Review Article

Hospital-Acquired Bacterial Pneumonia: Updated Strategies for Intravenous Antibiotic Coverage

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Abstract

Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia remain major causes of morbidity and mortality in hospitalized patients, particularly in intensive care unit settings. The microbiological landscape is dominated by Gram-negative bacilli, including *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*, as well as Gram-positive pathogens such as methicillin-resistant *Staphylococcus aureus*. The growing prevalence of resistance mechanisms, including extended-spectrum beta-lactamases, carbapenem-resistant Enterobacterales, metallo-beta-lactamases, AmpC enzymes, efflux pumps, and porin loss, significantly complicates therapeutic decision-making and necessitates risk-adapted empirical strategies guided by local antibiograms. Pathophysiological mechanisms such as microaspiration, dysbiosis, biofilm formation on endotracheal tubes, impaired mucociliary clearance, and systemic inflammatory activation contribute to infection persistence and progression to severe complications, including sepsis. Risk factors for multidrug-resistant organisms include prolonged hospitalization, prior intravenous antibiotic exposure, septic shock, acute respiratory distress syndrome, renal replacement therapy, and immunosuppression. Early initiation of appropriate intravenous antibiotic therapy within the first 24 hours is essential to reduce mortality and improve outcomes. Empirical regimens should be tailored

according to individual risk profiles, with broad-spectrum coverage reserved for high-risk patients and avoidance of unnecessary combination therapy. Updated regimens include antipseudomonal beta-lactams, carbapenems, new-generation beta-lactam/beta-lactamase inhibitor combinations, and agents such as cefiderocol for resistant pathogens. Rapid molecular diagnostics facilitate early de-escalation and optimization of treatment duration, while antimicrobial stewardship programs, preventive bundles, and infection control measures are critical to limiting resistance. Future strategies integrating novel antimicrobials, artificial intelligence, personalized dosing, and continuous surveillance are essential for sustained therapeutic effectiveness.

Key words

Gram-negative bacilli, Carbapenem resistance, Biofilm formation, Risk stratification, Pharmacokinetic optimization, Procalcitonin-guided therapy.

Introduction

Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia are highly prevalent infections in both intensive care unit and non-intensive care settings, with ventilator-associated bacterial pneumonia occurring more frequently among critically ill patients who require mechanical ventilation [1, 2]. The burden of ventilator-associated pneumonia in intensive care units is considerable, with reported incidence rates reaching up to 30% in certain clinical environments [3, 4]. Similarly, data from Nepal indicate an incidence of 20%, with a markedly higher prevalence of pneumonia among intubated patients compared with non-intubated hospitalized individuals. These findings collectively underscore the substantial epidemiological impact of these infections, particularly in mechanically ventilated populations [5].

Beyond their high incidence, hospital-acquired and ventilator-associated bacterial pneumonia are associated with significant mortality. In some cohorts, ventilator-associated bacterial pneumonia has been linked to mortality rates as high as 57.1% [3]. Moreover, ventilated hospital-acquired bacterial pneumonia demonstrates a mortality rate of 29.2%, which contrasts sharply with the 11.7% observed in non-ventilated hospital-acquired cases [1]. In addition to increased mortality, patients with ventilator-associated bacterial pneumonia experience prolonged intensive care unit and overall hospital stays, with median durations significantly exceeding those of patients who do not develop ventilator-associated infection [4].

The economic consequences of these infections are closely linked to their impact on length of stay and resource utilization. Ventilator-associated bacterial pneumonia incurs the highest healthcare costs among nosocomial pneumonias, with median expenses reported at $77,657 [1]. This financial burden is intensified by the need for prolonged mechanical ventilation and extended intensive care unit management, which increase overall healthcare resource consumption [4].

