

Mortality Incidence of Systemic Lupus Erythematosus in Dr. Soetomo General Hospital Surabaya

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ABSTRACT

Introduction: Systemic Lupus Erythematosus (SLE) is a chronic systemic autoimmune disorder involving a multi-organ system. Fatal autoimmune causes usually characterize SLE with a high mortality rate. In 2012 the mortality rate of SLE in Dr. Soetomo General Hospital Surabaya was 22.9%. Recently covered data hasn't been published.

Methods: This study is a descriptive retrospective. The aim is to evaluate the mortality rate using the medical records of SLE patients. All SLE patients were admitted to Dr. Soetomo General Hospital Surabaya from May 2016 to May 2017. Patients' characteristics, disease activity, and causes of death are collected.

Results: There are a total of 176 patients, with 93.2% female, with a mean age of 29.5 and a mean duration of illness of 20 months. There were 39 deaths (22.2%), with the leading causes being a respiratory failure (33.3%), septic shock (28.2%), and undetermined (23.1%). Low levels of C3 (69.2%) and C4 (69.2%) are the most common immunology profile in dead patients. The therapy used the most is the corticosteroid pulse dose (46.2%).

Conclusion: It concludes that the decrease in mortality rate of SLE in Dr. Soetomo General Hospital, Surabaya is 0.7% from 2012 to 2017.

Keywords: Systemic Lupus Erythematosus, Mortality Incidence

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic systemic autoimmune disorder involving a multi-organ system. It has various clinical manifestations, from mild to fatal output. SLE is known as a fatal autoimmune. Therefore, the mortality rate is high. The mortality depends on the genetic factor, social economy, and environment (Indonesian Rheumatology Association, 2011). Nowadays, mortality in SLE patients is decreasing. This is because of improving therapy and early use of corticosteroids and immunosuppressive drugs. Patients in Dr. Soetomo General Hospital Surabaya are categorized as having a low social economy; therefore, the patient's obedience is low. This fact is estimated to trigger high mortality in Dr. Soetomo General Hospital Surabaya.

Mortality incidence of SLE in the world is still reputed as high. The mortality rate in Japan is 11.4% among 306 patients (Funauchi et al., 2007). In China, the mortality rate is 17.2% among 1372 patients (Xuebing et al., 2016). Meanwhile, the mortality rate in Malaysia is 20.2% among 494 patients (Yeap et al., 2001). In Europe, the mortality rate is 6.8% among 1000 patients (Cervera et al., 2003). In Dr. Soetomo General Hospital Surabaya, Yuliasih 2012 reported the mortality incidence was 22.9% from 153 patients (Yuliasih, 2012).

The death cause of SLE is divided into 2 phases. The early phase is because by the active SLE and infection, and the late stage is caused by atherosclerosis (Rees et al., 2012).

In the early phase, there is dysregulation of the immune system that cause extensive organ damage. If a significant organ is affected and there will be organ failure which can lead to death. In the early phase, the patient is given a high dose of an immunosuppressive drug, and the side effect is a risk of infection. Infection in immunocompromised patients is higher than in patients with normal immune systems. Mortality in the late phase is caused by the side effect of the drug, such as steroids which lead to atherosclerosis, and chronic inflammation leads to atherosclerosis. It explains why mortality of SLE in the late phase is caused by cardiovascular disease. Cohen and Li (1992) reported that the illness's duration and young age caused active SLE to become the essential factor in SLE mortality. Genetic factors and the environment also cause mortality in SLE (Cohen & Li, 1992). According to James (2014), some genes have a characteristic that is susceptible to SLE, and the interaction between genetic and autoimmune can lead to mortality. The environment increases SLE's severe organ damage and ultimately leads to mortality (Kamen, 2014). Mortality incidence of SLE in Indonesia is relatively high. Therefore author wanted to know the mortality incidence of inpatient SLE in Dr. Soetomo General Hospital Surabaya.

METHODS

This study was a descriptive retrospective study. It aimed to evaluate the mortality rate using medical records of SLE



patients. All SLE patients were admitted to Dr. Soetomo General Hospital Surabaya from May 2016 to May 2017. Patients' characteristics, disease activity, and causes of death are collected.

Criteria for inclusion in this study were patients' medical records with the main diagnosis of SLE and patients with death status recorded in medical records. The exclusion criteria in this study were patients' main diagnosis overlapped with connective tissue disease and mortality that was not recorded in the medical history.

