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Characteristics and evaluation of potential drug interactions among HIV/AIDS outpatients: a retrospective study at primary health center in a North Lampung regency, Indonesia

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Abstract: People living with HIV/AIDS require lifelong antiretroviral therapy (ART) and frequently experience complications and comorbidities that raise the risk of drug-drug interactions. This study aimed to characterize the patients, describe their medication use, and identify potential drug interactions among HIV/AIDS patients at a primary health center in North Lampung Regency. We performed a retrospective, descriptive review of medical records from January to December 2024. All eligible HIV/AIDS patients (N = 31) were included via total sampling. Drug interaction screening used the Lexicomp® application and Stockley's Drug Interactions. The results showed that most HIV/AIDS patients were male (74.19%), aged 36–45 years (41.93%), and classified as WHO clinical stage I (38.70%). The first-line ART regimen TLE (tenofovir + lamivudine + efavirenz) was prescribed to 54.8% of patients. A total of 35 potential interactions were identified: 65.7% were moderate pharmacokinetic, 28.6% minor pharmacokinetic, and 5.7% pharmacodynamic (2.9% major and 2.9% moderate). Moderate pharmacokinetic interactions predominated, underscoring the importance of proactive screening and ongoing medication review by pharmacists to prevent adverse events and optimize therapy in HIV/AIDS care.

Keywords: drug interactions, HIV/AIDS, patient characteristics, pharmacokinetic and pharmacodynamic mechanisms

Introduction

Human Immunodeficiency Virus (HIV) is a virus that targets and infects lymphocytes, especially CD4+ T cells, resulting in immune system deterioration and increasing the risk of progression to Acquired Immunodeficiency Syndrome (AIDS) [1]. AIDS is the advanced stage of HIV infection, characterized by severe immune system impairment and the emergence of opportunistic infections [2]. According to recent data from the World Health Organization (WHO), HIV continues to pose a significant global health challenge, with approximately 39.9 million people living with HIV worldwide and 630,000 AIDS-related deaths in 2023 [3]. However, only 77% of people living with HIV globally receive antiretroviral therapy, highlighting substantial treatment gaps [4].

Indonesia represents one of Asia's fastest-growing HIV epidemics, with an estimated 640,443 individuals living with HIV [5]. According to the latest estimates from UNAIDS in 2023, approximately 570,000 individuals were living with HIV in Indonesia, with only 64% knowing their status and merely 34% receiving antiretroviral therapy [6,7]. Data from SIHA (HIV/AIDS Information System) in 2023 indicated that Lampung Province was among the 30 provinces with the highest number of AIDS cases, reporting a total of 1,386 HIV/AIDS cases [8]. These figures highlight the ongoing burden of HIV/AIDS in Indonesia, particularly in Lampung Province, where prevalence rates remain a concern for public health authorities and place the region far from achieving the UNAIDS 95-95-95 targets.

Individuals with HIV/AIDS commonly present with complications and comorbid conditions [9], which may negatively impact their quality of life and necessitate adjunctive therapies. Opportunistic infections represent the most prevalent complications among HIV/AIDS patients, with common examples including pneumocystosis, toxoplasmosis, and progressive multifocal leukoencephalopathy (PML) [10,11]. Among individuals with HIV, frequently observed comorbidities include tuberculosis, mental

health disorders, anemia, cardiovascular conditions (e.g., hypertension), renal dysfunction, pneumonia, as well as hepatitis B and C infections [12,13]. Notably, tuberculosis remains the leading cause of death among people living with HIV, with HIV-infected individuals being 18 times more likely to develop active TB disease, and up to 70% of HIV-infected people in resource-limited settings experiencing TB coinfection [14,15].

Antiretroviral therapy (ART) is the primary form of treatment used for managing HIV/AIDS patients [16]. The main goals of this therapy are to suppress viral replication, improve quality of life, and prolong patient survival. Typically, ART is administered as a combination of three different antiretroviral drugs to ensure treatment efficacy [17,18]. However, the concurrent use of multiple medications increases the risk of drug interactions, which may alter the concentration of other drugs in the body and result in suboptimal therapeutic outcomes [19,20]. Recent research demonstrates that nearly half (47.5%) of HIV patients experience potential clinically significant drug interactions, with 77% classified as having potential clinical relevance [21].

Drug interactions may be triggered by various factors, including the pharmacokinetic and pharmacodynamic properties of the drugs, the patient's health condition, and the use of other medications not directly related to HIV therapy [22]. Most clinically significant interactions are mediated by the cytochrome P-450 system, particularly CYP3A4 enzymes, which are involved in the metabolism of many antiretroviral drugs, especially protease inhibitors and non-nucleoside reverse transcriptase inhibitors [23,24]. Risk factors for these interactions include age exceeding 42 years, having more than three comorbidities, and treatment with three or more antiretrovirals or protease inhibitor-based regimens [25]. The presence of comorbid conditions can significantly hinder the success of therapy, primarily due to drug interactions and adverse effects arising from the concurrent use of multiple medications [26].