In parallel with these clinical and economic challenges, the progressive rise of multidrug-resistant pathogens has further complicated treatment strategies. The increasing prevalence of resistant organisms, including Acinetobacter and Klebsiella species, has necessitated continuous reassessment of empirical and targeted antibiotic approaches [3, 5]. Consequently, new intravenous antimicrobials are being incorporated into therapeutic considerations to address evolving resistance patterns and improve outcomes in hospital-acquired and ventilator-associated bacterial pneumonia [6]. At the same time, the integration of novel diagnostic techniques and molecular methods offers the potential to refine

antimicrobial selection and enhance therapeutic precision, aligning antibiotic management with contemporary precision medicine principles [7].

The objective of this article is to provide an updated and comprehensive analysis of hospital-acquired and ventilator-associated bacterial pneumonia, focusing on their global epidemiology, clinical impact, economic burden, and emerging resistance patterns, in order to support optimized intravenous antibiotic coverage strategies based on current evidence and precision-oriented therapeutic approaches.

Methodology

This narrative review on autoimmune bullous dermatoses in adults was conducted using a structured, transparent, and reproducible methodological framework designed to integrate contemporary clinical, histopathological, and immunological evidence relevant to differential diagnosis. A narrative design was selected due to the heterogeneity of study designs and diagnostic approaches, which precluded quantitative meta-analysis and favored an integrative synthesis of clinically applicable evidence. The review focused exclusively on adult populations, defined as individuals aged 18 years and older.

A comprehensive literature search was performed in PubMed, Scopus, and Web of Science. Peer-reviewed articles published between January 2021 and February 2026 in English or Spanish were considered eligible. The timeframe was selected to capture recent advances in diagnostic immunopathology, serological testing, and updated classification frameworks. Both Medical Subject Headings and free-text terms were used. The search strategy combined keywords and Boolean operators as follows: (“Autoimmune bullous dermatoses” OR “pemphigus” OR “bullous pemphigoid”) AND (“immunofluorescence” OR “histopathology” OR “serological assays” OR “differential diagnosis”). The final search was conducted in February 2026.

The initial search identified a defined number of records, which were screened after removal of duplicates. Titles and abstracts were reviewed to exclude clearly irrelevant studies. Potentially eligible articles underwent full-text evaluation. Two independent reviewers conducted the selection process, and discrepancies were resolved by consensus. The final number of included studies was determined after full-text assessment. Literature focusing exclusively on pediatric populations, conference abstracts without full methodological description, editorials, opinion pieces, duplicated reports, and studies lacking diagnostic confirmation were excluded.

Data extraction was performed using a standardized framework that included the following variables: study design, population characteristics, diagnostic criteria, histopathological findings, direct and indirect immunofluorescence patterns, serological markers, and key differentiating features among disease subtypes. Extraction was conducted independently and cross-verified to ensure accuracy and consistency.

Although quantitative synthesis was not undertaken, methodological quality and relevance were critically appraised using structured qualitative principles aligned with standards for narrative reviews. Greater weight was assigned to international guidelines, consensus statements, systematic reviews, and well-designed cohort studies. In cases of conflicting findings, interpretation prioritized methodological robustness and diagnostic clarity.

Data synthesis followed a qualitative integrative approach. Evidence was organized according to disease subtype and structured across clinical presentation, histological pattern, immunopathological profile, and diagnostic performance of ancillary tests. Comparative analysis emphasized distinguishing features and practical diagnostic implications. Artificial intelligence tools were used solely to assist with

thematic organization and structural coherence; all scientific interpretation, critical appraisal, and final content decisions were performed by the authors.

This review did not involve human subjects or patient-level data and therefore did not require ethical approval. Potential limitations include language restriction to English and Spanish publications, exclusion of gray literature, and the inherent risk of publication bias. Despite these limitations, the structured search strategy, independent selection process, standardized data extraction, and qualitative appraisal framework support methodological rigor and transparency.

