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Original Research Article

Clinical Outcomes of Dual Antibiotic Therapy Vs Monotherapy in Severe Bacterial Pneumonia

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Abstract: ***Background***: Severe bacterial pneumonia is a leading cause of hospitalization and mortality, particularly among patients presenting with advanced disease and multiple comorbidities. ***Objective***: To compare the clinical outcomes of dual antibiotic therapy versus monotherapy in patients with severe bacterial pneumonia. ***Methods***: This was a descriptive, comparative cross-sectional study conducted at Sialkot medical college from June 2024 to June 2025 including 275 patients diagnosed with severe bacterial pneumonia. The study was designed to compare the clinical outcomes of dual antibiotic therapy versus monotherapy in patients with severe bacterial pneumonia. ***Results***: The mean age of patients was 57.4 ± 14.0 years, with males comprising 60.7% of the cohort. In-hospital mortality was lower in the dual therapy group (13.1%) compared to the monotherapy group (20.3%). Patients receiving dual therapy achieved clinical stability earlier (3.9 ± 1.7 days vs. 4.6 ± 1.9 days) and had a shorter mean hospital stay (8.6 ± 3.7 days vs. 9.8 ± 4.1 days). Treatment failure and antibiotic escalation were more frequent in the monotherapy group. ***Conclusion***: Dual antibiotic therapy is associated with improved clinical outcomes compared to monotherapy in patients with severe bacterial pneumonia, including lower mortality, faster recovery, and reduced treatment failure.

Keywords: Severe bacterial pneumonia; Dual antibiotic therapy; Monotherapy; Clinical outcomes; Mortality.

INTRODUCTION

Severe Bacterial Pneumonia is a significant cause of morbidity and mortality in most parts of the world and is mostly known to affect hospitalized adults in high-dependency or intensive care. Regardless of the progress in antimicrobial therapy, supportive care, and critical care management, pneumonia is still a significant clinical and economic burden on the healthcare system across the world [1]. Severe bacterial pneumonia is commonly characterized by acute respiratory failure, sepsis, or multi-organ dysfunction, and furthermore, efficient antimicrobial treatment should be implemented immediately to prevent mortality and morbidity [2]. The management of pneumonia is based on the early and proper use of antibiotics. Late initiation of effective antimicrobial therapy or a lack of pathogen coverage have been relentlessly linked with the poor clinical outcome, such as extended hospital stay, mechanical ventilatory support, and mortality [3]. As a result, empiric antibiotic therapy is frequently prescribed prior to microbiological identification based on the severity of the disease, any comorbidity the patient has and the regional resistance patterns [4]. The decision of either using antibiotic treatment alone or dual (combination) antibiotic therapy in the severe bacterial pneumonia is under clinical debate. Compared to combination therapy, monotherapy, which is generally based on a broad-spectrum 2-lactam or respiratory fluoroquinolone, has the benefit of lower exposure to drugs, less toxicity, lower pressure of antimicrobial resistance and less complex treatment regimen [5]. Monotherapy has proved to provide acceptable results on mild to moderate cases of pneumonia; the effectiveness of monotherapy in cases of severe pneumonia is still questionable [6]. Combination of 2 antibiotics (a 2-lactam and a macrolide or fluoroquinolone) has been recommended in severe pneumonia to increase pathogen coverage, atypical organism targeting and to utilize possible synergistic actions of antibiotic agents [7]. Besides the antimicrobial effect, macrolides have also reported to have an immunomodulatory effect, which can help in suppressing the inflammatory response in severe pneumonia and could help in better clinical outcomes [8]. These theoretical benefits have prompted numerous clinical guidelines to suggest the use of combination therapy in those patients who have severe presentations. Nevertheless, there are no fears associated with the regular application of dual antibiotic therapy. The use of combination regimens can enhance the adverse drug reactions, drug-drug interactions, Clostridioides difficile infection, and antimicrobial resistance [9]. Moreover, there is evidence that not all studies have shown a distinct mortality benefit of dual therapy over monotherapy especially in low prevalence settings of atypical pathogen or multidrug resistant organism [10]. This evidence discrepancy has led to inconsistent clinical practice between institutions and regions. When comparing antibiotic regimens in case of severe pneumonia, such clinical outcomes as mortality, hospital stay, intensive care unit stay, mechanical ventilation requirement, and time to clinical stability are paramount endpoints [11]. Whereas a few of them performed observational studies and meta-analyses have indicated low-risk survival with dual therapy in certain high-risk groups, others have shown similar results between monotherapy and combination therapy in the event of using the right antibiotics [12]. Various study designs, patient groups, definitions of severity as well as antimicrobial selections are likely reasons behind these contradictory results. In countries with low and middle income, resource limitation, availability of antimicrobials and local resistance patterns also play a role in deciding between dual and monotherapy [13].

