Journal Syifa Sciences and Clinical Research (JSSCR)
Volume 8 Nomor 2, 2026
Journal Homepage: http://ejurnal.ung.ac.id/index.php/jsscr, E-ISSN: 2656-9612 P-ISSN:2656-8187
DOI : https://doi.org/10.37311/jsscr.v4i1.xxxxx

Drug-Drug Interactions in Adult Acute Respiratory Infections Prescriptions at the Gorontalo Police Clinic: A Six-Month Retrospective Study

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ABSTRACT

Acute respiratory infection (ARI) is one of the most common conditions managed in primary care, and its treatment often involves multiple medications that may increase the risk of potential drug–drug interactions (DDIs). This study aimed to identify medication use patterns and to determine the frequency, severity, and mechanisms of potential DDIs in adult ARI prescriptions at the Gorontalo Police Clinic. This observational cross-sectional study used a retrospective approach based on outpatient medical record and prescription data collected from July to December 2023. A total of 110 eligible adult patients were included in the analysis. Potential DDIs were screened using the Drugs.com Interaction Checker and further reviewed with Stockley's Drug Interactions as a reference. Data were analyzed descriptively. The results showed that the median number of medications per patient was 4 (IQR 3–6), while polypharmacy was identified in 11 patients (10.0%). Potential DDIs were found in 2 of 110 patients (1.82%). All identified DDIs were moderate in severity, with no minor or major interactions detected. The interaction mechanism was exclusively pharmacodynamic, and both cases involved the combination of amoxicillin and chloramphenicol, indicating a potential antagonistic effect. In conclusion, potential DDIs in adult ARI prescriptions at the Gorontalo Police Clinic were uncommon but clinically relevant. Routine screening is needed to prevent potentially inappropriate antibiotic combinations in primary care practice.

Keywords:
Acute respiratory infection; Drug–drug interactions; Polypharmacy; Pharmacodynamic interaction; Primary care; Antibiotic prescribing

Received:	*Accepted:*	*Online:*
2025-06-04	*2026-03-12*	*2026-05-01*

1. Introduction

Acute respiratory infections (ARI) are categorised as upper respiratory tract infections or lower respiratory tract infections. These infections can be caused by various viral and bacterial pathogens and are a major cause of morbidity and mortality worldwide [1]. These infections cause 4.25 million deaths annually and are a leading cause of death worldwide [2]. In addition, the burden of ARI on the healthcare system is increasingly recognised, with increased utilisation of healthcare resources, hospitalisations, and outpatient visits caused by these infections [3].

According to data from the Gorontalo Provincial Health Office, of the 10 most common diseases with the potential to become extraordinary events, ARI ranks first with 6,787 cases [4].

The highest incidence of acute respiratory tract infections (ARI) occurs among adults. Data from the Gorontalo Provincial Health Office shows that the number of ARI cases from 2019 to 2021 totalled 5,785, consistently ranking among the top five of ten other diseases. In 2020, there were 1,514 cases (26.12%), and in 2021, there were 1,258 cases (21.88%). Although most ARI cases in adults are managed on an outpatient basis, symptomatic treatment often involves multiple medications, including antibiotics, antipyretics, and antitussives. This multi-drug symptomatic approach increases the likelihood of potential drug–drug interactions (DDIs) [5].

Patients with respiratory disorders often have additional illnesses and are usually treated with more than one medication to manage their respiratory conditions and other comorbidities. Thus, they are often exposed to polypharmacy (≥5 medications), which increases the risk of *drug-drug* interactions (DDIs) and *adverse drug reactions (*ADRs) [6].

Polypharmacy is defined as the administration of five or more medications simultaneously. It is a widespread and complex situation among patients with chronic diseases and is associated with age, gender, comorbidities, and the use of over-the-counter (OTC) medications and inappropriate health policies [7], [8], [9]. On the other hand, polypharmacy is also associated with an increased risk of drug-drug interactions (DDIs) in cases of concurrent administration of drugs that share interrelated pharmacological pathways [10]. DDIs are defined as the process by which the pharmacokinetics or pharmacodynamics of a drug are altered by the influence of another drug after combination. Pharmacokinetic interactions (PK DDIs) assess the effects of drug interactions by comparing the absorption, distribution, metabolism, and elimination (ADME) processes of drugs. Pharmacodynamic interactions (PD DDIs) are often divided into antagonistic, synergistic, and additive effects, which are assessed based on changes in drug effects [11].

