The Characteristic of Anti dsDNA and Organ System Involved in Systemic Lupus Erythematosus Patient at Hasan Sadikin General Hospital, Bandung

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Abstract

Background

Clinical manifestation of Systemic Lupus Erythematosus (SLE) may be varies in attacking various body tissue and organ system. Anti-dsDNA is the important antibody in determining diagnosis and prognosis of SLE. This study was conducted to explain the characteristics of anti-dsDNA and organ system involved in SLE patients.

Method

We used quantitative descriptive analysis methods. Data were collected from medical records of SLE patients who came to Dr. Hasan Sadikin Bandung General Hospital Rheumatology Clinic from September to November 2016. Using categorical descriptive research equation, we found that total minimum samples were 67 subjects. Data observed included the level of anti-dsDNA antibody and clinical manifestation of organ system involved.

Result

From 67 samples, there were 65 females which accounted for 97% of the research subjects. Distribution of organ system involved in our subjects was musculoskeletal (29%), mucocutaneous (27%), hematologic (21%), kidney (15%), neuropsychiatry (4%), lung involvement (4%) and cardiovascular (0%). Organ system involved related with strong positive anti-dsDNA were mucocutaneous (21,6%), hematologic (25%), musculoskeletal (12,5%), kidney (14,3%) and lungs (20%).

Conclusion

The most frequent organ system involved in SLE patients at our setting was musculoskeletal. The common organ involvement related with strong positive anti-dsDNA were mucocutaneous, musculoskeletal, and hematologic.

Keywords: anti-dsDNA, involvement of organ system, clinical manifestation, systemic lupus erythematosus

Introduction

Systemic Lupus Erythematosus is a chronic autoimmune disease marked by the production of autoantibody that attacks various body tissue and organ system (SLE).[1] Prevalence of lupus disease is estimated around 143.7 out of 100,000 populations, with the largest incidence about 23.2 out of 100,000 populations every year.[2] The prevalence of SLE in 24 countries in Asia ranges between 30-50 out of 100,000 populations, with Shanghai ranks first for the highest number of prevalences.[3] In the newer survey, Taiwan reported the prevalence, incidence, and mortality of lupus diseases in this country about 97.5, 4.97, and 1.2 out of 100,000 populations, respectively.[4]

Clinical manifestastion of SLE may vary on each patients, from slight discomfort to life threatening. It is included dysfunction on skin and mucous; muscoloskeletal system; kidney system; nervous system; immune system; and blood system.[5]clinical and laboratory manifestations, therapy and outcome were assessed. RESULTS: A cohort of 56 patients with a mean age at disease onset of 12.6 +/- 4.04 years (mean +/- 1SD Based on the criteria of revised *American College of Rheumatology* (ACR) 1997, the diagnosis of lupus disease may be enforced if it meets 4 of 11 criteria which are malar rash, discoid rash, photosensitivity, mouth ulcer, arthritis, serositis, renal failure, neurological failure, hematologic failure, immunologic failure, and positive antinuclear antibody (ANA).[6]

The autoantibody holds essential role in SLE pathogenesis. It was reported by a research conducted in North Sweden that the autoantibody that damages the nucleus antigen was detected 5.6 ± 4.7 years before the diagnosis on 63% individuals who were later inflicted by SLE.[7]suggesting a gradual development of these diseases. Therefore, we sought to identify autoantibodies in a northern European population predating the onset of symptoms of SLE and their relationship to presenting symptoms.\\n\\nMETHODS: The register of patients fulfilling the American College of Rheumatology criteria for SLE and with a given date of the onset of symptoms was coanalysed with the register of the Medical Biobank, Ume\u00e5, Sweden. Thirty-eight patients were identified as having donated blood samples prior to symptom onset. A nested case-control study (1:4 The anti-

dsDNA Antibody is an antibody that is highly related with SLE manifestation, especially lupus nephritis.[8]

In Indonesia, particularly at the Rheumatology Department in Hasan Sadikin General Hospital, there were no data about the characteristics of anti-dsDNA antibody and organ system involvement of Systemic Lupus Erythematosus patients. Knowledgement of the characteristics of anti-dsDNA antibody along with organ system involvement in SLE patients is hoped giving a better understanding of Systemic Lupus Erythematosus prognosis on each patients.

Method

Sampling method

We used quantitative descriptive with consecutive sampling methods. The minimum amount samples required in this research was 67 samples obtained from using the categorical descriptive research equation. Samples were collected from patients who came to Rheumatology Clinic of Hasan Sadikin Bandung General Hospital from September to November 2016. Inclusion criteria for this study were: age ≥17 years old and diagnosed as SLE patient according to medical record. Samples were excluded if no data about organ system involvement and no data about the level of anti-dsDNA.

