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ANTIMICROBIAL RESISTANCE PATTERNS IN WHO-CRITICAL PRIORITY PATHOGENS: A RETROSPECTIVE ANALYSIS OF ICU CLINICAL SAMPLES FROM A TERTIARY CARE HOSPITAL IN INDIA

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ABSTRACT

Background: Antimicrobial resistance (AMR) is a serious concern to world health, especially in intensive care units (ICUs) which harbour a predominant population of immunocompromised and vulnerable patients who are more susceptible to drug resistant pathogens. The World Health Organization (WHO) has identified certain pathogens as a critical priority pathogen and it includes *A. baumannii* (carbapenem-resistant), *P. aeruginosa* (carbapenem-resistant), and Enterobacteriaceae (carbapenem-resistant, resistant to third-generation cephalosporins). This study seeks to deliver a thorough investigation of AMR patterns in WHO-critical priority pathogens obtained from clinical samples in the intensive care unit of a tertiary care hospital in India. **Methods:** Clinical samples were obtained from the ICU from January 2021 to 2023. The microbiology laboratory processed these clinical samples using traditional culture techniques. Antibiotic susceptibility testing (AST) was conducted via disc diffusion methods in accordance with CLSI standards. The pathogens were classified based on the WHO priority list, and their resistance profiles were examined. **Results:** A total of 4,339 clinical samples were received from the ICU. From clinical samples, 850 (19.5%) WHO-critical priority pathogens were identified. The most common isolates were *A. baumannii* 365 (43%) followed by *K. pneumoniae* 192 (23%), *P. aeruginosa* 178 (21%), and *E. coli* 115 (13%). The resistance to carbapenems was observed to be 88% in *A. baumannii* and 36% in *P. aeruginosa*. In Enterobacterales, carbapenem resistance was found to be 54%, while resistance to third-generation cephalosporins was 81%. **Conclusions:** The antimicrobial resistance patterns observed in this study reflect a significant challenge in treating ICU infections in a tertiary care hospital in India. The high rates of resistance necessitate urgent action in implementing robust antibiotic stewardship programs and enhancing infection control practices to mitigate the spread of resistant pathogens. The data generated can aid in developing targeted treatment guidelines and policy decisions to combat AMR effectively.

KEYWORDS : Antibiotic resistance, WHO-Critical Priority pathogens, Intensive care unit, Infection, Hospital setting

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a major public health threat in the twenty-first century, posing significant risks to human health. The World Health Organization (WHO) identifies AMR as one of the ten foremost global threats to public health [1,2]. AMR constitutes a significant global health challenge that endangers human, animal, and environmental health, rendering it a primary focus within the One Health framework. AMR results from the inappropriate use and overuse of antimicrobials in healthcare, agriculture, and livestock husbandry [3]. The use of antimicrobials in livestock promotes resistance that may be transferred to humans via food chains, direct contact, or environmental contamination. The environment contributes as a reservoir for AMR according to the release of antimicrobials and resistant bacteria into soil and water bodies. If not addressed, AMR may lead to 10 million fatalities per year by 2050, compromising global health, food security, and the sustainability of the economy. Addressing AMR demands a One Health strategy that amalgamates surveillance, antimicrobial stewardship, research, regulatory frameworks, and public awareness to protect the health of humans, animals, and ecosystems. In hospital settings, AMR due to bacterial infections is a major source of morbidity and mortality among hospitalized patients, particularly among critically sick patients in intensive care units (ICUs) [2–4].