This study aims to identify and quantify the frequency, severity, and mechanisms of potential drug-drug interactions (DDIs) in adult acute respiratory infection (ARI) prescriptions at the Gorontalo Police Clinic over a six-month period.

2. Methods

Study design and setting

This observational, cross-sectional study was conducted in an outpatient primary-care clinic over a six-month period. The objective was to identify and characterise potential drug–drug interactions (DDIs) among patients treated for acute respiratory infection (ARI) and to describe the distribution of DDI severity and mechanisms within routine prescribing. ARI was defined according to standard public-health criteria for acute upper/lower respiratory tract syndromes [1].

Participants and eligibility

All consecutive adult outpatients with an ARI diagnosis during the study window were screened. Records were eligible if demographic and medication data at the index visit were complete; charts with missing essential variables (e.g., drug name, dose, or duration) were excluded by listwise deletion without imputation to preserve interpretability.

Data sources and variables

From electronic/printed charts we abstracted age, sex, diagnosis, comorbidities (if available), and the full medication list at the index visit, including prescription and over-the-counter products (generic name, dose, frequency, route, and intended duration). Multi-ingredient products were recorded as single drug items to avoid double counting of components unless individual constituents were explicitly prescribed.

Definitions

Polypharmacy was defined a priori as concurrent use of **≥5** medications at the index visit, consistent with commonly adopted thresholds and recent reviews [9],[10]. Potential DDIs were those flagged by an electronic interaction-checking resource and adjudicated per predefined rules (below). DDI mechanisms were classified as pharmacokinetic (PK) or pharmacodynamic (PD) following contemporary methodological guidance [12]. DDI severity categories (minor, moderate, major) followed the screening platform's operational definitions, with external confirmation when needed using a standard compendium [15].

DDI screening and adjudication

Each medication list was screened with the Drugs.com Interaction Checker (platform severity labels retained verbatim). For quality assurance, all candidate DDIs and any clinically ambiguous flags were independently reviewed by two pharmacists/clinicians; disagreements were resolved by consensus using Stockley's Drug Interactions as the reference standard compendium [15]. Where antibiotic combinations were involved, mechanistic plausibility for PD antagonism was additionally cross-checked against locally available evidence when relevant [16]. When regimen interpretation required contextualisation with national policy, the current antibiotic guideline framework was consulted [14].

Outcomes

Primary outcomes were (i) the proportion of patients with ≥1 potential DDI and (ii) the number and distribution of DDI pairs by severity (minor, moderate, major). Secondary outcomes were the distribution by mechanism (PK vs PD) and a descriptive listing of clinically salient pairs observed in the cohort.

Sample size rationale

Given the descriptive aim and the finite clinic throughput over six months, the sample comprised all eligible encounters within the time frame (total N = 110 in the final analysis set). No formal power calculation was performed; precision is conveyed via exact counts and proportions with 95% confidence intervals where informative.

Statistical analysis

Analyses were descriptive. Categorical variables are presented as n (%); continuous variables as median (IQR). For polypharmacy, the proportion with ≥5 concurrent items is reported. No hypothesis testing was planned. Data handling and tabulation were performed in Microsoft Excel 365 (Microsoft® 365 Apps for enterprise, Version 2308, 2023). Missing data were excluded listwise; no imputation was undertaken.

Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Committee, Universitas Negeri Gorontalo (KEPK UNG) under decision letter No. 227A/UN47.B7/KE/2024 (protocol 009022757111132025030400001), dated 21 October 2024. The committee waived individual informed consent in accordance with institutional policy and national guidance.

3. Results and Discussion

The study population consisted of ARI patients at the Gorontalo Police Clinic who met the exclusion and inclusion criteria. There were 150 ARI patients from July to December 2023. A total of 110 ARI patients met the exclusion and inclusion criteria. The results and discussion of this study are presented in three sections: characteristics of ARI drugs based on class, potential for drug interactions, and mechanisms of drug interactions. The research results are presented in tables in the form of percentages. This study has obtained permission from the Health Research Ethics Committee of Gorontalo State University.

