 DOI: 10.18231/2394-5478.2017.0100

Emergence of Extensively drug-resistant *Acinetobacter spp* in a tertiary care centre of Hyderabad, Telangana state

Swathi Akula[1,*], Guru Prasad Manderwad[2], Ravi Shankar Reddy Anukolu[3], HRV Rajkumar[4]

[1,2]Assistant Professor, [3]Professor, [4]Professor & HOD, Dept. of Microbiology, Kamineni Academy of Medical Sciences & Research Centre, Hyderabad, Telangana

***Corresponding Author:**
Email: swathi.sho@gmail.com

Abstract

Introduction: *Acinetobacter spp.*, a gram negative coccobacillus, were considered to be opportunistic pathogen till their role in hospital acquired infections was described. It has been declared as one of the ESKAPE pathogens which effectively escapes the effects of antimicrobial drugs due to several resistance mechanisms. Of utmost concern is the emerging drug resistance to Carbapenems.

Material and Methods: The clinical specimens received were processed according to standard microbiology procedures and the organism was identified as *Acinetobacter spp*. Antimicrobial susceptibility testing was performed and the organisms were classified as Multidrug resistant (MDR), Extremely drug resistant (XDR) and Pan drug resistant (PDR).

Results: *Acinetobacter* spp were isolated predominantly in endotracheal aspirates (58.1%), suction tip (21.2%) and tracheal tip cultures (4.96%). There was decreased antimicrobial susceptibility to aminoglycosides, β lactam and β lactam inhibitor combination, fluoroquinolones and carbapenems. Out of 143 isolates, MDR were 131 (91.6%) and XDR were 126 (88.1 %). However no isolate was PDR. Majority of MDR and XDR strains were isolated from respiratory intensive care unit (RICU) (65.7% and 63.6% respectively).

Conclusion: Rise in carbapenem resistance in *Acinetobacter spp.* is quite alarming, as it leads to unchecked use of colistin, a last resort antibiotic. To avoid antimicrobial resistance, antibiotics should be used cautiously and empirical therapy should be formulated based on local antimicrobial sensitivity pattern. Antibiotic de-escalation therapy should be practiced based on the culture and sensitivity report. As it is a nosocomial pathogen, the health care workers have to be trained properly in infection control practices to prevent the transmission of this notorious pathogen.

Keywords*: Acinetobacter spp*, Carbapenem resistance, Combination therapy, Antibiotic de-escalation therapy, Infection control

Introduction

Acinetobacter spp, gained importance because of the emergence of resistance to almost all the available antibiotics. It was considered to be a quiet onlooker until its association with nosocomial infections was established. [(1)] It is termed as an Iraqibacter as a sudden rise in the isolations of *Acinetobacter baumannii* has been reported in injured soldiers returning from Iraq and Afghanistan. [(2)]

A.baumannii was generally considered to cause opportunistic infections. Several recent studies reported infections of the skin, soft tissues, bloodstream and urinary tract. Literature reveals that the *A. baumannii* constitutes a total of 20% infections in intensive care units worldwide, in patients who are immunosuppressed, on invasive devices like ventilator machines, catheters etc.[(3,4)]

Acinetobacter spp causes severe infections mainly due to the presence of several virulence factors which facilitate its survival under extreme environmental conditions.[(5)] *A. baumannii* has been now categorised as one of the ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, A. baumannii, Pseudomonas aeruginosa, and Enterobacter spp*,) by WHO which can conquer the effects of antimicrobial drugs due to ability to accumulate diverse mechanisms of resistance.[(6,7)] The nonselective use of antimicrobials in the ICUs and the various bacterial mechanisms of resistance contribute to summation of resistance property for this untreatable, notorious pathogen

Although Carbapenems are recommended against *Acinetobacter* infections, the resistance rate has increased drastically in recent times.[(8,9)] The alarming reports of extreme drug resistance (XDR) and pan-drug resistance (PDR) need attention focus.[(10)] Several studies reported the prevalence of carbapenem resistant *Acinetobacter spp* in India ranging from 15.21%-87.26%.[(11-14)]

In the recent times, in our hospital, we noticed that the prevalence of antimicrobial resistance pattern for *Acinetobacter spp* is on rise. With this view, we undertook a study to evaluate the prevalence and antimicrobial susceptibility pattern of *Acinetobacter spp* at our centre.

