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Analysis of potential drug interaction in children under 10 years of age with acute respiratory tract infections at RSIA Sitti Khadijah hospital in Makassar

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ABSTRACT: Acute Respiratory Tract Infection (ARI) is one of the most prevalent diseases, triggered by various factors such as microorganisms and air pollution. This study aimed to analyze the risk of drug interactions in pediatric ARI patients under 10 years of age at RSIA Sitti Khadijah Makassar from July to December 2024. A non-experimental retrospective design was applied using data collected from outpatient medical records. The findings indicated that 75% of patients having potential drug interactions predominantly in the moderate category with a pharmacodynamic mechanism. The primary factor contributing to these interactions was the concurrent use of multiple drugs. Such interactions can alter therapeutic effectiveness by either enhancing or reducing drug effects; therefore, early identification and appropriate management of drug interactions are essential to optimize treatment outcomes and minimize adverse effects. Greater attention to potential drug interactions in pediatric ARI therapy is crucial to ensure treatment safety and effectiveness.

KEYWORDS: Acute Respiratory Tract Infection (ARI); drug interaction; pediatri; pharmacodynamic; retrospective study.

INTRODUCTION

Acute Respiratory Tract Infection, commonly called ISPA, is a disease that attacks the respiratory tract, starting from the nose to the alveoli. ISPA is caused by microorganisms, such as bacteria, viruses, and fungi. ISPA can attack anyone, especially vulnerable groups such as infants, toddlers, and the elderly. ISPA is one of the 10 most common diseases [1]. The global death rate from ARI is 4.25 million per year. [2]. In Indonesia, the province with the highest ARI rate is East Nusa Tenggara, which has a rate of 15.4%. Meanwhile, in South Sulawesi, the prevalence is 8.3%, which is higher than that in Southeast and North Sulawesi [3].

The use of drugs is said to be rational if the drug chosen is in accordance with the needs and objectives. One of the problems that can arise in the use of drugs is unwanted drug interactions, which can cause side effects [4]. Drug-related problems (DRPs) are part of pharmaceutical care, which occur when pharmacists or health workers find that the treatment provided is not appropriate or has not helped patients achieve the expected therapeutic results. DRPs often occur during patient treatment and can be problems that have already occurred or that may occur in the future. These problems can affect the healing process of the patient, either due to side effects, incorrect dosages, or inappropriate use of drugs [5]. This study was conducted at Sitti Khadijah Hospital for Women and Children in Makassar City. Data were obtained from medical records. It was stated that the number of patients with ISPA in the period July-December 2024 was 175, the largest disease category. Therefore, research was conducted on drug interactions with the aim of reducing and preventing the occurrence of treatment in patients with ISPA by providing appropriate drug therapy to reduce the incidence of drug interactions during therapy and also improve and assist in the provision of optimal therapy to increase the effectiveness, safety, and efficiency of treatment.

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MATERIALS AND METHODS

Time and place

This study used a non-experimental (observational) design and a cross-sectional approach. Data were collected retrospectively from the patients' medical records. The research and data collection were conducted at the Sitti Khadijah Women's and Children's Hospital (RSIA) in Makassar City from April to May 2025.

Population and sample

The population is the entire object to be studied according to certain characteristics. In this study, the population consisted of all outpatients diagnosed with acute respiratory infections (ARI) at Siti Khadijah Hospital for Women and Children (RSIA) in Makassar City during the period of July to December. The sample represented a portion of the population. The sample in this study consisted of outpatient medical records of children aged < 10 years who were diagnosed with ARI. This study used secondary data obtained from medical records, and patient confidentiality was maintained by anonymizing all personal information. Ethics approval for this study was obtained from the Health Research Ethics Committee.

