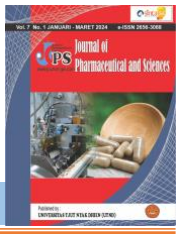
Journal of Pharmaceutical and Sciences
Electronic ISSN: 2656-3088 DOI: https://doi.org/10.36490/journal-jps.com
Homepage: https://journal-jps.com
REVIEW ARTICLE JPS. 2026, 9(4), 3488-3498



Analysis of Drug-Related Problems in Outpatient HIV Patient Based On PCNE Criteria: A Literature Review

Analisis Drug-Related Problems Pada Pasien HIV Rawat Jalan Berdasarkan Kriteria PCNE: Literatur Review

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Abstract

HIV (Human Immunodeficiency Virus) is a major health problem in the world and is a chronic disease that can be managed with antiretrovirals, but it also increases the risk of comorbidities. This review assesses drug-related problems (DRPs) in HIV patients using the Pharmaceutical Care Network Europe (PCNE) classification. A systematic search for articles published in the last 10 years was conducted using Google Scholar, Scopus, and PubMed. Three articles met the inclusion criteria, reporting DRP frequencies ranging from 58 to 183 cases, with 1,605 DRP causes identified in one of the studies. The most common problem domain was treatment safety, namely the incidence of adverse drug reactions with a total of 9 cases (15.5%), 87 cases (47.5%), and 475 cases (58.1%). The domains causing DRP that were frequently found were "Patient cannot understand instructions correctly" (C7.10) with 321 cases (19.1%), Patient non-compliance (C7.1) with 320 cases (19%), and inappropriate monitoring of therapy (C9.1) with 141 cases (8.4%). In conclusion, DRPs represent a major burden in HIV outpatient care, largely due to adverse drug reactions and patient-related factors. The role of the clinical pharmacist is critical to the identification, prevention, and resolution of DRP to optimize long-term antiretroviral therapy.

Keywords: *Antiretroviral therapy, HIV, Drug-Reated Problems, Pharmaceutical Care Network Europe, PCNE*

Abstrak

HIV (*Human Immunodeficiency Virus*) merupakan masalah kesehatan utama di dunia dan menjadi penyakit kronis yang dapat dikelola dengan antiretroviral, tetapi juga meningkatkan risiko komorbiditas. Tinjauan ini menilai masalah terkait obat (DRP) pada pasien HIV menggunakan klasifikasi Pharmaceutical Care Network Europe (PCNE). Pencarian artikel secara sistematis yang diterbitkan dalam 10 tahun terakhir dilakukan menggunakan Google Scholar, Scopus, dan PubMed. Tiga artikel memenuhi kriteria inklusi, melaporkan frekuensi DRP antara 58 sampai 183 kasus, dengan 1.605 penyebab DRP terindentifikasi dalam salah satu studi. Domain masalah yang paling umum adalah keamanan pengobatan, yaitu kejadian efek samping dengan jumlah 9 kasus (15.5%), 87 kasus (47.5%), dan 475 kasus (58.1%). Domain penyebab DRP yang banyak ditemukan adalah "Pasien tidak dapat memahami instruksi dengan benar" (C7.10) dengan 321 kasus (19.1%), Ketidakpatuhan pasien (C7.1) dengan 320 kasus (19%), dan Pemantauan monitoring terapi yang tidak tepat (C9.1) dengan 141 kasus (8.4%). Kesimpulannya, DRP merupakan beban utama dalam perawatan rawat jalan HIV, sebagian besar disebabkan oleh reaksi obat yang merugikan dan faktor-faktor yang berkaitan dengan pasien. Peran apoteker klinis sangat penting untuk identifikasi, pencegahan, dan penyelesaian DRP untuk mengoptimalkan terapi antiretroviral jangka panjang.

Kata Kunci: *Terapi antiretroviral, HIV, Drug-Reated Problems, Pharmaceutical Care Network Europe, PCNE*

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Article History:
Received: 16/05/2026,
Revised: 06/08/2026,
Accepted: 06/08/2026,
Available Online : 15/11/2026.
QR access this Article

https://doi.org/10.36490/journal-jps.com.v9i3.1711

Introduction

HIV is a major health problem in the world. UNAIDS data indicates that in 2023, there were 39.9 million people living with HIV worldwide. Women and girls accounted for 53% of this total. An estimated 30.7 million people living with HIV were receiving treatment [1]. Indonesia has the world's highest number of people living with HIV (PLWH) ranking 14th and the highest number of new HIV infections ranking 9th. In 2025, there were around 564,000, but only 63% of them were aware of their status. Of that number, 67% have undergone antiretroviral therapy (ARV), and only 55% have reached a viral load of undetectable, meaning that the virus is not detected and the risk of infection is very low [2].

