Risk factors of emerging multidrug resistant *Acinetobacter baumannii* in burn patients at Burn Unit of Dr. Soetomo Hospital during January 2020 to December 2021

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ABSTRACT

Introduction: Burn injury patients are at high risk of infection as a result of the nature of the burn injury itself, including prolonged hospital stays, antibiotics use, treatment procedures, etc. In this era, nosocomial infections caused by *Acinetobacter baumannii (A.ba)* have increased significantly. This study was conducted to investigate the micro-organism pattern and the risk factors for burn patients with multi-drug resistant (MDR) *Acinetobacter baumannii (A.ba)* in the Burn Unit at Dr. Soetomo Hospital.

Materials and Methods: We conducted a retrospective, observational study among burn patients with *A.ba* admitted to the Burn Unit at Dr. Soetomo Hospital from January 2020 to December 2021. Potential risk factors for MDR-*A.ba* were analysed by univariate and multivariate analysis. The patients diagnosed with MDR-*A.ba* wound infection were included in the case group. The patients diagnosed with non MDR, these are: (1) the patients isolated micro-organisms other than *A.ba*, (2) sterile isolates, and (3) the patients isolated as *A.ba* but not MDR, were included in the control group.

Results: A total of 120 burn patients were included in this study. During this study, 24% burn patients were found to have *Acinetobacter baumannii* and 79% (from 24% of *Acinetobacter baumannii*) had MDR-*A.ba*. According to univariate analysis, risk factors that significant were: Abbreviated Burn Severity Index (ABSI) (p = 0,002; OR: 6.10; CI: 1,68 - 21,57); hospital Length Of Stay (LOS) (p < 0,000; OR: 6.95; CI: 2,56 - 18,91) and comorbid (p = 0,006; OR: 3,72; CI: 1,44 - 9,58). But, after analysed by multivariate analysis, only ABSI was the significant factor (p = 0,010; OR: 1,70; CI: 1,23 - 2,36).

Conclusion: Based on univariate analysis, the significant risk factors for MDR-*A.ba* were: ABSI, hospital length of stay and comorbid. But after adjusted by multivariate analysis, only ABSI was the significant factor.

KEYWORDS:
Burns, Acinetobacter baumannii, multidrug resistance

INTRODUCTION

One of the major functions of the body skin is to ensure protection against microorganisms in the external environment. The burn wound can be considered as one of the major health problems in the world.[1]

Patients who are hospitalised after having a major burn injury are at high risk of developing hospital-acquired infections.[2] If patients survive in the initial 72 hours after a burn injury, infections are the most common cause of death.[2] In burn injuries, the most frequent and devastating pathogens are *Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Staphylococcus aureus. Acinetobacter spp.* are the most common gram negative MDR nosocomial agents.[3]

Recently, multidrug-resistant *Acinetobacter baumannii* (MDR-*A.ba*), defined as bacteria resistant to three or more classes of antibiotics including carbapenem, has arisen as a major causes of infection related healthcare.[4] MDR-*A.ba* are difficult to treat and high in mortality and morbidity, it is also associated with increasing in hospital stays.[4] Therefore, identifying risk factors for these nosocomial infections is needed to help reduce their occurence.[4]

The aim of this study was to investigate the micro-organism pattern and to assess the risk factors for burn patients with multidrug resistant *Acinetobacter baumannii* in the Burn Unit.

MATERIALS AND METHODS
Patients' Selection and Study Design
We conducted a retrospective and observational study of burn patients that were admitted to the Burn Unit of Dr. Soetomo Hospital, Surabaya, Indonesia from January 2020 to December 2021.

During the study period, wound cultures were routinely taken from all patients within 48 hours after hospitalized in Dr. Soetomo Hospital. Other cultures were collected from blood, urine and sputum/endotracheal aspirate for all patients admitted to the Burn Unit as indicated.

