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ANALYSIS OF POTENTIAL DRUG INTERACTIONS IN PNEUMONIA PATIENTS AT GUNUNG JATI REGIONAL HOSPITAL INSTALLATIONS, CIREBON

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ABSTRACT
Pneumonia patients with complex diseases require a variety of drugs so the possibility of drug interactions also increases. This study aims to determine patient characteristics, potential drug interactions, severity, description of the type of drug and number of interacting drugs, as well as the relationship between patient characteristics and drug interactions. This type of research is a retrospective analytical descriptive study. The research sample was the medical records of patients diagnosed with pneumonia who met the inclusion criteria. Determination of drug interactions using the Medscape application. The analysis uses a correlation test to determine the relationship between the number of drugs and comorbidities with potential drug interactions. The characteristics of patients based on age are 46-65 years (36%), the majority of gender is male (52%), the number of drugs most frequently used is ≥ 5 types of drugs (94%), the predominant comorbidity is asthma (19.3%). The number of potential drug interactions occurred in 60 patients (67%) out of a total of 90 pneumonia patients. The highest level of severity of potential drug interactions was 55.2%. The type and number of drugs that interacted most were dexamethasone with omeperazole (13.2%). The results of the Chi Square correlation test obtained a significance value of 0.00 where the significance result was <0.05, so it was concluded that the number of drugs used and comorbidities with drug interactions was correlated with an R value of 0.477, which means the correlation between the number of drugs used and comorbidities has a moderate level of correlation.

Keywords: Drug Interactions; Pneumonia; Medical records

1. INTRODUCTION

Pneumonia is a serious infection that can cause death if not properly treated. Pneumonia infection attacks the lungs at the end of the bronchioles and alveoli caused by invasion of pathogens such as bacteria, viruses, fungi and parasites. Pneumonia is prone to attack toddlers and the elderly, characterized by complaints such as fever, chills, cough with phlegm, or shortness of breath (Erviana, 2018).

The incidence of pneumonia is also high. According to data from the WHO (*World Health Organization*), 156 million cases of new pneumonia were found worldwide, and 61 million cases occurred in Southeast Asia. In 2015-2018, it was found that the incidence of pneumonia in children under five had increased by 3% from 94.12% to 97.30% (Azyenela et al., 2022). Based on data from the Cirebon District Health Service in 2020, pneumonia was found in 56.7% of children under five, namely 10,185 cases (Dinkes Cirebon, 2020). In children aged 29 days to 11 months, pneumonia is the main problem, resulting in 73.9% of deaths (Kemenkes RI, 2006).

The high morbidity and mortality rates of pneumonia in various countries have influenced the determination of patient care strategies. Correct treatment can determine the success of

pneumonia treatment. Antibiotics, which aim to kill bacteria, are the main therapy for treating pneumonia. Apart from antibiotic therapy, patients receive various other supportive treatments to achieve therapeutic success. Drug interactions occur due to the large number of treatments given to pneumonia patients (Azyenela et al., 2022).

Drug interactions are events in which changes in the pharmacokinetics and pharmacodynamics of a drug are caused by the influence of another drug. Patients with pneumonia have complex diseases that require a variety of medications. When a patient receives more drugs, the likelihood of drug interactions also increases (Erviana, 2018). According to Fatin and Pasha (2021), the potential for pneumonia drug interactions in one hospital in Bandung City was 480 interactions consisting of 5 minor interactions (1.04%), 214 moderate interactions (44.58%) and 261 major interactions (54.38%). According to Sari et al. (2019), his research found that there were 13 interactions (81.25%) between combinations of antibiotics and non-antibiotics in pneumonia patients at the Inpatient Hospital of Dr. Soedarso Pontianak with interaction severity levels major (25%), moderate (18.75%), and minor (37.50%). According to Farida (2022), of the 28 patients, there were 17 types of drugs that could cause drug interactions in pneumonia patients at Dr. Soedono Madiun. Previous studies have examined the relationship between drug interactions and the number of drugs used, but no research has been conducted regarding the correlation between drug interactions and comorbidities, especially pneumonia.

