Correlation between ESBL-Producing Bacteria Infection with Sepsis Severity of Patient in Medical Ward of Internal Medicine Department Dr. Soetomo General Hospital in 2016

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A B S T R A C T

Introduction: Sepsis is life-threatening condition that begins with infections that trigger pro-inflammation overresponse. Delaying antibiotic treatment in sepsis can cause serious condition. In ESBL-producing bacteria, the antibiotic resistance is common and it might cause harm to sepsis patient. This research aims to analyze the correlation between infections of ESBL-producing bacteria with sepsis severity.

Methods: This study was observational analytic on sepsis patient in Internal Medicine Ward of Dr. Soetomo General Hospital. The data were taken from medical records of the patient. The severity of sepsis was based on Surviving Sepsis Campaign 2012.

Results: A total 72 sepsis patients were included in this study, which consist of 40 patients with non-producing ESBL GNB and 32 patients with ESBL-producing bacteria. The most common bacteria in ESBL infection is *Escherichia coli* ESBL+ (75%) and non ESBL infection *is Acinetobacter baumanii* (27.5%). Septic shock is more common in patient with ESBL-producing bacteria (53.1% vs 22.5%). The correlation between ESBL infection and sepsis severity is significant and the power of correlation is low (p = 0.048; r = 0.234).

Conclusion: There is a correlation between ESBL-producing bacteria infection with sepsis severity and the power of correlation is low (p = 0.048, r = 0.234).

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Introduction

Sepsis is a condition caused by immune—overresponse due to infection. In sepsis, leukocyte is activated and pro-inflammatory response becomes overwhelmed.[1]

Blanco et al., (2008)[2] stated that the most prevalent causative bacteria was gram negative bacteria (50%) with Escherichia coli as the leading cause (37.2%) followed by Pseudomonas aeruginosa (20.9%) and Acinetobacter baumanii (10.9%). A study by Peirovifar et al., (2014)[3] concluded that the most prevalent ESBL-producing bacteria that cause sepsis in neonates was Klebsiella pneumoniae. Other research stated that ESBL-producing enterobacteriaceae infection was more fatale compared to the non ESBL (47.3% vs 22.4%), the treatment cost was also higher (215€.95 vs 115€). About 40-60% of the treatment cost was spent on antibiotics[4].

A study conducted by Lee et al., (2017)[5] showed that sepsis patient caused by ESBL-producing enterobacteriaceae happened more to fall into septic shock (26.2%) compared with sepsis patient due to non-ESBL producing (17.2%). Peirovifar et al., (2014)[3] also stated that 34 from 38 sepsis patient that die in Iran were caused by ESBL-producing bacteria. Blomberg et al., (2005)[6] also concluded that infections caused by ESBL-producing bacteria is more fatale compared to non ESBL-producing bacteria (71% vs 39%). The result of previous research indicates that the ESBL-producing bacteria infection caused more severe sepsis compared to the non ESBL bacteria.

Sepsis criteria has changed for several times since 1991. The 1991 SCCM/ACCP Consensus Conference divided sepsis into three groups, sepsis, severe sepsis, and septic shock[7]. Sepsis criteria was revised in 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference[8] and revised again in Surviving Sepsis Campaign in 2012 but still divides sepsis into three groups[9]. The latest sepsis criteria was made in 2016 by The Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) and divide sepsis severity into two groups, sepsis and septic shock[10.]

Methods

This study was observational analytic using cross-sectional design. The purpose of this study was to analyze the correlation between ESBL-producing bacteria infection with sepsis severity, particularly in Dr. Soetomo General Hospital. This study also showed the distribution of gram negative bacteria that causes sepsis and also the severity of sepsis within each group.

The population of this study was all inpatient sepsis patients in Internal Medicine Ward of Dr. Soetomo General Hospital from 1 January 2016 to 31 December 2016. Criteria for inclusion in this study was sepsis patient, hospitalized in Internal Medicine Ward during 1 January 2016 to 31 Desember 2016, culture has shown gram negative non ESBL or ESBL-producing, and the medical record is complete. The sepsis criteria used in this study was based on Surviving Sepsis Campaign 2012 that put sepsis into 3 classes (sepsis, severe sepsis, and septic shock). This criteria was chosen since it differentiated sepsis into more specific classes compared to the latest sepsis criteria that only divided sepsis into septic and septic shock.

The data of this study were obtained from medical records of sepsis patient that match the inclusion criteria. Data were analyzed using SPSS 23. Statistical analysis of correlation between the bacteria and sepsis severity was done by rank spearman test.

This study can be used as a reference for the upcoming or other studies in other centre about sepsis and also increase the awareness of sepsis and proper use of antibiotics.

Results

This study enrolled 72 sepsis patients with culture-positive isolate indicating gram negative bacteria infection (40 patients) and ESBL-producing bacteria infection (32 patients). The most prevalent bacteria for the non-producing ESBL gram negative bacteria was Acinetobacter baumanii (27.5%), followed by Escherichia coli (20%) and Klebsiella pneumoniae (17.5%). The most common ESBL-producing bacteria was Escherichia coli ESBL+ (75%), followed by Klebsiella pneumoniae ESBL+ (21.9%) and Klebsiella oxytoca (3.1%). The result is described in table 1.

Table 1. Distribution of bacteria from sepsis patient.