All levels of care are impacted by the healthcare burden that AMR poses, but critical care settings like ICUs are particularly impacted because patients with compromised immune systems are more prone to infections [5]. This can be explained by the fact that ICU patients with underlying health conditions and frequent medical device use are more likely to encounter nosocomial infections [6]. Furthermore, the high patient turnover rate and numerous opportunities for transmission may expose patients to resistant organisms. The WHO-designated "critical priority pathogens"—which include multi-drug resistant Gram-negative bacteria such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and members of the Enterobacteriaceae family (e.g., *Escherichia coli* and *Klebsiella pneumoniae*)—are among the most alarming contributors to this crisis [7]. A significant proportion of hospital-acquired infections (HAIs) originate by these bacteria, particularly in ICUs where invasive procedures, prolonged hospital stays, and extensive antibiotic use establish an environment that is favorable to the formation and transmission of resistant strains [8]. The problem is further complicated by the lack of newer antimicrobial agents, making treatment of common illnesses more difficult and increasing morbidity, mortality, and medical costs [9–12]. It is essential to understand the AMR profiles of pathogens in these environments to direct empirical therapy, enhance antibiotic stewardship initiatives, and influence infection prevention and control strategies. The present study addresses this issue by conducting a retrospective analysis of antibiotic resistance patterns in clinical samples obtained from the ICU of a tertiary care hospital in India that included pathogens classified as important priorities by the WHO. This study intends to shed light on resistance, identify the most harmful bacteria, and assist in the development of improved infection control measures by analyzing data across three years.

MATERIAL AND METHODS

Study Design And Setting

This study utilised a retrospective data analysis method, including the timeframe from January 2021 to December 2023. The study aimed to analyze the patterns of AMR in WHO-priority pathogens obtained from ICU patients.

Sample Collection

A total of 4,339 clinical samples, including blood, urine, LRT (Sputum, BAL) and pus (aspirates and exudates), and other specimens, were collected from ICU patients during this study. These samples were analyzed to identify pathogens and assess antimicrobial resistance patterns.

Clinical Sample Processing And Bacterial Identification

All clinical samples were processed in the Microbiology laboratory using conventional culture techniques [13].

Antibiotic Susceptibility Testing (AST)

All bacterial isolates were evaluated for antibiotic susceptibility using the disc diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines [14].

Retrospective Analysis of Clinical Data Using DHIS2

The clinical data was entered into a digital health information system (DHIS2) for streamlined record-keeping and management. DHIS2 is an open-source, no-cost platform designed to collect, report, analyze, and disseminate health data at both aggregate and individual levels. Subsequently, this data was retrospectively analyzed, focusing on various clinical samples to gain insights and identify patterns or trends relevant to the study. Based on the data analysis, clinical isolates were categorized according to the WHO priority list, focusing on carbapenem-resistant *A. baumannii*, *P. aeruginosa*, and Enterobacteriaceae. Resistance patterns were analyzed, particularly focusing on resistance to carbapenems (imipenem and meropenem) and third-generation cephalosporins (ceftriaxone).

RESULTS

WHO Priority Pathogens Isolated from Clinical Samples

Fig 1. shows the number of clinical samples received from ICUs. Out of 4339 clinical samples, blood samples were the most received samples (n=1928) flowed by urine (n=1195) and LRT samples (n=686).

Fig. 2 illustrates the distribution of various bacterial species in all the clinical samples received from ICUs. The most prevalent bacterial species was *A. baumannii* (21.8%) followed by *Staphylococcus aureus.* (19%) and *K. pneumoniae* (11.4%). The isolation rate of E. coli was 6.9% from these clinical samples.

Among WHO priority pathogens, *A. baumannii* (43%) was the most common bacterial species followed by *K. pneumoniae* (23%), *P. aeruginosa* (21%), and *E. coli* (13%) as shown in Fig. 3.

Carbapenem and Cephalosporin Resistance in WHO Critical Priority Pathogens

Table 1 shows antibiotic resistance patterns for *A. baumannii*, *P. aeruginosa*, and Enterobacteriaceae (*K. pneumoniae* and *E. coli*) against meropenem, imipenem, and ceftriaxone. The resistance rates to meropenem and imipenem were 88% and 82.3%, respectively, in *A. baumannii*, and in *P. aeruginosa* meropenem and imipenem resistance was 19% and 36% respectively. Among Enterobacterales, resistance to meropenem and imipenem was 54% and 39%, respectively, while ceftriaxone resistance was 81%.