A thorough grasp of DRP patterns is desperately needed to direct pharmacist-led quality improvement in outpatient HIV care given Indonesia's significant HIV treatment gap and the complicated polypharmacy load in PLWH [3,4]. Long-term ART has transformed HIV into a manageable chronic condition while increasing the risk of polypharmacy, comorbidity, and Drug-Related Problems (DRPs), which the Pharmaceutical Care Network of Europe (PCNE) defines as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [5,6]. Drug-related problems (DRPs) in HIV patients may include drug interactions, adverse drug reactions, non-adherence, and inappropriate drug selection, with incidence rates ranging from 24.9% to 83.2% across outpatient studies [5,7,8].

Therefore, this literature review aimed to evaluate and synthesize evidence on the incidence, types, and causes of DRPs in HIV outpatients based on the PCNE classification system, as a basis for developing evidence-based clinical pharmacy interventions in long-term HIV management. PCNE employs a structured system that distinguishes between problems, root causes, and interventions for the identification of DRPs [8].

This review comprehensively analyzes DRP domains based on the PCNE classification system—covering the problem (P) and cause (C) domains—while also being the first to synthesize this evidence with specific implications for clinical pharmacy practice in Indonesia and the first to apply this framework to an outpatient HIV population in a published literature review.

Method

This systematic literature review was conducted following the PRISMA 2020 guidelines to identify studies on Drug-Related Problems (DRPs) in HIV outpatients. A literature search was conducted on PubMed, Scopus, and Google Scholar for articles published between 2015 and 2025, using the following keywords specific to each database:

Scopus

("drug-related problems" OR "drug therapy problems" OR "medication-related problems" OR "adverse drug reactions" OR "drug interactions" OR "medication errors" OR DRP) AND (HIV OR AIDS OR "antiretroviral therapy" OR "antiretroviral drugs" OR ART OR HAART) AND (outpatient OR ambulatory OR "outpatient clinic" OR "HIV clinic" OR "pharmaceutical care" OR "clinical pharmacist")

Pubmed

("drug-related problems"[tiab] OR "medication-related problems"[tiab] OR "drug therapy problems"[tiab] OR "adverse drug reactions"[tiab] OR "medication errors"[tiab] OR DRP[tiab]) AND (HIV[tiab] OR AIDS[tiab] OR "antiretroviral therapy"[tiab] OR ART[tiab] OR HAART[tiab]) AND (outpatient[tiab] OR ambulatory[tiab] OR "clinical pharmacist"[tiab] OR "pharmaceutical care"[tiab])

Electronic ISSN : 2656-3088
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Google scholar
"drug-related problems" HIV outpatient "pharmaceutical care"

Inclusion criteria were established to ensure the validity and homogeneity of the analysis results. These criteria included: (1) original articles with an observational design (cohort, cross-sectional); (2) involving adult HIV patients (≥18 years) receiving ART; (3) classifying DRPs using the Pharmaceutical Care Network Europe (PCNE); (4) published between 2015 and 2025; and (5) available as full-text articles in English. Articles were excluded if they were literature reviews, inpatient studies, or did not contain relevant data on Drug-Related Problems (DRPs). All identified articles were imported into Rayyan.AI to remove duplicates. Titles and abstracts were screened against eligibility criteria, followed by a full-text review. Relevant data, including study design, sample size, and reported DRPs, were extracted using Microsoft Excel. The study selection process was documented using a PRISMA 2020 flowchart. The study selection process was documented using the PRISMA 2020 flow diagram (Figure 1).

Three of the 1,249 identified articles met all criteria and were included in the final analysis due to their sound methodology and meeting established quality standards. Due to variations in study design and characteristics, a meta-analytic analysis was not performed. Instead, a descriptive analysis was conducted to evaluate and compare the average prevalence of DRPs and the patterns of DRP types found in each study. This analysis provides a comprehensive overview of the trends and burden of DRPs in the studied population. The entire process was conducted using a transparent and systematic approach and based on the principles of evidence-based review, ensuring that the results were free from publication and selection bias. The decision to restrict publication to indexed open-access journals was intended to ensure the quality and replicability of the research results. The strategy for harmonizing the three different PCNE versions involves mapping equivalent codes across versions to enable more accurate data synthesis (Table 2 and Table 3).

