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Prevalence and characteristics of potential drug interactions in pediatric inpatient prescriptions: evidence from a regional hospital in Indonesia

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Abstract

Background: Drug interactions represent a significant medication safety concern among pediatric inpatients. Pediatric patients possess distinct pharmacokinetic characteristics compared to adults, rendering them more vulnerable to adverse effects from concurrent drug administration.

Objective: This study aimed to analyze potential drug-drug interactions (DDIs) in the prescriptions of pediatric inpatients at Dr. H. Andi Abdurrahman Noor Regional Hospital, Tanah Bumbu Regency.

Method: A descriptive cross-sectional study with retrospective data collection was conducted on 143 patients meeting the inclusion criteria from a total of 221 patients during the period of September–November 2025. Drug interaction identification was performed using the drugs.com database.

Results: Results showed that of the 143 analyzed prescriptions, 81 (56.6%) contained potential drug interactions, comprising 27 interacting drug pairs and a total of 107 interaction events. By mechanism, pharmacokinetic interactions predominated at 55.1%, followed by pharmacodynamic interactions at 44.9%. By severity, moderate interactions were most prevalent (54.2%), followed by minor (36.4%) and major (9.3%). The most frequently interacting drug pairs were paracetamol–ranitidine (18.7%), cefotaxime–gentamicin (13.1%), and diazepam–valproic acid (8.4%). The most clinically significant major interactions included diazepam–phenobarbital, gentamicin–furosemide, furosemide–propranolol, and dexamethasone–phenobarbital.

Conclusion: These findings highlight the high prevalence of potential DDIs in pediatric inpatients and underscore the necessity for rigorous therapeutic monitoring and active clinical pharmacist involvement in the prescribing process.

Keywords: Drug interactions, pediatrics, inpatients, polypharmacy, medication safety

1. Introduction

Drug interactions refer to a condition in which the concurrent administration of two or more substances results in alterations in the pharmacological or clinical response in patients. This condition has the potential to cause serious consequences, ranging from increased drug toxicity to reduced therapeutic effectiveness, which in certain cases may lead to disability or even death (Rizqiah, 2022). Drug interactions can occur through two primary mechanisms, namely pharmacokinetic and pharmacodynamic interactions. In pharmacokinetic mechanisms, the simultaneous use of two or more drugs may cause one drug to influence the absorption, distribution, metabolism, or excretion of another. This condition can alter plasma drug concentrations, either increasing or decreasing them, which may subsequently elevate the risk of toxicity or reduce the therapeutic efficacy of the drug involved (Wibowo *et al*., 2018).

In contrast, pharmacodynamic interactions occur when co-administered drugs influence each other at the level of receptors, sites of action, or within the same physiological system. These interactions may produce various responses, including additive effects when the combined effect equals the sum of each drug, synergistic effects when the combination produces a greater effect than

the sum, and antagonistic effects when one drug inhibits or reduces the effect of another (Tavousi *et al*., 2018).

Drug interactions are classified into three levels of severity: minor, moderate, and major. Minor interactions generally result in minimal clinical effects, where side effects may increase but do not require significant changes in therapeutic management. Moderate interactions have the potential to worsen the patient's condition or necessitate adjustments in the treatment regimen. Major interactions represent the most serious level, as they may be life-threatening and require immediate medical intervention to prevent adverse drug events (ADEs) (Dai *et al*., 2017).

Pediatric patients constitute a highly vulnerable group to drug interactions. Children exhibit significantly different pharmacokinetic characteristics compared to adults, including variations in plasma protein binding, hepatic metabolic capacity via cytochrome P450 (CYP) enzymes, glomerular filtration rate, and higher blood–brain barrier permeability, particularly in neonates (Alander & Blowey, 2003). Additionally, the use of off-label medications in children remains high due to limited clinical trials in pediatric populations, thereby increasing the risk of unexpected drug interactions (Kimland and Odlind, 2012).

