

THE USE OF EMPIRICAL ANTIBIOTICS IN THE CRITICAL CARE UNIT

PERVAIZ R^{1*}, AHMED H¹, AWAD AHA²

¹Department of Critical Care Medicine, Bahria International Hospital, Lahore, Pakistan

²Department of Critical Care Medicine, Rashid Hospital, Dubai Health, UAE

*Corresponding author's email address: drizwanpervaiz@gmail.com

(Received, 28th March 2024, Revised 16th April 2024, Accepted 20th May 2024, Published 29th May 2024)

ABSTRACT

Antimicrobial therapy plays a crucial role in managing infections in critically ill patients, yet its indiscriminate use can lead to adverse outcomes. Here, we propose a systematic approach for guiding empirical antimicrobial therapy in intensive care unit (ICU) patients with suspected infections. Diagnostic evaluation, including imaging, laboratory tests, and physical examination, is essential to assess the necessity of antimicrobial treatment. Despite advances, no gold standard biomarker for differentiating infection from inflammation necessitates thorough diagnostic assessment. Prompt microbiological sampling is crucial for accurate diagnosis and tailored treatment. Emergency initiation of antimicrobial therapy is recommended for conditions like sepsis and septic shock, emphasizing the need for timely intervention. Pathogen profiling and consideration of multidrug resistance risk factors are essential for selecting appropriate empirical therapy. Customized evaluation based on patient characteristics and regional trends is paramount for optimal antibiotic selection. Pharmacokinetic and pharmacodynamic parameters should guide dosing to ensure adequate antibacterial levels while minimizing adverse effects. Future research should focus on AI-powered decision-making systems, optimal timelines for starting or postponing therapy, and the environmental impacts of antibiotic use to enhance patient outcomes and reduce antimicrobial resistance.

Keywords: Antimicrobial Therapy, Empirical Treatment, Critical Care, Sepsis, Septic Shock, Diagnostic Evaluation, Microbiological Sampling

INTRODUCTION

Patients who are critically sick often have infections that might progress to sepsis or septic shock. In these cases, prompt and effective antimicrobial therapy is critical (1, 2). Our goal is to offer a systematic method for recommending empirical antimicrobial agents in advance to patients in the intensive care unit (ICU) who may have an infection.

Evaluating the necessity and urgency

The Necessity

Antimicrobial treatment is essential for most infections, but it can be harmful when used excessively. Thus, a thorough diagnostic evaluation is necessary (3). Imaging, laboratory tests, and physical examination are all included in a diagnostic assessment. Interpreting this data is crucial for intensivists, who consider each test individually and incorporate it into the more extensive decision-making process. Multidisciplinary care for severely ill patients may involve ICU doctors, referring physicians, surgeons, microbial scientists, and infectious disease experts. (4).

Even after much investigation, no gold standard biomarker can differentiate infection from other inflammatory conditions. Compared to clinical evaluation alone, the 2021 Surviving Sepsis Campaign Guidelines (SSCG) recommend against utilizing procalcitonin for sepsis diagnosis and antibiotic start. (5).

Before beginning an antimicrobial regimen, microbiological sampling should be carried out to avoid unduly delaying treatment. This is crucial for diagnosis and enabling specific treatment later on. (6).

Blood cultures and samples from potential infection sites must be obtained. (7) Quick molecular and microbiological methods can help with early and more customized antibacterial treatments. A wide range of commercial tests are available, making it possible to identify potentially relevant pathogens more quickly. Newly available clinical data often shows that these tests are more sensitive and specific than

conventional culture-based investigations. Prompt and correct interpretation will require in-depth knowledge and competence to ensure the right action is taken. More studies are needed to comprehend the influence of antibiotic use on patient outcomes.

The urgency

Emergency medical care is necessary for conditions like sepsis and septic shock. (8) The SSCG recommends starting antibiotic treatment as soon as possible within one hour of identifying an increased likelihood of sepsis or possible septic shock (9).

The medical evaluation window is prolonged in patients reporting suspected sepsis without shock to reduce the dangers associated with the misuse of antibiotics and to enable a more comprehensive assessment. (9) With close patient monitoring, there is a simple recommendation for postponing antimicrobial therapy in patients who have a low chance of infection and no shock (2). Prior studies suggest that in some highly supervised intensive care units, delaying the initiation of antibiotic medication until the first microbiological results are available might be acceptable for less critically sick patients. (10). This would enable more accurate treatment tailoring. Nevertheless, conclusive results are still elusive. Rapid diagnostic technology is about to transform this field.

