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Cost-Effectiveness Analysis of Antibiotics in Pneumonia Patients with Diabetes Mellitus Type 2

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ABSTRACT

Background: *Pneumonia poses a high clinical and economic burden, particularly in patients with type 2 diabetes mellitus (DM). Selecting the appropriate antibiotic is essential to ensure both clinical effectiveness and cost efficiency. This study aimed to evaluate the cost-effectiveness of fluoroquinolone monotherapy compared to beta-lactam–macrolide combination therapy in BPJS inpatients with pneumonia and comorbid type 2 DM at Prof. Dr. Sulianti Saroso Infectious Diseases Hospital (RSPI) during 2023–2024.*

Methods: *This retrospective observational study used a cost-effectiveness analysis (CEA) approach, drawing on medical record data. Effectiveness was measured based on the Pneumonia Severity Index (PSI) and length of stay, while total direct medical costs were analyzed to calculate the Average Cost-Effectiveness Ratio (ACER).*

Results: *There was no significant difference in effectiveness or total direct medical costs between the two regimens. However, fluoroquinolone monotherapy had lower total costs (Rp10,090,591) and a smaller ACER value than the beta-lactam–macrolide combination (Rp13,386,045), suggesting that monotherapy was more cost-effective despite similar clinical outcomes.*

Conclusion: *Although statistical differences were not significant, fluoroquinolone monotherapy appeared more cost-effective than beta-lactam–macrolide combination therapy for pneumonia patients with comorbid type 2 DM. These findings may support pharmacoeconomic-based decision-making in antibiotic selection. The study's limitations include a small sample size, a single-center setting, and a retrospective design, which may affect generalizability.*

INTRODUCTION

Pneumonia is a lung disease caused by bacterial, viral, or fungal infections and can occur at any age. The disease is characterized by inflammation of the lung tissue, leading to symptoms such as fever, cough, and shortness of breath. In addition to infectious causes, exposure to chemical or physical agents may also contribute to lung inflammation [1]. Globally, pneumonia remains a major cause of death, with an estimated 2.18 million deaths reported in 2021,

predominantly among individuals aged over 70 years, particularly in sub-Saharan Africa and Southeast Asia [2]. In Indonesia, the prevalence of pneumonia has increased—from 4.0% [3] to 10.8% [4] nationally, and from 3.8% to 9.0% [3–5].

Pneumonia also imposes a significant economic burden. In the United States, inpatient care costs amount to approximately USD 9.5 billion annually, while in Indonesia, pneumonia ranks among the 10 highest BPJS claims, with an average inpatient cost of IDR 3.89–7.12 million per episode and a total claim exceeding IDR 900 billion [6,7]. The burden is greater among patients with comorbid conditions, especially type 2 diabetes mellitus (DM). Diabetic patients have a 3.2-fold higher risk of developing pneumonia, with mortality rates reaching 20–30% [8]. Hyperglycemia impairs immune responses by reducing phagocytic activity and neutrophil function, thereby prolonging infection and recovery time [9,10]. Antibiotic therapy is the mainstay of pneumonia management. However, inappropriate or irrational antibiotic use may contribute to antimicrobial resistance, increased adverse effects, and higher treatment costs [11].

The two regimens commonly used in adult pneumonia are fluoroquinolone monotherapy and beta-lactam–macrolide combination therapy [12,13]. Choosing between these regimens requires consideration of both clinical and economic factors. Pharmacoeconomic studies, particularly cost-effectiveness analyses, provide valuable insights by comparing treatment outcomes with costs incurred [14]. Pharmacoeconomic analysis is important because it accounts for drug costs, hospitalizations, side effects, and therapeutic failure [15,16]. Although the initial costs are higher, appropriate therapy can reduce length of stay and complications [17,18].

Previous studies have yielded mixed results: beta-lactam–macrolide combinations reduce mortality in pneumococcal CAP [19], whereas fluoroquinolone monotherapy is more cost-effective in elderly patients [20] and more clinically effective than the combination [21]. In diabetic patients, IV ceftriaxone or a beta-lactam–macrolide combination may be used [22], whereas levofloxacin has shown less effectiveness than ceftriaxone [23]. Based on this, the study was conducted to analyze the cost-effectiveness of fluoroquinolone monotherapy and beta-lactam–macrolide combination therapy in patients with pneumonia and type 2 diabetes mellitus at Prof. Dr. Sulianti Saroso Infectious Diseases Hospital in the period 2023–2024.

