

Multidrug Resistant *Acinetobacter* Infection in Surgical Intensive Care Unit in a Tertiary Care Center in North India

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ABSTRACT

Introduction: *Acinetobacter* is nowadays a common threat in hospital, acquired especially in critically ill patients admitted to intensive care unit. This study was done to determine the presence of MDR *Acinetobacter* species in patients admitted in surgical intensive care unit in our hospital, so that timely steps are taken to prevent their spread, protect patients from inappropriate therapy and ensure proper infection control measures.

Material and Methods: Prospective study was designed in the Department of Microbiology and surgical intensive care unit, Sher I Kashmir Institute of Medical Sciences, Soura J&K, between December 2015 to March 2016. The samples were inoculated on 5% sheep blood agar and MacConkey agar and incubated overnight aerobically at 37°C. After the isolation of typical colonies, the identification was done as per standard microbiological techniques. Antibiotic susceptibility was performed according to CLSI recommendations.

Results: A total of 77 non duplicate samples were received from surgical ICU. Out of these 77 samples, 48 were positive and 29 samples were sterile. Out of 48 positive samples, 30 isolates of *Acinetobacter* spp were isolated. Maximum 23.3% were from the 60-70 year age group and maximum were obtained from tracheal aspirate 96.6%. Twenty five patients had prolonged hospital stay i.e. ≥ 7 days where as only 5 of the patients were in the hospital for ≤ 7 days before the *Acinetobacter* was isolated from their samples. Twenty eight were on ventilator support. Twenty nine (96.6%) isolates were resistant to Amikacin, and Tobramycin each. Higher resistance was also seen for Tetracycline, Tigecycline, Gentamicin, Levofloxacin and Cefotaxime (93.3% each). Twenty seven (90%) of isolates were resistant to Cefepime, 86.6% of isolates were resistant to Meropenem and Imipenem each. All the *Acinetobacter* isolated (100%) were sensitive to Polymyxin B. Nineteen isolates (63.3%) were sensitive to Piperacillin+tazobactam.

Conclusion: Risk factors in ICU patients like advanced age, ventilator support, prolonged hospital stay should raise suspicion of MDR *Acinetobacter* infection and the antibiotic should be given only after susceptibility test.

Keywords: MDR *Acinetobacter* in ICU, Nosocomial Infections, Antibiotic Resistance.

Acinetobacter has also been isolated from soil, water, fish, meat, vegetables, hospital air, tap water faucets, sink basins, bed mattresses, bedside urinals and respiratory therapy equipments. Colonization and infections occur more commonly during the warmer and more humid months.^{12,13} *Acinetobacter baumannii* has been involved in an increasing number of outbreaks around the world, especially in intensive care units (ICUs), where it can persist for long periods.^{14,15} Although the available beds in the ICUs generally represent only a fraction (10%) of the total hospital beds, infection rates in these units are disproportionately higher (8–10 times) than those observed in other hospital units. Although considered of low virulence, this micro-organism causes a wide spectrum of nosocomial infections in debilitated individuals in wounds, urinary and respiratory tracts, bacteraemia, and particularly ventilator-associated pneumonia in ICU patients.⁷ The ability of this micro-organism to rapidly develop antimicrobial resistance and to colonize various body sites of hospitalized patients, its capacity for long-term survival (up to several months) on moist and dry environmental surfaces, and its ease of spread between patients, have led to an important role in hospital-acquired infection.^{14,16,17} Carbapenem resistance is now observed worldwide in *A. baumannii* isolates, leading to limited therapeutic options. Several carbapenem-hydrolyzing lactamases have been documented in *A. baumannii*.¹⁸ Carbapenems, which were the drug of choice, are no longer being used for treatment of acinetobacter infections.¹⁹ The understanding and recognition of *Acinetobacter* infections in the ICU is critically needed. With this background, the present study was undertaken to determine the presence of MDR *Acinetobacter* species in patients admitted in surgical intensive care unit in our hospital, so that timely steps are taken to prevent their spread, protect patients from inappropriate therapy and ensure proper infection control measures.

MATERIAL AND METHODS

This prospective study was done over a period of 4 months from December 2015 to March 2016, in the Department of Microbiology, Sheri Kashmir Institute of Medical Sciences (SKIMS), a 700 bedded tertiary care hospital in North India.