Table I: Univariate analysis of risk factors for burn patients between MDR-A.ba vs non MDR

Risk factors	MDR-Ab (n = 23)	Non MDR (n = 97)	Total	R squared	OR (CI 95%)	p-value
Sex						
• Male	17	68	85	0.001	0.83 (0.29 -2.31)	0.476
• Female	6	28	35			
Age (years)						
• <=60	21	89	110	0.000	1.06 (0.21 - 5.36)	0.608
• >60	2	8	10			
% TBSA						
• <=3 (<30%)	0	6	6	0.012	1.25 (1.14 - 1.37)	0.271
• >=4 (> 31%)	23	91	114			
ABSI						
• <=7	3	46	49	0.092	6.10(1.68- 21.57)	0.002
• >=8	20	51	71			
Length of stays (days)						
• <=20	7	73	80	0.177	6.95 (2.56 - 18.91)	0.000
• >=21	16	24	40			
Duration of previous antibiotics (days)						
• <=10	8	37	45	0.036	1.44 (0.05 - 1.98)	0.060
• >=11	15	20	35			
Cause						
• Fire	18	61	79	0.016	0.47 (0.16 - 1.38)	0.123
• Others	5	36	41			
Inhalation injury						
• Yes	7	23	30	0.004	1,408 (0.516 - 3.841)	0.336
• No	16	74	90			
Comorbid						
• Yes	12	22	34	0.066	3.72 (1.44 - 9.58)	0.006
• No	11	75	85			

TBSA: Total body surface area, ABSI: Abbreviated Burn Severity Index, MDR-A.ba: Multidrug resistance Acinetobacter baumannii, OR: Odds ratio

Table II: Multivariate analysis for risk factors in burn patients between MDR-A.ba vs non MDR.

Risk factors	Multivariate analysis		
	OR	95% CI	p value
ABSI	1.70	1.23 - 2.36	0.010
Length of stay (days)	3.03	0.24 - 37.90	0.390
Comorbid	2.00	0.68 - 5.911	0.210

ABSI: Abbreviated Burn Severity Index, OR: Odds ratio, CI: Confidence interval

The risk factors for MDR-*A.ba* in burn patients were identified as sex, age, inhalation trauma, comorbid diseases, causes of burn injuries, hospital length of stay, day of exposure to antibiotics, Abbreviated Burn Severity Index (ABSI) and Total Body Surface Area (TBSA).

Patients were excluded from this study if they did not undergo bacterial culture, died before 48 hour and had incomplete dat.

Burn patients were divided into two group, case and control groups. The patients diagnosed with MDR-*A.ba* wound infection were included in the case group. Patients diagnosed with non MDR, such as those who isolated micro-organisms other than *A.ba*, (2) sterile isolates and(3) those who isolated as A.ba but not MDR, were included in the control group.

Multidrug-resistant MDR-*A.ba*, defined as strains resistant to three or more classes of antibiotics including carbapenem, has emerged as a major cause of healthcare associated infection.

Statistical Analysis
Numeric data were presented with standard deviation (SD). Continuous variables were analysed using Student's t-test. The Mann-Whitney U test is used when the data in not normally distributed. Potential risk factors for MDR-*A.ba* were analysed by univariate and multivariate analysis. Odds ratio (OD) and 95% confidence intervals (CI) were calculated using binary logistic regression for each model. p value < 0.05 represented statistical significance. Statistical analysis was calculated using SPSS version 15.0.

RESULTS
During the period of this study, from January 2020 to December 2021, a total number of 143 burn patients were admitted to the Burn Unit.

