Advances in Healthcare Research
Volume 4, Issue 2 (2026). 214-231
DOI: https://doi.org/10.60079/ahr.v4i1.737
OPEN ACCESS
e-ISSN: 2985-9808

Analysis of Patient Characteristics on Potential Drug Interactions in Intensive Care Unit (ICU) Patients at Dr. R Soedjati Purwodadi Grobogan Hospital

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ARTICLE HISTORY

Submitted	:	January 06, 2026
Reviewed	:	January 24, 2026
Revised	:	February 19, 2026
Accepted	:	February 26, 2026
Published	:	February 28, 2026

Conflict of Interest Statement:
The author(s) declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ABSTRACT

Purpose: This study aimed to analyze patient characteristics associated with potential drug interactions among Intensive Care Unit (ICU) patients at Dr. R Soedjati Purwodadi Grobogan Hospital. It was hypothesized that patient-related factors, particularly the number of prescribed drugs, would influence the occurrence of potential drug interactions.

Research Method: This quantitative observational study employed a retrospective cross-sectional design using ICU medical records from January to October 2025. Drug interaction screening was conducted using Medscape and Drug Interaction Checker. The variables included age, sex, comorbidities, number of drugs, interaction severity, and interaction mechanism. Data were analyzed using univariate and bivariate analysis.

Results and Discussion: A total of 255 potential drug interactions were identified, with most classified as moderate (56.9%) and pharmacodynamic (62.7%). Most patients were elderly, female, and had comorbidities. Statistical analysis showed no significant relationship between age, sex, or disease history and potential drug interactions, whereas the number of drugs prescribed was significantly associated with interaction occurrence ($p < 0.001$).

Implications: These findings emphasize that polypharmacy is the main determinant of potential drug interactions in ICU patients. Strengthened clinical monitoring, prescription review, and pharmacist involvement are needed to improve medication safety in intensive care settings.

Keywords: drug interactions; ICU patients; polypharmacy; patient characteristics; medication safety; pharmacodynamic interactions.

1. Introduction

Space Intensive Care Unit (ICU) is a unit in a hospital that treats patients with critical life-threatening conditions. A study shows that on average ICU patients can be prescribed up to 17 types of drugs in the first 24 hours of treatment, treatment in the ICU requires speed and precision and involves a variety of drugs that are generally given by injection (parenteral). This condition makes ICU patients at high risk related to the emergence of drug use problems including drug interactions. Drug interactions occur when the effects of a drug change due to co-use with other drugs, herbs, chemicals, foods, or beverages. The complexity of modern medicine and the use of many drugs (polypharmaceuticals) increase the risk of drug interactions. Based on how they work, drug interactions can be categorized into two types: pharmacokinetic and pharmacodynamic interactions. Pharmacokinetic interactions occur when one

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drug affects and alters the absorption, spread, metabolism, and excretion (ADME) process of another drug while pharmacodynamic interactions are related to the impact on the receptor level. These interactions can have two possible impacts: an increase in the effectiveness of one drug (synergistic effect) or a decrease in the effectiveness of one drug (an antagonistic effect) (Adi & Soetrasno, 2022). The drug interactions that occur will affect the length of the patient's hospitalization. Length of treatment is defined as a measure of how many days a patient is hospitalized during a treatment period (Retnowati, 2021). The longer the patient stays in treatment, the greater the chance of increased patient complications, such as infection and patient care costs (Nabila hakim 2019, 2023)

Data obtained from the World Health Organization (WHO) in 2016 shows that the number of patients admitted to intensive care units (ICUs) continues to increase every year. Between 9.8% to 24.6% of patients per 100. 000 people forced to be admitted to ICU due to very serious health conditions (Augustine, 2020). The high number of critical patient cases in the ICU certainly triggered the occurrence of drug interactions, in a previous study in a hospital in Brazil, showing a high prevalence of drug interactions in the ICU, with 405 drug pairs potentially having moderate (74%) and severe (67%) interactions. The risk of drug interactions was reported in 2.2%–30% of inpatients and 9.2%–70.3% in outpatients, approximately 11.1% of patients may experience symptoms due to drug interactions. Prevalence of drug-related problems in Intensive Care Unit (ICU) at Indonesian Hospitals is quite high, reaching 73.9% in critical patients. Another study showed 100% of patients with acute coronary heart disease in the ICU had the potential to experience drug interactions, which was dominated by moderate severity (63.7%). Ekawati (2010) conducted a study on 70 patients treated during March and April 2010 and found that most drug interactions were pharmacodynamic (54.87%) and pharmacokinetic (20.35%). The most common interactions are with diuretics, especially furosemide. The prevalence related to drug interactions in Central Java Province also faces similar challenges, Based on SKI 2018 data, Central Java is often one of the provinces with the largest proportion of chronic disease cases in Indonesia, such as hypertension and diabetes mellitus, which are directly correlated with increased drug use and polypharmacy risk.