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INTRODUCTION

Acinetobacter is a gram-negative coccobacillus that has emerged as an important nosocomial pathogen. It is ubiquitous in the outside environment and has been isolated from hospital personnel, and hospital equipments, surviving on a variety of surfaces and aqueous environments.¹⁻⁶ Nowadays, there are more than 20 species reported.⁷ However, the most common, known to cause major nosocomial infections in the ICU is *Acinetobacter baumannii*, making up to 80 percent of total clinical isolates and has been reported worldwide.⁸⁻¹¹ Besides human skin,

Clinical samples were collected from patients admitted in surgical intensive care unit (SICU). Demographic data concerning the name, hospital number, age, sex, site, and date of specimen collection, previous antibiotics taken 48 h before specimen collection, diagnosis, and ICU specialty were recorded. Samples taken from ICU included tracheal aspirate, blood from central venous catheter, abdominal drain fluid, sputum and wound swab.

Isolation and identification

The samples received in the laboratory were inoculated on 5% sheep blood agar and MacConkey agar and incubated overnight aerobically at 37°C. After the isolation of typical colonies, the identification was done as per standard microbiological techniques.^{20,21}

Susceptibility Testing

Antibiotic susceptibility was performed for each isolate by the Kirby-Bauer disc diffusion method using CLSI recommendations.²² The following Antibiotics were included Cefepime (30µg), Cefotaxime (30µg), Ceftazidime (30µg), Ceftriaxone (30µg), Ciprofloxacin (5µg), Levofloxacin (5µg), Amikacin (30µg), Gentamicin (10µg), Tobramycin (10µg), Tetracyclin (30µg), Imipenem (10µg), Meropenem (10µg), Ampicillin-Sulbactam (10/10µg) Piperacillin-tazobactam (100/10µg), Ticarcillin-clavulanate (75/100 µg), Tigecycline (15µg) and Polymyxin B (300µg). Susceptibility results were interpreted by CLSI standards.

RESULTS

A total of 77 non duplicate samples were received from surgical ICU during a period of four months in the department of microbiology SKIMS. Out of these 77 samples, 48 (62.33%) were positive and 29 (37.66%) samples were sterile. Out of 48 positive samples, 30 isolates of *Acinetobacter spp.*, 8 isolates of *Klebsiella spp.*, 6 *MRSA*, 2 isolates of *Escherchia coli* and 1 isolate of *Enterococcus* were isolated and confirmed by different methods according to the CLSI guidelines.

For isolates confirmed to be *Acinetobacter spp.* maximum 23.3% were isolated from patients belonging to age group of 60-70 years followed by 16.7% from the age group of 20-40 years, 13.3% in the age group of 40-60 years, 6.7% isolates were from the age group of 10-20 years and 3.3% of isolates were from the age group of 0-10 years. Seventeen (56.7%) isolates were from males and 13 (43.3%) were from females. The maximum numbers of *Acinetobacter* strains were obtained from tracheal aspirate 96.6%, followed by 3.3% from wound swab whereas none of the other samples yielded any *Acinetobacter*. Twenty five (83.3%) patients whose cultures were positive for *Acinetobacter* had prolonged hospital stay i.e; ≥ 7 days where as only 5 (16.6%) of the patients were in the hospital for ≤ 7 days before the *Acinetobacter* was isolated from their samples. Out of 30 patients whose samples were positive for *Acinetobacter species*, 28 (93.3%) were on ventilator support and 2 (6.6%) patients had undergone surgery in last seven days before isolation of *Acinetobacter*.

Before the isolation of *Acinetobacter species*, 23 of the patients were on the following antibiotics which included Ceftriaxone (12), Imipenem (1), Levofloxacin (5), and Cefaperazone (5), whereas only 7 patients had no history of antibiotic intake.

In the present study, Twenty nine (96.6%) isolates were resistant to Amikacin, and Tobramycin each. Higher resistance was also seen for Tetracycline, Tigecycline, Gentamicin, Levofloxacin, and Cefotaxime (93.3% each). Twenty seven (90%) of isolates were resistant to Cefepime, 86.6% of isolates were resistant to Meropenem and Imipenem each, 83.3% to Ciprofloxacin. Ceftriaxone resistance was seen in 80% of the isolates. All the *Acinetobacter* isolated (100%) were sensitive to Polymyxin B. Nineteen isolates (63.3%) were sensitive to Piperacillin+tazobactam, 46.6% of the isolates were sensitive to Ampicillin+sulbactam (Figure -1).

