ANTIBIOTIC RESISTANCE LEVEL OF *ACINETOBACTER BAUMANNII* STRAINS ISOLATED FROM SEPTICEMIA PATIENTS AT MILITARY HOSPITAL 103 (2015 - 2020)

Le Van Nam[1], Vu Thi Trang[2]

SUMMARY

***Objectives**: To describe antibiotic resistance of Acinetobacter baumannii (A. baumannii). **Subjects and methods**: Cross-sectional descriptive study on 44 A. baumannii strains were isolated from septicemia patients at Military Hospital 103 during the period from January 2015 to June 2020. **Results**: Over 60.0% of A. baumannii strains were resistant to antibiotics of penicillin, broad-spectrum cephalosporin, fluoroquinolone; and 48.6% to 75.0% strains were resistant to carbapenem antibiotics. 51.4% to 87.5% strains were susceptible to aminoglycoside antibiotics; 80.8% strains were susceptible to colistin. However, 19.2% of strains were resistant and intermediate to colistin; MDR accounted for 13.5% and XDR was 48.7%. Besides, 64.9% of antibiotics were not prescribed in accordance with microbiological results. Mortality occurred in 59.1%. **Conclusion**: A. baumannii strains isolated from septicemia patients' blood were highly resistant to antibiotics, which makes it difficult to choose appropriate antibiotics when not having antimicrobial susceptibility testing results.*

**Keywords: Septicemia; Acinetobacter baumannii; Antibiotic resistance.*

INTRODUCTION

A. baumannii is considered as one of many causes of hospital-acquired sepsis. Along with the highly increasing number of antibiotics, *A. baumannii* is regarded as the first priority in control and treatment recently. In clinical, *A. baumannii* can be resistant to all current antibiotics due to a profound resistance regimen. Study COMPACT II conducted in 5 countries in Asia - Pacific area (2012) stated that in Vietnam, the rate of resistance to carbapenem of *A. baumannii* is the highest among negative Gram bacteria, making up 89.5% [3]. The degree of antibiotic resistance was one important cause leading to failure in treatment and the increase in the rate of mortality among sepsis patients in Vietnam. This rate can considerably decrease if patients take empiric antibiotics early. Moreover, strategies of encouraging appropriate use of antibiotics will help prevent antibiotic conditions as well as optimize resources of hospitals [4]. However, epidemiology and some treatment results related to antibiotic resistance of microorganisms of sepsis in general and

[1]*Military Hospital 103,* ***Vietnam Military Medical University***

[2]*Hai Duong Medical Technical University*

Corresponding author: Le Van Nam (levannam@vmmu.edu.vn)

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of *A. baumannii* in particular in Vietnam have not been studied clearly. Knowledge about sepsis, antibiotic resistance, and its impacts on patients is very important in clinical management and the use of appropriate antibiotics. This article aimed: *To show the data about antibiotic resistance of A. baumannii among patients with sepsis in 6 years at Military Hospital 103.*

SUBJECTS AND METHODS

1. Subjects

The study was conducted among 44 patients diagnosed with sepsis by *A. baumannii* and treated at Military Hospital 103 from January, 2015 to June 2020.

* *Inclusion criteria:* Based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), patients need to adapt to these requirements:

+ SOFA score ≥ 2 points consequent to infections.

+ Blood culture isolates of *Acinetobacter* spp.

+ Over 18 years old.

* *Exclusion criteria:* Positive blood cultures ≥ 2 pathogens.

2. Methods

* *Study design:* Cross-sectional combined retrospective and prospective study.

* *Methods:* Antibiogram: Blood samples were retrieved and tested microbiologically by standard procedures. Tests were performed at the Department of Microbiology, Military Hospital 103, using the VITEK 2 COMPACT system (Bio Merieux). Data collection through medical records, all medical records were registered under unified form.

* *Research contents:*

- Classification of a source of infection: Community-acquired infections (CAI) are infections that were present upon admission or developed within 48 hours of hospital admission. Hospital-acquired infections (HAI) are infections which were occurred > 48 hours after hospital admission.

