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Acinetobacteria Baumannıı Infection in the Intensive Care Unit-Risk Factors and Antibiotic Resistance

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Abstract:, In this study, we tried to elucidate the increased carbepenem resistance in healthcare-associated acinetobacter baummani infections and the factors affecting mortality in the intensive care unit. A total of 70 subjects that were positive for acinetobacter baumannii colonisation have been included in the analysis. The data on age, gender, smoking, comorbidities, steroid usage and antibiotic treatment within the first 24 hours has been recorded. Septic shock patients who did not respond to intense fluid replacement and required dopamine infusion for the treatment of hypotension were also interpreted. The results of antibiogram culture, duration of noninvasive and invazive mechanical ventilation, hospital stay and mortality information have all been investigated. The APACHE and SOFA scores of the first admission day have been calculated. Invasive mechanical ventilation has been conducted to 66 patients and the median duration of administration was 19.5±23.94 (1-138, range: 138) days. The APACHE II score was 24.69±8.37 and SOFA score was 10.43±3.42. The mean hospital stay was 26.03±24.23 (1-139, range 138) days. The mean time to observe positive culture from hospital admission was 15.55±1.19 days. Patients with both meropenem and imipenem resistance were considered carbapenem resistant. By 2010, it was observed that both imipenem and meronem resistance reached 100%. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010. © 2022 NTMS.

Keywords: A. baumannii; Antibiotics Resistance; Intensive Care Unit.

1. Introduction

Healthcare-associated infections are more prevalent in intensive care unit patients. The risk factors associated with *acinetobacteria baumannii* at ICU can be elaborated as longer hospital stay, immune supression, older age, comorbid disease, major trauma or burn, previous antibiotic usage, invasive procedures, long term catheterization and mechanical ventilation (1). The rate of healthcare-associated infections are 5-10 times higher in the intensive care unit compared to inpatient clinics. The other importance lies beneath the

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fact that healthcare-associated infections are related with increased mortality, morbidity and healthcare costs (2). Hospital acquired infections are major health problem in intensive care units (3). *Acinetobacteria baumannii* is a gram negative, aerob cocobasilius and is one of the most frequent reasons of nasocomial infections (4). Although *acinetobacteria baumannii* has been identified as a beneficial species previously, currently it is treated as a health status threat due to its resistance to polypharmacy (5).

In this study we aimed to evaluate the *acinetobacteria baumannii* infection in our respiratory ICU with the annual parameters, demographics data and the change of carbepenem and other antibiotic resistance.

2. Material and Methods

The current study has been conducted in the respiratory intensive care unit between August 2006-July 2010 as a retrospective analysis. Ethical approval was obtained from the ethics committee of Dicle University Medical Faculty (Ethics Committee Number:190-21.09.10). Research and Publication Ethics was complied with in our study. The bacterial cultural analysis have been conducted to all patients and 70 subjects that were positive for *acinetobacter baumannii* reproduction have been included in the analysis.

The data on age, gender, smoking, comorbidities, steroid usage and antibiotic treatment within the first 24 hours has been recorded in the analysis. Septic shock patients who did not respond to intense fluid replacement and required dopamine infusion for the treatment of hypotension were also interpreted. The results of antibiogram culture, duration of non-invasive and invazive mechanical ventilation, hospital stay and mortality information have all been investigated for the analyis. Age, smoking, duration of IMV, hospital stay,

2.1. Statistical Analyses

Statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics of continuous variables were shown with mean and standard deviation (SD) values. The chi-square test was used to compare the nominal variables between the two groups. Student's t test was used to compare the mean values of scalar data between the two groups. Shapiro-Wilk test was performed to evaluate whether the data is distributed normally. The hypotheses were bidirectional and $p \leq 0.05$ value was accepted as statistically significant at 95% confidence interval.

3. Results

We had 84 samples of 70 patients *acinetobacter baumanni* cultures. The details of baseline demographic parameters of the patients are shown in Table 1.