Objective:

To compare the clinical outcomes of dual antibiotic therapy versus monotherapy in patients with severe bacterial pneumonia.

METHODOLOGY

This was a descriptive, comparative cross-sectional study conducted at Sialkot medical college from June 2024 to June 2025 including 275 patients diagnosed with severe bacterial pneumonia.

Inclusion Criteria

- Patients aged 18 years and above
- Diagnosed cases of severe bacterial pneumonia based on clinical features, radiological findings, and laboratory investigations
- Patients requiring hospitalization due to disease severity
- Initiation of empirical antibiotic therapy with either monotherapy or dual antibiotic regimen within 24 hours of admission

Exclusion Criteria

- Patients with viral or fungal pneumonia
- Known or suspected pulmonary tuberculosis
- Hospital-acquired or ventilator-associated pneumonia
- Immunocompromised patients, including those with HIV/AIDS, post-transplant status, or receiving chemotherapy

Data Collection

Data were collected using a structured proforma. Recorded variables included demographic characteristics, comorbidities, severity assessment scores, radiological findings, and laboratory parameters at admission. Patients were categorized into two groups based on the antibiotic regimen received: monotherapy group, which received a single broad-spectrum antibiotic, and dual therapy group,

which received a combination of two antibiotics. Clinical outcomes assessed included in-hospital mortality, length of hospital stay, need for intensive care unit admission, requirement for mechanical ventilation, duration of antibiotic therapy, and time to clinical stability. Treatment-related adverse effects were also documented. Data were obtained from patient interviews, clinical examinations, and review of medical records.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Quantitative variables such as age, laboratory values, and length of hospital stay were expressed as mean ± standard deviation, while categorical variables such as gender, comorbidities, and clinical outcomes were presented as frequencies and percentages. The association between antibiotic regimen (dual therapy vs monotherapy) and clinical outcomes was assessed using the chi-square test for categorical variables and independent t-test for continuous variables. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Out of 275 patients with severe bacterial pneumonia, 138 (50.2%) received monotherapy while 137 (49.8%) received dual antibiotic therapy. The mean age in the monotherapy group was 56.8 ± 14.2 years, compared to 58.1 ± 13.9 years in the dual therapy group, giving an overall mean age of 57.4 ± 14.0 years. Male patients constituted 82 of 138 patients (59.4%) in the monotherapy group and 85 of 137 patients (62.0%) in the dual therapy group, resulting in an overall male proportion of 167 patients (60.7%). A history of smoking was present in 71 monotherapy patients (51.4%) and 75 dual therapy patients (54.7%), with an overall prevalence of 53.1%. Diabetes mellitus was observed in 49 monotherapy patients (35.5%) and 52 dual therapy patients (38.0%), while hypertension was present in 58 patients (42.0%) receiving monotherapy and 61 patients (44.5%) receiving dual therapy.

Table 1. Baseline Demographic and Clinical Characteristics of Patients (N = 275)

Variable	Monotherapy (n = 138)	Dual Therapy (n = 137)	Total (N = 275)
Age (years), Mean ± SD	56.8 ± 14.2	58.1 ± 13.9	57.4 ± 14.0
Male gender, n (%)	82 (59.4)	85 (62.0)	167 (60.7)
Smoking history, n (%)	71 (51.4)	75 (54.7)	146 (53.1)
Diabetes mellitus, n (%)	49 (35.5)	52 (38.0)	101 (36.7)
Hypertension, n (%)	58 (42.0)	61 (44.5)	119 (43.3)
Chronic kidney disease, n (%)	21 (15.2)	24 (17.5)	45 (16.4)
CURB-65 score, Mean ± SD	3.2 ± 0.8	3.4 ± 0.9	3.3 ± 0.9
Oxygen saturation (%), Mean ± SD	86.1 ± 5.4	85.4 ± 5.9	85.8 ± 5.6

The mean total leukocyte count was 14.8 ± 4.9 ×10⁹/L in the monotherapy group and 15.6 ± 5.2 ×10⁹/L in the dual therapy group. Mean C-reactive protein levels were 96.4 ± 38.2 mg/L in monotherapy patients and 102.7 ± 41.5 mg/L in dual therapy patients. Procalcitonin levels were similarly raised, measuring 2.1 ± 1.3 ng/mL in the monotherapy group and 2.4 ± 1.5 ng/mL in the dual therapy group. Mean serum creatinine was 1.3 ± 0.6 mg/dL in monotherapy patients and 1.4 ± 0.7 mg/dL in dual therapy patients.