METHODS

This study is an observational, cost-effectiveness analysis design conducted retrospectively using medical records of pneumonia patients with comorbid type 2 diabetes mellitus at Sulianti Saroso Infectious Diseases Hospital (SSIDH) during the period January 2023–December 2024. The study sample consisted of 36 patients who met the inclusion and exclusion criteria. Data collected included patient characteristics, antibiotic therapy type, length of hospitalization, and direct medical costs. The effectiveness of therapy was measured using the Pneumonia Severity

Index (PSI) and length of hospitalization (LOS), while cost analysis was conducted using the Average Cost-Effectiveness Ratio (ACER). Statistical tests included comparative analysis of effectiveness and costs between groups and correlation between effectiveness and costs.

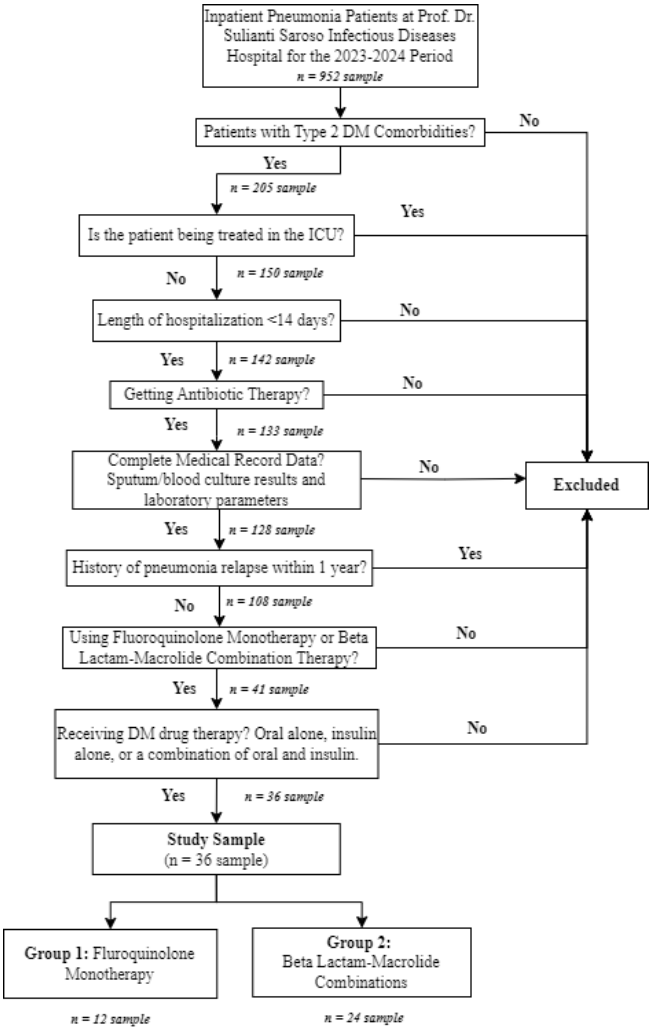

Figure 1. Flowchart of Study Sample Selection

RESULTS

Of the 36 patients included in this study, the majority were female (58.33%) compared to male patients (41.67%). The median age of participants was 61 years, with the largest proportion in the 56–65-year age group (44.44%), followed by those aged >65 years (30.56%). Most patients were hospitalized in 2024 (69.44%), while the rest were from 2023 (30.56%). Clinical characteristics showed variation in severity according to the Pneumonia Severity Index (PSI), with the majority classified as moderate to severe. In terms of therapy, patients were treated either with fluoroquinolone monotherapy or a combination of beta-lactam and macrolide

antibiotics. Direct medical costs and clinical outcomes, including length of stay (LOS), were analyzed to evaluate the cost-effectiveness of both therapeutic approaches (Table 1).

Table 1. Patient Characteristics Based on Gender and Age

Characteristics	Number of Patients	Percentage
Year		
2023	11	30,56%
2024	25	69,44%
Gender		
Man	15	41.67%
Woman	21	58.33%
Age		
18-25	0	0
26-35	0	0
36-45	1	2.78%
46-55	8	22.22%
56-65	16	44.44%
>65	11	30.56%

In terms of drug utilization, antibiotics were administered either as single fluoroquinolone therapy or as a combination of beta-lactam and macrolide. The majority of patients received the combination regimen (66.67%), while a smaller proportion received fluoroquinolone monotherapy (33.33%). Regarding diabetes mellitus therapy, half of the patients were managed with single insulin therapy (50%), followed by those who received a combination of oral agents and insulin (41.67%). Only a small proportion of patients were treated with oral antidiabetic drugs alone (8.33%) (Table 2).

