



The Impact of Multidrug-Resistant Organisms Infection on Outcomes in Burn Injury Patients at Sanglah General Hospital, Bali

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Abstract

BACKGROUND: Research related to the impact of multidrug resistant organisms (MDRO) infection on clinical outcomes in burns is still limited.

AIM: This study evaluated the effect of MDRO infection on morbidity and mortality of burn patients.

METHODS: A single-center retrospective cohort study was conducted on burn patients admitted to the burn unit of Sanglah General Hospital, Bali, between 2018 and 2020. MDRO patients were described as those who had at least one positive MDRO culture. All other patients were included in the non-MDRO group. Measurement and analysis included mortality and five indicators of morbidity: length of stay, duration of antibiotic therapy, sepsis, pneumonia, and acute kidney injury (AKI).

RESULTS: Significant associations of MDRO infection were found for duration of antibiotic therapy (0 vs. 7 days), sepsis (odds ratio [OR] 13.90 [95% Confidence interval (CI) 95% 2.88–67.10]), pneumonia (OR 12.67 [95% CI 3.26–49.23]), and mortality (OR 9.75 [95% CI 2.00–47.50]). No significant association was found for the length of stay and the incidence of AKI. Multivariate analysis found that MDRO infection increased risk of sepsis (OR 36.53 [95% CI 2.05–652.45], pneumonia (OR 10.75 [95% CI 1.87–61.86]) and mortality (OR 57.09 [95% CI 1.41–2318.87]). Multivariate analysis of MDRO infection with duration of antibiotic therapy found no independent variables that were significantly related.

CONCLUSION: These research findings suggest that MDRO infections are associated with increasing length of antibiotic treatment, sepsis, pneumonia, and mortality in burn patients.

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Introduction

Burn cases have increased every year with high morbidity and mortality rates, especially in developing countries. Burns result in high morbidity and mortality rates with significant physical, psychological, and economic impacts.

With the development and advancement of burn management over the past 50 years, infection remains the leading cause of death in burn patients. Research conducted over the past decade has shown that infection is linked to 42 percent to 65 percent of burn deaths [1]. According to the 2016 National Burn Repository Report in the United States, infection cause 7 out of 10 burn complications, pneumonia, urinary tract infections (UTIs), and cellulitis, ranking first [2]. Mortality increased twofold in burn patients with infection than burns without infection [3], [4].

Because of the compromised immune system of burn patients, infection control and prevention can be complicated. Reduced T-cell function and the disruption of the defensive skin layer due to burns, resulting in infections that can quickly spread to patients [1], [5]. Infection risk in burn patients is increased by prolonged care and intensive devices such as urinary catheters and central venous access [6].

The duration of treatment in burn patients increases the risk of infection due to Multi-Drug Resistance Organism (MDRO). The longer the patient is treated, the higher the patient's chances of suffering from an infection due to MDRO bacteria [7], [8]. Apart from the length of stay, prophylactic antibiotics, insufficient eschar excision, and intrusive equipment raise the risk of MDRO bacteria infection [8], [9], [10]. MDRO bacteria are resistant to various kinds of antibiotics that are used today. The development of new antibiotics is still not being developed so that the presence of MDRO bacteria

in patients with burns requires special attention [8]. Early exposure of burns to MDRO bacteria can significantly accelerate the progression of infection in burns [7].

Many studies have identified the distribution of MDRO bacteria in burn patients, but few researchers have investigated the impact of MDRO bacteria on morbidity and mortality in burn patients. This study investigated the differences in morbidity and mortality in burn patients infected with MDRO bacteria at the national burn unit referral hospital for the east part of Indonesia.

Method

A single-center retrospective study was performed on pediatric and adult burn patients admitted to the burn unit of Sanglah General Hospital Bali between 2018 and 2020 after receiving permission from the institutional review board. Sampling was done by consecutive sampling and stopped when it meets the minimum criteria for the number of samples. Patients with total burn surface area (TBSA) 20% or more and who have been examined for wound bed culture or blood culture or urine culture during treatment were included. MDRO patients were described as those who had at least one positive MDRO culture.

Age, sex, burn mechanism, admission time, percentage of TBSA, depth of burn, inhalation injury, length of stay, duration of antibiotic therapy, tangential excision, and skin graft procedure were all taken from the electronic medical record. Furthermore, we collected data on the incidence of sepsis, acute kidney injury (AKI), pneumonia, and mortality.

