CLINICAL CONDITIONS AND RISK FACTORS OF *ACINETOBACTER BAUMANNII* PRODUCING METALLO BETA-LACTAMASES AMONG HOSPITALIZED PATIENTS

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ABSTRACT

Purpose: The study aimed to determine the clinical conditions and risk factors associated with MBL produced by A.bumannii among hospitalized patients.
Subjects and Methods: The clinical samples were collected from inpatients and subcultured on routine culture media for growth. Identification of bacteria along with antimicrobial sensitivity testing was done by VITEK®2 compact (bioMerieux). Isolates that were resistant to Meropenem and/or Imipenem were followed to detection of MBL by using metallo-β-lactamases by imipenem EDTA combined disc test (IMP-EDTA CDT) method. Demographic and clinical data of each patient were collected in terms of the type of infection, hospital-stay, associated factors, and outcome till discharge.
Results: A number of 73(86.9%) isolates of A.baumannii were resistant to carbapenem. out of 73 carbapenem-resistant isolates, 64(87.7%) were found to be MBL positive. The patients with age more than 60 years i.e. 35.9% (23/64) were found to be more common in MBL positive isolates of A. baumannii. The difference in the distribution of MBL positive and MBL negative cases with endotracheal intubation and in Surgery during the last 30 days of incubation was found to be statistically significant. The mortality rate of patients infected by MBL positive isolates of A.baumannii was 12.5%.
Conclusion: The MBL positive strains among carbapenem-resistant isolates of A.baumannii were high. endotracheal intubation and Surgery during the last 30 days were independently associated with MBL positive cases.

INTRODUCTION

The word *Acinetobacter* came from the Greek word 'akinetose' which means non-motile. The first isolate of *Acinetobacter* was reported in 1911 from the soil by Beijerinck (Almasaudi, 2018). Since 1986, *Acinetobacter baumannii* has established itself as the most frequent species of *Acinetobacter* genus in clinical samples and has become a formidable pathogen responsible for a number of nosocomial infection outbreaks (Cisneros & Rodríguez-Baño, 2002). The reports of multidrug-resistant isolates *A.bumannii* have increased during the last decade, probably due to the increasing use of antimicrobial agents (Mohammed & Singh, 2019).

A. baumannii becomes a common organism in a hospital environment. The most important locations in medical care where *A. baumannii* has been found include urine collection bags, a container of distilled water, moist bedding articles, a multidose vial of medication, intravenous nutrition, and inadequately sterilized reusable arterial pressure transducers (Paterson, 2006).

Length of stay in the hospital particularly in the intensive care unit (ICU) and indwelling devices like mechanical ventilation, primary venous catheterization, and urinary catheterization are some of the common risk factors which are responsible for the development of carbapenem-resistant isolates of *A.baumannii* (Lee et al., 2017; Ellis et al.,2015). Identification of the risk factors associated with infection by strains producing carbapenemases is necessary for better management and prevention (Hong et al., 2015).

The present study aimed to identify the clinical conditions and risk factors of MBL among isolates of *A.baumannii* from various clinical specimens among hospitalized patients of Shree Krishna Hospital, Karamsad.

METHODOLOGY

A cross-sectional study was conducted from 30 September 2017 to 28 February 2018. The study was approved by the Human Research Ethics Committee (HREC) of H.M Patel Centre for Medical Care and Education, India. The clinical samples like pus, endotracheal aspirates, blood, sputum, body fluid, etc received in the Microbiology laboratory from hospitalized patients for culture & sensitivity. Identification of *A.baumannii* along with antimicrobial sensitivity testing was done by VITEK$^®$2 Compact microbiology systems (bioMerieux, France). Isolates that were resistant to Meropenem and/or Imipenem were followed to detection of metallo-β-lactamases (MBL) by using metallo-β-lactamases by Imipenem EDTA combined disc test (IMP-EDTA CDT) method. Demographic and clinical data of each patient were collected in terms of the type of infection, hospital stay, associated factors, and outcome till discharge. Statistical analysis was performed using the statistical package for social science (SPSS) software version 20.0. The results were presented as descriptive statistics in terms of relative frequency. A Chi-square test was used to analyze the results wherever needed. A P-value of < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Table 1: Distribution of MBL status in relation to carbapenem-resistant isolates of *A. baumannii* (n=73).

Types of Isolates	*A. baumannii* n=73(%)
MBL Positive	64(87.7)
MBL Negative	9 (12.3)
Total	73(100)

Table 2: Distribution of Age group/years in relation to MBL status in total isolates of *A. baumannii* (n=84).

