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Original Research Article

# Adverse Drug Reactions to Anti Retro Viral Therapy in a Tertiary Care Teaching Hospital

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**Abstract**

**Introduction:** Acquired immune deficiency syndrome (AIDS) is a persistent and possibly lethal illness of the immune system caused by the Human immunodeficiency virus (HIV). Highly active antiretroviral therapy (HAART), a blend of minimum 3 medications which had helped very much in reducing morbidity and mortality to a significant extent. All drugs used in treatment of HIV has many side effects related to it and is one of the main causes for altering or stopping drug management also irregular intake of drugs leads to poor compliance. Hence proper assessment of ADRs may help treating doctors to alter the medicament for managing HIV infection. Hence objective of our study is to estimate risk factors causing adverse drug reaction in relation to ART among HIV patients, and also to evaluate the causality and Severity of ADRs.

**Material and Methodology:** This research work was done as an observational study by pharmacology department along with ART center in a tertiary care hospital. In our study 200 patients were included who were started with HAART and were for a period of next one year they were followed. Causality assessment of ADRs was done by Naranjo scale and Severity assessment of ADRs by Hartwig and Seigel's severity scale.

**Results:** In our study out of the 200 patients 75 (37.5%) had experienced ADRs. System wise most of ADRs were connected to Hematological (32%), GIT (27%) and CNS (23%). The majority of the ADRs were with ZLN regimen (74%). Naranjo causality evaluation revealed 62 % were possible, 31 % were probable and 7% were definitive ADRs. Also 49% were mild and 51% were moderately severe in intensity based on Hartwig & Seigels scale.

**Conclusions:** Adverse drug reaction among PLHA on management with ART regimen is an important health issue compliance to treatment. So, constant monitoring is necessary to thwart life-threatening ADR and to improve treatment outcome.

**Keywords**: ADR; HAART; HIV, AIDS.

## Introduction

Human immune deficiency virus (HIV) infection and its development to acquired immune deficiency syndrome (AIDS) is a worldwide calamity It influences healthy lifestyle and socioeconomic status [1]. Worldwide AIDS is a notable health issue, with an estimation of around fifty million of the world population will be affected by 2024 [2]. South Indian mainly Tamilnadu has a share of 55% of HIV infected individuals in India [3].

Highly active antiretroviral therapy (HAART) is a blend of minimum three medicaments required until death. Medical benefits of HAART are due to its efficiency in reducing severity and unrelenting reduction of viral replication. But these are not devoid of side effects. Most of the drugs used in the management of HIV has one or the other adverse effects, hence it's been difficult to manage such patients with minimal adverse effects keeping both in balance. The NRTIs are linked with lactic acidosis and hyperlipidemia. While the NNRTIs are related with psychiatric illness, rashes and lipid aberrations. Protease inhibitors are linked with GIT related issues and dyslipidemia.

Apart from ADR depending on the type of ART regimen, CD4 count and viral load are two important factors influencing the occurrence of ADR [4]. Most of the ADRs can be sufficiently coped with proficient clinical observing at all levels. Hence, observing and recording of ADRs in AIDS patients on ART shoulders great significance. Hence objective of our study is to estimate risk factors causing adverse drug reaction in relation to ART among HIV patients. And also to evaluate causality and Severity of ADRs.

## Material and Methods

This research work was done as an observational study by pharmacology department along with ART center in a tertiary care hospital. We have assessed associated risk factors of ADRs developed due to ART. This study was done as a prospective observational study for a period of one year from April 2021 to March 2022. 200 patients who fulfilled inclusion criteria and exclusion criteria were assessed. Approval was obtained from Institutional ethical committee.

Patients who were established as having of HIV on treatment with ART of both gender were included and those who were not willing to participate were excluded.

At follow-up, detailed assessments with importance on any new abnormal signs perceived after commencement of ART were noted. Naranjo algorithm [5] was used for causality assessment. Hartwig & Seigel's Severity scale was used to assess severity [6].

## Results

In our study 200 laboratory confirmed HIV patients who are on ART were assessed and followed up for 6 months. Among which 75 (37.5%) developed side effects. 101 were men and 99 were women in our study group.

Coming to age distribution all were above 18, among which 84.5% were in the middle of 18 to 50 years, rest 15.5% were above 50 years. In our study 85% of ADR was seen in sexually active age group less than fifty years, rest 15 % of reactions was seen in above fifty year of age. Among 75 patients developed ADR, 39 were male and 26 were females.

We also evaluated transmission mode and it was generally heterosexual (98%). Similarly, 97% of ADR was seen in above mode of transmission patients. According to WHO staging most of ADRs were in patients with Stage I (83%).

We also evaluated viral load based on CD4 count, 8.5% had CD4 < 50, 15.5% had count

in the middle of 51 to 100, 15% had count ranging from 101 to 200, 42% had count ranging from 201 to 350 and rest 19% had CD4 > 350. 47 percent of reactions were seen in count 201 to 350 followed by 27 percent of reaction in count ranging from 101 to 200.

Zidovudine+ Lamivudine+ Nevirapine was the most frequently used combination in 68.5% of study population. In our study of 200 patients, reactions started early with 87% manifesting in first two weeks and rest 13% by four weeks and later Among our study population various regimens are used and ZLN combination had higher incidence of side effects (74%) followed by ZLE (15%) and TLE combination (6%).

**Table 1: Correlation of ADRs with Regimen**

| ART | Adverse drug reactions | |
|---|---|---|
| | No. of patients | % |
| ABAC+LAMI+NEVI | 0 | 0 |
| TENO+LAMI+EFAV | 5 | 6 |
| TENO+LAMI+NEVI | 4 | 5 |
| ZIDO+LAMI+EFAV | 11 | 15 |
| ZIDO+LAMI+NEVI | 55 | 74 |

System wise classification of adverse reaction was done and blood related reaction like anemia was most common and was present in 24 participants (32%), Digestive system related reactions was seen in 20 patients (27%), Neurological reactions was noted in 21 percent of patients and Dermatology related in 12 percent of study population.