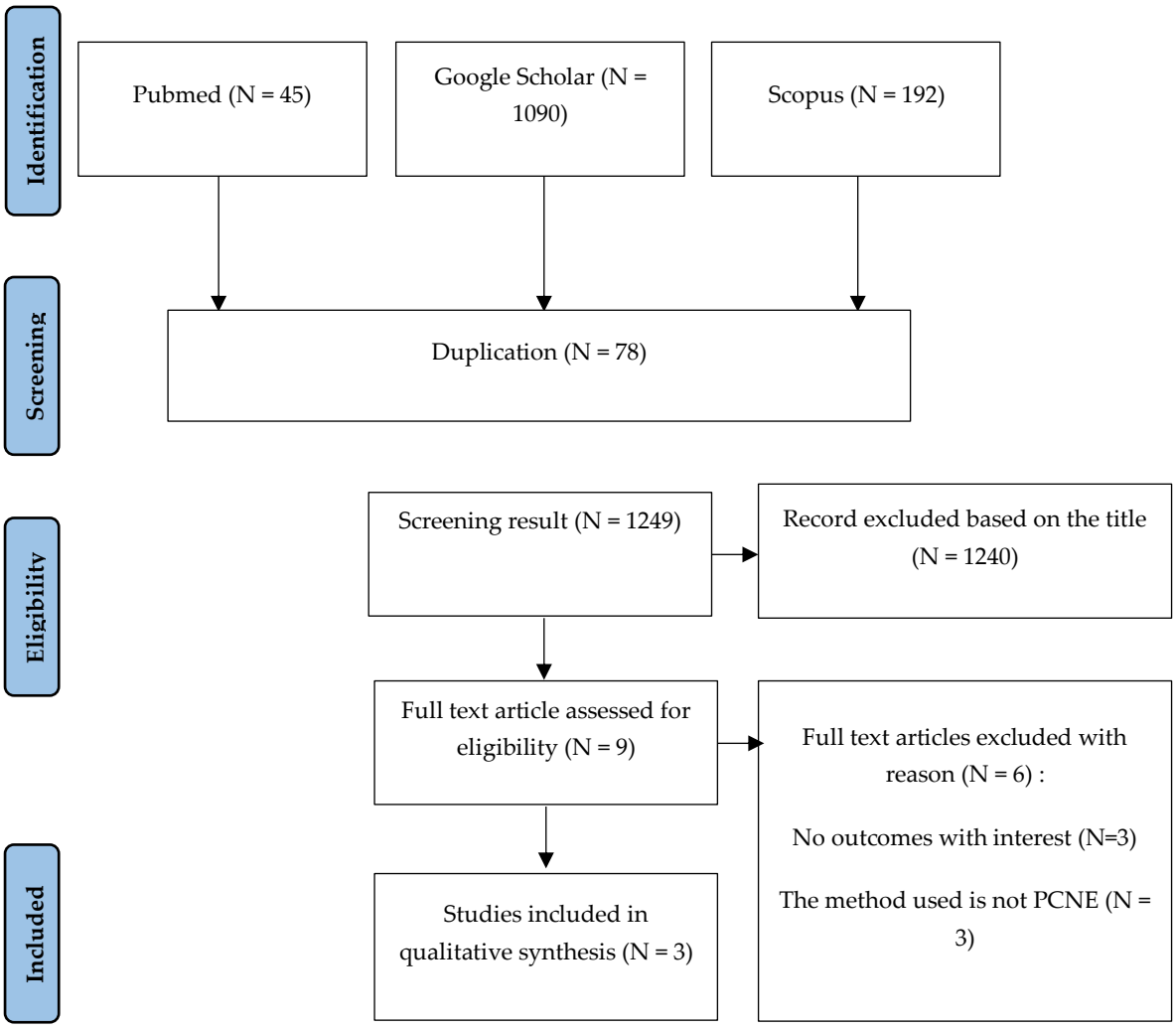


Figure 1 Article selection stages using PRISMA

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Result and Discussion

Table 1 Article quality assessment

Author (year)	Design	Instrument	Score	Category
Kara et al. (2019) [4]	Cross-sectional	JBI	5/8	Moderate bias risk
Che Pa et al. (2024) [6]	Retrospective cohort	NOS	5/9	Moderate bias risk
Gopinath et al. (2018) [7]	Prospective observational	JBI	4/9	High bias risk

Quality assessment using the Joanna Briggs Institute (JBI) and Newcastle-Ottawa Scale (NOS) classified the articles as having high and moderate risk of bias, while the interpretation was conducted with caution (Table 1).

