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A 5-year surveillance on antimicrobial resistance of *Acinetobacter* isolates at a level-I trauma centre of India

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Abstract:

INTRODUCTION: *Acinetobacter* spp. has emerged as a major cause of nosocomial outbreaks. Multiple antibiotic resistance is an important problem in *Acinetobacter* isolates in recent years. The aim of this study was to evaluate the rate of antimicrobial resistance and changes in resistance pattern over a period of 5 years (2012–2016) in *Acinetobacter* spp. isolated from trauma patients.

MATERIALS AND METHODS: *Acinetobacter* spp. was identified by VITEK 2 and antibiotic susceptibility of isolates was investigated by disc-diffusion method and VITEK 2 automated system. Interpretation of susceptibility results was based on the Clinical and Laboratory Standards Institute guidelines.

RESULTS: Out of the total 16,210 isolates obtained throughout the period of 5 years, *Acinetobacter* spp. accounted for 3744 (28.9%). Out of which, the species which was maximally isolated was *Acinetobacter baumannii* (98.5%), followed by *Acinetobacter Iwoffii* (1.4%) and *Acinetobacter hemolyticus* (0.1%). The highest number of clinical isolates of *Acinetobacter* were recovered from neurosurgical ward ($n = 1210$), followed by the neurosurgical intensive care unit (ICU) ($n = 1000$) and surgical ICU ($n = 948$) and the most common sample of *Acinetobacter* isolation was from tracheal aspirate (37.1%), followed by wound swab (18.8%). The highest level of resistance was observed against ciprofloxacin (96%), followed by cefepime (95%), ceftazidime (95%), piperacillin (95%), and amikacin (92%). The trend of antibiotic resistance was found to be statistically significant ($P < 0.001$) for most of the antibiotics being tested such as amikacin and carbapenems.

CONCLUSION: The high rate of antibiotic resistance of the *Acinetobacter* strains indicated that there is an urgent need for controlled antibiotic usage and appliance of hospital infection control measures.

Key words:

Antimicrobial, infection, resistance, surveillance

Introduction

Infections due to multidrug-resistant (MDR) bacteria are responsible for significant morbidity and mortality.^[1] Of these MDR organisms, *Acinetobacter* spp. remains one of the most dreadful opponents, as its unique and multifarious resistance mechanism allows it to elude the activity of variety of currently known and available drugs. *Acinetobacter* spp. are aerobic Gram-negative bacteria that do not ferment glucose and are pervasive

in the environment. In hospital settings, these nosocomial pathogens affect severely ill patients and cause a wide spectrum of infections. *Acinetobacter* spp. alone is responsible for approximately 10.6% of mortality due to MDR health-care-associated infections, with an estimated cost ranging from US\$33,510 to \$129,917.^[2,3] The infections caused by *Acinetobacter* spp. are often associated with invasive operative procedures and devices.^[4] It has also been implicated in wound infections, endocarditis, peritonitis, ventriculitis, abdominal and urinary tract infections, and meningitis.^[4]

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Acinetobacter spp. are resistant to many antibiotics because of the low permeability of its outer cell membrane and constitutive expression of certain efflux pumps, and it can accumulate components of resistance mechanisms encoded on plasmids, integrons, and transposons in hospital settings associated with high antibiotic consumption.^[5] Besides that, *Acinetobacter* has the ability to survive for a long period of time on hospital equipments.^[6]

In recent years, the drug resistance rates of *Acinetobacter* are increasing worldwide, particularly with the appearance of carbapenem-resistant *Acinetobacter*.^[7] In several studies, infection with MDR *Acinetobacter* has been associated with increased mortality.^[8] The trend in increasing antimicrobial resistance (AMR) limits the choice of effective antimicrobial agents. Thus, continuous surveillance of AMR of *Acinetobacter* is very important for the selection and implementation of proper empirical therapy for seriously ill patients.

The aim of this study was to determine the antibiotic resistance patterns of *Acinetobacter* that cause infections in the intensive care units (ICUs) and wards at a Level 1 trauma care center in a developing country and to follow the variation in resistance pattern from 2012 to 2016.

Materials and Methods

The present study was a retrospective cross-sectional study of all the nonduplicate isolates (i.e., similar isolates obtained over a 2-week period were regarded as one) of *Acinetobacter* that were collected and processed by the microbiological laboratory in our hospital from January 2012 to December 2016. The study hospital is a 186-bedded, tertiary care, Level 1 trauma center in India. Blood, respiratory tract specimens, urine, pus from wounds, cerebrospinal fluid (CSF), tissue sample, pleural fluid and other biological specimens collected from patients admitted to any unit of the hospital, and follow-up patients were eligible for inclusion. Samples sent by the clinicians in our hospital are generally from symptomatic patients only, and the history of the patients is generally communicated along with the samples. Thus, the processing of the samples was done based on the clinical history such that overreporting of organisms or processing of colonizers can be avoided. All the results were noted from the microbiology database and the resistance pattern was observed and analyzed.