Sampling was based on specific inclusion and exclusion criteria. The inclusion criteria were as follows: patients with ARI who visited the outpatient department of RSIA Siti Khadijah, Makassar City; aged between 1 month and 10 years; diagnosed with ARI as documented in the medical records during the specified period; received two or more types of medication; with or without comorbid conditions; and had complete medical record data. The exclusion criteria included hospitalization and damaged, incomplete, or illegible medical records.

Data analysis

The data are presented in the form of a table with a descriptive presentation. Drug interaction analysis was performed theoretically using the Stockley book. Drug Interactions, Drug.com, Drugbank.com, and Journal.

RESULTS

Table 1. Demographic data characteristics of patients with ISPA.

Category	Sub category	Number of patients	Percentage
Gender	Male	40	62.5%
	Female	24	37.5%
Age	1-6 Month	2	3.12%
	7-11 Month	8	12.50%
	1-5 Years	38	59.38%
	6-10 Years	16	25.0%
Total		64	100%

Data source : Medical record data from Siti Khadijah Hospital in Makassar City

Based on Table 1, there were 40 (62.5%) male and 24 (37.5%) female ISPA patients. At the age of 1-6 months there were 2 (3.125%) patients age 7-11 months there were 8 (12.50%) patients, at the age–1-5 years there were 38 (59.38%) patients age 6-10 years there and 16 (25.0%).

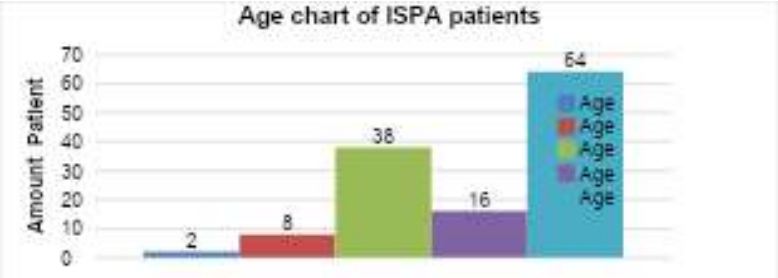

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Figure 1. Graph age patient.

Table 2. Characteristics of the number of drugs in patients with ISPA.

Number of drug combinations	Number of patients	Presentation
One Combination	2	3.13%
Two Combinations	17	26.56%
Three Combinations	31	48.44%
Four Combinations >	14	21.88%
Total	64	100%

Based on Table 2, the characteristics of the number of drugs in patients diagnosed with Acute Respiratory Tract Infection (ARI) at the Sitti Khadijah Hospital for Women and Children, Makassar City, in the period July–December 2024, the number of drugs with one combination was 2 (3.13%), two combinations 17 (26.56%), three combinations 31 (48.44%), and four or more combinations 14 (21.88%).

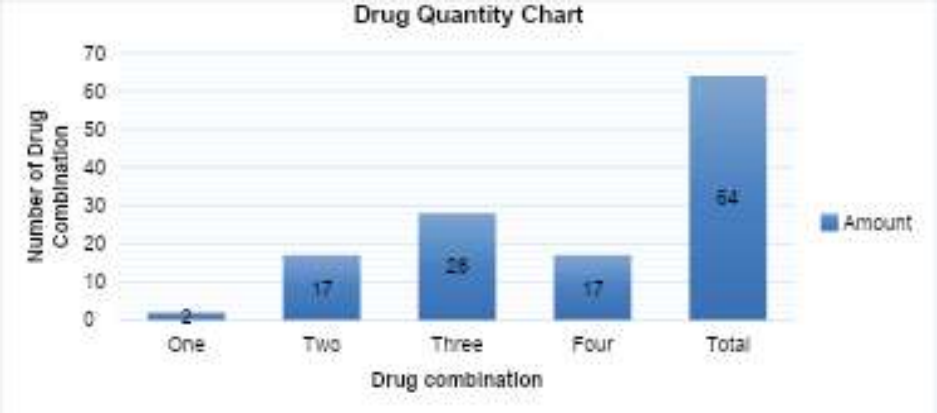

Figure 2. Drug quantity chart.