Table 2. Distribution of Antibiotic Drug Use and DM Therapy

Drug Use	Number of Patients	Percentage
Antibiotics		
Single Fluoroquinolone	12	33.33%
Beta Lactam-Macrolide Combination	24	66.67%
DM Therapy		
Oral Single	3	8.33%
Single Insulin	18	50%
Oral & Insulin Combination	15	41.67%

With regard to hospitalization outcomes, the majority of patients experienced a length of stay (LOS) between 6 and 10 days, accounting for 69.44% of the study population. A smaller proportion of patients had shorter hospitalizations of ≤5 days (13.89%), while 16.67% required prolonged care of more than 10 days. These findings indicate that most patients required

approximately one week of hospitalization for the management of pneumonia with type 2 diabetes mellitus comorbidity (Table 3).

Table 3. Distribution of Patients Based on Length of Stay (LOS)

Patient LOS	Number of Patients	Percentage
≤ 5 days	5	13.89%
6-10 days	25	69.44%
> 10 days	6	16.67%
Total	36	100%

Analysis of the relationship between antibiotic therapy type and patient length of stay (LOS) showed that those receiving single fluoroquinolone therapy had an average LOS of 7.23 days, while patients treated with a beta–lactam–macrolide combination had a slightly longer LOS of 7.54 days. Statistical analysis using the Independent T-Test revealed no significant difference between the two groups ($p = 0.853$), suggesting that both antibiotic regimens yielded comparable hospitalization durations (Table 4).

Table 4. Distribution of Patient LOS Duration Based on Antibiotic Class

Use of Antibiotic Therapy	Average LOS	*p-value*
Single Fluoroquinolone	7.23	0.853
Beta Lactam-Macrolide Combination	7.54	
Average	**7.52**	

* Independent T-Test

Evaluation of the effectiveness of antibiotic therapy based on changes in the Pneumonia Severity Index (PSI) and length of stay (LOS) showed comparable outcomes between the two treatment groups. Patients receiving single-fluoroquinolone therapy had an average PSI reduction of 10.00 and an average LOS of 7.23 days, resulting in an effectiveness value of 1.489. Meanwhile, those treated with a beta–lactam–macrolide combination achieved a slightly higher PSI reduction of 10.42, but with a longer LOS of 7.54 days, resulting in a comparable effectiveness score of 1.481. Overall, both regimens demonstrated nearly equal clinical effectiveness in improving patient outcomes (Table 5).

Table 5. Effectiveness of Antibiotic Therapy

Antibiotic Therapy	Average ΔPSI (initial PSI – final PSI)	Average LOS	Effectiveness ($\frac{\Delta PSI}{LOS}$)
Single Fluoroquinolone	10.00	7.23	1,489
Beta Lactam-Macrolide Combination	10,4167	7.54	1,481
Average	**10,278**	**7.52**	**1,484**

Analysis of the average direct medical costs revealed noticeable differences between the two antibiotic therapy groups. Patients receiving single-fluoroquinolone therapy incurred a total direct medical cost of Rp10,090,591, which was lower than Rp13,386,045 in the beta–lactam–macrolide combination group. The largest cost components in both groups were examination and supporting costs, followed by service fees and other drug costs. Interestingly, while antibiotic costs were slightly higher in the fluoroquinolone group, other components, such as medical device and BMHP costs, medical procedure fees, and service fees, were markedly higher in the beta–lactam–macrolide combination group. Despite these numerical differences, statistical analysis showed no significant difference in overall direct medical costs between the two groups (p = 0.568) (Table 6).

Table 6. Overview of Average *Direct Medical Costs*

Types of Direct Medical Costs	**Average *Direct Medical Cost***	
	Single Fluoroquinolone	**Beta Lactam-Macrolide Combination**
Antibiotic Costs	Rp540,205	Rp412,684
Other Drug Costs	Rp2,270,687	Rp2,363,130
Medical Device and BMHP Costs	Rp229,325	Rp803,224
Examination and Supporting Costs	Rp3,575,571	Rp3,552,358
Medical Procedure Fees	Rp378,871	Rp2,107,183
Service Fee	Rp1,851,475	Rp2,520,173
Accommodation Fees	Rp1,211,125	Rp1,589,583
Administrative Fees	Rp. 33,333	Rp37,708
Total	**Rp10,090,591**	Rp13,386,045
p-value	**0.568**	

* Mann-Whitney Test

The cost-effectiveness analysis was further evaluated using the Average Cost-Effectiveness Ratio (ACER). Patients who received single fluoroquinolone therapy showed a lower ACER value (Rp6,776,756.88) compared to those treated with the beta–lactam–macrolide combination (Rp9,038,517.89). This indicates that, although both regimens demonstrated similar levels of effectiveness, fluoroquinolone therapy required lower costs per unit of effectiveness gained. These findings suggest that single-fluoroquinolone therapy is the more cost-effective option for treating pneumonia in patients with type 2 diabetes mellitus (Table 7).