Non-invasive mechanical ventilation has been conducted to 43 patients and the median duration of administration was 5.15±6.52 (1-39, range: 38) days. Invasive mechanical ventilation has been conducted to 66 patients and the median duration of administration was 19.5±23.94 (1-138, range: 138) days.

The APACHE scores has been calculated according to lowest figures at the admission of ICU. The APACHE II score was 24.69±8.37 and SOFA score was 10.43±3.42. The mean hospital stay was 26.03±24.23 (1-139, range 138) days.

The mean time to observe positive culture from hospital admission was 15.55±1.19 days. The distribution of 84 samples were as follows: n=40 (47.6) from blood, n=26 (31%) deep tracheal aspiration material, n=7 (8.3%) from urine, n=7 (8.3%) from wound, n=4 (4.8%) from catheter. The antibiotics used within the first 48 hours of ICU stay were ceftriaxone n=29 (41.4), cefoperazone/sulbactam n=7 (9.9%), piperacillin/tazobactam n=3 (4.3%), levofloxacin n=6 (8.6%), meropenem n=8 (11.5%) and imipenem n=6 (8.5%).

3.1. Annual Resistance Rates

The annual resistance rates are shown in Table 2. There was a positive trend of bacterial colonisation starting from 2007 to 2009. We did not analyze 2006 due to limited number of cases n=1 (1.2%). The annual resistance distribution was n=14 (16.7%) in 2007, n=35 (41.7%) in 2008, n=27 (32.1%) in 2009 and n=7 (8.3%) in in 2010 (until June).

3.2. Carbepenem resistance

Patients with both meropenem and imipenem resistance were considered carbapenem resistant. By 2010, it was seen that both imipenem and meronem resistance reached 100%. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010 (Table 2).

3.3. Mortality Rate

The mortality rate, age, smoking, duration of IMV, hospital stay, APACHE II and SOFA scores were elaborared in Table 3. Regarding all the patients with acinetobacter baumannii colonisation the mortality rate has been observed as 87.1% (n=61). Age, smoking, duration of IMV, hospital stay, APACHE II and SOFA scores did not Show any statistical correlation with mortality.

Table 1: Baseline Demographics of the Study Population.

Baseline Demographics	*n (%)*
Gender	
Female	25 (35.7%)
Male	45 (64.3%)
Smoking	
Yes	30 (42.9%)
No	40 (57.1%)
Steroid Usage	
Yes	32 (45.7%)
No	37 (52.9%)
Dopamine Requirement	
Yes	60 (85.7%)
No	10 (14.3%)
Hospital Stay	
Yes	55 (78.6%)
No	15 (21.4%)
Outcome	
Alive	9 (12.9%)
Exitus	61 (87.1%)
Comorbid Disease	66(94.3%)
Chronic Obstructive Pulmonary Disease	26 (37.1%)
Congestive Heart Failure/Coronary Artery Disease	15 (21.4%)
Renal Failure	
Pulmonary thromboembolism	14 (20%)
Diabetes mellitus	9 (12.9%)
Cerebro-vascular event	9 (12.9%)
Pulmonary Tuberculosis History	9 (12.9%)
Malignity	6 (8.6%)
Hypertension	6 (8.6%)
Para-pulmonary effusion	5 (7.1%)
Bronchiectasia	4 (5.7%)
Muscle Disease	4 (5.7%)
	4 (5.7%)

Table 2: Annual antibiotic resistance rates (%).