The data above is not representative, especially in the city of Purwodadi, although there have been no studies that clearly evaluate the potential for drug interactions in the ICU room of Dr. R Soedjati Purwodadi Hospital, several previous studies at this hospital have indicated the complexity of drug prescribing. A study on the pattern of antibiotic use in inpatients at dr. R. Soedjati Soemodiardjo Purwodadi Hospital showed the existence of polypharmacy and the use of combination drugs that have the potential to trigger drug interactions. Based on Yeni's (2010) research, examining the evaluation of drug prescribing in elderly schizophrenia patients in this hospital also highlights the importance of examining the suitability of prescribing patterns, which implicitly includes potential drug interactions. Therefore, this study aims to evaluate the potential for drug interactions in the ICU room of one of the hospitals in Purwodadi City, the results of this study are expected to provide an overview of how great the potential for drug interactions in the ICU, especially the city of Purwodadi and increase the vigilance of health workers to prevent unwanted drug reactions, decreased therapy effectiveness, and drug toxicity. Based on the above phenomenon, the author was interested and set the title of the study as follows: "Evaluation of Potential Drug Interactions in Inpatients in the Intensive Care Unit of RSUD DR. R Soedjati Purwodadi Grobogan."

The remainder of this paper is organized as follows. Section 2 provides a literature review and hypothesis development. Section 3 presents the research method and design. Section 4 provides the results and discussion. Section 5 is Concluding Remarks and Recommendations.

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2. Literature Review and Hypothesis Development

2.1 Drug Interactions

Drug interactions are one of the manifestations of eight categories Drug-Related Problems (DRP) significant in clinical practice. This phenomenon is identified as a condition or event in the management of pharmacological therapies that has the potential to affect the patient's overall clinical output. Definitively, drug interactions occur when the efficacy or effect of a therapeutic agent changes due to the presence of other substances (Awortwe & Cascorbi, 2020). In addition to being triggered by combinations between drugs, these interactions can also occur through simultaneous consumption with herbal ingredients, environmental chemicals, and food and beverage intake. (Di et al., 2023). Drug Related Problem (DRP) or Drug-Related Problems is defined as a situation related to real or potential drug therapy, which may hinder the achievement of the desired treatment results or have the potential to cause toxic effects in the body (Hanutami et al., 2023). Giving two or more types of drugs at the same time has the potential to cause interactions. These interactions may result in a decrease or increase in the working effects of the medications taken. If left undetected, drug interactions can have adverse impacts because therapy cannot be optimized. The negative impacts include the appearance of side effects and the failure to achieve treatment goals.

2.2 Intensive Care Unit (ICU) Room

An intensive care unit or ICU is a special room to treat individuals who are experiencing serious conditions, emergency situations, or those who are at high risk of deteriorating conditions. This room is intended for patients with survivable conditions, who require intensive therapy, cutting-edge technology, monitoring both invasive and non-invasive, and the use of patented medicines (Ekawati Hijriyah, 2010). The ICU has differences compared to other treatment rooms. The focus of treatment in the ICU is on the patient's condition and the device used (Herawati and Faradilla, 2017).

Intensive care units (ICUs) are provided by a group of professionals from a variety of disciplines that include specialists, pharmacists, nurses, and medical consultants from areas such as surgery, pediatrics, and anesthesia. Ideally, the ICU should have a team of 31 experts for patient evaluation and handling. Large hospitals may have multiple ICUs that focus on different specialties, such as cardiac care units (CCUs), pediatric intensive care units (PICUs), neonatal intensive care units (NICUs), and surgical intensive care units (SICUs) for patients after surgery.

3. Research Method

This type of research is a quantitative research. The research design used was observational with a cross-sectional method, and data collection was carried out based on the medical records of patients treated in the intensive care unit (ICU) retrospectively. Affordable population is a research activity by limiting the population with certain characteristics that can be reached by researchers. The range chosen by the researcher is ICU patients for the period from January to October 2025. After a preliminary study was conducted, there were 446 patient populations treated in the Intensive Care Unit (ICU) room of Dr. R Soedjati Purwodadi Grobogan Hospital during this period. So the minimum number of samples is 232 patients, based on the calculation above, the medical record data to be taken is 232 patients. Sampling was carried out by purposive sampling. Data collection techniques are a method used in research to

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obtain information directly from the field to answer the problems that have been formulated. (Intan Adevia Rosnarita, 2025) The aspect studied in this study is the results of the number of drug interactions in the ICU room of Purwodadi Hospital. The information collection technique in this study applies the observation method with a backward-looking approach. The data collected includes, among others, medical record numbers, patient age, gender, and records on drug administration. The data analysis method in this study is univariate and bivariate analysis.

4. Results and Discussion

4.1 Analysis Results

4.1.1 Patient Characteristics

The results showed that the majority of patients in the elderly age group (≥ (60 years) were 110 patients, the adult age group (26-59 years) was 95 patients, and the adolescent age group (12-25 years) was 19 patients. Patients with female sex were more than men, namely 114 (50.9%) and men as many as 110 (49.1%). A total of 232 patients at the hospital had 206 comorbid patients with a percentage (92%) and no comorbidities as many as 18 (8%). Patients with consumption (< 5 drugs) were 127 patients (56.7%), consumption (5-9 drugs) as many as 83 patients (37.1%), and drug consumption (10) was 14 patients (6.3%)

Table 1. Patient Demographic Data

Characteristics	Remarks	Quantity	Percentage(%)
Age	Teenagers : 12-25 years old	19	8,5%
	Adults : 26-59 years old	95	42,4%
	Senior : ≥ 60 years old	110	49,1%
	Total	224	100%
Gender	Women	114	50,9%
	Male	110	49,1%
	Total	224	100%
Comorbidities	There	206	92%
	None	18	8%
	Total	224	100%
Number of Drugs	< 5 Drugs	127	56,7%
	5-9 Drugs	83	37,1%
	≥ 10 Drugs	14	6,3%
	Total	224	100%

Source: *Primary Data, 2025*

4.1.2 Research Results

The results of potential drug interactions with minor severity were obtained 61 incidents with a percentage (23.9%), moderate 145 incidents with a percentage (56.9%), and a major 49 incidents with a percentage (19.2%).

