

A Study of Adverse Drug Reactions to Antiretroviral Therapy in Patients Attending the Government General Hospital Vijayawada

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Abstract

Background: Adverse drug reactions (ADRs) can lead to non-adherence to antiretroviral therapy (ART) and are also the major causes of hospitalization and higher cost of treatment.

Aims and Objectives: The aims of this study were to analyse the pattern of ADRs, causality, and severity among HIV-infected patients.

Materials and Methods: It was a retrospective analysis conducted over 3 months from May 2021 to August 2021. ADRs due to antiretroviral drugs (ARVs) were collected from the Government General Hospital, Vijayawada. The WHO-UMC scale was used for assessing the causality and Hartwig–Siegel scale for severity of reactions.

Results: A total of 580 ADRs due to ART were received. Among them 360 were female patients and 220 are male patients. 89% ADRs were of mild grade of severity. Most of the ADRs were related to gastrointestinal system. Causality assessment of ADRs was probable in 320(55.17%) patients and possible in 260 (44.82%) patients.

Conclusion: Maximum number of ADRs was of mild nature suggesting that the ART is well tolerated among the patients. Further studies need to be conducted to fully understand the determinants of ADRs due to ART in a statistically significant manner.

Keywords: Adverse Drug Reactions; Antiretroviral Therapy; Human Immunodeficiency Virus.

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Introduction

The advent of antiretroviral therapy (ART) has revolutionized the management of human immunodeficiency virus (HIV) infection, transforming it from a universally fatal disease into a chronic, manageable condition.[1] With the widespread availability of highly active ART, there has been a remarkable decline in HIV-related morbidity, mortality, and opportunistic infections, accompanied by substantial improvement in the quality of life of patients. The success of ART has been largely attributed to its ability to achieve sustained viral suppression, restore immune function, and reduce HIV transmission.

Despite these benefits, the use of antiretroviral drugs (ARVs) is not without challenges. Long-term ART is associated with a wide spectrum of adverse drug reactions (ADRs), ranging from mild gastrointestinal disturbances, dermatological

manifestations, and metabolic complications to severe, life-threatening conditions such as hepatotoxicity, hypersensitivity reactions, pancreatitis, and lactic acidosis.[2–7] These ADRs often contribute to poor adherence, regimen modification, or discontinuation of therapy, which in turn jeopardizes treatment outcomes. Furthermore, ADRs are a significant cause of hospitalization and increase the overall cost of HIV care. [8]

The choice of an optimal ART regimen, therefore, should not only prioritize efficacy and viral suppression but also emphasize safety, tolerability, and patient-specific factors such as comorbidities, concomitant medications, and potential drug–drug interactions. In particular, the toxicity profile of ARVs plays a crucial role in determining treatment success. Drugs such as non-nucleoside reverse

transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and nucleoside reverse transcriptase inhibitors (NRTIs) have well-documented toxicity profiles, and newer agents continue to be evaluated for their safety in both short- and long-term use.

Globally, pharmacovigilance data on ART-related ADRs remain inadequate, especially in resource-limited settings where HIV burden is disproportionately high and treatment options may be constrained. Most of the available evidence originates from clinical trials, which often underestimate ADRs compared to real-world clinical practice. There is, therefore, a pressing need for systematic studies that analyze the pattern, severity, and causality of ADRs in diverse patient populations.

In this context, the present study seeks to evaluate the adverse drug reactions associated with ART among HIV-infected patients, with particular attention to their clinical presentation, severity, and causal relationship with antiretroviral agents. Such data are expected to provide valuable insights for clinicians in optimizing ART regimens, improving adherence, and ultimately enhancing treatment outcomes.

Aim and Objectives

Aim: To analyse the pattern, severity, and causality of adverse drug reactions (ADRs) associated with antiretroviral therapy (ART) among HIV-infected patients.

Objectives

1. To determine the incidence and types of ADRs occurring in patients receiving ART.
2. To assess the severity of ADRs using standardized severity assessment scales.
3. To evaluate the causality relationship between suspected drugs and reported ADRs.
4. To identify the most common ART regimens associated with ADRs.
5. To analyse the impact of ADRs on treatment adherence, regimen modification, or discontinuation.
6. To generate evidence that may contribute to safer prescribing practices and better patient outcomes in HIV management.