Table 3. Characteristics of drug classification for patients with ISPA.

Drug classes	Amount	Presentation
Mucolytic	62	24.60%
Antihistamin	59	22.62%
Cephalosporin	54	21.43%
Corticosteroids	45	17.86%
Macrolides	9	3.57%
Antipyretic	8	2.78%
Multivitamin	7	2.98%
Aminoglycosides	5	1.98%
Bronchidilator	2	3.17%
Sulfonamides	1	0.40%
Antimetic	1	0.40%
Non-steroidal	1	0.40%
Total	262	100%

Based on the characteristics of drug classification in patients with a diagnosis of ARI, the drug classification was as follows: Mucolytic 64 (24.4%), Antihistamine Group 61 (23.3%), Cephalosporin Group 54 (21.8%), Corticosteroid Group 46 (17.6%), Macrolide Group 8 (3.1%), Antipyretic Group 7 (2.7%), Multivitamin Group 7 (2.7%), Aminoglycoside Group 5 (2.3%), Bronchodilator Group 2 (0.8%), Sulfonamide Group 1 (0.38%), Antiemetic Group 1 (0.4%), Nonsteroid Group 1 (0.4%).

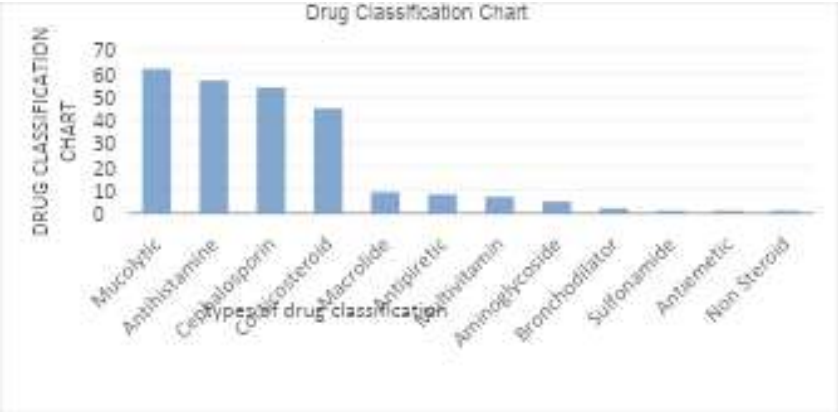

Figure 3. Classification chart.

Table 4. Potential drug interactions in patients with ISPA.

Potential drug interaction	Amount	Presentation
There is	48	75%
No	16	25%
Total	64	100%

Based on the potential for drug interactions were observed in 48 patients (75%) and no drug interactions were observed in 16 patients (25%).

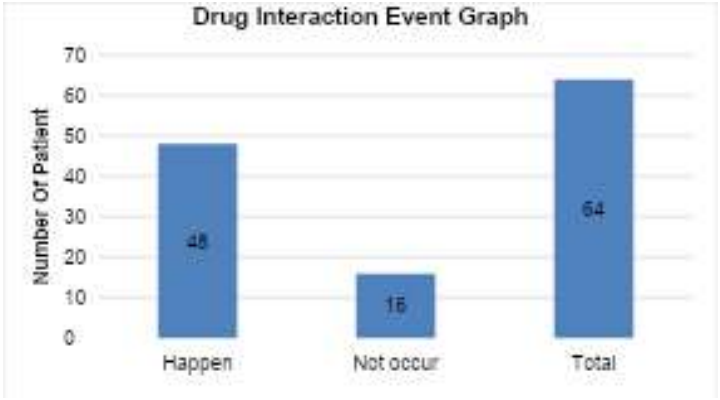

Figure 4. Drug interaction event graph.

Table 5. Interaction mechanisms.

Interaction mechanism	Number of occurrences	Presentation
Pharmacodynamics	52	96.3%
Pharmacokinetics	2	3.7%
Total	54	100%

Pharmacodynamic drug interaction mechanisms, there were 52 (96.3%) and 2 (3.7%) pharmacokinetic interaction mechanisms.