Table 2. An overview of the article analysis findings

Referensce	Research Methods	Country	Sample	Type PCNE	Result			
					Total Problem	Total Cause	ARV regimen	Analysis
[4]	Cross sectional	Turkey	181	V7.0	58	58	Not specifically mentioned	1. A total of 58 DRPs were identified in 45 patients. 2. The most frequent DRPs identified were effect of drug treatment not optimal accounting for 26 (44.8%) and untreated indication accounting for 19 (32.8%).
[6]	Cohort	Malaysia	355	V9.1	817	1605	Not specifically mentioned	1. Treatment safety was the most frequent problem domain, accounting for 475 (58.14%), followed by treatment effectiveness (P1) at 340 (41.62%). The most common cause domain was patient-related (C7), accounting for 937 (58.38%).
[7]	Observational	India	125	V5.1	183	183	1. AZT + 3TC + NVP 2. TDF + 3TC + EFV 3. AZT + 3TC + EFV 4. TDF + 3TC + ATV/r	1. A total of 183 DRPs were identified in 104 patients, resulting in a rate of 1.75 DRPs per patient. 2. Adverse reactions were the most frequently occurring problem domain, accounting for 123 (67.21%) problems. Drug/dosage selection was the most common cause, accounting for 124 (67.75%) problems

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Table 3 PCNE standardization across versions (V5.1, V7.0, V9.1)

Description	PCNE V7.0	PCNE V9.1	PCNE V5.1
No effect of drug treatment	P1.1	P1.1	Not mentioned
Effect of drug treatment not optimal	P1.2	P1.2	Not mentioned
Unnecessary drug-treatment	P1.3	P3.1	Not mentioned
Untreated indication	P1.4	P1.3	Not mentioned
Adverse drug event	P2.1	P2.1	P/1/P1.2/P1.3
Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes	P3.1	Not mentioned	Not mentioned
Non-adherence	C7.1	C7.1	C4.1
Inappropriate drug according to guidelines/formulary	C1.1	C1.1	Not mentioned
Inappropriate drug (within guidelines but otherwise contraindicated)	C1.2	Not mentioned	Not mentioned
No indication for drug	C1.3	C1.2	Not mentioned
Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	C1.4	C1.3	Not mentioned
No or incomplete drug treatment in spite of existing indication	Not mentioned	C1.5	Not mentioned
New indication for drug treatment presented	C1.9	Not mentioned	Not mentioned
Inappropriate drug form (for this patient)	Not mentioned	C2.1	Not mentioned
Drug dose too low	C3.1	C3.1	Not mentioned
Drug dose too high	C3.2	C3.2	Not mentioned
Dosage regimen too frequent	C3.4	C3.4	C2.1
Dose timing instructions wrong, unclear, or missing	Not mentioned	C3.5	C3.1
Prescribed drugs not available	C5.1	C5.1	C5.1
Necessary information not provided	Not mentioned	C5.2	Not mentioned
Wrong drug, strength, or dosage advised (OTC)	Not mentioned	C5.3	Not mentioned
Wrong drug or strength dispensed	C5.4	C5.4	Not mentioned
Inappropriate timing of administration and/or dosing intervals	C6.1	C6.1	C2.1
Drug overadministered	C6.3	C6.3	C2.3
Drug not administered at all	C6.4	C6.4	Not mentioned
Patient uses/takes less drug than prescribed or does not take the drug at all	C7.1	C7.1	C4.1
Patient uses/takes more than prescribed	Not mentioned	C7.2	Not mentioned
Patient takes a drug that interacts	C7.4	C7.4	Not mentioned
Patient takes food that interacts	C7.5	C7.5	C4.10
Patient stores drug inappropriately	C7.4	C.76	Not mentioned
Inappropriate timing or dosing intervals	Not mentioned	C7.7	Not mentioned
Patient administers/uses the drug in a wrong way	C7.5	C7.8	Not mentioned
Patient unable to use drug/form as directed	C7.8	C7.9	Not mentioned
Patient unable to understand instructions properly	Not mentioned	C7.10	Not mentioned
No or inappropriate outcome monitoring (including TDM)	C8.1	C9.1	Not mentioned
Other cause: Insufficient supply	C8.2	C9.2	C6.1
No obvious cause	C8.3	C9.3	C6.2