Materials and Methods

It is a retrospective study of ADRs due to ART conducted over 3 months from May 2019 to August 2019. This Study was approved from Institutional Ethics Committee later the data was collected as part of pharmacovigilance program and analysed. These ADRs were collected from patients attending OP in government general hospital, Vijayawada after obtaining their prior consent to participate in the study. Children are not included in the study, demographic details, medical history, details of ARVs, and other concomitant medications prescribed were collected. An expert committee which included pharmacologist and clinical expert assessed the causality of adverse reactions using WHO-UMC causality assessment system. [9]

Two drug regimens were followed Efavirenz+ Lamivudine+Tenofovir (E+L+T) regimen and Zidovudine+Lamivudine+Nevirapine (Z+L+N) regimen. Hartwig and Siegel scale was used for analysing the severity of adverse events. [10] The data was analyzed and presented as numbers and percentages.

Results

- A total of 580 ADRs due to ARVs were received.
- In that 360 (62.06%) were females and 220(37.94%) were male patients [Figure 1].

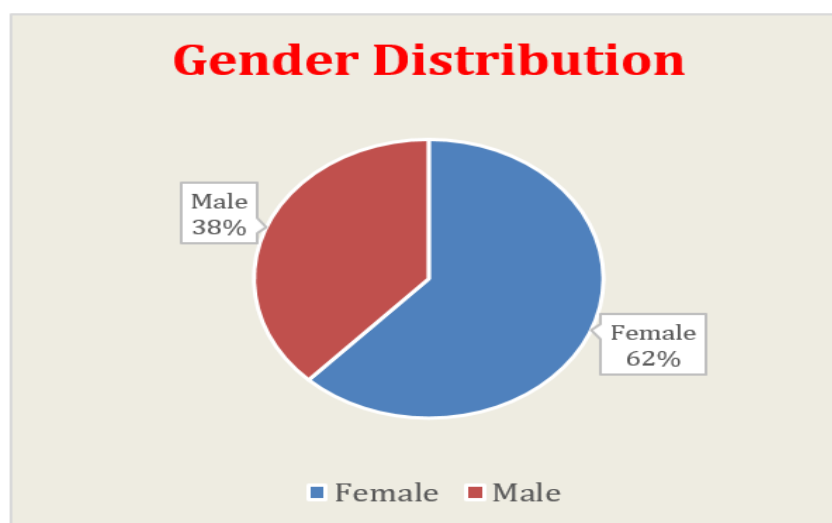


Figure 1: Gender distribution

Higher prevalence of ADRs was in the age group of 31–40 years [Figure 2].

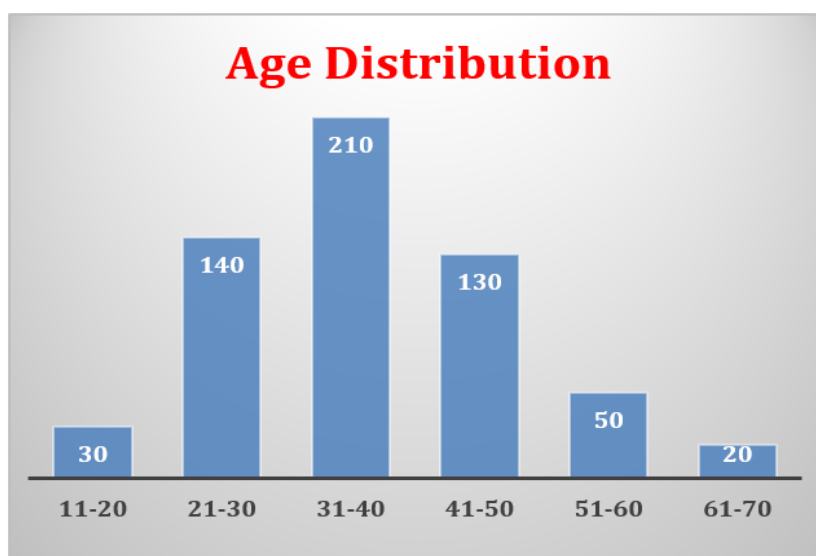


Figure 2: Age distribution

Figure 3 shows the severity of ADRs. Regarding severity of ADRs, most of them were of mild nature.

