ORIGINAL RESEARCH

Clinical profile and incidence of infection in Systemic Lupus Erythematosus patients at Medical Inpatient Installation, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016

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Article Info	ABSTRACT
  *Corresponding author Betty Agustina betty-a-t@fk.unair.ac.id	**Background:** Systemic Lupus Erythematosus (SLE) is an autoimmune disease with unknown aetiology. SLE attacks multiple organs with diverse clinical manifestations. Most patients get immunosuppressant therapy that suppresses immune system, causing the body to be susceptible to infection. **Objective**: to describe clinical manifestations, laboratory abnormalities, and incidence of infections in SLE patients hospitalized at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016. **Materials and Methods**: Cross-sectional descriptive observational study used medical records of 273 SLE patients hospitalized at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016. **Results**: Clinical manifestations found in this study were malar rash 7.33%, discoid rash 2.93%, oral ulcer 8.42%, allopecia 16.48%, arthritis 26.74%, serositis 13.19%, kidney 35.9%, neurology 24.91%, anemia 73.71%, leucopenia 32.67%, lymphopenia 76.89%, and thrombocytopenia 33.86%. Laboratory abnormalities found in this study were hematology (anemia 73.71%, leucopenia 32.67%, lymphopenia 76.89%, thrombocytopenia 33.86%), kidney function (high serum creatinine levels 39.66%, high BUN levels 41.2%, hypoalbuminemia 62.6%), urine (proteinuria 68.21%, hematuria 51.79%) and liver function (high ALT levels 36.65%, high AST levels 29.86%). Infection occurred in 33.7% patients. The most common infections were pneumonia (70.65%), urinary tract infections (51.09%), and sepsis (35.87%). **Conclusion**: The most common clinical manifestations experienced by SLE patients are hematological disorder, kidney disorder, and arthritis. Prominent laboratory abnormalities are anemia, lymphopenia, and proteinuria. Infection is a common complication, with the most common types pneumonia, urinary tract infection, and sepsis.

BACKGROUND

SLE is a chronic autoimmune disorder which can cause complications in several organs. This disorder occurs because the formation of various types of antibodies in the patient's body, including antinuclear antibody which is used as one of the diagnostic criteria (Anggraini, 2016).The exact cause of SLE is unknown until now. Several factors that are thought to play a role in the incidence of SLE in Indonesia are genetic, immunological, hormonal, and environmental (Ministry of Health, Republic of Indonesia, 2017). SLE is an autoimmune disease that attacks multiorgan so that the clinical manifestations depend on the target organ that is attacked. This results in difficulty in establishing a diagnosis. These difficulties often have an impact on diagnosis errors, so that it may result in delayed management of the case (Li, et al., 2013).

One of the criteria for establishing a diagnosis of SLE was made in 2012. According to Systemic Lupus International Collaborating Clinics (SLICC), a diagnosis can be made if it meets 4 criteria, at least 1 clinical criterion and 1 immunological criterion. The diagnosis can also be made by Lupus Nephritis (LN) as a single clinical criterion accompanied by evidence of ANA or anti ds-DNA. These clinical criteria include malar rash, discoid rash, oral ulcer, nonscarring alopecia, arthritis, serositis, kidney, neurology, hemolytic anemia, leukopenia, and thrombocytopenia. Meanwhile, immunological criteria include ANA, anti ds-DNA, anti Sm, anti-phospholipid antibodies, and complement (Bakula, et al., 2019). SLE is generally not a life-threatening disease, but this condition can change if organ involvement has been found. Organ dysfunction is the major cause of death. Complications may involve various organs, such as kidney, hematology, and neuropsychiatry.

Kidney manifestations are found in most patients with SLE. Few patients show clear clinical symptoms, but urine examination often shows proteinuria. LN is one of the major causes of death in patient with SLE. As many as 26% of cases end in End Stage Renal Disease (ESRD). It is important to predict the risk factors for progressive kidney abnormalities by looking at serum creatinine and albumin (Domingues, et al., 2018).

Hematological abnormalities play important role in determining prognosis. Frequent manifestations are anemia, leukopenia, and thrombocytopenia. Anemia with autoimmune pathology and decreased erythropoietin production due to inflammation in the kidneys are common. Leukopenia is often followed by decreased lymphocyte counts. Hematological disorders are closely related to corticosteroid use (Ratnadi, et al., 2015).

Abnormalities of liver function occur in 9.3% to 59.7% of patients with SLE. This disorder is defined as double increase in alanine aminotransferase (ALT) and aspartate aminotransferase (AST). It has strong influence on the disease activity. It has not been proven as a result of long-term corticosteroid use (Liu, et al., 2015).