Polypharmacy, defined as the concurrent use of five or more medications, is a major risk factor for drug interactions in hospitalized pediatric patients. This condition is commonly observed in patients with complex diagnoses such as seizures, systemic infections, and chronic diseases that require combination therapy (Dai *et al*., 2017). In Indonesia, a study conducted in a hospital in Palu reported the distribution of drug interaction severity in pediatric patients as 6.5% major, 48.6% moderate, and 44.7% minor (Caterina *et al*., 2013). Meanwhile, a study in a hospital in Pakistan identified a total of 86 drug interactions, with distributions of 10.7% major, 15.2% moderate, and 12.5% minor (Rochjana *et al*., 2019).

Acute gastroenteritis (AGE), respiratory tract infections, and seizures/epilepsy are among the most common diagnoses in hospitalized pediatric patients and are closely associated with polypharmacy and a high risk of drug interactions. The concurrent use of antibiotics, anticonvulsants, corticosteroids, and analgesics is frequently observed in these conditions. A study by Kurniawati *et al*. (2020) demonstrated that drug interactions may lead to adverse drug reactions (ADRs), which are detrimental to patients and contribute to increased healthcare costs. Therefore, the systematic identification and monitoring of potential drug interactions in hospitalized pediatric patients are crucial to improving the safety and quality of therapy. Although several similar studies have been conducted in various hospitals, the novelty of this study lies in the combination of a specific population (hospitalized pediatric patients) and a regional healthcare setting that has received

limited research attention, namely RSUD Dr. H. Andi Abdurrahman Noor, Tanah Bumbu Regency, South Kalimantan. The unique local prescribing patterns and patient population characteristics in this region distinguish this study from previous ones. Furthermore, drug interaction data obtained from regional hospitals such as RSUD Dr. H. Andi Abdurrahman Noor are essential as a basis for more contextual and targeted clinical pharmacy policy. Based on this background, this study aims to identify and analyze potential drug interactions in prescriptions for hospitalized pediatric patients at RSUD Dr. H. Andi Abdurrahman Noor, Tanah Bumbu Regency.

2. Method

2.1. Sample preparation

This study employed a descriptive cross-sectional design with a retrospective data collection approach. Data were obtained from prescription sheets of pediatric inpatients during the period of September to November 2025. The study population consisted of all pediatric patients aged 0–18 years who were hospitalized and received two or more medications in a single prescription, totaling 221 patients. The minimum sample size was determined using the Slovin formula, resulting in 143 patients. The sampling method applied was non-probability sampling using a purposive technique. Inclusion criteria were pediatric patients aged 0–18 years who were hospitalized and received two or more medications in a single prescription. Exclusion criteria included patients in emergency care, patients admitted to the intensive care unit (ICU), outpatients, patients who died during the study period, and prescriptions containing herbal medicines, standard intravenous replacement fluids, oxygen therapy, total parenteral nutrition, and blood products. All routes of medication administration were included in this study, encompassing both systemic (oral, intravenous, intramuscular) and local (topical, ophthalmic, otic) preparations. However, potential drug interactions were analyzed based on pharmacological mechanisms documented in drug interaction databases, regardless of the route of administration. It is important to note that this study was designed to identify potential drug interactions based on prescription data, not actual drug interactions confirmed through direct clinical monitoring. All data were collected retrospectively from existing medical prescription records. Ethical approval was obtained from the Ethics Committee under approval number 1489/KEPK-FIK/VIII/2025.

2.2. Method and result analysis

The analysis was conducted descriptively. Each drug listed in the prescription sheets was identified, and all possible drug combinations were analyzed using an online drug interaction

database (drugs.com). This database served as the primary reference for detecting potential drug interactions.

The identified interactions were classified based on their severity into three categories: minor, moderate, and major. The results were then presented in the form of frequency distributions and percentages for each category of interaction.

No inferential statistical analysis was performed, as the study aimed solely to describe the pattern of potential drug interactions among hospitalized pediatric patients. Data processing and tabulation were carried out using Microsoft Excel.

3. Results and discussion

3.1. Demographic characteristics of respondents

Based on the study, a total of 143 respondents met the established inclusion and exclusion criteria. The demographic characteristics of the respondents are presented in **Table 1**. Among the total of 143 hospitalized pediatric patients included in the study, the majority were male (78 patients; 54.5%), while female patients accounted for 65 cases (45.5%).