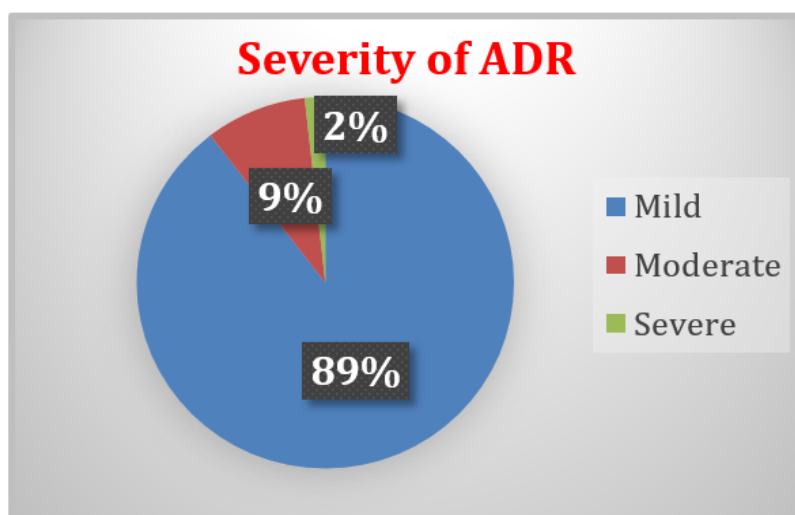


Figure 3: Severity of ADR

Majority of the ADRs were related to gastrointestinal system followed by dermatological system [details are provided in Table 1].

Table 1: Systems affected by ADRs due to ARVs regimens

Systems affected	E+L + T	Z+L + N	Total
	Regimen	Regimen	n (%)
Gastrointestinal system	160	40	200 (34.5)
Dermatology	140	30	170 (29.3)
Central nervous system	60	20	80 (13.8)
Musculoskeletal system	50	20	70 (12)
Others	40	20	60 (10.3)
E+L + T regimen: Efavirenz+Lamivudine+Tenofovir regimen, Z+L + N regimen: Zidovudine+Lamivudine+Nevirapine regimen, ARVs: Antiretroviral drug, ADRs: Adverse drug reactions			

Majority of the ADRs were attributed to E+L+T regimen as compared to Z+L+N regimen. Only two

cases of anaemia were reported due to zidovudine, and skin rashes were reported more with efavirenz.

Causality assessment of ADRs was probable in 320(55.17%) patients and possible in 260 (44.82%) patients.

Discussion

The present study was conducted with the aim of analyzing the pattern, severity, and causality of adverse drug reactions (ADRs) associated with antiretroviral therapy (ART) in HIV-infected patients. With the introduction of ART, HIV infection has been transformed from a fatal disease into a chronic, manageable condition. However, as observed in our findings, adverse drug reactions remain a significant challenge in ensuring long-term adherence, optimizing therapeutic regimens, and improving patient outcomes. This discussion contextualizes the results of the present study with reference to existing literature, explores possible explanations for the findings, and highlights their clinical and public health implications.

Pharmacovigilance in India and ADR Reporting: Pharmacovigilance in India is still evolving, with reporting of ADRs remaining poor, particularly in government hospitals. Except for centers attached to medical colleges, where academic and research interest fosters better reporting practices, most government hospitals lack a robust system for monitoring and recording ADRs.

This is concerning given that the majority of HIV patients in India seek care in government facilities rather than in private hospitals. Under-reporting of ADRs hinders the availability of accurate safety data, thereby affecting rational decision-making in ART policy. The findings of this study, therefore, assume particular importance as they provide real-world data on ADRs in a resource-constrained, government hospital setting.

Our study reinforces the need for strengthening India's Pharmacovigilance Programme (PvPI) and integrating ADR reporting into routine HIV care. Regular sensitization and training of healthcare providers, along with user-friendly reporting systems, may encourage better documentation. Given that ADRs are a major determinant of adherence, generating more robust data will help physicians anticipate common problems and modify regimens accordingly.

Demographic Distribution of ADRs

Gender Differences: The majority of patients who experienced ADRs in this study were females. This finding is consistent with a study conducted in South Africa [11], where females were also found to have a higher predisposition to drug-related toxicity. Several explanations have been proposed in the literature. Women may be more vulnerable due to differences in body composition, hormonal

influences, and pharmacokinetic variations such as drug absorption, metabolism, and clearance. Additionally, cultural and socioeconomic factors may delay access to care in women, increasing the chances of presenting with advanced disease, polypharmacy, and higher susceptibility to ADRs.

Previous studies in India have also reported a similar trend, suggesting that gender-specific factors should be considered while tailoring ART regimens. For instance, women have been found to be more prone to nevirapine-induced rash and hepatotoxicity. Recognizing such trends can guide clinicians in monitoring high-risk groups more closely.

Age Distribution: In our study, ADRs were most prevalent in the 31–40 years age group, consistent with studies conducted in Kadapa [12] and Dhule [13]. This can be explained by the epidemiology of HIV in India, where the majority of patients fall into the economically productive and sexually active age group. The social and financial pressures faced by individuals in this age group may also contribute to stress-related health issues and polypharmacy, further compounding the risk of ADRs.