Pathogen profiling

When deciding on an empirical therapy, the probable causative pathogen or pathogens must be assessed by identifying their species and susceptibility pattern. (11). This procedure considers the region's ecology, concomitant comorbidities, the infection source, and the possibility of multidrug-resistant (MDR) organisms. Significant antimicrobial pressure and barrier-breaching measures cause a high frequency of MDR infections in intensive care units. (12). Hospitalization for five days or more in the previous ninety days, recent antibiotic therapy, and a history of colonization or infection with multidrug-resistant organisms are other conventional risk factors that must be investigated. (13). Empirical antimicrobial selection guidelines based on MDR prevalence thresholds have been

developed.(14) . However, the broad ranges of these thresholds confine their uniform application, and they are primarily based on expert judgment utilizing different criteria. It's commonly

acknowledged that a lower threshold(5–10%) for eliminating hard-to-treat pathogens applies to people who are more seriously sick. (15).

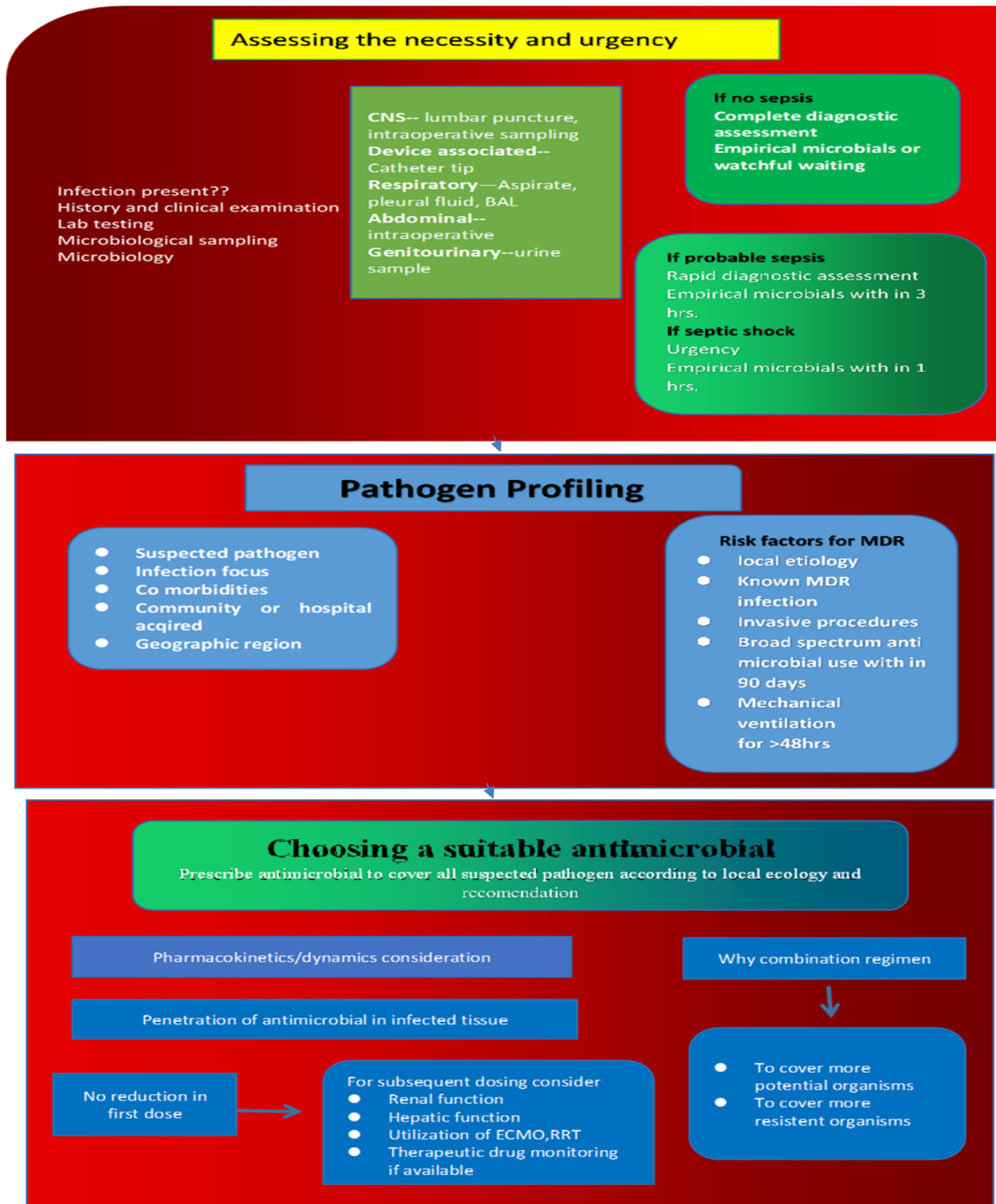


Figure 1 A systematic approach to the prescription of empirical antibiotic therapy

Choosing a suitable antimicrobial

There isn't a single empirical antibiotic regimen that has been recognized as the best. Again, a customized evaluation is essential, considering the degree of illness, the suspected infection source, immunodeficient condition, and patient-associated MDR risk variables (16). There are many challenges when incorporating regional ecological trends into global principles. Therefore, it is essential to support the formulation of hospital-specific standards to adequately address unique environmental factors and requirements. The selected agent must provide a spectrum encompassing the most likely causing pathogens. (2). Beta-lactams are one of the most often used groups in this scenario (17). When it is determined to be necessary, combining several drugs to encompass a wider variety of species and resistance patterns is considered acceptable (18). More controversial is the application of multiple medicines together to target a single susceptible infection to speed up pathogen clearance or stop resistance from developing (19). The SSCG advises against combination therapy in individuals with documented susceptibilities or those at a lower risk for MDR infection (20). It's important to follow relevant recommendations when certain medications are recommended as adjunctive therapy. Regularly assessing the treatment spectrum and duration is crucial for reducing environmental pressure (3).

Choosing the right empirical antibiotic needs careful evaluation of pharmacokinetic and pharmacodynamic parameters to provide enough antibacterial dosage at the site of infection while minimizing potential adverse effects (21). Accurate dosing, involving quantity, mode, and frequency, is crucial for optimal therapy (22). Sepsis patients typically require higher initial dosages or more frequent dosage intervals due to increased drug distribution and clearance during the first phase, based on the agent employed (23). After reaching a steady state level, adjust the dose based on the patient's clinical situation (e.g., end-organ failure, undergoing extracorporeal procedures) and mode of antimicrobial clearance (18). Therapeutic medication monitoring can help optimize dosing and reduce adverse reactions.

Upcoming Horizons

Diagnosing and determining the underlying microbes causing sepsis is crucial for improving therapy efficacy and reducing antimicrobial exposure. AI-powered decision-making systems that use patient, environment, and microbiological data are a potential field of research.

Well-designed studies are needed to define timelines for ICU doctors to start or postpone empirical therapy, assess the effectiveness of combination medicines over single-agent treatments, and determine the best settings for their usage. Studying the environmental effect of antibiotic selection at the patient, hospital, and international levels is essential.

DECLARATIONS**Data Availability statement**

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declared absence of conflict of interest.

AUTHOR CONTRIBUTION**RIZWAN PERVAIZ**

Conception of Study, Development of Research Methodology Design, Review of manuscript, Review of Literature.

HASSAN AHMED

Conception of Study, Manuscript revisions, critical input.

AHMED HOSSAMELDIN AHMED AWAD

Drafting article. Coordination of collaborative efforts. , Final approval of the manuscript.