Materials and Method

A retrospective study was conducted in the Dept. of Microbiology of our tertiary care centre to identify the prevalence and antimicrobial susceptibility pattern of *Acinetobacter spp*. Isolates of *Acb Complex* obtained between July 2016 to June 2017 were included in the study. A total 4420 clinical samples were processed in Microbiology laboratory using standard microbiological

procedures like microscopy, culture and antimicrobial susceptibility testing.

All isolates which were oxidase negative, catalase positive, non-motile and non-fermenting were identified as *A. baumanii*.[15] Antimicrobial susceptibility testing of the isolated organisms was performed by the disk diffusion method by Kirby Bauer method. Antimicrobials tested were amikacin(30 µ g), gentamicin(10 µ g), cefotaxime, ceftazidime(30 µ g), ciprofloxacin(5 µ g), piperacillin-tazobactam(75+10 µ g), cefoperazone-sulbactam(75+30 µ g), imipenem(10 µ g), meropenem(10 µ g). Colistin Ezy MICTM Strip (0.016-256 mcg/ml) (Himedia) was used to determine the minimum inhibitory concentration(MIC). Interpretation of the zone diameters and breakpoints of MICs was done as per clinical laboratory and standards institute (CLSI) guidelines 2016. The drug resistance pattern of *Acinetobacter spp* is further classified in our study as Multidrug-resistant (MDR) which resistant to at least three classes of antimicrobial agents — including all penicillins and cephalosporins (including inhibitor combinations), fluoroquinolones, and aminoglycosides.), Extensively drug-resistant (XDR) which is resistant to the three classes of antimicrobials described above (MDR) along with carbapenems, and Pan drug resistant (PDR) which is resistant to polymyxins and tigecycline.[11]

Results

During this study period, a total 4420 clinical samples were processed in the Department of Microbiology. Out of these, 878 (19.8%) samples were culture positive, in which *Acinetobacter spp* were isolated in 143(16.2%) samples. The male to female ratio was 1.75:1 (91 males and 52 females). *Acinetobacter spp* infection was significantly seen in the older age group (59.4% in >50yrs). Most of the *Acinetobacter spp* were isolated from the ICUs (92.3%) (Fig. 1)

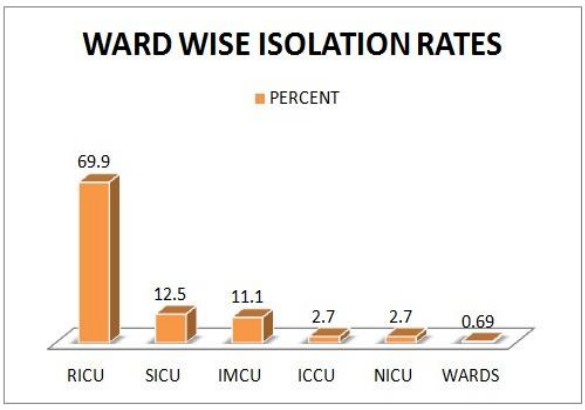

Fig. 1: Ward wise isolation rates

The various samples received and rate of *A.baumanii* isolation is shown in Table 1.

Table 1: Clinical specimens and Acinetobacter isolation

Specimens	No (%)
ET Aspirate	82(58.1)
Suction Tip	30(21.2)
Tracheal Tip	07(4.96)
Wound Swab	08(5.67)
Tissue	05(3.5)
Sputum	04(2.8)
Urine	03(3.1)
Blood	02(1.3)
Bal	01(0.7)
Pleural Fluid	01(0.7)
Total	143

* The No. in the parenthesis indicates percentage

A.baumanii was predominantly isolated from various respiratory specimens like ET aspirates (58.1%), suction tip (21.2%) and tracheal tip cultures (4.96%).