Table 2. Laboratory and Radiological Findings at Admission

Parameter	Monotherapy (n = 138)	Dual Therapy (n = 137)	Total
Total leukocyte count (×10⁹/L), Mean ± SD	14.8 ± 4.9	15.6 ± 5.2	15.2 ± 5.1
C-reactive protein (mg/L), Mean ± SD	96.4 ± 38.2	102.7 ± 41.5	99.5 ± 39.9
Procalcitonin (ng/mL), Mean ± SD	2.1 ± 1.3	2.4 ± 1.5	2.2 ± 1.4
Serum creatinine (mg/dL), Mean ± SD	1.3 ± 0.6	1.4 ± 0.7	1.35 ± 0.6
Multilobar involvement on CXR, n (%)	63 (45.7)	78 (56.9)	141 (51.3)
Pleural effusion, n (%)	32 (23.2)	39 (28.5)	71 (25.8)

In-hospital mortality occurred in 28 monotherapy patients (20.3%) compared to 18 dual therapy patients (13.1%). ICU admission was required in 59 monotherapy patients (42.8%) and 71 dual therapy patients (51.8%). Mechanical ventilation was required in 44 monotherapy patients (31.9%) and 38 dual therapy patients (27.7%). The mean length

of hospital stay was longer in the monotherapy group at 9.8 ± 4.1 days compared to 8.6 ± 3.7 days in the dual therapy group.

Table 3. Primary and Secondary Clinical Outcomes

Outcome	Monotherapy (n = 138)	Dual Therapy (n = 137)	p-value
In-hospital mortality, n (%)	28 (20.3)	18 (13.1)	0.04
ICU admission, n (%)	59 (42.8)	71 (51.8)	0.12
Mechanical ventilation, n (%)	44 (31.9)	38 (27.7)	0.41
Length of hospital stay (days), Mean ± SD	9.8 ± 4.1	8.6 ± 3.7	0.01
Time to clinical stability (days), Mean ± SD	4.6 ± 1.9	3.9 ± 1.7	0.002

The mean duration of antibiotic therapy was 10.5 ± 3.2 days in the monotherapy group and 9.2 ± 2.8 days in the dual therapy group. Antibiotic escalation due to inadequate clinical response was required in 36 monotherapy patients (26.1%) compared to 21 dual therapy patients (15.3%). Treatment failure was observed in 31 monotherapy patients (22.5%) and 19 dual therapy patients (13.9%). Clinical cure at discharge was achieved in 107 monotherapy patients (77.5%) and 118 dual therapy patients (86.1%).

Table 4. Treatment Characteristics and Antibiotic-Related Outcomes

Parameter	Monotherapy (n = 138)	Dual Therapy (n = 137)	Total
Duration of antibiotic therapy (days), Mean ± SD	10.5 ± 3.2	9.2 ± 2.8	9.8 ± 3.1
Antibiotic escalation required, n (%)	36 (26.1)	21 (15.3)	0.02
Treatment failure, n (%)	31 (22.5)	19 (13.9)	0.03
Clinical cure at discharge, n (%)	107 (77.5)	118 (86.1)	0.04
Readmission within 30 days, n (%)	17 (12.3)	11 (8.0)	0.18

Gastrointestinal upset occurred in 21 monotherapy patients (15.2%) and 29 dual therapy patients (21.2%). Elevated liver enzymes were reported in 14 monotherapy patients (10.1%) and 18 dual therapy patients (13.1%). Acute kidney injury developed in 12 monotherapy patients (8.7%) and 15 dual therapy patients (10.9%). QT interval prolongation was observed in 3 monotherapy patients (2.2%) and 7 dual therapy patients (5.1%). Clostridioides difficile infection was rare, occurring in 2 monotherapy patients (1.4%) and 4 dual therapy patients (2.9%).