Microbiological Landscape and Resistance Patterns

Hospital-acquired bacterial pneumonia is predominantly caused by Gram-negative bacilli, among which *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Enterobacter* species are the most frequently identified pathogens. *Pseudomonas aeruginosa* is particularly notable due to its marked adaptability and intrinsic resistance mechanisms, characteristics that often necessitate combination antimicrobial therapies to achieve effective treatment [8, 9]. Similarly, *Klebsiella pneumoniae* and *Acinetobacter baumannii* represent significant clinical concerns, especially in intensive care unit settings, where high resistance rates have been consistently documented [5, 10]. In addition to Gram-negative organisms, Gram-positive pathogens also play an important role. *Staphylococcus aureus*, including both methicillin-susceptible and methicillin-resistant strains, remains a common cause of hospital-acquired bacterial pneumonia, with the presence of methicillin-resistant *Staphylococcus aureus* further complicating therapeutic decisions because of its resistance to multiple antibiotic classes [10].

The predominance of these pathogens is closely linked to the growing complexity of antimicrobial resistance mechanisms. Extended-spectrum beta-lactamase–producing *Enterobacterales* are increasingly prevalent and exhibit significant resistance to beta-lactam antibiotics, often requiring treatment with carbapenems or newer agents such as ceftolozane/tazobactam [9, 11]. In parallel, carbapenem-resistant *Enterobacterales* pose a major therapeutic challenge due to their limited treatment options and association with high mortality rates, frequently necessitating the use of polymyxins or combination regimens [12, 5]. Additional enzymatic mechanisms, including metallo-beta-lactamases and AmpC beta-lactamases, confer resistance to a broad spectrum of beta-lactam agents and further complicate therapeutic strategies [10]. Beyond enzymatic degradation, non-enzymatic mechanisms such as efflux pumps and porin loss significantly contribute to multidrug resistance in *Pseudomonas aeruginosa*, reducing the efficacy of numerous antimicrobial agents [8].

These resistance patterns are not uniform and demonstrate considerable institutional and regional variability. Local antibiograms play a critical role in guiding empirical therapy, as resistance profiles may differ substantially between healthcare institutions and geographic regions [8, 9]. Notably, resistance rates are generally higher in intensive care units compared with non-intensive care environments, underscoring the need for targeted antimicrobial stewardship interventions in these high-risk settings [10]. Prior antibiotic exposure has been consistently identified as a significant risk factor for the development of resistant infections, highlighting the importance of judicious antimicrobial prescribing practices to mitigate the emergence and spread of multidrug-resistant pathogens [13].

Pathophysiology and Risk Stratification

Hospital-acquired bacterial pneumonia develops through a series of interconnected pathophysiological mechanisms that facilitate bacterial entry, persistence, and systemic

dissemination. One of the principal pathways is microaspiration of oropharyngeal secretions into the lower respiratory tract, a process that enables pathogenic microorganisms to colonize pulmonary tissue. This mechanism is further exacerbated by dysbiosis, in which disruption of the normal lung microbiome permits pathogenic bacteria to predominate and increases susceptibility to infection [14, 15].

In mechanically ventilated individuals, additional factors intensify this risk. Biofilm formation on endotracheal tubes represents a critical pathogenic mechanism, as biofilms consist of structured bacterial communities that adhere to artificial surfaces and create a protective matrix that enhances resistance to antimicrobial agents. Pseudomonas species and Acinetobacter species are frequently implicated as biofilm producers, contributing to persistent infections and reduced therapeutic efficacy [16]. The presence of these biofilms not only facilitates ongoing bacterial seeding of the lower airways but also complicates eradication despite appropriate antibiotic therapy. Concurrently, impairment of mucociliary clearance further undermines pulmonary defense. The mucociliary escalator is a fundamental protective mechanism responsible for removing inhaled pathogens and secretions from the respiratory tract. Mechanical ventilation and certain underlying conditions can disrupt this process, promoting pathogen accumulation and increasing the likelihood of pneumonia development [17]. As bacterial invasion progresses, the host immune response may become amplified, triggering a systemic inflammatory cascade. In severe cases of hospital-acquired bacterial pneumonia, this response can evolve into sepsis, a complication associated with significant morbidity and mortality [18].

