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Risk Factors for Acquisition of Carbapenem Resistant *Acinetobacter baumannii* in Intensive Care Unit of a Tertiary Care Hospital

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Abstract: ***The rise of Carbapenem resistant Acinetobacter baumannii (CRAB) in intensive care units has been associated with certain risk factors as confirmed by various studies. The study was carried out to assess these risk factors for acquisition of CRAB in patients of Intensive care units of a teratiary care hospital. Prospective case control study was conducted from Sep 2010 to Aug 2012. Cases were patients from whose clinical sample Acinetobacter baumanii were isolated. They were grouped into CRAB and Carbapenem sensitive Acinetobacter baumanii (CSAB) groups based on meropenem sensitivity testing. Their demographic and clinical details were recorded and compared as risk factors for acquisition of CRAB. Various independent risk factors for acquisition of CRAB were assessed. Out of all the factors none came to be significant for acquisition of CRAB over CSAB. The study has brought out that various risk factors are not significant in acquisition of CRAB over CSAB.***

Keywords: *Acinetobacter baumanii.*, Carbapenem Resistance, Risk Factors

1. Introduction

Acinetobacter baumannii (AB) has established itself as important pathogen, especially in intensive care units (ICUs). The development of resistance against multiple antimicrobials has severely restricted the therapeutic options available for infected patients, and increased the length of stay of these patients in ICUs with mortality [1, 2].

2. Literature Survey

This pathogen also has the unique ability of up regulating and acquiring new antibiotic resistant determinants from environment. Despite intensive efforts, acquisition of multi-drug resistant (MDR) AB has beenl a problem due to the great ability of AB to disseminate and colonize human and environmental reservoirs [3, 4]. Carbapenems are usually the antibiotics of choice for treating serious infections caused by *A. baumannii*. However, reports of Carbapenem resistant *A. baumannii* (CRAB) strains have been rising steadily during the past few years, and these isolates are often multidrug-resistant. This emergence of CRAB has become a worldwide problem and a troublesome development that threatens the continued successful treatment of *Acinetobacter* infections [3, 4, and 5]. Recently, major endemic and epidemic outbreaks of MDR AB have occurred in critically ill patients throughout the world.

3. Problem Definition

Various studies using different methodologies for analysis of risk factors associated with the acquisition of AB have been published in different journals. However, more data regarding the risk factors for acquisition of CRAB infection are needed in order to prevent infections in patients in ICUs. Aim of this study was to assess various risk factors for acquisition of CRAB in patients admitted to intensive care unit at a tertiary care hospital.

4. Methodology

This prospective study was conducted at the Department of Microbiology and Intensive Care Unit of a tertiary care institute after approval of the Institutional ethical committee between Sep 2010 and Aug 2012. A total number of 245 non repeat specimens received from ICU surgery and ICU medicine during Dec 2010 to May2012 in Department of Microbiology were processed for routine aerobic culture. Specimens were collected using strict aseptic precautions and were transported to the laboratory as per guidelines for transportation of clinical specimens for aerobic bacteriology. Amongst these 245 specimens, 80 cultured *Acinetobacter baumannii* in laboratory and were included as study strains. Identification of the genus *Acinetobacter* was done by standard laboratory protocols as suggested by Koneman E W et al (6^{th} ed). Detailed clinical histories, co-morbidities and various risk factors of patients were meticulously recorded. Antimicrobial susceptibility test was performed by using Kirby Bauer Disc Diffusion method as per Clinical Laboratory Standard Institute (CLSI) guidelines (2010). All the isolates showing resistance to Meropenem were subjected to MIC by Agar Dilution as per CLSI guidelines (2010). Isolates with MIC range of $\geq$8 µg/ml for Meropenem were considered Carbapenem Resiatant *Acinetobacter baumanni*, and Isolates with MIC range of <8 µg/ml for Meropenem were considered Carbapenem Sensitive *Acinetobacter baumannii.* Scheme of categorization is presented in **Fig 1.**

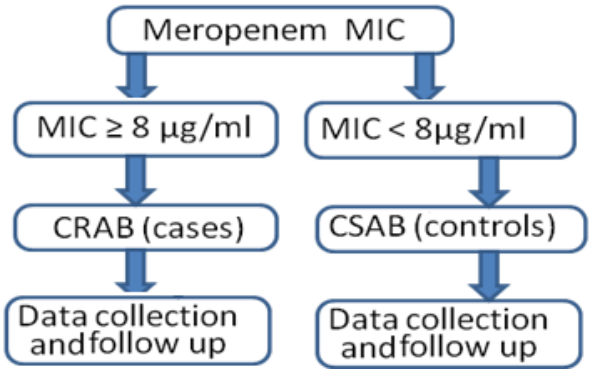

Figure 1: Categorization of Isolates in CRAB (Carbapenem resistant Acinetobacter baumannii) and CSAB (Carbapenem sensitive Acinetobacter baumannii) groups

