

Acinetobacter - A Hard to Treat Resilient ICU Pathogen

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ABSTRACT

Objective: To isolate Acinetobacter sp and identify MDR (multidrug resistant) and XDR (extensively drug resistant) isolates from intensive care unit in a tertiary care hospital, Lahore.

Methodology: This cross-sectional research was performed retrospectively in a tertiary care hospital, Lahore from January 2022-December 2022. It consisted of 435 specimens from ICU patients processed for culture and sensitivity in microbiology section of Pathology Laboratory, SMCH. The specimens included blood, pus, urine, cerebrospinal fluid, and other body cavity fluids, sputum, bronchial aspirates, wound swabs, ETT, etc. The specimens were cultured on Blood agar (Oxoid UK) and Mac Conkey agar (Oxoid UK) but CLED agar (Oxoid UK) was used for urine. After overnight incubation at 37°C, Acinetobacter sp were identified by morphology and biochemical reactions using Analytical profile index (API) 20 NE (Biomerieux, France).

Results: One hundred and seventy-five cases revealed Gram negative bacteria (GNB) and 31 (17.71%) of the GNB were Acinetobacter sp. Fifteen isolates of Acinetobacter sp were obtained from respiratory secretions, 7 from pus, 6 from urine, 2 from ETT, and 1 isolate from blood sample. A total of 31 isolates were obtained. Thirteen (41.9%) Acinetobacter isolates were MDR and 9 (29.0%) turned out to be XDR. The remaining 9 isolates exhibited satisfactory susceptibility.

Conclusion: Acinetobacter sp. is responsible for a significant bulk of drug resistant ICU associated infections and is increasingly developing resistance as evident by 41.9% MDR and 29.0% XDR isolates.

Key words: Acinetobacter sp, Intensive care units (ICUs), Infections, Gram negative bacteria.

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Introduction

The World Health Organization (WHO), reports an incidence of more than 24% nosocomial sepsis with a very high mortality rate. This is further worsened if infection is caused by drug resistant bacteria. Hence, Intensive care unit (ICU) associated infections are among the major causes of death worldwide.¹ A multicenter study in Punjab, Pakistan revealed a high prevalence of 33.3% ICU associated infections among HCAs.² An Intensive care unit (ICU) is the potential site for developing Health care associated infections (HAIs) at a rate much higher than other areas of health care facility.³ Among ICU associated

infections, ventilator associated pneumonia has the highest incidence followed by surgical site infections (SSIs), catheter associated urinary tract (CA-UTI), central line associated bloodstream (CLABSI), and gastrointestinal tract infections.⁴ The etiological agents causing ICU associated infections vary considerably from region to region, and even from hospital to hospital. Not only this but also the microbes isolated among different sections of a same health care facility also differ. This demonstrates the role of colonization of hospital surfaces with the causative bugs.⁵ Though gram positive and gram negative bacteria, all are implicated in such infections and among

gram positive microbes, *Staphylococcus aureus* is the predominant pathogen. However, the major bulk of ICU infections is constituted by Gram-negative bacteria.⁶ Such infections are associated with therapeutic failures, increase morbidity, and eventually very poor prognosis. The poor outcome owes to extensive antibiotic resistance especially among gram negative bacterial isolates particularly *Pseudomonas aeruginosa*, *Acinetobacter sp* and *Klebsiella pneumoniae*.^{7,8}

Multiple outbreaks of ICU infections have been reported recently and among the pathogens, *Acinetobacter* is a major culprit.⁹ *Acinetobacter species* especially *A.baumannii* is a non-fermenting gram negative coccobacillus (NFGNB) that requires aerobic environment for growth and has widespread distribution.¹⁰ The bacterium, previously considered as a commensal, has become a significant pathogen in seriously sick, hospitalized patients. It causes multiple diseases such as blood stream infections, catheter associated UTI, hospital-acquired pneumonia, etc.¹¹ According to various studies, around 7.9% of ventilator-associated pneumonitis and 5 to 15% of BSIs are associated with infection with *Acinetobacter sp.*, resulting in approximately 28-84% death rate in the Intensive care units.^{12,13} The main concern and the most troublesome issue is the extreme ability of this organism for acquisition of multidrug resistance.¹⁴