This study aimed to determine patient characteristics (gender, age, number of drugs, and comorbidities), description of the number of potential drug interactions, severity of drug interactions, description of the type and number of interacting drugs, and relationship between the number of drugs used and potential comorbidities. Drug interactions in pneumonia patients at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022.

2. METHODS

This was a non-experimental study with a retrospective data collection. This study was conducted from January to June 2023 at the Inpatient Installation at RSD Gunung Jati Cirebon. The population in this study comprised inpatients diagnosed with pneumonia at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022. Sampling was carried out by total sampling, taking all inpatients diagnosed with pneumonia at RSD Gunung Jati Cirebon in 2022 who met the inclusion criteria. The medical records used in this study included 90 patients. The inclusion criteria were as follows: medical records of patients with a primary diagnosis of pneumonia with or without comorbidities at the Inpatient Installation of RSD Gunung Jati Cirebon in 2022; medical records of pneumonia patients who received 2 or more types of drugs in the patient's treatment while inpatient; patients who have complete medical records, including: gender, age, diagnosis, name and number of drugs used, and comorbidities. The exclusion criteria in this study were patients' medical records that could not be read because they were damaged. The course of research: research permits and code of ethics, determination of sample size; data collection includes age and gender, diagnosis of disease, medicine name; processing and analysis of data. Data analysis in this study used descriptive analysis to examine patient characteristics, potential drug interactions, the severity of potential drug interactions (contraindicated, serious, monitor, or minor), and determine the description and types of drugs that interact with drug use in patients with pneumonia. The results of the analysis were in the form of a description of potential interactions in the form of percentages and tables. A Chi Square correlation test was also carried out to determine the relationship between the number of drugs and comorbidities and the potential for drug interactions in pneumonia patients at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022. This research received an Ethical Exemption certificate with No.014/LAIKETIK/KEPPKRSGJ/IV/2023 from RSD Gunung Jati Cirebon.

3. RESULTS AND DISCUSSION

The total sample in this study comprised 90 medical records of pneumonia patients at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022 who met the inclusion criteria. The data were collected in the form of patient characteristics such as age, gender, patient's main diagnosis, comorbidities, and data on medications received by the patient.

3.1. Patient Characteristics

Based on the results of this research, the characteristics of pneumonia patients at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022 are shown in **Table 1**.

Table 1. Characteristics of pneumonia patients in the RSD inpatient installation Gunung Jati Cirebon in 2022

Patient Characteristics	Group Variables	Number of Patients	Percentage (%)
Age	0-5 years	12	12%
	6-11 years	1	1%
	12-25 years	3	3%
	26-35 years old	4	4%
	36-45 years old	10	11%
	46-65 years old	36	40%
	>65 years	25	28%
	Total	**90**	**100%**
Gender	Man	47	52%
	Woman	43	48%
	Total	**90**	**100%**
Amount of medication used	2-4 drugs	5	6%
	≥ 5 drugs	85	94%
	Total	**90**	**100%**
Comorbidities	Patients with comorbidities	85	94%
	Patients without comorbidities	5	6%
	Total	**90**	**100%**

Based on **Table 1** of 90 patients with pneumonia, the results showed that patients in the age range of 46-65 years and those aged over 65 years were the largest group diagnosed with pneumonia. This is in accordance with the statement from Farida & Soleqah (2016) that in old age there are changes in anatomy and physiology and a decrease in body endurance. Anatomical and physiological changes resulting from the aging process have important consequences for the functional reserve of the lungs, ability to overcome decreased lung compliance, and increased airway resistance to infection. The next most frequent pneumonia patients were patients aged 0-5 years. This is caused by the body's immunity not being fully developed, the airways being rather narrow, and the high prevalence of pathogenic bacteria in the nose and throat area. In addition, malnourished children are 6.25 times more likely to get pneumonia than well-nourished children (Efliana et al., 2016).

52% more men were diagnosed with pneumonia than women. This is because the size of the respiratory tract of men is smaller than that of women, and the immune system of women is higher than that of men. According to Efliana et al. (2016) it was found that too much testosterone in men can reduce the immune response. Therefore, men are more susceptible to the disease than women are. In addition, pneumonia patients are dominated by male patients because pneumonia deaths are related to smoking. Long-term exposure to cigarette smoke in healthy adults can increase the risk of lung disease, bronchitis, and pneumonia (Farida & Soleqah, 2016).