From a public health perspective, ADRs in this age group have serious consequences, as treatment interruptions can lead to disease progression and reduced workforce productivity. Tailored counselling, adherence support, and early identification of ADRs in this group are therefore critical.

Pattern of ADRs

System Organ Class Involvement: The most common system affected by ADRs in our study was the gastrointestinal (GI) system, followed by the dermatological system and central nervous system (CNS). This pattern has been reported in previous studies [14,15] and is consistent with the pharmacological properties of many antiretroviral drugs.

Gastrointestinal ADRs such as nausea, vomiting, diarrhea, and abdominal discomfort are often associated with nucleoside reverse transcriptase inhibitors (NRTIs) and protease inhibitors (PIs). These ADRs, although usually mild, are distressing and negatively impact adherence.

Dermatological ADRs, particularly rash, are well-documented with non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine and efavirenz. While most rashes are mild, Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life-threatening conditions reported in some cases.

CNS ADRs, including insomnia, dizziness, and vivid dreams, are most often associated with

efavirenz. These ADRs can impair quality of life and are a leading cause of regimen discontinuation.

The predominance of mild ADRs in this study suggests that ART is largely well tolerated in most patients. Importantly, most ADRs did not require specific treatment, underscoring the importance of patient counselling and reassurance to prevent unnecessary discontinuation.

Severity of ADRs: The majority of ADRs were of mild severity, requiring only symptomatic management or no intervention. This aligns with findings from several other studies conducted in India and abroad, where mild ADRs outnumbered severe ones.

However, even mild ADRs can adversely affect adherence if not adequately addressed through counselling. Severe ADRs, though less frequent, pose significant clinical challenges. For instance, severe hepatotoxicity or hypersensitivity reactions necessitate immediate discontinuation of therapy and replacement with safer alternatives. In resource-limited settings, where treatment options are restricted, such changes can be difficult to implement.

Causality Assessment: Causality assessment using the WHO scale revealed that most ADRs were “probable,” followed by “possible.” None were classified as “definite,” primarily because rechallenge was not attempted due to ethical concerns and risk of recurrence. Additionally, the high incidence of polypharmacy in HIV patients—often due to concomitant treatment for opportunistic infections and comorbidities—complicated the exclusion of alternate causes.

In contrast, some other studies have used Naranjo’s scale [13,16], where the majority of ADRs were categorized as “possible.” Differences in causality assessment tools highlight the need for standardization to facilitate comparison across studies.

Nevertheless, the predominance of “probable” ADRs in this study strengthens the association between ART and the observed reactions.

Comparison with Other Studies: The findings of this study are in concordance with several national and international reports. Similar patterns of ADRs have been documented in African cohorts, where gastrointestinal disturbances and dermatological reactions were predominant. However, the proportion of CNS ADRs appears to be relatively higher in Indian studies, possibly due to the widespread use of efavirenz-based regimens.

In developed countries, where newer agents such as integrase strand transfer inhibitors (INSTIs) are more widely used, the ADR profile differs, with weight gain and metabolic complications being

increasingly reported. The reliance on older first-line regimens in India explains why gastrointestinal and dermatological ADRs remain the most common.

Clinical and Public Health Implications

The results of this study have several practical implications:

1. **Patient Counselling:** Mild ADRs should be explained to patients as expected and manageable side effects. This reassurance can prevent unnecessary discontinuation.
2. **Individualized Therapy:** Gender- and age-specific predispositions should be considered when initiating ART. Women and patients in the 31–40-year age group require closer monitoring.
3. **Strengthening Pharmacovigilance:** Routine ADR reporting should be institutionalized in government hospitals, supported by training programs for healthcare professionals.
4. **Policy Implications:** Findings from such studies can inform national ART guidelines by highlighting the need for safer alternatives or modifications in monitoring protocols.
5. **Adherence Support:** Since ADRs are a leading cause of noncompliance, integrating pharmacovigilance with adherence counselling will improve treatment success.

Limitations of Present Study

There were few limitations in the present study. The analysis was based on voluntary reporting of ADRs, so there could be chances of underreporting. We did not go into the details of the frequency of prescription of individual drug regimens. More comprehensive and large-scale studies have to be conducted to overcome the limitations of the present study.

Conclusion

The success of ART depends on the treatment adherence, and one of the most common reasons for poor compliance is occurrence of ADRs. The present study found that ADRs due to ART were more common in age group of 31–40 years and more prevalent among females. Most of the ADRs were of mild nature and casualty assessment of ADRs were probable for majority of cases, suggesting that the ART is well tolerated among the patients.

Further studies need to be conducted to completely understand the various factors affecting the occurrence of ADRs due to ART in a statistically significant manner.

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