Mucocutaneous Manifestation of Systemic Lupus Erythematosus Patients At Rheumatology Outpatient Clinic In Dr. Hasan Sadikin General Hospital

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Abstract

Background: Systemic Lupus Erythematosus (SLE) is an autoimmune systemic disease which symptoms induced by Ultraviolet rays exposure. It commonly affects women and causes wide range of symptoms. One of the organs affected is mucocutaneous. Our study aims to determine mucocutaneous manifestations of SLE patients in Rheumatology Outpatient Clinic in Dr.Hasan Sadikin General Hospital, Bandung.

Methods: A descriptive study with prospective cross-sectional design conducted. Data were obtained by interviewing SLE patients as primary data and accessing medical record as secondary data. Ninety-six SLE patients met the inclusion and exclusion criteria were included.

Results: From ninety-six subjects, 94.8% subjects are working indoors. Mucocutaneous manifestation were found in most patients. Based on American College of Rheumatology (ACR) criteria, we found mucocutaneous manifestations, such as: oral ulcers in 67 patients (69.8%); malar rash in 63 patients (65.6%); photosensitivity rash in 51 patients (53.1%), and discoid rash erythematous in 21 patients (21.9%). Specific LE cutanoeus manifestation based on Gilliam classification were found in our study subjects, such as papulosquamous/ psoriasisform (19.5%) , morbilliform (17.7%), vesicobullous annular SCLE (13.5%), annular SCLE (6.3%), and TEN-like LE (1%). Non-specific LE cutaneous manifestations based on Gilliam classification were also found in our study subjects, such as oral ulcers (69.8%), photosensitivity rash (53.1%), alopecia (86.5%), Raynaud's Phenomenon (39.6%), nail abnormalities (24.0%), periungual telangiectasia patients (13.5%), vasculitic lesions (12.5%), thrombophlebitis (44.8%), bullous lesion (5.2%) and erythema multiforme (5.2%).

Conclusion: Mucocutaneous manifestations in SLE patients based on ACR criteria found most in this study is oral ulcers. Based on Gilliam classification specific LE cutanoeus manifestation was not found in all SLE patients, while non-specific LE mucocutaneous manifestations mostly found is alopecia.

Keywords: American College of Rheumatology (ACR) criteria, Gilliam classification, Mucocutaneous manifestations, Systemic Lupus Erythematosus

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that targeted cytoplasm and nucleous of body cells. It causes wide manifestations from the most outer organ to the internal organs. Organ damages may varies, from mild to severe.[1,2] About 5,000,000 people around the world are affected by SLE. United Kingdom reported the prevalence of 97 cases per 100,000 people in 2012.[1]

Signs and symptoms of SLE can be varied. Genetic is predisposition factor which plays role in SLE pathogenesis.[6] Asian reported more severe clinical manifestations and higher mortality rate compared to the American and European. SLE can be found in all groups age and both male and female, but it is more common found in females during their fertile period. [1, 3-5]A study by Kaplan MJ in 2011 and Denny MF in 2010 stated that abnormal immune cells such as monocytes, macrophages, dendritic cells and others innate system components are found in SLE patients. Involvement of IFN-α initiate the development of the flares' signs and symptoms in SLE.[7-11]

SLE is also known as "the great imitator where the presence of those manifestations may be not specific. Manifestations, such as fever, malaise, arthralgia and headache are frequently found in SLE patients. Those symptoms are also found in others autoimmune diseases and hormone abnormalities.[12,13] In 1982, American College of Rheumatology (ACR) publised criterias used to diagnosis SLE based on signs and symptoms detected in SLE patients.[8,14] Many organ systems can be affected by SLE, included mucocutaneous, renal, cardiovascular, gastrointestinal, pulmonary and hematogenous. From all above, the most frequent clinical manifestation found in SLE patients is cutaneous involvement, which explained the reason why SLE originally described as a dermatological disease. Further, four of eleven diagnostic criteria of SLE in revised ACR criteria are skin lesions.[7, 13, 15, 16]

Skin is the most outer organ and also the largest organ of the body. It play role as body defense mechanism by acting as a barrier between the inner body and the environment.[17] Disruption of the skin, such in SLE patients, can affect its normal function, thus lead to secondary infection.[18]

Based on skin lesions characteristics, the manifestation of SLE in skin can be classified into 2 categories: specific and non-specific. Specific skin lesion is directly showed the specific characteristic of skin manifestations of SLE and severity of ilness, whereas non-specific skin lesion shows the progression of disease.[19-21] Specific skin lesions are divided into acute cutaneous lesion, subacute cutaneous lesion and chronic cutaneous lesion. Acute cutaneous lesion is normally widespread and localized. Subacute cutaneous lesion consists of papulosquamous lesion and annular lesion. Chronic cutaneous lesion comprised thick and red, scaly patches. Nonspecific skin lesion is characterized by several manifestations such as photosensitivity, mucosal ulceration and alopecia. [20-22]

By its nature, West Java especially Bandung geographical location, received high exposure of sunlight can become the predisposing factor for the development of SLE manifestation. There have not been any study about mucocutaneous manifestation of SLE patients in Bandung. The objective of this study is to configure the manifestations of mucocutaneous in SLE patients in Rheumatology Outpatient Clinic in RSUP Dr. Hasan Sadikin (RSHS), Bandung.