- Definition of antibiotic resistance: Multidrug-resistance (MDR) means acquired non-susceptibility to at least one agent in three or more antimicrobial categories. Extensively-drug resistance (XDR) is defined as non-susceptibility to at least one agent in all, but two or fewer antimicrobial categories, and pandrug-resistance **(**PDR) as non-susceptibility to all agents in all available antimicrobial categories.

- Antibiotic therapy was considered appropriate if the antibiotics had in vitro sensitivity to isolated strains.

- Outcomes of patients: Fatal cases were defined as patients who died in a hospital or were discharged with a diagnosis of brain death and the expectation that they would die imminently within hours or days.

* *Data processing:* Data were entered and analysed using SPSS 22.0.

RESULTS

From January 2015 to June 2020, we collected 44 *A. baumannii* strains and 37 antibiogram results from 44 septicemia patients by *A. baumannii* for study.

1. Characteristics of source of infection and clinical outcomes

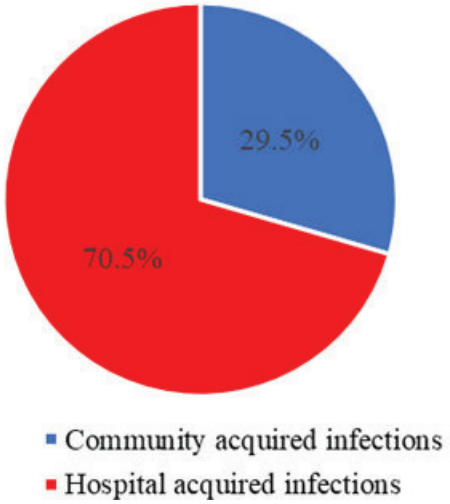

Chart 1: Classification of a source of infection.

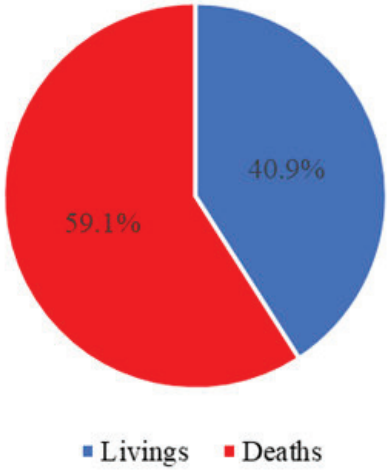

Chart 2: The rates of mortality.

2. Antibiotic resistance of *A. baumannii* strains

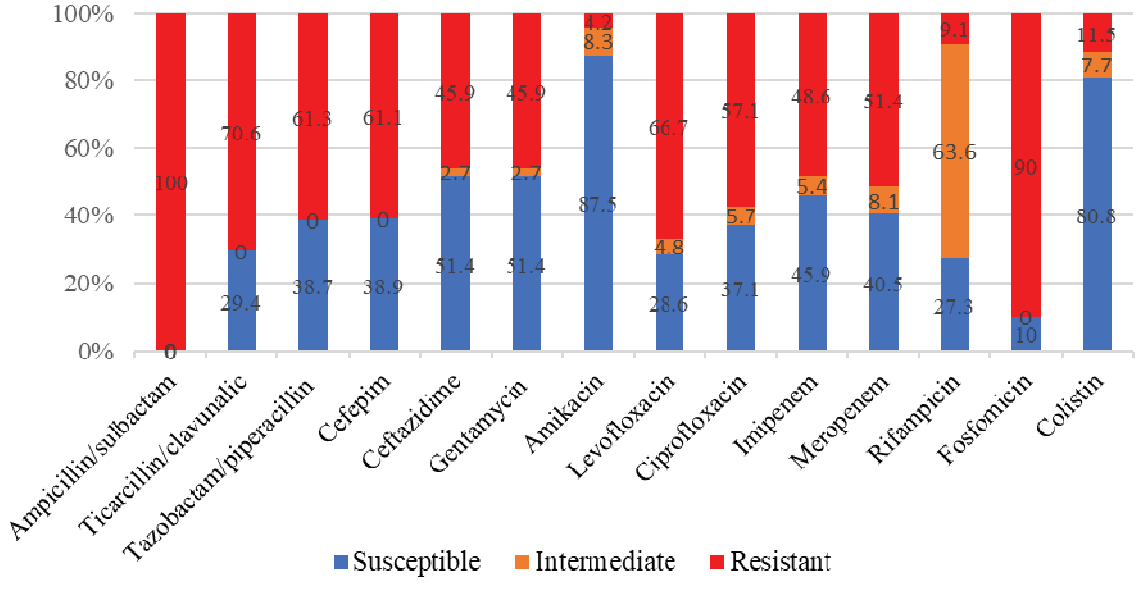

Chart 3: Antibiotic resistance of *A. baumannii* isolates.