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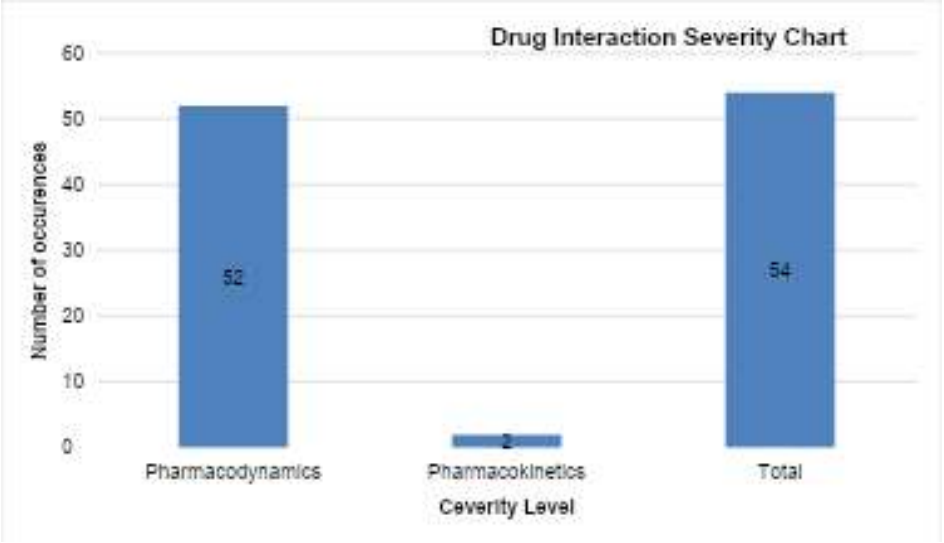

Figure 5. Drug interaction severity chart.

Table 6. Based on category.

Category	Amount	Presentation
Minor	1	1.9%
Moderate	53	98.1%
Major	-	-
Total	54	100%

Based on the drug interaction category, there was one minor (1.8 %) and 54 moderate (98.2 %) interactions, and no major interactions.

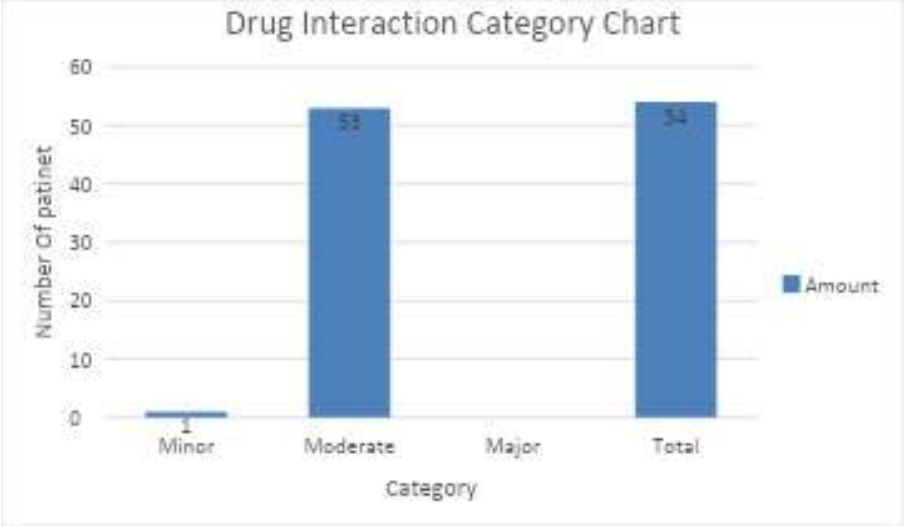

Figure 6. Drug interaction category chart.

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Table 7. Types of drug ınteraction events.

