ORIGINAL ARTICLE

Antimicrobial Susceptibility Pattern of Acinetobacter Baumannii and Rate of Carbapenem Resistance at a Tertiary Care Hospital in Karachi

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ABSTRACT:

Objective: To know frequency of carbapenem resistance in Acinetobacter baumannii and its antimicrobial susceptibility pattern at PNS Shifa Hospital Karachi.

Methodology: This study was carried out at PNS Shifa Hospital, Karachi, from 1st January 2015 till 31st October 2016. Samples from patients having different sites of infection were received in the laboratory from different wards of hospital and inoculated on culture plates. After 24 hours incubation, identification of non-lactose fermenter colonies of Acinetobacter baumannii was done by conventional methods. Antimicrobial susceptibility was recorded for ß-lactam group of antimicrobials, ß-lactam/ß-lactamase inhibitor combination group, tetracyclines, fluoroquinolones and aminoglycosides as per CLSI guidelines.

Results: During the study period, a total of 117 Acinetobacter baumannii isolates were identified from culture of different samples representing 5.0% of all bacterial isolates (n=2352) and 7.5% of all Gram-negative bacilli (n=1559) throughout the hospital. Out of one hundred and seventeen isolates, 52.1% (n=62) were found carbapenem resistant. Higher percentages of Acinetobacter baumannii were isolated among samples received from medical wards (26.4%). Percentage of Acinetobacter baumannii isolated was highest from the blood culture specimens (22.2%). Isolates showed higher resistance against ceftriaxone (84.6%) followed by cotrimoxazole (65.8%) and ciprofloxacin (63.2%). Comparatively low resistance against doxycycline and minocycline (23.9%), and tigecycline (38.9%) was observed. Resistance pattern to other antimicrobials was gentamycin (54.7%), amikacin (55.6%), piperacillin-tazobactam (48.7%), cefoperazone-sulbactam (51.35%), meropenem (52.1%) and imipenem (52.1%).

Conclusion: Carbapenem resistance in Acinetobacter baumannii is increasing and therapeutic options left to treat are highly toxic especially for patients with co-morbidities.

Keywords: Acinetobacter baumannii, Carbapenems, Frequency, Antimicrobial susceptibility pattern

INTRODUCTION:

Acinetobacter baumannii (AB) is catalase positive, oxidase negative and non-motile gram negative rod. It survives in aqueous environment, therefore it colonizes irrigating and intravenous solutions in hospital settings.[1,2,3] It has become clinically important due to its ability for outbreaks and resistance to antibiotics including carbapenems.[2,3,4,5] Associated risk factors with multidrug-resistant Acinetobacter baumannii include older age, prolong hospital stay, using drainage catheters for longer duration, prior antimicrobial therapy and intensive care unit (ICU) stay.[5,6,7,8] In the last 10 years, the incidence of Acinetobacter baumannii infections and carbapenem resistance has increased in a number of regions in the world.[8,9]

Carbapenems belong to ß-lactam group of antibiotics. These antimicrobials target cell wall of bacteria. This group includes meropenem, imipenem, doripenem and ertapenem. Carbapenems have been used as most effective and safe antimicrobials against gram negative rods till resistance against these antimicrobials developed.[9,10] Since ten years, resistance have been reported from hospitals of several countries against it. Many clinicians still believe that it is the most effective antimicrobial against gram negative rods. In most of hospitals carbapenems are used as empirical treatment to treat infections until culture reports are being obtained.[10]

It is important to know carbapenem resistance rate and susceptibility to other antimicrobials in hospitals and community of local settings. The purpose of this study was to provide data to clinicians regarding recent susceptibility pattern of carbapenems related to Acinetobacter baumanii infections.

METHODOLOGY:

A descriptive study was conducted at PNS Shifa Hospital Karachi from 1st January 2015 to 31st October 2016.

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Repeat samples from same patients were excluded from the study. Samples of wound/pus swab, naso-bronchial lavage, blood, sputum, urine, pleural fluid, tracheostomy tip, central venous line tip, sinus fluid and endotracheal tube tip were received in the microbiology laboratory from medical and surgical wards, intensive care unit (ICU), neonatal and pediatric wards/ ICU and out patients department (OPD) for culture and sensitivity.