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Table 2. Frequency of Potential Drug Interactions Based on Severity

Types of Interactions	Quantity	Percentage (%)
Minor	61	23,9%
Moderate	145	56,9%
Major	49	19,2%
Total	255	100%

Source: *Primary Data, 2025*

Table 3. The Relationship between Patient Characteristics and Potential Interactions

Patient Characteristics		Severity of Interactions			Quantity	Percentage (%)
		Minor	Moderate	Major		
Age	Teenagers (12-25 years)	6	8	6	20	7,8%
	Adults (26-59 years)	19	72	25	116	45,5
	Elderly (≥60)	36	65	18	119	46,7
			Total		255	100%
Gender	Women	40	104	49	180	70,2
	Male	21	41	13	75	29,8%
			Total		255	100%
Disease History	There	61	141	49	251	98,4%
	None	0	4	0	4	1,6%
			Total		255	100%
Number of Drugs	<5 drugs	8	21	10	39	15,3%
	5-9 drugs	49	116	36	201	78,4%
	≥ 10 drugs	4	8	3	15	6,3%
			Total		255	100%

Source: *Primary Data, 2025*

4.1.3 Relationship between Patient Characteristics and Potential Interactions

Based on the results of the research that has been conducted, it shows the relationship between patient characteristics and the severity of potential drug interactions. Based on the age group, the most potential drug interactions were found in the elderly (≥60 years), namely at moderate severity as many as 65 events, then minor interactions as many as 36 events and major as many as 18 events, in the adult age group (26-59 years) showed a fairly high number of interactions with 72 moderate, 19 minor, and 25 major events. Meanwhile, in the adolescent group (12-25 years) the number of potential drug interactions was relatively lower and dominated by moderate 8 events and 6 minor events, with very few major events. Based on the gender, female patients experienced more potential drug interactions than men, at the moderate level as many as 104 incidents, followed by minor as many as 40 incidents and major as many as 49 incidents. In male patients, the most potential drug interactions also occurred at the moderate level, namely 41 events, then minor interactions as many as 21 events and major as many as 13 events. Patients with a history of disease showed a much higher number of potential drug interactions than patients without a history of disease, in this group, there were 141 moderate interactions, followed by 61 minor events, and 49 major events. Based on the number of drugs used,

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patients who received <5 drugs had the potential for interaction at the moderate level of 21 events, 8 minor events and 10 major events. Then in patients with 5-9 drugs, the potential for interaction is quite high with the dominance of moderate levels of 116, minor 49 and major 36, while in patients with the use of ≥10 drugs, the number of potential interactions is moderate 8, minor 4, and major 3 events.

Table 4. Frequency of Potential Drug Interactions Based on Mechanism of Action

Types of Interactions	Quantity	Percentage (%)
Pharmacodynamics	160	62,7
Pharmacokinetics	95	37,3
Total	255	100

Source: *Primary Data, 2025*

Based on the results of the study, there were 160 potential drug interactions with pharmacodynamic working mechanisms (62.7%) and pharmacokinetic interaction working mechanisms as many as 95 (37.3%).

Table 5. The Relationship of Patient Characteristics with the Mechanism of Drug Interactions that Occur

Patient Characteristics		Interaction Mechanism		Quantity	Present (%)
		Pharmacodynamics	Pharmacokinetics		
Age	Teenagers (12-25 years)	13	7	20	7,8%
	Adults (26-59 years)	72	44	116	45,5%
	Elderly (≥60)	75	44	119	46,7%
		Total		255	100%
Gender	Women	104	75	179	70,2%
	Male	56	20	76	29,8%
		Total		255	100%
Disease History	There	157	94	251	98,4%
	None	3	1	4	1,6%
		Total		255	100%
Number of Drugs	<5 drugs	27	12	39	15,3%
	5-9 drugs	121	79	200	78,4%
	≥ 10 drugs	11	5	16	6,3%
		Total		255	100%

Source: *Primary Data, 2025*

Table 5 shows the results of the relationship between patient characteristics and the drug interaction mechanism that occurs, which is divided into two, namely pharmacodynamic and pharmacokinetic mechanisms, with different distributions in each patient's characteristics. Based on age group, the drug interaction mechanism was most found in elderly patients (≥60 years) with a pharmacodynamic mechanism of 75 events, and pharmacokinetics as many as 44 events with a percentage of 46.7% then in the adult group (26-59 years) with a drug interaction mechanism was also

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OPEN ACCESS
e-ISSN: 2985-9808

quite high, namely 72 pharmacodynamic events and 44 pharmacokinetic events of 10.03%, then in the adolescent age group (12-25 years) the number of drug potential was relatively higher low, with a percentage of 7.8% each. Based on the sex of female patients, there were 104 pharmacodynamic events and 75 pharmacokinetic events. In male patients, drug interaction mechanisms consisted of 56 pharmacodynamic events and 20 pharmacokinetic events. Patients with a history of disease showed the highest number of drug interaction mechanisms compared to other characteristics, namely 157 pharmacodynamic events and 94 pharmacokinetic events, with a percentage of 98.4%, whereas in patients without a history of disease the number of drug interaction mechanisms was relatively low, with 3 pharmacodynamic events and 1 pharmacokinetic event. Based on the number of drugs used, patients who received <5 drugs had drug interaction mechanisms, namely 27 pharmacodynamic events and 12 pharmacokinetic events. In patients with the use of 5-9 drugs, 121 pharmacodynamic events and 79 pharmacokinetic events were found, while in patients with the use of ≥ 10 drugs, the mechanism of drug interactions was 11 pharmacodynamic events and 5 pharmacokinetic events. The incidence of interactions in the use of ≥10 drugs is the least because there are not many patients with the consumption of ≥10 drugs.