Antibiotic	2007	2008	2009	2010
Cefotaxime	100	100	100	100
Trimethoprim + Sulfamethoxazole	92.3	85.7	96.3	71.4
Piperacillin Sodium	100	100	100	100
PiperacillinTazobactam	No Data	95.5	100	85.7
Chloramphenicol	100	100	No Data	No Data
Aztreonam	100	91.7	No Data	No Data
Cefepime Hydrochloride	61.5	80	100	100
Ceftazidime	92.3	91.4	96.3	100
Levofloksasin	100	90.3	95.8	71.4
Cefoperazone/Sulbactam Sodium	No Data	0	9.1	16.7
Ciprofloxacin	92.3	91.4	96.3	100
Imipenem	61.5	74.3	81.5	100
Meropenem	58.3	71.4	81.5	100
Colistin	No Data	0	No Data	0

Table 3: Comparison of risk factors on alive and exitus patients.

	EXITUS	ALIVE	P
Age (year)	63.34±15.9	55.67±22.09	0.20
Smoking (packs/year)	61.22±32.75	21.67±10.40	0.05
APACHE II	24.4±8.7	26±5.4	0.50
SOFA	10.49±3.46	10.0±3.31	0.69
IMV (days)	15,84±17.25	42.25±46.76	0.15
Duration of hospital stay (days)	21.5±17.8	56.6±38.36	0.03

$p \leq 0.05$ statistical significance.

A majority of the patient with smoking habit died (n=27/30). A statistical sginificance has been observed in the annual cigarette consumption was 61.22±32.75 packs in the mortality group and 21.67±10.40 packs/year in the alive individuals (p=0.05). One other significant data was duration of hospital stay between mortality group and alive subjects (p=0.03). Systemic steroid utilization, hospital stay, dopamin infusion, comorbid disease and gender differences did not generate any significance on dead and alive patients.

4. Discussion

In this study we have analyzed bacterial colonisation in order to detect the antibiotic resistance to acinetobacter baumannii. In our study, it was seen that the carbenem resistance of *A. Baumannii* reached 100%. In a recent systematic review, 24 studies were evaluated and, A. baumannii and carbapenem resistant strains were reported to account for 20.9% (95% CI 16.5-26.2) and 13.6% (95% CI 9.7-18.7) of all nosocomial infections, respectively (6).

We have investigated the *acinetobacter baumannii* treatment resistance in our intensive care unit with respect to mortality factors in the literature. We assume that the outcomes of this study will contribute to the patient management in the ICU.

The selection of edfective antibiotic at a sufficient dose is crucial forthe treatment success of healthcare-associated infections (7). At this stage the importance of resistance rates plays an important role for convenient treatment at the intensive care unit (8). The acinetobacter baumannii has developed resistance to dysinfectants and major antimicrobial agents thus becoming a severe healthcare-associated infection (9). *Acinetobacter baumannii* has developed strong resistance to sefthazidime 92.5% *(n=37/40)* and izolated *acinetobacter baumannii* cultivates this resistance to this antibiotic group (10). Since carbapenem group antibiotics are the last option in the treatment of *A. baumannii* infections, carbapenem resistance is of particular importance. In the study of Deveci et al., among 127 *A. baumannii* strains isolated from patients diagnosed with healthcare-associated infections between 2007 and 2010, 5 of 26 strains in 2007, 18 of 31 strains in 2008, 10 of 35 strains in 2009. In 2010, 20 of 35 strains and 20 of 35 strains were obtained from intensive care patients. While the sensitivity rate for imipenem was 50% in 2007, it was 20% in 2010. Similarly, increased carbepenem resistance was noted in our study. In the current research, by 2010, it was seen that *A.baumani* resistance reached 100% both imipenem and meronem resistance. Meronem resistance was 58.3% in 2007, 71.4% in 2008, 81.5% in 2009, and 100% in 2010. Imipenem resistance was 61.5% in 2007, 74.3% in 2008, 81.5% in 2009, and 100% in 2010. However lower resistance rates has been achieved in the European studies as mortalities was not always clearly identified due to comorbidities (12). In a previous article by Jang et al, they have declared that comorbid diseases played a major role than infection itself on mortality rates (13). Lahmer et al published that the rate mortality due to *acinetobacter baumannii* was 100% on sepsis cases (14). Similarly Leão et al emphasized that there is a relation between mortality and *acinetobecter baumanii* in sepsis patients at intensive care unit (15). A cohort study with septic shock patients in ICU has shown a mortality rate of 49.6% (16). On the contrary, no statistical significance has been achieved between the patients in septic shock that required dopamine and individuals with no sepsis in our study.

