Original Article

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Predictors of In-Hospital Mortality in Patients with Infective Endocarditis: A Single-Center Study

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Abstract

Background: Infective endocarditis remains a life-threatening condition with high in-hospital mortality, necessitating identification of predictive clinical factors.

Objective: To identify predictors of in-hospital mortality in infective endocarditis (IE) patients.

Methods: This single-center retrospective study included 88 patients with IE aged ≥ 18 years treated at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, between September 2019 and May 2023. During hospitalization, data regarding clinical characteristics, blood cultures, and clinical outcomes were assessed to identify the predictors of in-hospital mortality. Data were analyzed using chi-square and binary logistic regression.

Results: Among 88 patients with IE, the majority were male (56.8%) and aged < 60 years old (78%). More than two-thirds of patients had valvular heart disease. During treatment, 22 patients (25%) underwent cardiac surgery, and the total in-hospital mortality rate was 35.2%. Although not statistically significant, in-hospital mortality rate was lower in operated patients (22.7% vs 39.4%). In multivariate analysis, septic shock was the only significant predictor of in-hospital mortality (OR 40, 95% CI: 4.7–339, p<0.001)

Conclusion: Septic shock is a strong predictor of in-hospital mortality among patients with infective endocarditis. Invasive management by cardiac surgery does not significantly decrease the mortality risk.

Keywords: Infective endocarditis, in-hospital mortality, septic shock

Introduction

Infective endocarditis (IE) is a rare yet potentially life-threatening disease which involves the endocardial surface.[1] Recent data shows that the annual incidence of infective endocarditis (IE) worldwide is estimated to be 3-10 cases per 100,000 persons per year, with a continual increase observed each year.[2,3] In spite of the advancements in diagnostic capability, enhanced antimicrobial treatments, and improved techniques for surgical intervention in the modern era, infective endocarditis continues to be a dynamically developing condition with sustained high rates of mortality and morbidity.[4]Current evidence suggests an in-hospital mortality rate of around 20%, with a 6-month mortality rate of approximately 30%, rising to as high as 51% at 10 years, even with modern treatment.[5–7]

The epidemiological features of IE have shifted lately due to the changes in medical approaches and demographic changes.[1]

Previous studies have revealed significant differences in developing countries, characterized by higher rates of culture-negative infective endocarditis (IE), zoonotic infections, and increased mortality, with considerable regional variations. However, data on IE in developing countries, especially in South-East Asia, remain scarce.[2] There is a lack of information regarding the incidence of Infective Endocarditis (IE) in Indonesia, as well as information on mortality rates and factors influencing the mortality. Analyzing mortality rates and identifying predictors for fatal outcomes is crucial for recognizing modifiable factors and understanding treatment patterns to enhance overall outcomes. This approach aids in recognizing patients at the highest risk of death, guiding the necessity for escalated care interventions. Therefore, this study aimed to describe the clinical characteristics of patients with IE and to identify predictors of in-hospital mortality.

Methods

This was a retrospective and single-center study that included all consecutive IE patients aged ≥ 18 years old hospitalized in Dr. Hasan Sadikin General Hospital between September 2019 to May 2023. The total of 88 patients diagnosed with definite and possible IE in accordance with the modified Duke criteria were included in this study. Demographic data, clinical characteristics, microbiological findings, as well as surgical procedures and hospitalization outcomes were retrieved from the patient's medical records.

A multivariate analysis was performed on factors with a p-value of <0.05 in the univariate analysis to find the independent predictor of in-hospital mortality. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics software, version 27. This study was approved by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia (Ethical approval number: LB.02.01/X.6.5/101/2020).

Results

Between September 2019 until May 2023, there were 88 cases of definite and possible IE that were hospitalized in RSUP Dr. Hasan Sadikin based on modified Duke Criteria. Among the participants, 56.8% of the participants (50 patients) were male, while the remaining 43.2% (38 patients) were female. with the mean age was 43.47 ± 16.92 years. Baseline characteristics of the patients are summarized in Table 1.

Most patients (95.5%) had native valve involvement. Of all patients, 28.4% of patients exhibited congenital heart disease. Additionally, over two-thirds of the patients (68.2%) had underlying valvular heart disease, with only 9.1% suffering from rheumatic heart disease. Diabetes mellitus affected 4.5% of patients, while 20.5% were diagnosed with hypertension. Moreover, 9.1% of patients on hemodialysis therapy, and 5.7% were identified as intravenous drug users.

In this study, the predominant complication observed among the subjects was heart failure, affecting 51.1% of the cases. Other complications included stroke in 17%, septic shock in 15.9%, glomerulonephritis in 10.2%, vasculitis in 4.5%, spondylodiscitis in 3.4%, and pulmonary embolism in 2.3% of the cases.