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Table 4. Distribution of The Problems of Drug-Related Problems in HIV patient Based on PCNE Classification

Primary Domain	Code	Problem	Number (%)
Treatment effectiveness	P 1.1	No effect of drug treatment/therapy failure	1 (1.7) [4]
	P 1.2	Effect of drug treatment not optimal	26 (44.8) [4], 340 (41.6) [6]
	P 1.3	Unnecessary drug-treatment	1 (1.7) [4]
	P 1.4	Untreated indication	19 (32.8) [4]
Treatment safety	P 2.1	Adverse drug event (possibly) occuring	9 (15.5) [4], 475 (58.1) [6]
Others	P 3.1	Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes	2 (3.4) [4]
	P 3.2	Unnecessary drug-treatment	2 (0.2) [6]
Drug selection	C 1.1	Inappropriate drug according to guidelines/formulary	1 (1.7) [4]
	C 1.2	Inappropriate drug (within guidelines but otherwise contraindicated)	10 (17.2) [4]
	C 1.3	No indication for drug	1 (1.7) [4]
	C 1.4	Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements	9 (15.5) [4], 124 (7.4) [6]
	C 1.6	No or incomplete drug treatment in spite of existing indication	11 (19) [4], 2 (0.1) [6]
	C 1.9	New indication for drug treatment presented	1 (1.7) [4]
Drug form	C 2.1	Inappropriate drug form (for this patient)	3 (0.2) [6]
Dose selection	C 3.1	Drug dose too low	1 (1.7) [4], 1 (0.1) [6]
	C 3.2	Drug dose too high	5 (8.6) [4]
	C 3.4	Dosage regimen too frequent	2 (0.1) [6]
	C 3.5	Dose timing instructions wrong, unclear, or missing	1 (0.1) [6]
Dispensing	C 5.1	Prescribed drugs not available	8 (0.5) [6]
	C 5.2	Necessary information not provided	3 (0.2) [6]
	C 5.3	Wrong drug, strength, or dosage advised (OTC)	6 (0.4) [6]
	C 5.4	Wrong drug or strength dispensed	4 (0.2) [6]
Drug use process	C 6.1	Inappropriate timing of administration and/or dosing intervals	6 (10.3) [4]
	C 6.3	Drug overadministered	1 (1.7) [4]
	C 6.4	Drug not administered at all	7 (12.1) [4]
Patient related	C7.1	Patient uses/takes less drug than prescribed or does not take the drug at all	2 (3.4) [4], 320 (19) [6]
	C 7.2	Patient uses/takes more than prescribed	1 (0.1) [6]
	C 7.4	Patient takes a drug that interacts	93 (5.5) [6]
	C 7.5	Patient takes food that interacts	85 (5) [6]
	C 7.6	Patient stores drug inappropriately	3 (0.2) [6]
	C 7.7	Inappropriate timing or dosing intervals	126 (7.5) [6]
	C 7.8	Patient administers/uses the drug in a wrong way	3 (5.2) [4], 1 (0.1) [6]
	C 7.9	Patient unable to use drug/form as directed	1 (0.1) [6]
	C 7.10	Patient unable to understand instructions properly	321 (19.1) [6]
Others	C 9.1	No or inappropriate outcome monitoring (including TDM)	141 (8.4) [6]
	C 9.2	Other cause: Insufficient supply	94 (5.6) [6]
	C 9.3	No obvious cause	344 (20.4) [6]

Source: [4]Kara et al. (2019), [6]Che Pa et al. (2024)

The three studies reviewed used various methodological designs as listed in Table 2, namely cross-sectional studies (n=181), cohort studies (n=355), and observational studies (n=125). Variations in study populations, data collection methods, and PCNE versions (V5.1 vs. V7.0 vs. V9.1) enrich the analytical perspective but make a comprehensive quantitative synthesis more challenging, necessitating standardization across them (Table 3). Differences in DRP prevalence across studies may be influenced by identification methods, standard definitions, environmental factors, genetic characteristics (age, comorbidities, duration of therapy), and incomplete medical record data [9]. The classification of DRPs according to the PCNE across all included studies is discussed in Tables 4 and 5. The incidence rates of DRPs in the three reviewed studies showed varying results: the study by Kara et al. identified 58 DRPs in 45 of 181 patients (24.9%) [4], Che Pa et

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al. identified 817 "problem" domains and 1,605 "cause" domains among 355 patients [6], and Gopinath et al. identified 183 DRPs among 104 patients out of 125 [7]. This highlights the complexity of the study populations, ART regimens, research methods, and PCNE versions. Another study conducted by Aderemi-Williams et al. on 100 HIV patients using the Cipolle instrument identified 215 problems with antiretroviral therapy [10].