Table 6. The Relationship between Age and Potential Drug Interactions

Age	p-value
Teenagers (12-25 years)	
Adults (26-59 years)	0,199
Seniors 60 years old)(≥	

Source: *Primary Data, 2025*

Before the Chi-square statistical test was carried out, a normality test was carried out using shapiro wilk first, the results of the normality test were obtained p = <0.001 the results of the Chi-square statistical test between age and the type of interaction obtained a value of p = 0.199. A p-value greater than 0.05 indicates that there is no age relationship with the occurrence of potential drug interactions.

Table 7. Sex Relationship with Potential Drug Interactions

Gender	p-value
Male	
Women	0,143

Source: *Primary Data, 2025*

The results of the normality test on the relationship between sex and the potential for drug interactions using shapiro wilk showed a result of <0.001, the Chi-square statistical test obtained a value of p = 0.143. A p-value greater than 0.05 indicates that there is no relationship between sex and the occurrence of potential drug interactions.

Table 8. The Relationship between Disease History and Potential Drug Interactions

History of the disease	p-value
History of the disease	0,075

Source: *Primary Data, 2025*

The results of the normality test on the relationship between disease history and potential drug interactions were obtained with the result of p = <0.001, Chi-square statistical test obtained a value of

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p = 0.075. A p-value greater than 0.05 indicates that there is no relationship between disease history and potential drug interactions.

Table 9. The Relationship between the Number of Drug Administration and the Potential for Drug Interactions

Quantity	p-value
<5 drugs	< 0.001
5-9 drugs	
≥	
Seniors 60 years old)(≥	

Source: *Primary Data, 2025*

The results of the normality test on the amount of drug use with potential drug interactions were obtained with the result of p = <0.001, the results of the Chi-square statistical test obtained a value of p = <0.001. A p value of less than 0.05 indicates that there is a relationship between the amount of medication administration and the occurrence of potential drug interactions.

4.2 Discussion

4.2.1 Patient Characteristics

4.2.1.1 Age

The results showed that the majority of patients treated in the ICU room were in the elderly age group (≥60 years) as many as 110 patients (49.1%), followed by the adult group (26–59 years) as many as 95 patients (42.4%), and the adolescent group (12–25 years) as many as 19 patients (8.5%). The dominance of this elderly group shows that elderly patients are the group that needs the most intensive care. Increasing life expectancy and high prevalence of chronic diseases in the elderly contribute to the increasing need for advanced health services. The elderly generally have more complex clinical conditions than other age groups. This led to them being treated more often in the ICU for close monitoring and intensive therapy. The age distribution illustrates that the study population is dominated by biologically and clinically vulnerable groups.

4.2.1.2 Gender

The results showed that the distribution of patients by gender was relatively balanced, with 114 patients (50.9%) for women and 110 patients for men (49.1%). This proportion shows that both men and women have almost equal opportunities to undergo treatment in the ICU room. Biological differences between men and women can affect the body's response to disease and drug therapy. Hormonal factors, body composition, and enzyme expression of drug metabolism are important aspects that distinguish the two. Therefore, gender is an important characteristic that needs to be analyzed in the context of the safety and effectiveness of drug therapy. This distribution provides a basis for understanding the potential variation in pharmacological responses between sexes.

4.2.1.3 Comorbidities

The results showed that most patients had a history of disease or comorbidities as many as 206 patients (92%), while patients without comorbidities were 18 patients (8%). This high comorbidity rate indicates that the majority of ICU patients have more than one medical condition that requires simultaneous

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treatment. The presence of comorbidities increases the complexity of clinical conditions as well as the need for more diverse therapies. Patients with comorbidities generally require a combination of medications to control each of the diseases suffered. This has the potential to increase the complexity of the treatment regimen. This condition makes comorbidities an important characteristic in the context of drug therapy safety. This distribution reflects the high clinical burden on the study population.

Based on this discussion, it can be concluded that the high number of comorbidities in this study is in line with the theory of multimorbidity and polypharmacy explained by WHO (2016; 2019) and the theory of physiological changes due to chronic diseases according to Mangoni and Jackson (2004). Research by Alhawassi et al. (2020) supports that patients with comorbidities have a higher risk of drug-related problems, while research by Al-Qerem et al. (2021) suggests that good therapeutic management can lower such risks. This difference confirms that comorbidity is an important factor but is still influenced by the quality of therapy management. Thus, the characteristics of comorbidities in this study have a strong theoretical and empirical foundation in the context of the safety of drug use.