Clinical parameters definition

TBSA was calculated using the Rule of Nine by Wallace. The total number of burns depth divided into partial-thickness burns and full-thickness burns recorded in the medical record. According to the International Expert Proposal for Interim Standard Definitions for Acquired Resistance, MDRO is classified as a bacterial isolate resistant to at least one antibiotic from three antibiotic classes [11]. The period between admission and discharge from the hospital, or death, was known as length of stay. Duration of antibiotic therapy is defined as the duration of antibiotic use from the beginning of antibiotic use in the patient until it was declared stopping or the patient died. Tangential excision is defined as removing eschar tissue in full-thickness burns and coverage by split-thickness skin graft (STSG). Tangential excision is divided into two types, early tangential excision (performed in 1 week after the burn incident) and delayed tangential excision (performed 1 week after the burn incident). Inhalation trauma is defined as the onset of inhalation distress due to exposure to heat irritants to

the respiratory tract, as recorded in the medical record. Sepsis was defined according to the 2007 American Burn Association Consensus Conference [12]. Pneumonia is defined according to the definition of pneumonia from the Infectious Diseases Society of America [13]. AKI Network criteria are used to review the incidences of AKI [14]. The comorbid disease is a history of chronic disease suffered by the patient before being exposed to burns. MDRO patients were described as those who had at least one positive MDRO culture. All other patients were included in the non-MDRO group.

Microbiology

Blood culture is performed if the patient is suspected of having sepsis. When the patient is clinically suspected of having pneumonia, quantitative alveolar lavage bronchoscopy is performed. When a patient is suspected of developing a UTIs, a urine culture is done. In cases of possible burn skin infection, aerobic and anaerobic wound cultures were conducted. Many of the cultures were carried out according to normal procedures. All cultures were performed according to standard protocols. The antibiotic resistance of all cultured pathogens was determined after the bacterial strains were identified.

Statistical analysis

The statistical analysis was conducted using SPSS 26.0. Descriptive analysis was performed to assess age, sex, TBSA, depth of burn mechanism burns, culture results, the incidence of inhalation trauma, sepsis, pneumonia, AKI, and comorbid diseases. It is presented as mean if it is normally distributed; if it is not normally distributed, it is presented in the median, with the maximum and minimum values. The relationship between MDRO and non-MDRO bacteria with sepsis, AKI, and pneumonia was analyzed using chi-square analysis or Fischer exact. The relationship between MDRO bacteria and non-MDRO bacteria in burns with the length of stay and duration of antibiotic therapy was analyzed using Mann-Whitney analysis because data distribution was not normal. For the length of stay and duration of antibiotic use, dichotomous categorization was carried out with median as the cutoff point for multivariate analysis. Multiple logistic regression test was performed to determine the magnitude of the influence of the MDRO infection compared to others variable on the occurrence of the sepsis, AKI, pneumonia, and mortality.

Results

Over the 3 years, 271 patients were admitted, and 70 patients met the inclusion criteria. After met the

minimum requirement of sample size for the cohort study, we divide 35 patients with MDRO infection and 35 patients with non MDRO infection. Table 1 summarizes the baseline characteristic of research samples.

Table 1: Baseline characteristic of research samples

Variables	Value
Sex	
Male	52 (74.3)
Female	18 (25.7)
Age	35.61 (\pm 20.60)
Comorbidity	4 (5.71%)
Mechanism of Burn	
Fire	41 (58.6%)
Non-Fire	29 (41.4%)
Admission time	
<8 h	40 (57.1%)
>8 h	10 (42.9%)
TBSA (%), median (IQR)	29.00 (23.38–40.00)
Depth of burn	
Partial-thickness	6 (8.6%)
Full-thickness	64 (91.4%)
Inhalation Trauma	13 (18.6%)
Tangential Excision and Skin Grafting	
Without tangential excision	16 (22.8%)
Early tangential excision and skin graft	27 (38.6%)
Delayed tangential excision and skin graft	27 (38.6%)
Length of stay (days), median (IQR)	20.00 (14–32.5)
Duration of antibiotic therapy (days), median (IQR)	6.00 (0.00–10.00)
Sepsis	18 (25.7%)
Pneumonia	22 (31.4%)
AKI, n (%)	7 (10.00%)
Mortality	15 (21.4%)

TBSA: Total burn surface area; IQR: Interquartile range; AKI: Acute kidney injury.