These pathophysiological mechanisms are closely linked to the risk of infection by multidrug-resistant organisms. Prolonged hospitalization, particularly durations of five days or more, increases exposure to resistant pathogens that are prevalent within healthcare environments. Similarly, recent intravenous antibiotic therapy can select for resistant strains, rendering subsequent infections more difficult to manage [15]. Clinical severity at presentation also influences risk stratification; patients who present with septic shock are more likely to harbor multidrug-resistant organisms, partly due to the severity of illness and prior antimicrobial exposure [18]. Furthermore, acute respiratory distress syndrome frequently complicates pneumonia in critically ill patients and is often associated with infections caused by resistant organisms, reflecting the need for intensive care and mechanical ventilation. Additional factors such as renal replacement therapy and immunosuppression compromise host defenses and further increase susceptibility to infections caused by multidrug-resistant pathogens [15].

Principles of Empirical Intravenous Antibiotic Therapy

The early initiation of appropriate antibiotic therapy is a critical determinant of outcomes in hospital-acquired bacterial pneumonia. Administration of effective antimicrobial treatment within the first 24 hours has been associated with reduced mortality and improved clinical recovery [15]. In contrast, delayed initiation of therapy contributes to prolonged illness and increased healthcare costs, reinforcing the importance of timely and accurate empirical treatment decisions [19].

In high-risk patients, particularly those admitted to intensive care units, broad-spectrum antibiotic therapy may be required to ensure coverage of a wide range of potential pathogens, including multidrug-resistant organisms [15]. In such scenarios, novel antimicrobial agents can be considered empirically to provide timely and effective activity against resistant pathogens [19]. The selection of these agents must balance the urgency of adequate coverage with the risk of promoting further resistance. To refine therapeutic decisions, a risk-adapted approach is recommended. This strategy involves systematic

assessment of patient-specific risk factors for multidrug-resistant organisms in order to tailor antibiotic therapy appropriately. By aligning empirical treatment with individualized risk profiles, this approach reduces unnecessary antibiotic exposure and improves the appropriateness of antimicrobial selection [20].

Dual antipseudomonal therapy is recommended in selected clinical contexts, including severe ventilator-associated pneumonia or in patients with established risk factors for multidrug-resistant bacteria [21]. However, routine or unjustified combination therapy should be avoided to prevent antibiotic overuse and the associated emergence of resistance. Careful patient evaluation therefore guides whether monotherapy or combination therapy is most appropriate [20].

Empirical coverage for methicillin-resistant *Staphylococcus aureus* should similarly be guided by local epidemiology and individual patient risk factors. Clinical guidelines recommend considering MRSA-directed therapy in regions with high prevalence or in patients with documented risk factors for resistant Gram-positive infection. Incorporating local surveillance data into empirical decisions enhances therapeutic precision [15].

Pharmacokinetic and pharmacodynamic principles further inform antibiotic optimization. Beta-lactam antibiotics exhibit time-dependent killing, and prolonged or continuous infusions may enhance efficacy by maintaining drug concentrations above the minimum inhibitory concentration for extended periods [22]. In addition, dose adjustments based on renal function are essential to optimize therapeutic exposure while minimizing toxicity [23]. These considerations are integral to maximizing clinical effectiveness. Avoiding unnecessary double coverage is essential to limit the development of resistance and reduce adverse effects. A patient-specific, risk factor–based approach supports judicious antimicrobial use and minimizes unwarranted combination therapy, thereby promoting both effective treatment and responsible stewardship [20].