Method

We used a descriptive, prospective cross-sectional design. Data were attempted from SLE patients who came to Rheumatology Outpatient Clinic in RSHS from September 2016 to November 2016. It is consisted of primary and secondary data. Primary data is the data which obtained from direct interviews. Secondary data is the data obtained from medical record, it was used to recheck the accuracy and precision of the interviews.

For sampling method, we used convenience sampling methods. The minimal sample's number for this study is 96 patients. The inclusion criteria were: 15 years old or more, diagnosed as SLE patients based on American College of Rheumatology's (ACR) criteria, attend to the Rheumatology Outpatient Clinic during the interview period. The exclusion criteria was patient who rejects to be interviewed. Patients met those criteria would be interviewed using a questionnaire. Data collected included demographic characteristics such as gender, age and occupation; and mucocutaneous findings which enlisted in ACR criteria and Gilliam classification. After the interview, we crosschecked the information obtained with their medical record.

All data were inserted to Microsoft Office Excel and analyzed by using descriptive analysis within Statistical Packages for Social Sciences (SPSS) version 20. The study has been approved by Health Research Ethics Committee, Faculty of medicine, Padjadjaran University and with permission from board of director of RSHS.

Result

Ninety-six SLE patients were included to our study. The distribution data of SLE patients that comprised in this study based on the listed characteristics can be observed in following table.

Table 1 Demographic characteristics of SLE patients interviewed

Characteristics	Frequency (n=96) N (%)
Gender	
Male	3 (3.1%)
Female	93 (96.9%)
Age	
15-24	23 (24.0%)
25-34	29 (30.2%)
35-44	29 (30.2)
45-54	14 (14.6%)
≥55	1 (1.0%)
Occupation	
Indoor	91 (94.8%)
Outdoor	5 (5.2%)

Most subjects were female (96.9%). Patients' age were categorized into 5 age groups with 10 years of time interval. Patients was frequently found in group age of 25-34 and 35-44 years old with 29 subjects (30.2%) in each group. The study noted that 91 samples (94.8%) of our study worked indoor.

SLE patients normally experienced several mucocutaneous manifestations at a time. Table 2 and Table 3 below show the mucocutaneous manifestation based on ACR revised criteria and Gilliam LE-Cutaneous classification.

Table 2. Revised ACR Criteria Mucocutaneous Manifestation

Characteristic	Frequency (%)
Malar Rash	63 (65.6%)
Discoid Rash Erythematous	21 (21.9%)
Photosensitivity Rash	51 (53.1%)
Oral Ulcers	67 (69.8%)

Table 3. Gilliam Classification Mucocutaneous Manifestation

Characteristics	Frequency (%)
Specific	
Morbilliform	17 (17.7%)
Papulosquamous/psoriasiform	19 (19.8%)
Vesiculobullous annular SCLE	13 (13.5%)
Toxic epidermal necrolysis–like LE	1 (1%)
Annular SCLE	6 (6.3%)
Non specific	
Photosensitivity Rash	51 (53.1%)
Alopecia	83 (86.5%)
Oral Ulcers	67 (69.8%)
Bullous lesions	5 (5.2%)
Raynaud's phenomenon	38 (39.6%)
Vasculitis lesions	12 (12.5%)
Erythema multiforme	5 (5.2%)
Periungual telangiectasia	13 (13.5%)
Nail abnormalities	23 (24%)
Thrombophlebitis	43 (44.8%)

Based on Revised ACR criteria, the most frequent mucocutaneous manifestation found are oral ulcers, accounted for 69.8% of all subjects. Based on the Gilliam Classification, the most common LE-specific mucocutaneous manifestations is papulosquamous/ psoriasiform 19.8%, and the least common found is toxic epidemal necrolysis-like LE 1%. As for LE non-specific mucocutaneous manifestations, the majorly cutaneous manifestatsion found is alopecia 86.5%, and the least found are bullous lesion and erythema multiforme manifestation which accounted for 5.2%, respectively.

