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Original Article

Acinetobacter baumannii in Hematology Practice: Clinical Factors Affecting the Course of Infection

Abdülkadir Karışmaz[1], İstemi Serin[2], Ceyda Aslan[3], Mehmet Hilmi Doğu[3], Elif Suyani[4]

[1]*University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Hematology, İstanbul, Turkey*
[2]*Ağrı İbrahim Çeçen University, Ağrı Training and Research Hospital, Clinic of Hematology, Ağrı, Turkey*
[3]*University of Health Sciences Turkey, Derince Training and Research Hospital, Clinic of Hematology, Kocaeli, Turkey*
[4]*İstinye University Faculty of Medicine, Department of Hematology, İstanbul, Turkey*
[5]*University of Heath Sciences Turkey, Adana City Training and Research Hospital, Clinic of Hematology, Adana, Turkey*

ABSTRACT

Aim: Hematological malignancies are inherently risk factors for *Acinetobacter baumannii (A. baumannii)* infection. In this study, we aimed to reveal the clinical features of *A. baumannii* infection in patients with hematological malignancies and identify factors affecting the course of the infection.

Methods: The data of 49 subjects who were diagnosed and followed-up at the University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Hematology between October 2014 and July 2019 were analyzed retrospectively.

Results: Twenty-two (44.9%) subjects were diagnosed with acute myeloid leukemia, 15 (3.6%) subjects with lymphoma, 9 (18.4%) subjects with ALL, and 3 (6.1%) subjects were diagnosed with other hematological malignancies. Thirty-nine (79.6%) patients died during follow-up. Thirty-five (71%) subjects required intensive care unit (ICU) and were transferred to the ICU. Twenty-two (95.7%) of the subjects with neutrophil count <100/mm^3 and seventeen (65.4%) of the subjects with neutrophil count >100/mm^3 died (p=0.009). In the univariate analysis, neutrophil count <100/mm^3 had an impact on the occurrence of death in subjects with *A. baumannii* infection (p=0.026, HR=11.64). The number of patients who died was comparable between those treated with or without colsitin/tigecycline (p=0.253). The number of subjects who died was comparable between those who were treated with or without a carbapenem-type antibiotic (p=0.076).

Conclusion: Further studies are needed to identify factors affecting the course of *A. baumannii* infection in patients with hematological malignancies.

Keywords: *Acinetobacter baumannii (A. baumannii),* hematology, mortality, prognosis

Introduction

Acinetobacter baumannii (*A. baumannii*) is a Gram-negative pathogen that can spread easily by clinging to surfaces and can be a severe infectious agent in clinical practice due to its strong virulence factors [1]. Carbapenems, beta-lactam antibiotics, and polymyxins are frequently used, but multidrug-resistant *A. baumannii* can be a severe infection agent with difficulties that can be experienced during treatment [2-6].

A. baumannii-related mortality has been reported to range between 30% and 73% among critically ill patients [7,8]. Septic shock and mortality are quite high, especially within 30 days of the onset of infection [9]. Some mortality factors associated with *A. baumannii* infection include but are not limited to, advanced age, recent surgery, presence of immunosuppressive treatment, presence of invasive procedures such as catheterization and mechanical ventilation, presence of comorbidities such as acute renal failure, acute respiratory failure, septic shock, inappropriate use of antibiotics, and low platelet and albumin levels [10,11]. It is also important to determine whether there is an infectious agent due to colonization, especially in patients with a history of intensive

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Address for Correspondence: İstemi Serin MD, Ağrı İbrahim Çeçen University, Ağrı Training and Research Hospital, Clinic of Hematology, Ağrı, Turkey
E-mail: serinistemi@hotmail.com **ORCID ID:** orcid.org/0000-0003-1855-774X
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care unit (ICU) admission, which may lead to the unnecessary use of antibiotics [11].

Hematological malignancies are inherently risk factors for *A. baumannii* infection [10]. Data on the course of infection in hematologic malignancies, factors influencing the course of infection and mortality are limited. In this study, we aimed to reveal the clinical features of *A. baumannii* infection in patients with hematological malignancies and to identify factors affecting the course of the infection, as observed in our clinic.

Methods

Patients with co-existing hematological malignancies and *A. baumannii* infection were included in this study. The data of 49 patients who were diagnosed and followed at the University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Hematology, between October 2014 and July 2019, were analyzed retrospectively. Patients diagnosed with urinary infection, ventilator-associated pneumonia, or catheter-related bloodstream infection were included in the study. The only exclusion criterion was A. *baumannii* infection-related septic shock.