REFERENCES

- Heming N, Azabou E, Cazaumayou X, Moine P, Annane D. Sepsis in the critically ill patient: current and emerging management strategies. *Expert Review of Anti-Infective Therapy*. 2021;19(5):635-47.
- Niederman MS, Baron RM, Bouadma L, Calandra T, Daneman N, DeWaele J, et al. Initial antimicrobial management of sepsis. *Critical care*. 2021;25:1-11.
- Bassetti S, Tschudin-Sutter S, Egli A, Osthoff M. Optimizing antibiotic therapies to reduce the risk of bacterial resistance. *European journal of internal medicine*. 2022;99:7-12.
- Schmid S, Schlosser S, Gülow K, Pavel V, Müller M, Kratzer A. Interprofessional collaboration between ICU physicians, staff nurses, and hospital pharmacists optimises antimicrobial treatment and improves quality of care and economic outcome. *Antibiotics*. 2022;11(3):381.
- Wentowski C, Ingles DP, Nielsen ND. Sepsis 2021: a review. *Anaesthesia & Intensive Care Medicine*. 2021;22(11):676-84.
- Pak TR, Rhee C, Klompas M. Timing and spectrum of antibiotic treatment for suspected sepsis and septic shock: why so controversial? *Infectious Disease Clinics of North America*. 2022;36(4):719-33.
- Yu D, Larsson A, Parke Å, Unge C, Henning C, Sundén-Cullberg J, et al. Single-sampling strategy vs. multi-sampling strategy for blood cultures in sepsis: a prospective non-inferiority study. *Frontiers in Microbiology*. 2020;11:1639.
- Gavelli F, Castello LM, Avanzi GC. Management of sepsis and septic shock in the emergency department. *Internal and emergency medicine*. 2021;16(6):1649-61.
- Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Critical care medicine*. 2021;49(11):e1063-e143.
- Denny KJ, De Wale J, Laupland KB, Harris PN, Lipman J. When not to start antibiotics: avoiding antibiotic overuse in the intensive care unit. *Clinical Microbiology and Infection*. 2020;26(1):35-40.
- Kumar A. BACTERIAL ISOLATES FROM INFECTED WOUNDS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERN.
- Stull JW, Weese JS. Nosocomial and Multidrug-Resistant Infections. *Clinical Small Animal Internal Medicine*. 2020:1055-62.
- Kumar NR, Balraj TA, Kempegowda SN, Prashant A. Multidrug-Resistant Sepsis: A Critical Healthcare Challenge. *Antibiotics*. 2024;13(1):46.
- Parra-Rodriguez L, Guillamet MCV, editors. *Antibiotic decision-making in the ICU. Seminars in Respiratory and Critical Care Medicine*; 2022: Thieme Medical Publishers, Inc.
- Chlebowski C. *The Virus and the Host: Protect Yourself from Infectious Disease by Reducing Toxicity, Improving Immunity, and Minimizing Chronic Illness*: Chelsea Green Publishing; 2022.

16. Fujii M, Karumai T, Yamamoto R, Kobayashi E, Ogawa K, Tounai M, et al. Pharmacokinetic and pharmacodynamic considerations in antimicrobial therapy for sepsis. *Expert Opinion on Drug Metabolism & Toxicology*. 2020;16(5):415-30.
17. Rafailidis PI, Falagas ME. Benefits of prolonged infusion of beta-lactam antibiotics in patients with sepsis: personal perspectives. *Expert Review of Anti-infective Therapy*. 2020;18(10):957-66.
18. Garcia E, Ly N, Diep JK, Rao GG. Moving from point-based analysis to systems-based modeling: integration of knowledge to address antimicrobial resistance against MDR bacteria. *Clinical Pharmacology & Therapeutics*. 2021;110(5):1196-206.
19. Pacios O, Blasco L, Bleriot I, Fernandez-Garcia L, González Bardanca M, Ambroa A, et al. Strategies to combat multidrug-resistant and persistent infectious diseases. *Antibiotics*. 2020;9(2):65.
20. Egi M, Ogura H, Yatabe T, Atagi K, Inoue S, Iba T, et al. The Japanese clinical practice guidelines for the management of sepsis and septic shock 2020 (J-SSCG 2020). *Journal of intensive care*. 2021;9:1-144.
21. Póvoa P, Moniz P, Pereira JG, Coelho L. Optimizing antimicrobial drug dosing in critically ill patients. *Microorganisms*. 2021;9(7):1401.
22. Koch BC, Muller AE, Hunfeld NG, De Winter BC, Ewoldt TM, Abdulla A, et al. Therapeutic drug monitoring of antibiotics in critically ill patients: current practice and future perspectives with a focus on clinical outcome. *Therapeutic Drug Monitoring*. 2022;44(1):11-8.
23. Rawson TM, Wilson RC, O'Hare D, Herrero P, Kambugu A, Lamorde M, et al. Optimizing antimicrobial use: challenges, advances, and opportunities. *Nature Reviews Microbiology*. 2021;19(12):747-58.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. © The Author(s) 2024