DISCUSSION

This study offers a thorough examination of carbapenem and third-generation cephalosporin resistance in WHO-critical priority pathogens isolated from clinical samples collected from the ICU of a tertiary care hospital in India. Due to their high resistance levels and significant public health impact, the WHO has designated Enterobacterales resistant to carbapenems and third-generation cephalosporins as critical priority pathogens [15]. In our study, most of the clinical samples received from the ICU patients were from blood samples (n=1928) followed by urine samples (n=1195). This highlights that bloodstream infections and urinary tract infections (UTIs) are the most frequent types of infections encountered in the hospital environment. Similarly, a study conducted in European ICUs reported that bloodstream infections and UTIs were among the most common HAIs, with a significant number of blood samples collected for diagnostic purposes [16].

Among the WHO priority pathogens, *Acinetobacter spp., Klebsiella spp., Pseudomonas spp.,* and *E. coli* are the most harmful bacteria affecting ICU patients [17]. In our findings, *A. baumannii* (21.8%) was the most prevalent bacterial species, followed by *S. aureus* (19%) and *K. pneumoniae* (11.4%). *A. baumannii* is known for its ability to survive in the hospital environment and its resistance to multiple antimicrobials, making it a formidable pathogen in ICU settings [18]. This is consistent with findings from a study in Ethiopia, where *Acinetobacter spp.* and *K. pneumoniae* were also among the most common isolates in ICU environments [19]. *P. aeruginosa* and Enterobacteriaceae are Gram-negative bacteria that pose major healthcare challenges due to their prevalence and limited treatment options. *P. aeruginosa*, an opportunistic pathogen, primarily causes HAIs in immunocompromised patients [20]. Similar to our findings, a study in a Bangladeshi ICU found that *Acinetobacter spp.* (34%) and *Klebsiella spp.* (22%) were the most common gram-negative bacteria isolated from ICU patients [21]. This study also highlighted the high prevalence of multidrug-resistant (MDR) strains, particularly among *Acinetobacter spp*. and *Pseudomonas spp*. The Extended Prevalence of Infection in Intensive Care (EPIC III) study, which included data from 88 countries, reported that gram-negative pathogens such as *Klebsiella spp*., *E. coli*, *Pseudomonas species*, and *Acinetobacter spp.* were the most common in ICU patients [22].

The antibiotic resistance patterns observed in our study are concerning, with high resistance rates to meropenem and imipenem in *A. baumannii* (88% and 82.3%, respectively) and significant resistance in *P. aeruginosa* (19% and 36%, respectively). These findings are in line with global reports of increasing carbapenem resistance in these pathogens [23]. For Enterobacterales, resistance to meropenem and imipenem was 54% and 39%, respectively, while resistance for 3rd generation cephalosporin was 81%. Our findings align with WHO data, which report that *A. baumannii* (91%) and *P. aeruginosa* (82%) exhibit the highest global carbapenem resistance. Additionally, the study noted that in the Indian subcontinent, *A. baumannii* shows over 50% resistance, while *P. aeruginosa* ranges between 31% and 50% resistant to carbapenems [24]. Our results aligned with the surveillance data from the ICMR Antimicrobial Resistance Surveillance and Research Network (AMRSN) locations in India, indicating around 80% carbapenem resistance in *A. baumannii* and approximately 30% resistance in *P. aeruginosa* [25]. Similar to our findings, the WHO data has identified high carbapenem resistance in *E. coli* (55%). However, the carbapenem resistance was lower in our study than WHO data which shows *K. pneumoniae* (70%) resistance [26]. The 2017 WHO has reported the highest global carbapenem resistance in *A. baumannii* (91%) and *P. aeruginosa* (82%), contributing to their classification as Critical Priority infections [27]. This is consistent with data from other regions, where high resistance rates to third-generation cephalosporins and carbapenems have been documented. The carbapenem resistance at our hospital exceeded that reported in a study from Japan, where cephalosporin resistance in *K. pneumoniae* and *E. coli* varied between 16% and 30%. [28]. while carbapenem resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa* ranged from 31–50% [28].