Of the 90 patients diagnosed with pneumonia in 2022, treatment patterns were grouped into 2 based on the number of drugs received, namely 2-4 drugs and ≥5 drugs. From the research results, it is known that 6% of patients who receive 2-4 drugs and 94% of patients receive ≥ 5 drugs. When a patient receives many drugs (polypharmacy), the potential for drug interactions also increases (Reyaan et al., 2021).

The severity of pneumonia is influenced by comorbidities. The results of this study revealed that the patient had multiple diseases at the same time. Comorbidities in pneumonia patients cause a large number of drugs to be received by patients because, apart from prescribing drugs for the main disease, patients also receive drugs for comorbidities that may worsen the patient's health condition. As shown in **Table 2**, the dominant comorbidity was asthma, namely 28 patients (19.3%).

Table 2. Distribution of patients based on comorbidities

Comorbidities	Number of patients	Percentage (%)
Asthma	28	19.3%
Post Tuberculosis Obstruction Syndrome	17	11.7%
Dyspepsia	8	5.5%
Diabetes	7	4.8%
Pleura effusion	7	4.8%
Anemia	6	4.1%
Chronic Obstructive Pulmonary Disease (COPD)	5	3.4%
Chrinic Kidney Disease (CKD)	5	3.4%
Acute Respiratory Failure	5	3.4%
Hyponatremia	5	3.4%
Congestive Heart Failure (CHF)	5	3.4%
Malnutrition	3	2.1%
Hyperglycemia	3	2.1%
Hypocalemia	3	2.1%
Feeding difficulties	3	2.1%
Hypoalbumin	3	2.1%
Diarrhea	3	2.1%
Coronary Artery Disease (CAD)	2	1.4%
Stroke	2	1.4%
Hypertension	2	1.4%
Atrial fibrillation	2	1.4%
Human Herpes Virus (HHV)	2	1.4%
Gastroenteritis	2	1.4%
Hypertensive Heart disease (HHD)	2	1.4%
Radiculophaty Lumbal	1	0.7%
Generalized Anxiety Disorder (GAD)	1	0,7%
Hemophilia	1	0.7%
Hipoglycemia	1	0.7%
Hypercalemia	1	0.7%
Low intake	1	0.7%
Syndrom nefrotic	1	0.7%
Hepatic failure	1	0.7%
Bronchitis	1	0.7%
Coronary artery fistula	1	0.7%
Syok septic	1	0.7%
Hypotiroid	1	0.7%
Tumor Paru	1	0.7%
Parkinson	1	0.7%
Epilepsy	1	0.7%
Total	145	100%

3.2. Identify Potential Drug Interactions

Based on the results of research on pneumonia patients at the Inpatient Installation at Gunung Jati Hospital, Cirebon in 2022, of 90 patients, 60 (67%) experienced drug interactions,

while 30 (33%) did not experience drug interactions. Patients with pneumonia are at high risk of experiencing drug interactions because of the large number of drug therapies given. Because patients with pneumonia usually have accompanying or comorbid diseases, they usually receive 5 or more types of medication (polypharmacy). The results of this research are in accordance with the results of other studies (Fatin & Pasha, 2021), which stated that the number of patients with potential drug interactions in pneumonia patients in one of the Bandung City hospitals was 195 (48.51%) out of 402 patients analyzed. The number of potential drug interaction incidents among patients with pneumonia is shown in **Table 3**.

Table 3. Description of potential drug interaction events

Criteria	Number of Patients	Percentage (%)
Number of patients with potential drug interactions	60	67%
Number of patients who have no potential for drug interactions	30	33%
Total	**90**	**100%**

3.3. Description of the Severity Level of Potential Drug Interactions

Drug interactions can be classified according to their severity. The severity of drug interactions is divided into 4 categories: contraindicated, serious, monitored, and minor. Based on the results of research at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022, the results showed that the severity of potential drug interactions that occurred most frequently were drug interactions in the monitor category, with an incidence of 75 drug interactions (55.2%). Monitor interactions are drug interactions that have potential effects that may occur and require monitoring or medical treatment. The next highest level of severity of drug interactions was minor, with 46 interactions (33.8%). Drug interactions are included in the minor category if the effects are mild and do not cause a change in therapy (Reyaan et al., 2021). The severity is minor, and the effects are not disturbing or significantly visible; therefore, no special management is required (Agustina et al., 2023).