Age group/years	MBL Positive n=64(%)	MBL Negative n=20(%)
≤ 1-20	14(21.8)	3(15.0)

21-40	14(21.8)	9(45.0)
41-60	13(20.3)	2(10.0)
>60	23(35.9)	6(30.0)
Total	64(100)	20(100)

During the study period, 2843 non-duplicated clinical specimens were processed for culture and sensitivity tests that yielded 947(33.3%) pathogenic organisms. A number of 737(77.8%) out of 947 were found to be gram-negative bacteria of which 235(31.9%) were no fermenting gram-negative bacteria (NFGNB). The prevalence of *A. baumannii* was 8.9% out of total pathogenic bacteria, 11.4% out of gram-negative bacteria, and 35.7% out of NFGNB.

As seen in table number 1, a number of 73(86.9%) isolates of *A.baumannii* were resistant to carbapenem. Out of 73 carbapenem-resistant isolates, 64(87.7%) were found to be MBL positive. the patients with age more than 60 years i.e. Also, 35.9% (23/64) were found to be more common in MBL positive isolates of *A. baumannii* followed by age group of 1-20 and 21-40 years i.e. 14 (21.8%, each), table 2.

Table 3, Comparison of clinical conditions, co-morbidities, Indwelling/devices and outcome of patients with MBL positive and MBL negative isolates of *A.baumannii*.

Parameters	MBL Positive n=64(%)	MBL Negative n= 20(%)	P-value
Age, mean+_ SD (y)	46.67+_26.03	41.60+_21.39	0.431
Clinical Condition Acute febrile/ septicemias	10 (15.6)	3(15.0)	>0.999
Soft tissue infection	10(15.6)	2(10.0)	0.722
Respiratory tract infection	38(59.4)	11(55.0)	0.798
Trauma/head injury	3(4.7)	2(10.0)	0.588
Surgical conditions	3(4.7)	2(10.0)	0.588
Co- morbidities			
Diabetes mellitus	10(15.6)	0(0.0)	0.108
Neoplastic conditions	15(23.4)	7(35.0)	0.383
Hypertension	4(6.2)	2(10.0)	0.625
Using steroid	6(9.4)	1(5.0)	>0.999
Surgery during last 30 days	18(28.2)	1(5.0)	*0.033
Lung dysfunction	16(25.0)	4(20.0)	0.770
Cardiac dysfunction	2(3.1)	0(0.0)	>0.999
Liver dysfunction	8(12.5)	4(20.0)	0.467
Kidney dysfunction	11(17.2)	2(10.0)	0.724
Indwelling/devices			
Ventilator	48(75.0)	15(75.0)	>0.999
Renal dialysis	8(12.5)	3(15.0)	0.718
Tracheostomy	19(29.7)	3(15.0)	0.251
Endotracheal intubation	22(34.3)	2(10.0)	*0.046
Bronchoscopy	5(7.8)	1(5.0)	>0.999
Duration stay/day			
0-2	2(3.1)	2(1.0)	0.238
3-5	7(10.9)	5(25.0)	0.146
6-10	13(20.3)	5(25.0)	0.756
11-30	26(20.6)	5(25.0)	0.289

>30	16(25.0)	3(15.0)	0.541
Clinical outcome			
Improved	40(62.5)	15(75.0)	0.421
DAMA	16(25.0)	4(20.0)	0.769
Expired	8(12.5)	1(5.0)	0.679

*indicates significance at 5% level

DAMA=discharge against medical advice

As can be seen from Table 3, the most common clinical conditions in MBL positive cases of *A.baumannii* were respiratory tract infection (59.4%) followed by acute febrile/ septicemias, and soft tissue infection (15.6%, each).

Surgery during the last 30 days was the commonest co-morbidity in MBL positive isolates of *A.baumannii* i.e. 28.2% (18/64) followed by lung dysfunction in 25.0% (16/64) and neoplastic conditions in 23.4% (15/64). MBL negative strains in the surgery during the last 30 days were found to be statistically significant with a p-value of 0.033.

The highest 48(75.0%) frequency of indwelling /devices in MBL positive isolates of *A. baumannii* were of ventilator followed by endotracheal intubation and tracheostomy i.e. 48(75.0%), 22(34.3%), and 19(29.7%) respectively. The difference in the distribution of MBL positive and MBL negative strains in endotracheal intubation was found to be statistically significant with a p-value of 0.046.