A total of 110 outpatient records of adults diagnosed with acute respiratory infection (ARI) were analysed. The majority of patients were male (n = 98; 89.09%), with an overall median age of 30 years (IQR 26–35). According to the clinical records, most encounters reflected uncomplicated ambulatory presentations consistent with the epidemiological predominance of upper-tract ARI in primary care settings [1].

Table 1. Patient demographics and medication characteristics

Characteristic	Value
Age, years — median (IQR)	30 (26–35)
Male, n (%)	98 (89.09%)
Female, n (%)	12 (10.91%)
Number of medications per patient — median (IQR)	4 (3–6)
Polypharmacy (≥5 concurrent items), n (%)	11 (10.0%)

The prescribing pattern revealed a median of 4 drug items per encounter (IQR 3–6), with a total of 238 individual drug items identified across all prescriptions (**Table 1**). The most frequently dispensed classes were combination cold preparations (OTC), followed by antibiotics (e.g., amoxicillin, chloramphenicol), antipyretic–analgesics (paracetamol, ibuprofen), antitussives/expectorants, and vitamin–mineral supplements (Table 2). These combinations reflect the empirical, symptomatic approach commonly applied to ARI management in primary care [1].

Table 2. Medication profile by therapeutic class at index visit

Therapeutic class	n	% of items
Combination cold preparations (OTC)	70	29.41
Antibiotics	46	19.33
Antihistamines	33	13.87
Mucolytics	31	13.03
Multivitamins	27	11.34
Analgesics/antipyretics	20	8.40
Corticosteroids	11	4.62
Total	238	100

From a pharmacological standpoint, the concurrent use of multiple agents within a single visit increases the potential for interaction events, particularly among antimicrobial and symptomatic drug classes with overlapping pharmacodynamic pathways [12]. Although the per-patient medication load was moderate, such polytherapy can still generate pairwise combinations of clinical relevance. Similar prescription patterns and polypharmacy thresholds have been reported in other ambulatory cohorts, underscoring the need for routine interaction screening in outpatient ARI practice [9], [10].

Polypharmacy, Medication Load, and Potential DDIs

Polypharmacy—defined a priori as the concurrent use of ≥5 medications—was observed in 11/110 patients (10.0%). The per-patient medication load at the index visit was median 4 items (IQR 3–6). Potential drug–drug interactions (DDIs) were identified in 2/110 patients (1.82%). All detected DDIs were moderate in severity on the screening platform, with no minor or major events recorded (**Table 3**).

Table 3. Medication load, polypharmacy, and potential DDIs (N = 110)

Measure	**Result**
Medication items per patient — median (IQR)	4 (3–6)
Polypharmacy (≥5 concurrent items), n (%)	11 (10.0%)
Patients with ≥1 potential DDI, n (%)	2 (1.82%)
DDI severity — Minor, n (%)	0 (0%)
DDI severity — Moderate, n (%)	2 (100%)
DDI severity — Major, n (%)	0 (0%)

The observed polypharmacy proportion and median medication count are consistent with ranges reported in ambulatory cohorts and with operational thresholds commonly used to characterise polypharmacy [9],[10]. From a pharmacological perspective, increasing medication count expands the combinatorial space for interaction pairs particularly in ARI regimens that often combine antimicrobials with symptomatic therapies thereby justifying routine interaction screening even when average medication load remains moderate [12]. The exclusive presence of moderate events aligns with Stockley's descriptors, which emphasise the need for caution and/or monitoring rather than absolute avoidance, supporting point-of-care electronic checks in primary care workflows [15].

Mechanism and Clinically Salient Pairs

All identified interaction events were pharmacodynamic (PD = 2; 100%), with no pharmacokinetic (PK) interactions (0; 0%), a pattern consistent with ARI regimens that typically combine antibiotics with symptomatic therapies [12]. The dominance of PD mechanisms indicates that clinical effects are driven primarily by antagonism or synergy at pharmacological targets, rather than exposure changes, so management hinges on selecting compatible combinations and monitoring clinical response rather than PK-based dose adjustments [12], [15].

Both events involved amoxicillin–chloramphenicol, classified as PD antagonism with moderate severity by the screening platform and concordant with Stockley's descriptors [15]. This pair is known to reduce antibacterial effectiveness due to opposing mechanisms of action an observation also supported by local in-vitro data against *Salmonella typhi* [16]. In ambulatory practice, the amoxicillin–chloramphenicol combination should therefore be avoided unless there is compelling microbiological justification and close monitoring of therapeutic response [15], [16].