The level of severity of the interactions that occurred the least was the serious category of drug severity, with an incidence of 15 interactions (11%). Serious severity can potentially be life threatening or cause permanent damage (Agustin & Fitrianingsih, 2021). The results of this study did not identify any contraindication level drug interactions. Contraindication interactions have the highest level of drug interaction severity, which requires close monitoring of undesirable clinical effects if both drugs are given simultaneously (Fitriani et al., 2016). A description of the Severity Level of Potential Drug Interactions is shown in **Table 4**.

Table 4. Description of the severity level of potential drug interactions

Criteria	Number of Interactions	Percentage (%)
Contraindications	0	0%
Serious	15	11%
Monitors	75	55.2%
Minor	46	33.8%
Total	**136**	**100%**

The number of disease diagnoses given to patients will increase the number of drugs given for therapy. This increases the potential for drug interactions to occur during therapy. By administering three or more drugs, it is possible that potential drug interactions will arise during therapy (Bhagavathula et al., 2014). Based on **Table 4**, the most common severity of drug interactions is the monitor category with an incidence of 75 drug interactions (55.2%). Monitor interactions are drug interactions that have the potential to provide effects that may occur and

require monitoring or medical treatment. The next most common severity of drug interactions was minor interactions with 46 (33.8%). A drug interaction is categorized as minor if the effect is mild and does not cause a change in therapy (Reyaan et al., 2021).

The least severity of interaction was the serious category of drug severity with an incidence of 15 interactions (11%). Serious severity has effects that can be potentially life-threatening or can cause permanent damage (Agustin & Fitrianingsih, 2021). The results of the study did not find any contraindication level drug interactions. Contraindicated interactions are the highest severity level of drug interactions that require close monitoring of undesirable clinical effects when the two drugs are administered simultaneously (Fitriani et al., 2016).

3.4. Description of the Type and Amount of Interacting Drugs

It was found that there were 60 pneumonia patients (67%) who experienced drug interactions at the RSD Gunung Jati Cirebon Inpatient Installation in 2022, here are the 3 most frequent drug interactions at the Gunung Jati RSD Cirebon Inpatient Installation in 2022.

3.4.1. Dexamethasone and Omeprazole

The concomitant use of dexamethasone and omeprazole may decrease the levels or effects of omeprazole by affecting the hepatic/intestinal metabolism of CYP3A4 (Medscape). Based on the research results, the most frequent drug interactions occurred with the use of dexamethasone and omeprazole with 18 interactions (13.2%) with minor drug interaction severity.

3.4.2. Dexamethasone and Levofloxacin

The concomitant use of dexamethasone and levofloxacin increases the risk of tendon rupture (Medscape). Based on the research results, there were 12 drug interactions in the use of dexamethasone and levofloxacin (8.8%), with the severity of drug interactions monitored.

3.4.3. Aminophylline and Omeprazole

The concomitant use of aminophylline and omeprazole increases the toxicity of aminophylline and may decrease aminophylline levels or effects by affecting CYP1A2 liver enzyme metabolism (Medscape). There were 10 drug interactions in the use of aminophylline and omeprazole (7.4%), with minor drug interactions.

An overview of the types, numbers, and interactions of pneumonia patients at the Gunung Jati RSD Cirebon Inpatient Installation in 2022 is shown in **Table 5**.

3.5. Relationship Between Number of Drugs Used and Concomitant Diseases

Polypharmacy or the simultaneous use of more than or the same 5 types of drugs can increase the risk of interactions between drugs. Polypharmacy can cause drug interactions, side effects, and problems, thereby affecting patient clinical outcomes. Polypharmacy is classified into 2 categories: minor and major polypharmacy. Minor polypharmacy is a medication sheet containing 2-4 medications, while major polypharmacy is a medication sheet containing ≥ 5 medications (Reyaan et al., 2021). Polypharmacy can be detrimental to children because of their limited physiological conditions (Getachew et al., 2016). The greater the number of drugs used, the greater is the potential number of drug interactions. The relationship between the number of drugs used and drug interactions in patients with pneumonia at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022 is shown in **Table 6**.