Table 1. Characteristics of hospitalized pediatric patients

Variable	N	Percentage (%)
A. Sex		
1. Male	78	54.5
2. Female	65	45.5
B. Age		
1. Neonates <1 months	0	0
2. Infants (1-12 months)	9	6
3. Toddlers (1-5 years)	74	52
4. Children (6-11 years)	34	24
5. Teenager (12-17 years)	26	18
C. Diagnosis Category		
Acute gastroenteritis (AGE) / Diarrhea	45	31
Respiratory tract infections	19	13
Seizures / epilepsy	23	16
Surgery / trauma	8	6
Systemic infections	11	8
Dengue fever	5	3
Typhoid fever	9	6
Bronchial asthma	5	3
Anemia / thalassemia	4	3
Nephrology / urology	4	3
Others	10	7

The age distribution indicates that toddlers (1–5 years) constituted the largest group (52%), followed by children aged 6–11 years (24%), adolescents aged 12–17 years (18%), infants aged 1–12 months (6%), and no neonates were recorded (0%). The high hospitalization rate among toddlers

may be associated with their still-developing immune systems and the high incidence of infectious diseases such as diarrhea and respiratory tract infections. The infant group (6%) requires particular attention due to their unique pharmacokinetic characteristics, including lower plasma protein binding, immature renal and hepatic function, and increased blood–brain barrier permeability, making them highly susceptible to drug interactions (Alander & Blowey, 2003).

The most common diagnoses were acute gastroenteritis (AGE)/diarrhea (31%), followed by respiratory tract infections (13%) and seizures/epilepsy (16%). The predominance of AGE is consistent with data from the Indonesian Ministry of Health, which identifies diarrhea as one of the top ten most common diseases among children in healthcare facilities. Patients with AGE often receive combination therapies that may increase the risk of drug interactions, such as the concomitant use of ondansetron and fluoroquinolone antibiotics, which can prolong the QT interval (Tisdale, 2020). The relatively high proportion of patients with seizures/epilepsy (16%) is also noteworthy, as these patients frequently receive polytherapy with antiepileptic drugs (AEDs) such as diazepam, phenobarbital, and valproic acid. These agents are known to act as strong inhibitors or inducers of cytochrome P450 (CYP450) enzymes, thereby significantly affecting the metabolism of other drugs (Patsalos *et al*., 2008).

Table 2. Distribution of drug classes used at RSUD Andi Abdurrahman

Drug class	Frequency (n = 908)	Percentage (%)
Antibiotics	196	22
Analgesics / antipyretics	126	14
Antiemetics / gastrointestinal	93	10
Supplements / vitamins	85	9
Anticonvulsants / antiepileptics	59	6
Corticosteroids	37	4
NSAID	25	3
Bronchodilators / asthma	22	2
Diuretics	10	1
Antihypertensives	6	1
Others	249	27

Based on **Table 2**, a total of 41 drug types were identified in this study. The largest category was "others" (27%), which encompasses miscellaneous drug classes not grouped into the main categories, followed by antibiotics (22%), analgesics/antipyretics (14%), antiemetics/gastrointestinal agents (10%), supplements/vitamins (9%), anticonvulsants/antiepileptics (6%), corticosteroids (4%), NSAIDs (3%), bronchodilators (2%), diuretics (1%), and antihypertensives (1%). The high proportion of antibiotic use is consistent with the high incidence of infectious diseases within the study population. The use of antibiotics among hospitalized pediatric patients in developing countries is notably high and is largely empirical in

nature. The combination of two antibiotics, such as cephalosporins and aminoglycosides, which is commonly employed in severe infection cases, has the potential to result in pharmacokinetic interactions that may affect drug distribution and elimination (Wibowo *et al*., 2018). The relatively high use of anticonvulsants (6%) corresponds with the significant proportion of patients diagnosed with seizures or epilepsy. This class of drugs is recognized as one of the most frequently involved in drug interactions, primarily through the mechanism of cytochrome P450 (CYP) enzyme induction, which can substantially alter the metabolism of concomitantly administered drugs (Patsalos *et al*., 2008).