A total of 67% of the cases exhibited negative blood cultures. The most frequently isolated microorganisms were Streptococci (12.5%) and coagulase-negative staphylococci (8%).

The in-hospital mortality rate in this study was 35.2% (31 patients). Among the 22 patients who underwent cardiac surgery, 5 experienced in-hospital mortality, while 17 survived. For the 66 patients treated solely with medical treatment, 26 experienced in-hospital mortality, with 40 patients surviving. Although not statistically significant, in-hospital mortality rate was lower in operated patients (22.7% vs 39.4%) shown in Table 3. Univariate analysis showed that diabetes mellitus, septic shock, and spondylodiscitis were significantly associated with in-hospital mortality. However, multivariate analysis (Table 2) identified only septic shock as an independent predictor of in-hospital mortality (OR 40, 95% CI 4.7–339, p<0.001).

Discussion

In the current study, a notable finding indicates that septic shock emerged as the significant predictor in-hospital mortality. Among the 88 patients included, 14 (15.9%) experienced septic shock, with only one surviving. This finding aligns with Marques *et al*., where 20% of infective endocarditis (IE) cases were associated with septic shock, attributing one-third of the mortality.[8] Similarly, Ayad *et al*. demonstrated a statistically significant association between septic shock and mortality (p=0.01).[9]

Table 1 Characteristics of Patients with Infective Endocarditis and Their Association with In-Hospital Mortality (Univariate Analysis)

Characteristics	Total (n=88)	Univariate		
		Died (n=31)	Survived (n=57)	p-value
Age >60 years	19 (21.6%)	9 (29%)	10 (17.5%)	0.327
Sex				
Male	50 (56.8%)	18 (58.1%)	32 (56.1%)	1.000
Female	38 (43.2%)	13 (41.9%)	25 (43.9%)	
Predisposing conditions				
Prosthetic valve	4 (4.5%)	2 (6.5%)	2 (3.5%)	0.611
Congenital heart disease	25 (28.4%)	5 (16.1%)	20 (35.1%)	0.102
Valvular heart disease	60 (68.1%)	25 (80.6%)	35 (61.4%)	0.107
Rheumatic heart disease	8 (9%)	3 (9.7%)	5 (8.8%)	1.000
Diabetes mellitus	4 (4.5%)	4 (12.9%)	0 (0%)	0.013
Hypertension	18 (20.4%)	7 (22.6%)	11 (19.3%)	0.93
On Hemodialysis	8 (9%)	5 (16.1%)	3 (5.3%)	0.124
IV drug users*	5 (5.7%)	3 (9.7%)	2 (3.5%)	0.34
Complications				
Heart failure	45 (51.1%)	17 (54.8%)	28 (49.1%)	0.772
Septic shock	14 (15.9%)	13 (41.9%)	1 (1.8%)	<0.001
Glomerulonephritis	9 (10.2%)	5 (16.1%)	4 (7%)	0.269
Spondylodiscitis	3 (3.4%)	3 (9.7%)	0 (0%)	0.041
Vasculitis	4 (4.5%)	3 (9.7%)	1 (1.8%)	0.123
Pulmonary embolism	2 (2.27%)	1 (3.2%)	1 (1.8%)	1.000
Stroke	15 (17%)	7 (22.6%)	8 (14%)	0.471
Culture Findings				
Staphylococcus aureus	1 (1.1%)	0 (0%)	1 (1.8%)	1.000
CoNS*	7 (7.9%)	2 (6.5%)	5 (8.8%)	1.000
Streptococci	11 (12.5%)	4 (12.9%)	7 (12.3%)	1.000
Enterococci	2 (2.27%)	1 (3.2%)	1 (1.8%)	1.000
Gram negative bacteria	4 (4.5%)	3 (9.7%)	1 (1.8%)	0.123
Gram positive bacteria	1 (1.1%)	0 (0%)	1 (1.8%)	1.000
Negative culture	59 (67%)	20 (64.5%)	39 (68.4)	0.893
Treatment				
Cardiac surgery	22 (25%)	5 (16.1%)	17 (29.8%)	0.246

Notes: IV: intravenous; CoNS: *coagulase-negative staphylococci*

Table 2 Multivariable Logistic Regression Analysis of Predictors for In-Hospital Mortality in Patients with Infective Endocarditis

Variable	p-value	Odds Ratio (OR)	95% Confidence Interval (CI)
Septic shock	<0.001	40	4.7-339
Spondylodiscitis	0.999	1	
Diabetes mellitus	0.999	1	