The potential for drug interactions increases with the increase in comorbidities in patients diagnosed with pneumonia. Pneumonia with comorbidities has a high potential to cause drug interactions because if there are comorbidities in patients with pneumonia, additional drug therapy is required. If the more drugs given to a patient, the greater the possibility of drug interactions occurring. So, it can be concluded that the large number of drugs and the presence of comorbidities in pneumonia patients have an influence on the potential for drug interactions. The relationship between comorbidities and drug interactions in pneumonia patients at the Inpatient Installation at RSD Gunung Jati Cirebon in 2022 can be seen in **Table 7**.

Table 5. An overview of the types and numbers and interactions of pneumonia patients at the Gunung Jati RSD Cirebon inpatient installation in 2022

No.	Interacting Drugs		Severity level	Amount	Percentage
1.	Alprazolam	Codein	Monitor	1	0.7%
2.	Amikacin	Thiamine	Minor	1	0.7%
3.	Aminophylline	Dexamethasone	Monitor	7	5.1%
4.	Aminophylline	Metilprednisolon	Monitor	1	0.7%
5.	Aminophylline	Omeprazole	Minor	10	7.4%
6.	Atorvastatin	Azitromycin	Monitor	1	0.7%
7.	Atorvastatin	Metilprednisolon	Monitor	1	0.7%
8.	Azitromycin	Cetirizine	Monitor	1	0.7%
9.	Azitromycin	Bicnat	Monitor	1	0.7%
10.	Bicnat	Concor	Monitor	1	0.7%
11.	Candasertan	Concor	Monitor	1	0.7%
12.	Candasertan	Gentamicin	Monitor	1	0.7%
13.	Candasertan	Spironolactone	Monitor	1	0.7%
14.	Ceftriaxone	Furosemide	Minor	1	0.7%
15.	Clobazam	Cetirizin	Monitor	1	0.7%
16.	Clobazam	Codein	Monitor	1	0.7%
17.	Clobazam	Codein	Minor	1	0.7%
18.	Clopidogrel	Meloxicam	Monitor	1	0.7%
19.	Clopidogrel	Topamax	Monitor	1	0.7%
20.	Concor	Miniaspi	Monitor	1	0.7%
21.	Concor	Nicardipine	Monitor	1	0.7%
22.	Concor	Spironolactone	Monitor	1	0.7%
23.	Dexamethasone	Ciprofloxacin	Monitor	1	0.7%
24.	Dexamethasone	Furosemide	Minor	3	2.2%
25.	Dexamethasone	Levofloxacin	Monitor	12	8.8%
26.	Dexamethasone	Lansoprazole	Minor	1	0.7%
27.	Dexamethasone	Metronidazole	Monitor	1	0.7%
28.	Dexamethasone	Omeprazole	Minor	18	13.2%
29.	Dexamethasone	Ondansetrone	Monitor	9	6.6%
30.	Digoxin	Furosemide	Monitor	1	0.7%
31.	Digoxin	Ketorolac	Monitor	1	0.7%
32.	Digoxin	Lansoprazole	Monitor	1	0.7%
33.	Digoxin	Levofloxacin	Serius	1	0.7%
34.	Digoxin	Moxifloxacin	Monitor	1	0.7%
35.	Digoxin	Omeprazole	Serius	2	1.5%
36.	Digoxin	Omeprazole	Monitor	3	2.2%
37.	Digoxin	Sucralfate	Serius	2	1.5%
38.	Digoxin	V-Block	Monitor	1	0,7%
39.	Furosemide	Metilprednisolon	Minor	2	1.5%
40.	Furosemide	V-Block	Monitor	1	0.7%
41.	Isoniazid	Pyrazinamide	Minor	1	0.7%
42.	Ketorolac	Furosemide	Monitor	1	0.7%
43.	Ketorolac	Levofloxacin	Monitor	1	0.7%
44.	KCI	Vascon	Monitor	1	0.7%
45.	Lansoprazole	Metilprednisolon	Minor	2	1.5%
46.	Levofloxacin	Metilprednisolon	Monitor	1	0.7%
47.	Levofloxacin	Ondansetron	Serius	9	6.6%
48.	Miniaspi	Furosemide	Monitor	1	0.7%
49.	Miniaspi	Levemir	Monitor	2	1.5%
50..	Miniaspi	Metilprednisolon	Minor	1	0.7%
51.	Miniaspi	Ramipril	Serius	1	0.7%
52.	Miniaspi	Ramipril	Monitor	1	0.7%