The elevated prevalence of resistance in the "critical priority" organisms, despite the 2015 global action plan's declaration, is of paramount importance and must be considered a significant health hazard. This study cannot estimate real incidence; however, the observed geographical variances underscore the necessity for infection control of resistant diseases to be informed by local epidemiology. Large health institutions must systematically monitor and evaluate growing AMR patterns and trends to prioritize, plan, and execute facility-specific policies and recommendations for the optimal utilization of antimicrobials. Another study of ICU-acquired infections in lower-middle-income countries (LMICs) found that multidrug-resistant Gram-negative species, especially *A. baumannii* and *P. aeruginosa*, played a dominant role in ICU settings. The high resistance patterns observed underscore the need for targeted infection control measures based on local epidemiology and enhanced antimicrobial stewardship. Tackling this issue is essential for reducing elevated healthcare expenses, extended hospitalizations, and increased mortality linked to resistant diseases.

CONCLUSION

The rapid emergence and spread of antibiotic-resistant bacteria are a global concern in ICUs. Overall, our study's findings highlight the critical need for ongoing surveillance and targeted interventions to manage and mitigate the impact of antimicrobial resistance in ICUs. The differences noted in LMICs underscore the importance of considering regional variations in infection patterns and healthcare practices when interpreting these results. This information may enhance physicians' awareness regarding the prognostic significance of fast "critical priority" AMR infection tests upon admission and assist in the selection of early medications. Future research should focus on exploring novel antimicrobial agents and strategies to mitigate the impact of antibiotic-resistant pathogens in critical care environments. We encourage large healthcare institutions to frequently monitor and assess evolving antimicrobial resistance (AMR) patterns and trends to prioritize, strategize, and execute facility-specific policies and guidelines for the optimal utilization of antimicrobials. The findings are expected to inform clinical decision-making, enhance antimicrobial stewardship, and guide infection control strategies in similar healthcare environments.

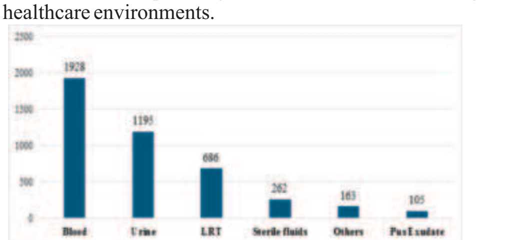

Fig 1. Showing The Number Of Clinical Samples Received From ICUs.

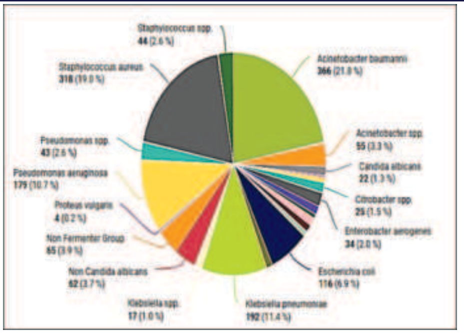

Fig 2. Showing Number And Percentage Of Different Bacterial Isolates Isolated From Clinical Samples Received From ICUs.

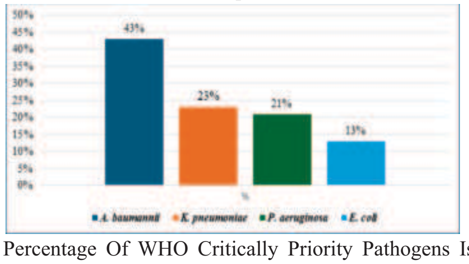

Fig 3. Percentage Of WHO Critically Priority Pathogens Isolated From Clinical Samples Received From ICUs.

Table 1. Showing Carbapenem And Third-generation Cephalosporin Resistance In WHO Critically Priority Pathogens.