This study is designed to isolate *Acinetobacter sp.* from ICU patients and identify the MDR (multidrug resistant) and XDR (extensively drug resistant) isolates. This data would guide towards redesigning antibiotic policy and infection control policy

Methodology

This cross-sectional research was conducted retrospectively from January 2022-December 2022. The study consisted of 435 samples processed for culture and sensitivity in microbiology section of Pathology laboratory, SMCH from ICU patients. The specimens included blood, pus, urine, Cerebrospinal fluid, and other body cavity fluids, sputum, bronchial washings, ETT, etc. The study was commenced after approval of Institutional review board (IRB NO. SMDC/SMRC/305-23). Specimens were cultured on Blood and Mac Conkey agar (Oxoid UK). While CLED agar (Oxoid UK) was used for Urine. After incubating the plates for 16-18 hours at 37°C, these were examined for colony morphology and bacterial identification. *Acinetobacter sp* were recognized by morphology and biochemical reactions using Analytical profile index (API) 20 NE (Biomerieux, France) according

to manufacturer's protocol. The antibiotic sensitivity of the bacterium was determined by modified Kirby Bauer disc diffusion technique using Clinical Laboratory Standard Institute guidelines¹⁵. Following antibiotic discs (Oxoid/UK) were used.

Piperacillin (PRL), Cefotaxime (CTX), Ceftriaxone (CRO), Ceftazidime (CAZ), Cefepime (FEP), Tazobactam-piperacillin(TZP), Amikacin (AK), Ciprofloxacin (CIP), Levofloxacin (LEV), Co-trimoxazole (SXT), Imipenem (IMP), Meropenem (MEM), and Doxycycline (DO).

Acinetobacter sp. were recognized as MDR, XDR according to the following criteria

Criteria of MDR and XDR in *Acinetobacter* spp.^{16,17}

MDR: The isolate not-sensitive to ≥ 1 agent in ≥ 3 antimicrobial categories.

XDR: The isolate not-sensitive to ≥ 1 agent in all but ≤ 2 categories.

The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 25. Frequencies and percentages were calculated for the study variables. The ≤ 0.5 p value was significant statistically.

Results

Of 435 specimens received in microbiology laboratory, 231 yielded positive growth. One hundred and seventy five cases revealed Gram negative bacteria (GNB).Out of 175, 104(59.42%) were Enterobacteriaceae, 40(22.8%) *Pseudomonas aeruginosa* and 31 (17.71%) of the GNB were *Acinetobacter sp.* (Table I)

Table I: Frequency and percentage of gram negative bacteria isolated from ICU.

Bacteria isolated	N (%)
Gram negative Bacteria	175 (100%)
Enterobacteriaceae	104(59.42%)
<i>Pseudomonas aeruginosa</i>	40(22.8%)
<i>Acinetobacter sp</i>	31(17.7%)

The distribution of *Acinetobacter sp* among different specimens is demonstrated in Figure 1. The data shows that 15 isolates of *Acinetobacter sp* were obtained from pus, followed by 7 from respiratory tract secretions such as sputum and bronchial washings, and 6 from urine, 2 from ETT and 1 isolate from Blood sample.