Table 7. Calculation of *the Average Cost-Effectiveness Ratio* (ACER) Value

Code	**Use of Antibiotic Classes**	**Average *Direct Medical Cost* (C)**	**Average Effectiveness (E)**	**ACER (C/E)**
a	Single Fluoroquinolone	Rp10,090,591	1,489	Rp. 6,776,756.88
b	Beta Lactam-Macrolide Combination	Rp13,386,045	1,481	Rp. 9,038,517.89

DISCUSSION

This study involved 36 pneumonia patients with comorbid type 2 diabetes mellitus at Prof. Dr. Sulianti Saroso Infectious Diseases Hospital (RSPI) during January 2023–December 2024. Most patients were hospitalized in 2024 (69.44%), and the majority were female (58.33%). The largest age group was 56–65 years (44.44%), followed by >65 years (30.56%). Although pneumonia is generally reported more often in men, previous studies have found no consistent gender-related differences in incidence or outcomes [24]. This variation may be associated with health-seeking behaviors and hormonal differences that affect immune response [25]. The predominance of older patients aligns with findings by Weber and Kim et al. that immunosenescence and comorbidities such as diabetes, hypertension, and chronic lung disease increase pneumonia susceptibility and severity [26].

Antibiotic use in this study showed that the beta-lactam–macrolide combination was prescribed more frequently (66.67%) than fluoroquinolone monotherapy (33.33%). This reflects clinicians' adherence to national guidelines that recommend both options depending on disease severity and patient condition [13]. Combination therapy is often used to broaden the antibacterial spectrum in moderate to severe infections [12], whereas monotherapy may be chosen when the causative organisms and sensitivities are well known. This is in accordance with the Indonesian Pulmonary Physicians Association (PDPI) recommendation that beta-lactam–macrolide combinations are suitable for severe pneumonia without risk of MRSA or Pseudomonas aeruginosa [27].

The findings of this study indicate that both antibiotic regimens fluoroquinolone monotherapy and beta-lactam–macrolide combination showed relatively similar clinical effectiveness, as reflected by comparable PSI score reduction and length of stay (LOS). These results differ from the study by Lai et al. (2024), which reported slightly lower outcomes for monotherapy [28], but align with the findings of Holland & Jahnke (2021), who observed no significant differences in lung function, need for additional therapy, or adverse events between the two regimens [29]. Variations across studies may result from differences in patient populations, pneumonia severity, and comorbid conditions [30].

Regarding diabetes management, half of the patients received insulin monotherapy (50%), followed by combined insulin–oral therapy (41.67%) and oral monotherapy (8.33%). This distribution reflects the need for strict glycemic control, as hyperglycemia in diabetes compromises immune function and increases susceptibility to infection [31]. Insulin remains the preferred option due to its rapid onset and dose flexibility [32]. The small proportion of patients on oral agents is consistent with Rusli et al. (2024), who noted that oral therapy is generally reserved for patients with stable, well-controlled diabetes [33].

Most patients were hospitalized for 6–10 days (69.44%), with an average LOS of 7.52 days. These results align with studies reporting average LOS of 7–11 days among CAP patients with diabetes [34–36]. LOS is influenced by factors such as age, disease severity, and comorbidities [37–39]. In this study, LOS did not differ significantly between fluoroquinolone monotherapy (7.23 days) and beta-lactam–macrolide combination therapy (7.54 days; $p = 0.853$), suggesting that the choice of antibiotic regimen did not significantly affect the duration of recovery. According to national guidelines, the duration of hospitalization should be adjusted based on clinical improvement [13,40]. Differences in LOS between antibiotic regimens can be due to infection severity, clinical response, and the complexity of the patient's medical condition [41].