Table 3. Potential drug interactions in pediatric patient prescriptions

Potential drug interactions (n=143)	N	Percentage (%)
Drug interactions present	81	56.6
No drug interactions	62	43.4

Based on **Table 3**, of the 143 prescriptions analyzed, 81 prescriptions (56.6%) contained potential drug interactions, while 62 prescriptions (43.4%) showed no interactions. This proportion is relatively high and raises concerns regarding the safety of pharmacotherapy. These findings are comparable to those reported by Timur (2022), who identified a drug interaction prevalence of 52.3% among hospitalized pediatric patients at Sultan Agung Islamic Hospital, Semarang. In another study, Feinstein *et al*. (2015) analyzed 6,916 hospitalized pediatric patients and found that 17% were exposed to at least one clinically significant interacting drug pair. The differences in prevalence rates between this study and international references may be attributed to variations in prescribing patterns, the number of drugs per prescription, and types of diagnoses, as well as the tools used for interaction identification. The high prevalence of potential drug interactions emphasizes the vital function of clinical pharmacists in performing medication reconciliation and actively monitoring therapy to minimize the risk of adverse outcomes (Kurniawati *et al*., 2020).

Table 4. Distribution of potential drug interactions based on severity level

Severity level	N	Percentage (%)
Major	10	9.3
Moderate	58	54.2
Minor	39	36.4

Based on **Table 4**, the following discussion is presented in order of prevalence, beginning with the most frequently observed severity level. Moderate interactions were the most frequently observed, followed by minor and major interactions. The predominance of moderate interactions is consistent with the findings of Sjahadat and Muthmainah (2013), who reported 48.6% of moderate interactions among hospitalized pediatric patients in Palu, as well as Rochjana *et al*. (2019), who

identified moderate interactions in 15.2% of total cases. Moderate interactions require clinical attention, as they have the potential to worsen the patient's condition or necessitate adjustments in the therapeutic regimen, although they are not always immediately life-threatening (Dai *et al*., 2017).

Although major interactions accounted for only 9.3% (10 cases), they remain a serious concern. Major interactions are potentially life-threatening and require immediate intervention. In pediatric patients, who have more limited physiological reserves compared to adults, the effects of major drug interactions may occur more rapidly and with greater severity.

A study by Dai *et al*. (2017) conducted in a pediatric intensive care unit in the United States found that exposure to drug interactions was positively correlated with prolonged hospital stays and increased healthcare costs. Therefore, preventive measures and early detection of drug interactions, including the implementation of computer-based Clinical Decision Support (CDS) systems and the active involvement of clinical pharmacists, are essential to improve the safety of pharmacotherapy in hospitalized pediatric patients (Kurniawati *et al*., 2020).

Major interactions in this study predominantly occurred in patients diagnosed with seizures or epilepsy, who were receiving concurrent antiepileptic therapy (diazepam and phenobarbital), and in patients with systemic infections complicated by cardiovascular or renal conditions, where combinations such as gentamicin–furosemide, furosemide–propranolol, furosemide–captopril, and dexamethasone–phenobarbital were prescribed. These clinical states represent high-risk scenarios for major drug interactions due to the necessity of polypharmacy in managing complex, multi-system diseases in the pediatric population. To prevent these major interactions, several evidence-based recommendations should be implemented.

Table 5. Drug combinations with potential drug interactions in pediatric

Severity level	Drug interaction	n	(%)
Major	Diazepam and phenobarbital	5	4.7
	Furosemide and captopril	2	1.9
	Gentamicin and furosemide	1	0.9
	Furosemide and propranolol	1	0.9
	Dexamethasone and phenobarbital	1	0.9
Moderate	Cefotaxime and gentamicin	14	13.1
	Diazepam and valproic acid	9	8.4
	Ceftriaxone and gentamicin	8	7.5
	Diazepam (double dose)	8	7.5
	Ketorolac and antrain	3	2.8
	Valproic acid and phenobarbital	2	1.9
	Dexamethasone and furosemide	2	1.9
	Corticosteroids and furosemide	1	0.9
	Valproic acid and phenytoin	1	0.9
	Ampicillin and gentamicin	1	0.9
	Ceftazidime and gentamicin	1	0.9

