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# Analysis of Antibiotic Therapy Accuracy and Drug Interaction in Pneumonia Inpatients at The Islamic Hospital Jakarta Cempaka Putih

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**Keywords:** Treatment accuracy, Drug interactions, Polypharmacy, Pneumonia.

**Abstract:** Polypharmacy may increase the risk of drug interactions affecting toxicity and therapeutic efficacy in pneumonia patients. This study aimed to analyse evaluation of pneumonia management, polypharmacy, relationship between polypharmacy and occurrence of drug-drug interactions, and relationship between drug-drug interactions and length of hospital stay of pneumonia patients. The study design used a quantitative descriptive approach with cross-sectional and retrospective data collection and a total sample of 113 samples that met the criteria. Analyses were performed using Spearman's rho correlation test to assess the association of polypharmacy with drug interactions, and the association of drug interactions with length of hospital stay. Medication accuracy was measured using PDPI (The Indonesian Lung Doctors Assosiaciation) guidelines, drug interactions using drugs.com and/or Medscape.com. Results showed 59.29% of patients were female, with the majority aged over 65 (55.65%). Most patients (91.15%) paid with BPJS, 62.61% were hospitalised for 1-5 days and 81.74% had comorbidities. Treatment accuracy in this study was 49.56%. 106 drug interactions were identified in a total of 226 cases. 66% of the interactions were pharmacodynamic with moderate severity (79%), such as the interaction between combivent and ondansetron. Mild pharmacokinetic interactions were common, especially between ranitidine and paracetamol (22 cases). There is a correlation between polypharmacy and drug interactions with a p-value 0.000 and there is a correlation between the number of drug interactions and length of hospitalisation with p-value 0.000. Conclusion of this study is polypharmacy increases the risk of drug interactions and affects the length of hospital stay in pneumonia patients.

## Introduction

Pneumonia is one of the acute conditions of the lower respiratory tract caused by infectious agents (1). There is pain when breathing and difficulty in inhaling oxygen due to disturbances in inhalation (2). Additional symptoms indicating the presence of pneumonia include discomfort when inhaling air and experiencing coughing. Pneumonia is a sharp infection in the lungs affecting the alveoli, the air sacs in the lungs, caused by various microorganisms including viruses, bacteria, fungi, and parasites (3). Pneumonia is a leading cause of hospitalization among adults and children in the United States, resulting in over 800,000 hospitalizations and over 400,000 emergency department visits in 2014 (4). According to the WHO report, acute respiratory tract infections are the 3rd leading cause of death worldwide. In 2015, the number of deaths due to acute respiratory tract infections reached 3.2 million worldwide. The incidence of pneumonia reached 9.2 million deaths in one year worldwide, with 92% of cases in Asia and Africa. Globally, the death toll from pneumonia in 2019 in the 15-69 age group reached 551,524 (5).

Meanwhile, preliminary data from the Jakarta Provincial Health Office in early 2023 also showed an increase in pneumonia cases compared to early 2022 (6). Based on data from the Jakarta Provincial Central Bureau of Statistics, in 2018 there were 14,629 cases of pneumonia in Jakarta, which then increased to 19,973 cases in 2021. According to data from the Jakarta Health Office between January and June 2023, there were 638,291 cases of acute respiratory tract infections (ARI) recorded (7). This increase in cases, based on research resulted in findings indicating a relationship between increased nitrogen dioxide (NO2) levels and pneumonia rates in Jakarta (8, 9). Air pollution of various kinds, such as dust, dirt, or gases (CO, NO, and SO) in the air, can be a long-term health problem, one of which is pneumonia (10).

Therapeutic treatment for pneumonia patients generally involves antibiotics. Antibiotics need to be selected based on culture results; however, empirical antibiotic choices can be

applied while waiting for more accurate culture results (2). According to the American Thoracic Society and the Infectious Diseases Society of America in 2019, therapy for community-acquired pneumonia involves the use of antibiotics such as amoxicillin, doxycycline, macrolides, cephalosporins, and fluoroquinolones (11). In addition to antibiotic therapy, for maximum treatment outcomes, pneumonia therapy also requires supportive treatment (12). Supportive treatment consists of several drugs such as antihistamines, antipyretics, antitussives, and vitamins. If patients have comorbidities or underlying diseases, they will receive more therapy, potentially leading to polypharmacy treatment and the risk of unexpected drug interactions (13).