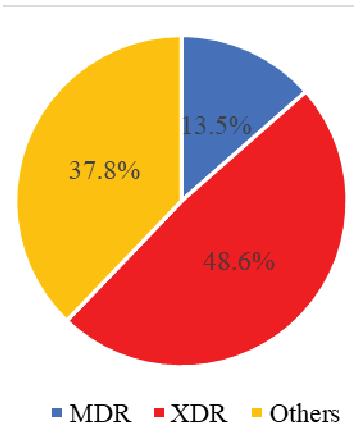

Chart 4: Classes of antibiotic resistance of *A. baumannii* isolates.

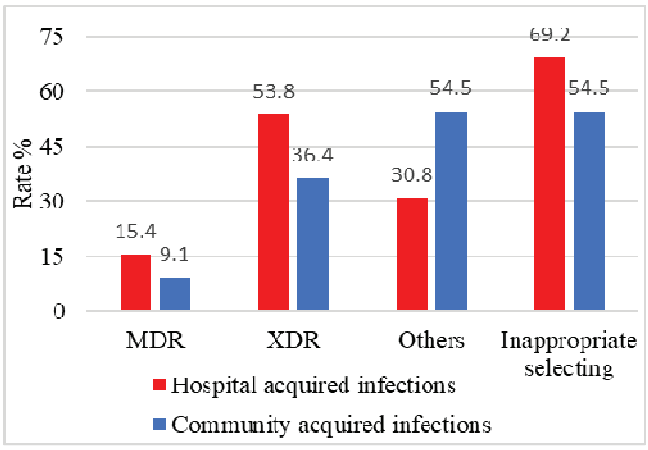

Chart 5: Types of antibiotics and choices of antibiotics following sources of infections.

Table 1: Relation between antibiotic resistances and treatment results.

Characteristics	Number of patients (n)	Rate %	Livings		Deaths		p
			n	%	n	%	
MDR	5/37	13.5	2/17	11.8	3/20	15.0	1.000
XDR	18/37	48.6	8/17	47.1	10/20	50.0	
Resistance to imipenem	19/37	51.3	8/17	47.1	11/20	55.0	0.746
Resistance to meropenem	21/37	56.8	9/17	52.9	12/20	60.0	0.746
Resistance to colistin	5/26	19.2	1/11	9.1	4/14	28.6	0.341
Selecting inappropriate empirical antibiotic regimens	24/37	64.9	9/17	52.9	15/20	75.0	0.291