Various risk factors were assessed for acquisition of CRAB from the data (given in master charts) collected for both the groups i.e. CRAB and CSAB. Statistical analysis was done by Chi Square test and Student's Paired T test wherever appropriate. *P* value ≤ 0.05 was considered significant.

5. Results

Out of 245 non repeat specimens of ICU patients, *Acinetobacter baumannii* strains were isolated from 80 specimens. Month wise distribution of these isolates is given in **Table 1**.

Table 1: Month wise distribution of Acinetobacter baumannii

Months	Dec 10	Jan 11	Feb 11	Mar 11	Apr 11	May 11
No of isolates	5	27	9	10	16	13
% (N=80)	6.25	33.8	11.25	12.5	20	16.25

It is evident that most isolates of *Acinetobacter baumannii* (33.8%) were isolated alone in the month of Jan 2011. Specimen wise isolation of *Acinetobacter baumannii* is given in **Table 2**.

Table 2: Total sample distribution (n=245)

Infection	Total no of sample processed-No (%)	Growth of *Acinetobacter* – No (%)	Growth of other organisms–No (%)
Respiratory infection	82(33.45)	44(53.65)	38 (46.25)
Blood stream infection	68(27.75)	22(32.35)	46 (67.65)
Surgical site infection	46(18.77)	13(28.26)	33 (71.74)
Urinary tract infection	32(13.06)	01(3.12)	31 (96.88)
Others	17(6.93)	00(00)	17 (100)
Total	245(100)	80(32.65)	165 (67.35)

Out of all samples respiratory samples constituted maximum, 33.45% (82/245) of total specimens from ICU. *Acinetobacter baumannii* were isolated from 53.6% (44/82) of total respiratory specimen. Out of all the specimens from which *Acinetobacter baumannii* was isolated respiratory specimens contributed the most 55% (44/80). **Fig 2** gives distribution of *Acinetobacter baumannii* with respect to specimen.

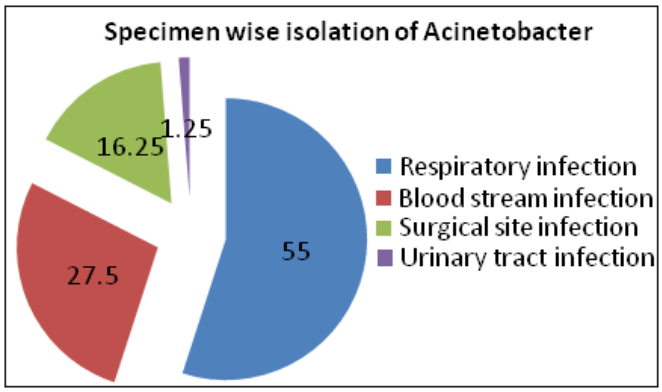

Figure 2: Specimen wise isolation of Acinetobacter

Demographic and clinical details of the 80 subjects from whom *Acinetobacter baumannii* was isolated were collected. Amongst 80 subjects, a total of 49 (61.25 %) were admitted to Surgery ICU (ICU-S) while 31 (38.75 %) were admitted to Medical ICU (ICU-M). Amongst these 80 subjects 48 (60%) were male while 32 (40%) were female. Age ranged from 16 yrs to 93 yrs with median and mean age 57.0 and 55.0 yrs respectively. Maximum subjects were of age group above 60 yrs. Origin of subjects is an important factor in colonization of bacteria leading to subsequent infection. 46(57.5%) subjects were directly admitted to the ICU, 23 (28.8%) were transferred in from other hospitals and 11(13.8%) were transferred to ICU from different wards of the hospital. A total of 22 (27.5%) subjects had received antibiotic in the past. ICU stay of study subjects ranged from 03 to 32 days with mean ICU stay for Surgery and Medical ICU 12.9 and 10.6 respectively. During the ICU stay these subjects underwent invasive procedures because of which they were at the risk of ICU acquired infection. Some of such important interventions are presented in **Table 3**.

