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Antibiotic Sensitivity Pattern of Blood Isolates of *Acinetobacter* Species in a Tertiary Care Hospital: A Retrospective Analysis

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Abstract: Problem statement: Multi-drug resistant *Acinetobacter* bacterium is one of the major causes of sepsis in ICUs in tertiary care hospitals in India. In this report we describe the antibiotic sensitivity patterns of *Acinetobacter* species isolated from blood over a one year period at a tertiary care hospital. **Approach:** We retrospectively analyzed the sensitivity pattern of *Acinetobacter* species isolated from blood during the period 1/6/2010 to 31/5/2011. Isolation and identification were performed using the best alert system and VITEK2 respectively. Sensitivities were determined by Kirby Bauer disc diffusion and broth dilution using VITEK2 -AST cards. **Results:** The total number of *Acinetobacter* species isolated during the study period was 72, out of which 57 (79%) were *A. baumanii*, 7 (9.7%) were *A. Iwofii* and 3 (5.2%) were *A. Junii*. One each from *A. calcoaceticus*, *A. ursingii* and *A. denitrificans* were isolated. All of the *baumanii* isolates were sensitive to polymyxin B and 61.4% were sensitive to tigecycline. Only 25% of the isolates in *baumanii* group were sensitive to meropenem and imipenem. In the *non-baumanii* group however, 73% were sensitive to carbapenems. **Conclusion:** There is a very high incidence of resistance to most antibiotics, including carbapenems. All of the *Acinetobacter* isolates tested are sensitive to polymyxin B. Tigecycline is the only other drug with reasonable susceptibilities, but this drug is not recommended for primary bacteriemias. If *Acinetobacter* sepsis is suspected, empiric therapy with polymyxins, followed by de-escalation after sensitivity results are back, is advisable.

Key words: *Acinetobacter*, polymyxin B, colistin, tigecycline, carbapenems

INTRODUCTION

Members of the genus *Acinetobacter* are ubiquitous, free living, aerobic, Gram negative cocco-bacilli that prefer a moist environment and can be easily obtained from soil, water, food and sewage (Dougari 2011).

They are usually considered to be opportunistic pathogens and cause nosocomial infections in hospitalized patients like bacteremia, pneumonia, meningitis and Urinary Tract Infection (UTI) (Towner, 1997; Bergogne-Berezin *et al*., 1996).

Antimicrobial resistance among nosocomial isolates of *Acinetobacter* complicates therapy and adversely affects clinical outcomes and treatment costs (Brusselaers *et al*., 2011; Harris *et al*., 1999). The presence of resistance to most antibiotic classes requires the use of older and more toxic drugs like colistin for tackling Multi-Drug Resistant (MDR) strains (Fritsche *et al*., 2005).

We analyzed the resistance pattern of *Acinetobacter* species grown in blood culture in patients during a one year period.

MATERIALS AND METHODS

All isolates of *Acinetobacter* from blood over a period of 1 year (1/6/2010 to 31/5/2011) were included in this study. Isolation and identification was performed using the Bac Talert and the VITEK 2 machine respectively. Antibiotic sensitivities were determined by Kirby Bauer disc diffusion and broth dilution using VITEK2 and AST cards and interpreted according to CLSI criteria.

RESULTS

The total number of *Acinetobacter* species isolated during the study period was 72, out of which 57 (79%) were *A. baumanii*, 7 (9.7%) were *A. Iwofii* and 3 (5.2%)

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were *A. junii*. One each from *A. calcoaceticus*, *A. haemolyticus*, *A. ursingii*, *A. denitrificans* were isolated. One isolate did not belong to any of the above species.

All the isolates in the *Acinetobacter baumanii group* were sensitive to polymyxin B (Table 1). 61.4% were sensitive to tigecycline. Sensitivities of imipenem, meropenem and doripenem were 24.55, 24.5 and 22.5% respectively. Only 12.5% of the isolates were sensitive to cefuroxime whereas for cefotaxime and ceftriaxone it was 12.2 and 10.5% respectively. Cefepime and ceftazidime had marginally better sensitivities when compared with other cephalosporins (28% each). Cefaperazone + sulbactam combination had better sensitivities (33%) when compared to piperacillin + tazobactam (21%).

The 15 isolates of non Baumanii group differed significantly from the Baumanii group, which had much greater sensitivities to all classes (Table 2).

Table1: The antibiotic sensitivity pattern of 44 isolates of *A. baumanii*

Antibiotic	Sensitive (%)	Intermediate (%)
Polymyxin B	44 (100)	
Tigecycline	27 (61.4)	15(34.09)
Cefaperazone/sulbactam	19(33.3)	4(7)
Amikacin	14(24.5)	1(1.75)
Ciprofloxacin	16(28)	
Cotrimoxazole	13(22.8)	
Piperacillin/tazobactam	12(21)	
Imipenem	14(24.5)	
Doripenem	13(22.8)	
Meropenem	14(24.5)	
Cefuroxime	7(12.2)	
Cefotaxime	7(12.2)	
Ceftriaxone	6(10.5)	
Cefepime	16(28)	
Ceftazidime	16(28)	
Aztreonam	8(14)	

Table 2: Antibiotic sensitivity pattern of 15 isolates of non baumanii group

Antibiotic	Sensitive (%)	Intermediate (%)
Polymyxin B	4 out of 4(100)	
Tigecycline	3out of 4(75)	
Cefaperazone+sulbactum	11(73)	
GM/Amikacin	12(80)	1(6.6)
Cipro/Oflox	10(66.6)	
Cotrimoxazole	7(46.6)	1(6.6)
Piperacillin+Tazobactam	11(73)	
Imipenem	11(73)	
Doripenem	11(73)	
Meropenem	11(73)	
Cefuroxime	7(46.6)	
Cefotaxime	7(46.6)	
Ceftriaxone	7(46.6)	
Cefepime	12(80)	
Ceftazidime	10(66.6)	
Aztreonam	7(46.6)	1(6.6)

