doi.org/10.36721/PJPS.2026.39.4.REG.15307.1

Efficacy and influencing factors of piperacillin sodium tazobactam sodium combined with moxifloxacin in the treatment of severe pneumonia in the elderly

Huacheng Li[1], Weixi Zhong[2] and Jian Sun[2]*

[1]Internal Medicine Department, Shanghai Yuhua Rehabilitation Hospital, Building C, Building 2, No.227 Huilong Road, Xujing Town, Qingpu District, Shanghai, China

[2]Emergency Medicine Department of Shanghai Sixth People's Hospital, No. 600, Yishan Road, Xuhui District, Shanghai, China

Abstract: **Background**: Elderly patients with severe pneumonia face elevated mortality from complex, often resistant, polymicrobial infections. **Objective**: This investigation aimed at assessing the efficacy and determinants of PTZ plus moxifloxacin for severe elderly pneumonia. **Methods**: Retrospectively, this study evaluated 120 elderly severe pneumonia patients (2021–2024), grouped by treatment: Control (n=60): IV piperacillin-tazobactam (PTZ), 4.5g q6h; observation (n=60): PTZ + daily moxifloxacin 400mg. Primary outcomes: pathogen resistance/clearance; secondary: 30-day mortality, readmission, CURB-65, ventilation duration, serum biomarkers. Logistic regression identified mortality factors; adverse events were recorded. **Results**: Baseline characteristics were comparable between groups (P>0.05). The observation group demonstrated superior primary outcomes (P<0.001) and pathogen clearance (P=0.013). No significant intergroup differences were found in secondary outcomes, including mortality, readmission, PLT and adverse events. Post-treatment CURB-65≥3, PCT and CRP significantly correlated with 30-day mortality (all P<0.001). **Conclusion**: The moxifloxacin-PTZ regimen enhanced microbial clearance without affecting survival, readmission, or adverse event rates, supporting its targeted clinical use.

Keywords: C-Reactive protein; Drug resistance; Moxifloxacin; Piperacillin/tazobactam; Procalcitonin; Rate of bacterial clearance; Severe pneumonia; 30-day mortality

Submitted on 29-09-2025 – Revised on 31-10-2025 – Accepted on 13-11-2025

INTRODUCTION

Among the elderly, pneumonia represents a substantial clinical burden. The reported annual incidence ranges from 25 to 44 cases per 1,000 among non-hospitalized older individuals, a rate that is fourfold higher than that observed in younger adults under 65 (Janssens and Krause, 2004). The disease carries a grave prognosis in this demographic; studies report that up to 30% of elderly patients hospitalized with community-acquired pneumonia (CAP) do not survive, with mortality escalating to as high as 57% in cases of nursing home-acquired pneumonia (NHAP) (El-Solh *et al*., 2001; Cui *et al*., 2021). This elevated risk and severity are largely driven by age-related physiological decline in organ function and a higher prevalence of comorbid conditions, which collectively impair the resilience of the respiratory and immune systems, among others (Janssens and Krause, 2004). Compounding this vulnerability is the complex and often resistant microbiology that characterizes severe pneumonia in the elderly. The etiological landscape is frequently mixed, featuring a combination of Gram-negative bacilli (e.g., *Pseudomonas aeruginosa, Klebsiella pneumoniae* and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli*), Gram-positive cocci (including *Streptococcus pneumoniae* and methicillin-resistant *S. aureus* (MRSA)) and atypical pathogens (Cilloniz *et al*., 2022; Haessler *et al*., 2022; Tahmasebi Babaeizad *et al*., 2024). Of particular concern is the growing incidence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria in this population. Risk factors such as prolonged hospitalization, recurrent antibiotic exposure and ICU stays further exacerbate this challenge, rendering conventional single-antibiotic regimens increasingly inadequate.

Current guidelines for managing CAP recommend empirical antimicrobial regimens that provide coverage against likely pathogens (Mandell *et al*., 2007; Lee *et al*., 2018). In severe CAP, the spectrum of causative organisms extends beyond typical bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Klebsiella pneumoniae* and *Staphylococcus aureus* (Jeon *et al*., 2011; Kang Ryoo *et al*., 2017; Seo *et al*., 2017), to include less common agents like *Legionella* and *Pseudomonas* species (Mandell *et al*., 2007; Lee *et al*., 2018). Due to the inherent and variable resistance profile of *Pseudomonas*, current guidance advises initiating combination antibiotic therapy when such infection is suspected, with subsequent de-escalation based on antimicrobial susceptibility testing results (Mandell *et al*., 2007; Lee *et al*., 2018). Among the preferred agents for severe CAP in recent years are β-lactam antibiotics and fluoroquinolones. Piperacillin-

**Corresponding author:* e-mail: sunjian09kh78@hotmail.com

tazobactam (PTZ), a broad-spectrum β-lactam/β-lactamase inhibitor combination, exhibits activity against a wide range of Gram-positive and Gram-negative aerobic and anaerobic bacteria (Lee *et al*., 2003). Its mechanism of action involves the disruption of bacterial cell wall synthesis. The piperacillin component, a ureidopenicillin, demonstrates in vitro efficacy against *Enterobacteriaceae* and *Pseudomonas aeruginosa* (Van der Auwera *et al*., 1993; Gomon, 2023). The addition of tazobactam extends its utility by inhibiting a broad array of β-lactamases produced by Enterobacteriaceae and other aerobic and anaerobic pathogens, both Gram-negative and Gram-positive (Samaha-Kfoury and Araj, 2003). This synergy not only expands the antibacterial spectrum of piperacillin but also establishes its clinical role in managing diverse infections (Perry and Markham, 1999). It should be noted, however, that the in vitro activity of PTZ against ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* is generally reduced compared to non-ESBL-producing isolates (Jacoby and Munoz-Price, 2005). Despite this, the combination has been well-established as an effective treatment for abdominal infections, lower respiratory tract infections, complicated urinary tract infections, gynecological infections and febrile neutropenia (Perry and Markham, 1999).

Moxifloxacin, a fourth-generation fluoroquinolone characterized by its 8-methoxy structure, exerts antibacterial effects through inhibition of bacterial DNA replication. It demonstrates potent in vitro activity against a broad spectrum of pathogens, including typical Gram-positive and Gram-negative aerobes, as well as atypical and anaerobic organisms and is available in both oral and intravenous formulations (Guo *et al*., 2024; Memoona Shakoor *et al*. 2024; Naaz *et al*., 2025). Notably, moxifloxacin retains its efficacy against penicillin-resistant *Streptococcus pneumoniae* and has received FDA approval for the treatment of CAP involving such resistant strains (Brueggemann *et al*., 1997; Jones *et al.,* 2000). Furthermore, it remains active against various pathogens exhibiting resistance to macrolides and tetracyclines-such as *Moraxella catarrhalis* and *Haemophilus influenzae*-and maintains coverage against atypical organisms including *Legionella pneumophila*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* (Miravitlles 2005; Miravitlles and Anzueto, 2008; Burkhardt and Welte, 2009).

Given the limited evidence regarding the clinical efficacy of β-lactam/fluoroquinolone combinations in elderly patients with severe pneumonia, a systematic assessment of the PTZ plus moxifloxacin regimen-encompassing its clinical effectiveness, safety and predictors of response-is of significant clinical importance. This study aims to address this gap by generating high-quality, evidence-based data through rigorous methodological design and analysis. The findings are expected to inform optimal antibiotic selection, support the development of individualized treatment strategies, enhance patient prognosis and ultimately contribute to elevating the standard of care for severe pneumonia in the geriatric population.

