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Original Research Article

A Cross-Sectional Study of Adverse Drug Reaction in Hiv Patients Taking Antiretroviral Treatment from Government Medical College, Kozhikode

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Abstract:

Introduction: The human immunodeficiency virus (HIV) is a retrovirus that infects cells of the immune system. As the infection progresses, the person becomes more susceptible to opportunistic infections due to affected immune system by HIV, which may leads to an advanced stage known as acquired immunodeficiency syndrome (AIDS) within 10-15 years. The duration can be significantly slows down by different antiretroviral regimens used in Anti-retroviral Therapy (ART). So the present study was conducted with objectives, to estimate the adverse drug reaction (ADR), and to assess their causality, severity in patients under ART.

Methodology: Approximately 152 patients were recruited by following certain set of inclusion and exclusion criteria since July 2015 to June 2016. The collected data was analysed by SPSS software (Descriptive, Chi-square test). The p value <0.05 was considered statistically significant.

Results: Out of 152 patients (75 were males and 77 were females), 21 (13.8%) patients had experienced ADRs, comprising 11(52.4%) male patients and 10 (47.6%) female patients. The majority of ADRs occurred in patients aged 41-50 years constituting 9 (42.9%). The majority of ADRs were related to hematological 10 (47.6%), cutaneous 4 (19.1%), gastrointestinal 3 (14.3%), hepatotoxicity 2 (9.5%) and neurological 2 (9.5%). Most adverse drug reactions occurred in the first 4 weeks of antiretroviral therapy. Out of the total ADRs, 13 (61.9%) had mild, 7 (33.3%) moderate intensity and 1(4.8%) had severe ADRs. WHO causality assessment showed 42.9% probable and 57.1% possible ADRs.

Conclusion: ADRs are more likely to occur within the first four weeks after initiating treatment with highly active antiretroviral therapy (HAART). In order to prevent occurrence of severe ADRs and to improve ART adherence close monitoring of the patient is required during therapy.

Keywords: Adverse drug reactions (ADRs); Antiretroviral therapy (ART); Human Immunodeficiency Virus (HIV).

Introduction

The human immunodeficiency virus (HIV) is a retrovirus that infects cells of the immune system. As the infection progresses, the person becomes more susceptible to opportunistic infections due to the affected immune system by HIV, which may lead to an advanced stage known as acquired immunodeficiency syndrome (AIDS) within 10-15 years[1]. HIV remains a major global public health issue, having claimed 40.1 million [33.6–48.6 million] lives so far with ongoing transmission in all countries globally(1). In 2021, 1.5 million [1.1 million–2.0 million] new HIV infections occurred, and 28.7 million individuals received antiretroviral medication[2].

Timely updated antiretroviral therapy has led to a significant reduction in the rates of illness and prolongs the life span of the patient[3]. Over 25% of HIV-infected individuals abandon their ART during the first year of therapy as a result of adverse drug reactions (ADRs), which are the most prevalent cause of ART cessation[4].

ADRs significantly affect public health as they impose a financial burden on society and healthcare systems, which led to a science called pharmacovigilance with the objectives, to ensure the safe and rational use of medicines and prevent avoidable negative consequences of pharmacotherapy in patients. Healthcare practitioners in India lack knowledge about medication safety monitoring and get inadequate training in this area.

So this cross-sectional study was conducted with the objectives, to estimate the adverse drug reaction (ADR), and to assess their causality, and severity in patients under ART. The finding of the study may help physicians to gain knowledge of adverse effects due to ART and promote the early recognition and reversal of potentially serious adverse effects to improve tolerability and adherence to ART.

Materials and Methods

A cross-sectional hospital based study was conducted in HIV positive patients attending from July 2015 to December 2015 at the ART center of Medical College Hospital, Kozhikode. The study was approved by the institutional ethics committee (Ref.No. GMCKKD/RP 2014/IEC/31/12dt1y/1/14). The permission to conduct the study in the medical college ART center Calicut was sanctioned by Kerala Aids Control Society in adherence with guidelines (No.5091/15/M&E/KSACS).

The sample size was calculated and approximated to 152, based on prevalence of ADR in previous studies. The patients under there different regimen (Zidovudine + Lamivudine + Nevirapine, Tenofovir+ Lamivudine + Nevirapine and Tenofovir + Lamivudine + Efavirenz) were selected by simple random sampling technique with an inclusion and exclusion criteria.

Inclusion Criteria:

1. HIV positive patients of both sex aged from 18-60 years under ART≤1Year.
2. Willing to give consent

Exclusion Criteria:

1. Patient taking antitubercular drugs, potential hepatotoxic drugs, nephrotoxic drugs, and other drugs interact with Anti-retroviral drugs.
2. Patients on second line drugs
3. Pregnant women on ART
4. Patients less than 18 years of age
5. Patients more than 60 years of age.

The patients were informed about the study in the local language and the undersigned consent form was obtained. Data was collected by visiting the ART center every Monday till the sample size was obtained from July 2015. At every visit, 10 patients were studied. The data was collected from pretested semi-structured proforma which includes sociodemographic profile, adverse

drug reaction of ART affecting gastrointestinal, hematological, neurological, cutaneous, musculoskeletal, hepatic, renal systems, and the laboratory investigation details. The causality and severity of ADR were assessed in accordance with the WHO causality assessment scale[5] and the modified Hartwig and Siegel Severity Assessment Scale respectively[6]. The data was analysed by applying descriptive statistics, a chi-square test in SPSS software. The p-value of < 0.05 was considered statistically significant.

Results

Out of 152 patients included in the study, 75 (49.3%) were males and 77 (50.7%) were females. The patients were in three different regimens i.e. 117 patients were on AZT+3TC+NVP, 35 were on TDF+3TC+NVP, and No patients were on TDF+3TC+EFV.

The observed data showed that 21 patients suffered from ADRs, out of them 11 were (52.4%) males and 10 (47.6%) were females (Table 1).

Table 1: Demographic characteristics of the patients

		Numbers	Percentage
Sex			
	Males	75	49.3
	Females	77	50.7
Regimen			
	AZT+3TC+NVP	117	76.97
	TDF+3TC+NVP	35	23.03
	TDF+3TC+EFV	0	0
ADRs			
	Present	21*	13.8
	Absent	131	86.2
WHO stage	Stage 1	33	21.7
	Stage 2	111	73.0
	Stage 3	8	5.3
* = Males: 11(52.4%); Females: 10 (47.6%)			

Concerning age, the majority of ADRs occurred in patients aged between 41-50 (42.9%) years, and the least number of ADRs occurred in patients aged between 51-60 (4.8%). According to WHO staging of patients, 33 (21.7%), 111 (73.0%), and 8 (5.3%) patients were distributed in stage 1, stage 2, and stage 3 respectively (Table 1).

In relation to Regimen, 20 (95.2%) and 1(4.8%) suffered patients were on AZT+3TC+NVP and TDF+3TC+NVP respectively.

The data showed that the majority of ADR occurred with AZT+3TC+NVP regimen with a P value of 0.032 (Table 2).

Table 2: Correlation of adverse drug reaction with regimen

Regimen	Number	Percentage
AZT+3TC+NVP	20	95.2
TDF+3TC+NVP	1	4.8
TDF+3TC+EFV	0	0
Chi square = 4.586, d.f (1), p value = 0.032		

The Majority of the patients in the study fell in WHO stage 2 which showed a greater number of ADRs (77.96%). A greater number of ADRs occurred within first 4 weeks of treatment (52.3%) and patients with D4 count <200 cells/µL (52.4%). Based on Table 3, Out of 21 ADRs 12(57.1%) were possible and 9(42.9%) were probable ADRs with a p-value of 0.191. According to Table 4, data shows that 13 (61.9%) were mild, 7 (33.3%) were moderate, and 1 (4.8%) was severe ADRs assessed by using Modified Hartwing and Siegel severity scale with p value 0.000.

Table 3: Causality assessment using the World Health Organization-Uppsala Monitoring Centre Scale

WHO Causality Scale	Number	Percentage
Probable	9	42.9
Possible	12	57.1
Total	21	100
WHO Causality Scale	Number	Percentage

Table 4: Severity Assessment using Modified Hartwig and Siegel Assessment Scale

Severity	Number	Percentage
Mild	13	61.9
Moderate	7	33.3
Severe	1	4.8

The observed ADRs were mainly related to haematological 10 (47.6%), cutaneous (19.1%), gastrointestinal 3 (14.3%), hepatotoxicity 2 (9.5%), and neurological 2 (9.5%).

Discussion:

The present observational study was conducted on 152 patients who are under different HAART regimens from July 2015 to December 2016. They were Zidovudine + Lamivudine + Nevirapine, Tenofovir+ Lamivudine + Nevirapine and Tenofovir + Lamivudine + Efavirenz. Among 152 patients 75 were males and 77 were females. Out of the study population, 21 patients had experienced ADRs which was around 13.8%. Among 21 patients, 11 patients were males and 10 were females with 52.4% and 47.6% respectively. The study findings were supported by Singh et.al and Sharma et.al with miner deviations [7], [8].

Bonfati et .al. in his study observed that women were more susceptible to ART-induced ADRs than men in contrast to the present study[9].

In the present study, ATR-induced ADRs were higher in patients receiving AZT+3TC+NVP comprising 5.2% when compared to 4.8% with TDF + 3TC + NVP, which may be due to more number of patients in the study were received this regimen. However serious side effects are more varied with nucleoside analogs like zidovudine, didanosine, stavudine, lamivudine, and tenofovir [10]. The present study was supported by Sadiq et.al., who concluded that most of the ADRs were with the Zidovudine-based combination[11].

The majority of ADRs were related to haematological around 47.6 % [10], of all anaemia was the most frequent ADR observed in the study, and was supported by a study conducted by Namme luma et al reported that 3.8% of haematological ADRs, out of them anaemia was the most common and severe in association with ATZ based regimen[12]. Cutaneous ADRs observed in the present study were 19.1% including maculopapular rashes, which was supported by Divakar et.al., and Sharma, Mustafa et.al., who observed rashes as ADR about 6.25% and 10% of their study

population respectively [13],[14]. But with Max and Sherer et.al., a study says that rashes can occur in 5 % to 24 % of patients(15). Hepatotoxicity was observed in 9.5 % of the present study population which was supported by MartineZ et.al., and Sulkowski et.al., with 12.5% and 15.6% respectively[16], [17]. GIT ADRs were observed in 14.3% of present study patients, of them nausea and vomiting most common with ATZ-based regimen. Peripheral neuropathy was also observed in 9.5% patients though the main causing drugs are stavudine, didanosine, and zalcitabine[18].

Among all the adverse reactions observed in the present study 13 (61.9 %) were mild, 7 (33.3%) were moderate, and 1 (4.8%) was severe. WHO causality assessment showed 42.9% probable and 57.1% of possible ADRs in the present study.

Conclusion

Antiretroviral therapy is becoming more effective, but it is also more challenging due to its related ADRs most likely to occur during the first four weeks of treatment. This may result in non-compliance which is a major global issue with ATR against virus in terms of adherence, efficacy, and resistance. Hence it is prudent to recognise these ADRs as early as possible. To avoid the emergence of serious ADRs and to increase ART adherence close monitoring, reporting of ADRs, and patient education about ART-associated ADRs are necessary throughout therapy.

References:

1. HIV and AIDS [Internet]. [cited 2023 May 10]. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids
2. UNAIDS Geneva. Global HIV & AIDS statistics — Fact sheet [Internet]. https://www.unaids.org/en. 2023 [cited 2023 May 10]. Available from: https://www.unaids.org/en/resources/fact-sheet
3. Palella FJ, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining Morbidity and Mortality among Patients with Advanced Human Immunodeficiency Virus Infection. N Engl J Med. 1998 Mar 26;338(13):853–60.
4. Monforte A d'Arminio, Lepri AC, Rezza G, Pezzotti P, Antinori A, Phillips AN, et al. Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naïve patients: AIDS. 2000 Mar;14(5):499–507.
5. WHO. The use of the WHO-UMC system for standardised case causality assessment [Internet]. [cited 2023 May 17]. Available from: https://www.who.int/publications/m/item/WHO-causality-assessment
6. Petrova G, Stoimenova A, Dimitrova M, Kamusheva M, Petrova D, Georgiev O. Assessment of the expectancy, seriousness and severity of adverse drug reactions reported for chronic obstructive pulmonary disease therapy. SAGE Open Med. 2017 Jan 31;5:2050312117690404.
7. Singh H, Dulhani N, Tiwari P, Singh P, Sinha T. A prospective, observational cohort study to elicit adverse effects of antiretroviral agents in a remote resource-restricted tribal population of Chhattisgarh. Indian J Pharmacol. 2009 Oct;41(5):224–6.
8. Sharma A, Vora R, Modi M, Sharma A, Marfatia Y. Adverse effects of antiretroviral treatment. Indian J Dermatol Venereol Leprol. 2008;74(3):234–7.
9. Bonfanti P, Valsecchi L, Parazzini F, Carradori S, Pusterla L, Fortuna P, et al. Incidence of Adverse Reactions in HIV Patients Treated With Protease Inhibitors: A Cohort Study. JAIDS J Acquir Immune Defic Syndr. 2000 Mar 1;23(3):236.
10. Fellay J, Ledergerber B, Bernasconi E, Furrer H, Battegay M, Hirschel B, et al.

Prevalence of adverse events associated with potent antiretroviral treatment: Swiss HIV Cohort Study. The Lancet. 2001 Oct;358(9290):1322–7.
11. Sadiq S, Gupta S, Khajuria V, Tandon V, Mahajan A, Gupta M. Adverse drug events due to Antiretroviral Therapy in a Northern Indian Tertiary Care Institution. Natl J Physiol Pharm Pharmacol. 2016;6(3):205.
12. Namme Luma H, Doualla MS, Choukem SP, Temfack E, Ashuntantang G, Achu Joko H, et al. Adverse drug reactions of Highly Active Antiretroviral Therapy (HAART) in HIV infected patients at the General Hospital, Douala, Cameroon: a cross sectional study. Pan Afr Med J. 2012 Jul 27;12:87.
13. Marfatia Y, Sharma A, Modi M, Sharma A. Stavudine *vs* . Zidovudine as antiretroviral therapy. Indian J Sex Transm Dis AIDS. 2007;28(1):26.
14. Srikanth BA, Babu SC, Yadav HN, Jain SK. Incidence of adverse drug reactions in human immune deficiency virus-positive patients using highly active antiretroviral therapy. J Adv Pharm Technol Res. 2012;3(1):62–7.
15. Max B, Sherer R. Management of the Adverse Effects of Antiretroviral Therapy and Medication Adherence. Clin Infect Dis. 2000 Jun 1;30(Supplement 2):S96–116.
16. Martínez E, Arnaiz JA, Podzamczer D, Dalmau D, Ribera E, Domingo P, et al. Substitution of nevirapine, efavirenz, or abacavir for protease inhibitors in patients with human immunodeficiency virus infection. N Engl J Med. 2003 Sep 11;349(11):1036–46.
17. Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. JAMA. 2000 Jan 5;283(1):74–80.
18. Reliquet V, Mussini J, