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Emergence of Multidrug resistant Acinetobacter baumannii as Nosocomial Pathogen: Clinical Significance and Antimicrobial Sensitivity

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Abstract:
Background: *Acinetobacter baumannii has emerged as an important pathogen globally in various infections especially in hospital acquired infections.*
Objectives: *This study was conducted to determine the prevalence, risk factors, and antibiotic resistance pattern of Acinetobacter baumannii from various clinical samples.* ***Materials and Methods:*** *The study included a total of 4269 clinical samples, collected from patients at a multi super speciality hospital in Dehradun, India from September 2013 to August 2014. Identification and sensitivity of Acinetobacter baumannii were performed by fully automated Vitek 2 compact system.*
Results: *From total 4269 culture samples, 102 (2.39%) Acinetobacter baumannii were isolated. Maximum 59 (57.8%) isolates were obtained from respiratory secretions followed by blood 16 (15.7%) and pus 10 (9.8%). Elderly age, multiple hospitalization, prolonged ICU stay and invasive procedure were found to be significant risk factors. Out of 102 isolates, 95 (93.14%) were resistant to more than two classes of antibiotics (multidrug resistant) and 89 (87.26%) were resistant to carbapenems. 4 isolates (3.92%) were resistant to tigecycline while no isolate was resistant to Colistin.*
Conclusion: *The study will help to implement better infection control strategies and improve the knowledge of antibiotic resistance patterns of Acinetobacter baumanii in our region.*
Key words: *Acinetobacter species, antibiotics, multidrug resistance, nosocomial*

I. Introduction

Members of the genus Acinetobacter are ubiquitous, free living organisms that prefer moist environment and can be easily obtained from soil, water, food and sewage [1]. They are usually considered to be opportunistic pathogens, and of recent have been reported to cause a number of outbreaks of nosocomial infections in hospitalized patients like septicaemia, pneumonia, wound sepsis, endocarditis, meningitis and urinary tract infection (UTI) [2,3]. Although acknowledged to be an opportunist in hospitalised patients, community acquired infections are reported and they can cause infections in virtually every organ system [4].

Interpreting the significance of isolates from clinical specimens is often difficult, because of the wide distribution of Acinetobacter in nature and its ability to colonise healthy or damaged tissue [5]. In our study, undertaken over a period of one year (September 2013-August 2014) at Max Super Speciality Hospital, Dehradun, India, a 200 bedded multi super speciality hospital, we report the significance of infections caused by Acinetobacter baumannii and their antimicrobial susceptibility pattern.

II. Material and Methods

During the study period, total 4269 clinical samples were processed in microbiology laboratory. Paired blood cultures were processed with Biomerieux BacT/Alert 3D system. All the clinical samples including positive blood culture bottles were inoculated on MacConkey agar and Columbia agar with 5% sheep blood. Urine samples were additionally inoculated into CLED agar. Inoculated plates were incubated at 37°C for 24 - 48 hours. Colonies of Acinetobacter baumannii were white/cream coloured, smooth, circular with entire edges on Columbia agar and were nonfermenter with a pinkish tint on MacConkey agar. Microscopy showed gram negative coccobacilli on gram stain. Oxidase test was negative. [6,7].

Identification and sensitivity of Acinetobacter baumannii were performed by fully automated Vitek 2 compact system of Biomerieux diagnostics. Antimicrobials tested were amikacin, gentamicin, cefepime, ceftazidime, ciprofloxacin, levofloxacin, ampicillin-sulbactam, piperacillin-tazobactam, doxycycline, co-trimoxazole, cefoperazon-sulbactam, ticarcillin-clavulanate, imipenem, meropenem, doripenem, colistin and tigecycline as per CLSI.[8]

'Multidrug resistant (MDR) Acinetobacter sp.' is defined as isolate that is resistant to at least three classes of antimicrobial agents - all penicillins and cephalosporins (including inhibitor combinations), fluoroquinolones and aminoglycosides. 'Extensive drug resistant (XDR) Acinetobacter sp.' shall be the MDR isolate that is also resistant to carbapenems. 'Pandrug resistant (PDR) Acinetobacter sp.' shall be the XDR isolate that is also resistant to polymyxins and tigecycline. [9]

III. Results

From a total of 4269 culture samples processed, 1866 (43.71%) were culture positive. Out of 1866 positive cultures, 102 (5.47%) isolates belonged to the Acinetobacter baumannii.

