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Drug Resistant Acinetobacter Baumannii: Pattern of Infection and In Vitro Tigecycline Activity

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ABSTRACT

Objective: The purpose of this study is; firstly, to find out the prevalence of drug resistant Acinetobacter baumannii, secondly, to find the most common site of infection by Acinetobacter baumannii, and thirdly, to assess the in vitro effectiveness of tigecycline against drug resistant Acinetobacter baumannii, in our hospital setting. **Study Design:** Retrospective/Observational study. **Setting:** Charsada Teaching Hospital affiliated with Jinnah Medical College Peshawar. **Period:** One year from January 2016 to December 2016. **Methodology:** All the reports occurring during this study period with positive diagnosis for Acinetobacter were retrieved from the archives, irrespective of patient's age and gender. Only one isolate of Acinetobacter per patient was considered in the study. The organisms were identified and species determined manually. Susceptibility for antimicrobial agents was determined according to criteria of CLSI 2016. MIC for tigecycline in the isolates was determined by E-test. **Results:** On analyzing all the Acinetobacter isolates (n=391) during one year time, it was found that the large majority of these isolates were of Acinetobacter baumannii (96.2%), while only few were of Acinetobacter lwoffii (3.8%). Multidrug resistant Acinetobacter baumannii represented about one third (31%) of all the Acinetobacter baumannii isolates. Most of the isolates of Acinetobacter baumannii were from skin and soft tissue wounds (44.4%), followed by isolates from respiratory secretions (42.7%), urine (6.8%), blood (5.2%) and CSF (0.9%) (Table II). The isolates of Acinetobacter baumannii showed maximum sensitivity to Tigecycline (88.9%), followed by Colistin (81.2%) and Polymyxin (79.5%) (Table III). **Conclusions:** Drug resistant Acinetobacter baumannii is present in 31% of isolates, it is most commonly isolated from infected wounds and respiratory tract secretions in debilitated patients, and also Tigecycline is an excellent treatment choice for infections caused by drug resistant Acinetobacter baumannii.

Keywords: Acinetobacter baumannii, Tigecycline, Wound infections, Respiratory tract secretions.

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INTRODUCTION

Gram negative organisms (GNOs) isolated from various body sites respond variably to commonly used antibiotics. However; multidrug resistant gram-negative organisms (MDRGNOs) have emerged as a result frequent and injudicious use of antibiotics, thereby remarkably reducing the number of antibiotics available to treat these infections. Acinetobacter baumannii is the forerunner amongst MDRGNOs acquired in health care settings (nosocomial infections) and is very resistant to commonly used antibiotics[1]. Interestingly, Acinetobacter baumannii is a virulent, capable of causing infections of the seriously ill host[2].

Acinetobacter is one of the commonest bacteria causing hospital acquired/nosocomial infections[2]. It is found as either an infecting or colonizing organism in seriously ill hospitalized patients. It can colonize the moist skin of axillae, groins and toe webs of in-patients as well as health care staff[3]. In patients it commonly involves the organ systems with high fluid content like respiratory tract secretions, cerebrospinal fluid, urine, peritoneal fluid, fluid drains, catheters and wounds, whereas it is uncommon for it to be found on dry parts of the skin and in feces[2].

The various mechanisms involved in the development of antibiotic resistance include production of antimicrobial inactivating enzymes, reduced access to bacterial targets, and mutations that change the targets for the antimicrobials. A single or a combination of these mechanisms may be at work in a particular case[3]. Moreover, genetic studies have revealed association of antibacterial resistance with certain mutations.

The purpose of this study is; firstly, to find out the prevalence of drug resistant Acinetobacter baumannii, secondly, to find the most common site of infection by Acinetobacter baumannii, and thirdly, to assess the in vitro effectiveness of tigecycline against drug resistant Acinetobacter baumannii, in our hospital setting.