The risk factors for drug resistant *Acinetobacter spp* are shown in the Table 2.

Table 2: Risk factors associated with drug resistant *Acinetobacter spp*

	% of Drug resistant Acinetobacter spp isolated
Age >50yrs	59.4%
Mechanical ventilation	64%
Previous antibiotics	81.2%
Any other comorbidities*	57%
Mortality	28%

*Comorbidity includes road traffic accident, Congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus, end stage renal disease, asthma, cancer, human immunodeficiency virus

Most of the patients (64%) were mechanically ventilated and 81.2% received previous antibiotics.

The antimicrobial resistance pattern of *Acinetobacter baumannii i*s given in Table 3.

Table 3: Antibiotic susceptibility pattern of A.baumanii

Antimicrobial agent	Resistant (%)
Fluoroquinolones	131(91.6)
Aminoglycosides	129(90.2)
BL+BLIs	128(89.5)
Carbapenems	126(88.1)
Polymyxins	0

* The No. in the parenthesis indicate percentage

Beta lactam+betalactam inhibitor (BL+BLI) combination, aminoglycosides and fluoroquinolones showed decreased antimicrobial susceptibility (10.5%, 9.8% and 8.4% respectively) and carbapenems showed

antimicrobial susceptibility of 11.9%. All the isolates were susceptible to polymyxins.

Out of 143, MDR isolates were 131 (91.6%) and XDR isolates were 126(88.1%) and no isolate was PDR. Majority of MDR and XDR strains were isolated from RICU (65.7% and 63.6% respectively) followed by SICU, IMCU, ICCU, NICU, and wards. (Fig. 2)

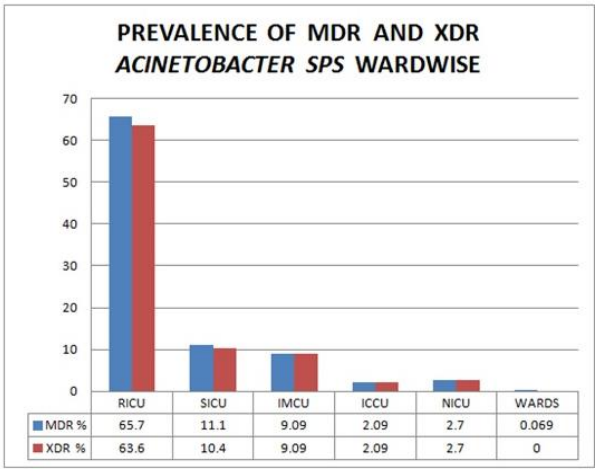

Fig. 2: Prevalence of MDR and XDR Acinetobacter spp ward wise

Discussion

Acinetobacter baumannii, over the past two decades, has emerged as one of the most difficult to treat pathogens due to its phenomenal ability to acquire drug resistance determinants. Multidrug resistant *A. baumanii* strains are now being reported, which is of utmost concern for the healthcare community. In synergy with this, *A. baumanii* has the freakish ability to survive for prolonged periods in the hospital environment, thus increasing the likelihood of nosocomial spread. The organism targets the most vulnerable hospitalized patients, admitted in the ICUs, use of invasive procedures, on treatment with the broad spectrum of antibiotics. As from literature reviews dating back to the 1970s, hospital-acquired pneumonia is still the most common infection caused by this organism. However, in more recent times, infections involving the central nervous system, skin and soft tissue, and bone have been reported by few authors.[2]

In the present study, Out of 878 culture positive samples, *Acinetobacter spp* were isolated in 143(16.2%) samples, which constitute 3.23% of the total samples. Similar prevalence was reported by a study from Delhi,[16] Pune.[17] In comparison a slightly lower prevalence was reported in Dehra Dun[10] and Mangalore[18] and higher prevalence rates were reported in Lucknow[19] and Maroc.[8] The *Acinetobacter spp* is a colonizer of skin, wounds, gastrointestinal and respiratory tracts. It is known to survive in tropical and humid climatic conditions and has an ability to be transmitted through contamination of fomites in hospital wards.