Of the 143 burn patients, 120 patients were included, and 23 patients were excluded because of incomplete data and no isolates culture (Figure 1). There were 23 MDR-*A.ba* burn patients and 97 non MDR burn patients. Of the 97 non-burn
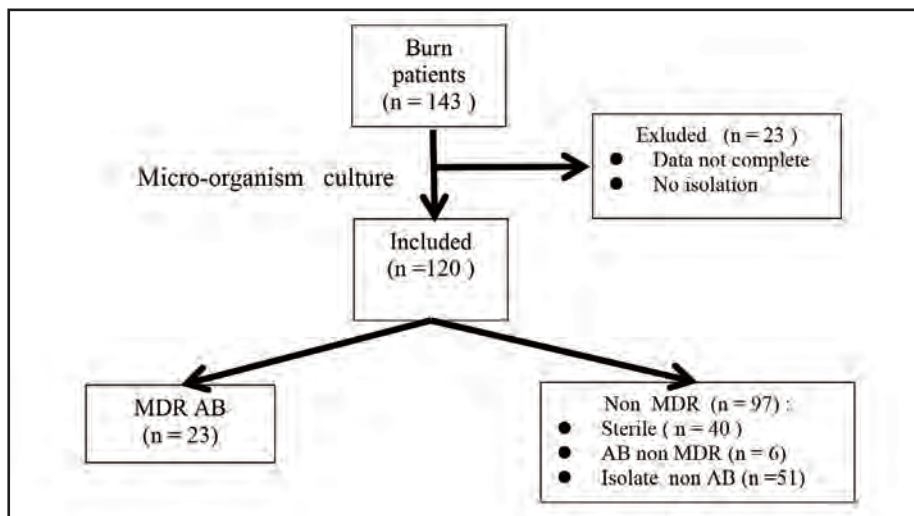
Fig. 1: Selection process in burn patients. MDR multi-drug resistant. A.ba Acinetobacter baumannii

patients, 40 patients (41%) had sterile isolate culture, six patients (6%) had Acinetobacter baumannii non MDR and 51 patients (53%) had positive isolate non *Acinetobacter baumannii*.

Table I showed the causative agents isolated from burn patients. Of the 120 burn patients, there were 80 patients (67%) with positive culture and 40 patients (37%) with negative cultures.

The most frequently isolated pathogens were *Pseudomonas aeruginosa* (35), *Staphylococcus sp* (30), *Acinetobacter baumannii* (29) and *Klebsiella* (20). Of the 29 patients with Acinetobacter, 23 patients (79%) were MDR-*A.ba*, and only six patients were *Acinetobacter* non MDR.

Univariate analysis of baseline and risk factors associated with MDR-A.ba infection is presented in Table I. According to the univariate analysis, there were no significant difference associated with risk factors, such as sex, age, TBSA and cause of burns and inhalations injury. But, there were significant difference associated with ABSI ($p = 0,002$; OR: 6.10; CI: 1,68 - 21,57), hospital length of stay ($p < 0,000$; OR: 6.95; CI: 2,56 - 18,91) and comorbid ($p = 0,006$; OR: 3,72; CI: 1,44 - 9,58). But, after analysed by multivariate analysis, only ABSI was the significant factor ($p = 0,010$; OR: 1,70; CI: 1,23 - 2,36) (Tabel II).

Of the 120 burn patients, there were 44 patients (37%) death and 76 patients (63%) discharged alive. In MDR-A.ba group, there were nine patients (20%) death and 35 patients (80%) in non MDR. But, there was no significant difference between MDR-A.ba and non MDR group ($p = 0.784$).

DISCUSSION
Infection become a major cause of morbidity and mortality in patients with burn injury.[2] The Infectious Diseases Society of America (IDSA) identifies *Acinetobacter baumannii* as one of the seven pathogens that threaten the health system because of its ability to survive on patient skin and environmental surfaces, this pathogen transmits and spreads very quickly.[5]

Likewise in the burn unit, this pathogen often causes extraordinary events.[4]

Acinetobacter baumannii, previously categorised as a low pathogenicity bacterium, has evolved into a high pathogenicity bacteria because it is resistance to more than one type of antibiotic (multi drug resistance/MDR to extremely drug resistance *Acinetobacter baumannii*/XDR-*Ab*) which causes world health problems due to nosocomial outbreaks in hospitals throughout the world.[5]

During hospital treatment, the spread of this pathogen can occur from invasive medical devices used, such as intravenous lines, catheters, endotracheal tubes, ventilators, ward bed, to objects carried by medical personnel, such as trolleys, food, and direct contact from medical personnel.[6,7] We didn't investigate the source of pathogen in our hospital. However, in our burn unit, we have limitation of isolation room, therefore, in a very large number of patients were placed in the same room which increase the risk of cross contamination.

