# CHANGING TRENDS OF AEROBIC BACTERIA ISOLATED AND SUSCEPTIBILITY PATTERN OF ACINETOBACTER SPECIES IN INTENSIVE CARE UNIT

### LATIF S.<sup>1</sup> AND ANWAR M.S.<sup>2</sup>

Department of <sup>1</sup>Microbiology, Services Institute of Medical Sciences Department of <sup>2</sup>Pathology, CMH, Lahore Medical College, Lahore – Pakistan

## ABSTRACT

Background and Objectives: Microorganisms isolated in Intensive Care Unit (ICU) setting change over time and may be different in different hospitals. For empiric therapy the knowledge of commonly isolated organisms is important. Multi drug resistance is common in the Acinetobacter species isolated from patients admitted in medical intensive care unit (MICU). The presence of multi drug resistant (MDR) bacteria leads to increased morbidity and mortality, is an economic burden on the already stretched resources of our nation.

Methods: In this retrospective cohort study specimens received from the patients admitted in the medical ICU of Services Hospital Lahore (SHL) during the period January 2009 to October 2009 and January 2013 to March 2014 were analyzed. The bacterial isolates obtained were identified on the basis of colony morphology, Gram staining reaction and biochemical tests. The sensitivity pattern of Acinetobacter spp. to various antibiotics was noted.

Results: In 2009, 379 bacterial isolates were obtained from 640 culture specimens received from MICU. Gram-positive bacteria isolated were 111 (29%), enterobacteriacae were 122 (32%) and non-fermenters were 146 (39%). During the period from January 2013 to March 2014, 462 bacteria were isolated from 801 specimens. Gram positive bacteria were 20 (4.3%), enterobacteriacae 121 (26.3%) and non-fermenters were 321 (69.4%). Sixty-six Acinetobacter species were isolated from Jan-Oct, 2009. Imipenem resistant strains were 40(60.6%) of these 18 were found to be resistant to all antibiotics studied. Tige-cyclin (TGC) sensitivity was not performed in 2009. From January 2013 to March 2014 one hundred and eighty-nine Acinetobacter species were isolated. One hundred and fifty-four Acinetobacter species were tested for imipenem/meropenen sensitivity out of these 114 (74%) were resistant. One hundred and eighty Acinetobacter species were tested for sensitivity to tigecycline and only 13 (7.2%) were resistant. Nine were resistant to all antibiotics tested including TGC.

Conclusion: It is observed that the prevalence of non-fermenter bacteria is increasing while Gram positive bacteria and enterobacteriacaea are decreasing in MICU patients. This situation is alarming as not only the prevalence of the non-fermenter, Acinetobacter species increasing so is the imipenem resistance which has increased from 60.6% to 74% within two years. The presence of resistance to imipenem in bacteria indicates resistance to multiple drugs and in extreme case, to all the antibacterial drugs available. The treatment of infections caused by MDR or pan-drug resistant bacteria is not always possible. Thus it is very important to control, detect and treat these bacteria early.

Key Words: Intensive care unit, Antibiotic therapy, Acinetobacter species, Multi drug resistance.

## **INTRODUCTION**

Organisms causing infections in intensive care units change over time and so does their antibiotic sensitivity pattern, this knowledge is important to select antibiotic therapy.<sup>1</sup>

Multi-drug resistant organisms, some of which are resistant to all available antibiotics are frequently seen in intensive care setting of hospitals. These organisms can cause pneumonia, blood stream infections, device related infections, urinary tract infections and surgical site infections.<sup>2-4</sup> Acinetobacter is a Gram-negative non fermentative bacteria. It has the ability to survive for prolonged periods on dry and wet surfaces. It is often resistant to multiple drugs and has the ability to cause infection outbreaks in hospital settings especially in the intensive care unit (ICU) where patients are already immunocompromised. Few antibiotics are available for treatment and the cost of treatment is higher if infected with Acinetobacter spp. Infected patients have a longer stay in hospital along with increased morbidity and higher mortality.<sup>4-7</sup> The Services Hospital, Lahore (SHL) is a 1450-bed tertiary care teaching hospital. There are four ICUs; surgical, pediatric, neonatology and medical. The medical ICU has a capacity of 10-beds.