We isolated *A. baumanii* from various clinical samples including endotracheal tubes, tracheal secretions, body fluids, urine, wound swabs and other samples, but most commonly from respiratory tract 119 (84.3%). In a study conducted by Jean Uwingabiye et al,[8] Anil Chaudhary et al,[11] Lakshmi et al,[15] Jimmy B. Vaidya et al,[20] Amandeep Kaur et al[21] and Sridevi et al[18] the occurrence of *Acinetobacter spp* in respiratory specimens was reported to be 44.67%,57.8%, 62%, 64%,68.7% and 31.94% respectively. In the present study, the significant risk factors noted for *Acinetobacter* infection were age ≥50 years, longer (≥7 days) duration of stay in the hospital, having undergone any invasive procedures like intubation, mechanical ventilation, tracheostomy and catheterization. A prolonged hospital stay in a high-risk unit, use of mechanical ventilation and underlying co-morbid conditions have been identified as the significant risk factors in previous studies.[11,15] In our study, 91.6% isolates were MDR & 88.1% isolates were XDR while no isolate was PDR. Our study correlates with a study from Maroc (76%), [8] Dehradun (89%) [11] Mangalore (76.84%) [18] in which the prevalence of MDR and XDR was very high.

In India, less prevalence of XDR strains has been reported from Delhi (15.21%)[16] and Luck now (23.91%).[19] A similar study conducted at NIMS, Hyderabad in 2014 have reported the prevalence of 77% MDR strains and 13% XDR strains.[15] It is alarming to see the resurgence of XDR *Acinetobacter spp* as a dominant hospital-acquired pathogen.

Carbapenems are the drug of choice for treating *Acinetobacter* infections, Literature revealed the occurrence of carbapenem resistant *Acinetobacter baumannii* worldwide. Colistin and tigecycline have become the last alternatives in the treatment. In our study, all *Acinetobacter baumannii* isolates were sensitive to Colistin. A similar observation was made by Anil Chaudhary et al,[11] Lakshmi et al[15] and Sreedevi Sridhar et al. [18] It is worrying to note that several reports from India have shown the resistance rate to colistin between 1.49%[16] -19.6 %.[19] In our study colistin resistance was not found, may be due to its selective use only in cases with carbapenem-resistant gram-negative bacteria.

As our hospital is a super speciality centre, we receive patients who are previously admitted else were and treated with high-end antibiotics. In the study, a majority of the isolates were resistant to gentamicin, amikacin, ciprofloxacin, piperacillin/ tazobactam and Imipenem. This scenario clearly states that XDR isolates are on the rise, probably due to indiscriminate use of antibiotics in healthcare settings. It is a time to re-emphasize the use of broad-spectrum antibiotics with caution at proper dose and proper duration.

The principle of antibiotic de-escalation therapy is widely practiced for the management of life-threatening infections. Early administration of broad-spectrum antibiotics followed by sequential de-escalation provides

maximum benefit for the individual patient and reduces the selection pressure fueling the development of resistance. De-escalation strategies provide a clinical balance between using broad spectrum empirical antimicrobial agents and delaying the initiation of targeted therapy pending the bacteriological culture results. Several studies have shown that de-escalation therapy leads to a reduced spectrum of antibiotic use, shorter duration of therapy and reduced mortality. [22,23]