In this study it was found that the incidence of *Acinetobacter baumannii* were quite high, counted as 29%. Another study conducted by Song et al and Atilla & Kilic each reported almost the same results 21% and 30%.[7,8]

Acinetobacter baumannii microbes were found, 23 (79%) were categorised as MDR-*A.ba*. Likewise, the results of research by Song et al. and Atilla & Kilic, namely 59% and 88%, respectively.[7,8]

In this study, burn patients with *Acinetobacter baumannii* ranked third after Pseudomonas and Staphylococcus. Meanwhile, according to the results of a study by Song et al., *Acinetobacter baumannii* is in second place after *Staphylococcus Microbes*. Meanwhile, the results of Atilla & Kilic's study show that Acinetobacter baumannii ranks first.[7,8]

Certain risk factors increase the incidence of Acinetobacter baumannii. In our study, it was found that significant risk factors for the occurrence of MDR-*A.ba* were ABSI ($p = 0.002$),

length of stay (p = 0.000) and comorbid factors (p = 0.006). However, after multivariate analysis, ABSI was the only significant risk factor. Statistically, this means that when all variables are analysed simultaneously, length of stay and comorbidities do not play a role in increasing the risk of MDR-*A.ba*. Multivariate analysis allows for the examination of the combined effects of multiple variables, which can lead to different result than univariate analysis. The possibilities of confounding factors which can affect the result in this study are medication and treatment in previous hospital, since our hospital is the last referral hospital in Eastern Indonesia.

ABSI is an assessment to predict the survival rate in burn patients in arrival. This scoring consists of five variables, namely gender, age, presence/absence of inhalation trauma, full thickness burns and extent of burns.[9] Tsolakidis, et al showed that patients who developed infections tended to have higher TBSA, higher ABSI score and longer hospital stays. In this study, a retrospective study was conducted on 252 burn patients. In our study, the small population size of patients may limit the clinical applicability of the data.[10]

Jung et al. reported the results of his research regarding risk factors for MDR-*A.ba*, such as the use of endotracheal tubes, central venous catheters and previous use of antibiotics. Given this, they suggest that clinicians minimize the use of invasive devices and remove them as early as possible.[11]

Song et al. conducted a study by comparing the MDR-A.ba vs. Non-MDR-*A.ba* groups (non-*Acinetobacter* positive cultures, sterile culture and culture of *Acinetobacter* non MDR-A.ba).[7] From the results of this study, it was concluded that the significant risk factors for the occurrence of MDR-*A.ba* were length of stay, TBSA, intubation and causes of burns. However, after multivariate analysis, only length of stay and TBSA were significant.

Meanwhile, according to the results of Wong et al.'s study, the independent risk factors for causing MDR-A.ba were the acute physiology and chronic health evaluation (APACHE) II score at hospital admission and the number of invasive devices installed.[12]

Atilla & Kilic reported the results of their research, namely that significant risk factors contributing to Acinetobacter baumannii were the use of invasive devices, length of stay in hospital, length of stay in ICU and TBSA.[8]

Based on the research results of Munier et al. It can be concluded that the incidence of nosocomial MDR-*A.ba* infection in the burn unit is very high. The increased risk of nosocomial infection in MDR-*A.ba* burn patients is associated with factors: simplified acute physiology score (SAPS II), ABSI, *Acinetobacter baumannii* colonisation, invasive procedures and more than two skin grafts.[4]

CONCLUSION
In conclusions, this retrospective-observational study found a moderate high incidence of MDR-*A.ba* nosocomial infection in burn patients. A univariate analysis showed that Abbreviated Burn Severity Index (ABSI), hospital length of stay and comorbid, were statistically significant. But, after multivariate analysis was adjusted, ABSI was the only significant factor.

Due to increased drug resistance, wider research and further studies are necessary to control hospital infections.

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