**Table 2: System wise distribution of ADRs**

| System | Adverse drug reactions | |
|---|---|---|
| | No. of patients | % |
| Neurological | 16 | 21 |
| Digestive system | 20 | 27 |
| Hematological | 24 | 32 |
| Renal | 2 | 2 |
| Skin | 9 | 12 |
| Miscellaneous | 4 | 6 |

Causality assessment showed that 62 percent of reactions were possible, 31 percent was probable and 7 percent was definitive. In our study group 51 percent of ADRs were found to be moderate, 49 percent were mild in severity based on HS scale.

**Table 3: Causality assessment**

| Causality Assessment | Adverse drug reactions | |
|---|---|---|
| | No. of patients | % |
| Definitive | 5 | 7% |
| Possible | 47 | 62% |
| Probable | 23 | 31% |
| Unlikely | 0 | 0 |

## Discussion

The starting of HAART in HIV management have caused a noteworthy drop in HIV associated sickness and death [7] regrettably, one fourth of affected population stop intake of medicine due to management fiasco, adverse effects or non-compliance as early as at the start of treatment. Despite the fact introduction of newer drugs carry on, struggles to make the most of the efficacy of presently available management modality is real with minimal ADR. It is perilous to expect, identify and treat any adverse reaction if at all it happens which is expected almost with all drugs and combinations used in management of the disease.

In our study participants it was witnessed that, 37.5% of PLHA developed reaction to anti-retroviral medicines. We compared our results with previous study and in a study done by Luma *et al* [8] the incidence of reactions was 19.5 percent which was less than ours, wjile in another study by Rajesh *et al* [9] it was 43.85 percent comparable to ours. These disparities in the prevalence of side effects is attributed to concomitant drugs used for handling other illness developed during the course of disease [10].

A Study from Kadapa [11] displayed that patients with an average age ranging from 30 to 40 years were frequently infected. Literature shows that sexually active population has more incidence of disease and hence more ADRs.

Coming to gender influence the frequency of side effects in men (51%) and women (49%) didn't had noteworthy variance. Lihite *et al* [12] displayed similar finding the reason being dissimilarities between male and female in BMI and lipid configuration, genetic variances of numerous enzymes.

Uneducated patients exhibited more adverse effects (54 percent) than educated in our study which was comparable to work done by Modayil *et al* [13] which may be due to unawareness and dearth of knowledge about illness.

ADRs were more among study group with Clinical stage I comprising 83% in our study. Divakar *et al* [10]. interpreted ADR among patients with WHO Clinical stage I & II was 26.5% which was not comparable to our study.

Adverse drug reaction may hinge on the baseline CD4+ count at initiation of management. In our study 47 percent of reactions were seen in count 201 to 350 followed by 27 percent of reaction in count ranging from 101 to 200. Rajesh *et al* [9] displayed incidence of adverse effects as 79.8% when CD4 ≤ 200 which s way higher than our study.

ADRs were common with ZIDO+LAMI+NEVI combination encompassing 74 % followed by 15% with the ZIDO+LAMI+EFAV combination which may be because zidovudine-based regimen is in common use. Kennath *et al* [14] interpreted that side effects were very minimal in patients in stavudine-based and tenofovir-based combination. In contrast to this one study done in Chhattisgarh showed stavudine based was the most common combination which caused reactions [15].

System wise classification of adverse reaction was done and blood related reaction like anemia was most common and was present in 24 participants (32%), Digestive system related reactions was seen in 20 patients (27%), Neurological reactions was noted in 21 percent of patients and Dermatology related in 12 percent of study population. Luma *et al* [8] presented 3.8% of blood related reactions of which anemia was the most frequently encountered. This is due to myelosuppression. One another study done

by Agarwal *et al* [16] reported high frequency of Zidovudine related anemia.

Digestive tract related events was next frequent adverse reaction we faced (27%). Lihite *et al* [12] displayed 31.25% of adverse events were related to Digestive system. These were identified mostly in early part of treatment with ART and is mostly self-limiting.

Adverse effects related to central nervous system were encountered in our study encompassing 21 percent of it, most frequently encountered were neuropathy, vertigo and psychiatric manifestations. Lihite *et al* [12] depicted that 16.25% ADRs were neurology related comparable to our study. Rashes were seen in 12 percent of patients with the nevirapine related combinations. Sharma *et al* [10]. described rashes in 10 percent of study population he took.

Naranjo causality assessment scale [5] was applied to evaluate the type of adverse events. Anshu K *et al* [17] exposed 66.04 percent were 'probable' and 33.96 percent were 'possible'. These was dissimilar from Rajesh *et al* [9] study where most (63.5 percent) were probable. In our study 62 percent was possible and 31 percent was probable.

Severity of the ADRs is measured by using HS scale [6] Among 75 adverse events in our study, 49% were mild and 51% were moderate in severity, which is not comparable to one which was done by Srikanth *et al* [11] where 90.14 percent of reactions were moderate and 9.85 percent were mild.

## Conclusion

Adverse drug events are bound to happen while starting management of illness and vigilant watching is mandatory to avert complications. Zidovudine containing combinations have more predisposition for developing adverse events. Hence it is better to start with Tenofovir combinations. Adverse drug reaction among PLHA on management with ART regimen is an important health issue compliance to treatment. So, constant monitoring is necessary to thwart life threatening ADR and to improve treatment outcome.

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