METHODOLOGY

Study Design: Retrospective observational study

Place of Study: Pathology laboratory of Charsada Teaching Hospital affiliated with Jinnah Medical College Peshawar

Period: One year from January 2016 to December 2016

All the reports occurring during this study period with positive diagnosis for Acinetobacter were retrieved from the archives, irrespective of patient's age and gender. Isolates from only one isolate of Acinetobacter per patient was considered in the study. The organisms were identified and species determined manually. Susceptibility for antimicrobial agents was determined according to criteria of CLSI 2016. MIC for tigecycline in the

isolates was determined by E-test (supplied by bioMerieux) on Muller-Hinton agar (Oxoid Microbiology Products). Non-susceptibility for Tigecyline was defined as MIC of ≥ 4 ugm/ml for Acinetobacter baumannii[4]. Multi drug resistant (MDR) Acinetobacter baumannii were defined as isolates resistant to penicillin/cephalosporin, fluoroquinolones and aminoglycosides. Extensively drug resistant (XDR) Acinetobacter baumannii were defined as isolates of MDR additionally resistant to carbapenems. Pan drug resistant (PDR) Acinetobacter baumannii are isolates of XDR additionally resistant to tigecycline, colistin and polymyxin.

Acinetobacter baumannii isolates were tested for multiple antibiotics by disc diffusion method; the antibiotics used were ampicillin-sulbactum, ceftazidime, ciprofloxacin, imipenem, tobromycin, amikacin, cepftriaxone, trimethoprim-sulphamethoxazole, doxycycline, tigecycline, colistin and polymyxin.

RESULTS

On analyzing all the Acinetobacter isolates (n=391) from different body sites, starting from January 2016 to December 2016, it was found that the large majority of these isolates were of Acinetobacter baumannii (n=376, 96.2%), while only few were of Acinetobacter lwoffii (n=15, 3.8%) (Table I).

Table 1: Types of Acinetobacter Species Isolated

Sr. No.	Acinetobacter	Isolates	%
1.	Acinetobacter baumannii	376	96.2
2.	Acinetobacter lwoffii	15	3.8

Multidrug resistant Acinetobacter baumannii represented about one third (n=117, 31%) of all the Acinetobacter baumannii isolates (n=376). Most of the isolates of Acinetobacter baumannii were from skin and soft tissue wounds (n=52, 44.4%), followed by isolates from respiratory secretions (n=50, 42.7%). Urine isolates for Acinetobacter baumannii were the third most common (n=8, 6.8%), while blood (n=6, 5.2%) and CSF (n=1, 0.9%) isolates followed in frequency. (Table II).

Table 2: Types of Specimens and Acinetobacter Isolates

	Types of Specimen	No. of isolates	Percent isolates
1	Wounds	52	44.4
2.	Respiratory Secretions	50	42.7
3.	Urine	8	6.8
4.	Blood	6	5.2
5.	CSF	1	0.9
	Total	**117**	**100**

The isolates of Acinetobacter baumannii showed maximum sensitivity to tigecycline (n=104, 88.9%), followed by Colistin (n=95, 81.2%) and Polymyxin (n=93, 79.5%) (Table III).

Table 3: Antibiotic Sensitivity of Acinetobacter baumannii

Sr. No.	Antibiotic	No. of isolates	Percent Sensitive
1.	Tigecycline	104	88.9
2.	Colistin	95	81.2
3.	Polymyxin	93	79.5

DISCUSSION

Gram negative organisms (GNOs) are commonly isolated from specimens received from various body sites and they variably respond to the commonly used antibiotics. Unfortunately, because of different reasons many multidrug resistant gram-negative organisms (MDRGNOs) have emerged over the time, thereby remarkably reducing the number of antibiotics available at hand to treat these infections. Acinetobacter baumannii is the forerunner amongst MDRGNOs acquired in health care settings and is very resistant to treatment[1].

