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Original Research Article

A retrospective evaluation of anti-retroviral therapy regimen modifications due to adverse drug reactions in a tertiary care hospital

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ABSTRACT

Background: Antiretroviral therapy (ART) has transformed HIV infection into a chronic manageable disease and substantially improved survival among people living with HIV. Despite these advances, adverse drug reactions (ADRs) remain a major cause of treatment modification, potentially affecting adherence, treatment continuity, and long-term outcomes. Real-world pharmacovigilance data describing ADR-driven ART regimen changes in Indian settings remain limited. Aim was to evaluate the frequency and pattern of ART regimen modifications attributable to ADRs reported to the adverse drug reaction monitoring centre (AMC) of a tertiary care teaching hospital.

Methods: A retrospective observational study was conducted using suspected ADR reporting forms received at the AMC, department of pharmacology, Mysore Medical College and Research Institute between January 2022 and December 2024. Data regarding patient demographics, ADR characteristics, suspected antiretroviral agents, and regimen modifications were extracted and analysed using descriptive statistics. The association between ADR type and regimen modification was assessed using the Chi-square test.

Results: A total of 93 ART-related ADR reports were analysed. Among them, 67 patients (72.0%) required modification of their ART regimen following an ADR. Renal ADRs were the most frequently reported reactions (67.7%), with tenofovir-based regimens accounting for the largest proportion of implicated drugs. Patients experiencing renal toxicity were significantly more likely to undergo regimen modification compared with those experiencing non-renal ADRs (χ^2=24.45, p<0.001). Substitution from tenofovir-containing regimens to alternative regimens, particularly abacavir-based combinations, represented the most common modification pattern.

Conclusions: ADRs continue to be an important determinant of ART regimen modification in routine clinical practice. Renal toxicity, predominantly associated with tenofovir-containing regimens, emerged as the leading reason for treatment substitution. These findings highlight the importance of vigilant pharmacovigilance, timely recognition of drug-related toxicity, and routine renal function monitoring to support safer and more sustainable ART use.

Keywords: Adverse drug reactions, Antiretroviral therapy, HIV, Pharmacovigilance, Renal toxicity, Tenofovir

INTRODUCTION

Antiretroviral therapy (ART) has transformed HIV infection into a manageable chronic condition, substantially reducing morbidity and mortality among people living with HIV.[1] However, adverse drug reactions (ADRs) continue to pose significant challenges by affecting adherence, tolerability, and long-term treatment outcomes.[2] The multidrug combinations used in ART increase the potential for pharmacokinetic and pharmacodynamic interactions, thereby elevating the risk of toxicity.[3]

Globally, the prevalence of ADRs among individuals receiving ART varies widely depending on treatment composition, demographic characteristics, comorbidities,

and monitoring standards.[4] Several drug-specific toxicities have been well documented, including zidovudine-induced anemia, nevirapine-associated hepatotoxicity and hypersensitivity reactions, efavirenz-related neuropsychiatric disturbances, and tenofovir-associated renal dysfunction.[5-8] Although dolutegravir is generally considered a well-tolerated agent, mild creatinine alterations have been reported in some patients.[9]

Spontaneous reporting systems such as the Pharmacovigilance Programme of India (PvPI) and World Health Organization (WHO) guidelines emphasize structured monitoring to identify regimen-limiting toxicities early.[1,10] However, Indian evidence specifically correlating ADRs with regimen modifications remains limited because of under-reporting, incomplete documentation, and variability across treatment centres.[11] Previous studies have shown that 20-40% of patients may require ART modification due to ADRs, particularly hematological, hepatic, neurological, and renal toxicities.[12-14] Tenofovir-associated renal toxicity continues to be a major contributor to treatment substitution in several Indian cohorts.[8,11]

Given these concerns, systematic evaluation of ADR-induced ART regimen modifications using real-world pharmacovigilance data is essential. Such evidence may support safer regimen selection, earlier detection of toxicity, and improved treatment continuity in high-burden tertiary care settings.

METHODS

Study design

This was a retrospective observational study conducted using duly filled suspected adverse drug reaction (ADR) reporting forms received at the adverse drug reaction monitoring centre (AMC), department of pharmacology, Mysore Medical College and Research Institute, Mysore. The study period included reports submitted between January 2022 and December 2024.

Study population and sampling

Inclusion criteria

All ADR reporting forms involving patients receiving ART and contained complete information required for analysis.

Exclusion criteria

ADR forms with incomplete demographic or regimen-related details.

The source population comprised all patients enrolled in the ART centre of the tertiary care hospital during the study period.

Data collection

A predesigned and pretested structured proforma was used to extract relevant information from the ADR forms. The following variables were collected: patient demographics: age, sex, weight. ART regimen details: initial regimen, duration of therapy, nature of regimen modification (drug/substitution/dose/frequency/duration). ADR characteristics: type of reaction, suspected drug(s), time to onset, clinical management. Causality assessment: performed using the Naranjo adverse drug reaction probability scale.