Research innovation and significance

This study provides a new idea and basis for the choice of drugs for the treatment of severe pneumonia in the elderly. Piperacillin sodium tazobactam sodium combined with moxifloxacin can significantly improve the pathogen clearance rate and reduce the pathogen drug resistance rate, but it has little effect on mortality and readmission rate. It has effectively challenged the universal applicability of the combined antibiotic therapy with heavy punches, promoted the profound change of the anti-infection treatment strategy from "wide coverage" to "precision" and "descending the ladder" and emphasized that future research should pay more attention to regulating host response rather than just strengthening sterilization.

MATERIALS AND METHODS

Research object

This retrospective controlled clinical study was conducted by researchers not involved in patient treatment, who completed all data collection and analysis. This study enrolled 120 severe pneumonia patients admitted between January 2021 and December 2024. According to the study protocol, participants were randomized to receive different treatments. The first cohort (n=60) underwent treatment with intravenous PTZ (4.5 g every 6 hours). The observation group (n=60) received additional moxifloxacin administered once daily at 400 mg. Evaluations were performed before and after treatment to assess the clinical efficacy of the combination of PTZ and moxifloxacin in treating severe pneumonia. The study flow chart is presented in Fig. 1.

Inclusion criteria

(1) Patients with primary or secondary diagnosis of pneumonia and primary diagnosis of respiratory failure, acute respiratory distress syndrome, respiratory arrest or septicemia; (2) Only patients who received the combination of tazobactam sodium in piperacillin sodium and moxifloxacin or only tazobactam sodium in piperacillin sodium were included (Haessler *et al*. 2022; Oh *et al*. 2024).

Exclusion criteria

(1) Patients who do not meet the criteria of severe CAP; (2) Pneumonia diagnosed 48h after hospitalization; (3) Use vancomycin or carbapenems within 48 hours of hospitalization; (4) transfer during hospitalization; (5) Incomplete observation of the whole clinical process; (6) Died within 48 hours of hospitalization (Oh *et al*. 2024).

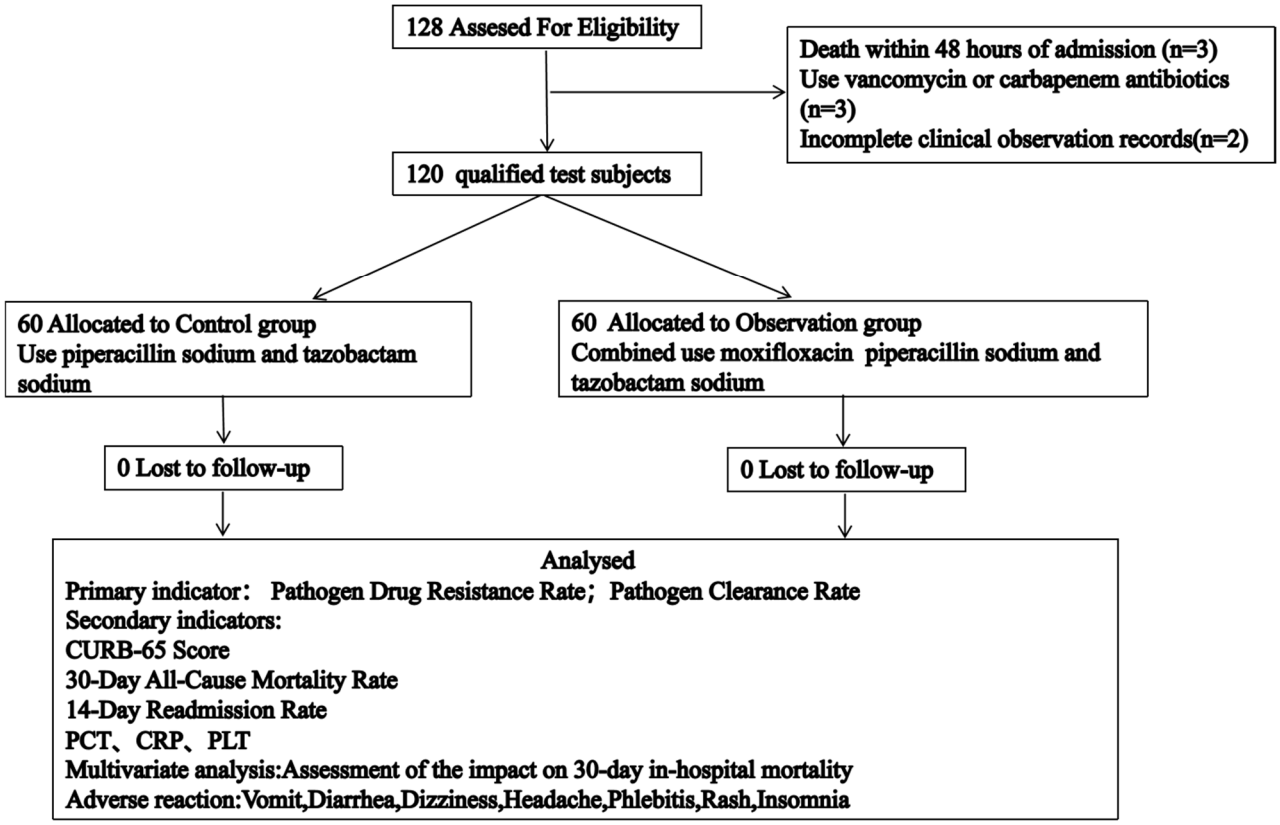

Fig. 1: Research flowchart.

Ethical statement

This clinical study was conducted in accordance with the principles of the Helsinki Declaration and other relevant ethical guidelines (Serra 2025) and received approval from the hospital ethics committee prior to its initiation. The researchers were required to thoroughly explain the study's purpose, procedures and potential risks to all participants or their legal representatives and to obtain written informed consent.

Sample size calculation

This study is a retrospective clinical controlled trial, which is assigned to the observation group or the control group according to the treatment method. An independent samples t-test was applied to the data. The sample size was established a priori using G-Power software (Kim *et al*., 2017). The selection effect is 0.6, the threshold (α) was set at 0.05 (bilateral) and the statistical power (1-β) is 0.80. These parameters lead to 44 participants in each group, a total of 88 participants. In the end, 120 participants were included in this study, which exceeded the target sample size and met the statistical requirements of the study.

Treatment methods

120 patients with severe pneumonia were randomized to two treatment groups following different therapeutic protocols. Control group (60 cases): PTZ (Pfizer) was given and the specific scheme was intravenous injection every 6 hours, 4.5 g (Harris *et al*., 2018) each time; Observation group (60 cases): Moxifloxacin (Avelox, Bayer Pharmaceuticals Corporation, West Haven, CT) was added to the control group's treatment, administered intravenously at a daily dose of 400 mg (Katz *et al*., 2004).

Observation indicators

Baseline indicators: Baseline information of patients was collected, including age, sex, BMI, smoking history, CURB-65 score, pathogen infection type, etc.