Bactec plus aerobic and anaerobic medium (BD; USA) were used and incubated in the Bactec FX (BD, USA) automated blood culture system. After obtaining the culture signal, Gram-stained microscopic examination of the positive blood culture bottle was performed. Microscopic examination revealed Gram-negative coccobacilli. The blood samples were then inoculated in 5% sheep blood (Oxoid, UK), eosin methylene blue (EMB, Oxoid, UK), and chromogenic *Candida* agar (AEM Medical, Turkey). The cells were incubated for 24 h at 37 °C under aerobic conditions. Species-level identification was performed in line with the manufacturer's recommendations using the VITEK-2 Compact (bioMérieux, France) system. A 0.5 McFarland (DensiChek Plus, bioMérieux, France) bacterial suspension from pure bacterial colonies was used for identification. All isolates in this study were identified as *A. baumannii using* the VITEK-2 Compact (bioMérieux, France) system, and their antimicrobial susceptibility was determined. Antibiotherapy was revised according to the antibiogram results.

The data, including age, diagnosis, antibiotic treatment, and ICU history, of the subjects were reviewed through the hematology department's database. Laboratory tests performed to assess the biochemical and metabolic status of the subjects included measurements of complete blood count and kidney and liver function.

The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital of Local Ethics Committee (approval date and number: 09/08/2019-1949).

The experimental procedures were based on the Declaration of Helsinki and relevant institutional regulations. Informed consent to publish the article was obtained from the subjects.

Statistical Analysis

The Statistical Package for the Social Sciences 24 package was used for statistical analysis. Data were presented as numbers and percentages or median and range, as appropriate. x^2 Fisher's exact test was used to analyze categorical values in subject groups. Regression analysis was used to evaluate the effect of neutrophil count on the occurrence of death. All p values were 2-sided with statistical significance at 0.05

Results

The characteristics of the participants are summarized in Table 1. The median age of the subjects was 49 years (range 19-76), with 39 males and 10 females. Twenty-two (44.9%) subjects were diagnosed with acute myeloid leukemia, 15 (3.6%) subjects with lymphoma, nine (18.4%) subjects with acute lymphoblastic leukemia and three (6.1%) with other hematological malignancies. The median numbers of white blood cells and neutrophils were 3,961/mm^3 (range, 100-32,200) and 2,417/mm^3 (range, 0-2,005). The number of

Table 1. The characteristics of the subjects

Patients' characteristics	N=49
Age, years, median (range)	49 (19-76)
Gender, n (%)	
Female	10 (20%)
Male	39 (80%)
Diagnosis, n (%)	
Acute myeloid leukemia	22 (44.9%)
Acute lymphoblastic leukemia	9 (18.4%)
Lymphoma	15 (30.6%)
Other	3 (6.1%)
WBC, mm^3, median (range)	3.961 (10-32,200)
Platelet count, mm^3, median (range)	43.977 (1.000-315,000)
Neutrophil count, mm^3, median (range)	2417 (0-20,050)
Hemoglobin, gr/dL, median (range)	8.4 (5.5-13.7)
C-reactive protein, mg/L (range)	99 (1.8-452)
Procalcitonin, µg/L, median (range)	9.8 (0.04-158)
Number of neutrophil count, n (%)	
<100 mm^3	23 (47%)
>100 mm^3	26 (53%)
Number of neutrophil count, n (%)	
>1,000 mm^3	16 (32%)
500-1,000 mm^3	3 (6%)
100-500 mm^3	7 (14%)
<100 mm^3	26 (53%)
Intensive care requirement, n (%)	
Present	35 (71%)
Absent	14 (29%)
Use of colistin/tigecycline	
Present	13 (26.5%)
Absent	36 (73.5%)
Use of a carbapenem	
Present	28 (57.1%)
Absent	21 (42.9%)

WBC: White blood cell count

subjects with neutrophil count >1,000/mm^3 was 16 (32%), between 500-1,000/mm^3 was three (6%), between 100-500/mm^3 was seven (14%), and the number of subjects with neutrophil count <100/mm^3 was 23 (47%). The number of subjects with neutrophil counts >100/mm^3 was 26 (53%). The median C-reactive protein level was 36.6 mg/L (range, 1.8-452), and the median procalcitonin level was 0.975 µg/L (0.04-158) (Table 1).

Thirty-nine (79.6%) patients died during follow-up. Thirty-five (71%) subjects required ICU and were transferred to the ICU (Table 1). Although all subjects (100%) in the ICU died, four (28.6%) of the subjects not requiring ICU also died (p=0.000). Twenty-two (95.7%) of the subjects with neutrophil count <100/mm^3 and seventeen (65.4%) of the subjects with neutrophil count >100/mm^3 died (p=0.009) (Table 2). In the univariate analysis, neutrophil count <100/mm^3 had an impact on the occurrence of death in subjects with *A. baumannii* infection (p=0.026, HR=11.64).

When the subjects were analyzed based on their antibiotherapy, the number of subjects treated with either colistin or tigecycline was 13 (26.5%) and that treated with a carbapenem-type antibiotic was 28 (57%). The number of subjects who died was comparable between those who were treated with colsitin/tigecycline or not (p=0.253). The number of subjects who died was comparable between those who were treated with a carbapenem-type antibiotic and those who did not (p=0.076) (Table 2).