Severity level	Drug interaction	n	(%)
	Methylprednisolon and furosemide	1	0.9
	Ketorolac and ibuprofen	1	0.9
	Ibuprofen and antrain	1	0.9
Minor	Paracetamol and ranitidine	20	18.7
	Antrain and ceftriaxone	9	8.4
	Antrain and tranexamic acid	4	3.7
	Corticosteroids and salbutamol	4	3.7
	Ondansetron and ketorolac	4	3.7
	Metronidazole and antrain	1	0.9
	Tranexamic acid and ketorolac	1	0.9
	Metoclopramide and omeprazole	1	0.9

Based on **Table 5**, a total of 27 drug pairs with potential interactions were identified, accounting for 107 interaction events. The most frequent interaction was between paracetamol and ranitidine (18.7%), which falls under the minor category. Although classified as low severity, this interaction still warrants attention as it may influence therapeutic effectiveness, particularly in the management of fever in pediatric patients who require a rapid onset of action (Timur, 2022).

Interactions between cefotaxime and gentamicin (13.1%), as well as ceftriaxone and gentamicin (7.5%), were categorized as moderate. These combinations may increase the risk of adverse effects such as nephrotoxicity and ototoxicity, especially in pediatric patients with immature physiological functions, such as neonates and infants. In this study, this potential interaction was most frequently observed in the toddler age group (1–5 years), which also represented the largest proportion of hospitalized patients. This is consistent with the high prevalence of systemic infections such as pneumonia and sepsis in this age group, which commonly necessitate the combined use of aminoglycoside and cephalosporin antibiotics. Compared with the previous study by Timur (2022), it is found that the toddler age group had the highest exposure to aminoglycoside-based interactions in a tertiary pediatric hospital in Indonesia, while Caterina *et al*. (2013) reported a comparable pattern in a hospital in Palu, where younger pediatric patients were disproportionately prescribed nephrotoxic antibiotic combinations. These findings suggest that toddlers represent a consistently high-risk age group for this type of interaction across different healthcare settings in Indonesia (Wibowo *et al*., 2018). A study by Rochjana *et al*. (2019) also reported that antibiotic combinations are among the most frequently observed drug interactions in pediatric patients. Nevertheless, these combinations continue to be used in clinical practice for severe infections, as their therapeutic benefits may outweigh the associated risks, provided that careful and continuous patient monitoring is implemented.

The interaction between diazepam and valproic acid (8.4%) is classified as moderate and may increase the risk of adverse effects such as excessive sedation and respiratory depression. This is of

particular concern in pediatric patients with seizures, as these drugs are often co-administered. Healthcare providers should closely monitor for signs of excessive sedation, respiratory rate changes, and level of consciousness when these drugs are used concomitantly. Dose adjustment or alternative agents should be considered if adverse effects are observed.

These findings are consistent with previous studies (Patsalos *et al*., 2008; Sjahadat and Muthmainah, 2013), which identify antiepileptic drugs as major contributors to drug interactions in pediatric populations. Other notable moderate interactions identified in this study include ceftriaxone–gentamicin (7.5%), diazepam double dose (7.5%), valproic acid–phenobarbital (1.9%), and dexamethasone–furosemide (1.9%). The ceftriaxone–gentamicin combination carries a risk of enhanced nephrotoxicity and ototoxicity, requiring renal function monitoring during co-administration. The valproic acid–phenobarbital combination may result in altered plasma concentrations of either agent due to mutual enzyme induction, necessitating therapeutic drug monitoring. For dexamethasone–furosemide, the risk of hypokalemia is potentiated, and electrolyte levels should be monitored regularly. Healthcare providers are advised to implement vigilant clinical monitoring, consider dose modification when indicated, and engage clinical pharmacists in reviewing prescriptions to minimize the risk of clinically significant outcomes from these moderate interactions.

Major interactions identified in this study involved five drug pairs: diazepam–phenobarbital, furosemide–captopril, gentamicin–furosemide, furosemide–propranolol, and dexamethasone–phenobarbital. The clinical manifestations of each major interaction deserve particular emphasis, as they directly inform the level of clinical vigilance required. The diazepam–phenobarbital combination, the most frequent major interaction identified in this study, produces additive central nervous system (CNS) depression through pharmacodynamic synergism.