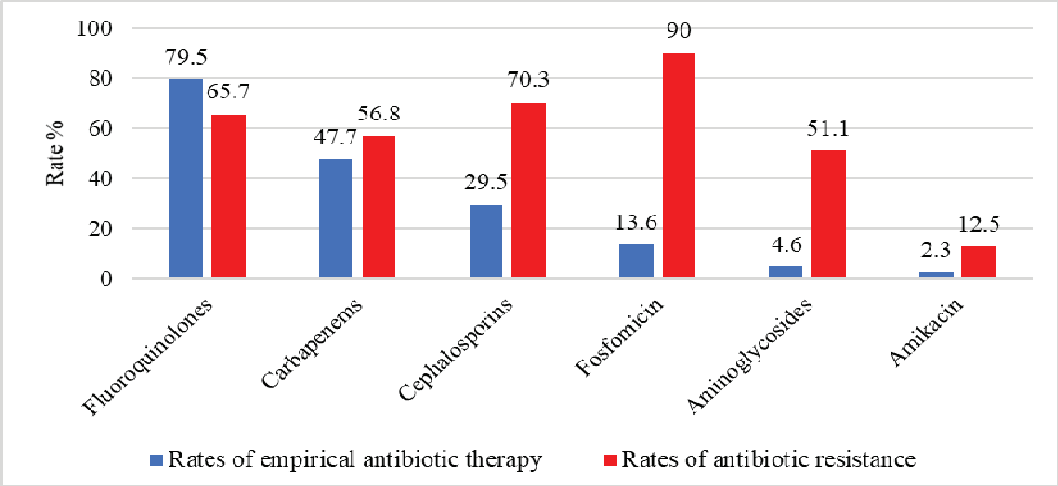

Chart 6: The rates of empirical antibiotic therapy and rates of antibiotic resistance.

DISCUSSION

1. Characteristics of the source of infection and clinical outcomes

Statistics showed *A. baumannii* caused about 1.8% of infections related to medical care in the US and Europe. More seriously, the rate was double compared to that in the Middle East and Asia [5]. Prominently, Vietnam was among Asian countries which had the highest rate of hospital-acquired infections [6]. Our study reported 70.5% associated *A. baumannii* patients by hospital-acquired infections and only 29.5% caused by community infections. The similar results by Olaniyi Ayobami (2019) when data from 16 countries of Europe, the East Medirrance and Africa showed that the rate of *A. baumannii* cases caused by hospital-acquired infections was 25.1/1000 patients (95%CI: 12.8 - 48.5) and up to 56.6/1000 patients (95%CI: 33.9 - 92.8) in ICU [7]. That is not only a big threat to hospitals, nursing homes but also to patients who undergo medical procedures. A multicenter study carried out in Southeast Asia (including Vietnam) stated that *Acinetobacter* spp. was one of highly fatal agents (1%) which should be taken into consideration [8].

The mortality rate of our patients was 59.1%, higher than the result gained by Nguyen Thi Thanh Ha (2015) (50.8%, p = 0.178) and Tran Le Tien (2015) (39.3%, p = 0.008) regarding sepsis caused by *A. baumannii* in a few years ago [1, 2]. A study by Wisplinghoff (2000) showed that the mortality rate among *A. baumannii* sepsis patients (31.5%) was higher than Gram-negative sepsis patients (27.9%) [9]. Although it is very hard to differentiate between a sepsis death by *A. baumannii* or by underlying medical conditions, our results along with other domestic and international studies showed that sepsis caused by *A. baumannii* leads to a higher mortality rate compared to Gram-negative sepsis in particular and sepsis caused by microorganism by common [1, 2, 9]. The higher mortality rate caused by *A. baumannii* is intimately closed to the antibiotic resistance of the bacteria [10].

2. Antibiotic resistance of *A. baumannii* strains

Our *A. baumannii* strains had higher antibiotic resistance ranging from 4.2% to 100%. Among them, 62.5% to 100% strains were resistant to antibiotic groups of penicillin; 45.9% to 66.7% were resistant to groups of broad-spectrum cephalosporin and 57.1% to 66.7% were resistant to groups of fluoroquinolone. The rate of MDR was 13.5%, XDR was 48.7% and currently we have not recorded PDR. Compared to results by Nguyen Thi Thanh Ha (2011 - 2012) and Tran Le Tien (2012 - 2015), we realised that the rate of antibiotic resistance of *A. baumannii* to each antibiotic tended to increase through time [1, 2]. Antibiotic resistance of carbapenem was highly similar to results by Nguyen Thi Thanh Ha and Tran Le Tien (the number of imipenem and meropenem strains in their study and ours were 66.2%, 42.9%, 48.6% and 62.4%, 48.7%, 51.4%, respectively) [1, 2]. In recent years, there were many reports on *A. baumannii* strains resistant to the majority of current antibiotics; however, most of

them were still susceptible to colistin. However, it was alarming that the number of *A. baumannii* strains resistant to colistin was ceaselessly increasing over time. Our results showed 19.2% of them were resistant to colistin while this rate was 0% in Nguyen Thi Thanh Ha's study and 8.7% in Tran Le Tien's study [1, 2].