The highest number of MBL positive cases had a stay of 11-30 days followed by more than 30 days of hospital stay i.e 26 (20.6%) and 16 (25.0%) respectively. The distribution of DAMA and expired cases were found to be more percentage in MBL positive isolates than MBL negative isolates.

Discussion

The prevalence of Metallo beta-lactamase among carbapenem-resistant isolates of *A. baumannii* in this study was found to be 87.8%. This is higher than the previous studies reported in India by Gupta V *et al* (2006), Karthika RU *et al* (2009) and Singla *et al* (2013) i.e. 7.5%, 70.9% and 57.5%, respectively (Gupta, Datta, & Chander, 2006; Singla et al., 2013). Also, the rate is higher when compared to 6.2% by Mesli *et al* (2013) from Algeria (Mesli et al., 2013), 3.2% by Ryoo NH *et al* (2010) from Korea (Mesli et al., 2013), and 27.1% by El-Ageery SM *et al* (2014) from Saudi Arabia (El-Ageery & Al-Hazmi, 2014). But the rate is lower when compared to the percentage of 96.0% by Aksoy MD *et al.* (2015) from Turkey (Aksoy et al., 2015) and similar to 86.86% by Noori M *et al* (2014) from Iran (Noori et al., 2014).

In this study, the significant difference in MBL positive and MBL negative cases of *A.baumannii* was identified only in endotracheal intubation (34.3% Vs 10.0% p= 0.046) and other devices such as ventilator use (75.0% Vs 75.0% p=>0.999), renal dialysis (12.5% Vs 15.0% p=0.718), tracheostomy (29.7% Vs 15.0% p= 0.251) and bronchoscopy (7.8% Vs 5.8% p= >0.999). To the best of the author's knowledge, there is no previous study reporting the association between clinical devices in

patients and the infection with MBL positive isolates of *A. Baumannii.* However, Zhou H *et al* (2019) in their study on multidrug resistance *A. baumannii* (MDRAB) found use of clinical devices to be statistically significant in comparison to non-multidrug resistance *A. baumannii* (Non-MDRAB) i.e. central vein catheterization (74.8% Vs 62.5% p=<0.001), urinary catheter (91.2% Vs 32.8% p=<0.001) mechanical ventilation (78.5% Vs 18.8% p= 0.0257) and tracheal intubation (79.9% Vs 21.9% p=<0.001) (Zhou et al., 2019).

In this study, only surgical procedures done before 30 days (28.2% Vs 5.0% p=0.033) were found to be significance as compared to MBL negative, other co-morbidities as as: diabetes mellitus (15.6% Vs 0.0% p=0.108), neoplastic conditions (23.4% Vs 35.0% p=0.383), hypertension (6.2% Vs 10.0% p=0.625), use of steroids (9.4% Vs 5.0% p=>0.999), cardiac dysfunction (3.1% Vs 0.0% p=>0.999), kidney dysfunction (17.2% Vs 10.0% p=0.724), liver dysfunction (12.5% Vs 20.0% p= 0.467), lung dysfunction (25.0% Vs 20.0% p= 0.770).

More importantly, there is a dearth of studies on co-morbidities in cases infected by MBL positive isolates of *A. Baumannii.* Huang ST *et al* (2012) reported that the co-morbidities observed in carbapenem-resistant and carbapenem susceptible isolates of *A. baumannii* were steroid use (43.5% Vs 36% p=0.372), hypertension (33.9% Vs 32.3% p=0.95), chronic kidney disease (25.8% Vs 17.1% p=0.197), diabetes mellitus (24.2 Vs 24.4 p=>0.999), Chronic obstructive pulmonary disease COPD (22.6% Vs 15.9% p=0.324) and liver cirrhosis (1.6% Vs 6.1 p=0.297) and were not significantly associated (Huang et al., 2012).

In this study, the mortality rate of a patient infected by MBL positive isolates of *A. baumannii* was 12.5%. Pandy Y *et al* (2016) reported that the mortality rate of patients infected by *A. baumannii* was 27.2% which is higher than our findings (Pandya et al., 2016).

CONCLUSION

The MBL positive strains among carbapenem-resistant isolates of *A.baumannii* were high. endotracheal intubation and Surgery during the last 30 days were independently associated with MBL positive cases. The distribution of DAMA and expired cases were found to be more prevalent in MBL positive isolates than in MBL negative isolates. The results of this study could be useful for clinicians and the infection control system in hospitals.

CONFLICTS OF INTEREST

There are no conflicts of interest

FUNDING

No Funds were received for completing this study.

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