Table 2 shows the various types of bacteria found in MDRO and non-MDRO patients. The majority of cultured bacteria (80 %) were Gram-negative, with MDRO accounting for 59 % of Gram-negative bacteria. *Acinetobacter baumannii* was the most common MDRO (37.1%)

Table 2: Gram-negative and gram-positive bacteria that are most often cultured

	Non-MDRO patients (%) (n = 35)	MDRO patients (%) (n = 35)
Gram-negative bacteria		
<i>Pseudomonas aeruginosa</i>	9 (25.8)	12 (34.2)
<i>Acinetobacter baumannii</i>	4 (11.4)	13 (37.1)
<i>Klebsiella pneumoniae</i>	2 (5.7)	6 (17.1)
<i>Serratia marcescens</i>	1 (2.8)	0 (0.0)
<i>Proteus mirabilis</i>	3 (8.5)	0 (0.0)
<i>Enterobacter cloacae</i>	1 (2.8)	1 (2.8)
<i>Morganella morganii</i>	1 (2.8)	0 (0.0)
<i>Escherichia coli</i>	2 (5.7)	0 (0.0)
<i>Burkholderia cepacia</i>	0 (0.0)	1 (2.8)
Gram-positive bacteria		
<i>Staphylococcus aureus</i>	8 (22.8)	3 (8.5)
<i>Staphylococcus haemolyticus</i>	2 (5.7)	0 (0.0)
<i>Bacillus sp.</i>	1 (2.8)	0 (0.0)

MDRO: Multidrug-resistant organism.

Results are given as number of patients with a positive culture and the total percentage of these patients in the total patient population.

Significant associations of MDRO infection were found for the length of antibiotic treatment, sepsis, pneumonia, and mortality and are shown in Table 3. No significant association was found for the length of hospital stay and the incidence of AKI. The median duration of antibiotics in subjects with MDRO infection was 7 days. MDRO infection was found to be associated with the risk of sepsis and pneumonia with odds ratio (OR) 13.90 (95% Confidence interval [CI] 2.88–67.10) and 12.67 (95% CI 3.26–49.23), respectively. The OR for mortality was 9.75 (95% CI 2.00–47.50)

Table 3: Bivariate Analysis of MDRO and Non MDRO

Variables	Non-MDRO (n = 35)	MDRO (n = 35)	p
Length of stay (days), median (IQR)	20.0 (12.0–28.0)	21.0 (14.0–34.0)	0.533
Duration of antibiotic therapy (days), median (IQR)	0.0 (0.0–7.0)	7.0 (4.0–12.0)	< 0.001
Without sepsis	33 (94.3%)	19 (54.3%)	< 0.001
Sepsis	2 (5.7%)	16 (45.7%)	
Without pneumonia	32 (91.4%)	16 (45.7%)	< 0.001
Pneumonia	3 (8.6%)	19 (54.3%)	
Without AKI	32 (91.4%)	31 (88.6%)	1.000
AKI	3 (8.6%)	4 (11.7%)	
Non mortality	33 (94.3%)	22 (62.9%)	0.001
Mortality	2 (5.7%)	13 (37.1%)	

MDRO: Multidrug-resistant organism; IQR: Interquartile range; AKI: Acute kidney injury.

Multivariate analysis was carried out to determine the independence of the association of MDRO infection on the duration of antibiotic therapy, sepsis, pneumonia, and mortality.

Multivariate analysis of MDRO infection with duration of antibiotic therapy found no independent variables that were significantly related. Two variables were significantly and independently associated in the multivariate analysis for sepsis outcome, namely MDRO infection and TBSA. MDRO infection was shown to increase the risk of sepsis in subjects, with an OR of 36.53 (95 % CI 2.05–652.45). For an OR of 1.06 (95 % CI 1.00–1.13), the larger the TBSA, the greater the chance of sepsis. Subjects with MDRO infection were also found to have an increased risk of pneumonia with an OR of 10.75 (95% CI 1.87–61.86). The other variables were not found to be significantly and independently associated with the risk of pneumonia. MDRO infection was associated with an increased mortality risk with an OR value of 57.09 (95% CI 1.41–2318.87). With an OR value of 1.13 (95 % CI 1.04–1.22), larger TBSA burns are associated with a higher risk of death Table 4.