The clinicians can modify their antibiotic dosing by understanding time-dependent versus concentration-dependent antimicrobial activity of the drug. Clinical literature is emerging on the use of extended infusions of beta-lactams to treat gram-negative bacteria (e.g. increasing the dose of meropenem to 2gm every 8 hrs and infusion time to 3hrs). Several unconventional combination therapies have been postulated but often include colistin as a part. Colistin plus glycopeptides/ carbapenems/ tigecycline/ minocycline can be used as a combination therapy. A double carbapenem therapy, especially with Ertapenem, is most effective in reducing mortality, especially in colistin-resistant isolates. A triple combination therapy including carbapenem + rifampicin or sulbactam against Carbapenem resistant A. baumanii has been proposed. However, we recommend using the antibiotics with utmost precautions and only clinical settings when indicated. Newer therapeutic options include Eravacycline, Omadacycline, Plazomicin, Bal 30072 (beta-lactam), S 649266 (Cephalosporin) which are still in clinical trials.

Being a nosocomial pathogen, the spread of extensively drug-resistant *Acinetobacter spp* can be curtailed by following simple infection control practices. The infection control protocol in the ICUs can be reviewed and all the health care workers have to be trained properly. The important measures that can be strictly implemented are hand hygiene, scrubbing of the patients using 4% chlorhexidine body wash, environmental cleaning with regular wet mopping schedules, high surface cleaning, regular cleaning of suction bottles, trolleys and other patient care items, proper maintenance of wounds to avoid infection. [24] A checklist can be prepared to monitor the adherence to all the above and reviewed periodically by the hospital infection control team.

Conclusion

In our study, we found 88.1% *Acinetobacter baumannii* isolates were XDR and all were sensitive to colistin. Older age, admission in ICU with associated co-morbidity, and use of invasive procedures were found to be the risk factors for acquisition of *A. baumanii* infection. This in turn would prolong the hospital stay and cost burden to the patients. To avoid drug resistance, antibiotics should be used with caution and empirical antibiotic therapy should be determined based on local antimicrobial sensitivity pattern of the prevalent organisms of the hospital. Antibiotic de-escalation therapy, the practice of using broader spectrum antibiotics, earlier in treatment, for a shorter duration of time – and then switching to narrow spectrum of antibiotic (if possible the therapy can be discontinued), once the infection is accurately diagnosed and under control should be practiced. Every hospital should have an antibiotic policy prepared in concordance with the national guidelines. Increasing carbapenem resistance rates in *Acinetobacter spp*. is of concern as it leads to increased usage of colistin-a last resort antibiotic.

References

1. Taneja N, Singh G and Sharma M. Emergence of tigecycline & colistin resistant Acinetobacter baumanii in patients with complicated urinary tract infections in north India. Indian J Med Res 2011; 133:681-684.
2. Peleg AY, Seifert H, Paterson DL. Acinetobacter baumannii: emergence of a successful pathogen. Clin Microbiol Rev 2008; 21:538-82.
3. Lee CR, Lee JH, Park M, Park KS, Bae IK, Kim YB et al. Biology of Acinetobacter baumannii: Pathogenesis, Antibiotic Resistance Mechanisms, and Prospective Treatment Options. Front Cell Infect Microbiol 2017; 13:55-59.
4. Singh H, Thangaraj P, Chakrabarti A. Acinetobacter baumannii: A Brief Account of Mechanisms of Multidrug Resistance and Current and Future Therapeutic Management. J Clin and Diagn Res 2013; 4:1-4.
5. Lin, M. F., and Lan, C. Y. Antimicrobial resistance in Acinetobacterbaumannii: from bench to bedside. World J. Clin. Cases 2014; 2:787–814.
6. Boucher HW, Talbot GH, Bradley JS, Edwards JE, Gilbert D, Rice LB et al. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis 2009;48:1-12
7. Gordon NC, Wareham DW. Multidrug-resistant Acinetobacter baumannii: mechanisms of virulence and resistance. Int J Antimicrob Agents 2010; 35:219-26.
8. 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;23:191-196
9. Kim DH, Choi JY, Kim HW, Kim SH, Chung DR, Peck KR, et al. Spread of carbapenem-resistant Acinetobacter baumannii global clone 2 in Asia and AbaR-type resistance islands. Antimicrob Agents Chemother. 2013; 57:5239–5246.
10. Doi Y, Husain S, Potoski BA, McCurry KR, Paterson DL. Extensively Drug-Resistant Acinetobacter baumannii. Emerg Infect Diseases 2009; 15:980-982.
11. Chaudary A, Pandya N. Emergence of multi drug resistant Acinetobacter baumannii as nosocomial pathogen. J Dent Med Sci 2015; 14:40-44.
12. Bhattacharyya S, Bhattacharyya I, Rit K, Mukhopadhyay PK, Dey JB, Ganguly U et al. Anti-biogram of Acinetobacter *spp* isolated from various clinical specimens in a tertiary care hospital in West Bengal, India. Biomed Res 2012. ISSN: 0970-938X (Print) | 0976-1683 (Electronic).
13. Dash M, Padhi S, Pattnaik S, Mohanty I, Misra P. Frequency, risk factors, and anti-biogram of Acinetobacter species isolated from various clinical samples in a tertiary care hospital in Odisha, India. Avicenna J 2013; 3:97-102.