Bacteria	Frequency (n)	Percentage (%)
Non-producing ESBL GNB		
Acinetobacter baumanii	11	27,5
Escherichia coli	8	20
Klebsiella pneumonia	7	17,5
Burkholderiacepacia	2	5
Pseudomonas aeruginosa	2	5
Citrobacter freundii	1	2,5
Empedobacter brevis	1	2,5
Enterobacter aerogenes	1	2,5
Enterobacter cloacae	1	2,5
Pantoea agglomerans	1	2,5
Proteus vulgaris	1	2,5
Providencia rettgeri	1	2,5
Providencia stuartii	1	2,5
Pseudomonas spp	1	2,5
Raoultella orthinolytica	1	2,5
Total	40	100
ESBL-producing bacteria		
Escherichia coli ESBL +	24	75
Klebsiella pneumoniae ESBL+	7	21,9
Klebsiella oxytoca ESBL+	1	3,1
Total	32	100

Source: research data, processed

From 72 patients, we put the patient into 3 classes (sepsis, severe sepsis, and septic shock) based on Surviving Sepsis 2012 criteria. In non ESBL-producing gram negative bacteria group, the most common condition was severe sepsis (52.5%) and in the ESBL-producing bacteria group, the most common condition was septic shock (53.1%). The correlation between ESBL-producing bacteria infection with sepsis severity was analyzed using rank-spearman method. The p-value is 0.048 and the correlation coefficient is 0.234. This result stated that there is a low correlation between ESBL-producing-bacteria infection with sepsis severity. The result is described in table 2.

Table 2. Rank-spearman correlation test.

Group	Sepsis Severity			r*	p**
	Sepsis	Severe sepsis	Septic shock		
Non-producing ESBL GNB	10 (25.0%)	21 (52.5%)	9 (22.5%)	0.234	0.048
ESBL-producing bacteria	7 (21.9%)	8 (25%)	17 (53.1%)		
Total	17 (23.6%)	29 (40.3%)	26 (36.1%)		

Source: research data, processed

* correlation coefficient

* correlation between groups, significant in <0.05

Discussion

Distribution of bacteria in sepsis patient

The most prevalent bacteria for the non-producing ESBL gram negative bacteria was *Acinetobacter baumanii* (27.5%), followed by *Escherichia coli* (20%) and *Klebsiella pneumoniae* (17.5%). The result of this study is different from several studies. Blanco, *et al.*[2] stated that *Eschericia coli* is the most common gram negative bacteria that caused sepsis and *Acinetobacter baumanii* was at the fourth position. Lochan *et al.,*[11] also stated that *Acinetobacter* is the third most common gram-negative bacteria that cause sepsis, below *Escherichia coli* and *Klebsiella pneumoniae.* This result can be different from two studies above because those two studies did not differ between ESBL and non ESBL-producing gram negative bacteria. In the other hand, Khanna *et al.,* showed that 46.2% of *Eschericia coli* and 55.5% of *Klebsiella pneumoniae* in hospitalized patient are found to be ESBL+[12].

Acinetobacter baumanii is an anaerobic-gram-negative-bacteria that is likely to cause nosocomial and opportunistic infections. This bacteria is also stated as one of the leading cause of sepsis and cause a high mortality rate in ICU patients[13]. *Acinetobacter baumanii* is quite alarming since they are likely to be resistant to many antibiotics. The high infection number of *Acinetobacter baumanii* in this study could also indicate that nosocomial infection was also high and it could be dangerous.

In ESBL-producing bacteria group is *Escherichia coli ESBL+* (75%). The result of this study is almost the same with the study conducted by Shaikh *et al.,*[14] and Sakellariou *et al.,*[15] that also reported that the most prevalent ESBL-producing bacteria was also *Escherichia coli ESBL+*. Different results came from Kuntaman *et al.,*[15] and Dewan *et al.,*[16] which showed that *Klebsiella pneumoniae ESBL+* is the most common bacteria that is isolated from the patients.

Correlation between ESBL-producing bacteria infection and sepsis severity

This research concluded that there is a significant correlation (p-value 0.048) between ESBL-producing bacteria infection and severity and the power of correlation is low (correlation coefficient 0.234). This result is quite similar with other studies. A study conducted by Lee *et al.,* (2017)[5] showed that sepsis patient caused by ESBL-producing *enterobacteriaceae* happened more to fall into *septic shock* (26.2%) compared with sepsis patient due to non - ESBL producing *enterobacteriaceae* (17.2%). Peirovifar *et al.,* (2014)[3] also stated that 34 from 38 sepsis patient that die in Iran were caused by ESBL-producing bacteria. Blomberg *et al.,* (2005)[6] also stated that infections caused by ESBL-producing bacteria is way more fatale than infection caused by non ESBL-producing bacteria (71% vs 39%). The result of previous research indicated that the ESBL-producing bacteria infection caused more severe sepsis compared to the non ESBL bacteria. The result of this study also matched the theory that stated the resistance to antibiotics can raise the risk of sepsis patient to fall into worse condition such as septic shock or even death.[9]

Conclusion

There is a correlation between ESBL-producing bacteria infection with sepsis severity and the power of correlation is low (p = 0.048, r = 0.234).

CONFLICT OF INTEREST

The author stated there is no conflict of interest in this study.

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