Table 5. Distribution of The Problems of Drug-Related Problems in HIV patient Based on PCNE Classification

Primary Domain	Code	Problem	Number (%)
Adverse reactions	P 1.1	Side effect suffered (non-allergic)	87 (47.5) [7]
	P 1.2	Side effect suffered (allergic)	33 (18) [7]
	P 1.3	Toxic effects suffered	3 (1.6) [7]
Drug use problem	P 4.1	Drug not taken/administered at all	39 (21.3) [7]
	P 4.2	Wrong drug taken/administered	9 (4.9) [7]
Interactions	P 5.1	Potential interaction	12 (6.6) [7]
Drug/dose selection	C 1.1	Inappropriate drug selection	1 (0.5) [7]
	C 1.2	Inappropriate dosage selection	1 (0.5) [7]
	C 1.4	Pharmacokinetic problems incl. Ageing/ deterioration in organ function and interactions	9 (4.9) [7]
	C 1.7	New symptom/indication revealed/presented	1 (0.5) [7]
	C 1.8	Manifest side effect, no other cause	112 (61.2) [7]
Drug use process	C 2.1	Inappropriate timing of administration and/or dosing intervals	14 (7.7) [7]
	C 2.3	Drug over used/over administered	3 (1.6) [7]
Information	C 3.1	Instructions for use/taking not known	2 (1.1) [7]
Patient/psychological	C 4.1	Patient forgets to use/take drug	39 (21.3) [7]
	C 4.3	Patient suspects side-effect	1 (0.5) [7]

Source: [7]Gopinath et al. (2018)

Therapy Safety

Therapeutic safety, particularly adverse drug reactions (P2.1), was the most dominant "problem" domain in this review; specifically, the study by Che Pa et al. identified 475 cases (58.14%) [6]. The study by Gopinath et al. involved 123 cases, with 87 cases (47.5%) of non-allergic adverse drug reactions (P1.1), 33 cases (18%) of allergic adverse drug reactions (P1.2), and 3 cases (1.6%) of toxic effects (P1.3) [7]. In the study by Kara et al., the incidence rate of adverse drug reactions was 9 cases (15.5%) [4]. A study conducted in Tasikmalaya, Indonesia, reported 120 cases among 400 HIV patients, with the most common adverse drug reactions being dizziness (n=43), nausea (n=18), rash (n=16), and vomiting (n=13) [11]. Another study in Surabaya, Indonesia, reported 123 cases among 72 HIV patients, with the most common adverse drug reactions being dizziness (n=56), nausea and vomiting (n=41), and rash (n=15) [12].

Adverse drug reactions such as dizziness may be caused by efavirenz (2% to 28%) and lamivudine (21% to 35%). Gastrointestinal adverse drug reactions such as nausea and vomiting may be caused by efavirenz (2% to 12%), tenofovir (8% to 11%), and lamivudine (15% to 33%). Rashes may be caused by nevirapine (13%) and efavirenz (5% to 26%) [13]. For side effects such as nausea or vomiting, additional medications like domperidone are typically administered; paracetamol is given for headaches; and chlorpheniramine maleate—or a combination of dexamethasone and dexchlorpheniramine maleate, along with salicylic talc—is used for rashes or itching. If side effects are severe, the medication is substituted while symptomatic treatment is continued [14].

Risk factors for drug side effects may be associated with a CD4 count <200 cells/mm^3 (OR = 1.00, 95% CI: 1.00–1.02; p = 0.04) and a low level of education (OR = 3.27, 95% CI: 1.34–7.95; p = 0.009). Drug side effects in HIV patients can be caused by drug interactions (OR = 5.66; p = 0.02) [15].