Another complication that is the highest cause of hospitalization in SLE is infection. The most common infections are pneumonia, sepsis, skin infections, urinary tract infections, and opportunistic infections. Sepsis and opportunistic infection have the highest mortality rate (Wichainun, et al., 2013). Considering the clinical, especially laboratory profile of SLE patients has not been widely discussed and the high mortality due to infection, the researchers were interested in conducting this study.

OBJECTIVE

This study aimed to describe clinical manifestations, laboratory abnormalities, and incidence of infection in SLE patients in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

MATERIALS AND METHODS

This study was a descriptive cross sectional observational study used secondary data in the form of medical record. Population used in this study was SLE patients who were admitted at Medical Inpatient Installation, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia from 1 January 2016 to 31 December 2016. The sample used in this study was all SLE patients who were admitted at Medical Inpatient Installation, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia from 1 January 2016 to 31 December 2016. The inclusion criteria were SLE patients who were admitted at Medical Inpatient Installation, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016. Exclusion

criteria were the status of patient's medical records who were not found in the medical record section at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. Dependent variables were clinical manifestations, laboratory abnormalities, and infection in SLE patients. Independent variable was SLE patients admitted at Medical Inpatient Installation, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016. Data obtained through medical records, processed using Microsoft Excel 2016, then presented in the table form.

RESULTS

Demography

SLE patients admitted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2016 were 280 patients, but there were 273 medical records found. Patients were mostly female (94.87%) than male (5.13%). The most age range were 25-44 (49.08%) and 15-24 years (40.29%). Patients who survived were 92.31% and the remaining 7.69% died.

Clinical manifestations

Clinical manifestations based on complaints and examination results listed on medical records and grouped according to SLICC 2012 criteria.

Table 1. Clinical manifestations in SLE

Clinical Manifestation	Percentage (%)
Malar rash	7.33
Discoid rash	2.93
Oral ulcer	8.42
Nonscarring alopecia	16.48
Arthritis	26.74
Serositis	13.19
Kidney	35.90
Neurology	24.91
Anemia	73.71
Leukopenia	32.67
Lymphopenia	76.89
Thrombocytopenia	33.86

Source: research data, processed

The most common manifestations were hematology (anemia, leukopenia, lymphopenia, thrombocytopenia), kidney, and arthritis.

Laboratory abnormalities
Hematology

About 251 of the 273 samples were examined for hematology. The hematological laboratory examinations were leukocytes, lymphocytes, erythrocytes, haemoglobin, and platelets. The number of leukocytes was not much different between leukopenia (32.67%), normal (35.46%), and leukocytosis (31.87%). Most patients had low lymphocyte count (76.89%). Hematological abnormalities were also found as the lower count of erythrocytes (58.96%), haemoglobin (73.71%), and thrombocytopenia (33.86%) (Table 2). The erythrocyte index which had a normal value in the majority of patients showed that the dominant type of anemia was normochromic normocytic.

Kidney Function

Kidney function was examined from BUN, serum creatinine, albumin, and urine examination. Total 250 patients were examined for BUN, 237 patients for serum creatinine, and 246 patients for albumin. Urine examination was performed on 195 patients. Kidney function was also seen in patients with complications of LN. Total 98 patients with LN, 75 patients were examined for BUN, 77 patients were examined for serum creatinine, and 67 patients were examined for albumin. Urine examination was performed on 77 patients (Table 3).

Liver function

Liver function was evaluated from alanine aminotransferase (ALT) and aspartate aminotransferase (AST) level. From a total of 273 samples, 221 patients were examined for ALT and AST. Table 4 shows a high ALT (36.65%) and high AST (29.86%) levels. It shows impaired liver function.

Table 2. Hematology in SLE

Type of Examination	Percentage (%)
Leukocyte Count	
Low	32.67
Normal	35.46
High	31.87
Lymphocite Count	
Low	76.89
Normal	22.31
High	0.80
Erythrocyte Count	
Low	58.96
Normal	40.24
High	0.80
Erythrocyte Index: MCV	
Low	45.02
Normal	50.60
High	4.38
Erythrocyte Index: MCH	
Low	35.06
Normal	53.39
High	11.55
Erythrocyte Index: MCHC	
Low	16.33
Normal	49.80
High	33.86
Haemoglobin	
Low	73.71
Normal	24.30
High	1.99
Thrombocyte Count	
Low	33.86
Normal	64.94
High	1.20

