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Mortality In Patients With Respiratory And Nonrespiratory Carbapenem Resistant-Multidrug Resistant Acinetobacter Infections

Nosheen Nasir
Aga Khan University, nosheen.nasir@aku.edu

S Mahmood
Aga khan University, syed.mahmood@aku.edu

SHORT COMMUNICATION

MORTALITY IN PATIENTS WITH RESPIRATORY AND NON-RESPIRATORY CARBAPENEM RESISTANT-MULTIDRUG RESISTANT ACINETOBACTER INFECTIONS

Nosheen Nasir, Syed Faisal Mahmood

Section of Infectious Diseases, Department of Medicine, Aga Khan University Hospital Karachi-Pakistan

Background: Mortality from carbapenem-multi-drug resistant *Acinetobacter* infections may vary according to site of infection. The objective of this study was to compare mortality in respiratory vs. non-respiratory infection with Carbapenem-Multi-drug Resistant Acinetobacter (C-MRAB). **Methods**: We conducted a prospective cohort study to compare mortality rate in patients with respiratory vs. non-respiratory infection (n=30 each). **Results**: Results showed that mortality was 40% in the respiratory group compared to 23% in non-respiratory group; the difference was not statistically significant (p=0.165, RR=1.71, CI=0.73-3.75). There was a significantly higher prior admission rate in patients with respiratory infection (p=0.028). Logistic regression did not reveal any modifier effect from other variables. **Conclusion**: This study showed no significant difference in mortality in patients with carbapenem-multi-drug resistant acinetobacter respiratory vs. non-respiratory infections.

Keywords: *Acinetobacter*; Mortality; Respiratory; *Acinetobacter baumannii*; Pneumonia

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INTRODUCTION

Acinetobacter baumannii is a gram-negative, aerobic, nonfermenting coccobacillus which is often implicated in nosocomial infections.[1,2] *Acinetobacter baumannii* has been associated with pneumonia, bacteraemia, wound infections, urinary tract infections, central line associated bacteraemia and meningitis.[3,4] Infections caused by Acinetobacter sp. are especially difficult to treat due to increasing carbapenem resistance and surveillance studies have shown that the percentage of carbapenem-resistant isolates have gradually increased over the last ten years in Europe, North America, South Asia and Latin America.[5–8]

The associated crude mortality rate with carbapenem multidrug resistant *Acinetobacter baumannii* (C-MRAB) is high, ranging from 26–68%.[3,9,10] C-MRAB infections are also associated with increased morbidity and a prolonged length of hospital and ICU stay.[11] While the increased mortality may be related directly to limited therapeutic options, poor outcomes may also be due to inappropriate empirical therapy and the site of infection. Erbay *et al* identified that amongst the sites of infection, pneumonia causing bacteraemia was associated with the greatest mortality.[1] However, as there has been no comparison of outcomes with other sites of infection we a study to evaluate if respiratory infections with C-MRAB were associated with a higher mortality as compared to non-respiratory infections with C-MRAB.

MATERIAL AND METHODS

We conducted a prospective observational cohort study at a 600, bedded tertiary referral hospital in Karachi, Pakistan. All adult patients (age greater than 18 years) presenting between the 1st of March 2011 and 31st of August 2011, with a positive culture for C-MRAB from any site active infection were included. Patients with samples sent as an outpatient or those with a polymicrobial infection were excluded. Patient's medical records were reviewed to obtain information regarding age and gender, medical diagnoses, co-morbidities, antimicrobial therapy and in-hospital mortality, length of hospital stay and readmission rate within 1 year of discharge as well as biological sample, species of Acinetobacter and antibiotic susceptibility.

Data was entered into SPSS version 16. For purpose of the analysis, we assumed that respiratory infections were associated with higher risk of mortality and were considered as the 'exposed' (at higher risk) while the non-respiratory group were considered 'non-exposed'. Significance of difference of mortality between these two groups was determined using Chi square test. Relative risk of mortality was calculated for the two groups. Influence of confounding variables (gender, source of positive culture, diagnoses, comorbid) on mortality was determined using logistic regression. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 patients with Acinetobacter infection were included in the study with an equal number in reparatory and non-respiratory arms. In the non-respiratory group, most patients had a urine tract infection (n=15), followed by wound infections (n=7) and vascular catheter infections (n=6). Overall, the mean age of our patients was 53.7 years ranging between 18–88 years (SD±20.0 years). There were 53% males and 47%

females. No significant differences in age or gender were found amongst patients with respiratory and the non-respiratory C-MRAB infections. Among the co-morbidities, 30% of patients with respiratory infections had ischemic heart disease as compared to 6% in non-respiratory infections (p=0.22).

The commonest principal diagnosis on admission was sepsis, 56% in respiratory and 53% in non-respiratory group; followed by trauma 10% in respiratory and 16% in non-respiratory group. Out of the 60 total patients with C-MRAB infection, 19 expired whereas 41 were discharged from the hospital (Table-1). Although a greater proportion of patients died in the respiratory group (40%) compared to non-respiratory group (23%), the difference was not statistically significant (p=0.165, RR=1.71, CI=0.73–3.75, Figure-1). There was a significantly higher prior admission rate in patients with respiratory infection as compared to non-respiratory group (p=0.028).