Previous research at Respira Yogyakarta Hospital found 79 drug interaction incidents in pneumonia treatment. Of the total potential interactions, 16.48% were classified as major, 22.78% as moderate, and 60.76% as minor. A similar study was also conducted at Dr. Soedarso Pontianak Regional General Hospital in 2019, where 13 out of 30 samples showed drug interactions in combination antibiotic therapy with non-antibiotics. The severity rates were 25% for major, 18.75% for moderate, and 37.50% for minor (14).

According to a WHO report, household air pollution causes the premature deaths of 3.2 million people annually, due to diseases related to household air pollution. Particulates and other pollutants in households lead to lung inflammation, disrupt the immune response, and reduce the oxygen-carrying capacity of the blood. Additionally, previous research has found a correlation between increased nitrogen dioxide (NO2) levels and pneumonia cases in Jakarta. Air pollution comes in various forms, such as dust, dirt, or gases (CO, NO, and SO gases) in the air. Long-term exposure to air pollution can lead to health problems, one of which is pneumonia (15). According to IQAir on August 15, 2023, Jakarta ranked as the fourth worst city in the world with an air quality index of 157, indicating unhealthy air (16).

The Jakarta Provincial Government is one of the provinces in Indonesia with very high pollution levels, both due to environmental factors and human factors. Based on the high pollution problem resulting in increased pneumonia rates and also based on the problem of polypharmacy treatment of pneumonia patients undergoing hospitalization, the author intends to conduct research on the evaluation of polypharmacy drug interactions in adult pneumonia patients in the inpatient of Islamic Hospital Jakarta Cempaka Putih.

# Methodology

## Study Design

This research employed a cross-sectional design with retrospective data collection from adult inpatients diagnosed with pneumonia between January and December 2023. Ethical approval was obtained from the Ethics Committee of the Faculty of Pharmacy, Pancasila University (No. 001/KEPK-FFUP/V/2024).

## Study Setting and Population

This study was conducted at Jakarta Islamic Hospital Cempaka Putih between January and December 2023 on inpatients diagnosed with pneumonia. Inclusion criteria were adult patients (≥17 years) with pneumonia, with or without comorbidities, who received treatment with more than five medications. Exclusion criteria were incomplete or unclear medical records, concomitant infectious diseases, hospitalization of less than 24 h, referral cases, and records of deceased patients.

## Data Collection Procedures

The data source for this study was patient medical records. The variables assessed included antibiotic evaluation, defined as the appropriateness of dosage, frequency, route of administration, indication, and adherence to clinical guidelines, as well as drug interaction analysis, which encompassed the severity and mechanism of interaction (pharmacokinetic or pharmacodynamic). Adherance antibiotics used was evaluated using the pneumonia management guidelines issued by the Indonesian Society of Respirology (PDPI), by comparing the medications prescribed to patients. In this study, we defined the use of antibiotics as rational when the type, dose, and frequency of the antibiotic were appropriate; if any of these aspects were inappropriate, the antibiotic use was considered irrational. The evaluation included, among others, the type of antibiotic, drug dosage, and route of administration while drug–drug interactions were identified using *Drugs.com, Medscape*, and *Stockley's Drug Interactions.* The correlation analysis with Spearman's rho was applied to determine the association between polypharmacy and the number of drug–drug interactions.

## Outcomes Measures

This study obtained data on the number of medication appropriateness cases compared with the guidelines, the number of drug–drug interactions identified, and the length of hospital stay, which was then compared with the number of drug–drug interactions.

## Data Analysis

Sociodemographic data were grouped to describe patient characteristics, including age, gender, and length of hospital stay. Drug use data encompassed the type, quantity, and class of medications administered to adult pneumonia patients, while clinical assessment data included diagnoses, dosages, administration rules, and potential drug–drug interactions. Drug interactions were classified into pharmacokinetic interactions, occurring when co-administered drugs affect absorption, distribution, metabolism, or excretion, and pharmacodynamic interactions, which occur when drugs act on similar receptors or physiological pathways.