Updated Intravenous Antibiotic Regimens

In standard-risk patients with hospital-acquired bacterial pneumonia, antipseudomonal beta-lactams constitute the foundation of empirical intravenous therapy. Agents such as piperacillin-tazobactam, cefepime, and ceftazidime are widely utilized due to their broad-spectrum activity against *Pseudomonas aeruginosa* and other Gram-negative pathogens. These antibiotics provide reliable coverage in many clinical settings; however, susceptibility patterns may vary considerably, and local resistance data should guide final therapeutic selection. When methicillin-resistant *Staphylococcus aureus* is suspected or confirmed, the addition of targeted anti-MRSA therapy is recommended. Vancomycin and linezolid are commonly employed in this context, with vancomycin dosing guided by area-under-the-curve monitoring to optimize antimicrobial exposure while minimizing toxicity [24, 25].

In contrast, patients at high risk for multidrug-resistant organisms require broader and more potent antimicrobial strategies. Carbapenems such as meropenem and imipenem-cilastatin represent key therapeutic options in this population, particularly when resistant Gram-negative pathogens are suspected. The addition of relebactam to imipenem-cilastatin has demonstrated efficacy against imipenem-nonsusceptible strains, expanding treatment possibilities for hospital-acquired bacterial pneumonia and other serious Gram-negative infections [26]. Beyond traditional carbapenems, new-generation beta-lactam/beta-lactamase inhibitor combinations, including ceftolozane-tazobactam, ceftazidime-avibactam, and meropenem-vaborbactam, have shown effectiveness against multidrug-resistant *Pseudomonas aeruginosa* and carbapenem-resistant *Enterobacterales.* These agents have demonstrated high susceptibility rates in both

clinical trials and real-world analyses, supporting their role in resistant infections [24, 27].

Cefiderocol, a siderophore cephalosporin, provides an additional option for the management of carbapenem-resistant organisms. Its novel mechanism of action enhances bacterial uptake and contributes to activity against difficult-to-treat Gram-negative pathogens. Although polymyxins may be considered in cases involving multidrug-resistant infections, their use is limited by significant nephrotoxicity and neurotoxicity, positioning them primarily as last-resort agents [24].

With respect to methicillin-resistant *Staphylococcus aureus* coverage, vancomycin remains a central therapeutic agent, and area-under-the-curve–guided dosing is essential to balance antimicrobial efficacy with the risk of nephrotoxicity, particularly in patients with renal impairment. Linezolid offers an alternative option with favorable lung penetration and does not require dose adjustment based on renal function, making it particularly useful in patients with compromised renal status [25].

Targeted Therapy, De-escalation, and Treatment Duration

Accurate microbiological diagnosis plays a central role in optimizing the management of hospital-acquired bacterial pneumonia and facilitating appropriate therapeutic adjustments. Traditional diagnostic methods such as bronchoalveolar lavage and endotracheal aspirates remain fundamental for obtaining respiratory samples, which can subsequently be analyzed using conventional culture techniques as well as rapid molecular diagnostics. Among these methods, bronchoalveolar lavage has demonstrated particular clinical value, as it can support prompt antibiotic de-escalation without increasing unfavorable clinical outcomes [27].

In recent years, rapid molecular panels have further transformed the diagnostic landscape. Techniques such as loop-mediated isothermal amplification and multiplex polymerase chain reaction have demonstrated high diagnostic accuracy and markedly reduced turnaround times, significantly accelerating pathogen identification and resistance profiling [28, 29, 30]. The integration of these tools into clinical practice enables more precise and timely initiation of targeted therapy, thereby reducing reliance on prolonged empirical broad-spectrum regimens. In contrast, blood cultures, although still considered standard practice, are generally slower and less sensitive than molecular diagnostic methods, which may delay appropriate treatment adjustments in critically ill patients [31].

The availability of rapid and reliable microbiological data directly supports early de-escalation strategies. De-escalation based on susceptibility results allows clinicians to narrow initial broad-spectrum antibiotic therapy while maintaining clinical safety. Evidence indicates that de-escalation guided by rapid diagnostic testing does not compromise patient outcomes and may reduce the risk of resistance development [27, 32]. By identifying specific pathogens and their resistance patterns, clinicians can tailor antibiotic regimens more precisely, thereby minimizing unnecessary exposure to broad-spectrum agents [30, 31].