Table 4. Clinically salient DDI pairs identified

Drug pair (generic)	Mechanism	Severity	n	Practical implication
Amoxicillin – Chloramphenicol	PD (antagonism)	Moderate	2	Avoid unless strongly justified; consider alternatives and/or close monitoring [15], [16].

Note: Mechanism and severity classifications follow the PK/PD framework and platform nomenclature, confirmed against Stockley's Drug Interactions [12], [15].

Quality Assurance, Context, and Integrated Interpretation

All interaction findings originated from electronic screening and were subsequently audited by two independent reviewers (pharmacist/clinician) and confirmed against Stockley's Drug Interactions; there were no material disagreements, and the platform's severity labels were retained [15]. This process minimises misclassification and ensures that events labelled moderate are interpreted as requiring caution and/or monitoring rather than constituting absolute contraindications [15]. The dominance of pharmacodynamic (PD) mechanisms observed is congruent with the PK/PD classification framework and with ARI regimens that commonly combine antibiotics with symptomatic therapies [12].

In the policy context, antibiotic prescribing patterns broadly align with Ministry of Health Regulation No. 28/2021, although occasional legacy combinations—such as amoxicillin–chloramphenicol—may still appear in routine practice, underscoring the continued importance of pharmacist-led interaction screening at prescribing/dispensing points [14],[15]. Taken together, the DDI burden in this cohort is low but non-zero (1.82% of patients), exclusively moderate PD and concentrated in a single clinically salient pair; these observations support routine interaction checks and prescriber–pharmacist feedback loops in primary care to avoid PD antagonism that could compromise antibacterial effectiveness [12],[16]. Given the descriptive, single-site design, estimates should be interpreted cautiously and validated in multi-centre studies that evaluate clinical outcomes and guideline adherence.

This study has several limitations. As a retrospective descriptive study conducted at a single primary-care clinic over a six-month period with a relatively small sample (N = 110), the findings may not be generalizable to other healthcare settings. The analysis relied on secondary data from medical records and prescriptions, which may contain incomplete or inconsistent information, and did not capture important factors such as patient adherence, unrecorded over-the-counter medication use, dose adjustments, or prescribers' clinical rationale. Potential DDIs were identified using the Drugs.com Interaction Checker and confirmed against Stockley's Drug Interactions; however, no cross-platform validation was performed, so some under- or over-detection remains possible. In addition, the study evaluated only potential DDIs and did not assess actual clinical outcomes, adverse events, or guideline concordance. The low number of detected interaction events (2/110; 1.82%) also precluded further risk-factor analysis, while the classification of pharmacokinetic and pharmacodynamic mechanisms was based on pharmacologic references rather than patient-level biomarker or pharmacokinetic data. Therefore, the findings should be interpreted cautiously and validated in larger, multi-centre studies that include clinical outcome assessment.

4. Conclusion

In this six-month primary-care cohort (N = 110), medication use for ARI was dominated by combination symptomatic therapy alongside targeted antibacterials. Potential drug–drug interactions were uncommon but present: 2/110 patients (1.82%) had a moderate, pharmacodynamic DDI, both involving the pair amoxicillin–chloramphenicol. No minor or major DDIs were detected. The mechanism profile was exclusively pharmacodynamic (100%), consistent with antagonism at the pharmacological target level rather than pharmacokinetic displacement. Clinically, the amoxicillin–chloramphenicol combination should be avoided unless there is compelling microbiological justification and close monitoring. Future research should (i) validate these descriptive estimates in multi-centre cohorts with larger samples; (ii) incorporate cross-platform DDI checks (e.g., Micromedex/Lexicomp) to assess detection concordance; (iii) evaluate clinical outcomes (symptom resolution, adverse events, treatment failure) linked to flagged DDIs; and (iv) assess guideline concordance and the impact of integrated electronic DDI screening and pharmacist feedback on prescribing quality in primary care.

Acknowledgements:

The authors sincerely thank Gorontalo Police Clinic for granting permission and facilitating the data collection process. The authors also acknowledge the support provided by the Department of Pharmacy, Faculty of Sports and Health, Gorontalo State University in facilitating access to academic resources and literature databases.

Conflict of Interest:

The authors declare that there are no conflicts of interest related to the publication of this article.

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