This study obtained data from medical records of patients with the main diagnosis of SLE (ICD M32). Death status is recorded in patients' medical records. The patient's medical records recorded age, gender, and duration of illness. ANA test results were obtained from the patient's medical records, C3 was obtained from the patient's medical records and had low output (less than 50), and C4 was obtained from the patient's medical records and had low work (less than 20). Profile of therapy was obtained from patient's medical records, recorded use of corticosteroid pulse dose (500-1000 mg for three days continuously) and pulse dose (less than 500 mg), and immunosuppressive drug (cyclophosphamide, Sandimmune, and Imuran). Mortality incidence was measured using the mortality rate formula: total death patients divided by full patient times with 100%.

RESULTS

This study's total number of samples was 176 patients with SLE, and 39 patients were dead and inpatient in Dr. Soetomo Hospital, Surabaya, who met the inclusion and exclusion criteria.

$$\begin{aligned} \text{Mortality incidence} &= \frac{\text{total death patients}}{\text{total patients}} \times 100\% \\ &= \frac{39}{176} \times 100\% \\ &= 22\% \end{aligned}$$

Table 1. General Characteristics of The Patients

Characteristics	Case n (%) N=176	Death n (%) N=39
Age		
0 – 14 years	2 (1.1)	0 (0)
15 – 30 years	99 (56.3)	20 (51.3)
31 – 50 years	68 (38.6)	17 (43.6)
> 50 years	7 (4)	2 (5.1)
Mean age	29.5	31.7
Sex		
Male	12 (6.8)	5 (12.8)
Female	164 (93.2)	34 (87.2)
Duration of illness		
< 1 years	36 (20.5)	7 (17.9)
1 – 4 years	127 (72.2)	29 (74.4)
5 – 9 years	12 (6.8)	3 (7.7)
≥ 10 years	1 (0.5)	0 (0)
Mean duration	1.7	1.7

Table 2. Immunology Profile of The Patients

Characteristics	Case n (%) N=176	Death n (%) N=39
ANA test		
Available data	97 (55.1)	21 (53.8)
No data	79 (44.9)	18 (46.2)
Result		
< 10 (negative)	14 (14.4)	2 (9.5)
10 – 20 (intermediate)	9 (9.3)	1 (4.8)
> 20 (positive)	74 (76.3)	18 (85.7)
C3		
Available data	130 (73.9)	27 (69.2)
No data	46 (26.1)	12 (30.8)
Result		
< 50	60 (46.2)	15 (55.6)
50 - 120	62 (47.7)	11 (40.7)
> 120	8 (6.2)	1 (3.7)
C4		
Available data	126 (71.6)	27 (69.2)
No data	50 (28.4)	12 (30.8)
Result		
< 20	57 (45.2)	14 (51.9)
20 - 50	49 (38.9)	9 (33.4)
> 50	20 (15.9)	4 (14.8)

Table 3. Therapy Profile of The Patients

Characteristics	Case n (%) N=176	Death n (%) N=39
Corticosteroid		
Pulse dose	20 (11.7)	18 (46.2)
Non pulse dose	152 (86.7)	18 (46.2)
Immunosuppressive drug		
Cyclophosphamid	70 (39.8)	17 (43.6)
Sandimmun	74 (42.0)	13 (33.3)
Immuran	42 (23.9)	14 (35.9)

Table 4. Causes of Death

Causes of death	Death n (%) N=39
Septic shock	11 (28.2)
Respiratory failure	13 (33.3)
Intracranial haemorrhage	2 (5.1)
Cardiovascular event	4 (10.3)
Undetermined	9 (23.1)

Among 1483 outpatients with type 2 diabetes mellitus, the patient's medical record data about the duration of type 2 diabetes mellitus can be obtained in 220 patients. The number of patients that suffers type 2 diabetes mellitus with less than five years are 79 patients (35.9%), more than five years are 134 patients (61%), and no previous history of diabetes mellitus or just knowing the disease when visited Dr. Soetomo Hospital are seven patients (3.1%).