Main indicators

(1) Comparison of drug resistance rate of pathogens:

After venipuncture, inject bioMérieux BacT/ALERT® FA/FN Plus blood culture bottles, first inject anaerobic bottles and then aerobic bottles, each bottle is 8-10 ml, indicating the sampling time, location and suspected diagnosis disease and then put them into bioMérieux BacT/ALERT® 3D automatic blood culture instrument after inspection. After incubation at 37°C, if they are positive, they will be immediately stained with Gram and then the plates will be transferred. The drug diffuses in agar, forming a concentration gradient. After overnight culture, the diameter of bacteriostatic circle was measured. The larger the inhibition zone, the more sensitive it is to the drug. The smaller it is, the more resistant it is (Mansour-Ghanaei *et al*. 2022).Blood cultures were collected from all patients on the third day after admission. From the initial positive blood culture, clinical data were recorded every day until the fifth day after grouping according to the

treatment plan (the first day is the grouping day, which must be carried out within 72 hours after the initial blood culture collection).On the fifth day, the main treatment plan can choose to stop all antibiotics or continue to use the allocated drugs or change to progressive therapy(Harris *et al*. 2018).

(2) Comparison of pathogen clearance rate

After venipuncture, the blood culture bottles of bioMérieux BacT/ALERT® FA/FN Plus were injected and then the anaerobic bottles were injected, each bottle was 8-10 ml, indicating the sampling time, location and suspected diseases. After inspection, they were put into the Biomé rieux Bact/Alert 3D automatic blood culture instrument, incubated at 37℃ and if they were positive, they were immediately stained with Gram and transferred to the seed plate for identification.

Secondary indicators

(1) Confusion, Urea nitrogen, Respiratory rate, Blood pressure, Age ≥65 years (CURB-65) score

The British Thoracic Association (BTS) recommended using CURB-65 score to evaluate the prognosis of CAP (Agusti *et al*., 2023). It contains five indicators, namely, disturbance of consciousness, urea nitrogen> 7 mmol/L, respiratory rate ≥30 beats/min, hypotension (systolic blood pressure<90 mmHg or diastolic blood pressure≤60 mmHg) and patient's age reaching or exceeding 65 years (Guo *et al*., 2011). If each indicator meets the requirements, you will get 1 point, with the total score ranging from 0 to 5 points (2001). Patients with CURB-65 score 3 have a high risk of death and should be treated in intensive care unit (highly dependent or intensive care unit); Patients who score 2 face a moderate mortality risk and should be offered either short-term hospitalization or closely supervised outpatient care; Patients with a score of 0 or 1 have a lower risk of death and can be treated at home (Mandell *et al*., 2007; Lim *et al*., 2009). CURB-65 score at admission and 30-day mortality were counted.

(2) Clinical outcome:30-day all-cause mortality

The cause of death was determined according to the medical records written by the attending doctor. The death certificate lists all the related causes of death except the main cause of death and is the main record of evidence. According to relevant certificates, discharge records and death records, the cause of death caused by the aggravation of pneumonia is determined as pneumonia (Oh *et al*., 2024).

(3) Re-admission rate 14 days after treatment

Count the people who were cured and discharged from hospital. The day of discharge was the first day and they were continuously observed for 14 days from discharge and the number of readmission cases within 14 days was recorded (Guo *et al*., 2011; Unal Cetin *et al*., 2025).

(4) C-Reactive Protein (CRP), Procalcionin (PCT), Platelet (PLT)

CRP, PCT: 5 mL of fasting venous blood of patients was collected by a golden hat serum tube as a test sample and the serum was separated by BeckmanMicrofuge®20R centrifuge at 1500 g/min for 10min and then detected by ABBOTT ARCHITECT C8000 automatic biochemical analyzer at 600nm wavelength (Huang *et al*., 2024).

PLT: The patient's 5 mL fasting venous blood was collected with purple cap anticoagulation tube as the test sample and the BeckmanMicrofuge®20R centrifuge was used for 1500 g/min. After centrifugation for 10min, the serum was separated and tested with ABBOTT CELL-DYN blood analyzer (Huang *et al*., 2024).

(5)Mechanical ventilation time

Non-invasive ventilator (NIV) ventilates through face mask or nasal mask, without establishing artificial airway (such as tracheal intubation) (Ferrer *et al*., 2024). The first day is the day of mechanical ventilation treatment within 48 hours after admission and the patient continued to breathe spontaneously for more than 24 hours until he was successfully separated from the ventilator for the first time. If the patient failed to withdraw from the machine successfully, the end point of observation was the time of death or tracheotomy.

(6)Analysis of influencing factors of 30-day all-cause mortality

The effects of treatment methods, age, sex, smoking history, CURB-65 score, PCT and CRP on 30-day mortality were analyzed by binary Logistic (Huang *et al*., 2024).

(7) Adverse drug events

Vomiting, diarrhea, dizziness, headache, rash, phlebitis and insomnia (Frank *et al*., 2002; Gin *et al*., 2007).

The formula for calculating the incidence of adverse reactions is as follows: the incidence of adverse reactions =(number of patients with adverse reactions/total number of patients in each group) *100%.

Statistical analysis

Statistical software SPSS25.0 was used to analyze and process all the figures used in this study. The measurement data were expressed as ($\bar{x} \pm s$). T test was used for the data that conformed to the normal distribution, such as age, BMI and CURB-65 score comparison, etc. Chi-square test was used for the classified counting data such as gender, smoking history, pathogen drug resistance rate, pathogen clearance rate, clinical outcome, readmission rate and adverse events between groups. Represented by "n, %". $P<0.05$ is statistically significant.

RESULTS

Baseline characteristics by group

Table 1 displays a comparison of baseline characteristics between the control group (n=60) and the observation group (n=60).No significant differences were observed between the groups in terms of age, sex, BMI, smoking history, CURB-65 score, or type of microbial infection ($P>0.05$), demonstrating that the baseline profiles were well-balanced and comparable.

Table 1: Baseline characteristics [mean ±SD, n (%)]

Variables	Control group (n=60)	Observation group (n=60)	*95% CI*	$\chi^2/t/Z$	*P*
Age (years)	76.30±8.20	77.13±7.46	-3.697 to 1.964	-0.606	0.545
BMI (kg/m^2)	21.75±4.35	22.45±4.65	-2.329 to 0.926	-0.854	0.395
Gender					
Male	39 (65.00)	37 (61.70)	-	0.144	0.850
Female	21 (35.00)	23(38.30)			
History of smoking	18 (30.00)	20 (33.30)	-	0.154	0.845
The CURB-65 Score	2.58±0.79	2.57±0.67	-0.248 to 0.282	0.125	0.901
Infection type					
Stenotrophomonas maltophilia	8 (13.30)	7 (11.70)	-	0.076	0.783
Klebsiella pneumoniae	7 (11.70)	11 (18.30)	-	0.076	0.783
Streptococcus pneumoniae	2 (3.30)	1 (1.70)	-	0.342	0.559
Escherichia coli	3 (5.00)	3 (5.00)	-	0.000	1.000
Pseudomonas aeruginosa	9 (15.00)	8 (13.30)	-	0.069	0.793
Staphylococcus aureus	5 (8.30)	5 (8.30)	-	0.000	1.000
Total infection rate	23 (46.9)	26 (43.3)	-	0.310	0.577
Post-treatment survival rate (for infections)	12(52.2)	17(65.4)	-	0.882	0.348
Hospitalization duration(days)	16.30±2.94	15.63±2.41	-3.097 to 1.633	1.349	0.180
PCT(ng/mL)	0.82 (0.58,1.03)	0.94 (0.78,1.16)	-	-0.202	0.840
PLT($\times10^9$/L)	173.50 (152.25,187.00)	177.00 (168.00,191.00)	-	-0.163	0.871
CRP(mg/L)	79.40 (70.88,87.25)	79.20 (70.10,90.53)	-	-0.079	0.937
Application of mechanical ventilation within 48 h	7(11.70)	12 (20.00)	-	1.563	0.211

Note: BMI: Body Mass Index; PCT: Procalcitonin; PLT: Platelet; CRP: C-Reactive Protein; CURB-65: Confusion, Urea, Respiratory rate, Blood pressure, Age ≥65 score. The same below.