In primary healthcare settings, particularly in developing countries like Indonesia, the management of HIV drug interactions faces unique challenges due to limited specialized training and monitoring capabilities [27,28]. The co-occurrence of HIV and tuberculosis infection, prevalent in Indonesian settings, introduces additional complexity as drug-drug interactions between anti-TB and antiretroviral medications can significantly impact treatment efficacy, safety, and overall patient well-being [29,30]. Therefore, a thorough understanding of potential drug interactions is essential in the management of patients with HIV/AIDS, particularly in resource-limited primary care settings.

This study aimed to identify the types and prevalence of potential drug interactions in patients living with HIV/AIDS at a primary health center in North Lampung Regency. The findings of this study were expected to provide valuable insights and useful information to guide healthcare professionals in improving the quality and standard of healthcare services, particularly in primary care settings where most HIV patients receive their ongoing care.

Methods

This study is a non-experimental, descriptive study conducted retrospectively by collecting data from patients' medical records. The study population consisted of HIV/AIDS patients undergoing outpatient treatment during the period of January to December 2024. Sampling was performed using a total sampling method based on predefined inclusion and exclusion criteria.

Based on the conducted study, a total of 31 patients met the inclusion and exclusion criteria. The inclusion criteria for this study were HIV/AIDS patients who received treatment at the primary health center during the period of January to December 2024, patients aged ≥18 years, and those receiving more than one medication. The exclusion criteria included patients with incomplete medical record data (missing information on age, sex, diagnosis, or prescribed medications). This study received ethical clearance from the Ethics Committee of Jendral Ahmad Yani Regional General Hospital, Metro City, with reference number: 370/596/KEPK-LE/LL-02/2025.

The variables in this study include the potential for drug interactions in HIV/AIDS patients, analyzed based on the mechanism of interaction (pharmacokinetic or pharmacodynamic) and the severity level (severe, moderate, or mild). Data obtained from the medical records of HIV/AIDS patients at primary health center included patient characteristics (such as gender, age, clinical stage, complications, and comorbidities) as well as treatment-related information. The data were analyzed based on a literature review using the Lexicomp 2025 application and the Stockley's Drug

Interactions Ninth Edition to identify potential drug interactions. The results were presented in tables and percentages, and described narratively.

Results

Patient demographic and clinical characteristics

Patient characteristics were categorized by gender, age, clinical stage, presence of complications, and comorbidities. Details are presented in Table 1.

Complications and Comorbidities

Table 2 shows the spectrum of complications and comorbidities; note that one patient may have >1.

Drug utilization profile

The percentage of drug use among outpatient HIV/AIDS patients at the primary health center (January–December 2024) was obtained from 31 patient prescriptions. All medications were administered orally. The ARV and non-ARV profiles are shown in Tables 3 and 4.

Table 1. Characteristics of HIV/AIDS patients

Characteristics	N = 31	
	Frequency (n)	Percentage (%)
Gender		
Male	23	74.19
Female	8	25.81
Age (years)		
18 – 25	8	25.81
26 – 35	8	25.81
36 – 45	13	41.94
46 – 55	2	6.45
Clinical stage		
I	12	38.71
II	5	16.13
III	8	25.81
IV	6	19.35
Complication		
Present	26	83.87
Absent	5	16.13
Comorbidity		
Present	2	6.45
Absent	29	93.55

Table 2. Complications and comorbidities observed in patients with HIV/AIDS

Incidence	Disease	Frequency (n)	Percentage (%)
Complications	Tuberculosis (TB)	16	48.48
	Syphilis	3	9.09
	Hand, foot, and mouth disease	2	6.06
	Fever	2	6.06
	Oral candidiasis	1	3.03
	Acute otitis media	1	3.03
	Suspected tuberculosis	1	3.03
	Skin abscess	1	3.03
	Pulmonary tuberculosis	1	3.03
	Chronic suppurative otitis media	1	3.03
	Opportunistic infection	1	3.03
Comorbidity	Dyspepsia	1	3.03
	Gout arthritis	1	3.03
	Hyperthyroidism	1	3.03
Total		33	100

Note: One patient may experience more than one complication and/or comorbidity

Table 3. Antiretroviral (ARV) drug utilization in HIV/AIDS patients

Combinations	Frequency (n)	Percentage(%)
TLE (TDF + 3TC + EFV)	17	54.84
TLD (TDF + 3TC + DTG)	8	25.81
Duviral (AZT + 3TC) + NVP	3	9.68
Forstavir EM (TDF + FTC) + Aluvia (LVP/r)	1	3.23
ABC + 3TC + Aluvia (LVP/r)	1	3.23
Forstavir EM (TDF + FTC) + NVP	1	3.23
Total	31	100.00

Note: ABC: abacavir; AZT: zidovudine; 3TC: lamivudine; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; LPV/r: lopinavir/ritonavir; NVP: nevirapine; TDF: tenofovir disoproxil fumarate.