Source: research data, processed

Table 3. Kidney function in SLE and LN

Type of Examination	SLE (%)	LN (%)
Kidney Function		
BUN		
Low	25.20	5.33
Normal	33.60	20.00
High	41.20	74.67
Serum Creatinine		
Low	6.75	5.19
Normal	53.59	32.47
High	39.66	62.34
Albumin		
Low	62.60	77.61
Normal	37.40	22.39
High	0	0
Urine Protein		
Normal	31.79	10.39
High	68.21	89.61
Leukocyte		
Normal	62.05	57.14
High	37.95	42.86
Erythrocyte		
Normal	48.21	15.58
High	51.79	84.42

Source: research data, processed

Table 4. Liver function in SLE

Type of Examination	Percentage (%)
ALT	
Normal	76.92
High	36.65
AST	
Normal	70.14
High	29.86

Source: research data, processed

ANA, C3, C4

The ANA examination results were found in 31 patients. Results of C3 and C4 examinations were found in 18 patients. Some patients had positive ANA examination results (87.1%), low C3 (38.89%), and low C4 (66.67%).

Infection

Infection was one of the most common complications in SLE patients. Table 5 shows the type of infection based on the diagnosis made by the clinician recorded in the medical record. Most infections were pneumonia (70.65%), urinary tract infections (51.09%), and sepsis (35.87%).

Table 5. Type of infection in SLE

Type of Infection	Percentage (%)
Pneumonia	70.65
Urinary Tract Infection	51.09
Sepsis	35.87
Lower Respiratory Tract Infection	13.04
Tuberculosis	7.61
Cerebral Infection	5.43
Dengue High Fever	2.17
Candidiasis	2.17

Source: research data, processed

DISCUSSION

Demography

The results showed that SLE patients were dominated by female. Most patients consisted of age group of 25-44 years followed by age group of 15-24 years. This was in accordance with profile data in Indonesia that SLE mostly affected women of productive age (15-44 years) (Ministry of Health, Republic of Indonesia, 2017). The number of patients died were 21 patients (7.69%). The major cause of death was septic shock. This result was different from the situation in Indonesia that in 2015, 8.23% of the patients died (Ministry of Health, Republic of Indonesia, 2017). This difference could have been be caused by the improvement in managing of SLE patients in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia compared to other hospitals in Indonesia.

Clinical manifestations

The most common manifestations are hematology (anemia, leukopenia, lymphopenia, thrombo-cytopenia), kidney, and arthritis. The presenting manifestation of arthritis is joint pain. Other clinical manifestations that often appear are serositis, neurology, and alopecia. Serositic manifestations may include pleural effusion and pericardial effusion. Neurological manifestations are seizures, behavioral changes, depression, and decreased consciousness.

According to a previous research in Semarang, Indonesia, the most frequent clinical manifestations are arthritis, kidney, and anemia (Putra, et al., 2018). In the UK, manifestations that most often occur in patients with SLE are musculoskeletal, constitutional, and mucocutaneous (Nightingale, et al., 2017). Musculoskeletal manifestations are the most frequent, while kidney disorders and other organs show signs in a small proportion of patients (Gergianaki & Bertsias, 2018). These three studies show that musculoskeletal manifestations (arthritis) are the most frequently used criteria for the diagnosis of SLE (Putra, et al., 2018; Nightingale, et al., 2017; Gergianaki & Bertsias, 2018).

The differences in the results of this study were cutaneous manifestations, especially malar rash, which should have high incidence (Putra, et al., 2018; Nightingale, et al., 2017). This difference might have resulted from the recording of the data. The manifestations written in the medical records were those found at that moment, while in other studies the manifestations were observed for several years. Clinical manifestations that occur in patients with SLE are very diverse and do not always appear together.

Laboratory abnormalities

Hematology

SLE patients tend to experience leukopenia. This happens because of immunosuppressant therapy which suppresses the work of the immune system (Wiseman, 2016). The result does not have much different between patients who experienced leukopenia and leukocytosis. Leukocytosis that is found in many patients indicates high incidence of infection. Immunosuppressant therapy which decreases the immune system makes the body vulnerable to infection. Low use of corticosteroids shows a relationship to decreased incidence of infection in SLE patients in United States, although this result should be evaluated thoroughly (Anastasiou, et al., 2018).

Low haemoglobin levels showed an incidence of anemia in 73.71% of patients. The type of anemia that occurs is seen from the erythrocyte index that show normal values in most patients. It means that the type of anemia that often occurs is normochromic normocytic. This type of anemia usually occurs due to loss of blood, hemolysis, chronic disease, and renal insufficiency. Blood loss in SLE is associated with long-term corticosteroid use. Hemolysis can occur in underlying autoimmune diseases, such as AIHA. Chronic disease and renal insufficiency occur due to long inflammatory process. Haemoglobin levels have relationship with disease activity in SLE (Reyes-thomas, et al., 2011).