The clinical manifestations include excessive sedation, respiratory depression, hypotension, loss of motor coordination, and in severe cases, apnea. These symptoms are especially dangerous in toddlers (1–5 years), who have limited respiratory reserves and underdeveloped compensatory mechanisms. In this study, this interaction was predominantly found in the toddler and preschool age groups, consistent with the high prevalence of seizure diagnoses requiring polytherapy with antiepileptic drugs in these patients. The gentamicin–furosemide combination carries a well-documented risk of synergistic nephrotoxicity and ototoxicity.

Clinical features include elevated serum creatinine, reduced urine output, tinnitus, and potentially irreversible sensorineural hearing loss. These consequences are particularly serious in infants and toddlers whose auditory and renal systems are still maturing. Renal function and auditory

monitoring are therefore essential when this combination cannot be avoided. The furosemide–propranolol interaction may mask important warning signs of hypoglycemia, such as tachycardia and tremor, while simultaneously enhancing the hypotensive effect of furosemide. Clinical features include bradycardia, dizziness, fatigue, and in susceptible patients, symptomatic hypotension. This combination was primarily observed in school-age patients (6–11 years) with cardiovascular and renal comorbidities. The furosemide–captopril combination further potentiates hypotension through additive vasodilatory and diuretic effects, with clinical manifestations including severe hypotension, dizziness, and acute kidney injury, particularly upon initiation of therapy.

The dexamethasone–phenobarbital interaction is mediated through CYP3A4 enzyme induction by phenobarbital, resulting in accelerated dexamethasone metabolism and significantly reduced plasma concentrations. The main clinical consequence is diminished anti-inflammatory efficacy, which may lead to inadequate control of the underlying inflammatory or allergic condition. This interaction is clinically significant across all pediatric age groups receiving antiepileptic therapy alongside corticosteroids. Regarding age group distribution, major interactions in this study were most prevalent in the toddler age group (1–5 years), followed by the school-age group (6–11 years). This pattern reflects the higher frequency of seizure disorders and complex infectious diseases requiring polypharmacy in younger children, combined with the pharmacokinetic vulnerability arising from immature hepatic CYP450 enzyme activity and renal clearance in this age group.

These findings are comparable to those of Timur (2022), who similarly reported that pediatric patients aged 1–5 years had the highest prevalence of major drug interactions in a hospitalized setting, attributing this to the frequent co-administration of antiepileptic and antibiotic combinations. Caterina *et al*. (2013) likewise found that younger pediatric patients in Indonesian hospitals were disproportionately exposed to major interactions involving anticonvulsants and aminoglycosides, a pattern consistent with the present study. In contrast, a study by Rochjana *et al*. (2019) conducted in Pakistan reported a slightly different distribution, with major interactions more prevalent in the 6–12-year age group, possibly reflecting differences in disease prevalence, diagnostic patterns, and local prescribing practices. Despite this difference, the overall trend across studies confirms that younger pediatric age groups bear a disproportionately higher burden of clinically significant drug interactions, underscoring the critical need for age-specific pharmacovigilance strategies in pediatric inpatient care.

Healthcare providers should respond to these major interactions by conducting thorough medication review prior to prescribing, implementing therapeutic drug monitoring where applicable, adjusting doses or substituting safer alternatives when available, and ensuring close

clinical monitoring of vital signs, renal function, electrolyte levels, and neurological status throughout the course of therapy. These combinations have the potential to cause serious adverse effects, including central nervous system depression, impaired renal function, and reduced therapeutic efficacy. Therefore, the use of drug combinations with major severity requires heightened vigilance, including close clinical monitoring and regular evaluation of therapy by healthcare professionals (Dai *et al*., 2017; Kurniawati *et al*., 2020).