Table 3 Management Type and In-Hospital Mortality in Patients with Infective Endocarditis

Treatment	In-hospital Death		Total
	Yes (%)	No (%)	
Cardiac surgery	5 (22.7)	17 (77.3)	22
Only medical treatment	26 (39.4)	40 (60.6)	66

Septic shock remains a concerning and potentially fatal condition, with mortality rate often exceeding 40%. While infective endocarditis (IE) primarily affects the inner surface of the heart, particularly the heart valves, it also manifests as a bloodstream infection, clinically characterized by the presence of sepsis-related signs and symptoms. With IE being the primary site of infection, the development of sepsis can lead into subsequent progression to septic shock. The mortality of septic shock depends on many factors, for instance the type of organism that causes severe sepsis.[10] A large meta-analysis of 510 studies reported that gram-negative bacteremia was associated with a higher mortality compared with gram-positive bacteremia. The most common bloodstream infections were due to coagulase-negative Staphylococcus and E. coli.[11]

The observed in-hospital mortality rate of 35.2% in this study is higher than the reported range in the literature (15–32%).[12–17] Despite the inherent surgical risks in IE patients, current evidence indicates that surgical intervention may confer a survival advantage of up to 20% in the first year. The recent guidelines recommend surgical intervention for patients with acute infective endocarditis, especially in those experiencing heart failure, uncontrolled infection, or presenting a high risk or established embolism.[18] Notably, this center deviates from the approach seen in other institutions, where cardiac surgery is employed in 40-69.7% of cases.[13,14,16] At this center, cardiac surgery is conducted in only 25% of cases. Some of the patients with guideline-recommended indications for surgery are not actually operated. Among the reasons given are poor prognosis irrespective of treatment, hemodynamic instability, death before surgery, and refusal for surgery.

In this study, although management by cardiac surgery was associated with a lower mortality rate (22.7% vs 39.4%), it was not statistically significant in univariate analysis, and management by cardiac surgery did not remain as a factor of better prognosis in the multivariate analysis (OR 0.452, 95% CI 0.149-1.377, p=0.246). This result aligns with the findings of Delahaye *et al*. in 2007, which stated that although surgery showed a lower mortality rate (14.4% vs 19.3%), this difference did not reach statistical significance in the univariate analysis. Furthermore, in their multivariate model, surgery did not remain a significant factor for a better prognosis (OR: 0.723, 95% CI 0.388-1.349).[19] However, this contrasts with findings by Marques *et al*. study in Italy, which indicated that cardiac surgery served as a main protective factor against mortality.[8] Moreover, Krajinovic *et al*. research in 2018 demonstrated that management by cardiac surgery had a favorable impact not only in in-hospital mortality but also on the one-year follow-up of IE patients with sepsis and septic shock. However, among patients without sepsis, there was no significant difference between those undergoing cardiac surgery and those receiving only medical treatment.[10]

The key to diagnosing infective endocarditis lies in identifying the responsible microorganisms, primarily through blood

cultures. This process is essential for promptly initiating targeted antimicrobial therapy specific to the identified organism. Unfortunately, this study revealed that microbial presence was not identified in two-thirds of the patients. Similar to the study done by Zhang *et al*., blood cultures were negative in 56.7% of cases.[20] A potential reason for the observed low detection rate in this study could be attributed to the administration of antibiotics before blood collection, fastidious slow-growing microorganisms or by truly non-cultivable intracellular bacteria, and errors during sample collection.[21–23]

This study holds strength as research in infective endocarditis is relatively scarce, particularly within Indonesia. This study also stands as one of the few focusing on the predictors of in-hospital mortality in patients with infective endocarditis in Indonesia. However, this research presents certain limitations that warrant consideration. Firstly, its execution within a tertiary care center introduces the possibility of referral bias, potentially skewing the findings toward more severe cases or specific demographics within that setting. Additionally, the sample size in this study was relatively limited, which could impact the generalizability of the results to broader populations. Another constraint arises from its retrospective design, relying solely on available data within medical records, which may lack comprehensive information or have inherent inconsistencies. Moreover, this study did not perform specific analyses related to sex or gender differences. As such, potential variations in clinical outcomes between male and female patients were not explored and remain an area for future investigation.

In conclusion, despite advances in antimicrobial and surgical therapies, IE remains a challenging condition with high in-hospital mortality. In this study, in-hospital mortality rate remained high (35.2%). Septic shock was a strong predictor of in-hospital mortality in this study, and independently increased the risk of in-hospital mortality of infective endocarditis patients. Nevertheless, invasive management by cardiac surgery did not significantly decrease the mortality risk.

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