Comparison of drug resistance rate of pathogens

Comparing the pathogens isolated from patients in the control group and the observation group, it can be seen from table 2 that the drug resistance rates of *Stenotrophomonas maltophilia* and *Staphylococcus aureus* are significantly lower than those in the control group (*P*=0.003;0.038). Generally speaking, the resistance rate of *Stenotrophomonas maltophilia* to fluoroquinolones was low (28.6%), but the resistance rate to tazobactam sodium in piperacillin sodium was extremely high (100%). *Staphylococcus aureus* was obviously resistant to piperacillin sodium tazobactam sodium (100%), but it was not resistant to moxifloxacin (*P*=0.0038).In addition, the resistance rates of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* to piperacillin sodium tazobactam sodium and moxifloxacin were low. Nevertheless, while the two treatment regimens showed no significant statistical difference (*P*>0.05), table 2 demonstrates high resistance in *Streptococcus pneumoniae* to PTZ and in *Escherichia coli* to moxifloxacin. Furthermore, the difference between these resistance rates was also not statistically significant-a finding that is likely due to the low detection rates for both organisms. The above results show that patients mainly infected with *Stenotrophomonas maltophilia* and Staphylococcus aureus need to choose the combined treatment scheme. For the treatment of *Streptococcus pneumoniae*, the sample size needs to be expanded for further determination.

Comparison of pathogen clearance rate and readmission rate

According to the baseline characteristics presented in table 1, 23 patients in the control group and 26 in the observation group were identified with pathogenic infections. Following treatment, 12 patients survived in the control group, compared to 17 in the observation group. The pathogen clearance rate and readmission rate of patients who were infected with pathogens and survived after 30 days of treatment were compared between the control group and the observation group. As can be seen from table 3, the pathogen clearance rate of the observation group was significantly higher than that of the control group, with statistical significance (*P*=0.013). Adjunctive moxifloxacin therapy was associated with improved pathogen clearance compared to PTZ alone in elderly patients with severe pneumonia, resulting in greater anti-infective treatment effectiveness. No statistically

significant disparity in readmission rates was demonstrated between the other two groups (*P*=0.800). The results showed that both treatment methods had good therapeutic effect on bacterial infection and the effect was similar in preventing reinfection and the readmission rate of both groups was at a low level.

30-day comparison of all-cause mortality

A comparison was made of the 30-day all-cause mortality rates between the control and observation groups. As presented in table 4, no statistically significant difference was observed in 30-day mortality between the two groups (*P*=0.184). Given the current sample size, the findings demonstrate that the combination therapy did not significantly boost early-stage survival rates in elderly patients with critical pneumonia compared to monotherapy. Both treatment strategies were equally effective in reducing patient mortality.

Analysis and comparison of PLT, PCT and CRP levels between the two groups before and after treatment

The PLT, PCT and CRP of patients in the control group and the observation group were compared respectively. As can be seen from table 5, there was no significant difference in PLT, PCT and CRP between the two groups before treatment (all *P*>0.05). After treatment, the levels of PCT and CRP in the control group and the observation group decreased significantly (all *P*<0.05), but there was no significant difference in PLT (all *P*>0.05). After treatment, PLT, PCT and CRP (PLT:173.00 (150.50,188.75) in the observation group and the control group; PCT:0.46 (0.24,0.57); CRP: 63.05 (36.70,106.80), the PCT and CRP of the observation group (PCT:0.30 (0.15,0.85); CRP:20.00 (17.10,101.98) were significantly lower than that of the control group (*P*=0.013, 0.001). The adjunctive use of moxifloxacin exhibits a marked therapeutic effect on severe pneumonia in the elderly, leading to improved clinical outcomes.

Analysis and comparison of mechanical ventilation time between the two groups before and after treatment

Table 6 presents a comparison of mechanical ventilation time in the control and observation groups. Both groups showed comparable baseline characteristics prior to treatment (all *P*>0.05). Post-intervention, a substantial decrease in mechanical ventilation time was observed in both groups (all *P*<0.05). However, post-treatment comparison revealed no significant difference between the observation group (5.54±2.07 days) and the control group (5.54±2.06 days) (*P*=0.99). The findings suggest that adding moxifloxacin offered no significant benefit in shortening mechanical ventilation time for elderly patients with severe pneumonia.

CURB-65 score analysis and comparison between the two groups before and after treatment

Comparing the CURB-65 scores of patients in the control group and the observation group, it can be seen from Table 7 that there was no significant difference in CURB-65 scores between the two groups before treatment (all *P*>0.05). After treatment, a significant reduction in CURB-65 scores was observed in both the control and observation groups (both *P*<0.05). After treatment, the CURB-65 score (score: 0.50 (0.00, 1.00) of the observation group was compared with that of the control group and the CURB-65 score (score: 0.00 (0.00, 1.00) of the observation group decreased significantly (*P*=0.03).The findings reveal that the combination regimen including moxifloxacin provides a marked reduction in mortality rates for elderly individuals suffering from severe pneumonia.

Evaluate the influencing factors of 30-day mortality

Table 8 shows the results of multivariate analysis. No association was found between combination therapy and all-cause in-hospital mortality. But CURB65≥3 (or: 0.020; 95%*CI*, 0.004–0.096; *P*<0.001), PCT (OR:0.002;95%*CI,* 0.000–0.020; *P*<0.001) and CRP (or: 0.047; 95%*CI*, 0.008–0.270; *P*<0.001) showed a significant correlation with all-cause.

Comparison of adverse reaction incidence for the two groups

As can be seen from table 9, during the treatment period, two patients in the control group suffered from vomiting, one patient with diarrhea, one patient with dizziness and one developed a rash, resulting in an overall adverse reaction rate of 8.3%, while one patient in the observation group suffered from vomiting, one patient with diarrhea and one developed a rash, yielding an adverse reaction rate of 6.7%. The results showed that there was no significant difference in the incidence of adverse reactions between piperacillin sodium tazobactam sodium and piperacillin sodium tazobactam sodium combined with moxifloxacin in the treatment of elderly patients with severe pneumonia (*P*=0.769).

DISCUSSION

This study evaluated the efficacy and safety of combination therapy with PTZ and moxifloxacin versus PTZ monotherapy in elderly patients with severe pneumonia. The principal findings indicate that the combination regimen confers distinct microbiological advantages. Most notably, the observation group exhibited significantly lower resistance rates for *Stenotrophomonas maltophilia* and *Staphylococcus aureus*, a result consistent with previous reports by (Grabein *et al*., 2024), which strongly echoed our findings. Given that the baseline characteristics and pathogen distribution were well-balanced between the two groups, these observed microbiological benefits are more likely attributable to the expanded antibacterial coverage and potential synergy of the combination therapy, rather than to confounding patient or pathogen factors. The mechanistic basis for the reduced resistance rates can be elucidated as follows. *Stenotrophomonas maltophilia* frequently carries metallo-β-lactamases, which hydrolyze the β-lactam ring of PTZ, thereby conferring resistance (Grabein *et al*., 2024).