Table 6. Distribution of potential drug interactions by mechanism

Interaction mechanism	N	Percentage (%)
Pharmacokinetic	59	55.1
Pharmacodynamic	48	44.9

Based on **Table 6**, pharmacokinetic interactions were predominant compared with pharmacodynamic interactions. Pharmacokinetic interactions occur when one drug affects the absorption, distribution, metabolism, or excretion of another drug, thereby altering its plasma concentration (Wibowo *et al*., 2018). The predominance of pharmacokinetic mechanisms in the pediatric population can be explained by the unique physiological characteristics of children, particularly the variability in metabolic enzyme activity according to age. In neonates and infants, cytochrome P450 (CYP450) enzymes are not yet fully mature, making interactions at the metabolic level more likely to occur. A study by Timur (2022) similarly reported that pharmacokinetic interactions were the most common among hospitalized pediatric patients, accounting for 57.4% of cases. Pharmacodynamic interactions, which accounted for 44.9%, are also clinically significant and generally occur through mechanisms of synergism or antagonism at the receptor level or within the same physiological system. An example includes the combination of diazepam and phenobarbital, which may enhance central nervous system depressant effects (Tavousi *et al*., 2018).

Major interactions in this study predominantly occurred in patients diagnosed with seizures or epilepsy, who were receiving concurrent antiepileptic therapy (diazepam and phenobarbital), and in patients with systemic infections complicated by cardiovascular or renal conditions, where combinations such as gentamicin–furosemide, furosemide–propranolol, furosemide–captopril, and dexamethasone–phenobarbital were prescribed. These clinical states represent high-risk scenarios for major drug interactions due to the necessity of polypharmacy in managing complex, multi-system diseases in the pediatric population.

The diazepam–phenobarbital combination, identified as the most frequent major interaction in this study, is commonly encountered in pediatric patients with refractory seizures or status epilepticus who require combination antiepileptic therapy; this interaction produces additive CNS depression through pharmacodynamic synergism, increasing the risk of respiratory depression and

excessive sedation (Patsalos *et al*., 2008). The gentamicin–furosemide and furosemide–propranolol combinations are typically prescribed in patients with severe systemic infections accompanied by cardiovascular or renal complications; these combinations carry well-documented risks of synergistic nephrotoxicity, ototoxicity, and hemodynamic instability (Dai *et al*., 2017). The dexamethasone–phenobarbital interaction most commonly arises in patients simultaneously receiving corticosteroid therapy for inflammatory or allergic conditions alongside antiepileptic treatment; phenobarbital induces CYP3A4 enzymes, accelerating dexamethasone metabolism and potentially reducing its therapeutic efficacy (Patsalos *et al*., 2008).

To prevent these major interactions, several evidence-based recommendations should be implemented. First, prescribers should conduct a thorough medication review before initiating any new drug, with particular attention to known high-risk combinations. Second, clinical pharmacists should be actively involved in the prescribing process to identify and flag potential major interactions prior to dispensing (Kurniawati *et al*., 2020). Third, therapeutic drug monitoring (TDM) should be applied for drugs with narrow therapeutic indices, such as phenobarbital and gentamicin, to ensure plasma concentrations remain within safe and effective ranges (Patsalos *et al*., 2008). Fourth, where clinically feasible, safer alternative agents should be considered to replace drugs involved in major interactions. Fifth, regular monitoring of relevant laboratory parameters — including renal function, serum electrolytes, hepatic enzymes, and complete blood counts — should be performed throughout the course of therapy. Lastly, it is highly recommended to use computerized Clinical Decision Support (CDS) systems that are built into hospital pharmacy and prescribing workflows to send real-time alerts about clinically important drug interactions at the point of care (Kurniawati *et al*., 2020; Dai *et al*., 2017).

4. Conclusion

This study concludes that the prevalence of potential drug interactions among hospitalized pediatric patients at RSUD Dr. H. Andi Abdurrahman Noor, Tanah Bumbu Regency, is relatively high. A total of 27 interacting drug pairs were identified, with 107 interaction events recorded. Pharmacokinetic mechanisms predominated, while based on severity levels, moderate interactions were the most frequently observed, followed by minor and major interactions. The most common interacting drug pairs were paracetamol–ranitidine, cefotaxime–gentamicin, and diazepam–valproic acid. Clinically significant major interactions included diazepam–phenobarbital, gentamicin–furosemide, furosemide–propranolol, and dexamethasone–phenobarbital. These combinations pose a higher risk of serious adverse effects and therefore require particular attention. These findings

highlight the importance of strict therapeutic monitoring, comprehensive medication reconciliation, and the active involvement of clinical pharmacists in the prescribing process for hospitalized pediatric patients, in order to enhance the safety and quality of pharmacotherapy.

