method in the selection of subjects and all medical records of patients who fit the criteria in the given period were used. This study was approved by the Health Research Ethics Committee Dr. Hasan Sadikin General Hospital.

Medical records were used as a tool to obtain information required on each subject. Medical records of 56 children in the Department of Child Health at Dr. Hasan Sadikin General Hospital who had the disease from January 2010 to December 2014 were obtained and analyzed. The subjects were selected according to diagnosis by the clinician on the basis of the criteria by the American College of Rheumatology 1997.⁷ Any records that were incomplete were excluded. The age, gender, chief complaint, other symptoms, lab findings, radiologic findings, echocardiogram findings, and other findings were recorded for each patient. The frequency of each individual finding was determined by percentage and tabulated.

Results

The results in the tables were obtained from medical records of 56 patients with SLE who were admitted to the Department of Child Health from 2010 to 2014. The frequencies were calculated based on epidemiological features and the individual manifestations were categorized according to the diagnostic criteria.⁷

The frequencies of gender and age ranges are tabulated in Table 1. Out of the 56 subjects, more females had SLE and the female to male ratio was 4.6:1. Patients in the age group of 11 to 15 who had SLE were seen to be the greatest

Table 1 Clinical Characteristic of SLE in Children at Dr. Hasan Sadikin General Hospital from The Period of 2010 to 2014

	n(%) (n= 56)
Age (years)	
1-5	7 (12.5)
6-10	20 (35.7)
11-15	29 (51.8)
Gender	
Male	10 (17.9)
Female	46 (82.1)

Table 2 Clinical Manifestations in Children with SLE according to The Diagnostic Criteria

Manifestation	n(%) (n= 56)
Malar Rash	37(66.1)
Discoid Rash	17(30.4)
Photosensitivity	8(14.3)
Oral ulcers	18(32.1)
Non-erosive Arthritis	31(55.4)
Pleuritis or Pericarditis	11(19.6)
Renal disorder	36(64.3)
Neurologic disorder	2(3.6)
Hematologic disorder	47(83.9)
Immunologic disorder	24(42.9)

(51.8%), followed by patients between the ages of 6 to 10 (35.7%).

The frequencies of the clinical manifestations based on the diagnostic criteria of The American College of Rheumatology as been calculated and tabulated in Table 2. As seen in Table 2, hematologic involvement (83.9%) and malar rash (66.1%) were found to be the most common clinical manifestation. A high frequency of patients had associated symptoms of dermatologic changes, with 66.1% of them presented malar rash and 30.4% of them presented discoid rash (Table 2).

The manifestations have subsequently been described in more detail and categorized according to the clinical examinations in Tables 3 and 4. A large number of patients had a chief complaint of fever (41.1%), followed by a rash (28.6%) and joint pain (25.0%)

Table 3 Chief Complaints in Children with SLE

Chief Complaints	n(%) (n= 56)
Fever	23(41.1)
Rash	16(28.6)
Joint pain	14(25.0)
Pale	6(10.7)
Palpebral edema	3(5.4)
Dyspnea	1(1.8)

Table 4 Laboratory and Radiologic Findings in Children with SLE

Manifestation	n(%) (n= 56)
Laboratory Examinations	
Blood Test	
Complete Blood Count	
Anemia	40 (71.4)
Leukopenia	20 (35.7)
Thrombocytopenia	13 (23.2)
Antibody Tests	
Reactive Antinuclear antibody test	46 (82.1)
Pattern of Antinuclear antibody by immunofluorescence:	
Speckled pattern	23 (41.1)
Homogenous pattern	10 (17.9)
Positive titer of Anti-dsDNA	44 (78.6)
Urine Tests	
Proteinuria	28 (50.0)
+1(≥30mg/dL)	8 (14.3)
+2(≥100mg/dL)	9 (16.1)
+3(≥300mg/dL)	11 (19.6)
Hematuria (≥ 5 erythrocytes/ HPF)	28 (50.0)
Presence of casts (Granular casts)	6 (10.7)
Radiologic Exams	
Abnormalities in Lungs	
Pleural Effusion	6 (10.7)
Pneumonia	2 (3.6)
Pneumothorax	1 (1.8)
Abnormalities in Heart	
Pericardial Effusion	6 (10.7)
Cardiomegaly	6 (10.7)
Mitral Regurgitation	1 (1.8)
Cardiomyopathy	1 (1.8)

(Table 3). Laboratory examinations are shown in Table 4. Anemia (71.4%) was the most common anomaly from the complete blood count examination, followed by leukopenia (35.7%) and thrombocytopenia (23.2%) (Table 4). From the antibody tests conducted on the patients, various patterns were found from the anti-nuclear antibody tests (Table 4). The most common antinuclear antibody pattern was found to be the speckled pattern

(41.1%) and followed by the homogenous pattern (17.9%).

The radiologic examinations and results from echocardiography, if any, were also recorded in Table 4. According to the abnormalities in the lungs and the heart, the most common abnormality in the lungs and the heart was found to be pleural effusion (10.7%) and pericardial effusion (10.7%) and cardiomegaly (10.7%) (Table 4).