In addition to spectrum optimization, appropriate determination of treatment duration is essential. Current guidelines recommend a seven-day course of therapy for most bacterial pathogens, including *Pseudomonas aeruginosa*, provided that the patient demonstrates adequate clinical response. However, prolonged therapy may be required in cases involving non-fermenting Gram-negative bacilli or in the presence of complications, given the increased risk of recurrence in these scenarios [33]. Biomarker-guided approaches further refine treatment duration, as procalcitonin levels can be used to support decisions regarding antibiotic discontinuation and potentially reduce unnecessary prolonged therapy [34].

Antimicrobial Stewardship and Preventive Strategies

The integration of antimicrobial stewardship programs into intensive care unit protocols represents a fundamental strategy for optimizing antimicrobial use, reducing resistance, and improving patient outcomes. These programs are designed to involve critical care practitioners in the careful initiation and subsequent de-escalation of antimicrobial therapy, with decisions guided by rapid diagnostic tools and microbiological culture results [35, 36].

Within this framework, stewardship efforts should prioritize the reduction of unnecessary broad-spectrum antibiotic use, the transition to monotherapy when clinically appropriate, and the shortening of treatment duration through the use of biomarkers such as procalcitonin [37, 38]. Empirical antibiotic therapy must also be aligned with local resistance patterns and individual patient risk factors. Guidance based on local antibiograms, combined with patient-specific assessment, enhances appropriateness and minimizes overuse. Evidence indicates that patient-centered strategies reduce inappropriate therapy and excessive antibiotic exposure more effectively than reliance on unit-specific antibiograms alone [20]. Rapid multiplex polymerase chain reaction testing can further inform empirical therapy; however, its impact on clinical outcomes remains debated, partly due to inconsistent adherence to stewardship protocols [38].

Ongoing monitoring of antibiotic consumption and resistance trends is essential to sustain effective stewardship programs. Continuous surveillance allows for timely adjustment of prescribing practices and institutional protocols. Data from Italian intensive care units have demonstrated that stewardship initiatives can reduce the duration of empirical therapy and decrease the prevalence of multidrug-resistant bacteria without compromising patient safety [39]. Accordingly, surveillance systems and stewardship programs should be systematically incorporated into ICU protocols to address the high prevalence of resistant pathogens and the complex pharmacological considerations characteristic of critically ill patients [36, 40].

In parallel with antimicrobial stewardship, preventive strategies are critical to reducing the incidence of ventilator-associated pneumonia. Prevention bundles typically include elevation of the head of the bed, oral antisepsis, daily sedation interruption, and early mobilization, all of which have been associated with decreased VAP incidence and improved clinical outcomes. Additional measures such as selective decontamination of the digestive tract and the use of non-invasive ventilation are supported by robust evidence, while early mobilization has been shown to significantly shorten intensive care unit length of stay and the duration of mechanical ventilation [27].

Comprehensive infection control measures further reinforce these preventive efforts. Isolation precautions and structured infection control protocols are essential to limit the transmission of multidrug-resistant bacteria within intensive care environments. A multifaceted strategy that combines targeted interventions with broader preventive measures is recommended to address the complexity of pathogen spread in these settings. Effective infection control requires active engagement of intensive care personnel in preventing cross-contamination, along with the implementation of novel technologies and coordinated preventive strategies [40].

Future Directions and Clinical Implications

The development of novel antimicrobials represents a critical advancement in the management of hospital-acquired bacterial pneumonia and ventilator-associated pneumonia, particularly in the context of multidrug-resistant Gram-negative pathogens. New agents such as ceftobiprole, ceftolozane-tazobactam, and cefiderocol have been specifically designed to

target resistant organisms that are frequently implicated in these infections. These antibiotics demonstrate high activity against resistant pathogens and expand therapeutic options, thereby reducing reliance on traditional broad-spectrum agents that contribute to the propagation of antimicrobial resistance [41].