Therapeutic Efficacy

The issue of treatment effectiveness particularly effect of drug treatment not optimal (P1.2) was the next dominant DRP domain in the study by Che Pa et al., accounting for 340 cases (41.6%) [6]. In the study by Kara et al., 26 cases (44.8%) of effect of drug treatment not optimal were found, followed by 19 cases (32.8%) of untreated indications (P1.4) [4]. In addition to effect of drug treatment not optimal, issues with treatment effectiveness can be influenced by non-adherence to treatment. In the study by Gopinath, 39 cases (21.3%) of drug not taken/administered at all were found, 12 cases (6.6%) of potential interaction, and 9 cases (4.9%) of wrong drug taken/administered [7]. These issues can reduce treatment effectiveness, which risks increasing

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viral load in patients. In another study, treatment nonadherence was found in 67 cases (81.7%) [16]. The effectiveness of antiretroviral therapy can be improved, in part, through clinical interventions by pharmacists and physicians, such as adherence education, management of medication adverse drug reactions, and regular monitoring of drug interactions, which can increase CD4 counts by up to 84% [17].

Risk factors for antiretroviral therapy failure include patient non-adherence to treatment (OR = 5.90; 95% CI 3.50–9.94; moderate strength of evidence) and a CD4 count < 200 cells/mm³ (OR = 4.82; 95% CI 2.44–9.52; low strength of evidence) [18].

Drug Selection

The domains of medication selection were identified in all three studies, which had different numbers of cases. In the study by Kara et al., the causes of medication selection included inappropriate medications (in accordance with guidelines but contraindicated) (C1.2) in 10 cases (17.2%), inappropriate drug combinations, or combinations of drugs and herbal medicines, or drugs and dietary supplements (C1.4) in 9 cases (15.5%), and no or incomplete drug therapy despite indications (C1.6) in 11 cases (19%) [4]. A study by Che Pa et al. found inappropriate drug combinations, or combinations of drugs and herbal medicines, or drugs and dietary supplements (C1.4) in 124 cases (7.4%) [6]. A study by Gopinath et al. in the domain of drug selection attributed the issue to manifest adverse drug reactions, no other cause in 112 cases (61.2%) [7].

A study conducted in Pontianak, Indonesia, identified 110 (69.35%) interactions involving 7 types of ARVs and 55 types of non-ARVs. Regarding severity, 15.45% (n=17) of the interactions were classified as major, 60% (n=66) as moderate, and 24.55% (n=27) as minor. In terms of mechanism, 90% (n=99) of the interactions occurred via pharmacokinetic mechanisms and 2.37% (n=3) via pharmacodynamic mechanisms, while the mechanisms for 7.27% (n=8) of the interactions were unknown [19]. Several factors influencing drug interactions include polypharmacy and age, particularly among the elderly. This is due to the emergence of various diseases with advancing age especially cardiovascular and central nervous system disorders leading to polypharmacy rates as high as 44%, which triggers drug interactions and results in 31% of patients receiving inappropriate therapy [20]. One way to avoid interactions between HIV medications and other drugs is to routinely screen for interactions using drug interaction software or databases, such as Liverpool HIV Drug Interactions.

Patient Factors

Patient-related causes were the most prevalent cause of DRP across all included studies. In the study by Che Pa et al., patient factors (C7) accounted for 952 cases in the cause domain. Inability to understand medication instructions (C7.10) accounted for 321 cases (19.1%), nonadherence to medication (C7.1) accounted for 320 cases (19.0%), inappropriate dosing time or interval (C7.7) accounted for 126 cases (7.5%), patients taking medications that interact (C7.4) accounted for 93 cases (5.5%), and patients consuming foods that interact with medications (C7.5) accounted for 85 cases (5%) [6]. In the study by Gopinath et al., patients forgetting to take their medication (C4.1 in PCNE V5.1) accounted for 39 cases (21.3%) [7]. In a study by Kara et al., patients took fewer medications or none at all (C7.1) in 2 cases (3.4%) [4]. In a study by Arifiani et al., nonadherence to treatment among HIV patients occurred in 38 out of 111 patients (34.2%) [21].

A study conducted in Padang, Indonesia, found that 34.3% (n=12) of people living with HIV/AIDS (PLWHA) were non-adherent to antiretroviral (ARV) medication and 40% (n=23) did not achieve successful ARV therapy outcomes; a significant association was observed between adherence and the success of ARV therapy (p=0.000) [22]. HIV patients nonadherence to antiretroviral therapy contributes to treatment discontinuation, which can lead to drug resistance, necessitating dose increases and, of course, adversely affecting patient health [23]. Factors influencing patient adherence include support from healthcare providers, family, friends, and self-motivation [24]. Medication adherence can be improved through patient education and the provision of an antiretroviral adherence pocket guide [25]. Another strategy to address the root causes of medication-related problems is effective communication between healthcare professionals and patients—utilizing simple language, visual aids, and the "teach-back" method to ensure patients understand the instructions [26].