Organism	Meropenem n/n (%)	Imipenem n/n (%)	Ceftriaxone n/n (%)
A. baumannii	158/180 (88%)	145/176 (82.3%)	-
P. aeruginosa	12/63 (19%)	32/88 (36%)	-
Enterobacteriaceae (K. pneumoniae and E. coli)	45/84 (54%)	51/131 (39%)	94/116 (81%)

Authors' Contributions: IK: conceptualization, methodology, formal analysis, investigation, resources, supervision, visualization, and writing—original draft, AC: investigation, supervision, resources, VM: conceptualization, methodology, formal analysis, investigation, visualization, and writing—original draft

Conflict Of Interest: None

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REFERENCES

1. Tadesse TY, Molla M, Yimer YS, Tarekegn BS, Kefale B. Evaluation of antibiotic prescribing patterns among inpatients using World Health Organization indicators: A cross-sectional study. SAGE Open Med. 2022. doi:10.1177/20503121221096608
2. Allel K, Day L, Hamilton A, Lin L, Furuya-Kanamori L, Moore CE, et al. Global antimicrobial-resistance drivers: an ecological country-level study at the human–animal interface. Lancet Planet Heal. 2023. doi:10.1016/S2542-5196(23)00026-8
3. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. Veterinary World. 2022. doi:10.14202/vetworld.2022.743-749
4. Uc-Cachón AH, Gracida-Osorno C, Luna-Chi IG, Jiménez-Guillermo JG, Molina-Salinas GM. High prevalence of antimicrobial resistance among gram-negative isolated bacilli in intensive care units at a tertiary-care hospital in Yucatán Mexico. Med. 2019. doi:10.3390/medicina55090588
5. Moolchandani K, Sastry AS, Deepashree R, Sistla S, Harish BN, Mandal J. Antimicrobial resistance surveillance among intensive care units of a tertiary care hospital in South India. J Clin Diagnostic Res. 2017. doi:10.7860/JCDR/2017/23717.9247
6. Warren DK, Zack JE, Elward AM, Cox MJ, Fraser VJ. Nosocomial primary bloodstream infections in intensive care unit patients in a nonteaching community medical center: A 21-month prospective study. Clin Infect Dis. 2001. doi:10.1086/322483
7. Nisa TT, Nakatani D, Kaneko F, Takeda T, Nakata K. Antimicrobial resistance patterns of WHO priority pathogens isolated in hospitalized patients in Japan: A tertiary center observational study. PLoS One. 2024. doi:10.1371/journal.pone.0294229
8. Atik TK, Atik B, Kilinç O, Bektöre B, Duran H, Selek BM, et al. Epidemiological evaluation of an acinetobacter baumannii outbreak observed at an intensive care unit. Saudi Med J. 2018. doi:10.15537/smj.2018.8.22431
9. Ahmed SK, Hussein S, Qurbani K, Ibrahim RH, Fareeq A, Mahmood KA, et al. Antimicrobial resistance: Impacts, challenges, and future prospects. J Med Surgery, Public Heal. 2024. doi:10.1016/j.glmedi.2024.100081
10. Muteeb G, Rehman T, Shahwan M, Aatif M. Origin of Antimicrobials and Antibiotic Resistance , and Their Impacts on Drug Development : A Narrative Review. 2023; 1–54.
11. Ganesh Kumar S, Adithan C, Harish BN, Sujatha S, Roy G, Malini A. Antimicrobial resistance in India: A review. Journal of Natural Science, Biology and Medicine. 2013. doi:10.4103/0976-9668.116970
12. Nagarjuna D, Mittal G, Dhanda RS, Gaind R, Yadav M. Alarming levels of antimicrobial resistance among sepsis patients admitted to ICU in a tertiary care hospital in India - A case control retrospective study. Antimicrob Resist Infect Control. 2018. doi:10.1186/s13756-018-0444-8