No.	Interacting Drugs		Severity level	Amount	Percentage
53.	Miniaspi	V-Block	Monitor	1	0.7%
54.	Omeprazole	Neurobion	Minor	1	0.7%
55.	Omeprazole	Ciprofloxacin	Monitor	1	0.7%
56.	Ramipril	Furosemid	Minor	1	0.7%
57.	Ramipril	KSR	Monitor	1	0.7%
58.	Ramipril	Spironolacton	Monitor	2	1.5%
59.	Sentraline	Codein	Minor	1	0.7%
60.	Sentraline	Codein	Monitor	1	0.7%
61.	Sentraline	Loratadine	Minor	1	0.7%
62.	Simvastatin	Metilprednisolon	Serius	1	0.7%
63.	Simvastatin	Metilprednisolon	Monitor	2	1.5%
64.	Sucralfate	Lansoprazole	Minor	1	0.7%
66.	Sucralfate	Moxifloxacin	Monitor	1	0.7%
67.	Sucralfate	Vitamin D	Minor	1	0.7%
	Total			**136**	**100%**

Table 6. Relationship between the number of drugs used and drug interactions

Potential Event	Concomitant Diseases			
	There is		There isn't any	
	Amount	Percentage	Amount	Percentage
Interaction Occurs	57	67%	3	60%
No Interaction Occurs	28	33%	2	40%
Total	**85**	**100%**	**5**	**100%**

Table 7. Relationship between comorbidities and drug interactions

Potential Event	Concomitant Diseases			
	There is		There isn't any	
	Amount	Percentage	Amount	Percentage
Interaction Occurs	57	67%	3	60%
No Interaction Occurs	28	33%	2	40%
Total	**85**	**100%**	**5**	**100%**

The results of the Chi Square correlation test obtained a significance value of 0.00 where the significance result was < 0.05, so it was concluded that the number of drugs used and comorbidities with drug interactions was correlated with an R value of 0.477, which means the correlation between the number of drugs used and comorbidities has a moderate level of correlation. The relationship between the number of drugs used and comorbidities with drug interactions using the Chi Square correlation test can be seen in the **Table 8**.

Table 8. The relationship between the number of drugs used and comorbidities with drug interactions using the Chi Square Correlation Test

	Value	Df	Asymptotic Significance (2-sided)	R	Sig. F Change
Chi Square correlation test				.477	.000

Predictors: (Constant), Comorbidities, Number of drugs used

4. CONCLUSION

Based on the results of this study, from 90 patient medical records, the results of the most patient characteristics based on age were 46-65 years (36%), the most male gender (52%), the greatest number of drugs used was ≥ 5 types of drugs (94%), the most comorbidities were asthma (19.3%). The number of potential drug interactions occurred in 60 patients (67%). The highest severity of potential drug interactions was 55.2%. The type and number of drugs that interacted

the most was dexamethasone with omeperazole (13.2%). Chi Square correlation test results showed that there was a significant relationship between the number of drugs used, the type of comorbidities with drug interactions.

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6. AUTHOR DECLARATION

Authors' Contributions and Responsibilities

The authors made substantial contributions to the conception and design of the study. The authors took responsibility for data analysis, interpretation, and discussion of results. The authors read and approved the final manuscript.

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Availability of Data and Materials

All data are available from the authors.

Competing Interests

The authors declare no competing interest.

Additional Information

No additional information from the authors.

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