Data collection

Data about organ involvement were collected from patients' medical records.

Anti-dsDNA data that we analyzed were taken on the day of the patient came to clinics. Anti-dsDNA test were done using QUANTA Lite dsDNA ELISA with interpretation: negative (<200 IU/ml); equivocal (201-300 IU/ml); moderate positive *(301-800 IU/ml)*; and strong positive*(>800 IU/ml)*[9]

Statistical analysis

The analysis was conducted descriptively by counting the number, percentage, and cross tabulation. The variables in this research were the patients' characteristics (age, gender, occupation, educational attaintment), the anti-dsDNA antibody characteristics (negative, equivocal, moderate positive, and strong positive), and the patients' clinical manifestation based on the involvement of organs which includes mucocutaneous, musculoskeletal, hematology, renal, cardiovascular, lungs and neuropsychiatry. The patients data were then analyzed by data processing application in the computer and presented in the form of tables.

Ethic

This study has been approved by Health Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran with letter No. 922/UN6.C1.3.3/KEPK/PN/2016.

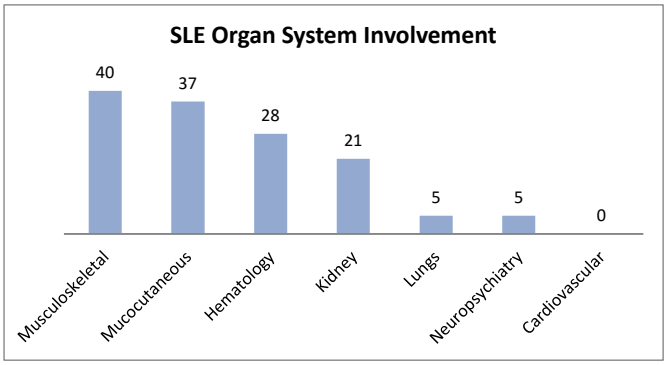
Results

Table 1. Subjects' Demography

Characteristic (N=67)	Frequency N(%)
Gender	
Female	65 (97%)
Male	2 (3%)
Age	
17-26	18 (27%)
27-36	18 (27%)
37-46	17 (25%)
47-56	9 (13%)
≥57	5 (8%)
Occupation	
Indoor	61 (91%)
Outdoor	6 (9%)
Educational Attainment	
No Education	0 (0%)
Elementary School	10 (15%)
Junior High School	11 (16%)
Senior High School	34 (51%)
University	12 (18%)

Sixty-seven subjects who meet the study criteria were included. We found 65 female patients (97%) of the subjects. The subjects' aged were ranged between 20-60 years old. Most of the subjects were comprised of females of productive age, whose age 17-46 accounted for 79% of all subjects. Most research subjects were engaged in indoor activities, reaching up to 61 people (91%) with their occupation as housewives. Most achieved educational attainment was at the level of senior high school, reaching up to 34 people (51%), followed by 12 people at college level (18%).

Figure 1. Organ System Involvement



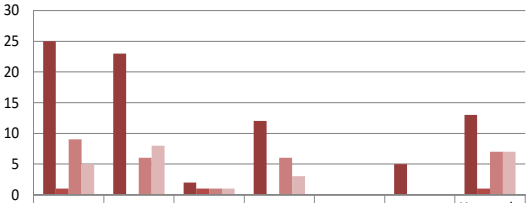
From figure 1 we can see that the most common organ system involvement is musculoskeletal, reaching up to 40 cases (59.7 %), followed by mucocutaneous at 37 cases (55.2 %), hematology at 28 cases (41.8 %), kidney at 21 cases (31.3 %), neuropsychiatry at 5 cases (7.5 %) and lungs at 5 cases (7.5 %). There was no case of the cardiovascular involvement reported.

Table 2. Characteristic of Anti-dsDNA

Anti-dsDNA (N=67)	N(%)
Negative	41 (61%)
Equivocal	2 (3%)
Moderate Positive	14 (21%)
Strong Positive	10 (15%)

We found that majorly subjects has negative anti-dsDNA which amount for 41 subjects (61%). Only 10 subjects (15%) show strong-positive anti-dsDNA level.

Figure 2. The Characteristic of Anti-dsDNA and Organ System Involvement



	MS	MC	Lungs	Kidneys	CV	NP	Hematology
Negative (41)	25	23	2	12	0	5	13
Equivocal (2)	1	0	1	0	0	0	1
Moderate Positive (14)	9	6	1	6	0	0	7
Strongly Positive (10)	5	8	1	3	0	0	7

MS: musculosceletal; MC: mucocutaneous; CV:cardiovascular; NP: neuropsychiatry

The research data showed us that patients with negative anti-dsDNA had frequent clinical manifestation on musculoskeletal system (60.9%), mucocutaneous (56.1%), and hematology (31.7%). Meanwhile, patients with strong positive anti-dsDNA had more common clinical manifestation in mucocutaneous (80%), hematology (70%), musculoskeletal system (50 %). All neuropsychiatry involvement had negative anti ds-DNA.