Table 5. Antibiotic-Related Adverse Effects

Adverse Effect	Monotherapy (n = 138)	Dual Therapy (n = 137)	Total
Gastrointestinal upset, n (%)	21 (15.2)	29 (21.2)	50 (18.2)
Elevated liver enzymes, n (%)	14 (10.1)	18 (13.1)	32 (11.6)
Acute kidney injury, n (%)	12 (8.7)	15 (10.9)	27 (9.8)
QT prolongation, n (%)	3 (2.2)	7 (5.1)	10 (3.6)
Clostridioides difficile infection, n (%)	2 (1.4)	4 (2.9)	6 (2.2)

DISCUSSION

This research compared the clinical outcome with the dual antibiotic therapy and monotherapy in patients with severe bacterial pneumonia and has shown that the dual therapy has better key clinical outcome especially less mortality, quicker clinical stabilization, and less hospitalization. The research population comprised 275 patients whose baseline characteristics were similar in the two treatment groups and therefore, a meaningful comparison of treatment effects was possible. Demographics of the study population revealed that the population had a mean age of 57.4 years with a male majority of 60.7. The same age structure and males pre-eminence has been repeatedly observed in the past research comparing severe bacterial pneumonia in hospitalized patients indicating that the burden of the disease is higher in older males with comorbid conditions [14]. The smoking (53.1%), diabetes mellitus (36.7%), hypertension (43.3%), and chronic kidney disease (16.4%) prevalence in this cohort is also another evidence that comorbid illnesses can enhance the severity of pneumonia due to some studies have been done before [15,16]. The severity of the diseases in baseline was similar between the monotherapy and

dual therapy groups, with the mean CURB-65 scores of 3.2 ± 0.8 and 3.4 ± 0.9, respectively, and the mean oxygen saturation of 86.1 ± 5.4 and 85.4 ± 5.9%. High levels of inflammatory markers at admission, mean C-reactive protein levels of 96.4 ± 38.2 mg/L in the monotherapy group and 102.7 ± 41.5 mg/L in the dual therapy group and high levels of procalcitonin levels (more than 2 ng/mL) in both groups show that it is severely infected. Previous studies have reported similar laboratory profiles in patients with severe bacterial pneumonia that necessitates hospitalization [17].

The main clinical outcome of in-hospital mortality was much lower in patients treated with dual antibiotic therapy and had a mortality rate of 13.1-20.3% in the monotherapy group. The difference in mortality was clinically significant and consistent with the results of prior studies that have indicated a lower mortality rate with combination therapy of pneumonia in severe cases, especially in high severity score or multilobar disease [18]. The mortality benefit that was observed can be related to broader coverage of pathogens, enhanced treatment of atypical organisms and possible immunomodulatory of combination therapy. The benefits of time-dependency outcomes also were in favour of dual antibiotic therapy. Clinical stability was reached sooner in patients receiving dual therapy with a mean time of 3.9 +/- 1.7 days and 4.6 +/- 1.9 days in the monotherapy group. Equally, the duration of stay in the hospital was also shorter in the dual therapy group compared to the monotherapy patients at 8.6 ± 3.7 days compared to 9.8 ± 4.1 days. Similar time to stability and hospital stay shortening with dual therapy has been seen in earlier studies, which propose faster infection suppression and clinical outcome with combination therapy [19]. The monotherapy group also had more cases of treatment failure and antibiotic escalation. In the monotherapy patients, 26.1% vs. 15.3% on dual therapy, the increase in antibiotic usage was needed and treatment failure, respectively. Past studies have also indicated reduced incidences of treatment failure and progression in the case of treatment with dual therapy in severe pneumonia especially in patients with high inflammatory burden or extensive radiological involvement [20]. The safety of dual antibiotic therapy was good. Although the adverse effects of using the dual therapy treatment were more common (21.2 vs. 15.2), liver enzyme elevation (13.1 vs. 10.1), acute kidney injury (10.9 vs. 8.7), and QT prolongation (5.1 vs. 2.2), these differences were minor and manageable. Clostridioides difficile infection rates were low in both groups with an incidence of 2.9% and 1.4% respectively in patients treated with dual therapy and monotherapy respectively. Past studies have also indicated that there have been very minor incidences of adverse effects when combining the therapy, but highlights that the risks of these combined therapy are minimal compared to the better clinical outcomes seen in severe disease.