DISCUSSION

Acinetobacter has become one of the most important causes of nosocomial infections (Gerner-Smidt, 1995; Gulati *et al*., 1999) and causes considerable mortality as it has acquired many antibiotic resistance genes including the novel carbapenemases. It is an opportunistic pathogen associated with a wide spectrum of infections including nosocomial pneumonia, meningitis, endocarditis, skin and soft tissue infections, urinary tract infections, conjunctivitis, burn wound infections and bacteremia (Bergogne-Berezin and Towner, 1996). The common form of resistance to carbapenems is mediated by lack of drug penetration (i.e., porin mutations and efflux pumps) and/or carbapenem hydrolyzing beta-lactamase enzymes including the Metallo-Betalactamases (MBL). Acquired MBLs are encoded mobile gene cassettes of organism and such strains are often resistant to different groups of antimicrobial agents with transferable properties to various types of bacteria (Pitout *et al*., 2005).

Resistance rates to carbapenems vary significantly depending on the geographical region. In Greece, the proportion of imipenem-resistant *A. baumanii* isolates from patients hospitalized between 1996 and 2007 in tertiary care hospitals in several regions of the country rose from no resistance to 85% (ICUs), 60% (medical wards) and 59% (surgical wards) GSSAR. Bloodstream isolates from the same dataset exhibited even higher resistance rates. The prevalence of imipenem resistance in *A. baumanii* isolated from a burns unit of USA was found to be as high as 87% (2007) (Trottier *et al*., 2007).

Initial Indian studies in the 21st century showed that *Acinetobacter* species were fairly sensitive. For instance, Suri *et al*. (2000) demonstrated *Acinetobacter* in patients from a neurosurgical unit and it was sensitive to ciprofloxacin, amikacin cefotaxim and ceftriaxone. Singh *et al*. (2002) showed *Acinetobacter* which was sensitive to amikacin. Prashanth and Badrinath (2004) from JIPMER Pondichery isolated *Acinetobacter* which was sensitive to amikacin and ceftazidime. Isolates were resistant to ciprofloxacin and cefotaxime (Prashanth and Badrinath, 2004). Gladstone *et al*. (2005) from Vellore reported a prevalence of 14% carbapenem-resistant *Acinetobacter* spp., isolated from tracheal aspirates.

Banerjee *et al*. (2005) isolated *Acinetobacter* from different body fluids which has good sensitivities for gentamycin. Prashanth and Badrinath (2006) showed gradually increasing resistance of *Acinetobacter*. Gaur *et al*. (2008) noted resistance to meropenem in 6.4% of *Acinetobacter* species. As

recently as in 2010, one study from Ahmedabad showed few were carbapenem resistant (Patel *et al*., 2010).

However there are now several Indian studies showing an increased prevalence of MDR *Acinetobacter*. Our study shows that 75% of our isolates were carbapenem resistant. This is concordant with recent reports from elsewhere in India. In 2009 a study from Rohtak showed that the resistance of *Acinetobacter* to meropenem had increased to 25.6% (Goel *et al*., 2009). In the same study the resistance to amikacin was 87.2% and ciprofloxacin was 89.7%. In Delhi, India (2006), the prevalence of carbapenem resistance in *Acinetobacter* spp. isolated from different clinical samples was found to be almost 35%. Sinha *et al*. (2007), but the latest studies show resistance to carbapenem is seen in up to 89% of isolates (Jaggi *et al*., 2011). In our study the level of carbapenem resistance was very high in the Baumanii group. Karthika *et al*. (2009) in their study showed the presence of bla IMP1 carbapenemase genes in South Indian population. Though bla VIM-2 is the most common carbapenemases seen in other parts of world (Yum *et al*., 2002; Poirel *et al*., 2000; Walsh *et al*., 2005), it was surprisingly absent in their study, though bla IMP1 gene was seen in 42% of isolates (Karthika *et al*., 2009). Our study showed 100% sensitivity to polymyxin. Tigecycline too retained activity against MDR isolates, although it is not recommended for primary bacteremias. However there have been reports of polymyxin resistant *Acinetobacter* from Greece, Slovakia and other parts of Europe (Gales *et al*., 2006; Souli *et al*., 2006). Polymyxin resistance has been reported from South Korea and the rates of resistance is alarming, 18.1 and 27.9% for polymyxin B and colistin respectively (Ko *et al*., 2007). Recently there has been an alarming study from Chandigarh where 3.5% of all strains and 16% of carbapenem resistant strains were resistant to polymyxin B and tigecycline (Taneja *et al*., 2011).

The antibiotic sensitivity pattern of non Baumanii group differed significantly from Baumanii group. Most of the isolates were sensitive to carbapenems and BL+ BLI combinations (73%).

The strength of our study is that only blood isolates were analysed, as samples from other sites may represent colonization and may not reuire therapy. The polymyxin group remains the only option as an empirical therapy if *Acinetobacter* bacteremia is suspected, as it showed 100% sensitivities to MDR *Acinetobacter*. Though tigecycline showed good antibiotic sensitivity in our study, it is not recommended for primary bacteremia due to low blood levels resulting inclinical failures.

CONCLUSION

There was a very high incidence of resistance to most antibiotic classes, including carbapenems, in *Acinetobacter* blood isolates in our center. All of the resistant isolates were however sensitive to polymyxin B. Tigecycline was the only other drug with reasonable susceptibilities. If *Acinetobacter* bacteremia is suspected, empiric therapy with the polymyxin group, followed by de-escalation after sensitivity results are back, is advisable.

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