All samples were inoculated on blood agar (oxoid) and MacConkey's agar (oxoid). Culture plates were incubated at 37° C in CO_2 incubator at ambient air for 24 - 48 hours. Techniques used for identification of Acinetobacter baumannii included colony morphology, catalase test, oxidase test, gram staining and species differentiation by biochemical reactions using API 20 NE (bioMerieux) were done.[2] Isolates showing grey, shiny, small colonies on blood agar, and oxidase negative non-lactose fermenting colonies on MacConkey's agar were included in study. All isolates were screened for carbapenem-resistant Acinetobacter baumannii (CRAB) with Imipenem 10µg and meropenem 10µg discs following Kirby-Bauer disc diffusion method according to clinical and laboratory standards institute (CLSI) guidelines.[11] The isolates with zone diameter equal to or less than 22mm against Imipenem disc and equal to or less than 18mm against meropenem disc were considered as CRAB as per CLSI guidelines[11]

Bacterial suspension equal to 0.5 McFarland solution of all isolated CRAB was inoculated on a Mueller-Hinton (oxoid) agar plate. Antimicrobial susceptibility or resistance against minocycline (30µg), tigecycline (15µg), doxycycline (30µg), cotrimoxazole (25µg), ciprofloxacin (5µg), amikacin (30µg), gentamycin (10µg), piperacillin-tazobactam (100/10µg), cefoperazone/sulbactam (75/30 µg) and polymyxin B (MIC) was carried out as per CLSI guidelines.[11] Descriptive statistics were applied and data was analyzed on IBM SPSS 22. The significance threshold was set at $P<0.05$.

RESULTS:

During the study period of two years, a total of 117 Acinetobacter baumannii isolates were identified from culture of different samples representing 5.0% of all bacterial isolates (n=2352) and 7.5% of all Gram-negative bacilli (n=1559) throughout the hospital. All Acinetobacter baumannii isolates were screened for carbapenem resistance. Out of one hundred and seventeen isolates, 62 (52.1%) were found to be carbapenem resistant. Most of the microorganisms were isolated in samples received from medical ward (26.4%) (Table-1).

Percentage of Acinetobacter baumannii isolated from different specimens has been shown in Table-2. It was highest from blood samples (22.2%).

In this study, the isolates showed higher resistance against ceftriaxone (84.6%) followed by other antimicrobials (Figure-1).

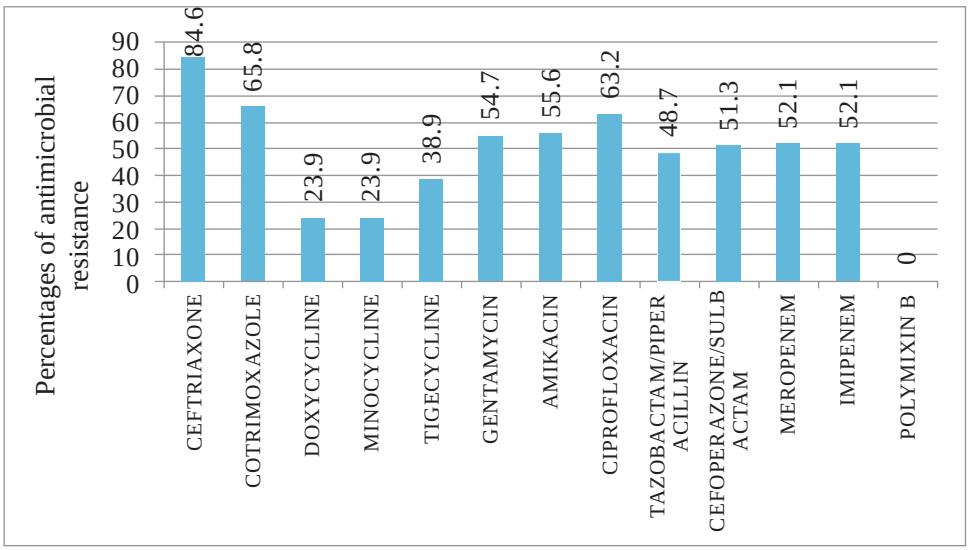
Table: 1
Percentages of Acinetobacter baumannii isolated from different wards of PNS Shifa Hospital from 2015-2016