Figure 2 demonstrates the frequency of MDR and XDR isolates of *Acinetobacter sp*. A total of 31 isolates were obtained. Thirteen *Acinetobacter* isolates were MDR and 9 turned out to be XDR. The remaining 9 isolates exhibited

satisfactory susceptibility. The sensitivity pattern of the isolates to all tested drugs is exhibited in Figure 3

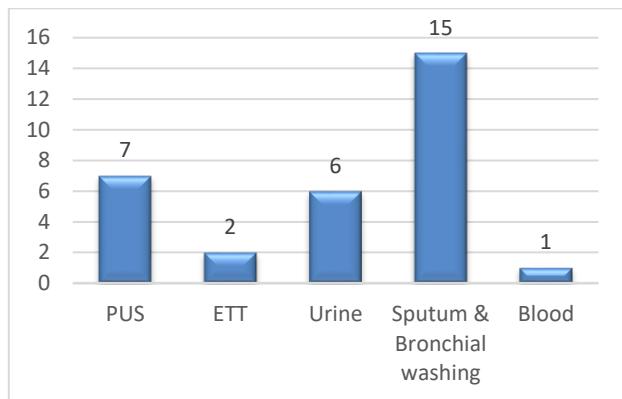


Figure 1. Distribution of *Acinetobacter* sp among various specimens.

Discussion

Acinetobacter, non fermenting gram negative bacterium is a major global challenge for the clinicians and the policy makers owing to its intrinsic resistance and its ability to develop non susceptibility to a wide array of antibiotics.

The current study assessed the frequency of *Acinetobacter* sp in ICU patients and identify the MDR and XDR strains so that a vivid picture of infections caused by the resilient bug can be demonstrated to the clinicians and help revise the empirical therapy. Hence, reducing the treatment failures and mortality among ICU patients.

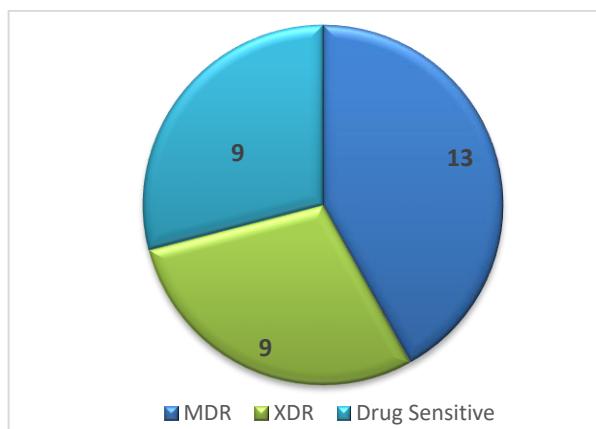


Figure 2. Frequency of MDR, XDR, and drug sensitive *Acinetobacter* sp in ICU.

In current study 175 specimens from ICU patients yielded Gram negative bacteria, out of which 31(17.7%) were identified to be *Acinetobacter* sp. Even a high percentage is evident in a study in Nepal, reporting 41% *Acinetobacter* species of Gram negative bacilli from ICU patients. The findings highlight the increasing cases of infections caused by *Acinetobacter* sp.¹⁸ The present study shows that 15 isolates of *Acinetobacter* sp were obtained from respiratory tract secretions such as sputum and bronchial washings, followed by 7 from pus, and 6 from urine, 2 from ETT and 1 isolate from Blood sample. The findings correspond to a Romanian study that reported 33 *Acinetobacter* isolates from bronchial lavage/washings, 2 from Central venous catheter followed by 1 from blood culture and 1 from urine sample.¹⁰