The gender (male:female) ratio was 2.2:1 (70 males, 32 females). Acinetobacter infection was significantly observed among in-patients and the elderly (58.82% isolates in ≥55 years age group), was associated with co morbidities and longer duration of stay in the hospital as suggested by higher numbers of isolates from ICU patients and was found in those who had undergone any invasive procedure [Table 1].

Table 1. Various risk factors & number of isolates.

	No of A.baumannii isolated (102)
1.Attended hospital as	
In patient	97
Out patient	5
2.Age	
≥55	60
<55	42
3. Ward	
ICU	75
Non ICU	27
4. invasive procedure	
Conducted	67
None	35
5. Gender	
Male	70
Female	32

Table 2. Sensitivity of tested antibiotics

Antibiotic	Sensitive (%)	Intermediate (%)	Resistant (%)
Amikacin	25(24.5)	8(7.8)	70(68.6)
Ampicillin+Sulbactam	2(1.9)	0	100(98.0)
Cefepime	4(3.9)	0	98(96.0)
Cefoperazon+Sulbactam	10(9.8)	13(12.7)	79(77.4)
Ceftazidime	5(4.9)	1(0.9)	96(94.1)
Ciprofloxacin	3(2.9)	0	99(97.1)
Co-trimoxazole	8(7.8)	0	94(92.2)
Colistin	102(100)	0	0
Doripenem	8(7.8)	0	94(92.2)
Doxycycline	3(2.9)	0	99(97.1)
Gentamicin	4(3.9)	3(2.9)	95(93.1)
Imipenam	7(6.9)	1(0.9)	94(92.2)
Levofloxacin	3(2.9)	15(14.7)	84(82.4)
Meropenam	8(7.8)	5(4.9)	89(87.3)
Pipera-tazobactum	5(4.9)	0	97(95.1)
Tigecycline	88(86.3)	10(9.8)	4(3.9)
Ticarcillin+Clavulanic Acid	5(4.9)	0	97(95.1)

Of the total 102 isolates of Acinetobacter baumannii, 97 (95.09%) isolates were from the hospitalized patients as compared to the 5 (4.90%) isolates from the OPD patients. Acinetobacter baumanii was predominantly isolated from respiratory secretions 69 (67.65%), blood 16 (15.69%), pus 10 (9.80%), urine, pleural & ascitic fluid cultures.The highest number of isolates 41(40.20%) were from the medical ICU followed by neurosurgical ICU 25(24.51%). Other locations of isolation were ward 20(19.60%), other ICUS 9(8.8%), emergency ward 2(1.9%).

The antibiotic sensitivity pattern of Acinetobacter baumannii is given in Table 2. Ampicillin-sulbactam showed lowest sensitivity of 1.9%. While higher antibiotics like Imipenem and Meropenem also showedlower sensitivity 6.9% and 7.8% respectively. Amikacin and Cefoperazone-sulbactam showed higher sensitivity than carbapenems, 24.5% and 9.8% respectively. 4 isolates (3.92%) were resistant to tigecycline while no isolate was resistant to Colistin. Out of 102 isolates, 95 (93.14%) were MDR and 89 (87.26%) were XDR. However No isolate was PDR.

IV. Discussion

Acinetobacter spp. are the second most common Non-fermenting bacteria after Pseudomonas species that are isolated from human specimens, especially among nosocomial infections.[10] In recent years, this species has emerged as the causative agent of important nosocomial infections in the ICUs, which is probably related to the increasingly invasive procedures used, the greater quantity of broad-spectrum antimicrobials used, and prolonged duration of stay in the hospital. Development of resistance to antimicrobials is a major problem in the treatment of Acinetobacter infections.[11]

In our study, out of total 1866 organisms isolated, 102 (5.47%) were Acinetobacter baumannii. Similar prevalence of 3.47% of the total organisms isolated was reported by Lone et al[12] and 3.32% by Mindolli PB et al[13]. In comparison, higher prevalence rates of 14% and 9.6% among hospital isolates were observed by Mostofi et al. in Iran and Joshi et al. in Pune, India, respectively.[14,15] Acinetobacter spp. can colonize skin, wounds, respiratory and gastrointestinal tracts.[16] It is a pathogen of tropical and humid environment, but some species can survive environmental desiccation for weeks, a characteristic that promotes transmission through fomite contamination in hospitals.[17]

We isolated Acinetobacter baumanii from various clinical samples including blood, urine, body fluids, tracheal secretions, endotracheal tubes, pus and other samples, but most commonly from respiratory tract 69 (67.65%). In a study conducted by A. Asensio et al in 2008 Acinetobacter was isolated from respiratory tract (42.2%), surgical wound (15.1%), urinary tract (12.9%), skin (11.7%).[18]