14. Anitha P, Ramaiah S. Beta lactamase in Acinetobacter Species: A Global Threat. Int J Pharm Biol Sci 2011; 2:1-4.
15. Sukanya S, laxmi V, Padmaja K. Prevalance of multi drug resistant Acinetobacter baumannii in clinical samples in a tertiary care hospital. Int J Infect control 2014; 11:1-5.
16. Perween N, Sehgal S, Krishna Prakash S. Geographical Patterns in Antimicrobial Resistance of Acinetobacter in Clinical Isolates. J Clin Diagn Res 2014; 8:10 -12.
17. Gupta N, Gandham N, Jadhav S, Mishra R. Isolation and identification of Acinetobacter species with special reference to antibiotic resistance. J Nat Sci Biol Med. 2015; 6:159–162.
18. Shridhar S, Bhat S. Clinicomicrobiological Study of infections caused by Acinetobacter species. Asian J Pharm Clin Res 2017; 10:223-224.
19. Islahi S, Ahmad F, Khare V, Mishra N, Yaqoob S, Shukla P et al. Prevalence and Resistance Pattern of Acinetobacter Species in Hospitalized Patients in a Tertiary Care Centre. Journal of Evolution of Medical and Dental Sciences 2014; 3:4629-4635.
20. Vaidya JB, Vijay N. Charde and Arun B. Prevalence of Multi drug resistance Acinetobacter baumannii in Central India (Nagpur). J Pharm Res 2015; 9:517-521.
21. Kaur A, Singh S, Gill AK, Kaur N, Mahajan A. Isolation of Acinetobacter baumannii and its antimicrobial resistance pattern in an intensive care unit (ICU) of a tertiary care hospital. International Journal of Contemporary Medical Research 2016; 3:1794-1796.
22. Joung MK, Lee J, Moon S, Cheong HS, Joo EJ, Joung Y et al. Impact of de-escalation therapy on clinical outcomes for intensive care unit-acquired Pneumonia. Crit Care 2011; 15:79-84.
23. Kosey, Raj Kumar. Antibiotic De-Escalation in The Intensive Therapy Unit- A Review Int J Pharm Sci Res 2016; 7:3596-3601.
24. Prevention of hospital acquired infections. A practical guide 2nd edition available at http://apps.who.int/medicinedocs/documents/s16355e/s16355e.pdf. Accessed on 19th June 2015.

How to cite this article: Akula S, Manderwad GP, Anukolu RSR, Rajkumar HRV. Emergence of extensively drug-resistant *Acinetobacter spp* in a tertiary care centre of Hyderabad, Telangana state. Indian J Microbiol Res 2017;4(4):448-452.