This study was done to see the bacteriological profile and the susceptibility pattern of the Acinetobacter species isolated from MICU. This will help select effective empiric antibiotic therapy.

### MATERIALS AND METHODS

It is a retrospective cohort study. Laboratory data of patients admitted in MICU at Services hospital, from year 2009 & 2013-14 was analyzed. The trends and frequency of isolated aerobic bacteria was recorded along with susceptibility patterns of Acinetobacter spp.

From Jan – Oct 2009, six hundred and forty specimens were received and processed at Microbiology laboratory of Services Institute of Medical Sciences (SIMS). Eight hundred and one specimens were processed from Jan 2013 to March 2014.

A variety of specimens such as tracheal swabs, blood, urine, central venous tips, body fluids, pus and sputum received, were inoculated on Blood agar and MacConkey agar plates and incubated at 35°C overnight. Identification was based on colony morphology, Gram stain reaction followed by biochemical tests which included oxidase test, catalase test, DNase, triple sugar iron (TSI), motility test, citrate utilization test and urease test.8 Antibiotic sensitivity was determined by Kirbey Bauer method on Mueller Hinton agar plates incubated at 35°C overnight. Antibiotics discs used included those of 3rd generation cephalosporin ceftazidime, (CAZ30) and 4<sup>th</sup> generation cephalosporin Cefepime (FEP30). Quinolone, ciprofloxacin (CIP5); cabapenem, imipenem or meropenem (IPM10, MEM); aminoglycoside gentamycin (CN10) amikacin (AK30); monobactam, Azactam (AZT); Antipseudomonal penicillin Piperacillin/Tazobactam (TZP110). Doxycycline (DO 30), Tigecycline (TGC15) and trimethoprim + sulfamethoxazole 1.25+23.75ug (SXT25) depending on availability. Discs were obtained from Oxoid. Susceptibility and tact was performed according to CLSI.9

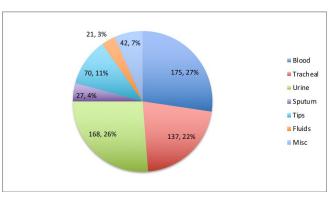
Tigecycline MICs were not done as recommended and 19mm zone of clearing around TGC was considered sensitive.

## RESULTS

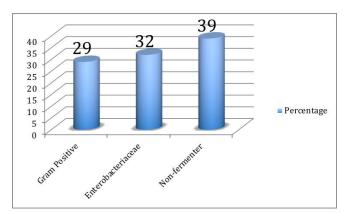
In year 2009, 640 specimens were received from January to October as shown in Figure 1.

Of the 640 specimens, growth was obtained from 294 (46%) of specimens. In the growth positive specimens, 379 bacterial isolates were obtained. The distribution of isolates was as shown in Figure 2.

Sensitivity pattern of 66 Acinetobacter SPP isolated was as shown in figure 3. Imipenem resistant Acinetobacter strains were 40 (60.6%). Out of these 18 were found to be resistant to all antibiotics studied.



**Fig. 1:** Specimens received from medical ICU in year 2009 (*n* = 640).



**Fig. 2:** Aerobic bacteria isolated in 2009 (n = 379).

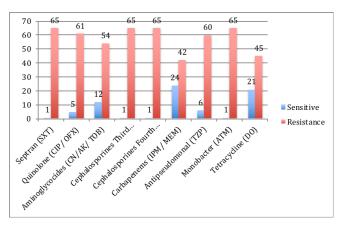


Fig. 3: Sensitivity pattern of Acinetobacter spp isolated in year 2009.

Tigecycline was not tested in 2009.

During the period January 2013 to March 2014, 801 specimens were received as shown in Figure 4.

Of the 801 specimens 451(56%) yielded growth. From the growth positive specimens four hundred and sixty two bacterial isolates were obtained. The distribution of isolates was as shown in Figure 5.