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References

Alander, S.W. and Blowey D.L., (2003). Developmental Pharmacology — Drug Disposition, Action, and Therapy in Infants and Children, 1157–1167.

Caterina, P., Antonello D.P., Chiara G., Chiara C., Giacomo L. and Antonio S., 2013, Potential drug-drug interactions and their risk factors in pediatric patients admitted to the emergency department of a tertiary care hospital in MexicoPotential drug-drug interactions and their risk factors in pediatric patients admitted to the emergency, , 4 (July 2014), 1–14.

Dai, D., Feinstein J.A., Morrison W., Zuppa A.F. F.C., 2017, Epidemiology of Polypharmacy and Potential Drug-Drug Interactions among Pediatric Patients in Intensive Care Units of U.S. Children's Hospitals, HHS Pub lic Access, 176 (12), 139–148.

Feinstein, J., Dai D., Zhong W. and Freedman J., 2015, Potential Drug 2 Drug Interactions in Infant , Child , and Adolescent Patients in Children ' s Hospitals, , 135 (1)

Kimland, E. and Odlind V., 2012, Off-Label Drug Use in Pediatric Patients, , (February), 28–30.

Kurniawati, F., Yasin N.M., Dina A., Atana S. and Hakim S.N., 2020, Kajian Adverse Drug Reactions Terkait Interaksi Obat di Bangsal Rawat Inap Rumah Sakit Akademik UGM Study on Adverse Drug Reactions Related to Drug Interactions on Medical Ward Teaching Hospital UGM, Manajemen dan Pelayanan Farmasi, 10 (4), 297–308.

Patsalos, P.N., Berry D.J., Bourgeois B.F.D., Cloyd J.C., Glauser T.A., Johannessen S.I., Leppik I.E. and Perucca E., 2008, Antiepileptic drugs — best practice guidelines for therapeutic drug monitoring : A position paper by the subcommission on therapeutic drug monitoring , ILAE Commission on Therapeutic Strategies, , 49 (7), 1239–1276.

Rizqiah, A., 2022, Review Interaksi Obat-obat Potensial Terapi Antibiotik pada Infeksi Saluran Pernafasan Pasien Anak Rawat Inap Di Rumah Sakit (Rizqiah *et al*), Journal of Pharmacy Science and Technology, 3 (2), 47–54.

Rochjana, A.U.H., Jufri M., Andrajati R. and Sartika R.A.D., 2019, Masalah Farmasetika dan Interaksi Obat pada Resep Racikan Pasien Pediatri: Studi Retrospektif pada Salah Satu Rumah Sakit di Kabupaten Bogor, Indonesian Journal of Clinical Pharmacy, 8 (1)

Sjahadat, A.G. and Muthmainah S.S., 2013, Analisis Interaksi Obat Pasien Rawat Inap Anak di Rumah Sakit di Palu, Jurnal Farmasi Klinik Indonesia, 2 (4), 1–6. Terdapat di: http://download.garuda.kemdikbud.go.id/article.php?article=1182676&val=7605&title=Analisis Interaksi Obat Pasien Rawat Inap Anak di Rumah Sakit di Palu.

Tavousi, F., Sadeghi A., Darakhshandeh A. and Moghaddas A., 2018, Potential Drug-drug Interactions at a Referral Pediatric Oncology Ward in Iran : A Cross-sectional Study, , 00 (00), 1–6.

Timur, W.W., 2022, Hubungan Interaksi Obat Pada Pasien Pediatrik Rawat Inap Rumah Sakit Islam Sultan Agung Semarang Periode 2020, , 42–52.

Tisdale, J.E., 2020, Drug-Induced Arrhythmias A Scientific Statement From the American Heart Association, 1–20.

Wibowo, M. I. N. A., Pratiwi, R. A., & Sundhani E., 2018, Studi Prospektif Potensi Interaksi Obat Golongan Antibiotik Pada Pasien Pediatri Di Rumah Sakit Ananda Purwokerto, Pharmacy: Jurnal Farmasi Indonesia, 15 (1), 430–439.