Discussion

Certain patterns can be derived from the results of the 56 patients. Based on the results in Table 1, there was a higher frequency of SLE in children from the ages of 11 to 15 compared to the other age groups. Systemic Lupus Erythematosus (SLE) was found to be rare in toddlers compared to children and adolescents. The age group of the children and adolescents also correlates with a study done by Silverman⁸, in which the global mean age of SLE in children was 12 to 13 years of age.² There was also a higher frequency of SLE in female children compared to male children as seen in Table 1. This finding is consistent with previous studies that have proven that there is a predominance in SLE in females compared to males and that the global male/female ratio has been reported to be of 1:2 to 1:5.² These prove that the frequencies and patterns of epidemiological features displayed in the children in Bandung, Indonesia, are actually similar to previous studies conducted in the rest of the world.

In this study, fever was the most common chief complaint. Fever in SLE tends to not have a specific pattern. The differential diagnosis of fever are chronic infections, autoimmune diseases, and malignancy.⁸ Therefore, it is essential to investigate the cause of fever to ensure that it is due to SLE.

The rash on the face was the second most common chief complaint, as seen in Table 3. In another study conducted by Silverman⁸, 60–80% of patients had skin involvement. Dermatologic involvement or changes that mostly found in SLE are malar rashes and discoid rash.⁹ In addition, SLE might also present other dermatologic changes, such as vasculitic skin lesions and bullous lesions.⁹

Joint pain was also a common chief complaint among the patients (Table 3). In the study done by Silverman⁸, 60–88% of patients had arthritis. Arthritis in SLE is described as non-erosive and involving two or more peripheral joints.⁷ It is important to differentiate arthritis from arthralgia whilst examining the patient. This is key as non-erosive arthritis is stated as a criteria of diagnosis of SLE, not arthralgia.

In this study, patients had a chief complaint of paleness as seen in Table 3. Paleness is commonly due to a low hemoglobin level and subsequent anemia. Normochromic, normocytic anemia is the type of anemia that is usually detected.⁸ However, hemolytic anemia has also been found in patients with SLE. This can be detected by a blood smear

and thereafter a positive direct Coombs test.⁸

There was a significantly high frequency of dermatologic, renal and hematologic involvement, as seen in Table 2. However, based on previous studies, renal involvement has been the most common clinical manifestation that was found in patients with SLE.^{2,8,10} In this study, hematologic involvement was the most common. It could be argued that renal involvement in the patients in this study was also significantly high (64.3%). The difference in data may be attributed to the difference in the number of patients available in both studies, which may have resulted in the study done previously to have had a wider and more diverse array of manifestations compared to the one being done in this study. Another reason for this difference may also have been that the patients in this study had been treated at an early stage before their disease could have progressed to a more severe one, which may have involved the renal system.

In this study, the antinuclear antibody (ANA) test used is an immunofluorescence test, which is directed towards Human Epithelial Type 2 (HEp-2) cells. The antinuclear antibodies (ANAs) target nuclear antigens such as histones, DNA, non-histone proteins bound to RNA and nucleolar antigens. The ANA test displays several patterns of antibodies such as homogenous, speckled and rim/peripheral. In SLE, the main patterns of staining is a homogenous pattern that reflects antibodies to chromatin and histones and a speckled pattern that reflects antibodies to Ro/SS-A and La/SS-B.⁹ These patterns are reflected in Table 4. In this study, the most commonly displayed pattern was speckled (41.1%) followed by homogenous (17.9%). This correlates with a study by Ghrahani et al.¹¹, which showed speckled pattern as the most common pattern with a frequency of 40.3%. The study by Ghrahani et al.¹¹ was also conducted in the Department of Child Health at Dr. Hasan Sadikin General Hospital but it was during a different time period. The reactive ANA test is sensitive to SLE as it indicates the disease. However, it does not rule out other autoimmune diseases. The result of the presence of antibodies to double-stranded DNA, as seen in Table 4, is extremely specific to SLE and confirms the diagnosis.

The wide array of chief complaints and associated symptoms may be due to the disease involvement of multiple systems. This may also be seen in the involvement of the heart and lungs (Table 4) where many subsequent disorders of the heart such as mitral

regurgitation and dilated cardiomyopathy and disorders of the lung such as pneumothorax and pneumonia may occur.

A drawback of this study is the inability to obtain an incidence rate or a prevalence rate. Dr. Hasan Sadikin General Hospital is a tertiary referral hospital, which means many patients may have been treated in previous healthcare services. Therefore, the total population and the number of patients are not truly representative of the population of patients in Bandung. This would subsequently lead to an inaccurate calculation of an incidence or a prevalence rate. To overcome the aforementioned drawback, a study could be conducted across multiple hospitals and healthcare services in Bandung. This would allow for a more widespread representation of the patients with SLE in Bandung.

Based on this study, it can be summarized that females have a greater tendency to have SLE and children between the ages 11 to 15 are the most likely to get SLE. Fever is the most common chief complaint among patients. Hematologic involvement and renal involvement were also found to occur most commonly among the patients.

Systemic Lupus Erythematosus is a disease with diverse and multiple presentations as seen in the data presented in this study. It is often hard to diagnose due to its mimicry with a vast number of diseases. Therefore, there is a need to determine the true cause of this disease before a diagnosis can be obtained. The patterns and data obtained in this study would allow clinicians in the geographical location to be able to identify the warning signs or common presentations of a child with SLE.

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