The mean length of stay was 18 days for the respiratory group and 19 days for non-respiratory group, and there was a 23% readmission rate among survivors (20% in respiratory group and 26% in non-respiratory group). To look for possible bias due to confounding variables, logistic regression was performed for outcome (discharged vs. died) in relation to categorical variables, i.e., group (respiratory vs. non-respiratory), gender, comorbid, diagnosis and nosocomial vs. community acquired infection. No statistically significant effect was observed.

Appropriate definitive antibiotic therapy with intravenous polymyxin B was instituted in 70% of patients in respiratory group and 53% in the non-respiratory group (p=0.388). However, no statistically significant difference was observed in terms of mortality in both groups who received polymyxin B containing regimen versus those who did not receive Polymyxin B (p=0.09).

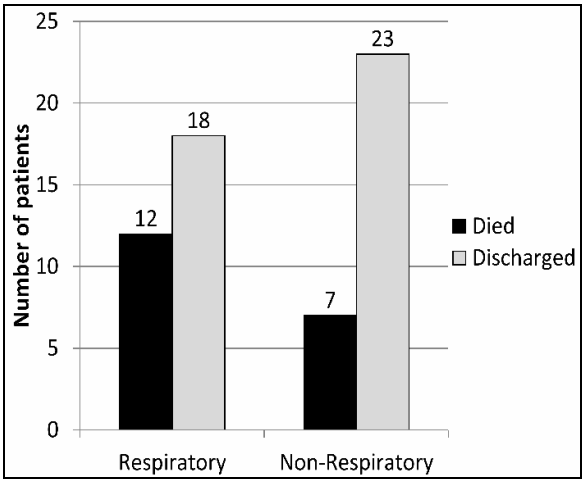

Figure-1: Comparison of outcome between respiratory and non-respiratory groups

Table-1: Patient characteristics in both groups

Patient Characteristics	Respiratory group (n=30)	Non-Respiratory group (n=30)	p-value
Gender			0.30
Male	18	14	
Female	12	16	
Primary Diagnosis			0.11
Tumour	2	4	
Pneumonia	5	0	
Sepsis	12	16	
Trauma	3	5	
Autoimmune	2	0	
Other	6	5	
Definitive anti-microbial therapy			0.388
Polymyxin	21	16	
Carbapenems	4	7	
Source of infection			
Tracheal	28	0	
Urine	0	15	
Sputum	2	0	
Wound	0	7	
Vascular catheter	0	6	
Other	0	2	
Outcome			0.165
Died	12	7	
Discharged	18	23	

DISCUSSION

Nosocomial infections with Acinetobacter are an emerging cause of morbidity and mortality in intensive care units worldwide. We compared the differences in outcomes between patients who had respiratory infection with C-MRAB and those with infection at other sites. We were not able to find a statistically significant difference in outcome in both groups although there was a trend towards greater mortality in patients with C-MRAB pneumonia. This is in contrast to studies from Europe[12,13] and South East Asia[14] which have shown increased mortality with respiratory infections. For example, Chen et al reported a mortality of 39% with C-MRAB respiratory tract infections compared to 3.8% with vascular catheter or urine catheter related infections (p=0.001)[15], while Erbay *et al*[1] found that the mortality with C-MRAB bacteraemia was significantly higher when associated with a respiratory infection 78% (p=0.009). Similarly, a study from India.[16] reported mortality rates of 50% in patients with C-MRAB ventilator associated pneumonia. However, none of these studies were specifically designed or powered to evaluate differences in outcomes of different C-MRAB infection sites. As a result, most patients with C-MRAB had a respiratory tract infection (which is the most common site), which may lead to the apparent increase in mortality. In our study, we attempted to control for this by enrolling an equal number of patients with respiratory and non-respiratory C-

MRAB infections. Moreover, most of these studies did not distinguish between C-MRAB infection and colonization. As a number of risk factors for colonization with C-MRAB (such as a high APACHE II score and ICU stay)[9,17] are associated with increased mortality, we attempted to control for this by not including patients who were colonized and only evaluating actively infected patients. While our study was limited by a small sample size and a heterogeneous comparator group, we did not find any difference in outcomes between respiratory and non-respiratory C-MRAB infections. Moreover, our study was a single centre study so the findings may not be generalizable to other settings.

CONCLUSION

In conclusion, our study highlighted that while mortality with C-MRAB infections is high, this is not related to the site of infection and may linked to the virulence of the organism or the lack of therapeutic options.

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Address for Correspondence:

Dr. S. Faisal Mahmood, Section of Infectious Diseases, Department of Medicine, Aga Khan University, PO Box 3500, Stadium Road, Karachi74800-Pakistan

Tel: +92 2134864574

Email: faisal.mahmood@aku.edu