Besides, *A. baumannii* has flexible genetic traits depending on each type of environment, capable of living in healthcare places; therefore, they can survive for long, accumulating antibiotic genes and becoming opportunistic pathogens, especially for severely ill patients [11]. This explained why our *A. baumannii* stemming from hospitals obviously had higher antibiotic resistance than other strains in the community. Specifically, 19.2% of resistant and intermediate *A. baumannii* strains were in a group of hospitals-acquired infections. Retrospective study by Chery Lim (2016) in 9 hospitals in Thailand stated that the rate of *A. baumannii* MDR in hospital-acquired sepsis was 3.8 times higher than infections in the community (75% and 20%). Moreover, 75% of strains stemming from hospitals were resistant to ceftazidime, 63% resistant to amikacin, 67% resistant to ciprofloxacin and 64% resistant to carbapenem. Prominently, 3% of *A. baumannii* isolates were resistant to colistin [12].

Using empirical antibiotic therapy in the early stages can help decrease the mortality rate among sepsis patients [2]. However, in reality, the current antibiotic state caused many difficulties in choosing antibiotics from the start for doctors when they treat infections caused by *A. baumannii*. Our preferred chosen antibiotics for hospital-acquired infections caused by Gram-negative were all highly resistant (the frequency of usage and the rate of antibiotic resistance of fluoroquinolones were 79.5%, 65.7%, respectively; broad-spectrum cephalosporin: 29.5%, 70.3%, respectively; aminoglycoside: 13.6%, 51.1%, respectively and carbapenem: 47.7% and 56.8%, respectively). The selection of an empiric antibiotic regimen was inappropriate in 64.9% of patients. The rate in the dead group was higher than in the alive group (75.0% and 52.9%, $p > 0.05$). The study by Kyeongman Jeon (2019) carried out in 977 patients infected by microorganisms in general in Korea stated that 68.6% of patients took empiric antibiotics. Among those, there were only 40% of antibiotics appropriate and effective against *A. baumannii* ($p = 0.810$) [13]. Marya D Zilberberg (2019) realised that MDR pathogens were inappropriate predictive factors for choosing empiric antibiotics (OR = 13.05, 95%CI: 7.0 - 24.3, $p < 0.001$). Especially, the inappropriateness of empiric antibiotic selection for *A. baumannii* was 73.9% [14]. Some studies reported that prior use of carbapenem, third-generation cephalosporins and fluoroquinolones were independent risk factors for the acquisition of multidrug resistant *A. baumannii* [10].

Among patients with *A. baumannii* resistant to antibiotics, the mortality is higher than the alive group. Besides, we also reported the death rate among *A. baumannii* - carbapenem and colistin resistant patients higher than the alive, especially with colistin (patients infected

with *A. baumannii* were dead). However, there are still some limitations, such as the majority of patients retrospective, small samples, and restriction on a hospital scale. Choosing inappropriate antibiotics from the beginning was just restricted in comparison with microgram results, not from examining the appropriate usage of antibiotics concentration in treatments. The results stated the differences did not give details about statistics. However, the study carried out by Youn Jeong Kim (2012) among 95 sepsis patients caused by *A. baumannii* showed that resistance to carbapenem (OR 7.29, 95%CI:1.57 - 33.8, p = 0.01) and inappropriate usage of antibiotics (OR 8.05, 95%CI: 1.65 - 39.2, p = 0.009) were separated factors to the casualty in 14 days of sepsis patients caused by *A. baumannii* [10]. Therefore, it is significantly necessary to carry out broader-scale studies about antibiotic resistance of *A. baumannii*, clinical and subclinical manifestations among sepsis patients.

CONCLUSION

Through 44 *A. baumannii* isolates from blood specimens of sepsis *A. baumannii* patients treated at Military Hospital 103, we come to some conclusions:

- 70.5% of sepsis patients were hospital-acquired, the mortality rate was 59.1%.

- *A. baumannii* isolates were highly resistant to antibiotics. Over 60% of them were resistant to penicillin, broad-spectrum cephalosporin, and fluoroquinolone. The rate of MDR strains was 13.5% and XDR was 48.7%; no PDR was recorded. 48.6% to 51.4% of strains were resistant to carbapenem and especially 19.2% were intermediate and resistant to colistin.

- The selection of an empiric antibiotic regimen was inappropriate in 64.9% of patients.

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