Data were organized to evaluate patient demographics, polypharmacy patterns, and interaction risk, as well as to examine the relationship between the number of concurrently used drugs and hospital stay. Inferential statistical analysis was performed using Spearman's rho correlation to assess the association between polypharmacy and interaction frequency, and between interaction frequency and length of hospital stay in pneumonia patients.

# Result and Discussion

## Patient Sociodemographic Characteristics

The study was conducted in DKI Jakarta, specifically at Islamic Hospital Jakarta Cempaka Putih. Data collection was carried out retrospectively using secondary data from the medical records of inpatients diagnosed with pneumonia during the period of January-December 2023. This study used total sampling technique, with 113 medical records of patients meeting the inclusion criteria selected as the research sample, and the patients' sociodemographic characteristics are presented in **Table 1**.

**Table 1.** Patient sociodemographic characteristics.

| Patient Characteristics | n | % |
|---|---|---|
| **Gender** | | |
| Male | 46 | 40.71 |
| Female | 67 | 59.29 |
| **Age (Years)** | | |
| 17-25 | 4 | 3.54 |
| 26-35 | 3 | 2.65 |
| 36-45 | 4 | 3.54 |
| 46-55 | 18 | 15.93 |
| 56-65 | 21 | 18.58 |
| >65 | 63 | 55.75 |
| **Fee Guarantee** | | |
| Insurance | 3 | 2.66 |
| BPJS | 103 | 91.15 |
| Private | 7 | 6.20 |
| **Comorbidity** | | |
| Yes | 92 | 81.42 |
| No | 21 | 18.58 |
| **Length of Stay (Days)** | | |
| 1-5 | 70 | 61.95 |
| 6-10 | 38 | 33.63 |
| 11-15 | 3 | 2.65 |
| >15 | 2 | 1.77 |
| **Polypharmacy (amount of drugs)** | | |
| 5-10 | 83 | 73.00 |
| 11-15 | 21 | 19.00 |
| 16-20 | 7 | 6.00 |
| 21-25 | 2 | 2.00 |

Based on findings at Islamic Hospital Jakarta Cempaka Putih, the total number of female patients was higher than male patients, with 67 female patients (59.29%) and 46 male patients (40.71%). Previous research yielded different results. Meilita's study (15) reported that male patients contributed 53%, while females contributed 47%. Similarly, previous study showed that male patients outnumbered females in four different hospitals, with 398 males (54.44%) and 333 females (45.56%) (16).

Age grouping was done to assess the distribution of pneumonia at the hospital. In this study, age groups were classified into six categories according to the classification by the Ministry of Health of the Republic of Indonesia in 2009: 17 to 25 years, 26 to 35 years, 36 to 45 years, 46 to 55 years, 56 to 65 years, and over 65 years. The results showed an increase in pneumonia cases with increasing age. This trend is consistent with the findings of RISKESDAS DKI Jakarta in 2018, which also showed a higher percentage of pneumonia patients with increasing age (17).

Previous study revealed that the distribution of pneumonia patients in the inpatient ward included 6% in the early elderly age group (46 to 55 years), 6% in the advanced elderly age group (56 to 65 years), and 10% in the geriatric age group (>65 years). The incidence of pneumonia increases 5 to 10 times in the elderly compared to adults (18).

In the results of this study, it was found that 103 patients (91.15%) used BPJS Health insurance, 3 patients (2.66%) used other insurance, and 7 patients (6.20%) paid independently or publicly without using health insurance. This is consistent with the previous research conducted, where the majority of patients used BPJS, namely 70.42% (19).

In this study, most pneumonia patients were hospitalized for 1-5 days (61.95%), followed by 6-10 days (33.63%), 11-15 days (2.65%), and more than 15 days (1.77%). The average length of hospital stay was 6 days, with the fastest patient being hospitalized for 2 days and the longest patient being hospitalized for 18 days. These findings are consistent with previous research indicating that most pneumonia patients are hospitalized for less than 10 days (2).