One hundred and eighty-nine *Acinetobacter* species were isolated. According to availability of anti-

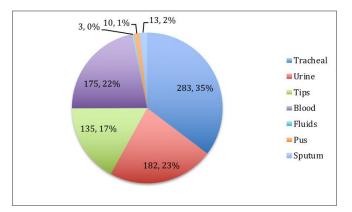
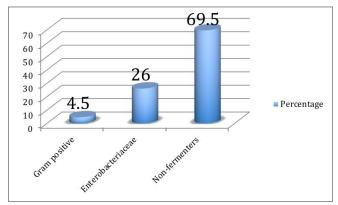


Fig. 4: Specimens received from medical ICU in 2013-2014 (n = 801).

biotic discs one hundred and fifty-four *Acinetobacter* species were tested for imipenem/meropenen sensitivity of which 114 were resistant (74%). One hundred and eighty *Acinetobacter* species were tested for sensitivity to tigecycline and only 13 were resistant (7.2%). Nine isolates were resistant to all antibiotics tested including TGC.

Sensitivity pattern of Acinetobacter sp isolated is shown in figure 6.



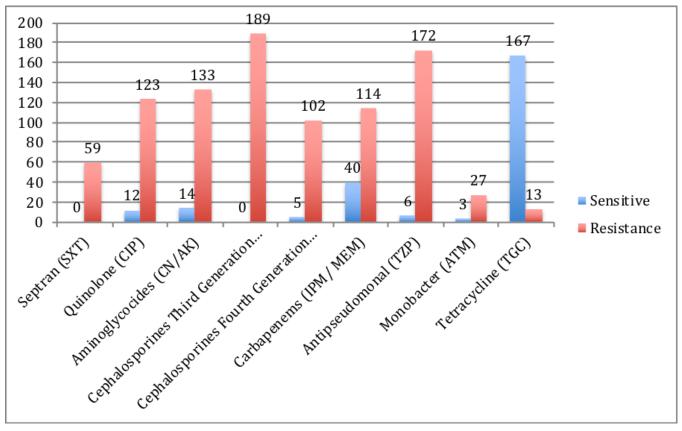
**Fig. 5:** Aerobic bacteria isolated in 2013-14 (n = 462).

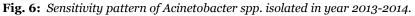
## DISCUSSION

The bacterial profile and sensitivity pattern of microorganisms varies in different hospitals and indeed in areas of the same hospital.<sup>10</sup> Therefore for appropriate empiric therapy to be selected it is essential to monitor these changing trends of bacteria isolated.

In 2009, 640 specimens were processed while in 2013-14 eight hundred and one specimens were processed at Microbiology laboratory of SIMS.

Growth was obtained from 46% of specimens in





2009 and 56% in 2013-14. This increase in growth positivity may be due to change in the type of specimens received in the laboratory. In 2009 most common specimens received were blood cultures (Figure 1). Positive yield was low from blood culture. In 2013-14 the most common specimens received were tracheal secretions with high positive growth rate as compared to blood cultures (Figure 4). In the ICU setting where assisted ventilation is required the high rate of positive growth in tracheal specimens, may be due to colonization of the ventilator tube which may result in infection.<sup>11-13</sup>

In 2013-14 there was a change in bacteriological profile at medical ICU of SHL as compared to 2009. This change was less pronounced in isolated Grampositive organisms and enterobacteriaece isolated while the yield of nonfermenter Gram negative organisms increased (Figure 2 & 5). This is in agreement with a *study carried out by Alp et al to see the changing pattern of antibiotic susceptibility in ICU over a ten year period.*<sup>14</sup>

The yield of isolated Acinetobacter species increased from 17.4% in 2009 to 33.3% in 2013-2014. It is lower than the 57.8% as seen in study conducted at Shifa international hospital and PIMS, Islamabad.<sup>7</sup>

The sensitivity of the isolated Acinetobacter species is shown in Figures 3&6. As a last resort, the treatment of resistant Acinetobacter infections is the carbapenem group of antibiotics.<sup>14</sup> It is alarming to see the rise in resistance to carbapenems from 60.6 to 74% in our MICU. Similarly in neighboring India a rise in resistance to carbapenems was seen; from 6% in 2003 to 74% in 2008.<sup>15</sup> In Taiwan the resistance rate was low initially but over time it has increased from 14.1% in 2003 to 46.3% in 2008.<sup>16</sup>