13. Sánchez-romero MI, Manuel J, Moya G, José J, López G, Orta N. Collection , transport and general processing of clinical specimens in Microbiology laboratory ☇. 2019;37: 127–134.
14. Clinical and Laboratory Standards Institute. 2019. pp. 604–604. doi:10.1007/978-3-662-48986-4_300416
15. Kaye KS, Belley A. Third-Generation Cephalosporin-Resistant Enterobacterales Are Critical Priority Pathogens, Too! Antimicrobial Agents and Chemotherapy. 2022. doi:10.1128/aac.00213-22
16. European Centre for Disease Prevention and Control. European Surveillance of Healthcare-Associated Infections in Intensive Care Units - HAI-Net ICU protocol, version 1.02. Stockholm: ECDC. 2015.
17. Mancuso G, Midiri A, Gerace E, Biondo C. Bacterial antibiotic resistance: the most critical pathogens. Pathogens. 2021. doi:10.3390/pathogens10101310
18. Howard A, O'Donoghue M, Feeney A, Sleator RD. Acinetobacter baumannii An emerging opportunistic pathogen. Virulence. 2012. doi:10.4161/viru.19700
19. Kindu M, Moges F, Ashagrie D, Tigabu Z, Gelaw B. Multidrug-resistant and carbapenemase-producing critical gram-negative bacteria isolated from the intensive care unit environment in Amhara region, Ethiopia. PLoS One. 2023. doi:10.1371/journal.pone.0295286
20. Wood SJ, Kuzel TM, Shafikhani SH. Pseudomonas aeruginosa: Infections, Animal Modeling, and Therapeutics. Cells. 2023. doi:10.3390/cells12010199
21. Haque S, Ahmed A, Islam N, Haque FKM. High Prevalence of Multidrug-Resistant Bacteria in the Trachea of Intensive Care Units Admitted Patients: Evidence from a Bangladeshi Hospital. Antimicrobials. 2024. doi:10.3390/antimicrobials13010062
22. Vincent J, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. The Extended Prevalence of Infection in the ICU Study: EPIC II. Crit Care. 2009.
23. Bou G, Cervero G, Dominguez MA, Quereda C, Martinez-Beltran J. Characterization of a nosocomial outbreak caused by a multiresistant Acinetobacter baumannii strain with a carbapenem-hydrolyzing enzyme: High-level carbapenem resistance in A. baumannii is not due solely to the presence of β-lactamases. J Clin Microbiol. 2000. doi:10.1128/jcm.38.9.3299-3305.2000
24. Arowolo MT, Orababa OQ, Olaitan MO, Osibeluwo BV, Essiet UU, Batholomew OH, et al. Prevalence of carbapenem resistance in Acinetobacter baumannii and Pseudomonas aeruginosa in sub-Saharan Africa: A systematic review and meta-analysis. PLoS One. 2023. doi:10.1371/journal.pone.0287762
25. Walia K, Madhumathi J, Veeraraghavan B, Chakrabarti A, Kapil A, Ray P, et al. Establishing Antimicrobial Resistance Surveillance & Research Network in India: Journey so far. Indian J Med Res. 2019. doi:10.4103/ijmr.IJMR_226_18
26. Iwu CD, Patrick SM. An insight into the implementation of the global action plan on antimicrobial resistance in the WHO African region: A roadmap for action. Int J Antimicrob Agents. 2021. doi:10.1016/j.ijantimicag.2021.106411
27. Seale AC, Gordon NC, Islam J, Peacock SJ, Scott JAG. AMR surveillance in low and middle-income settings - A roadmap for participation in the Global Antimicrobial Surveillance System (GLASS). Wellcome Open Res. 2017. doi:10.12688/wellcomeopenres.12527.1
28. Oka K, Matsumoto A, Tetsuka N, Morioka H, Iguchi M, Ishiguro N, et al. Clinical characteristics and treatment outcomes of carbapenem-resistant Enterobacterales infections in Japan. J Glob Antimicrob Resist. 2022. doi:10.1016/j.jgar.2022.04.004