



ANTIMICROBIAL RESISTANCE IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH INFECTION AT RSUP. H. ADAM MALIK MEDAN

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ABSTRACT **Introduction.** The main causes of death in SLE patients are major organ failure caused by infection, active disease and cardiovascular disease where in the last decades, the leading cause of death in SLE patients has changed from active disease to infection. SLE patients have a high risk of infection due to impaired intrinsic immune responses, immunosuppressant drug use and complications of vital organs from SLE disease. The still limited data on antimicrobial resistance patterns in SLE patients in Indonesia is the basis for this study. The purpose of this study was to investigate antibiotic resistance in SLE patients with infection at RSUP Haji Adam Malik Medan. **Methods.** Descriptive study was conducted at Adam Malik General Hospital Medan in January 2014 to December 2017. Data obtained through medical record at RSUP H. Adam Malik. Infection in SLE patients was based on positive culture results according to focal infection. **Result.** Patients with SLE infection were 122 with the most sex was female (91,8%) and mean age 32,08 + 11,1 year. The most infection sites were in the lungs (50,4%) and urinary tract (29,8%). Most microorganisms were *Escherichia coli* (26,7%) and *Klebsiella pneumonia* (22,9%). Ampicillin, Norfloxacin, Doxycycline, and Clindamycin are the most resistant antimicrobials in SLE patients with resistance values > 70%. **Conclusion.** *Escherichia coli* and *Klebsiella pneumonia* are the most common microorganisms found in SLE patients with infections at RSUPH. Adam Malik Medan. Resistant antimicrobials in SLE patients are Ampicillin, Norfloxacin, Doxycycline, and Clindamycin.

KEYWORDS : SLE, infection, antimicrobial resistance

1. INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by autoantibodies against a nucleus and complex immune system involving many organs in the body.¹ The prognosis of SLE patients is reported to have increased deaths by 3-5 times compared with the general population.² The main causes of death in SLE patients are major organ failure caused by active disease (flare), infection, and cardiovascular disease. Where in recent decades, the leading cause of death in SLE patients has changed from active disease to infection. Late diagnosis, poor treatment adherence, and persistent active disease of SLE are important predictors of the prognosis of SLE patient death.^{2,3}

SLE patients have a high risk of infection due to impaired intrinsic immune responses, immunosuppressant drug use, and vital organ complications.^{4,5} Infection in SLE patients is caused by consumption of steroids during their illness.³ Steroids are a drug used as anti-inflammatory and immunosuppression, leading to a decrease in the ability to fight infections and diseases.⁶

Of most recent study, infection is one of the leading causes of death in lupus patients other than cardiovascular complications.³ Differentiating infection from active disease in SLE patients is very difficult and challenges for rheumatologists. This is due to similar clinical symptoms between infection and active disease. In SLE patients with infections, antibiotic therapy is required with decreased immunosuppressant dose, while active disease is required to increase immunosuppressant dose.^{7,8} The limited data of antimicrobial resistance pattern in SLE patients in Indonesia became the background of this study.

2. METHODS

2.1 Patient Selection

This study was a descriptive study design on 122 consecutive SLE patients with infection that were admitted to General Hospital Haji Adam Malik Medan in January 2014 until December 2017. Data obtained through medical record at RSUP H. Adam Malik from 2014-2017. Diagnosis of SLE was made by according to American College of Rheumatology (ACR) 1997 revised criteria.⁹ Inclusion criteria was SLE patients with positive infection and exclusion criteria was non infection SLE patients. Culture according focal infection and details of infection and other clinical characteristics were recorded. This study was approved by local ethics committee.

2.2 Definition of bacterial infection

Diagnosis of bacterial infection based on the results of positive culture examination of pathogenic microorganisms. In this study, we examined culture according focal infection (blood, urine, sputum, pus) in each study subjects.

3. RESULTS

This study was followed by 122 patients who had been diagnosed with SLE with infections treated at Adam Malik General Hospital Medan Medan from 2014-2017. Based on **Tabel 1**, the patient with female gender as many as 112 people (91.8%) while the male is 10 people (8.2%). The mean age in this study was 32.08 + 11.1 years. Most of the occupation was 56 students (45.9%) followed by 38 (31.1%) housewives, 20 people (16.4%) and farmers 8 people (6.6%).

In this study, infected SLE patients may experience more than 1 site of infection site. Based on the location of the infection, it was found that most of the infections were lungs (50,4%), followed by urinary tract (29,8%), skin (16,8%) and gastrointestinal (3,0%).

Tabel 1. Basic characteristics of SLE patients

Characteristics	
Sex ^a	
Men	10 (8,2)
Women	112 (91,8)
Age ^b	32,08 + 11,1
Occupation ^a	
Student	56 (45,9)
Housewife	38 (31,1)
Entrepreneur	20 (16,4)
Farmer	8 (6,6)
Site of Infection ^a	
Lungs	66 (50,4)
Urinary tract	39 (29,8)
Skin	22 (16,8)
Gastrointestinal	4 (3,0)

^acategorical data : n (%)

^bnumeric data, mean ± SD

In SLE patients can occur infection with microorganisms more than 1 type of microorganisms. Based on the type of microorganisms, the

most types of microorganisms were *Escherichia coli* (26.7%) and *Klebsiella pneumonia* (22.9%). Followed by *Acinetobacter baumannii* (12.9%), *Pseudomonas aeruginosa* (10.7%), *Staphylococcus aureus* (9.2%) and others (7.7%). (Table 2).