Discussion

Most subjects are female, which ratio female to male is 31:1. As a comparison, study by Saigal *et al* conducted in Western India, also found higher ratio of SLE in female than in male, with ratio 11:1; and study by Budhoo *et al* in South African found 91.2% female from 408 samples. Saigal *et al*, Budhoo *et al* and this study enhanced the theory that SLE affects mostly on female.[15, 23] Most SLE patients were found in group age of 25-34 years old and 35-44 years old. Study by Jakes *et al* and Bhaskar *et al*, showed mean age found for SLE patients is 25.7-34.5 years old and 21-30 years old, where it is a close meet to the most age group found in this study.[3, 24] William stated that age from 15 to 44 years old is a fertile period for a female.[25] Therefore, it can be concluded that SLE mostly can affect female who is in childbearing age.

We found that more patients worked indoor than outdoor. Exposure to ultraviolet (UV) rays is one of the triggering factors of flares in SLE patients.[7, 8] Based on Mak, *et al* study, exposure of UV rays especially UV-B is actually a dose depend. SLE patients that exposed to higher UV ray would experience larger necrosis of the keratinocytes and have higher degree of inflammation.[26] In our study, eventhough most SLE patients worked indoor, to prevent the exposure of UV light, but most of them still showed mucocutaneous manifestastions. Factors that affects these manifestations should further be assessed.

Based on table 2, the mucocutaneous manifestations enlisted in American College of Rheumatology's criteria found most in this study is oral ulcers, followed by malar rash. It is rather different with Saigal, *et al* study, which noted that in Western India photosensitivity rash is the most common mucocutaneous manifestation, while in Bhaskar, *et al* study which held in Assam, Northeastern India found that oral ulcers is the common mucocutaneous manifestation.[15, 24] We sugested that the differences may be happened due to the difference level of disease activity of SLE when the study held. Unfortunately we did not analyze the corellation between SLE disease activity and the frequent mucocutaneous manifestations.

In the Gilliam classification comprises, mucocutaneous lesion is classified as specific and non-specific mucocutanous manifestations. It can be seen that both specific and nonspecific mucocutanous manifestations are found in SLE patients who attended our study. Yet, subject in our study experienced more non-specific mucocutaneous manifestations rather than the specific ones. Dubois mentioned that it is common that nonspecific mucocutaneous manifestation developed more in SLE patients.[21] Increase in SLE non-specific mucocutaneous lesion is the indication of higher disease activity.[27]

Among non-specific SLE mucocuteneous manifestations, alopecia is the most common non-specific SLE mucocuteneous manifestations (86.5%). It is consistent with Kole, *et al* study which also found 86.67% SLE patients developed non-scarring alopecia manifestations. But, study by Bhaskar, *et al.* only found 52.63% of the total patients had alopecia.[24, 27] Erythema multiforme and bullous lesion are the least manifestations in this study with rate 5.2% respectively. Bhaskar, *et al.* and Kole, *et al.* studies found erythema multiforme in 18.42% and 6.67% patients respectively; and bullous lesions in 7.89% and 10% of SLE patients respectively.[24, 27] These contrasts might be caused by the differences patients' lifestyles and the severity of illness.

Papulosquamous/psoriasiform is the most frequent specific SLE mucocuteneous lesions found (19.8%) in this study. Kuhn, *et al.* stated that papulosquamous/psoriasiform is a subacute lesion. Patients with subacute lesions may have either papulosquamous/psoriasiform or annular lesions. But, only few will have both.[28] In our study, only 6.3% patients had annular SCLE lesions. The discrepancy might occurred due to the difference degree of disease severity in patients. The lowest specific SLE mucocuteneous manifestations found in this study was toxic epidermal necrolysis–like LE with rate only 1%. Kole, *et al.* mentioned that there was a case of toxic epidermal necrolysis–like LE occurred in a patient after few series of relapse.[27] Kuhn stated that this kind of lesion can be occurred with almost same properties as drug eruption case.[28] Only small number of patient found with toxic epidermal necrolysis–like LE, since it is a fast-react mucocutaneous manifestation.[29]

Throughout the study, we realized several limitations. The researcher aware that time limitation is one of the concerns, even though we reached the minimal samples, but for the feasibility of time, we could only used convenience sampling methods which has lower confidence value than the systematic random sampling methods. We also had minimalized the recall errors by referring our primary data to patients' medical record. However, not all data were recorded in the medical records or the medical records were not available due to transferred to other outpatient clinics during the data collection.

Conclusion

Characteristic of SLE patients with mucocutaneous manifestations based on revised ACR criteria, arranged from most frequent, was oral ulcers, malar rash, photosensitivity rash and discoid rash erythematous. Non-specific SLE mucocuteneous manifestations were found more frequent compared to specific SLE mucocuteneous manifestations. The common manifestation of non-specific SLE mucocuteneous manifestation is alopecia. Several recommendations to improve our study is improving medical records management system in RSUP Dr. Hasan Sadikin and awareness of every doctors and physician on data importance on every intervention made on patients. Further, multiple center studies for SLE mucocutaneous manifestation prevalence and incidence are needed.

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