Discussion

We found female SLE patients were 32 folds more frequent to male SLE patients. This matched the previous studies, such as research conducted by Candace, et al which stated that female SLE patients were 6 times more common than male patients;[2] and research conducted by Somers, et al which stated female patients were 10 times more common in comparison to male patients[10] The age of the patients ranged between 20-60 years old, with the highest span between 17-36 years old. It is consistent with the study conducted by Yazdany, et al which mentioned the age span of SLE patients in San Fransisco ranged between 24 and 60 years old. [11] However, some literatures mentioned that SLE patients were commonly met at age ranged between 15-18 years old.[12]

Subjects whose have indoor occupation were up to 91%, as the sun light exposure may induces SLE flares. They confessed working as housewives with most activities were conducted indoor. However , it's not impossible for these housewives to get sun light exposure from their activities.[13]n = 263 The study also reported that the majorly subjects had attained at least senior high school level education (69%).

The most common clinical manifestation was the involvement of musculoskeletal (59.7%), followed by mucocutaneous (55.2 %) and hematology (41.8 %). It is consistent with the study conducted by Cabral, et al that the most common manifestation is the involvement of musculoskeletal (87.5%), followed by mucocutaneous (80.3%) and hematology (75%).[5]clinical and laboratory manifestations, therapy and outcome were assessed. RESULTS: A cohort of 56 patients with a mean age at disease onset of 12.6 +/- 4.04 years (mean +/- 1SD And also matched the research conducted by Jallouli, et al in Tunisia which states that musculoskeletal (84.2 %) and mucocutaneous (75.3 %) are the two most common manifestations.[14]

We found that most subjects had negative anti-dsDNA (61%), while moderate positive (21%) and strong positive anti-dsDNA (15%). This could be happened due to the anti-dsDNA test used in this study, QUANTA Lite dsDNA ELISA, which has high specificity (91.0%) but low sensitivity (54.1%). Thus causing patients with negative anti-dsDNA not cleared from their SLE ailment status.[15]

For negative, equivocal and moderate positive anti-dsDNA, the most common organ involvement was musculoskeletal, while for strong positive anti-dsDNA, the most common organ involvement was the mucocutaneous. Previous researches stated that persistent positive anti-dsDNA tend to show the involvement of kidney (30.2%) while persistent negative anti-dsDNA tend to show more serositis (82.3%).[16] However in our settings, kidney involvement happened in 31.3% of all subjects and dominated by the negative anti-dsDNA patients which accounted for 57.1% of all kidney involvement subjects. The difference might be occured due to the low sensitivity of our test in detecting anti-dsDNA. Study using anti-dsDNA test from CLIFT showed a correlation between positive anti-dsDNA with spesific manifestations, such as proteinuria, haematuria, pleuritis and leukopenia. When antibodies were confirmed by any immunoassay, the prevalence of malar rash, cutaneous vasculitis, alopecia,lymphopenia and non-haemolytic anaemia would be increased.[17] Anti-dsDNA is also play important role in developing lupus nephritis by the arrangement of immune complex between anti-dsDNA with autoantigen located at kidneys. However, research conducted by Atta, et al stated that the level of anti-dsDNA is not always related with kidney involvement. It explained that the synthesis of dsDNA antibodies depends on innate and acquired immunity, which is induced by bacterial DNA. [18] In addition, Yung and Chan also stated that organ involvement not only depends on the existence of anti-dsDNA. Other factors, such as cytokine, chemokine, proteolytic enzymes and oxidation process play roles in developing inflammation process which is responsibled in damaging organs.[19]

We realized some limitation of our study. Firstly, this research only used secondary data from medical record and had relatively short data collection period, between September to November 2016. Furthermore, we do not analyze any other factors that might affects spesific organ involvement, such as duration of disease, medication received, amount of sun light exposure, etc.

Summary

In concluison, the most frequent organ involved in SLE patients at Dr. Hasan Sadikin Bandung General Hospital Rheumatology Clinic is musculoskeletal. Most patients showed negative anti-dsDNA. The most common manifestation of positive anti-dsDNA is the involvement of mucocutaneous, musculosceletal and hematologic.

We strongly suggest for conducting more comprehensive study on a larger scale to provide more accurate results.

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