DISCUSSION

The incidence of *Acinetobacter* infection in the intensive care unit (ICU) is rising and causes a great concern to all clinicians and intensivists worldwide due to their extraordinary ability to develop resistance to multiple classes of antibiotics. *Acinetobacter* can infect virtually any body site, particularly the lower respiratory tract, the bloodstream, and the urinary tract.²³ In our study a total of 77 bacterial isolates were recovered from patients admitted to the SKIMS ICU over a period of 4 months. Out of these 30 (38.96%) were *Acinetobacter species*. One such study by Nahar A et al. 2012²⁴ reported a prevalence of 33.7% in ICU patients. In another study by Bhattacharyya S et al. 2013²⁵ studied the prevalence (33.3%) of *Acinetobacter species* in ICU patients. The results in both of these studies are concordant with our study. *Acinetobacter* is commonly isolated from skin and throat of healthy people and the colonisation rates tend to increase during ICU stay.²⁵

Maximum no. of acinetobacter species were found in the age group of 60-70 (23.3%) years. In older age groups, there is wide range of comorbid conditions, deranged immunity and the ICU stay predisposes such patients to more severe infections. In a study by Huidrom S et al. 2015²⁶ studied a wide range of age groups, youngest in the study being 23 years and the oldest being 86 years of age. The maximum no. of patients, 24 (38.7%) were observed in the elderly in the 60-70 years age group, which is concordant with our study.

Acinetobacter species were isolated more in males (56.7%) than females (43.3%). A slight male preponderance was observed in our study. Bhattacharyya S et al. 2013²⁵ isolated acinetobacter in male patients more commonly as compared to females patients with the male female ratio of 46:1. In a study by Huidrom H et al. 2015²⁶, 66.1% of acinetobacter were isolated from males and

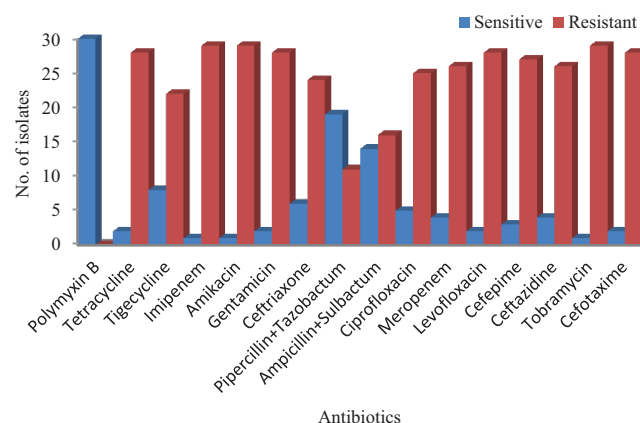


Figure-1: Antibiotic sensitivity pattern of *Acinetobacter* in ICU.

33.9% were from females.

Majority of the *Acinetobacter* species were isolated from tracheal aspirate (96.6%), followed by wound swab (3.3%). A study in Bangladesh by Nahar A et al. 2012²⁴ reported the isolation of *Acinetobacter* species from endotracheal tube (100%), followed by 54.3% from tracheal isolates, 36.4% from central venous catheter blood, 13.6% from peripheral blood and 12.5% from urine. In India a study by Bhattacharya S et al. 2013²⁵ reported the higher isolation of *Acinetobacter* species from urine (54%), followed by pus (23%), CSF (12%) and other samples (11%). The respiratory tract is an important site of colonisation and is the most important site of infection too. *Acinetobacter* have been isolated from nares, nasopharynx and tracheotomy sites.²⁵ This may be the reason for its higher isolation in respiratory samples.