Table 4: Multivariate analysis of all variables

Variables	OR (95% CI)			
	Length of antibiotic treatment	Sepsis	Pneumonia	Mortality
MDRO	2.58	36.53	10.75	57.09
Infection	(0.82–8.14)	(2.05–652.45) [†]	(1.87–61.86) [†]	(1.41–2318.87) [†]
Age	0.99	0.99	1.02 (0.98–1.07)	1.06
	(0.97–1.03)	(0.97–1.03)		(0.99–1.13)
Comorbidity	0.99	0.54	6.06	12.87
	(0.093–10.71)	(0.02–13.69)	(0.137–268.05)	(0.19–875.91)
Admission	1.19	5.16	3.72	2.05
Time > 8h	(0.40–3.55)	(0.73–36.41)	(0.74–18.65)	(0.17–24.18)
TBSA	1.00	1.06	1.03	1.13
	(0.96–1.04)	(1.00–1.13) [†]	(0.98–1.08)	(1.04–1.22) [†]
Inhalation	0.58	2.63	2.84	0.27
Trauma	(0.11–3.04)	(0.25–27.86)	(0.28–28.53)	(0.01–7.59)

OR: Odd ratio; CI: Confidence interval; MDRO: Multidrug-resistant organism; TBSA: Total burn surface area.

[†](p < 0.05) ** (p < 0.01).

Discussion

MDRO bacteria are resistant to various types of antibiotics so that choosing the right antibiotic is often difficult. This results in more extended use of antibiotics and the risk of causing side effects for patients, higher costs, and triggering bacteria that are more resistant than before [15]. The research results related to the association of MDRO bacteria with an increase in

the duration of antibiotic use were also found in the study by Van Langeveld *et al.* [16]. After conducting multivariate analysis in this study, no independent variable was significantly associated and independent with the length of treatment with antibiotics. This may be explained because, in addition to the type of bacteria, the long duration of antibiotics is also influenced by the clinical response of each patient and is also influenced by surgical interventions such as tangential excision and skin grafting [16].

A logical assumption is that patients infected with MDRO have a higher risk of developing sepsis or multiple organ dysfunction syndrome because of the difficulty of selecting effective antibiotics. This study succeeded in proving that MDRO-infected patients were more prone to suffer from sepsis (OR 13.90, 95% CI 2.88–67.10). Two variables were significantly and independently associated in the multivariate analysis for sepsis outcome, namely MDRO infection and TBSA. Subjects with MDRO infection were found to have an increased risk of sepsis with an OR of 36.53 (95% CI 2.05–652.45) and a p-value of 0.014. TBSA is a significant risk factor for sepsis, consistent with previous studies [17], [18], [19].

This study is the first to evaluate risk factors for pneumonia in burn patients where MDRO infection was found to be a significant risk factor (OR 10.75, 95% CI 1.87–61.86, p 0.008) compared to other factors. This may be due to the ineffective use of antibiotics in patients infected with MDRO, allowing bacteria to move hematogenously to the respiratory organs, resulting in pneumonia.

In this study, there was no relationship between MDRO bacteria and the occurrence of AKI. This may be explained by the small number of samples in which AKI only occurred in 7 cases (10% of cases). There was no association between length of stay and MDRO infection in this study. This is in line with Theodorou *et al.*, where there was no difference in length of stay between *Pseudomonas aeruginosa* MDRO and non-MDRO [20].

There were two variables associated significantly and independently with the risk of mortality, namely MDRO infection and burn area. MDRO infection was associated with an increased mortality risk with an OR value of 57.09 (95% CI 1.41–2318.87). This is in line with Pena *et al.*, which found an increase in mortality rates between *P. aeruginosa* MDRO compared to non-MDRO [21].

One of the study's strengths is that it looks at multiple MDROs instead of many other studies that have only looked at one pathogen's role in burn morbidity and mortality. The retrospective nature of the analysis and the small number of reported events such as AKI limited the methodological approach to univariable analysis.

This study is the first study in Indonesia to examine the relationship between MDRO infection

with the length of stay, length of antibiotic treatments, sepsis, pneumonia, AKI, and mortality in burn patients. More studies with a greater sample size are needed in the future to investigate further the effect of MDRO bacteria on morbidity and mortality in burn patients.

Conclusion

MDRO infection was shown in this study to increase the length of antibiotic treatment, sepsis, pneumonia, and mortality in burn patients, indicating that it is critical to prevent the spread of MDRO bacteria for reducing morbidity and mortality in burn patients. Strategies that can be taken are infection control with optimal handling, use of appropriate antibiotics and in accordance with the results of culture and germ patterns, and measures to improve the hygiene of health workers to prevent transmission between patients in the burn unit.

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