WARD	n=117	%
Medical ward	31	26.4
Adult intensive care units	26	22.2
Outpatient department	20	17.1
Neonatal intensive care unit	16	13.7
Surgical ward	14	12.0
Pediatric intensive care unit	07	6.0
Pediatric ward	03	2.6

Table: 2
Percentages of Acinetobacter baumannii isolated from different samples at PNS Shifa Hospital Karachi from 2015-2016

SAMPLE	n=117	Acinetobacter baumannii isolated%
Blood	26	22.2
Naso-bronchial lavage	21	17.9
Pus culture	21	17.9
Sputum	15	12.8
Endotracheal tube tip	12	10.3
Wound culture	05	4.3
Pleural fluid	06	5.2
Tracheostomy tube tip	04	3.4
Urine	04	3.4
Central venous catheter tip	03	2.6

Figure: 1
Percentages of Acinetobacter baumannii isolates resistant against different antimicrobials at PNS Shifa Hospital Karachi from 2015-16



DISCUSSION:

Acinetobacter Baumannii is a multidrug resistant, opportunistic microorganism, usually found in Intensive Care settings and recognized as a known nosocomial pathogen leading to different types of infections such as bacteremia, nosocomial or ventilator associated pneumonia, meningitis, and skin and soft tissue infections.[6,7,12]

Acinetobacter baumannii strains are classified as multi-drug resistant (MDR): non-susceptible to ≥1 agent in ≥3 antimicrobial categories, extensive drug resistant (XDR): non-susceptible to ≥1 agent in all but ≤2 antimicrobial categories and, pan-drug resistant (PDR): non-susceptible to all antimicrobial agents available.[13,14] However these definitions will change with developing resistance. Now Carbapenem resistance rates are increasing to such an extent that it is threatening the world and this situation is gradually becoming a routine phenotype for the microorganism.[14,15] Factors responsible for developing resistance include impermeable outer membrane, enzymes responsible for breakdown of antibiotics especially ß-lactamases, class D OXA-type and class B metallo-ß-lactamases allowing the organism to resist carbapenems, porin channel alterations and efflux pumps.[13,14]

In the present study, more than half of Acinetobacter baumannii (52.1%) isolates were resistant to carbapenems (meropenem and imipenem). Higher resistance (90%) to carbapenem was reported in a study conducted at hospital of Turkey in 2010-2012.[16] This shows increasing resistance in Acinetobacter baumannii to carbapenems from other countries as well. In our study 22.2% of total AB isolates were identified among samples received from adult ICU which was high as compared to a study conducted in ICU settings of different hospitals where AB related infection was19.2%, 17.1%, 14.8%, 13.8%, 5.6%, 4.4% and 3.7% in Asia, Eastern Europe, Africa, Central and South America, Western Europe, Oceania and North America respectively.[2] This shows increasing ICU related infections due to AB. In our study ICU related infections were high most likely due to improper use of disinfectants and room irrigation techniques before and after patient's discharge from hospital.

In the present study most of the AB were isolated from the blood culture specimen (22.2%) followed by respiratory tract, pus discharge and pleural fluid samples. According to some studies the mortality rates were high because of bacteremia.[14,15,17] While taking samples special consideration should be given to sampling techniques as in most of the wards proper aseptic techniques were not followed. Hence isolates could be contaminants or might have been introduced in blood during sampling.[6,7,18]