High carbapenem resistance is also seen in the nosocomial acinetobacter isolates in other hospitals in Pakistan. In Karachi, a retrospective study by Saleem et al, reported 71.3% resistance to carbapenems in Acinetobacter isolated from NICU from 2003-8.<sup>17</sup> In another study done on specimens received from ICU of patients admitted in AKU hospital, 90% of isolates of Acinetobacter species were cabapenem resistant.<sup>12</sup> In Islamabad in a study conducted by Begum et al<sup>18</sup> to study resistance mechanisms in Acinetobacter to carbapenems, 100% of Acinetobacter species. was resistant to carbapenems. Hassan et al in 2014 reported 65.5% resistance in Acinetobacter isolated from different hospitals of Pakistan.<sup>19</sup>

Findings in this study were in agreement with other South East Asian nations such as 72.2% resistance in Malaysia,<sup>20</sup> and 75.4% resistance in China.<sup>21</sup> In a prospective study carried out in Singapore in the year 2006-2007 carbapenem resistance in *Acinetobacter baumannii* was 70.5%.<sup>22</sup>

There is an increase in MDR Acinetobacter repor-

ted in USA. In a study on susceptibility pattern of 55,330 Acinetobacter species; resistance to carbapenems increased to 49.2% in 2008 from 20.6% in 2002. In the ICU setting resistance to carbapenems in 2008 was 55.2%.<sup>23</sup> The carbapenem resistant Acinetobacter species. reported in another study by Jennifer et al from USA is similar to ours. In this study 67 Acine-tobacter species collected from different hospitals in USA revealed 75% resistance to imipenem.<sup>24</sup>

It is very important that this organism should not be allowed to become endemic in hospitals for this rigorous implementation of standard and transmission based precautions are required.<sup>25</sup>

## CONCLUSION AND SUGGESTIONS

It is concluded that in the medical ICU at SHL there is a vast change in the organisms pattern isolated in the year 2009 as compared to year 2013-2014. The multiple drug resistant Acinetobacter species have increased in 2013-14; therefore continuous surveillance is required to be aware of the changes. Empiric antibiotic therapy should be instituted according to bacterial profile and sensitivity pattern of the isolates.

### **Author's Contribution**

SL: Collection of data, writing and formatting of article. AS: Contribution in data analysis and writing and formatting of results.

#### ACKNOWLEDGEMENT

The authors are obliged to Prof. Dr. Ghazala Jaffery, HoD Pathology SIMS for guiding and allowing this project to be carried out in the department.

## **Conflict of Interest:**

None.

#### REFERENCES

- 1. Tyckowska-Sieron R, Bartoszko-Tyczkowska A, Gaszynski W. Bacterial infections in intensive Care Unit patients analyzed on the example of Lodz Medical University Hospital No 1 in the period 2002-2015. Med Dosw Mikrobiol. 2016; 68 (1): 39-46.
- 2. Potron A, Poirel L, Nordmann P. Emerging broad-spectrum resistance in Pseudomonas aeruginosa and Acinetobacter baumannii: mechanisms and epidemiology. J Int antimic agents, 2015; 45 (6): 568-85.
- 3. Mathai AS, Oberoi A, Madhavan S, Kaur P. Acinetobacter infections in a tertiary level intensive care unit in northern India: Epidemiology, clinical profiles and outcomes. J infec pub heal. 2012; 5 (2): 145-52.
- 4. Niederman MS, Kollef MH. The road forward in the management of Acinetobacter infections in the ICU. J Inten Care Medi. 2015; 41 (12): 2207–2209.
- 5. Sunenshine RH, Wright M-O, Maragakis LL, Harris AD, Song X, Hebden J, et al. Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization. Emer Infec Dis. 2007; 13 (1): 97.
- 6. Dent LL, Marshall DR, Pratap S, Hulette RB. Multidrug

resistant Acinetobacter baumannii: a descriptive study in a city hospital. BMC Infec Dis. 2010; 10 (1): 196.