Drug name	Category	Mechanism	Frequency	Presentation
Ambroxol (Epexol) + Dexamethasone (Cortidex)	Moderate	Pharmacodynamics	39	70.91%
Paracetamol (Sanmol) + Ambroxol (Epexol)	Moderate	Pharmacodynamics	7	12.73%
Dexamethasone (Cortidex) + Erythromycin (Erysanbe)	Moderate	Pharmacodynamics	5	9.09%
Paracetamol (Sanmol) + Dexamethasone (Cortidex)	Moderate	Pharmacokinetics	1	1.82%
Salbutamol (Albuterol) + Dexamethasone (Cortidex)	Moderate	Pharmacodynamics	1	1.82%
Ibuprofen + Dexamethasone	Moderate	Pharmacodynamics	1	1.82%
IbuProfen + Cefadroxyl	Minor	Pharmacokinetics	1	1.82%

Based on the Drug Interaction Incident Ambroxol (Epexol) + Dexamethasone (Cortidex) was included in the moderate category with a pharmacodynamic mechanism of 39 (70.91%). Paracetamol (Sanmol) + Ambroxol (Epexol) is included in the moderate category, with a pharmacodynamic mechanism of 7 (12.3%). Dexamethasone (Cortidex) + erythromycin (Erysanbe) was included in the moderate category (n = 5, 9.09%). Paracetamol (Sanmol) + Dexamethasone (Cortidex) was included in the moderate category pharmacokinetically 1 (1.82%). Salbutamol + Dexamethasone was included in the moderate category with a pharmacodynamic mechanism of 1 (1.82%). Ibuprofen + Dexamethasone is included in the moderate category with a pharmacodynamic mechanism of 1 (1.82%). Ibuprofen + Cefadroxil is included in the minor category pharmacokinetically 1 (1.82%).

▪ DISCUSSION

Acute Respiratory Infection is a disease that attacks the upper or lower respiratory tract and is usually contagious. This disease is caused by several microorganisms and environmental factors [6]. Drug interactions occur when the effects of a drug change due to the presence of other drugs, herbal medicines, food, drinks, or other chemical agents in the body. Drug interactions are an important factor that can affect the body's response to treatment. Some drugs can affect each other's efficacy. Therefore, they can increase or decrease each other's effects, which can affect the desired therapeutic outcome [7].

As shown in Table 1, there were 40 male and 24 female patients. In the prevalence of ARI, it is said that most patients who have ARI are male, namely 83 (62.9%) and in women as many as 34 (37.1%) [8]. The most common age group was toddlers, namely the range of 2-5 years, namely 37 (72.5%) [9]. Factors that influence the type of male are more susceptible to Acute Respiratory Tract Infection (ARI) than females due to various biological, behavioral, and social factors. Biologically, men have an immune system that tends to be weaker in responding to infection than that of women, which can affect the body's ability to fight pathogens that cause ARI. Ages 1-5 years are very susceptible to ARI because their immune system is not yet mature, they are exposed to the environment, lack awareness of cleanliness, and lack immunization.

Based on Table 2, therapy with three-drug combinations was the most commonly administered treatment (28 patients, 43.75%), and one-drug combination therapy, which is 2 (3.125%). Taking two or more drugs simultaneously can cause drug interactions, namely, changes in drug effects that occur when the drugs interact with each other. This interaction can affect the mechanism of action of the drug, either by increasing or decreasing its effectiveness [10].