4.2.1.4 Number of Drugs

The results showed that most patients received <5 drugs as many as 127 patients (56.7%), followed by the group that received 5–9 drugs as many as 83 patients (37.1%), and ≥10 drugs as many as 14 patients (6.3%). This distribution suggests that most patients receive combination therapy, although not all of them fall into the extreme polypharmaceutical category. The administration of more than one drug in ICU clinical practice is common because patients usually experience complex conditions that require simultaneous therapy. Drug combinations are given to treat major diseases, comorbidities, and supportive therapies. Variations in the amount of these drugs are an important factor in the safety analysis of therapy. The more drugs used, the more complex the possible interactions that occur. Based on this discussion, it can be concluded that the distribution of the number of drugs in this study has theoretical relevance through the concept of polypharmacy according to WHO (2019) and the theory of drug interactions according to Mangoni and Jackson (2004). Research by Tesfaye et al. (2022) supports that an increase in the number of drugs is associated with an increased risk of potential drug interactions, while research by Al-Qerem et al. (2021) suggests that rational management of therapies can reduce these risks. This difference confirms that the number of drugs is an important factor but is still influenced by the quality of prescription and clinical monitoring. Thus, the characteristics of the number of drugs in this study have a strong theoretical and empirical foundation in the context of the therapeutic safety of ICU patients.

4.2.2 Frequency of Potential Drug Interactions Based on Severity

The results showed that the potential for drug interactions based on severity was most in the moderate category, which was 145 incidents (66.9%), followed by the minor category as many as 61 incidents (23.9%), and the major category as many as 49 incidents (19.2%). These data show that most of the drug interactions that occur have a potentially significant clinical impact and require monitoring or therapy adjustments. Although the major category is not dominant, its proportion is still significant and has the potential to cause serious effects if not managed properly. This distribution illustrates that patients have a risk of interactions that are clinically relevant and therefore require special attention in prescribing and monitoring therapy.

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Based on this discussion, it can be concluded that the dominance of moderate category interactions of 66.9% in this study is in line with the theory of Tatro (2014) and Stockley (2016) who stated that moderate level interactions are most often found in clinical practice. Three relevant studies, namely Ismail et al. (2021), Tesfaye et al. (2022), and Alhawassi et al. (2020), support the results of this study. Meanwhile, two other studies, namely Al-Qerem et al. (2021) and Alene et al. (2020), showed the dominance of the major category in certain populations. Thus, the severity of drug interactions in this study is influenced by the characteristics of the patient and the therapy pattern given and still requires optimal clinical monitoring.

4.2.3 The Relationship between Patient Characteristics and Potential Drug Interactions

4.2.3.1 The Relationship between Age and Potential Drug Interactions

Based on the results of the study, the elderly group (≥60 years) had the highest potential for drug interactions, namely 119 incidents (46.7%), followed by the adult group with 116 incidents (45.5%) and adolescents with 20 incidents (7.8%). This distribution suggests that increased age correlates with an increased risk of potential drug interactions. Although the gap between the elderly and adults is not too far, the elderly group still occupies the highest proportion. This indicates that the age factor has an important contribution to the occurrence of drug interactions. The increased incidence rate in the elderly may also reflect a higher complexity of the clinical condition. Epidemiologically, the elderly are indeed more susceptible to drug-related problems. Thus, age is an important variable in the evaluation of therapeutic safety. These findings are in line with the concept that the geriatric population is a group at high risk of drug-related problems.

Overall, age is associated with potential drug interactions. The elderly in this study showed a higher risk than other age groups. This can be explained through physiological changes, increased prevalence of chronic diseases, and the use of more drugs. Although the adult group also shows significant numbers, the elderly remain the most vulnerable group. These findings confirm the importance of monitoring therapy in geriatric patients. Evaluation of kidney and liver function needs to be done before administering certain drugs. A deprescribing approach can also be considered to reduce the risk of interaction. Thus, therapy management in the elderly must be carried out comprehensively.

4.2.3.2 Sex Relationship with Potential Drug Interactions

The results showed that women experienced more potential drug interactions (70.2%) than men (29.8%). This difference in proportion indicates a tendency that sex can influence the occurrence of drug interactions. Higher numbers in women may reflect variations in drug use patterns and biological factors. In addition, women generally have a higher number of health care visits. This condition has the potential to increase the number of drugs prescribed. The more drugs used, the more likely an interaction to occur. Therefore, this distribution is an important finding in the research. This data indicates that women are a group that needs special attention in therapy monitoring.

Overall, gender can influence potential drug interactions, although it is not the only determining factor. Women in this study showed a higher incidence rate. This is likely related to biological, social, and more drug use. However, this relationship still needs to be studied along with other variables such as the number of medications and disease history. A multidimensional approach is needed in assessing interaction risk. Thus, the management of therapy must take into account the individual characteristics

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of the patient. The role of health workers is very important in minimizing risks. Rational therapeutic evaluation is the main key to preventing interactions.

4.2.3.3 The Relationship between Disease History and Potential Drug Interactions

Most of the potential drug interactions occurred in patients with a history of disease (98.4%). This proportion shows that disease history is the dominant factor in the occurrence of drug interactions. Patients with chronic diseases generally require long-term therapy. Such therapy often involves a combination of several medications at once. The more complex the patient's clinical condition, the more complex the therapy regimen. This complexity increases the chances of interaction. Therefore, the history of the disease is an important indicator in risk assessment. This data confirms that comorbidities play a large role in potential drug interactions.