Drug Use Process

DRPs caused by the medication administration process were identified in Kara et al. [4] and Gopinath et al. [7]. The study by Kara et al. found 6 cases (10.3%) of inappropriate timing of administration and/or dosing intervals (C6.1) and 7 cases (12.1%) where medication was not administered at all [4]. The study by

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Gopinath et al. found 14 cases (7.7%) of inappropriate timing of administration and/or dosing intervals (C2.1) and 3 cases (1.6%) of medication overuse (C2.3) [7]. Another study reported 18 cases (20%) of patients who did not start antiretroviral therapy [9]. A study conducted in Palu, Indonesia, found that among HIV patients, instances of taking incorrect dosages (either low or high) were not observed; instead, 80% (n=20) failed to take or use the medication entirely, while 20% (n=5) took the medication at the wrong time [27].

Others

The category of DRP causes, which includes no medication monitoring results, such as therapeutic drug monitoring (C9.1), other causes (C9.2), and no clear reason (C9.3), was relatively high at 579 cases (34.4%) [6]. This indicates that many causes of DRPs are not specifically classified within the PCNE categories. The high proportion in the "other" category suggests that the PCNE classification needs to be updated or adjusted to accommodate specific causes of DRPs in the field. This high proportion also highlights the importance of clinical pharmacists documenting and analyzing complex causes of DRPs.

Findings regarding drug-related problems (DRPs) in Turkey, Malaysia, and India are relevant to the situation in Indonesia, where issues such as adverse drug reactions, drug interactions, and non-adherence to antiretroviral therapy persist. This may be attributed to the significant disparity in healthcare access between the western and eastern regions of Indonesia; the western region enjoys superior healthcare access, evidenced by better healthcare facilities and a larger medical workforce compared to the eastern region [28]. Patterns of Drug-Related Problems (DRPs) were also observed in other conditions, such as diabetes mellitus and hypertension. Inappropriate drug selection included drugs that were effective but unsafe (18%; n=18), ineffective drugs (12%; n=12), and inappropriate drug combinations (11%; n=11) [29].

Clinical Implications

The occurrence of Drug-Related Problems (DRPs) reported across the three studies—predominantly caused by patient-related factors such as an inability to understand medication instructions and non-adherence—indicates that the majority of DRPs among HIV outpatients can be prevented and resolved through clinical pharmacy interventions. Services such as pharmacist-led Communication, Information, and Education (CIE), the provision of antiretroviral adherence guidebooks, drug information services, and the HIV/AIDS Information System (SIHA) application influence adherence among HIV patients receiving antiretroviral (ARV) therapy [30].

The role of clinical pharmacists in the early detection and resolution of DRPs among HIV outpatients in Indonesia can be fulfilled through screening using standardized instruments during routine follow-ups, structured and patient-tailored medication counseling, and active collaboration among physicians, nurses, and pharmacists to address DRPs requiring regimen changes, the addition of therapy for untreated comorbidities, or referrals to other services [26, 27].

Study Limitations

Differences in study designs, such as cohort and cross-sectional studies, provide diverse perspectives that enrich our understanding of drug-related problems (DRPs) in HIV patients. However, methodological differences—along with variations in population characteristics and DRP classification tools (such as different versions of the PCNE classification)—pose challenges for conducting a comprehensive and consistent quantitative synthesis. These factors can influence clinical interpretation and the generalizability of findings. Furthermore, variations in sample sizes across studies—ranging from 125 to 355—may affect the weighting and comparability of reported clinical outcomes. Additionally, only studies utilizing the PCNE classification were included; studies employing other classification systems might yield different results. The review was limited to English-language articles, meaning significant studies in other languages may have been excluded. Finally, the articles were published within the last decade, a period during which the PCNE classification itself has undergone several revisions.

Conclusions

Based on available evidence from studies in Asia and the Middle East the distribution of DRPs according to the PCNE classification, medication safety in the form of adverse events remains the primary challenge in the management of HIV patients, followed by effect of drug treatment not optimal. These findings

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highlight the importance of continuous monitoring of drug response and adverse events, as well as the active involvement of clinical pharmacists in the early detection, evaluation, and prevention of DRPs. To enhance therapy outcomes, it is recommended to improve patient education regarding medication adherence and awareness of side effects.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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