Acinetobacter spp. was identified by VITEK 2 system (BioMerieux, Lyon, France) and antibiotic susceptibility of isolates was investigated by disc-diffusion method and VITEK 2-automated system. Interpretation of susceptibility results was based on the Clinical and Laboratory Standards Institute (CLSI) guidelines.^[9] The

standardized custom sensitivity panel used in the VITEK 2 included 25 different antimicrobials for susceptibility of all the Gram-negative isolates, but for the present study, only the resistance of *Acinetobacter* spp. to common anti-*Acinetobacter* agents was analyzed. The antibiotics tested were amikacin (30 µg), cefepime (30 µg), ceftazidime (30 µg), ciprofloxacin (5 µg), gentamicin (10 µg), imipenem (10 µg), levofloxacin (5 µg), meropenem (10 µg), piperacillin (100 µg), piperacillin/tazobactam (100/10 µg), trimethoprim/sulfamethoxazole (1.25/23.75 µg), and tigecycline (15 µg).

Resistance of *Acinetobacter* spp. to individual antimicrobials is presented in absolute numbers and percentages, and was analyzed as per year and hospital unit origin (ICU vs. non-ICU). Since the number of isolates of non-*baumannii* *Acinetobacter* spp. was not significant, the trend in the resistance pattern was not studied separately. All the statistical analyses were performed with STATA software (STATA Version 12.1, StataCorp, Texas-77845, USA). $P < 0.05$ was considered statistically significant.

Results

During the period of 5 years, 3744 isolates were collected and identified as *Acinetobacter*, which represented 28.9% of all the isolated strains. The mean age of the patients was 34 years, ranging from 1 to 96 years. Male patients (3133, 83.7%) outnumber female patients (611, 16.3%) from whom *Acinetobacter* spp. were isolated. In male patients, the mean age was 34 years with a range of 1–96 years, whereas in female patients, the mean age was found to be 35.3 years with a range of 1–90 years. *Acinetobacter* spp. were observed in patients of different age groups such as in <15 years of age (229, 6%), 15–24 years (902, 24%), 25–65 years (2473, 66%), and >65 years (140, 4%). This study is a part of Department of Science & Technology (DST)-funded project entitled “Molecular and epidemiological study of beta-lactamase producing Gram negative nosocomial pathogens in India,” and ethical clearance was obtained from the Institute Ethics Committee of AIIMS (Ref. No.-IEC/NP-123/2011).

Out of total 3744 isolates, the species which was most commonly isolated was *Acinetobacter baumannii* (3688, 98.5%), followed by *Acinetobacter lwoffii* (52, 1.4%), and *Acinetobacter hemolyticus* (4, 0.1%). *Acinetobacter* spp. were isolated most commonly from neurosurgery ward (1,210, 32%), followed by neurosurgical ICU (1000, 27%), surgical ICU (948, 25%), surgical ward (442, 12%), follow-up patients (65, 2%), orthopedic ward (41, 1%), and casualty (38, 1%). *A. hemolyticus* (4) were isolated from the follow-up patients. *A. lwoffii* (52) were isolated from the surgical ward (18), orthopedic ward (17), casualty (12), and neurosurgical ICU (5). *A.*

baumannii were isolated from neurosurgical ICU (9995), surgical ICU (948), surgical ward (424), follow-up patients (61), orthopedic ward (24), and casualty (26).

The *Acinetobacter* strains were maximally isolated from tracheal aspirate (1,391, 37.1%), followed by pus/wound swab (704, 18.8%), bronchoalveolar lavage (BAL) (612, 16.3%), blood (502, 13.4%), CSF (185, 4.9%), urine (100, 2.7%), central venous catheter tip (63, 1.7%), tissue sample (55, 1.5%), drain fluid (52, 1.4%), pleural fluid (23, 0.6%), sputum (4, 0.1%), bone fragments (2, 0.1%), and others (e.g., – ascites fluid, lavage fluid, debridement slough, etc.) (51, 1.4%). The resistance pattern of the *Acinetobacter* spp. (*A. baumannii*, *A. lwoffii*, and *A. hemolyticus*) isolated during the 5-year study period is described in Table 1. The analysis of the level of antibiotic resistance showed that resistance was maximum against ciprofloxacin (96%), followed by ceftazidime (95%), cefepime (95%), and piperacillin (95%). The lowest level

of resistance was observed against tigecycline (8%). Of the strains isolated, a total of 68 (1.8%) isolates only were found to be colistin resistant using the VITEK 2 system. Antibiotic resistance pattern of different antimicrobials by specimen origin (ICU vs. non-ICU) for *Acinetobacter* spp. is shown in Figure 1. The difference in the level of resistance was not found to be statistically significant for any antibiotic tested.