Overall, disease history has a strong relationship with potential drug interactions. The need for combination therapy and impaired organ function are the main factors. These findings are in line with various previous studies. The risk of interaction in patients with comorbidities cannot be ignored. Preventive approaches and routine monitoring are important steps. The role of pharmacists and clinicians is crucial in this process. With proper management, risks can be reduced to a minimum. Therefore, evaluation of disease history should be a major part of the assessment of therapy.

4.2.3.4 The Relationship of the Number of Drugs with Potential Drug Interactions

Based on the results of the study, patients who used 5–9 drugs had the highest interaction potential (78.4%). These findings show that the amount of drugs is a factor that greatly affects the occurrence of drug interactions. The 5–9 drug group dominated the incidence compared to the <5 drug and ≥10 drug groups. This indicates that the increase in the number of drugs is in line with the increasing complexity of the therapy. This complexity opens up greater opportunities for combinations of interactions. Any addition of a new drug has the potential to cause interactions with previously used drugs. Therefore, the amount of the drug is an important indicator in risk evaluation. This data reinforces the suspicion that polypharmaceuticals are closely related to drug interactions.

In addition to the number of drugs, the type of drugs used also affects potential interactions. Drugs with a narrow therapeutic index have a higher risk of causing serious clinical impacts. Combinations of drugs that act on the same physiological system also increase the risk. Therefore, not all combinations in polypharmaceuticals have the same risk. Clinical assessment needs to consider the pharmacological profile of each drug. Regular medication reviews are an important step in prevention. Rationalization of therapy can reduce unnecessary medications. This approach can reduce the risk of interaction even if the amount of the drug is quite large.

4.2.4 Frequency of Potential Drug Interactions Based on Mechanism of Action

The results showed that out of a total of 255 potential drug interaction events, pharmacodynamic mechanisms were the most dominant, with 160 events (62.7%), while pharmacokinetic mechanisms were 95 events (37.3%). These data show that most drug interactions that occur in ICU patients have more to do with the effect of drug action on receptors or physiological systems than with changes in metabolic processes or drug elimination. The dominance of pharmacodynamic mechanisms indicates that the combination of therapies given tends to have mutually reinforcing or opposing effects in the patient's body system. In critical patients, the use of drugs with cardiovascular, sedative, and anticoagulant effects

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DOI: https://doi.org/10.60079/ahr.v4i1.737
OPEN ACCESS
e-ISSN: 2985-9808

simultaneously has great potential to give rise to this type of interaction. Therefore, the distribution of this mechanism has significant clinical implications in intensive care practice.

In theory, pharmacodynamic interactions occur when two or more drugs act on the same receptor or physiological system resulting in additive, synergistic, or antagonistic effects. Katzung (2018) explains that pharmacodynamic interactions do not affect drug concentrations in plasma, but do affect emerging clinical responses. These interactions are often more noticeable through changes in the patient's vital signs or clinical manifestations. In clinical practice, a combination of antihypertensive, anticoagulant, or central nervous system depressants is often an example of pharmacodynamic interactions. This theory explains why in an ICU setting, where combination therapy is commonly used, pharmacodynamic interactions can be more dominant. Thus, the findings of this study have a strong theoretical basis.

Based on this discussion, it can be concluded that the dominance of pharmacodynamic mechanisms in this study is in line with the pharmacological theory according to Katzung (2018) and the drug interaction theory according to Mangoni and Jackson (2004). Three relevant studies, namely Tesfaye et al. (2022), Ismail et al. (2021), and Alhawassi et al. (2020), support that pharmacodynamic interactions are more common in inpatients. Meanwhile, two other studies, namely Al-Qerem et al. (2021) and Alene et al. (2020), showed pharmacokinetic dominance in certain populations. This difference confirms that the distribution of interaction mechanisms is influenced by the therapy pattern, organ condition, and patient characteristics. Thus, the results of this study have a strong theoretical and empirical foundation and still need to be understood in a specific clinical context.

4.2.5 The Relationship of Patient Characteristics with the Mechanism of Drug Interactions that Occur
4.2.5.1 Age Relationship with Drug Interaction Mechanisms

Based on the results of the study, the mechanism of drug interactions in all age groups is dominated by pharmacodynamic interactions rather than pharmacokinetics. In the elderly group (≥60 years), 75 pharmacodynamic and 44 pharmacokinetic events were found, while in the adult group there were 72 pharmacodynamics and 44 pharmacokinetic. Adolescents showed the lowest number of 13 pharmacodynamics and 7 pharmacokinetics. This pattern shows the consistency of dominance of mechanisms based on the effect of drug action in all age groups. Quantitatively, the difference between the two mechanisms is quite clear in the elderly and adults. This suggests that interactions due to synergistic or antagonistic effects occur more often than metabolic changes or drug elimination. The distribution indicates that clinical factors are more dominant than purely physiological factors. Thus, the pharmacodynamic mechanism is the main pattern in this study.

Overall, age was associated with the distribution of drug interaction mechanisms, but the dominance of the mechanisms in this study remained pharmacodynamic in all age groups. Age-related physiological changes do increase pharmacokinetic risk, but in clinical practice the combination of therapeutic effects more often gives rise to interactions. These findings show the importance of monitoring clinical effects rather than focusing only on organ function. Evaluation of combination therapy should be a priority in adult and elderly patients. With the right approach, the risk of excessive synergistic effects can be minimized. Therefore, clinical monitoring-based therapy management is essential. The dominance of pharmacodynamics is the main implication in this study.