The important factor in our work was to study the length of prior hospital stay. We divided the stay of patients into two groups i.e; ≤ 7 days and >7 days. It was found that 83.3% patients were having >7 days of hospital stay and 16.6% patients were having ≤ 7 days of hospital stay before isolation of *Acinetobacter*, which is clinically significant. A study made by Husni RN et al. 1999²⁷ reported the mean duration of time from admission to the ICU to infection was 12.8 days (range, 4 to 40). A study by Biendo M et al. 1999²⁸ reported the mean length of stay in the Intensive care units 16.7 days (range, 2 to 210 days), which is more or less in concordance with our study. *Acinetobacter* infection is facilitated by the ability of the bacterium to colonise hospital equipment and to persist on inanimate surfaces for prolonged periods of time ranging from 3 days to 5 months, and *Acinetobacter* spp. can be detected on various equipment including bedrails, curtains, ventilation equipments (e.g. AMBU bags, Ventilation filter).²⁵

Our study identified some risk factors for hospital acquired *Acinetobacter* species infection. Patients which were on ventilator support (93.3%) and underwent a recent surgery (6.6%) were prone to have *Acinetobacter* infection. Also 76.6% of the patients in our study were on broad spectrum antibiotics prior to isolation of *Acinetobacter*. Study reported by Ozdemir et al. 2011²⁹ stated that 92.3% of those patients had been mechanically ventilated, and 88.5% of them had been treated with multiple classes of antibiotics before the onset of infection were having *Acinetobacter* infection, the similar observation to this was seen in our study. A longer hospital stay prior to infection (≥ 7 days) was seen in 25 patients in our study, was a significant predictor of *Acinetobacter* infection. These results confirm that the length of hospital stay and antibiotic use prior to infection were significantly associated with increased risk of *Acinetobacter* infection.

High level of resistance was recorded for Amikacin, Tobramycin (96.6% each), followed by Tetracycline, Tigecycline, Gentamicin, Levofloxacin and Cefotaxime (93.3% each). Higher resistance was also seen for Cefepime (90%), Ceftazidime, Imipenem, Meropenem (86.6% each), followed by Ciprofloxacin, (83.3%), Ceftriaxone (80%). Lower resistance was seen in Ampicillin+sulbactam (53.3%) whereas all the isolates were sensitive to Polymyxin B. And the least resistance was seen in Piperacillin+tazobactam (36.6%). A similar study by Nahar A et al. 2012²⁴ reported that *Acinetobacter* species were 100% resistant to Amoxicillin, Cefuroxime, Ceftriaxone

and Gentamicin. High level of resistance was recorded for Amikacin (68.4%), Imipenem (66.7%) and maximum activity with an overall low resistance was showed in Colistin (10.5%), 6.6% of isolates were sensitive to Aztroenam and Cefotaxime. In our study, the acinetobacter isolates were found sensitive to some extent to Piperacillin+tazobactam (63.3%) followed by Ampicillin+sulbactam (46.6%) and Ceftriaxone (20%), whereas all the isolates were sensitive to polymyxin B. Study in India by Huidrom S et al. 2015²⁶ reported that most of the *Acinetobacter* spp. isolated were highly resistant to Ampicillin (83.9%), Amikacin (77.4%), Gentamicin (77.4%), Ceftazidime (85.5%), Ceftriaxone (62.9%), Cefotaxime (77.4%), Imipenem (40.3%), Meropenem (50.0%), cotrimoxazole (83.9%), Piperacillin-Tazobactam (46.8%). Out of the 62 isolates, 56 (90.3%) were MDR and all 62 isolates were sensitive to Colistin. The results obtained in our study are in concordance with the above study. Susceptibilities of *Acinetobacter* against various antimicrobials are considerably different among countries, centers and even among different wards of the same hospital, therefore such type of local surveillance studies are important in deciding the most adequate therapy for such infections.²⁶

CONCLUSION

In conclusion, *Acinetobacter* species were found to be resistant to most commonly used antibiotics. Only lower resistance was seen in piperacillin+tazobactam (36.6%). This hospital based epidemiological data has showed that a very high number of *Acinetobacter* isolates were MDR being only sensitive to Polymyxin B (100%), followed by Piperacillin+tazobactam (63.3%). This information is alarming and highlights the problem of the emerging infection of multidrug resistant *Acinetobacter* species especially in an ICU setting. It is a great challenge for the Physician to treat multidrug resistant *Acinetobacter* species. So, nationwide antibiotic policy and guidelines is necessary due to increased resistance patterns. Producing a local antibiogram database will improve the knowledge and antimicrobial resistance patterns at tertiary care hospital and will also help to improve treatment strategies.

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