In this study, a total of 91 patients (80.53%) had comorbidities, while 22 patients (19.47%) did not have any comorbidities. This distribution is consistent with previous research findings showing the prevalence of comorbidities in pneumonia patients. Among patients with comorbidities, cardiovascular disease was the most common secondary diagnosis (29.57%), followed by hypokalemia (19.89%) and hyponatremia (10.75%). These findings are consistent with other research indicating the correlation between pneumonia and heart failure as well as other cardiovascular comorbidities (20).

## Evaluation of Antibiotic Use

### Types of Antibiotics

In this study, the majority of pneumonia patients received single antibiotic therapy, with 73 patients (64.50%) receiving it, as shown in **Table 2**.Combination therapy with two antibiotics was used in 35 patients (30.97%), while combination therapy with three antibiotics was applied to 5 patients (4.42%). The initial selection of antibiotics was based on broad-spectrum empirical antibiotics while awaiting culture results. This finding is consistent with the study by Khairani *et al*., which showed the use of single antibiotics in 57.34% of patients, combination therapy with two antibiotics in 36.70% of patients, combination therapy with three antibiotics in 5.50% of patients, and combination therapy with four antibiotics in 0.46% of patients (19).

Based on the research findings, as presented in **Table 3**, 53% of the types of antibiotics used at Islamic Hospital Jakarta Cempaka Putih have complied with the pneumonia treatment guidelines recommended by the PDPI. However, 53 patients (47%) received antibiotics that did not adhere to these guidelines, primarily due to the use of single antibiotics other than levofloxacin and moxifloxacin. According to the PDPI, the recommended single antibiotics are only levofloxacin and moxifloxacin, while other antibiotics are recommended to be given in combination (3).

Previous research indicates that rational antibiotic use reached 76.5%, while irrational use accounted for 23.5%. The assessment of antibiotic rationality is based on the type, dose, and frequency of antibiotic administration. In terms of dosage accuracy, 94% of antibiotic therapy adhered to the PDPI guidelines, while 6% did not. Based on the frequency of antibiotic administration, 91% were in accordance with the PDPI guidelines. Examples of dosage and frequency inaccuracies in this study include the use of ceftazidime, which should be given at a dose of 2 grams every 8 h, but in this study, it was only given at 1 gram every 12 h. Additionally, levofloxacin was administered at a dose of 500 mg, whereas it should have been 750 mg (3). Dosages that

**Table 2.** Antibiotic use inpatients pneumonia.

| Antibiotic use | Antibiotics | n | % |
|---|---|---|---|
| Single use antibiotics | Ampicilin Sulbaktam 4x1.5 g | 1 | 0.88 |
| | Azithromycin 1x500 mg | 2 | 1.77 |
| | Cefixime 1x2 g | 1 | 0.88 |
| | Cefotaxime 2x1 g | 1 | 0.88 |
| | Cefotaxime 3x1 g | 3 | 2.65 |
| | Cefoperazone 3x1 g | 2 | 1.77 |
| | Ceftazidime 3x2 g | 1 | 0.88 |
| | Ceftriaxone 1x2 g | 35 | 30.97 |
| | Levofoxacin 1x750 mg | 24 | 21.24 |
| | Levofoxacin 1x500 mg | 3 | 2.65 |
| Two combination use antibiotics | Azithromycin 1x500 mg+Ceftriaxone 1x2 g | 9 | 7.95 |
| | Levofoxacin 1x500 mg+Ceftazidime 2x1 g | 1 | 0.88 |
| | Levofoxacin 1x750 mg+Ceftriaxone 1x2 g | 19 | 1.77 |
| | Levofoxacin 1x500 mg+Cefoperazone 2x1 g | 1 | 0.88 |
| | Levofoxacin 1x750 mg+Cefoperazone 3x1 g | 2 | 1.77 |
| | Levofoxacin 1x750 mg+Cefotaxime 3x1 g | 1 | 0.88 |
| | Levofoxacin 1x750 mg+Ceftazidime 2x1 g | 1 | 0.88 |
| | Moxifloxacin 1x400 mg+Meropenem 3x1 g | 1 | 0.88 |
| Three combination use antibiotics | Levofoxacin 1x750 mg+Ceftriaxone 1x2 g+Meropenem 3x1 g | 1 | 0.88 |
| | Levofoxacin 1x500 mg+Levofoxacin 1x750 mg+Ceftriaxone 1x2g | 1 | 0.88 |
| | Azitromisin 1x500 mg+Ceftriaxone 1x2 g+Cefoperazone 3x1 g | 1 | 0.88 |
| | Ceftriaxone 1x3 g+Ceftriaxone 1x2 g+Levofoxacin 1x750 mg | 1 | 0.88 |
| | Ceftriaxone 1x2 g+Levofoxacin 1x750 mg+Cefoperazone 3x1 g | 1 | 0.88 |

**Table 3**. Analysis of antibiotic therapy accuracy based on PDPI guidelines.

| Guideline Adherence | n | % |
|---|---|---|
| **Antibiotic Type** | | |
| Adherence | 60 | 53 |
| Non adherence | 53 | 47 |
| **Antibiotic Dosage** | | |
| Adherence | 106 | 94 |
| Non Adherence | 7 | 6 |
| **Antibiotic Usage Frequency** | | |
| Adherence | 103 | 91 |
| Non Adherence | 10 | 9 |

are too low or too high, as well as inappropriate frequency of administration, can affect antibiotic levels in the body, hinder therapeutic goals, and potentially lead to antibiotic resistance (21, 22). Doses of antibiotics that are too low will not reach the minimum effective level, while doses that are too high can have toxic effects (23, 24). These research findings are consistent, where the administration of cefotaxime, which should have been every 8 h according to the PDPI guidelines, was given every 12 h (19, 25).

## Drug Interactions

The concurrent use of medications in adult patients with pneumonia in 2023 resulted in 106 drug interactions, totaling 226 cases, as presented in **Table 4**.Pharmacodynamic interactions most frequently occurred at a moderate severity level, for example, there were 11 cases of interaction between combivent and ondansetron. This interaction can lead to irregular heart rhythms and prolonged QT interval, increasing the risk of ventricular arrhythmia. Major pharmacodynamic interactions were most common found in the use of potassium chloride with candesartan, totaling 4 cases, which increases the risk of hyperkalemia. Minor pharmacodynamic interactions were most often found in the combination of methylprednisolone with combivent, which can cause hypokalemia and increase the risk of ventricular arrhythmia (26).

**Table 4.** Drug interactions and severity level.

| Interactions and severity | n | % |
|---|---|---|
| **Pharmacodynamic (n=70)** | | |
| Additive | 12 | 17 |
| Synergistic | 38 | 54 |
| Antagonistic | 20 | 29 |
| **Severity Pharmacodynamic** | | |
| Mayor | 8 | 11 |
| Moderate | 55 | 79 |
| Minor | 7 | 10 |
| **Pharmacokinetics (n=36)** | | |
| Absorption | 13 | 36 |
| Distribution | 2 | 6 |
| Metabolism | 12 | 33 |
| Excretion | 9 | 25 |
| **Severity Pharmacokinetic** | | |
| Mayor | 1 | 3 |
| Moderate | 26 | 72 |
| Minor | 9 | 25 |

**Table 5**. Correlation polypharmacy and drug interaction.

| Correlation | | | |
|---|---|---|---|
| Polypharmacy | Drug Interaction | | |
| Polypharmacy | Correlation Coefficient | 1.000 | .573** |
| | Sig. (2-tailed) | .000 | |
| | N | 113 | 113 |
| Drug Interaction | Correlation Coefficient | .573** | 1.000 |
| | Sig. (2-tailed) | .000 | |
| | N | 113 | 113 |
| **Description:** **. Correlation is significant at the 0.01 level (2-tailed) | | | |

**Table 6.** Correlation drug interaction and length of stay at hospital.

| Correlation | | | |
|---|---|---|---|
| Drug Interaction | Length of Stay | | |
| Drug Interaction | Correlation Coefficient | 1 | .368** |
| | Sig. (2-tailed) | .000 | |
| | N | 113 | 113 |
| Length of Stay | Correlation Coefficient | .368** | 1 |
| | Sig. (2-tailed) | .000 | |
| | N | 113 | 113 |
| **Description:**** *Correlation is significant at the 0.01 level (2-tailed)* | | | |