Kidney function

The results showed that 35.9% of patients with SLE had complications in the form of LN. These results were in line with previous study that 35% of adults with SLE experienced kidney nephritis abnormalities. These complications reduce their life expectancy (Hahn, et al., 2012). In this study, SLE patients showed high BUN levels, high serum creatinine, and hypoalbuminemia in most cases. Urine examination showed proteinuria in most patients. These results indicated abnormal kidney function in

patients with SLE. The number of patients with normal and high levels of leukocytes in the urine was not much different. It indicates that proteinuria is better indicators of LN than leukocituria.

The results were in line with previous research, that proteinuria is an important factor in the diagnosis of kidney disorders. Albumin levels can determine the prognosis in patients with LN. Patients with albumin levels> 3.7g / dL have a better prognosis (Domingues, et al., 2018). The results of this study are also similar with previous study, that proteinuria can be an indicator of early detection of lupus nephritis. Proteinuria is also associated with disease activity. 24-hour urine collection is the most accurate choice, but the ratio of protein and serum creatinine can be a more practical choice (Reyes-thomas, et al., 2012).

Liver function

This study showed high ALT levels in 36.65% of patients and high AST in 29.86% of patients. This shows liver abnormalities in some patients with SLE. This was consistent with the statement that 9.3% to 59.7% of SLE patients have the opportunity to experience liver disorders (Liu, et al., 2016). The ratio of ALT and AST levels can indicate the etiology of liver abnormalities. ALT or AST levels which increase by at least double, affect the severity of disease in SLE (Ratnadi, et al., 2015).

ANA, C3, C4

ANA is one of the SLE markers. The sensitivity and specificity of ANA at 1:80 titer were 98% and 92%, whereas in 1: 160 titers were 90% and 96% (Wichainun, et al., 2013). Patients with clinical manifestations of fever and fatigue have almost normal levels of C3 and C4, but patients with arthritis, malar rash, and oral ulcers have low levels of C3 and C4. C3 and C4 levels are also inversely proportional to disease activity (Li, et al., 2013).

This study showed positive ANA examination in 87.1% of patients. Low C3 levels in 38.89% of patients and low C4 levels in 66.67% of patients. Low results can occur due to small number of patients who were examined for ANA, C3, and C4. It could also occur because some patients were not in the initial phase of disease when the examination was performed, so that the levels of ANA, C3, and C4 had dropped.

Infection

The results showed that infection was a common complication in patients with SLE, which was 33.7%. The three most common types of infections were pneumonia, urinary tract infections, and sepsis. This result was different from a study conducted in the United States, which found that the incidence of infections that accompany SLE were mostly pneumonia, sepsis, and skin infections (Tektonidou, et al., 2015). According to research in South Korea, the incidence of infection mostly attacks upper respiratory tract, pneumonia and sepsis (Jung, et al., 2019). The difference in location of research can be a factor that distinguishes this.

There are similarities in these three studies, the infection that attacks respiratory tract is most prevalent (Tektonidou, et al., 2015; Jung, et al., 2019). Airborne disease is the biggest challenge in dealing with the incidence of infection. Microorganism particles can be spread over a wide radius and then inhaled, consumed, and come into contact with other individuals who have never met directly with the source of the infection (Fernstrom & Goldblatt, 2013).

In this study, sepsis occurred in 35.87% patients. Culture was found to be positive in 4 patients. The microorganisms found were *Escherichia coli*, *Enterobacter cloacae, Streptococcus anginosus, and Candida spp.* This result was different from the research conducted in Surakarta, Indonesia, that the mostly found microorganisms in sepsis were *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Escherichia coli*, and *Acinetobacter baumannii* (Mahendra, 2016). The difference can be caused by differences in location and study population. The difference can also can be caused by the small amount of culture found in the medical record so that it is not representative.

Patients with infection complications are known to have corticosteroids (methylprednisolone), immunosuppressants (cyclophosphamide), and antibiotics (ceftriaxone, levofloxacin, ciprofloxacin) as therapy. The use of high dose corticosteroids is significantly associated with incidence of serious infection in SLE patients (Jung, et al., 2019).

CONCLUSION

The most common clinical manifestations experienced by SLE patients are hematological disorder, kidney disorder, and arthritis. Prominent laboratory abnormalities are anemia, lymphopenia, and proteinuria. Infection is common complication, with the most types are pneumonia, urinary tract infection, and sepsis.

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