Based on table 3, the most widely used drug class is mucolytics with 64 (24.4%), and the second most

widely used drug class is antihistamines with 61 (23.3%), while the fewest drug classes are bronchodilators with 2 (0.8%), and nonsteroids with 1 (0.4%). In cases of Acute Respiratory Tract Infection (ARI), coughing up phlegm is a common symptom that often appears. Mucolytic drugs can be used to overcome this condition. Mucolytics work by breaking down the chemical bonds in mucoproteins and mucopolysaccharides in phlegm, thereby reducing its viscosity and making it easier to cough out [11]. This is not in line with the results of the study Humaira Fadhilah et al., 2022 that based on the drug class, the most widely used ARI drugs are the antipyretic group as many as 78 (31.45%), the Antibiotic Group as many as 74 (29.84%), the Mucolytic Group is included in the third as many as 45 (18.15%). The use of antipyretics due to a viral or bacterial infection that enters the body through the respiratory tract can cause pain and fever as a response to an abnormal body condition. The use of antibiotics is included in the second treatment because ARI can also be caused by bacteria. Mucolytic drugs are also used in the treatment of ARI because ARI often causes coughing [11].

As shown in Table 4, potential drug interactions were identified in 48 patients (75%), whereas 16 patients (25%) did not experience potential drug interactions. One factor that may contribute to the high incidence of drug interactions is the concurrent use of multiple medications. The use of several drugs simultaneously can increase the risk of drug interactions, as each drug has the potential to interact with other drugs. The greater the number of medications consumed by patients, the higher the likelihood of interactions that may affect the effectiveness of the therapy.

Based on Table 5, there were 52 (96.3%) pharmacodynamic drug–drug interaction incidents and 2 (3.7%) pharmacokinetic drug–drug interaction incidents. Pharmacodynamic drug interactions occur more frequently than pharmacokinetic or unknown interactions. This is caused by most drugs at the receptor, site of action, or the system. the same physiological effects, which can cause additive, synergistic, or antagonistic effects. In addition, other studies have reported that interactions that often occur in drug use often occur in pharmacodynamic mechanisms [12].

Based on table 7. The results of the research that has been conducted show that the highest category percentage is the moderate category (98,1%) and the minor category as much as 1 (1.9%). This is in line with research conducted by Rahayu & Susilawati in 2023, which found that the most common drug interactions were moderate category as much as (54.16%), followed by minor interactions (41.67%)[13]. The potential for drug–drug interactions (DDIs) refers to the possibility of changes in the therapeutic effect of a drug due to the simultaneous administration of other drugs. Based on the category of drug interactions, there are three parts: minor, moderate, and major. Minor interactions generally do not significantly affect therapeutic outcomes and can still be tolerated; minor interactions do not require changes in the therapeutic regimen and can be managed with time adjustments. An example of a minor interaction in this study is the increase in the pharmacological effect of ibuprofen when administered with cefadroxil. Moderate interactions require further attention, such as monitoring the side effects in patients. Moderate category interactions need to be considered, especially in children, because their body development is still ongoing, which can affect the absorption, distribution, metabolism, and elimination of drugs. An example of a moderate interaction in this study is the increase in blood levels of dexamethasone when administered with erythromycin. Major interactions are dangerous because they cause serious clinical effects, such as life-threatening effects, and can cause permanent damage [12].

Based on Table 8. The results of the research that has been done based on the type of drug interaction showed that ambroxol (Epexol) + dexamethasone (Cortidex) is included in the moderate category, where the interaction mechanism, namely the severity of methemoglobinemia, can increase when dexamethasone is combined with ambroxol (pharmacodynamics) interactions occurred in 39 (60.9%) patients (Drug.com). Drug interactions between paracetamol and ambroxol are included in the moderate category, where the interaction mechanism, namely methemoglobinemia, can increase when combined (pharmacodynamics) in seven (10.93%) patients (Drugbank.com). The combination of paracetamol and ambroxol can cause a moderate category with a pharmacodynamic interaction mechanism; namely, simultaneous use can cause methemoglobinemia, a rare but serious and potentially fatal side effect [14].