Therapeutic effectiveness, expressed as PSI reduction per hospital day (ΔPSI/LOS), was nearly identical between regimens 1.489 for fluoroquinolone and 1.481 for combination therapy indicating clinical equivalence. Beta-lactam–macrolide combinations are typically selected to broaden antibacterial coverage, especially against atypical pathogens [13]; however, this study found no additional clinical benefit over single-agent fluoroquinolone therapy. Xu (2022) and Efriani (2025) also reported no significant difference between the two, although fluoroquinolones may offer faster symptom improvement and fewer side effects [42,43]. These outcomes suggest that variations in response may be more attributable to patient-specific factors, such as age, disease severity, or glycemic control, rather than to the antibiotic regimen itself [31].

From an economic standpoint, the average total direct medical cost (DMC) was lower in the fluoroquinolone group (Rp10,090,591) compared to the combination group (Rp13,386,045). Although this difference was not statistically significant ($p = 0.568$), it suggests a higher cost burden for combination therapy. The largest contributors to total cost were supporting examinations and medical services, while antibiotic expenses accounted for a relatively small portion. This pattern aligns with Haris et al. (2022), Aoralia (2022), and Nurjahan et al. (2024), who found that patients on combination therapy generally have more complex conditions requiring extended care and procedures, leading to higher overall costs [44–46]. In addition, diabetic comorbidity increases medical expenditures due to insulin and adjunctive drug needs, longer LOS, and intensive monitoring [47,48]

Cost-effectiveness analysis using the Average Cost-Effectiveness Ratio (ACER) showed that fluoroquinolone monotherapy was more cost-efficient, with an ACER of Rp6,776,756.88 per PSI point/day compared to Rp9,038,517.89 for the combination. Given that both regimens demonstrated similar effectiveness (1.489 vs. 1.481 PSI/day), this cost-effectiveness advantage stems primarily from lower overall costs rather than superior clinical outcomes. Mann–Whitney analysis confirmed no significant differences in cost ($p = 0.568$) or effectiveness ($p = 0.946$). A significant negative correlation between effectiveness and DMC ($\rho = -0.653$; $p < 0.001$) indicates that higher therapeutic effectiveness was associated with lower treatment costs.

Overall, fluoroquinolone monotherapy appeared more cost-effective than the beta-lactam–macrolide combination, achieving comparable outcomes at lower costs. However, therapy selection should remain individualized to the patient's condition and infection severity, consistent with national guidelines [13,40]. These findings are consistent with those of Rahardjoputro and Efriani [23,43], who reported shorter hospitalization and lower total costs with fluoroquinolone monotherapy. Combination therapy is typically used in more severe cases, thereby contributing to higher healthcare expenditures [46,48].

From a pharmacoeconomic perspective, these findings illustrate the principle of allocative efficiency, emphasizing that healthcare resources should favor regimens that achieve optimal clinical outcomes at minimal cost. In pneumonia with comorbid diabetes mellitus, rational antibiotic selection such as effective monotherapy can minimize hospitalization expenses while avoiding unnecessary combination therapy [8]. The observed negative correlation between treatment effectiveness and total cost reinforces the importance of early, appropriate therapy for both clinical recovery and cost reduction.

A key limitation of this study is the unequal sample distribution between treatment groups and its single-center, retrospective design, which may limit generalizability. Consequently, this study was restricted to ACER analysis without ICER calculation. Nevertheless, the results underscore the importance of rational antibiotic use, in accordance with the National Guidelines for Medical Services and PDPI recommendations (2022), which advocate monotherapy as the preferred option when clinically effective, reserving combination therapy for cases with clear indications [13,27].

CONCLUSION

This study found that fluoroquinolone monotherapy and beta-lactam–macrolide combination therapy were comparable in clinical effectiveness for patients with pneumonia and comorbid type 2 diabetes mellitus. However, fluoroquinolone monotherapy appeared more cost-efficient, showing similar outcomes at a lower overall treatment cost. Although the difference between regimens was not statistically significant, the findings suggest that single-agent fluoroquinolone therapy may be a more practical and cost-effective option for managing pneumonia in diabetic patients, provided it remains clinically appropriate. Nonetheless, these results should be interpreted with caution. The study’s retrospective design, small and unequal sample size, and single-center setting limit the generalizability of the findings. Future research with larger, prospective, and multi-center designs is recommended to confirm these results and to explore broader economic evaluations, such as cost-utility or cost-benefit analyses, to strengthen the evidence base for antibiotic selection in pneumonia patients with comorbidities.

DECLARATIONS

Ethics approval

This study was approved by the Ethical approval obtained from the Research and Community Service Ethics Committee of Sulianti Saroso Infectious Disease Hospital (No. PP.07.01/D.XXXIX.14/26/2025).

Conflict of interest

The authors declare no conflict of interest.

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