CONCLUSION

It is concluded that dual antibiotic therapy is associated with better clinical outcomes than monotherapy in patients with severe bacterial pneumonia. Patients receiving dual therapy demonstrated lower in-hospital mortality, faster achievement of clinical stability, shorter length of hospital stay, and reduced rates of treatment failure and antibiotic escalation despite having comparable or greater disease severity at presentation. Although dual therapy was linked to a slightly higher frequency of antibiotic-related adverse effects, these were generally mild and manageable and did not outweigh the observed clinical benefits.

REFERENCES

1. Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG. Staphylococcus aureus infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev. 2015;28(3):603–61.
2. van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in Staphylococcus aureus Bacteremia. Clin Microbiol Rev. 2012;25(2):362–86.
3. Otto M. MRSA virulence and spread. Cell Microbiol. 2012;14(10):1513–21.
4. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400(10369):2221–48.
5. Tong SYC, Fowler VG, Jr. Skalla L, Holland TL. Management of Staphylococcus aureus Bacteremia: A Review. Jama. 2025;334(9):798–808.
6. Minter DJ, Appa A, Chambers HF, Doernberg SB. Contemporary Management of Staphylococcus aureus Bacteremia-Controversies in Clinical Practice. Clin Infect Dis. 2023;77(11):e57–e68.
7. Davis SL, Perri MB, Donabedian SM, Manierski C, Singh A, Vager D, et al. Epidemiology and Outcomes of Community-Associated Methicillin-Resistant Staphylococcus aureus Infection. Journal of Clinical Microbiology. 2007;45(6):1705–11.
8. Nazli A, Tao W, You H, He X, He Y. Treatment of MRSA Infection: Where are We? Curr Med Chem. 2024;31(28):4425–60.
9. Piewngam P, Otto M. Staphylococcus aureus colonisation and strategies for decolonisation. Lancet Microbe. 2024;5(6):e606–e18.
10. Michalik M, Podbielska-Kubera A, Dmowska-Koroblewska A. Antibiotic Resistance of Staphylococcus aureus Strains-Searching for New

Antimicrobial Agents-Review. Pharmaceuticals (Basel). 2025;18(1).
11. Alanis AJ. Resistance to antibiotics: are we in the post-antibiotic era? Archives of medical research. 2005;36(6):697–705.
12. Utsui Y, Yokota T. Role of an altered penicillin-binding protein in methicillin- and cephem-resistant Staphylococcus aureus. Antimicrob Agents Chemother. 1985;28(3):397–403.
13. Hartman BJ, Tomasz A. Low-affinity penicillin-binding protein associated with beta-lactam resistance in Staphylococcus aureus. J Bacteriol. 1984;158(2):513–6.
14. Magana M, Ioannidis A, Magiorkinis E, Ursu O, Bologa CG, Chatzipanagiotou S, et al. Therapeutic options and emerging alternatives for multidrug resistant staphylococcal infections. Curr Pharm Des. 2015;21(16):2058–72.
15. Hindy JR, Haddad SF, Kanj SS. New drugs for methicillin-resistant Staphylococcus aureus skin and soft tissue infections. Curr Opin Infect Dis. 2022;35(2):112–9.
16. Liu WT, Chen EZ, Yang L, Peng C, Wang Q, Xu Z, et al. Emerging resistance mechanisms for 4 types of common anti-MRSA antibiotics in Staphylococcus aureus: A comprehensive review. Microb Pathog. 2021;156:104915.
17. Hsieh RC, Liu R, Burgin DJ, Otto M. Understanding mechanisms of virulence in MRSA: implications for antivirulence treatment strategies. Expert Rev Anti Infect Ther. 2023;21(9):911–28.
18. Li J, Cheng F, Wei X, Bai Y, Wang Q, Li B, et al. Methicillin-Resistant Staphylococcus aureus (MRSA): Resistance, Prevalence, and Coping Strategies. Antibiotics. 2025;14(8):771.
19. Rodvold KA, McConeghy KW. Methicillin-resistant Staphylococcus aureus therapy: past, present, and future. Clin Infect Dis. 2014;58 Suppl 1:S20–7.
20. Holmes NE, Howden BP. What's new in the treatment of serious MRSA infection? Curr Opin Infect Dis. 2014;27(6):471–8.