Table 2: Comparison of rate of drug resistance among patients [n (%)]

Variables	Control group	Variables	Observation group	Test	95% CI	χ^2	P
Stenotrophomonas maltophilia (n=8)	8 (100.00)	*Stenotrophomonas maltophilia* (n=7)	2 (28.60)	Chi-square test	-	8.571	0.003
Klebsiella pneumonia (n=7)	2(28.60)	*Klebsiella pneumonia* (n=11)	1 (9.10)	Chi-square test	-	1.169	0.28
Escherichia coli (n=3)	1 (33.30)	*Escherichia coli*(n=3)	2 (66.70)	Chi-square test	-	0.667	0.414
Pseudomonas aeruginosa (n=9)	1 (11.10)	*Pseudomonas aeruginosa* (n=8)	2 (25.00)	Chi-square test	-	0.562	0.453
Streptococcus pneumonia (n=3)	2 (66.70)	*Streptococcus pneumonia* (n=0)	0(0.00)	Chi-square test	-	1.333	0.248
Staphylococcus Aureus (n=5)	5 (100.00)	*Staphylococcus aureus* (n=5)	2 (40.00)	Chi-square test	-	4.286	0.038
Total	16(69.60)	Total	5(19.20)	Chi-square test	-	16.626	<0.001

Table 3: Comparison of rate of bacterial clearance and readmission after 30 days of treatment [n (%)]

Variables	Control group (n=11)	Observation group (n=17)	Test	*95% CI*	χ^2	*P*
Bacterial clearance	6 (54.50)	16 (94.10)	Chi-square test	-	6.212	0.013
Readmission rate	1 (16.70)	2 (12.50)	Chi-square test	-	0.064	0.800

Note: **P*<0.05 vs. Control group; The same below.

Table 4: Comparison of mortality rates [n (%)]

Variables	Control group (n=60)	Observation group (n=60)	Test	*95% CI*	χ^2	*P*
30-day mortality	44 (73.30)	50 (83.30)	Chi-square test	-	1.768	0.184

Note: **P*<0.05 vs.Control group; The same below.

Table 5: Comparison of PLT, PCT, CRP (M(P25,P75))

Indicator	Time	$M(P_{25},P_{75})$		*Z*	*P*
		Control group	Observation group		
PLT(×10⁹/L)	Before treatment	173.50(152.25,187.00)	175.00(153.50,187.00)	-0.163	0.871
	After treatment	173.00(150.50,188.75)*	175.00(163.25,190.25)*	-1.559	0.119
PCT(ng/mL)	Before treatment	0.82(0.58,1.03)	0.80(0.63,1.00)	-0.202	0.840
	After treatment	0.46(0.24,0.57)*	0.30(0.15,0.85)*	-2.491	0.013
CRP(mg/L)	Before treatment	79.40(70.88,87.25)	79.20(70.10,90.53)	-0.079	0.937
	After treatment	63.05(36.70,106.80)*	20.00(17.10,101.98)*	--3.262	0.001

Table 6: Comparison of mechanical ventilation ($\bar{x}$±s, days)

Indicator	Time	$\bar{x}$±s		*95% CI*	*t*
		Control group (n=7)	Observation group (n=12)		
Mechanical Ventilation	Before treatment	13.51±5.67	14.50±5.47	-6.55	4.58
	After treatment	5.54±2.07*	5.54±2.06*	-2.34	2.33

Table 7: Comparison of CURB-65 (M(P25, P75), score)

Indicator	Time	M(P25,P75)		*Z*	*P*
		Control group (n=60)	Observation group (n=60)		
CURB-65	Before treatment	2.00(2.00,3.00)	2.00(2.00,3.00)	-0.98	0.33
	After treatment	0.50(0.00,1.00)*	0.00(0.00,1.00)*	-2.24	0.03

Table 8: Multivariate analysis: Assessment of the impact on 30-day in-hospital mortality

Variables	*B*	*SE*	*Wald* χ^2	*P*	*OR*	*OR 95% CI*
Treatment	-0.01	0.79	0.00	0.99	0.99	0.21 to 4.69
Age	-0.96	1.86	0.27	0.61	0.39	0.10 to 14.68
Gender	-0.13	0.82	0.03	0.87	0.88	0.17 to 4.39
History of smoking	-0.92	0.81	1.08	0.30	0.40	0.07 to 2.25
The CURB-65 Score	-2.94	0.87	11.43	<0.001	0.05	0.01 to 0.29
PCT	-3.28	0.92	12.85	<0.001	0.04	0.01 to 0.23
CRP	-0.31	0.90	11.70	<0.001	0.05	0.01 to 0.27

Table 9: Comparison of adverse reactions of patients [n (%)]

Variables	Adverse reactions [n (%)]							
	Vomit	Diarrhea	Dizziness	Rash	Phlebitis	Headache	Insomnia	Total
Control group (n=75)	2	1	1	1	1	1	0	7 (11.7)
Observation group (n=75)	1	2	0	1	0	1	1	6 (10.0)
Test	Chi-square test							
χ^2	0.086							
P	0.769							

Note: **P*<0.05 vs. Before treatment; The same below.

Moxifloxacin, which exerts its antibacterial effect by inhibiting DNA gyrase and topoisomerase IV (Di Bonaventura *et al*., 2004; Shariati *et al*., 2022). This provides an alternative antibacterial pathway that is not affected by the β-lactamase-mediated resistance that can undermine PTZ efficacy. Therefore, the addition of moxifloxacin is theoretically expected to reduce the selective pressure for resistance that might emerge under PTZ monotherapy., Similarly, regarding *Staphylococcus aureus*, PTZ is effective against methicillin-sensitive strains (MSSA) but not against MRSA (Adedeji-Olulana *et al*., 2024). Moxifloxacin is active against some MRSA (Alseqely *et al*., 2021). The concurrent use of both agents not only broadens the spectrum of coverage but also introduces a dual-mechanism antibacterial strategy. This approach reduces the risk of resistance emergence that can occur under selective pressure from either drug alone, thereby lowering the overall resistance burden of *S. aureus*.

Furthermore, the observation group demonstrated comparatively low resistance rates for *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, consistent with reports by (Rahmel *et al*., 2017; Harris *et al*., 2018; Hsu *et al*., 2025). the This alignment may be explained by inherent potency of PTZ against these Gram-negative pathogens-including numerous ESBL-producing strains-due to the presence of tazobactam (Bhowmick *et al*., 2025). For organisms such as *K. pneumoniae, Escherichia coli* and *P. aeruginosa*, PTZ monotherapy alone exerts substantial antibacterial pressure, thereby limiting the marginal benefit contributed by the addition of moxifloxacin. Consequently, resistance rates remained low in both groups without statistically significant differences, underscoring the robustness of PTZ as foundational therapy for these core Gram-negative bacilli. With regard to Streptococcus pneumoniae, PTZ exhibits moderate in vitro activity, whereas moxifloxacin demonstrates strong efficacy. Nonetheless, no intergroup difference in resistance was observed in this study, likely due to the low overall detection rate of *S. pneumoniae*, which limited statistical power to discern potential differences.