Table 2. Pathogen microorganisms in SLE patients

Pathogens	n (%)
<i>Acinetobacter baumannii</i>	17 (12,9)
<i>Burkholderia cepacia</i>	4 (3,0)
<i>Escherichia coli</i>	35 (26,7)
<i>Enterobacter aerogenes</i>	3 (2,3)
<i>Klebsiella pneumonia</i>	30 (22,9)
<i>Pseudomonas aeruginosa</i>	14 (10,7)
<i>Raoultella ornithino</i>	3 (2,3)
<i>Stenotrophomonas maltophilia</i>	3 (2,3)
<i>Staphylococcus aureus</i>	12 (9,2)
Others	10 (7,7)

Antimicrobial Resistance and sensitivity of infected SLE can be seen in Figure 1. The results showed that Ampicillin have high antimicrobial resistance > 80%, followed by Norfloxacin, Doxycycline and clindamycin with resistance between 70%-80%. While antimicrobials that have good sensitivity are Ertapenem (100%), Amikacin (95%) followed by Cefuroxime and Vankomycin (83%).

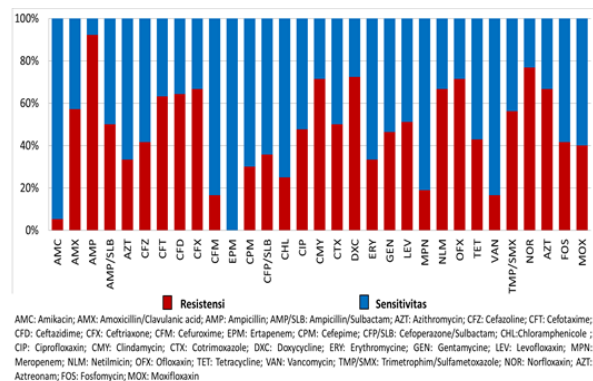


Figure 1. Antimicrobial resistance and sensitivity in SLE patients with infections

DISCUSSION

In this study, majority sex of the subjects research was woman (91,8%). This results was consistent with study conducted by Skare et al, of which 144 samples obtained SLE patients with gender of woman as much as 93.8% and in research conducted by Marpaung et al in Medan on 81 SLE patients, 88.9% was woman.^{10,11} The study of Bertias obtained the most SLE patient is woman, with ratio of ratio between woman and man that is equal to 10: 1.¹²

The mean age of SLE patients in this study was 32.08 ± 11.107 years. This results was consistent with the research conducted by Bertias et al, which in his study obtained the productive age was the most prevalence of SLE, 834 people (83%).¹² Ruiz-Iratorza et al, Skare et al, and Marpaung et al reported the mean age of SLE were 39.15 ± 11.65 years, 36.2 ± 18 years, and 28 ± 9.24 years, respectively.^{10,11,13}

The subjects of this study may have an infection of more than 1 infection site. Based on table 1. above, the majority site of infection were lungs (50.4%) and urinary tract infections (29.8%). These result was consistent with other studies where in that studies stated that the location of infection in patient SLE are on the respiratory tract, urinary tract, and skin.^{10,14,15,16}

The results of this study obtained the most microorganisms *Escherichia coli* (26.7%) and *Klebsiella pneumonia* (22.9%). Research conducted by Ruiz-Iratorza et al and Bosch et al in Spain found that *Escherichia coli* is the most common gram negative bacteria found in infected SLE. While *Staphylococcus aureus* is the most common gram-positive bacteria.^{15,17} Other studies conducted by Zandman-Goddart & Shoenfeld in Israel stated that most gram-negative microorganisms were *Salmonella* and *Escherichia coli*, whereas the most gram positive was coccus (39.85%).¹⁴ The study of

SLE patients with infections in the South China region resulted in the most microorganisms being *Escherichia coli* (24.6%) followed by *Acinetobacter baumannii* (13.4%) and *Staphylococcus aureus* (12.4%).¹⁶ In Asian populations, bacteria gram negative is the most cause of bacteremia in SLE patient while gram positive bacteria for western population. *Staphylococcus aureus* is the leading cause of gram-positive bacteremia whereas *Escherichia coli* is the most common cause of gram negative bacteremia.¹⁸

Pattern of antimicrobial resistance and sensitivity on SLE patient with infection according to figure 1. The results obtained that Ampicillin has high resistance rates > 80% followed by Norfloxacin, Doxycycline, Clindamycin and Ceftriaxone with resistance between 60% -80%. Some antimicrobials have good sensitivity such as Ertapenem (100%), Amikacin (95%) followed by Cefuroxime and Vankomycin (83%). The results were consistent with Chen et al, which showed resistance to Ampicillin (69%) and first-generation cephalosporine (23%).¹⁸ Based on the recommendations of IDSA (Infectious Disease Society of America), the use of third generation cephalosporin antimicrobials and gentamycin is the first choice in SLE patient with infection and pyelonephritis.^{19,20} In this study it can be seen that third generation cephalosporin antimicrobials (Ceftriaxone, Cefotaxime and Cefazidime) and Gentamycin have a high antimicrobial resistance (> 60%). A proper guide to empirical antimicrobial therapy is required in accordance with local bacterial surveillance and local drug sensitivity data in the treatment of infection with SLE.

CONCLUSION

Escherichia coli and *Klebsiella pneumonia* are the most common microorganisms found in SLE patients with infections at RSUP H. Adam Malik Medan. Antimicrobials resistant in SLE patients are Ampicillin, Norfloxacin, Doxycycline, and Clindamycin.

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