Table 3: Interventions at ICU

Mean days (SD)	ICU S	ICU M	Total
CVC	11.52(9.9)	8.21(7.7)	10.2(9.2)
Intubation	10.47(10.1)	6(4.9)	8.68(8.7)
Mech Venti	10.396(10.2)	5.93(4.8)	8.65(8.7)
Parental Nutrition	5.125(7.4)	1.43(3.6)	3.65(6.4)

Out of 80 isolates of *Acinetobacter baumannii*, 48 (60%) were found to be Carbapenem resistant i.e. Meropenem MIC$\geq$8 µg/ml and 32 (40%) were found to be Carbapenem sensitive i.e. Meropenem MIC<8 µg/ml by Agar Dilution method. Detail break up of samples into these two groups have been given in **Table 4.**

Table 4: Categorization of Isolates in CRAB and CSAB groups

Infection	CRAB (*N*=48) (%)	CSAB (*N*=32) (%)	Total (*N*=80) (%)
Pneumonia	28(58.33)	16(50)	44(55)
Blood stream infection	12(25)	10(31.25)	22(27.5)
Surgical site infection	07(14.58)	06(18.75)	13(16.25)
Urinary tract infection	01(2.08)	00(00)	01(1.25)
Total	48(100)	32(100)	80(100)

CRAB – Carbapenem resistant *Acinetobacter baumannii*
CSAB – Carbapenem sensitive *Acinetobacter baumannii*

Various risk factors for acquisition of Carbapenem resistant *Acinetobacter baumannii* isolates were assessed between two groups of CRAB and CSAB isolates from the data collected during follow up of patients. All the patients were further followed up for detail clinical and demographic data till their discharge from hospital or death.

1) **Sex distribution:** Amongst these subjects, 48(60%) were male while 32 (40%) were female. There was no major variation between sex distribution between two groups of CRAB and CSAB. P value as calculated was 0.78.
2) **Age distribution:** Age ranged from 16 yrs to 93 yrs. Mean ages of both the groups of patients were almost equal. P value as calculated was 0.88.
3) **Location:** 48(60%) of patients were from Surgical ICU, while 32(40%) of them were from Medical ICU.
4) **Origin of patients:** Majority of CRAB patients 25(52.0%) and CSAB patients 21(65.6) were admitted directly to ICU and were not transferred in from another hospital or ward. P value as calculated was 0.09.
5) **Relation to trauma:** Amongst these subjects, CRAB had13 (27.0%) patients of trauma, while CSAB had 8 (25%) patients of trauma. P value as calculated was 0.836.
6) **Past H/O Antibiotic:** Majority of patients in both CRAB 30(62.5%) and CSAB 28(87.5%) were without any previous history of antibiotics. P value calculated for both the groups was 0.07.
7) **Duration of ICU stay:** ICU stay ranged from 02 days to more than 20 days. All the isolates were isolates from patients after more than 48 hrs of admission signifying that all were nosocomial infections. Mean duration of stay for CRAB infection was 12.7 while for CSAB infection was 10.9. p value as calculated was 0.28.
8) **Duration of intervention:** Various interventions during ICU admission are major risk factors for CRAB acquisition. None of the intervention duration demonstrated significant p value.
9) **Outcome of patients:** Mortality in patients of CRAB was 14(29%) out of 49, while for that of CSAB 6(18.75%) out of 32. P value as calculated is 0.6.
10) A composite table showing assessment of all risk factors for acquisition of Carbapenem resistant *Acinetobacter baumannii* is being given in **Table 5.**

Table 5: Assessment of risk factors for acquisition of CRAB

Risk factors	CRAB (*N*=48) *n* (%)	CSAB (*N*=32) *n* (%)	Total (*N*=80) *n* (%)	*p* value
Female Sex	18 (37.5)	13(40.6)	31(38.7)	0.78
Other hospital	18(37.5)	5(15.6)	23(28.7)	0.09
RTA	13(27.1)	08(25)	21(26.2)	0.836
Past antibiotic history	18(37.5)	04(12.5)	12(15)	0.071
Past surgery history	08(16.67)	03(9.37)	11(13.75)	0.72
Unscheduled surgical	17(35.4)	13((40.1)	30(37.5)	0.38
Mortality	15 (31.25)	8 (25)	23 (28.75)	0.6
Risk factors	CRAB (SD ± Mean)	CSAB (SD ± Mean)	Total (SD ± Mean)	*p* value
Age (mean)	55.3 ± 17.0	54.7 ± 18.1	55.0 ± 17.3	0.88
Duration of antibiotic	18.6 ± 9.2	16.7 ± 7.5	18.44 ±8.97	0.0089
Duration of ICU stay	12.65 ± 7.7	10.7 ± 8.7	12.0 ± 7.8	0.28
Duration of CVC	10.5 ± 9.2	9.7 ± 9.2	10.2 ± 9.2	0.6
Duration of intubation	8.6 ± 8.2	8.8 ± 9.5	8.7 ± 8.7	0.096
Duration of ventilation	8.5 ± 8.2	8.7 ± 9.5	8.6 ± 8.7	0.12
Duration of parenteral nutrition	4.0 ± 6.5	3.1 ± 6.5	3.7 ± 6.4	0.65