Outcome measures

The primary outcome was the proportion of ART regimen modifications attributable to ADRs.

Secondary outcomes included the pattern of ADRs, suspected drugs, and causality assessment scores.

Statistical analysis

The collected data were manually entered and analyzed using Microsoft Excel 2019 and IBM SPSS Statistics for Windows, version 28.0. Categorical variables were expressed as frequencies and percentages. Associations between ADR characteristics and regimen modifications were assessed using the Chi-square test, with a p value <0.05 considered statistically significant.

Ethical considerations

The study was conducted following approval from the institutional ethical committee (IEC) of Mysore Medical College and Research Institute, Mysore, ensuring adherence to ethical standards and patient confidentiality.

RESULTS

A total of 93 suspected adverse drug reaction (ADR) reports associated with antiretroviral therapy (ART) were analysed.

Table 1: Demographic detail.

	Males	Females
Number of reports	62	31
Percentage	67	33

The gender distribution of ADR reports are as follow, 62 patients (67%) were males and 31 (33%) were females.

The causality assessment using Naranjo adverse drug reaction probability scale showed 74 cases (80%) categorized as ‘probable’ and 17 cases (18%) ‘possible’ (Figure 1).

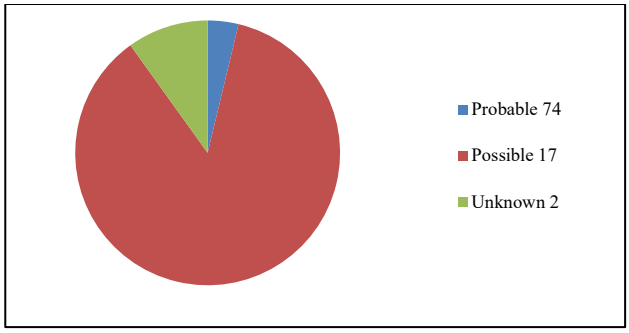

Figure 1: Causality assessment of ADRs using Naranjo scale.

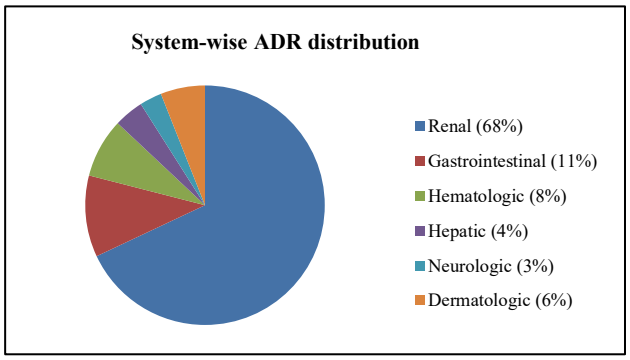

Figure 2: System-wise ADR distribution.

Among the 93 reports, 67 (72%) resulted in a modification of the ongoing ART regimen, while 26 (28%) did not require any change (Table 1). Renal adverse drug reactions constituted the predominant category, accounting for 63 cases (68%) of all ADRs, followed by gastrointestinal (11%), hematologic (8%), dermatologic (6%), hepatic (4%), and neurologic (3%) reactions (Figure 2).

Drug-wise distribution showed that tenofovir-based regimens were implicated in the highest proportion of ADRs (n=42), followed by lamivudine (n=10), dolutegravir (n=7), zidovudine (n=7), abacavir (n=6), nevirapine (n=4), and efavirenz (n=4). Among renal ADRs, tenofovir was the most frequently suspected drug (Figure 3).

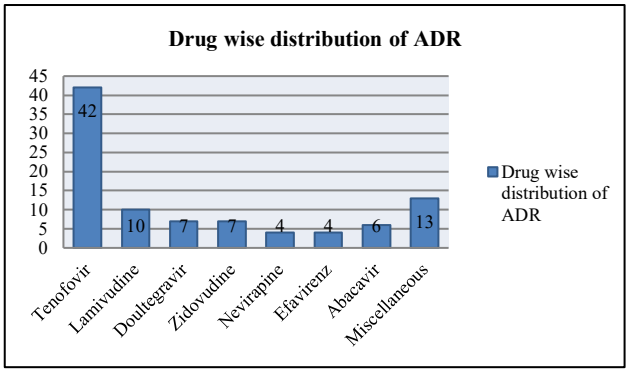

Figure 3: Drug wise distribution of ADR.

A statistically significant association was observed between the type of ADR and the need for regimen modification (Table 3). Patients experiencing renal ADRs were more likely to undergo ART regimen modification (55 of 63 cases), compared to those with non-renal ADRs (12 of 30 cases). This association was found to be statistically significant (χ^2=24.45, p<0.001), indicating that renal toxicity was a major determinant for ART substitution in this cohort.