The combination therapy also resulted in a significantly higher overall pathogen clearance rate, a finding consistent with previous studies (Cai *et al*., 2023; Reinert, 2009; Xu *et al*., 2024). This improvement is likely attributable to the expanded antibacterial spectrum-encompassing atypical pathogens and enhanced Gram-positive coverage-as well as potential synergistic effects, which collectively reduce the likelihood of inadequate initial antimicrobial coverage and promote more rapid and thorough eradication of pathogens. In line with the observations by (Huang *et al*., 2024), we also noted markedly lower levels of the inflammatory biomarkers CRP and PCT in the combination group, suggesting more effective control of systemic inflammation. CRP, as an acute-phase protein, reflects the intensity of the inflammatory response, while PCT serves as a more specific indicator of bacterial infection and is closely correlated with disease severity and prognosis. The enhanced anti-inflammatory effect observed with the moxifloxacin-containing regimen may be mediated through several mechanisms: first, accelerated and comprehensive pathogen clearance reduces the primary stimulus for inflammation; second, fluoroquinolones have been shown to exert direct immunomodulatory effects, including suppression of specific pro-inflammatory cytokines; and third, combination therapy may limit the emergence and spread of resistant bacterial strains, thereby reducing persistent inflammatory stimulation. Notably, however, the combination regimen did not confer a significant reduction in the duration of mechanical ventilation, a result consistent with the report by (Bahloul

et al., 2013). This may be explained by the fact that parenchymal lung injury and inflammatory edema resulting from pneumonia require a substantial period for repair-a process not substantially influenced by the choice of antimicrobial regimen. Even with effective and rapid microbial eradication, structural and functional recovery of lung tissue may follow a protracted course, particularly in elderly patients who often have underlying comorbidities such as chronic obstructive pulmonary disease or heart failure, which can further delay weaning from ventilatory support.

Multivariable analysis in this study identified the CURB-65 score and PCT level as significant predictors of 30-day mortality, corroborating the earlier findings reported by (Huang *et al*., 2024). As a multidimensional tool integrating consciousness, renal function, respiratory rate, blood pressure and age, the CURB-65 score provides a composite measure of illness severity and physiological reserve. In elderly patients, an elevated CURB-65 score often signifies advanced infection with depleted compensatory capacity, indicating a heightened risk of organ failure and mortality even after infection control is achieved. Similarly, PCT-a biomarker with high specificity for bacterial infection-serves as a valuable prognostic indicator. Elevated PCT levels reflect not only the severity of infection but also the intensity of the associated systemic inflammatory response, which can contribute directly to organ dysfunction. In older adults, age-related immune dysregulation, often termed immunosenescence, may lead to either an exaggerated or a blunted inflammatory reaction, further complicating disease progression and recovery.

No statistically significant differences were observed between the two groups in terms of mortality, readmission rate, or overall incidence of adverse events. Several factors may explain these findings. First, Effectiveness of the control group: The control regimen of PTZ monotherapy represents a highly effective treatment in its own right. The results from (Lai *et al*., 2023) establish that PTZ itself sets a high therapeutic benchmark, achieving favorable clinical outcomes in severe pneumonia, which may have limited the discernible marginal survival benefit from the addition of a second potent agent. Second, the advanced age and high baseline risk of non-infectious mortality in this specific patient population may have diluted any incremental survival benefit attributable to the antibacterial regimen. In younger individuals or those with fewer comorbidities, the advantages of combination therapy might translate more clearly into mortality reduction. Third, the distribution of pathogens in the study cohort could have influenced outcomes. In settings with a higher prevalence of resistant organisms such as MRSA or atypical pathogens, combination therapy may demonstrate more pronounced survival benefits. In this study, however, the efficacy of PTZ monotherapy against common Gram-negative pathogens such as Klebsiella pneumoniae and Pseudomonas aeruginosa may have narrowed the potential for further outcome improvement, creating a therapeutic "ceiling effect" that limited discernible differences in readmission and survival rates between the two regimens.

Finally, in terms of drug safety, The addition of moxifloxacin to the PTZ regimen did not introduce new or unexpected safety concerns, a finding consistent with the well-documented safety profile of moxifloxacin observed in other contemporary controlled trials (Li *et al*., 2021). This supports the conclusion that the combination, from a safety perspective, is a viable clinical option.

The findings of this study advocate for a more refined and evidence-based approach to the use of combination antibiotic therapy in elderly patients with severe pneumonia. Rather than applying combination regimens universally, treatment should be targeted toward those individuals most likely to derive clinical benefit, such as patients with suspected or confirmed infections due to resistant Gram-negative organisms or specific pathogens like *Stenotrophomonas maltophilia* and MRSA. Prospective randomized controlled trials should be carried out in the future, with special attention to high-risk subgroups of patients; Explore biomarkers that predict the benefits of combination therapy; Conduct pharmacoeconomic evaluation; Explore a more optimized drug delivery scheme; To establish a predictive model integrating clinical features, biomarkers and pathogenic information.

Research limitations

This study is a retrospective clinical controlled study. Although the data collection and analysis were completed by researchers who did not participate in patient treatment, the objectivity of the study was guaranteed to some extent, but the retrospective study itself has certain limitations. The research sample only comes from 126 patients in our hospital. Although it meets the basic statistical requirements, the sample size is relatively small and it does not cover groups with different economic levels and cultural backgrounds. Selection bias may have been present, potentially compromising the universality and representativeness of the research outcomes. On the other hand, the sample size of each pathogen may be insufficient, especially when the number of drug-resistant strains is small, which may lead to the failure to detect real differences (that is, false negative results). Finally, while we discuss potential mechanisms for the observed resistance patterns, this study did not perform molecular analyses. Future prospective studies incorporating such molecular epidemiology data would be valuable to confirm the mechanisms underlying the resistance trends observed in a clinical setting. The conclusion of this study provides some clinical reference value for the combination therapy, but its exact effectiveness and safety still need to be further verified by a well-designed, large-sample, multi-center prospective RCT.

CONCLUSION

The regimen combining PTZ with moxifloxacin represents a potent and targeted antimicrobial strategy for the management of severe pneumonia in the elderly. Its core value is not universally superior to powerful single drug, but lies in expanding the antibacterial spectrum, accurately covering specific difficult pathogens (such as *Stenotrophomonas maltophilia* and *Staphylococcus aureus*) and significantly reducing the risk of drug resistance, thus comprehensively improving the pathogen clearance rate. Although the scheme failed to improve the final survival rate of the elderly population in this study, its advantages in curbing drug resistance and ensuring the success rate of treatment cannot be ignored. Clinically, this combination should be considered for elderly patients with severe pneumonia, particularly when infections with *Stenotrophomonas maltophilia* or *Staphylococcus aureus* are suspected, or in settings with high rates of multidrug resistance. Future research should focus on prospective, randomized trials to validate these findings and on identifying biomarkers that can predict which patients will derive the greatest mortality benefit from such broad-spectrum combination therapy.

Acknowledgement
None

Author's contributions statement
Huacheng Li: Conceived and designed the research and analyzed data. Drafted and revised the manuscript critically for important intellectual content; Weixi Zhong: Contributed to the acquisition, analysis and interpretation of data and provided substantial intellectual input during the drafting and revision of the manuscript; Jian Sun: Participated in the conception and design of the study, played a key role in data interpretation and manuscript preparation All authors have read and approved the final version of the manuscript.

Funding
There was no funding.

Data availability statement
The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This clinical study was conducted in accordance with the principles of the Helsinki Declaration and other relevant ethical guidelines and received approval from the Shanghai Yuhua Rehabilitation Hospital ethics committee prior to its initiation (approval number: 20250012).

Conflict of interest
The authors affirm that they do not have any financial conflicts of interest.

Consent to participate
The researchers were required to thoroughly explain the study's purpose, procedures and potential risks to all participants or their legal representatives and to obtain written informed consent.

REFERENCES

Adedeji-Olulana AF, Wacnik K, Lafage L, Pasquina-Lemonche L, Tinajero-Trejo M, Sutton JAF, Bilyk B, Irving SE, Portman Ross CJ, Meacock OJ, Randerson SA, Beattie E, Owen DS, Florence J, Durham WM, Hornby DP, Corrigan RM, Green J, Hobbs JK and Foster SJ (2024). Two codependent routes lead to high-level MRSA. *Science,* **386**(6721): 573-580.