6. Discussion

6.1 *Acinetobacter baumannii :* emergence of successful nosocomial pathogen

The development of Multi Drug Resistance in Acinetobacter has been a major cause of concern in ICU infections. Recently, major endemic and epidemic outbreaks of MDR *Acinetobacter baumannii* have developed in critically ill patients throughout the world; aggressive control measures to prevent the transmission and colonization of this pathogen are currently limited.

Acinetobacter baumannii has been implicated in a wide spectrum of opportunistic diseases including septicaemia, pneumonia, endocarditis, meningitis, skin and wound infections and urinary tract infections in ICUs. [11] The greatest impact of *Acinetobacter* has been as a causative agent of nosocomial pneumonia, particularly ventilator associated cases. *Acinetobacter* pneumonia with multilobular cavitations, pleural effusion and broncho-pleural fistula formation has frequently been observed. [7] The incidence of MDR *Acinetobacter baumannii* bacteremia has increased; thus, efforts to identify factors that influence the survival of patients with this pathology have been made in various studies [7,8,9].

In this study *Acinetobacter baumannii* was isolated mainly from four different types of samples coming from ICU. The study revealed that *Acinetobacter* mostly colonizes respiratory tract in patients causing pneumonia and other respiratory conditions. This fact is also mentioned by Mandel et al [11] and by other researchers. [13, 14]

6.2 Prevalence of *Acinetobacter baumannii* in ICU

In this study, prevalence of *Acinetobacter baumannii* in ICU was estimated to be 32.7%. Out of which 42 (60%) are Carbapenem Resistant AB. Various studies have reported the prevalence of Imipenem resistance in Acinetobacter spp as 6—8% in the USA and Canada, 10% in Latin America, and 16% in Europe, however these prevalence studies were for hospital and not only for ICUs. [15, 16, 17]

6.3 Evaluation of risk factors for acquisition of Carbapenem resistant *Acinetobacter baumannii*

Various studies using different methodologies have analyzed different risk factors associated with the acquisition of

Acinetobacter baumannii. Most of them have addressed factors that influence the risk of infection with MDR AB, comparing to infection with non-MDR *Acinetobacter baumannii*, or non-*Acinetobacter baumannii.* Such studies have found factors such as male sex, longer duration of ventilation, longer duration of parenteral nutrition, past antibiotic history, longer duration of antibiotics and longer duration of ICU stay associated with increased risk of acquisition of infection with *Acinetobacter baumannii.*[18, 19, 20, 21, 22, 23, 24] These factors also include prior colonization, which was independently related to the development of MDR AB bacteremia and colonization. [1, 3] However, there is limited data on risk factors associated with the development of MDR AB bacteremia from colonization in ICUs. [18]

Jung et al 2010 showed that the presence of infection and respiratory failure at the time of ICU admission, recent central venous catheter insertion, and bacteremia caused by other microorganisms after colonization by MDR AB, and prior antimicrobial therapy, as independent risk factors for MDR AB bacteremia. [1]

In this study after statistical calculations, it was found all the risk factors like patient coming from other hospitals, with past antibiotic history, of road traffic accident cases, longer duration of antibiotics, longer duration of CVC and longer duration of ventilation were not found to be statistical significant for acquisition of Carbapenem resistant *Acinetobacter baumannii*. Even mortality rate also was not significantly higher in patients with CRAB infections. The study differs with several other studies which have found association of several risk factors for CRAB. [1, 3, 18, 19, 20, 21, 22, 23, 24]

7. Conclusion

7.1 This study differs from previous study by not founding any association of risk factors with acquisition of CRAB in ICU as has been previously found.

8. Future Scope

Further studies are recommended to ascertain various risk factors for acquisition of CRAB.

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