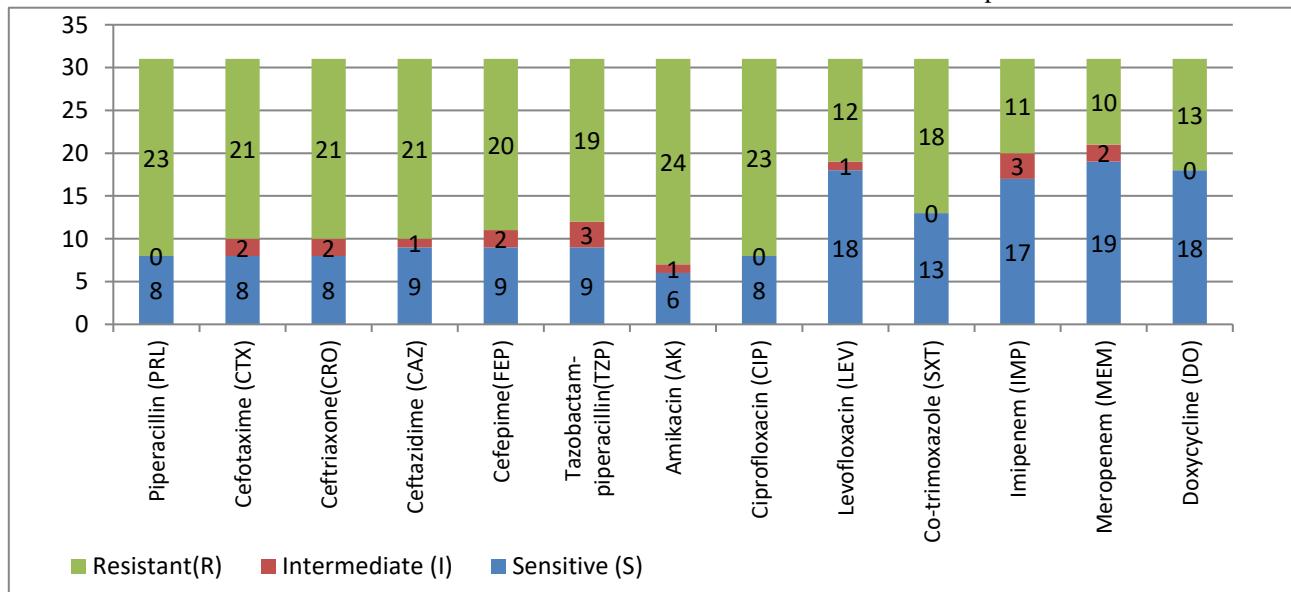


Figure 3. Antibiotic sensitivity of isolated *Acinetobacter* species.

Similarly, another study reported a very high percentage of respiratory secretions 44.67% yielding

Acinetobacter sp, thus proving *Acinetobacter* sp to be a major cause of ventilator associated pneumonitis in ICU.¹⁹

Our study results show that 13(41.9%) *Acinetobacter* isolates were MDR and 9(29.0%) were XDR. Such high resistance rate justifies increased morbidity and mortality associated with *Acinetobacter* infections. Around 30% MDR *Acinetobacter* isolates out of 2900 strains, were identified in a USA survey.²⁰ Another study comparing the regional variation of *Acinetobacter* susceptibility, reported more than 75% incidence in Africa and Asia. The prevalence was even higher than 90% in Europe and the Middle East.²¹ The underlying phenomenon for emergence of this alarming resistance is the selection pressure. In 2011, an ICU outbreak caused by MDR *Acinetobacter* sp was documented, reporting 4 out of 26 cases.²² However, much increased cases are being reported currently and deadly infections with MDR and XDR *Acinetobacter* isolates are on a surge. An Indian study reported even higher resistant rates than our study isolating around 88.02% MDR and 61.97% XDR in ICU.²³ A study on pediatric intensive care unit revealed 102 MDR/XDR *Acinetobacter baumannii* posing high risk of mortality.²⁴ A five year study concluded that the incidence of MDR *Acinetobacter* infections has risen from 89 % to 95% over a period of 4-5 years.²⁵ Another research conducted over 10 years reported 87% extensively drug resistant (XDR) *Acinetobacter* isolates.²⁶

Conclusion

Acinetobacter sp. are responsible for a significant bulk of drug resistant ICU associated infections and is increasingly developing resistance as evident by 41.9% MDR and 29.0% XDR isolates.

Limitations: It is a single centre study, hence reporting a very limited data. Future studies enrolling more hospitals and even different regions of the country would be required to give a more vivid picture of drug resistant *Acinetobacter* and its associated complications.