Agusti A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martinez FJ, Montes de Oca M, Mortimer K, Papi A, Pavord I, Roche N, Salvi S, Sin DD, Singh D, Stockley R, Lopez Varela MV, Wedzicha JA and Vogelmeier CF (2023). Global. initiative for chronic obstructive lung disease 2023 Report: GOLD Executive Summary. *Eur Respir J*, **61**(4): 2300239.

Alseqely M, Newton-Foot M, Khalil A, El-Nakeeb M, Whitelaw A and Abouelfetouh A (2021). Association between fluoroquinolone resistance and MRSA genotype in Alexandria, Egypt. *Sci Rep*, **11**(1): 4253.

Bahloul M, Chaari A, Dammak H, Ammar R, Medhioub F, Hamida CB, Chelly H and Bouaziz M (2013). Efficacy of corticosteroid therapy in severe decompensation of chronic obstructive pulmonary disease requiring mechanical ventilation. *Am J Ther*, **20**(6): 630-637.

Bhowmick T, Canton R, Pea F, Quevedo J, Santerre Henriksen A, Timsit JF and Kaye KS (2025). Cefepime-enmetazobactam: first approved cefepime-β- lactamase inhibitor combination for multi-drug resistant Enterobacterales. *Future Microbiol*, **20**(4): 277-286.

British Thoracic Society Standards of Care Committee (2001). BTS Guidelines for the Management of Community Acquired Pneumonia in Adults. *Thorax*, **56**(Suppl 4): Iv1-64.

Brueggemann AB, Kugler KC and Doern GV (1997). In vitro activity of BAY 12-8039, a novel 8-methoxyquinolone, compared to activities of six fluoroquinolones against *Streptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis*. *Antimicrob Agents Chemother*, **41**(7): 1594-1597.

Burkhardt O and Welte T (2009). 10 years' experience with the pneumococcal quinolone moxifloxacin. *Expert Rev Anti Infect Ther*, **7**(6): 645-668.

Cai LJ, Wei XL, Wei YQ, Guo XT, Jiang XJ, Zhang Y, Yu GP, Dai M, Ye JY, Zhou HS, Xu D, Huang F, Fan ZP, Xu N, Shi PC, Xuan L, Feng R, Liu XL, Sun J and Liu QF (2023). A single-center study on the distribution and antibiotic resistance of pathogens causing bloodstream infection in patients with hematological malignancies. *Zhonghua Xue Ye Xue Za Zhi*, **44**(6): 479-483.

Cilloniz C, Pericas JM and Rojas J (2022). Ceftaroline in severe community-acquired pneumonia. *Rev Esp Quimioter*, **35**(Suppl 1): 28-30.

Cui J, Li M, Cui J, Wang J, Qiang X and Liang Z (2021). The proportion, species distribution and dynamic trends of bloodstream infection cases in a tertiary hospital in China, 2010–2019. *Infection*, **50**(1): 121-130.

Di Bonaventura G, Spedicato I, D'Antonio D, Robuffo I and Piccolomini R (2004). Biofilm formation by *Stenotrophomonas maltophilia*: Modulation by quinolones, trimethoprim-sulfamethoxazole, and ceftazidime. *Antimicrob Agents Chemother*, **48**(1): 151-160.

El-Solh AA, Sikka P, Ramadan F and Davies J (2001). Etiology of severe pneumonia in the very elderly. *Am J Respir Crit Care Med*, **163**(3 Pt 1): 645-651.

Ferrer M, De Pascale G, Tanzarella ES and Antonelli M (2024). Severe community-acquired pneumonia: Noninvasive mechanical ventilation, intubation and HFNT. *Semin Respir Crit Care Med*, **45**(2): 169-186.

Frank E, Liu J, Kinasewitz G, Moran GJ, Oross MP, Olson WH, Reichl V, Freitag S, Bahal N, Wiesinger BA, Tennenberg A and Kahn JB (2002). A multicenter, open-label, randomized comparison of levofloxacin and azithromycin plus ceftriaxone in hospitalized adults with moderate to severe community-acquired pneumonia. *Clin Ther*, **24**(8): 1292-1308.

Gin A, Dilay L, Karlowsky JA, Walkty A, Rubinstein E, Zhanel GG (2007). PTZ: A beta-lactam/beta-lactamase inhibitor combination. *Expert Rev Anti Infect Ther*, **5**(3): 365-383.

Gomon, YM (2023). PTZ: prospects for use in real-world practice. *Real-World Data & Evidence*, **3**(3): 1-7.

Grabein B, Arhin FF, Daikos GL, Moore LSP, Balaji V and Baillon-Plot N (2024). Navigating the current treatment landscape of metallo-β-lactamase-Producing Gram-negative infections: What are the Limitations?. *Infect Dis Ther*, **13**(11): 2423-2447.

Guo Q, Li HY, Zhou YP, Li M, Chen XK, Liu H, Peng HL, Yu HQ, Chen X, Liu N, Liang LH, Zhao QZ and Jiang M (2011). Compliance with the CURB-65 score and the consequences of non-implementation. *Int J Tuberc Lung Dis*, **15**(12): 1697-1702.

Guo RQ, Yang J, Yang YB, Chen YN, Xiao YY, Xiang P, Dong MJ, He MF, Wang YT, Xiao YL, Ke HQ and Liu H (2024). Spectrum and antibiotic sensitivity of bacterial keratitis: A retrospective analysis of eight years in a tertiary referral hospital in Southwest China. *Front Cell Infect Microbiol*, **14**: 1363437.

Haessler S, Guo N, Deshpande A, Zilberberg MD, Lagu T, Lindenauer PK, Imrey PB and Rothberg MB (2022). Etiology, treatments and outcomes of patients with severe community-acquired pneumonia in a large U.S. sample. *Crit Care Med*, **50**(7): 1063-1071.

Harris PNA, Tambyah PA, Lye DC, Mo Y, Lee TH, Yilmaz M, Alenazi TH, Arabi Y, Falcone M, Bassetti M, Righi E, Rogers BA, Kanj S, Bhally H, Iredell J, Mendelson M, Boyles TH, Looke D, Miyakis S, Walls G, Al Khamis M, Zikri A, Crowe A, Ingram P, Daneman N, Griffin P, Athan E, Lorenc P, Baker P, Roberts L, Beatson SA, Peleg AY, Harris-Brown T, Paterson DL; MERINO Trial Investigators and the Australasian Society for Infectious Disease Clinical Research Network (ASID-CRN) (2018). Effect of PTZ vs meropenem on 30-day mortality for patients with *E coli* or *Klebsiella pneumoniae* bloodstream infection and ceftriaxone resistance: A randomized clinical trial. *JAMA*, **320**(10): 984-994.

Hsu WY, Kao TW, Cho HC, Ruan SY, Lee TF, Huang YT, Chien JY; TACTICS (TAiwan CollaboraTive Intensive Care Study) Group (2025). Performance of a hybrid capture-based target enrichment next-generation sequencing for the identification of respiratory pathogens and resistance-associated genes in patients with severe pneumonia. *Microbiol Spectr*, **13**(1): e0213024.

Huang SS, Qiu JY, Li SP, Ma YQ, He J, Han LN, Jiao LL, Xu C, Mao YM and Zhang YM (2024). Microbial signatures predictive of short-term prognosis in severe pneumonia. *Front Cell Infect Microbiol*, **14**: 1397717.