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4.2.5.2 Gender Relationship with Drug Interaction Mechanisms

The results showed that women experienced 104 pharmacodynamic interactions and 75 pharmacokinetic events, while men experienced 56 pharmacodynamic and 20 pharmacokinetic interactions. In both groups, pharmacodynamic mechanisms remained more dominant than pharmacokinetics. The difference in the total number of incidents between women and men is quite significant. This suggests that in addition to a higher number of interactions, the pattern of mechanisms in women also follows the trend of dominating the effects of drug work. Although males have lower numbers, the distribution of the mechanisms remains similar. Thus, pharmacodynamic mechanisms become the main patterns in both sexes. Physiologically, women have a higher body fat composition than men. This condition can affect the volume of distribution of lipophilic drugs. In addition, the activity of metabolic enzymes such as cytochrome P450 is reported to have variations between sexes. In theory, this difference has the potential to increase the risk of pharmacokinetic interactions in women. However, in this study, pharmacodynamic interactions remained more dominant. This suggests that although metabolic factors play a role, the combination of therapeutic effects more often triggers interactions. In other words, the clinical effects of drugs outweigh metabolic differences. Biological factors do not fully determine the mechanism of the interaction that occurs.

Overall, sex showed a difference in the number of interactions, but did not change the dominance pattern of interaction mechanisms. Pharmacodynamic mechanisms remain the most common in both women and men. These findings confirm that the combination of therapeutic effects more often triggers interactions than metabolic changes. Therefore, monitoring the clinical effects of drugs should be a top priority in pharmaceutical services. Biological factors do play a role, but they are not dominant in determining the mechanism. The therapeutic evaluation approach should take into account the complexity of the drug regimen. With proper management, the risk of interaction can be minimized. The dominance of pharmacodynamics is an important implication in this study.

4.2.5.3 The Relationship of Disease History with Drug Interaction Mechanisms

Based on the results of the study, most of the interactions occurred in patients with a history of disease, namely 157 pharmacodynamic events and 94 pharmacokinetics. In contrast, patients without a history of disease showed only 3 pharmacodynamic events and 1 pharmacokinetics. This difference is very significant and shows that the presence of comorbidities plays a major role in the occurrence of drug interactions. The dominance of pharmacodynamic mechanisms remained seen in groups with a history of disease. This indicates that the combination of the drug's working effects is the main factor. The more complex the patient's clinical condition, the more likely it is that combination therapy will be given. Thus, disease history is closely correlated with the distribution of drug interaction mechanisms. These data show the importance of evaluating therapy in patients with comorbidities.

Overall, the history of the disease has a strong relationship with the mechanisms of drug interactions. Patients with comorbidities show dominance of pharmacodynamic interactions due to combination therapies of chronic diseases. Although pharmacokinetic interactions have also been found, the amount is lower. These findings confirm the importance of evaluating therapy in patients with a history of the disease. Monitoring of clinical effects should be carried out periodically to prevent excessive synergistic effects. The role of pharmacists is very important in conducting medication reviews. With the right approach, the risk of interaction can be minimized. Pharmacodynamic dominance is an important implication in the management of patients with comorbidities.

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4.2.5.4 The Relationship between the Number of Drugs and the Mechanism of Drug Interactions

Based on the results of the study, the amount of medication used by patients showed a clear relationship with the mechanism of drug interactions. In patients with the use of <5 drugs, 24 pharmacodynamic and 15 pharmacokinetic events were found. In groups 5–9 of drugs, incidence increased significantly to 124 pharmacodynamics and 77 pharmacokinetics. Meanwhile, in patients with ≥10 drugs, 12 pharmacodynamics and 3 pharmacokinetics were found. This data shows that groups of 5–9 drugs have the highest number of interactions. The dominance of pharmacodynamic mechanisms remained consistent across all groups. This suggests that an increase in the number of drugs is directly proportional to an increase in the potential for interactions. The complexity of therapy is a major factor that affects the distribution of interaction mechanisms.

Overall, the amount of the drug has a strong relationship with the mechanism of drug interactions. Polypharmacy increases the risk of interaction both through pharmacodynamic and pharmacokinetic mechanisms. The dominance of pharmacodynamics shows that the combination of drug working effects is the main factor in this study. These findings confirm the importance of a thorough evaluation of the therapy regimen. Health workers need to conduct medication reviews, especially in patients with ≥5 drugs. Deprescribing efforts may be considered to reduce the risk of interaction. With proper therapy management, potential interactions can be suppressed. The number of drugs is an important indicator in the prevention of drug interactions.

4.2.6 The Relationship of Patient Characteristics with Potential Drug Interactions
4.2.6.1 The Relationship between Age and Potential Drug Interactions

The results showed that the relationship between age and potential drug interactions had a p-value of 0.199 ($p>0.05$), so there was no significant relationship between adolescent, adult, and elderly age groups on the incidence of potential drug interactions. Although descriptively the elderly have a higher number of events, statistically the difference is not meaningful. In theory, Mangoni and Jackson (2004) explain that the aging process causes pharmacokinetic changes in the form of decreased glomerular filtration rate, decreased hepatic metabolism, and changes in drug distribution due to increased body fat. These changes can increase the risk of drug accumulation and interactions. However, in this study, these physiological changes were not strong enough to produce significant differences between age groups. This suggests that the chronological age factor does not stand alone as a determinant of drug interactions. Thus, statistically age has not been shown to be significantly related.