Recommendations: To prevent the spread and control such resilient life-threatening bacterium, meticulous infection control practices and antimicrobial stewardship programs should be implemented in true letter and spirit. Further, strategies to restrict the colonization of hospital surfaces with this bacterium are direly needed. This would conserve our available antibiotics so that these life savers are optimally used when really needed.

References

- WHO launches first ever global report on infection prevention and control; News release. Geneva. 6 May 2022.
- Saleem Z, Hassali MA, Godman B, Hashmi FK, Saleem F. A multicenter point prevalence survey of healthcare-associated infections in Pakistan: Findings and implications. <https://doi.org/10.1016/j.ajic.2018.09.025>
- European Centre for Disease Prevention and Control. Surveillance Report- Annual Epidemiological Report for 2016 - Healthcare-Associated Infections in Intensive Care Units. 2016:11. Available at: https://ecdc.europa.eu/sites/portal/files/documents/AER_for_2016-HAI_0.pdf Accessed July 20, 2019.
- Eshrat B, Mehrabi Y, Etemad K, and Nazari S S. The national rate of intensive care units-acquired infections, one-year retrospective study in Iran. BMC Public Health.2021; 21(609):1-8. <https://doi.org/10.1186/s12889-021-10639-6>
- Esfahani B N, Basiri R, Mirhosseini S, Moghim S, & Dolatkhah S. Nosocomial Infections in Intensive Care Unit: Pattern of Antibiotic-resistance in Iranian Community. Adv biomed Res. 2017, 6, 54. <https://doi.org/10.4103/2277-9175.205527>
- Sieron R T, Tyczkowska A B, Gaszynski W. Bacterial infections in Intensive Care Unit patients analyzed on the example of the Lodz Medical University Hospital No 1 in the period 2002-2015. Med Dosw Mikrobiol. 2016; 68 (1):39-46. PMID: 28146621
- Gandra S, Tseng K T, Arora A, Bhowmik B, Robinson M L, Panigrahi B, Laxminarayan R, Klein E Y. The Mortality Burden of Multidrug-resistant Pathogens in India: A Retrospective, Observational Study. Clinical Infectious diseases. 2019; 69(4):563 570 <https://doi.org/10.1093/cid/ciy955>
- Sader HS, Farrell DJ, Flamm RK, and Jones RN. Antimicrobial susceptibility of gram-negative organisms isolated from patients hospitalized in intensive care units in United States and European hospitals. Diagn Microbiol Infect Dis. 2014; 78(4):443-448 <https://doi.org/10.1016/j.diagmicrobio.2013.11.025>
- Molter G, Seifert H, Mandraka F, Kasper G, Weidmann B, Hornei B, , et al. Outbreak of carbapenem-resistant *Acinetobacter baumannii* in the intensive care unit: a multi-level strategic management approach. J Hosp Infect. 2016;92(2):194-8 <https://doi.org/10.1016/j.jhin.2015.11.007>
- Lazureanu V, Poroşnicu M, Gândac C , Moisil, T, Bădițoiu L, Laza R, et al. Infection with *Acinetobacter baumannii* in an intensive care unit in the Western part of Romania. BMC Infect Dis. 2016;16:95. <https://doi.org/10.1186/s12879-016-1399-0>
- Lynch J P, Zhanel G G, Clark N M. Infections Due to *Acinetobacter baumannii* in the ICU: Treatment Options. Semin Respir Crit Care Med. 2017;38(3):311-325. <https://doi.org/10.1055/s-0037-1599225>
- Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. Crit Care. 2014;18:208. <https://doi.org/10.1186/cc13775>
- Timsit JF, Soubirou JF, Voiriot G, et al. Treatment of bloodstream infections in ICUs. BMC Infect Dis. 2014;14:489. <https://doi.org/10.1186/1471-2334-14-489>