Table 4. Non-ARV drug utilization in HIV/AIDS patients

Drug	Frequency (n)	Percentage (%)
Isoniazid	15	23.44
Cotrimoxazole	12	18.75
Vitamin B_6	7	10.93
Paracetamol	5	7.81
Vitamin B complex	5	7.81
Dexamethasone	4	6.25
Amoxicillin	3	4.68
Cetirizine	3	4.68
Chlorpheniramine	3	4.68
Diclofenac sodium	2	3.12
RHZE (rifampicin + isoniazid + pyrazinamide + ethambutol)	2	3.12
Antacid	1	1.56
Guaifenesin	1	1.56
Metronidazole	1	1.56
Total	64	100.00

Notes:
• RHZE is the standard intensive-phase TB regimen (rifampicin + isoniazid + pyrazinamide + ethambutol).
• Percentages are calculated as (n / 64) × 100 and rounded to two decimal places.

Table 5. Occurrence of potential drug interactions based on mechanism and severity level

Drug interaction categories		Drug-drug interaction	Sub-mechanism	n (%)	Total
Mechanism	**Severity**				
Pharmacokinetic	Major	-	-	-	94.28%
	Moderate	3TC >< Cotrimoxazole	PK - Excretion	11 (31.42)	
		DTG >< Isoniazid	PK - Excretion	5 (14.28)	
		TLE >< Dexamethasone	PK - Metabolism	3 (8.57)	
		EFV >< Rifampicin	PK - Metabolism	2 (5.71)	
		Paracetamol >< Isoniazid	PK - Metabolism	1 (2.85)	
		Cotrimoxazole >< Rifampicin	PK - Metabolism	1 (2.85)	
	Minor	EFV >< Isoniazid	PK - Metabolism	8 (22.85)	
		LPV/r >< Cetirizine	PK - Metabolism	1 (2.85)	
		ABC >< LPV/r	PK - Distribution	1 (2.85)	
Pharmacodynamics	Major	TDF >< Diclofenac sodium	PD	1 (2.85)	5.7%
	Moderate	TDF >< LPV/r	PD	1 (2.85)	
	Minor	-	-	-	
Total				35 (100)	100%

Note: 3TC: lamivudine; ABC: abacavir; EFV: efavirenz; DTG: dolutegravir; LVP/r: lopinavir/ritonavir; TDF: tenofovir; TLE: tenofovir + lamivudine + efavirenz

The most commonly used ARV combination was TLE, consisting of tenofovir (TDF), lamivudine (3TC), and efavirenz (EFV), used by 17 patients (54.83%). The TLD combination (TDF + 3TC + dolutegravir) was used by 8 patients (25.80%), while the Duviral combination (zidovudine [AZT] + 3TC) with nevirapine was used by 3 patients (9.67%). The profile of non-ARV drug use among HIV/AIDS patients is presented in Table 4.

Drug interactions

Potential drug interactions (mechanism and severity) were identified via Lexicomp and Stockley's Drug Interactions (9th ed.). Results are in Table 5.

Moderate pharmacokinetic interactions were most common (n = 23; 65.71%), followed by minor pharmacokinetic interactions (n = 10; 28.57%). Major and moderate pharmacodynamic interactions each occurred once (2.58%), and no major pharmacokinetic or minor pharmacodynamic interactions were observed.

Discussion

Based on patient characteristics, most individuals living with HIV/AIDS were male (74.19%). This finding is consistent with data from the HIV/AIDS Information System (SIHA) in 2023. Men's behaviors and social contexts may make them more vulnerable to HIV transmission than women [8]. The largest proportion of HIV/AIDS patients fell into 36-45-year-old age group (41.93%), which aligns with the 2024 report from the Directorate General of Disease Prevention and Control, Ministry of Health, Republic of Indonesia, stating that people aged 25–49 account for the highest number of HIV cases. Individuals in this age range are more likely to engage in risky behaviors—such as unprotected sex, substance abuse, or participation in MSM (men who have sex with men) networks—which increases their HIV risk [31,32].