Conceptually, the polypharmacy theory states that the risk of interactions increases due to the complexity of the therapy, not solely due to biological age (Morin et al., 2020). The elderly are indeed more physiologically vulnerable, but if the amount of drugs given is not much different from other age groups, then the risk of interaction can be equal. In this study, it is likely that the distribution of therapy between adults and the elderly is not very contrasting. This causes statistical tests to show no significant correlation.

It can be concluded that age biologically has the potential to increase the risk of drug interactions, but in this study it was not proven to be statistically significant. This is likely influenced by the relatively even distribution of the number of drugs and disease characteristics. Therefore, age was not a factor significantly related to the potential drug interactions in this study.

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4.2.6.2 Sex Relationship with Potential Drug Interactions

The results showed that the relationship between sex and potential drug interactions had a p-value of 0.143 ($p>0.05$), so there was no significant relationship between men and women on the incidence of drug interactions. Although women had a higher number of descriptively events, the difference was not statistically significant. In theory, Anderson (2008) explains that women have a higher body fat composition and variations in the activity of certain metabolic enzymes that can affect drug responses. However, these factors do not necessarily lead to a statistically increased drug interaction. In this study, gender was not proven to be the main determinant. This suggests that other clinical factors are more dominant than biological characteristics. Thus, sex was not significantly related to potential drug interactions. It can be concluded that although there are biological physiological differences between males and females, in this study gender was not significantly related to potential drug interactions. The factor of the number of drugs and the complexity of the therapy is more dominant. Therefore, gender is not a statistically influential variable in this study.

4.2.6.3 The Relationship between Disease History and Potential Drug Interactions

The results showed that the relationship between disease history and potential drug interactions had a p-value of 0.075 ($p>0.05$), so that statistically there was no significant relationship. Although descriptively almost all interaction events occurred in patients with a history of disease, the difference did not reach a significant level. In theory, WHO (2019) states that patients with comorbidities tend to undergo long-term combination therapy which increases the risk of drug interactions. Chronic diseases such as hypertension, diabetes mellitus, and cardiovascular disorders generally require more than one type of therapy. These conditions clinically increase the chances of interactions both through pharmacodynamic and pharmacokinetic mechanisms. However, in this study, the history of the disease was not proven to be statistically significant. This shows that the existence of the disease alone is not necessarily a determinant factor regardless of the amount and type of drugs used. It can be concluded that a history of the disease has the potential to increase the risk of drug interactions, but in this study it was not proven to be statistically significant. This is likely influenced by the homogeneity of the respondent characteristics and the distribution of the amount of drugs. Thus, disease history was not the main determinant in this study.

4.2.6.4 The Relationship between the Number of Drug Administration and the Potential Drug Interaction

The results showed that the relationship between the amount of drug administration and the potential for drug interactions had a p-value of 0.001 ($p<0.05$), so there was a significant relationship. This suggests that the more drugs are given, the higher the risk of potential drug interactions. In theory, Maher et al. (2014) explain that polypharmaceuticals increase the likelihood of drug combinations that can interact exponentially. Each addition of one drug increases the chances of an interaction occurring. This risk can occur through pharmacodynamic and pharmacokinetic mechanisms. In this study, the number of drugs was proven to be the most statistically influential factor. Thus, polypharmacy is the main determinant of potential drug interactions.

It can be concluded that the number of drug administration is the most influential factor on the potential for drug interactions. Polypharmaceuticals significantly increased risk and were consistent in various studies. Therefore, the amount of the drug was proven to be the main determinant in this study.

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5. Concluding Remarks and Recommendation

This study involved 232 ICU patients with various critical illness diagnoses. The majority of patients were in the elderly age group (≥ 60 years) at 47.8%, followed by the adult age group (26–59 years) at 39.7%, indicating that elderly patients were the group that needed the most intensive care. The results of the statistical test showed that age ($p = 0.199$), sex ($p = 0.143$), and disease history ($p = 0.075$) did not have a significant relationship with the occurrence of potential drug interactions. The distribution of the number of drugs showed that the majority of patients received less than 5 drugs (58.6%), but there was still a sizable proportion of patients with the use of 5–9 drugs (37.9%) and ≥ 10 drugs (3.4%), which clinically had the potential to increase the incidence of drug interactions. There was a significant relationship between the number of drugs given and the potential for drug interactions with a $p <$ value of 0.001, which suggests that the more drugs used, the higher the risk of potential drug interactions in ICU patients.

Most ICU patients have comorbidities, which is 92.2%, which has the potential to increase the complexity of therapy and the use of many drugs (polypharmaceuticals), thereby increasing the risk of potential drug interactions. The potential drug interactions that occur in ICU patients are most caused by pharmacodynamic mechanisms, which are 166 events (62.4%), compared to pharmacokinetic mechanisms as many as 96 events (36.4%). This suggests that drug interactions are more common due to the effects of drug action that affect each other. Based on severity, the most potential drug interactions were in the moderate category with 148 events (56.1%), followed by the minor category with 62 events (23.5%), and the major category with 53 events (20.1%). These findings suggest that most drug interactions require clinical monitoring and therapeutic adjustments.

Statement of Use of Generative AI

During the preparation of this work, the author used generative artificial intelligence tools to support the scientific writing process. Grammarly was used to check grammar, refine writing style, and improve clarity in scientific writing. All interpretations, analyses, and conclusions presented in this study are the sole responsibility of the author.

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