Jacoby GA, Munoz-Price LS (2005). The new beta-lactamases. *N Engl J Med*, **352**(4): 380-391.

Janssens JP and Krause KH (2004). Pneumonia in the very old. *Lancet Infect Dis*, **4**(2): 112-124.

Jeon EJ, Cho SG, Shin JW, Kim JY, Park IW, Choi BW and Choi JC (2011). The difference in clinical presentations between healthcare-associated and community-acquired pneumonia in university-affiliated hospital in Korea. *Yonsei Med J*, **52**(2): 282-287.

Jones ME, Staples AM, Critchley I, Thornsberry C, Heinze P, Engler HD and Sahm DF (2000). Benchmarking the in vitro activities of moxifloxacin and comparator agents against recent respiratory isolates from 377 medical centers throughout the United States. *Antimicrob Agents Chemother*, **44**(10): 2645-2652.

Kang YS, Ryoo SR, Byun SJ, Jeong YJ, Oh JY and Yoon YS (2017). Antimicrobial resistance and clinical outcomes in nursing home-acquired pneumonia, compared to community-acquired pneumonia. *Yonsei Med J*, **58**(1): 180-186.

Katz E, Larsen LS, Fogarty CM, Hamed K, Song J and Choudhri S (2004). Safety and efficacy of sequential i.v. to p.o. moxifloxacin versus conventional combination therapies for the treatment of community-acquired pneumonia in patients requiring initial i.v. therapy. *J Emerg Med*, **27**(4): 395-405.

Kim N, Fischer AH, Dyring-Andersen B, Rosner B and Okoye GA (2017). Research techniques made simple: Choosing appropriate statistical methods for clinical research. *J Invest Dermatol*, **137**(10): e173-e178.

Lai CC, Chen WC, Kuo LK, Wang YT, Fu PK, Ku SC, Fang WF, Chen CM, Tu CY, Cheng WC and Chen CH (2023). The clinical efficacy of cefoperazone-sulbactam versus PTZ in the treatment of severe community-

acquired pneumonia. *Medicine (Baltimore)*, **102**(28): e34284.

Lee MS, Oh JY, Kang CI, Kim ES, Park S, Rhee CK, Jung JY, Jo KW, Heo EY, Park DA, Suh GY and Kiem S (2018). Guideline for antibiotic use in adults with community-acquired pneumonia. *Infect Chemother*, **50**(2): 160-198.

Lee N, Yuen KY and Kumana CR (2003). Clinical role of beta-lactam/beta-lactamase inhibitor combinations. *Drugs*, **63**(14): 1511-1524.

Li Y, Zhu D, Peng Y, Tong Z, Ma Z, Xu J, Sun S, Tang H, Xiu Q, Liang Y, Wang X, Lv X, Dai Y, Zhu Y, Qu Y, Xu K, Huang Y, Wu S, Lai G, Li X, Han X, Yang Z, Sheng J, Liu Z, Li H, Chen Y, Zhu H and Zhang Y (2021). A randomized, controlled, multicenter clinical trial to evaluate the efficacy and safety of oral sitafloxacin versus moxifloxacin in adult patients with community-acquired pneumonia. *Curr Med Res Opin*, **37**(4): 693-701.

Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, Macfarlane JT, Read RC, Roberts HJ, Levy ML, Wani M, Woodhead MA; Pneumonia Guidelines Committee of the BTS Standards of Care Committee (2009). "BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax*, **64**(Suppl 3): iii1-55.

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG; Infectious Diseases Society of America; American Thoracic Society (2007). Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*, **44**(Suppl 2): S27-72.

Mansour-Ghanaei F, Poostizadeh G, Joukar F and Siavoshi F (2022). Efficacy of disc diffusion and agar dilution methods in evaluating helicobacter pylori susceptibility to antibiotics. *Middle East J Dig Dis*, **14**(2): 207-213.

Miravitlles M (2005). Moxifloxacin in respiratory tract infections. *Expert Opin Pharmacother*, **6**(2): 283-293.

Miravitlles M and Anzueto A (2008). Moxifloxacin: A respiratory fluoroquinolone. *Expert Opin Pharmacother*, **9**(10): 1755-1772.

Naaz S, Kaur A and Saeed M (2025). Targeting gram-positive bacterial resistance: An *in-silico* study of phytochemicals from lepidium draba. *Current Indian Science*, **3**.

Oh S, Jang W and Kim B (2024). Is the fluoroquinolone combination necessary for empirical antibiotic regimen in severe community-acquired pneumonia?. *Postgrad Med*, **136**(3): 337-345.

Perry CM and Markham A (1999). Piperacillin/tazobactam: An updated review of its use in the treatment of bacterial infections. *Drugs*, **57**(5): 805-843.

Rahmel T, Asmussen S, Karlik J, Steinmann J, Adamzik M and Peters J (2017). Moxifloxacin monotherapy versus combination therapy in patients with severe community-acquired pneumonia evoked ARDS. *BMC Anesthesiol*, **17**(1): 78.

Reinert RR (2009). The antimicrobial resistance profile of Streptococcus pneumoniae. *Clin Microbiol Infect*, **15 (**Suppl 3): 7-11.

Samaha-Kfoury JN and Araj GF (2003). Recent developments in beta lactamases and extended spectrum beta lactamases. *Bmj*, **327**(7425): 1209-1213.

Seo H, Cha SI, Shin KM, Lim JK, Yoo SS, Lee J, Lee SY, Kim CH, Park JY and Lee WK (2017). Clinical relevance of necrotizing change in patients with community-acquired pneumonia. *Respirology*, **22**(3): 551-558.

Serra ME (2025). Participation and education: The Declaration of Helsinki in today's context. *Arch Argent Pediatr*, **123**(3): e202410585.

Shakoor M, Sadiq N, Akbar M, Shafique M and Mustafa G (2024). Electrochemical Sensor based on molecularly imprinted polymer for the detection of moxifloxacin. *Russ. J. Electrochem.*, **60**(9): 728-736.

Shariati A, Arshadi M, Khosrojerdi MA, Abedinzadeh M, Ganjalishahi M, Maleki A, Heidary M and Khoshnood S (2022). The resistance mechanisms of bacteria against ciprofloxacin and new approaches for enhancing the efficacy of this antibiotic. *Front Public Health*, **10**: 1025633.

Tahmasebi H, Babaeizad A, Mohammadlou M, Alibabaei F, Banihashemian SZ and Eslami M (2024). Reemergence of *Mycoplasma pneumoniae* disease: Pathogenesis and new approaches. *Microb Pathog*, **196**: 106944.

Unal Cetin E, Kurtkulagi O, Kamis F, Das M, Simsek E, Cetin AU and Beyazit Y (2025). Advancing ICU mortality prediction in community-acquired pneumonia: Combining fibrinogen-to-albumin ratio, CT severity score, PSI and CURB-65. *Biomol Biomed*, **25**(9): 2083-2091.

Van der Auwera P, Duchateau V, Lambert C, Husson M, Kinzig M and Sorgel F (1993). Ex vivo pharmacodynamic study of piperacillin alone and in combination with tazobactam, compared with ticarcillin plus clavulanic acid. *Antimicrob Agents Chemother*, **37**(9): 1860-1868.

Xu Y, Zhou X, Zheng W, Cui B, Xie C, Liu Y, Qin X and Liu J (2024). Serotype distribution, antibiotic resistance, multilocus sequence typing and virulence factors of invasive and non-invasive *Streptococcus pneumoniae* in Northeast China from 2000 to 2021. *Med Microbiol I mmunol*, **213**(1): 12.