14. Uwingabiye J, Lemnouer A, Baidoo S, Frikh M, Kasouati J, Maleb A, et al. Intensive care unit-acquired *Acinetobacter baumannii* infections in a Moroccan teaching hospital: epidemiology, risk factors and outcome. *Germs*. 2017 Dec; 7(4): 193-205. <https://doi.org/10.18683/germs.2017.1126>
15. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 31st ed. CLSI supplement. M100S. Wayne (PA): Jan 2021.
16. Magiorakos A Srinivasan R B, Carey Y, Carmeli M E, Falagas C G, Giske S, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. European Society of Clinical Microbiology and Infectious Diseases, CMI, 2012; 18:268-81. <https://doi.org/10.1111/j.1469-0691.2011.03570.x>
17. Centers for Disease Control and Prevention (CDC). Antimicrobial-resistant phenotype definitions, last updated 1/2022. https://www.cdc.gov/nhsn/pdfs/ps-analysis-resources/phenotype_definitions.pdf (Accessed on August 03, 2022).
18. Siwakoti S, Subedi A, Sharma A, Baral R, Bhattarai N R, Khanal B. Incidence and outcomes of multidrug-resistant gram-negative bacteria infections in intensive care unit from Nepal- a prospective cohort study. *Antimicrobial Resistance & Infection Control* volume . 2018; 7(114) . <https://doi.org/10.1186/s13756-018-0404-3>
19. 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 African Medical Journal*. 2016; 23:191. <https://doi.org/10.11604/pami.2016.23.191.7915>
20. Denys GA, Callister SM, Dowzicky MJ. Antimicrobial susceptibility among gram-negative isolates collected in the USA between 2005 and 2011 as part of the Tigecycline Evaluation and Surveillance Trial (T.E.S.T.). *Ann Clin Microbiol Antimicrob* 2013; 12: 24 <https://doi.org/10.1186/1476-0711-12-24>
21. Lob SH, Hoban DJ, Sahm DF, Badal RE. Regional differences and trends in antimicrobial susceptibility of *Acinetobacter baumannii*. *Int J Antimicrob Agents* 2016; 47 (04) 317-323 <https://doi.org/10.1016/j.ijantimicag.2016.01.015>
22. Consales G, Gramigni E, Zamidei L, Bettocchi D, Raffaele A, Gaudio D. A multidrug-resistant *Acinetobacter baumannii* outbreak in intensive care unit: antimicrobial and organizational strategies. *J Crit Care*. 2011; 26 (5): 453459 <https://doi.org/10.1016/j.jcrc.2010.12.016>
23. Banerjee T, Mishra A, Das A, Sharma S, Barman H, and Yadav G. High Prevalence and Endemicity of Multidrug Resistant *Acinetobacter* spp. in Intensive Care Unit of a Tertiary Care Hospital, Varanasi. India. *J. Pathog.* 2018; ID 9129083. <https://doi.org/10.1155/2018/9129083>
24. Shi J, Sun T, Cui Y, Wang C, Wang F, Zhou Y, Yucai Zhang, et al. Multidrug resistant and extensively drug resistant *Acinetobacter baumannii* hospital infection associated with high mortality: a retrospective study in the pediatric intensive care unit. *BMC Infect. Dis* .2020; 20 <https://doi.org/10.1186/s12879-020-05321-y>
25. Odsbu I, Khedkar S, Khedkar U. High proportions of multidrug-resistant *Acinetobacter* spp. isolates in a district in Western India: a four-year antibiotic susceptibility study of clinical isolates. *Int. J. Environ. Res. Public Health*. 2018;15: 153 <https://doi.org/10.3390/ijerph15010153>
26. Kolpa M, Właszek M, Gniadek A, Wolak Z, and Dobros W, Incidence, microbiological profile and risk factors of healthcare-associated infections in intensive care units: a 10 year observation in a provincial hospital in Southern Poland, *Int J Environ Res Public Health*. 2018; 15:112. <https://doi.org/10.3390/ijerph15010112>