Clinical Stage I was the most common, observed in 38.70% of patients, mirroring a study at a Tasikmalaya hospital that reported most HIV diagnoses at Stage I [33]. Clinical stage informs decisions about initiating ART and ongoing patient monitoring, since higher stages carry a greater risk of opportunistic infections and related complications, often necessitating more medications [34].

Tuberculosis was the most frequent complication (48.48%). In HIV-infected persons, TB progresses more rapidly due to CD4+ T-cell depletion, which impairs granuloma formation against *Mycobacterium tuberculosis*. This is consistent with findings from Dr. Soetomo Hospital in Surabaya [35–37].

The first-line ARV regimen (TDF + 3TC + EFV) was used by 54.83% of patients, in line with WHO and Indonesian Ministry of Health guidelines [38,39]. The most commonly used non-ARV drug among HIV/AIDS patients was the antituberculosis drug isoniazid, accounting for 23.43%. Isoniazid is part of the standard TB treatment regimen alongside other first-line antituberculosis drugs. In addition, isoniazid is also used to treat latent TB infection, typically administered as monotherapy for a duration of 6 to 9 months [40,41].

Potential drug interactions can significantly affect clinical outcomes, as patients remain on lifelong ART plus supportive therapies. Moderate pharmacokinetic interactions predominated (65.71%), a pattern also seen at Dr. Soedarso Regional Hospital in Pontianak [42]. Pharmacokinetic interactions, which dominated the analysis results, have the potential to alter the plasma concentration of antiretroviral drugs, thereby reducing therapeutic efficacy or increasing the risk of toxicity [43]. Pharmacokinetic interactions occur when an administered drug influences the absorption, distribution, metabolism, or excretion (ADME) of another drug, thereby potentially increasing or decreasing the amount of the drug available to produce its pharmacological effect [44].

The most frequently observed moderate interaction was between lamivudine and cotrimoxazole, with 11 occurrences (31.42%). This interaction operates via a pharmacokinetic mechanism that may lead to increased levels of lamivudine in the body [45]. Other studies have reported that lamivudine clearance can be reduced by up to 31%, resulting in a 43% increase in steady-state concentration. Therefore, routine blood monitoring and close clinical supervision are recommended when this combination is used [46].

Pharmacodynamic interactions were less frequently observed but did occur, primarily at major and moderate severity levels. Pharmacodynamic interactions involve the modulation of a drug's pharmacological response due to the presence of another drug, either through antagonistic or additive mechanisms. These interactions typically occur at the level of the drug's receptor or site of action [44]. Pharmacodynamic interactions, although less frequent,

still pose a risk of additive or antagonistic effects that may worsen the immunological status of HIV/AIDS patients, interfere with the effectiveness of antiretroviral therapy, and increase the risk of complications or the development of drug resistance [47].

In this study, a major severity drug interaction was identified between tenofovir (TDF) and diclofenac sodium, with a 100% occurrence rate, involving a pharmacodynamic mechanism that can lead to nephrotoxicity [48]. The concomitant use of NSAIDs (non-steroidal anti-inflammatory drugs) with tenofovir may increase the risk of nephrotoxicity, particularly in patients with impaired renal function, low body weight, or those taking other medications that elevate tenofovir levels. Therefore, in patients at risk of renal impairment, alternative therapies to NSAIDs should be considered, and regular monitoring of renal function is strongly recommended.

The instability of drug concentrations resulting from interactions can lead to treatment failure, viral resistance, and increased morbidity and mortality. Therefore, early detection and management of potential drug interactions are critical for maintaining treatment success and improving clinical outcomes in HIV/AIDS patients [49,50]. Pharmacists at primary healthcare centers are expected to play an active role in monitoring potential drug interactions in HIV/AIDS patients, conducting therapy monitoring and evaluating clinical symptoms or relevant laboratory results, as well as providing patient education regarding possible interactions and adverse drug effects [51].

This study was limited by incomplete data, particularly regarding patients prior drug histories. The lack of such data may limit the ability to conduct a more in-depth analysis of factors influencing patient health outcomes. More comprehensive laboratory data and medical records would provide a clearer and more accurate understanding, thereby improving the validity and reliability of findings related to drug interactions.

Conclusion

Potential drug interactions, based on mechanism and severity, consisted of moderate pharmacokinetic interactions (65.71%), minor pharmacokinetic interactions (28.57%), major pharmacodynamic interactions (2.85%), and moderate pharmacodynamic interactions (2.85%). These findings indicate that the most frequently occurring potential drug interaction in this study was moderate pharmacokinetic interaction.

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Declaration of interest

None.

Contributors

NAN and ADA contributed to the study's conception, design, and manuscript revision. MAK conducted the data collection and analysis and drafted the manuscript.

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