Discussion

Real-life data on *A. baumannii* infection and its course in patients with hematological malignancies are limited, and the factors affecting the course of infection are not clear in this patient group. In this study, we aimed to determine the factors that influence the course of *A. baumannii* in patients with hematologic malignancies.

Table 2. Comparative characteristics of subjects who died and survived

	Dead patients N=39	Alive patients N=10	p value
Number of neutrophil count, n (%) <100 mm^3 >100 mm^3	22 (56.4%) 17 (43.6%)	1 (10%) 9 (90%)	0.009
Intesive care requirement, n, (%) Present Absent	35 (89.7%) 4 (10.3%)	0 (0%) 10 (100%)	0.000
Use of colistin/tigecycline Present Absent	12 (30.8%) 27 (60.2%)	1 (10%) 9 (90%)	0.184
Use of a carbapenem Present Absent	25 (64.1%) 14 (35.9%)	3 (30%) 7 (70%)	0.052

In a multicenter study examining the clinical characteristics and prognostic factors of *A. baumannii* infection in patients with hematological malignancies, a total of 40 patients with bacteremia were identified; 62.5% of them were diagnosed with acute leukemias. Neutropenia was detected in 67.5% of subjects, and neutropenic subjects had higher Acute Physiology and Chronic Health Evaluation Scores (APAHCE) and 30-day mortality than non-neutropenic subjects [12]. Carbapenem-resistant *A. baumannii* infection, neutropenia, high APAHCE, and Pitt bacteremia scores, and inappropriate antibiotic therapy were associated with 30-day mortality compared with carbapenem-susceptible infections [12]. In another multicenter study conducted on 46 patients with hematological malignancies, carbapenem-resistant *A. baumannii* cases were examined; a high SOFA score was associated with 7-day mortality, and appropriate antibiotic therapy was found to be protective in the first 48 hours [13].

Clinical data on *A. baumannii* and its course in patients with hematological malignancies have also been published. In a study that included critically ill hematological patients, 39 subjects with *A. baumannii* infection were included. Advanced age, aminoglycoside exposure, central venous catheterization, and nasogastric tube use were independent risk factors for *A. baumannii* infection [14]. In the multivariate analysis, low Glasgow coma score, neutropenia and immunosuppressive therapy, invasive mechanical ventilation, and severe sepsis were associated with mortality [14]. *A. baumannii* bacteremia was defined in 6% of subjects with hematologic malignancies, and 50% of these cases were fatal; all cases were carbapenem-resistant in another study [15]. In a study involving 154 patients with hematologic malignancies, nosocomial Gram-negative bacteremia was evaluated. Pitt bacteremia score, presence of aplastic anemia, bacteremia caused by glucose non-fermenting Gram-negative bacillus, inappropriate antibiotic therapy, presence of severe sepsis or septic shock, difficulty obtaining a microbiological culture, and need for ICU were associated with mortality. In the multivariate analysis, only bacteremia requiring ICU was associated with mortality [16].

In our study, *A. baumannii* infection was most frequently observed in the acute leukemia subgroup. Thirty-one (61%) of the subjects included in our study were diagnosed with acute leukemia, which was in accordance with the literature findings. Neutrophil count <100/mm^3 was found to have an impact on the occurrence of death in subjects with *A. baumannii* infection. Our study also showed that acute leukemia was the riskiest malignancy and that profound neutropenia was one of the most important risk factors. Although carbapenem administration did not have a significant effect on mortality, colistin/tigecycline administration did not have a significant effect. The need for ICU was associated with mortality, which is consistent with the literature.

Study Limitations

There are important limitations to our study. The most significant limitation of this study is that it was based on data from a single center. A further limitation is the retrospective

mortality prediction scores of subjects who were not included in the statistical analysis due to a lack of recorded data. In addition, antimicrobial susceptibility was not evaluated statistically.

Conclusion

In conclusion, in our study, we investigated the clinical features of *A. baumannii* infection in patients with hematological malignancies and the factors affecting the course of the infection in our clinic. Univariate analysis showed that neutrophil count <100/mm^3 had an impact on the occurrence of death in subjects with *A. baumannii* infection. The number of patients who died was comparable between those who were and were not treated with carbapenem-type antibiotic and those who were not. The need for ICU was associated with mortality. Further studies are needed to identify factors affecting the course of *A. baumannii* infection in patients with hematological malignancies.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital of Local Ethics Committee (approval date and number: 09/08/2019-1949). The experimental procedures were based on the Declaration of Helsinki and relevant institutional regulations.

Informed Consent: Retrospective study.

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We respectfully remember all the colleagues we lost in the fight against COVID-19.

Footnotes

Authorship Contributions

Data Collection or Processing: A.K., İ.S., M.H.D., Analysis or Interpretation: A.K., İ.S., M.H.D., Writing: A.K., İ.S., C,A., M.H.D., E.S.

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