Table 2: Comparison of regimen modification between Tenofovir-based and non Tenofovir-based regimens.

Regimen types	Modified due to ADR (N)	Not modified (N)	Total (n)	Percentage modified
Tenofovir-based (e.g., TLD, TDF+3TC+EFV)	48	8	56	85.7
Non-tenofovir-based (e.g., ZLE, ABC+LMV+DTG)	19	18	37	51.4
Total	67	26	93	72

TLD: Tenofovir + Lamivudine + Dolutegravir; TDF: Tenofovir Disoproxil Fumarate; 3TC: Lamivudine; EFV: Efavirenz; ZLE: Zidovudine + Lamivudine + Efavirenz; ABC: Abacavir; LMV: Lamivudine; DTG: Dolutegravir.

Table 3: Frequency and pattern of ART regimen modification in a tertiary care hospital.

Initial Regimens	Frequency of modification	Modified regimen	Frequency of modification
TLD	38	ABC+LMV	28
TDF+LMV+EFV	10	ABC+LMV+DTG	16
ZLE	7	TLD	7
ABC+LMV+DTG	4	ABC+LMV	4
AZT+LMV+NVP	4	unknown	-
TDF+LMV+NVP	2	Unknown	-
Tenofovir (alone)	2	unknown	-
Total	67	Total	55

TLD: Tenofovir + Lamivudine + Dolutegravir; TDF: Tenofovir Disoproxil Fumarate; EFV: Efavirenz; ZLE: Zidovudine + Lamivudine + Efavirenz; ABC: Abacavir; LMV: Lamivudine; DTG: Dolutegravir; AZT: Zidovudine; NVP: Nevirapine.

Table 4: Association of ART regimen modification and ADR.

ADR Types	Regimen Modified (N)	Not Modified (N)	Total
Renal ADR	55	8	63
Non-renal ADR	12	18	30
Total	67	26	93

χ^2=24.45, p < 0.001 (statistically significant). ADR: adverse drug reaction.

DISCUSSION

The present study highlights the significant burden of ADRs associated with ART, with renal toxicity emerging as the most frequent and clinically important ADR pattern. Similar findings have been reported in previous Indian studies where tenofovir-associated nephrotoxicity was identified as a major determinant of regimen modification.[5,11,12] However, the renal ADR proportion observed in the present study was higher than that reported by Shenoy et al and Patil et al.[13,14] This difference may be attributable to variations in demographic characteristics, comorbidities, referral patterns, and pharmacovigilance reporting practices.

The high burden of renal ADRs observed in this study emphasises the importance of baseline and periodic renal function assessment, particularly among patients receiving tenofovir-based regimens in resource-limited settings.

Drug-wise analysis demonstrated that tenofovir-based regimens were implicated most frequently, consistent with previous pharmacovigilance reports demonstrating renal tubular injury and elevated creatinine levels associated with tenofovir use.[8] Although dolutegravir is generally considered a well-tolerated agent, emerging evidence suggests that mild creatinine elevation may occur because of organic cation transporter-2 inhibition without true glomerular injury.[9]

The strong association observed between renal ADRs and regimen modification (χ^2=24.45, p<0.001) further emphasises the need for systematic renal monitoring when initiating or continuing tenofovir-based ART.

The regimen modification rate of 72% observed in the present study was higher than the 20-40% range reported in previous multicentric Indian studies.[12-15] This discrepancy may reflect improved ADR detection practices, tertiary care referral bias, greater burden of comorbidities, and increased accessibility to safer alternatives such as abacavir- and dolutegravir-based regimens.

Despite its strengths including real-world applicability and pharmacovigilance relevance, this study has certain limitations. Its retrospective design introduces the possibility of incomplete or inconsistent reporting. Additionally, the absence of ADR severity grading and long-term renal follow-up data restricts assessment of clinical progression.

Future prospective studies incorporating biomarker-based renal assessment, pharmacogenomics, and structured follow-up are warranted to better identify patients at risk of ART-related nephrotoxicity.

CONCLUSION

This retrospective pharmacovigilance study provides real-world evidence regarding the burden of ART-related ADRs, with renal toxicity emerging as the predominant cause of regimen modification in a tertiary care setting. Tenofovir-based regimens were significantly associated with renal ADRs, reinforcing the need for routine renal function monitoring during ART.

The observed shift towards abacavir- and dolutegravir-based regimens reflects evolving treatment trends favouring improved renal safety profiles. Strengthening pharmacovigilance systems, standardised ADR documentation, and early identification of drug-related toxicities may help minimise treatment interruptions and improve long-term therapeutic outcomes.

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