The interaction mechanism of dexamethasone (Cortidex) + erythromycin (Erysanbe chewable) is that erythromycin can increase dexamethasone levels in the blood. Patients may experience side effects such as

swelling, weight gain, high blood pressure, high blood glucose levels, and muscle weakness, where the form of interaction (pharmacodynamics) is 5 (9.09%) patients (Drug.com). This is in line with research conducted by Widodo, who found two cases with a percentage of 22.3%. Namely, there is an interaction of erythromycin and dexamethasone drugs between these two drugs occurs pharmacokinetically showing that dexamethasone can increase the activity of the CYP3A4 enzyme, which plays a role in erythromycin metabolism. This decreases erythromycin levels in the blood. If these two drugs are used together, there is a higher risk of bacterial resistance to erythromycin [15].

Paracetamol + Dexamethasone (Cortidex) was included in the moderate category, where the interaction mechanism is that dexamethasone is known to induce liver enzymes, especially CYP2EI, and can metabolize paracetamamol and increase its hypototoxic potential, where interactions occur in one (1.82%) patient. (DrugBank.com). The combination of paracetamol and dexamethasone can moderately increase the hepatotoxic activity of acetaminophen (pharmacokinetics) [14]. Salbutamol + Dexamethasone Category (moderate) where the interaction mechanism can cause an increased risk of hypokalemia when dexamethasone is combined with Salbutamol (albuterol) as much as 1 (1.56%) (Drugbank.com).

Ibuprofen + Dexamethasone (Cortidex) is included in the moderate category where the interaction mechanism is the use of dexamethasone with ibuprofen can increase the risk of side effects in the digestive tract such as inflammation, bleeding, ulceration and rarely, perforation where the form of interaction (Pharmacodynamics) as much as 1 (1.82%) patients (Drug.com). The cefadroxil + Ibuprofen Category (moderate) showed that the interaction mechanism has the potential for simultaneous nephrotoxicity, which can cause an increase in the degree of kidney damage. This combination of drugs can produce additive effects that contribute to an increase in the incidence or severity of kidney injury (DrugBank.com). The form of interaction is (pharmacokinetics) 1 (1.82%). The combination of cefadroxil and ibuprofen is a minor category where the interaction mechanism is that cefadroxil can increase the levels or effects of ibuprofen through a competitive mechanism in the anionic transport process in the kidney, which plays an important role in tubular clearance. When these two drugs are used together, they compete for binding to anionic transporters in the renal tubule, which can lead to increased concentrations of ibuprofen in systemic circulation. This has the potential to enhance the therapeutic effects of ibuprofen but can also increase the risk of side effects, such as impaired renal function [13].

Potential drug interactions pose a significant risk to patient safety. Moderate interactions can be minimized by adjusting the interval between drug administration, particularly in pharmacokinetic interactions, to avoid simultaneous drug intake. Following the identification of potential interactions, pharmacists play a critical role in assessing their clinical relevance, providing recommendations for therapy modification, monitoring patient outcomes, and educating patients to ensure the safe and rational use of medications [16].

In the implementation of patient-oriented pharmaceutical care, pharmacists play an important role in preventing and managing potential drug interactions by monitoring drug therapy during the provision of pharmaceutical services. After identifying potential interactions, appropriate actions should be taken based on the severity of the interaction. In addition, pharmacists must ensure that patients clearly understand the information provided, particularly regarding the proper use of medications, to minimize the risk of drug interactions [17].

▪ CONCLUSION

This study identified 54 potential drug interactions among 64 patients with Acute Respiratory İnfections (ARI) at Sitti Khadijah Hospital in Makassar, most of which were classified as moderate. The most frequently observed drug combinations were ambroxol–dexamethasone, ambroxol–paracetamol, and dexamethasone–erythromycin combinations. However, this study only identified potential drug interactions based on references and drug interaction databases and did not assess whether these interactions occurred clinically in patients. Therefore, the findings should be interpreted as potential drug–drug interactions rather than confirmed clinical events. These results highlight the importance of careful prescription review and

monitoring of drug combinations by healthcare professionals, particularly pharmacists, to reduce the risk of drug–drug interactions and improve the safety and effectiveness of therapy.

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