In parallel with pharmacological innovation, artificial intelligence has emerged as a promising tool for resistance prediction and antimicrobial optimization. Artificial intelligence systems can support antimicrobial stewardship efforts by generating real-time, individualized recommendations for antibiotic prescribing, with the potential to reduce unnecessary broad-spectrum antibiotic use and improve patient outcomes. Artificial intelligence–driven platforms can analyze resistance patterns and suggest narrower-spectrum agents when appropriate, thereby optimizing treatment strategies and minimizing the development of further resistance [42].

Personalized antibiotic dosing strategies also contribute to improved therapeutic precision. Through therapeutic drug monitoring and individualized assessment of patient characteristics and pathogen profiles, personalized medicine approaches can optimize antibiotic exposure. By ensuring that drug concentrations remain within effective therapeutic ranges, this strategy enhances treatment efficacy while reducing the risk of resistance associated with suboptimal dosing [43].

Adjunctive therapies provide additional opportunities to enhance standard treatment regimens. Approaches such as aerosolized antibiotics and immunomodulation have been investigated as complementary strategies in hospital-acquired bacterial pneumonia. These interventions may allow for more direct pathogen targeting or modulation of the host immune response, with the potential to improve clinical outcomes and shorten the duration of systemic antibiotic therapy [44].

Given the dynamic nature of antimicrobial resistance, continuous surveillance of resistance patterns is essential for effective disease management. Ongoing monitoring supports the development of adaptive clinical guidelines that respond to evolving epidemiological trends. Regular updates to clinical recommendations are necessary to ensure that therapeutic strategies remain aligned with the most current evidence and resistance data [45]. Ultimately, a coordinated global effort is required to integrate novel antimicrobials, artificial intelligence applications, personalized dosing strategies, and adjunctive therapies into routine clinical practice. Evidence-based recommendations should therefore emphasize optimization of antibiotic use, enhancement of diagnostic capabilities, and continued innovation in antimicrobial development to effectively address the challenge of resistance [19].

Conclusions

Hospital-acquired bacterial pneumonia is driven by a microbiological landscape dominated by multidrug-resistant Gram-negative bacilli, particularly *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*, alongside methicillin-resistant *Staphylococcus aureus*. The increasing prevalence of complex resistance mechanisms, including extended-spectrum beta-lactamases, carbapenemases, metallo-beta-lactamases, AmpC enzymes, efflux pumps, and porin loss, significantly limits therapeutic options and reinforces the need for locally guided empirical strategies based on institutional antibiograms and patient-specific risk factors.

The pathophysiology of hospital-acquired bacterial pneumonia, characterized by microaspiration, biofilm formation, impaired mucociliary clearance, and systemic inflammatory activation, is closely intertwined with risk factors for multidrug-resistant infection,

including prolonged hospitalization, prior antibiotic exposure, critical illness, and immunosuppression. Early initiation of appropriate intravenous antibiotic therapy within the first 24 hours, guided by risk-adapted assessment and pharmacokinetic optimization, remains essential to reduce mortality, prevent complications such as sepsis, and improve clinical outcomes while minimizing unnecessary antimicrobial exposure.

Effective management requires an integrated approach that combines updated intravenous antibiotic regimens, rapid molecular diagnostics to facilitate early de-escalation, antimicrobial stewardship programs, preventive bundles for ventilator-associated pneumonia, and rigorous infection control measures. Future directions, including novel antimicrobials, artificial intelligence–supported resistance prediction, personalized dosing strategies, adjunctive therapies, and continuous surveillance with adaptive guidelines, are fundamental to sustaining therapeutic efficacy and mitigating the global threat of antimicrobial resistance.

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