Discussion

Acinetobacter spp. has emerged as one of the major causes of hospital-acquired infections in critically ill patients.^[4] The drug resistance data during 2012–2016 in our hospital setup showed that the resistance rates of the majority of antibiotics increased throughout the period. The antibiotic resistance in our hospital has increased for all antibiotics from 2012 to 2016 by almost the same percentage. However, the increase in

Table 1: Resistance pattern of *Acinetobacter* spp. against different antimicrobials

Antimicrobials	2012 (%)	2013 (%)	2014 (%)	2015 (%)	2016 (%)	Total resistance (%)	Total sensitive (%)
Amikacin	965 (96.8)	1015 (93.1)	884 (94)	718 (90.1)	723 (84.5)	4305 (92)	375 (8)
Cefepime	955 (96)	1061 (97.3)	888 (94.5)	765 (96)	773 (90.3)	4442 (95)	238 (5)
Ceftazidime	975 (97.8)	1065 (97.7)	878 (93.4)	752 (94.4)	775 (90.5)	4445 (95)	235 (5)
Ciprofloxacin	981 (98.4)	1040 (95.4)	911 (97)	777 (97.5)	772 (90.2)	4481 (96)	199 (4)
Gentamycin	946 (94.9)	1022 (93.7)	889 (94.6)	749 (94)	711 (83)	4317 (92)	363 (8)
Imipenem	892 (89.5)	954 (87.5)	862 (91.7)	751 (94.2)	759 (88.7)	4218 (90)	462 (10)
Levofloxacin	890 (89.3)	831 (76.2)	661 (70.3)	666 (83.6)	701 (81.9)	3749 (80)	931 (20)
Meropenem	907 (91)	953 (87.4)	850 (90.4)	744 (93.4)	759 (88.7)	4213 (90)	467 (10)
Piperacillin	961 (96.4)	1053 (96.6)	901 (95.8)	780 (97.9)	774 (90.4)	4469 (95)	211 (5)
Piperacillin/tazobactam	944 (94.7)	1018 (93.4)	870 (92.5)	744 (93.4)	762 (89)	4338 (93)	342 (7)
Trimethoprim/sulfamethoxazole	688 (69.0)	951 (87.2)	798 (84.9)	710 (89.1)	605 (70.75)	3752 (80)	928 (20)
Tigecycline	N/A	85 (7.8)	45 (4.8)	61 (7.7)	89 (10.4)	280 (8)	3403 (92)