- 7. Tahseen U, Talib MT. Acinetobacter infections as an emerging threat in intensive care units. J Ayub Med Col Abbot. 2015; 27 (1): 113-6.
- 8. Cheesbrough M. District laboratory practice in tropical countries Part 2. Combridge 2nd ed: Camb Uni Press; 2006.
- 9. Wikler MA, Institute CLSI. Performance standards for antimicrobial susceptibility testing: sixteenth informational supplement. 16 ed: Clin Lab Stand Inst. 2006.
- 10. Bertrand X, Dowzicky MJ. Antimicrobial susceptibility among gram-negative isolates collected from intensive care units in North America, Europe, the Asia-Pacific Rim, Latin America, the Middle East, and Africa between 2004 and 2009 as part of the Tigecycline Evaluation and Surveillance Trial. Clin Therap. 2012; 34 (1): 124-37.
- Guo-xin M, Dan-yang S, Xi-zhou G, Jun-chang C, Rui W, Zhi-gang C, et al. Laboratory to clinical investigation of carbapenem resistant Acinetobacter baumannii outbreak in a general hospital. J Jundish Micro. 2014; 7 (1): 1-7.
- Sandiumenge A, Rello J. Ventilator-associated pneumonia caused by ESKAPE organisms: cause, clinical features, and management. Current Opinin Pulmo Medi. 2012; 18 (3): 187-93.
- 13. Irfan S, Zafar A, Guhar D, Ahsan T, Hasan R. Metallo- $\beta$ lactamase-producing clinical isolates of Acinetobacter species and Pseudomonas aeruginosa from intensive care unit patients of a tertiary care hospital. J Ind Med Micro. 2008; 26 (3): 243.
- 14. Alp E, Kiran B, Altun D, Kalin G, Coskun R, Sungur M, et al. Changing pattern of antibiotic susceptibility in intensive care units: ten years experience of a university hospital. Anaerobe. 2011; 17 (6): 422-5.
- 15. Goel N, Wattal C, Oberoi JK, Raveendran R, Datta S, Prasad KJ. Trend analysis of antimicrobial consumption and development of resistance in non-fermenters in a tertiary care hospital in Delhi, India. J Antimicro Hem. 2011; 66 (7): 1625-30.

- Su C-H, Wang J-T, Hsiung CA, Chien L-J, Chi C-L, Yu H-T, et al. Increase of carbapenem-resistant Acinetobacter baumannii infection in acute care hospitals in Taiwan: association with hospital antimicrobial usage. Plos one, 2012; 7 (5): e37788.
- 17. Saleem AF, Ahmed I, Mir F, Ali SR, Zaidi AK. Pan-resistant Acinetobacter infection in neonates in Karachi, Pakistan. J Infec Develop Count, 2009; 4 (01): 030-7.
- 18. Begum S, Hasan F, Hussain S, Shah AA. Prevalence of multi drug resistant Acinetobacter baumannii in the clinical samples from Tertiary Care Hospital in Islamabad, Pakistan. J Pak Med Sci. 2013; 29 (5): 1253.
- 19. Hasan B, Perveen K, Olsen B, Zahra R. Emergence of carbapenem-resistant Acinetobacter baumannii in hospitals in Pakistan. J Med Micro. 2014; 63 (1): 50-5.
- 20. Lean S-S, Suhaili Z, Ismail S, Rahman NIA, Othman N, Abdullah FH, et al. Prevalence and genetic characterization of carbapenem-and polymyxin-resistant Acinetobacter baumannii isolated from a tertiary hospital in Terengganu, Malaysia. ISRN Micro. 2014; 2014: 1-9..
- Tan TY, Hsu LY, Koh TH, Ng LS, Tee N, Krishnan P, et al. Antibiotic resistance in gram-negative bacilli: a Singapore perspective. Ann Acad Med Singapore, 2008; 37 (10): 819-25.
- 22. Mera RM, Miller LA, Amrine-Madsen H, Sahm DF. Acinetobacter baumannii 2002–2008: increase of carbapenem-associated multiclass resistance in the United States. Micro Drug Resis. 2010; 16 (3): 209-15.
- 23. Adams-Haduch JM, Onuoha EO, Bogdanovich T, Tian G-B, Marschall J, Urban CM, et al. Molecular epidemiology of carbapenem-non-susceptible Acinetobacter baumannii in the United States. J Clin Mmicro. 2011; 4a (11): 3849-54.
- 24. Doi Y, Husain S, Potoski BA, McCurry KR, Paterson DL. Extensively drug-resistant Acinetobacter baumannii. Emer Infec Dis. 2009; 15 (6): 980.
- 25. Myers C, Mangino J, Taylor D, Dunwoody L. Acinetobacter baumannii outbreak in an intensive care unit (ICU): Epidemiologic investigation and resolution. Am J Infec Cont. 2005; 33 (5): 107-8.