Overall, in the present study, the significant risk factors for Acinetobacter infection were age ≥55 years, admission in the hospital as inpatients, longer (≥7 days) duration of stay in the hospital, having undergone any invasive procedures like catheterization, intubation, tracheostomy and mechanical ventilation. A longer hospital stay in a high-risk unit, use of mechanical ventilation, admission as inpatient into the ICUs, and underlying co-morbid conditions have been identified as the risk factors in previous studies as well.[9,12,19]

In our study, 93.14% isolates were MDR & 87.26% isolates were XDR while no isolate was PDR. The other studies conducted by Bhattacharyya et al. in West Bengal and Mostofi et al. in Tehran reported the MDR isolates to be 29% and 54%, respectively.[20,14] Acinetobacter is ubiquitous in the hospital setting. Its ability to survive for long periods coupled with its ability to demonstrate a number of antimicrobial resistance genes has made Acinetobacter a successful hospital pathogen.[21]

Most of the patients who were admitted in our hospital had previously attended primary and secondary care hospitals and usually received combination of β-lactam antibiotics like third and fourth generation cephalosporins along with aminoglycosides or fluoroquinolones. Majority of the isolates in our study were resistant to commonly used antibiotics such as ceftazidime, cefepime, gentamicin, amikacin, tobramycin, ciprofloxacin, levofloxacin, and ampicillin/sulbactam. This means MDR isolates are increasing, probably due to indiscriminate use of these antibiotics in healthcare settings. It is re-emphasized that broad spectrum antibiotics should be used with caution. We found that imipenem, meropenem, doripenem and piperacillin/tazobactam were also highly resistance antibiotics against this pathogen suggesting increased PDR isolates. The resistance pattern observed by us was in contrast to those described in previous studies.[22,23] Mostofi et al. in their study had reported tobramycin (26%) was the least resistant drug followed by meropenem (31%) and piperacillin/tazobactam (40%), but imipenem (76%) showed high resistance to Acinetobacter spp.[14] Differences observed between the studies could be due to the methods and the resistance patterns that are influenced by the environmental factors and the antimicrobial patterns used. Although antibiotic resistance is a worldwide concern, it is first and foremost a local problem – selection for and amplification of resistant members of a species that are occurring in individual hospitals and communities, which can then spread worldwide.[24] There are many measures that may impact on antimicrobial resistance; reducing and restricting the use of antimicrobials to only those situations where they are warranted, at proper dose and for the proper duration is the most appropriate solution.[25]

Carbapenems have been the drug of choice for treating Acinetobacter infections, but unfortunately, carbapenem resistant Acinetobacter baumannii is becoming common worldwide.[26] Of the β-lactamases, those with carbapenemase activity are the most concerning for drug resistance and include the serine oxacillinase (belonging to Ambler class D OXA type) and the metallo-b-lactamases (Ambler class B).[27]

Colistin and tigecycline are new but last alternatives in the treatment of Acinetobacter species. In our study, all Acinetobacter baumannii isolates were sensitive to Colistin while 88 (86.3%) isolates were susceptible to tigecycline. Similar to our findings, Shareek et al. studied 44 isolates of A. baumannii and found that all were sensitive to colistin.[28] Taneja et al. in Chandigarh, India studied 224 A. baumannii isolates, out of which 50 (22.3%) isolates were resistant to carbapenems.The significant finding in their study was that eight (3.5%) isolates were resistant to both colistin and tigecycline. [29] Various authors have reported the resistance rate to colistin between 1.8% and 2%,[30,31] while resistance to tigecycline varies from being nonexistent to 66%.[32,33] We did not find any Acinetobacter isolate being resistant to colistin, which may be due to its selective use only in case of carbapenem-resistant gram-negative bacteria.

V. Conclusion

We found 93.14% Acinetobacter baumannii isolates were MDR & 87.26% were XDR and all of these isolates were sensitive to colistin while most were sensitive to tigecycline. Elderly age, being inpatients, longer duration of stay, associated co-morbidity, and invasive procedure were found to be the risk factors for acquisition of Acinetobacter baumanii infection. To avoid resistance, antibiotics should be used judiciously and empirical antibiotic therapy should be determined based on local antibiotic sensitivity pattern of the prevalent organisms of the hospital. Increasing carbapenem resistance rates in Acinetobacter spp. is alarming as it leads to increasing usage of last antibiotics colistin and tigecycline.

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