## Drug Interaction Incidence and Polypharmacy

In this study, out of 113 pneumonia patients, the average use of medications was 9 types of drugs per patient, with a maximum usage of 25 types of drugs and a minimum of 5 types of drugs. Out of this total, 92 patients (81.42%) experienced drug interactions. The same with another research the level of polypharmacy analysed was a minimum of 5 drugs and a maximum of 17 drugs received by patients during treatment, based on 182 samples. It is known that 108 patients (59.34%) were treated with 5-9 drugs and 74 patients (40.66%) were treated with ≥ 10 drugs (27).

Analysis conducted in SPSS revealed a p-value of 0.000, indicating a significant correlation between polypharmacy and the number of drug interactions (p-value <0.05). The Correlation Coefficient value of 0.573 suggests a strong correlation between polypharmacy and the number of drug interactions. These findings are consistent with a previous study, which a significant correlation between polypharmacy and the potential for drug interactions in pneumonia patients, patients receiving more than 5 types of medication were at a 10.1 times higher risk of experiencing drug interactions compared to those receiving fewer than 6 types of medication (13, 28).

Furthermore, there was a correlation between the length of hospital stay and the incidence of drug interactions, with a p-value of 0.000. However, this result contradicts with another study, which did not find a significant correlation between drug interactions and the length of hospital stay in pneumonia patients. This suggests that not all drug interactions affect the length of hospital stay, depending on the management and actions taken by healthcare professionals to address these interactions. In the **Table 4**, explain about correlation between Polypharmacy and drug interaction (2). As shown in **Table 5**, there was also a significant correlation between polypharmacy and the occurrence of drug interactions.

### Drug Interaction Incidence and Polypharmacy

Based on the SPSS analysis, as presented in **Table 6**, there is a fairly strong correlation between the length of hospital stay and the incidence of drug interactions, with a p-value of 0.000 and a correlation coefficient of 0.368. This is supported by the findings that the majority of drug interactions are moderate, meaning that the interaction requires additional care because of some of its effects (27). This result is in contrast to a previous study, which found no significant correlation between drug interactions and length of hospital stay in pneumonia patients. This finding suggests that not all drug interactions necessarily affect the length of hospital stay. It depends on how the interactions are managed by healthcare professionals (2) .

These findings highlight the importance of appropriate drug management and monitoring of drug interactions to improve the quality of pneumonia patient care. Compliance with antibiotic treatment guidelines is crucial to reduce the risk of antibiotic resistance and ensure therapy effectiveness. Education and training for medical professionals on appropriate drug use guidelines and the importance of monitoring drug interactions need to be enhanced (19).

The weakness of this study is that the data collection was retrospective, so that the interactions obtained in this study were only reported to the hospital. However, it was confirmed that these interactions did not cause any adverse effects on patients, and all patients were discharged with the doctor's permission.

This study provides a comprehensive overview of pneumonia patient profiles, antibiotic use, and drug interactions at Islamic Hospital Jakarta Cempaka Putih. These findings are expected to serve as a basis for improving clinical practices, particularly in terms of drug use management and monitoring of drug interactions, to enhance clinical outcomes and the quality of life of pneumonia patients. Further research is needed to develop effective intervention strategies for managing drug use and drug interactions in clinical settings.

## Conclusion

Antibiotic evaluation indicates that most prescriptions align with guidelines, while significant drug interactions occur in pneumonia patients, primarily through pharmacodynamic mechanisms. The strong correlation between polypharmacy and drug interactions confirms that the use of multiple medications can increase the risk of drug interactions in hospitalized pneumonia patients. These findings support our hypothesis that polypharmacy. Increases the risk of drug interactions and affects the length of hospital stay in pneumonia patients.

## Declarations

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### Conflict of Interest

The authors declare no conflicting interest.

### Data Availability

The unpublished data is available upon request to the corresponding author.

### Ethics Statement

This study was approved by the Ethics Committee of the Faculty of Pharmacy, Universitas Pancasila (No. 001/KEPK-FFUP/V/2024)

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# Additional Information

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