Acinetobacter is a pleomorphic, aerobic, non-fermentative, gram negative bacillus/coccobacillus found mostly in hospital settings[2,5]. It is found as either an infecting or colonizing organism in seriously ill hospitalized patients. It can colonize the moist skin of axillae, groins and toe webs of in-patients and even health care staff[3]. In patients it commonly involves the organ systems with high fluid content like respiratory tract secretions, cerebrospinal fluid, urine, peritoneal fluid, fluid drains, catheters and wounds, whereas it is uncommon for it to be found on dry parts of the skin and in feces[2]. It has been found on patient's clothes, bed linen, ventilators, door knobs, side tables and bed rails etc. It has been reported to survive for 11 days on laminated surfaces and for 12 days on stainless steel surfaces[6]. Also, it can form a bio-film over implants making the treatment of implant associated infections much more difficult[3]. In a study conducted in Portugal, 11% of the fruits and lettuce leaves (both considered as ready to eat foods) were found to contain Acinetobacter baumannii on their surfaces[7].

The various mechanisms involved in the development of antibiotic resistance have been broadly categorized as: 1. antimicrobial inactivating enzymes, 2. Reduced access to bacterial targets, 3. Mutations that change the targets for the antimicrobials. A single or a combination of these mechanisms may be at work in a particular case[3,8]. Moreover genetic studies have revealed association of antibacterial resistance with certain mutations. Ser83Leu mutations in GyrA is associated with fluoroquinolone resistance, mutations in various genes (aphA1, aphA6, aacC1, aadA1, etc) have been associated with class 1 integrons that encode aminoglycoside modifying enzymes causing resistance to gentamycin and tobramycin but not amikacin. ISAba1 element presence correlates with cephalosporin resistance. ISAba1-bla(OXA-51-) presence correlates with carbapenem resistance[9].

The common risk factors for acquiring Acinetobacter baumannii include: previous antibiotic therapy, invasive procedures, bed sores, prolonged hospitalization, deep penetrating wounds, and burn wounds[6].

In this study, 376 (96.2%) isolates of Acinetobacter baumannii were identified of which 117 (31.1%) isolates were resistant to penicillin, cephalosporin, aminoglycosides, fluoroquinolones and carbapenem. Ozgen et al in their study of 124 Acinetobacter baumannii isolates in Turkey during one-year period, 41.1% Acinetobacter baumannii isolates were found to be multidrug resistant[10]. This is 10% more than the figure in the present study; this could be due to the regional variation in the prevalence of Acinetobacter baumannii variants having different exposure to different antibiotics in their environment.

Most of the isolates of Acinetobacter baumannii were from wounds (n=52, 44.4%), while respiratory secretions (like sputum and endotracheal secretions) constituted the second commonest source (n=50, 42.7%). Urine isolates for Acinetobacter baumannii were the third most common (n=8, 6.8%), while blood (n=6, 5.2%0 and) and CSF (n=1, 0.85%) isolates followed in frequency (Table II). In a study conducted at a Medical University in Iran involving 800 cases by Abbasi et al, the most common sites of infection were wounds, respiratory tract, blood stream and urinary tract, the same pattern as in our study[11]. Some studies show slightly more cases of respiratory tract specimens as compared to the wound infections, his can be attributed to the disease pattern of patients attending that hospitals, surgical wards and ICUs with more patients of road traffic accidents and gunshot wounds (as our hospital) will show more wound infections than respiratory tract infections.

The isolates of Acinetobacter baumannii showed maximum sensitivity to tigecycline (n=104, 88.9%), followed by colistin (n=95, 81.2%) and polymyxin (n=93, 79.5%) (Table III). It can be inferred that 9 isolates of Acinetobacter baumannii were sensitive only to Tigecycline. In multiple studies conducted in different parts of the world tigecycline which is a derivative of minocycline has been found to be very effective against Acinetobacter baumannii with upto 97% sensitivity rate[12,13,14,15,16].

In conclusion, drug resistant Acinetobacter baumannii is present in 31% of isolates, it is most commonly isolated from infected wounds and respiratory tract secretions in debilitated patients, and also tigecycline is an excellent treatment choice for infections caused by drug resistant Acinetobacter baumannii.

CONCLUSION

Drug resistant Acinetobacter baumannii is present in 31% of isolates, it is most commonly isolated from infected wounds and respiratory tract secretions in debilitated patients, and also Tigecycline is an excellent treatment choice for infections caused by drug resistant Acinetobacter baumannii.

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