If the risk factors of *acinetobacter baumannii* infection was analyzed one can see that being male, comorbid disease *(respiratory and renal failure)*, high APACHE II score, longer stay at ICU, invasive mechanical ventilation, previous antibiotic usage, immuno-supression and septic shock were the major factors (17).

In another study conducted in burnt patients, a total of 30 patients infected with Multi-drug resistant *acinetobacter baummani* (MDR-AB) and 60 uninfected control cases were included in the study. This study showed that many factors contribute to multidrug resistance in *A. baumannii*. A combination of early detection of wound infections, appropriate antimicrobial treatments, surgical debridement and early wound closure may be effective in treatment (18). In another study in which a total of 70 newborns with extensive drug-resistant (XDR) *acinetobacter baummani* growth and 118 control newborns were included in the study, gestational age, mechanical ventilation, transfusion, parenteral nutrition, glycopeptide use, carbapenems, and aminoglycosides were found to be significantly associated associated with mortality (19).

On the contrary we did not found any statistical significance between exitus and alive individuals on age, comorbid disease, gender, hospital stay, systemic steroid usage, dopamine infusion requirement, systemic steroid administration duration of invasive mechanical ventilation, APACHE II and SOFA scores. The limited number of study population, heterogeneous patient profiles might be the reason of this issue. On the other hand all the risk factors above were not evenly present in the ICU patients.

According to previous research, the mortality rate of patients with *acinetobacter baumannii* colonisation ranges between 30-76% (20). In our study the mortality rate in *acinetobacter baumannii* clonized patients were 87.1% (n=61) (n=9, 12.9% were alive). The high rate of mortality in this study could be elaborated with 3 factors: older age, presence of comorbidities and being in the respiratory ICU.

Male gender has been elaborated as one of the risk factors in previous studies and this rationwas 64.3% in our research (21). The rate of smoking was 42.9% in our population and Wah-Shing Leung et al found a similar figure as 55.4% previously (22). The high rate of smoking could be attribured to the respiratory intensive care unit.

Preventing antibiotic resistance development to acinetobacter *baumannii* is one of the main objectives of intensive care patient management. A bacterial culture analysis should be conducted prior to initiating antibotic treatment on hospitalized patients. did not have a placebo group and the absence of a control group that did not receive both treatments.

5. Conclusions

Carbepenem resistance is increasing gradually and is a problem in terms of treatment. Having information about resistance would lead the physician in a more appropriate way for better treatment success. The antimicrobial regimen must be reassigned according to bacterial culture results. Increased carbapenem resistance is currently trending and this causes longer duration of hospital stay and increased mortality. Further studies should be conducted in this era with larger number of patients.

Limitations of the Study

The mail limitation of this study can be elaborated as the population only consisted of acinetobacter baumannii colonized individuals and lacking a control group. Nonetheless we still assume that this study will provide certain guidance to intensive care management.

Conflict of Interests

We do not have any conflicts of interest

Financial Support

We do not have financial resources to declare

Author Contributions

Data collection B.Ç, statistics E.K, spelling B.Ç and E.K, edit İ.H and M.K, translation and coordination T.K

Ethical Approval

Ethical approval was obtained from the ethics committee of Dicle University Ethics committee number: 192:21.09.10.

Data sharing statement

Data and materials are Available upon reguest: HYPERLINK "mailto:drbariscil@hotmail.com"drbariscil@hotmail.com

Consent to participate

Consent to participate was obtained from the participants.

Informed Consent

Informed consent was obtained from the participants

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