DISCUSSION

SLE is mainly found in patients of productive age. In this study, we obtained the mean age in dead patients is 31.7 years. The mean age in China is slightly above 38 years (Feng et al., 2011). In the Philippines, the mean age is 28.5 years; in Malaysia, the mean age is 26.9 years (Osio-Salido & Manapat-Reyes, 2010). The data above shows that the mean age of total and death patients is slightly different. The difference may be related to genetic factors, race and ethnicity, therapy, and social culture.

SLE is mainly known in the female sex. We obtained 34 dead patients with five female and 29 male patients, so the ratio is 7: 1. In Malaysia, the balance between female and male deceased patients is 6:1 (Teh & Ling, 2013). In China, the ratio between females and males in dead patients is 9:1 (Feng et al., 2011). From the data, we conclude that SLE is mainly found in the female sex. Wasef explained that it is related to the estrogen hormone (Wasef, 2004).

We obtained the duration of illness in total patient and death patient is same, that is 1 to 4 years, with the mean duration in 1.7 years. In Malaysia, the duration of illness is one year. In China, the duration of illness is two years (Feng et al., 2011). Singapore reported the duration of illness is 14 years. And in India, the duration of the illness varies from monthly to 30 years (Osio-Salido & Manapat-Reyes, 2010). This fact explained that there could be differences in the duration of illness. It is caused by factors such as education, disease severity, social culture, reference system, information from the internet, and social organization.

SLE is a systemic autoimmune disease. The presence of the immune complex in the organ causes inflammation and tissue damage. One of the classifications of SLE is the presence of a positive ANA test and C3 and C4 low-level complement. In this study, most patients have a high titer for the ANA test, and low levels of C3 and C4, in total patients and dead patients. Fernando dan Isenberg reported that 95% of patients with SLE have a positive result on the ANA test, and the result of C3 and C4 is normal to a low level (Fernando & Isenberg, 2005). This shows that the dead patients in this study have severe SLE.

The therapy used here is a corticosteroid and immunosuppressive drug. Maame and Caroline explained that a corticosteroid pulse dose is used when the nonpulse dose does not respond well or if the patients have severe manifestation (Amissah-Arthur & Gordon, 2010). In this study, 152 patients got a nonpulse corticosteroid dose, and 20 got a corticosteroid pulse dose. But 90% of patients that got corticosteroid pulse dose recorded death. And immunosuppressive cyclophosphamide was used the most, yet the patients still died. This shows that SLE in most patients here is severe. Because after using corticosteroid pulse dose and cyclophosphamide, the patients still die. In China, cyclophosphamide is mainly used with high doses of corticosteroids for severe SLE or with fatal manifestations (Xuebing et al., 2016).

In this study, the definite cause of death is unknown. For the septic shock, the infection data source was not recorded; therefore, it is hard to evaluate the cause of death. In Malaysia, organisms that cause death in SLE were *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Salmonella typhi*, and *Pseudomonas aeruginosa* (Teh & Ling, 2013). Patients with intracranial hemorrhage have a history of thrombocytes less than 5000 or are categorized as severe thrombocytopenia. And all patients with cardiovascular events have been diagnosed with SLE since 2014. But the cause of cardiovascular events itself is unknown. In Japan, the causes of death in SLE are cardiovascular disease, bronchopneumonia, renal failure, gastrointestinal hemorrhage, malignancy, and others (Funauhi et al., 2007). In China, the causes of death in SLE are infection, neuropsychiatric involvement, renal failure, pulmonary disease, and cardiovascular disease.

The limitation in this study is that we used secondary data, so there are many incomplete data. The cause of infection can not be evaluated because no data is recorded. And this study is not a cohort study.

CONCLUSION

The decrease in the mortality rate of SLE in Dr. Soetomo General Hospital, Surabaya, was 0.7% from 2012 to 2017. 39 (22.2%) of 176 SLE patients were recorded dead, with an age range of 15-30 years (51.3%); mostly were female sex (87.2%) and diagnosed with SLE for 1-4 years (74.4%). Mostly the cause of death in patients is a respiratory failure (33.3%). Low levels of C3 (69.2%) and C4 (69.2%) are the most common immunology profile in dead patients. Therapy that is used the most in corticosteroid pulse dose (46.2%).

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

ETHICS CONSIDERATION

This research was ethically cleared and approved by Ethical Committee for Health Research of Dr Soetomo General Academic Hospital certificate no.0201/KEPK/IV/2018.

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AUTHOR CONTRIBUTION

All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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