In our study there was higher resistance against ß-lactam antibiotics as compared to other groups of antimicrobials. Polymyxin B with 0%, tigecycline 38.9%, doxycycline 23.9% and minocycline 23.9% were among least resistant antimicrobials. However these antimicrobials have limitations related to their side effects.[19] There was no resistance against polymyxin B in our study. Similar data was found in a study conducted in National Hospital of Tropical Diseases (Hanoi, Vietnam) in 2009 where susceptibility rates against ß-lactam antimicrobials were low as compared to minocycline, tigecycline or doxycycline and all isolates were sensitive to polymyxin B.[20] However, some resistance (3%) was reported against polymyxin B in a study conducted in Songklanagarind Hospital in Songkhla Province, Thailand in 2010.[21] This was frightening as last resorts have been started compromising also. Moreover, problem globally was of less concern for pharmaceutical companies towards development of newer antimicrobials.[19,22] Keeping in view such threats studies have been done to evaluate in

vitro susceptibility of combination therapy like colistin and imipenem, colistin and rifampicin, cefoperazone/sulbactam combined with imipenem and combination of imipenem with rifampicin.[21] One limitation of our study was that Rifampicin was not included in this study. Cefoperazone/sulbactam combined with rifampicin had better response against AB infection.[21] According to different studies, combination therapy was superior to mono-therapy because of toxicity, and hetero-resistance to polymyxin B due to prolonged use.[21,23,24,25]

In our study, better options for treatment in case of carbapenem-resistant strains of AB were minocycline, doxycycline and Polymyxin B. The judicious use of these agents is the need of the day, as these are the last resorts available for treating such resistant pathogens. To overcome this challenge a multidisciplinary approach is needed to prevent infections.

CONCLUSION:

Laboratories play an important role in providing appropriate antibiogram related to pathogens isolated in hospitals. This study has demonstrated that Carbapenem resistance in Acinetobacter baumannii is increasing and therapeutic options left to treat are highly toxic especially for patients with co-morbidities. In this way, empirical treatment is guided following regional or local antimicrobial susceptibility pattern of pathogens.

REFERENCES:

1. Manchanda V, Sinha S, Singh N. Multidrug resistant Acinetobacter. J Glob Infect Dis. 2010; 2(3):291-304.
2. Uwingabiye J, Frikh M, Lemnouer A, Bssaibis F, Belefquih B, Maleb A, et al. Acinetobacter infections prevalence and frequency of the antibiotics resistance: comparative study of intensive care units versus other hospital units. Pan Afr Med J. 2016; 23:191-201
3. Zhong Q, Xu W, Wu Y, Xu H. Clonal Spread of Carbapenem Non-susceptible Acinetobacter baumannii in an Intensive Care Unit in a Teaching Hospital in China. Ann Lab Med. 2012; 32(6):413-9.
4. Hammoudi D, Moubareck CA, Hakime N, Houmani M, Barakat A, Najjar Z, et al. Spread of imipenem-resistant Acinetobacter baumannii co-expressing OXA-23 and GES-11 carbapenems in Lebanon. Int J Infect Dis. 2015; 36: 56-61.
5. Maragakis LL, Perl TM. Antimicrobial Resistance: Acinetobacter baumannii: Epidemiology, Antimicrobial Resistance, and Treatment Options. Clin Infect Dis. 20 08; 46(8):1254–63.
6. Fournier PE, Richet H, Weinstein RA. The Epidemiology and Control of Acinetobacter baumannii in Health Care Facilities. Clin Infect Dis. 2006; 42(5):692-9.
7. Thom KA, Johnson JK, Lee MS, Harris AD. Environmental contamination because of multidrug-resistant Acinetobacter baumannii surrounding colonized or infected patient. Am J Infect Control 2011; 39(9):711-5
8. Liu CP, Shih SC, Wang NY, Wu AY, Sun FJ, Chow SF, et al. Risk factors of mortality in patients with carbapenem -resistant Acinetobacter baumannii bacteremia. J Microbiol Immunol Infect. 2014.
9. Hussein NH, Al-Mathkhury HJF, Sabbah MA. Identification of Imipenem-Resistant Genes in Acinetobacter baumannii Isolated from Baghdad Hospitals. J Med Microb Diagn. 2014; 3(6):170.
10. Al-Dorzi HM, Asiri AM, Shimemri A,Tamim HM, Al Johani SM, Dabbagh TA et al. Impact of empirical antimicrobial therapy on the outcome of critically ill patients with Acinetobacter bacteremia. Ann Thorac Med. 2015; 10(4):256-262.
11. Clinical and Laboratory Standards institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 26th ed. Wayne, PA: 2016.
12. Silva GD, Domingues S. Insights on the Horizontal Gene Transfer of Carbapenemase Determinants in the Opportunistic Pathogen Acinetobacter baumannii. Microorganisms. 2016; 4(3):29.
13. Magiorakos AP, Srinivasan A, Carey R, Carmeli Y, Falagas M, Giske C, et al. Multidrug-resistant, extensively drug-resistant and pan-drug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Infect. 2012; 18(3): 268–81.
14. Guo N, Xue W, Tang D, Ding J, Zhao B. Risk factors and outcomes of hospitalized patients with blood infections caused by multidrug-resistant Acinetobacter baumannii complex in a hospital of Northern China. Am J Infect Control 2016; 44(4):37-9.
15. Park SY, Choo JW, Kwon SH, Yu SN, Lee EJ, Kim TH, et al. Risk factors for mortality in patients with Acinetobacter baumannii bacteremia. Infect Chemother. 2013; 45(3):325.
16. Altun HU, Yagci S, Bulut C, Sahin H, kinikli S, Adiloglu AK et al. Antimicrobial Susceptibilities of Clinical Acinetobacter baumannii Isolates With Different Genotypes. Jundishapur J Microbiol. 2014; 7(12):13347.
17. Kapoor K, Jain S, Jajoo M, Dublish S, Dabas V, Manchanda V. Risk Factors and Predictors of Mortality in Critically ill Children with Extensively-Drug Resistant Acinetobacter baumannii Infection in a Pediatric Intensive Care Unit. Iran J Pediatr. 2014; 24(5):569-74.
18. Javed A, Zafar A, Ejaz H, Zubair M. Frequency and antimicrobial susceptibility of Acinetobacter species isolated from blood samples of paediatric patients. Pak J Med Sci. 2012; 28(3):363-6.
19. Liu Q, Li W, Feng Y, Tao C. Efficacy and Safety of Polymyxins for the Treatment of Acinectobacter baumannii Infection: A Systematic Review and Meta-Analysis. PLoS ONE. 2014; 9(6).
20. Van TD, Dinh Q-D, Vu PD, Nguyen TV, Pham CV, Dao TT, et al. Antibiotic susceptibility and molecular epidemiology of Acinetobacter calcoaceticus–baumannii complex strains isolated from a referral hospital in northern Vietnam. J Glob Antimicrob Resist. 2014; 2(4):3 18-21.
21. Tunyapanit W, Pruekprasert P, Laoprasopwattana K, Chelae S. Antimicrobial susceptibility of Acinetobacter baumannii isolated from hospital patients. Sci Asia. 2014; 40(1):28.
22. Baadani AM, Thawadi SI, El-Khizzi NA, Omrani AS. Prevalence of colistin and tigecycline resistance in Acinetobacter baumannii clinical isolates from 2 hospitals in Riyadh Region over a 2-year period. 2013; 34(3):248-53.
23. Chu H, Zhao L, Wang M, Liu Y, Gui T, Zhang J. Sulbactam-based therapy for Acinetobacter baumannii

infection: a systematic review and meta-analysis. Braz J Infect Diseas. 2013; 17(4):389-94

24. Kempf M, Djouhri-Bouktab L, Brunel J-M, Raoult D, Rolain J-M. Synergistic activity of sulbactam combined with colistin against colistin-resistant Acinetobacter baumannii. Int J Antimicrob Agents. 2012; 39(2):180-1.
25. Cai Y, Chai D, Wang R, Liang B, Bai N. Colistin resistance of Acinetobacter baumannii: clinical reports, mechanisms and antimicrobial strategies. J Antimicrob Chemother. 2012; 67(7):1607-15