N/A = Not available

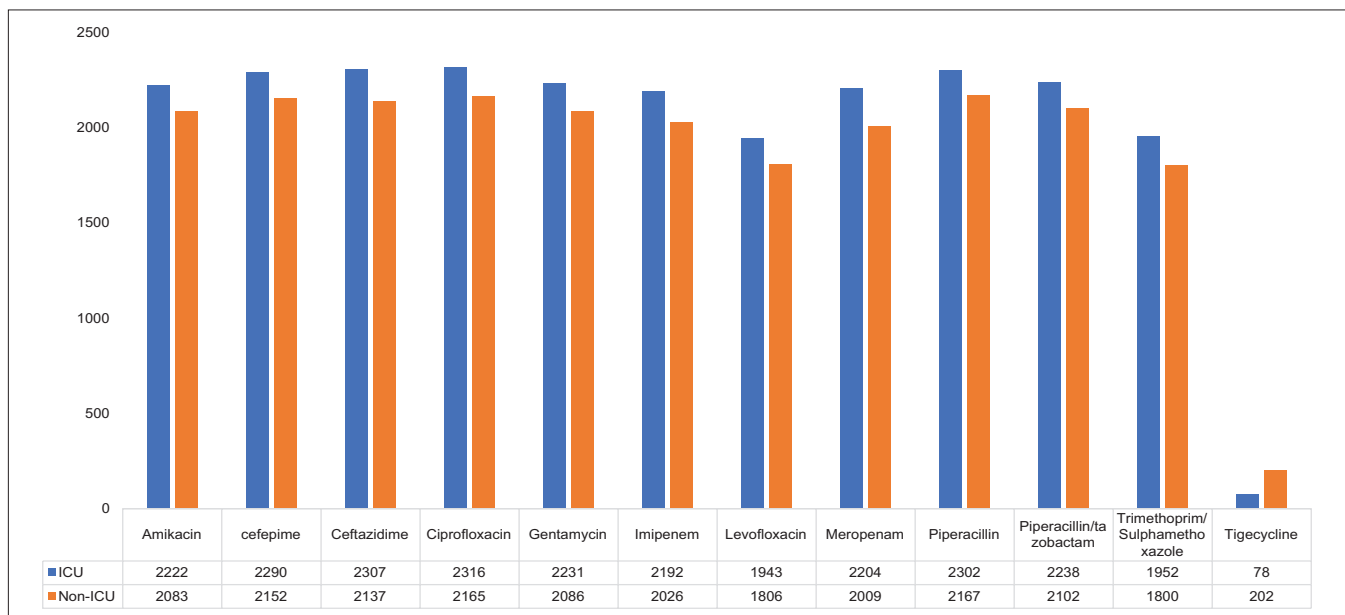


Figure 1: Resistance pattern of different antimicrobials in the intensive care unit versus nonintensive care unit setup throughout the period of 5 years

the level was maximum for amikacin. The antibiotic policy was introduced in our hospital setting in 2006, and the majority of antibiotics used were restricted and guided by rules. The antibiotic policy promoted the rational use of antimicrobial drugs, and certain antibiotic-resistant rates periodically reduced. However, all the antimicrobial-resistant rates did not decrease at the same time to cure infection, and there was a fluctuation. Rates of some antibiotics periodically increased also in our hospital settings.

Carbapenemase-resistant *Acinetobacter* is an increasing problem worldwide.^[10] In a study in Greece, the evolution of *Acinetobacter* isolates from carbapenem susceptible in the 1990s to carbapenem resistant in the 2000s was rapid. Resistance to imipenem in *Acinetobacter* isolates in hospitalized ICU patients increased from 0% in 1996 to 91% in 2006 of a Greek hospital.^[11] In our study also, we observed the proportion of carbapenem-resistant clinical isolates to be 80%–96%. In our hospital setup, 83.7% of patients infected with *Acinetobacter* isolates were males which shows the general trend of higher male preponderance in trauma centers.^[12]

Most of the studies have reported the predominance of *Acinetobacter* strains in bronchopulmonary samples.^[13] In this study also, the main isolation site of the *Acinetobacter* isolates was from tracheal sample (37.1%), followed by BAL (18.8%) followed by blood cultures (13.4%). It has been reported that among *Acinetobacter* species, *A. baumannii* is the main cause of *Acinetobacter* infections with the antibiotic resistance rate being very high causing more serious infections than other species of *Acinetobacter*.^[14] We have also found the same results in our study as the species which was maximally isolated was *A. baumannii* (98.5%).

In general, the *Acinetobacter* isolates are known for their resistance to various antibiotics despite their weak virulence, limiting the control and treatment due to these microorganisms.^[15] Our study shows that the rate of antibiotic resistance in our trauma care center is generally high and variable. Several authors have confirmed the high prevalence of these infections associated with high resistance in ICUs.^[16] The high proportion and the high resistance of these microorganisms in ICUs are related to the existence of numerous risk factors associated with *Acinetobacter* infection such as immunocompromised patients, longer hospital stay, use of invasive devices, the broad-spectrum antibiotics therapy, possible and frequent contaminations, cross transmission of this bacteria through environmental reservoirs, and contaminated hands of health-care workers.^[17]

For the beta-lactam antibiotics which are a large family playing an important role in antimicrobial treatment,^[18]

the high resistance of *Acinetobacter* clinical isolates to this class of antibiotics (ceftazidime, cefepime, imipenem, and piperacillin/tazobactam) has been described in the literature.^[19] In our study, the resistance rate was highest in ciprofloxacin, followed by ceftazidime, cefepime, and piperacillin. In our study, 1.8% of the isolates were found to be colistin resistant using the VITEK 2 system. These strains, however, could not be retested using the currently recommended microbroth dilution method. However, a major drawback of our study is that we did not test for the susceptibility to antibiotics such as ampicillin/sulbactam, minocycline, cefoperazone/sulbactam, or cefepime/tazobactam which have proved to have promising effect in the coming era of widespread antibiotic resistance.

Conclusion

The vast majority of *Acinetobacter* spp. in our hospital are MDR. The remaining therapeutic options for *Acinetobacter* infections are severely limited. Continuous surveillance of AMR of *Acinetobacter* sp. is extremely important for the selection of appropriate empirical therapy. Infection control practices and antimicrobial stewardship should be implemented in every hospital setting. The resistance pattern shown in the study could be used for updating the antibiotic policy of our institute.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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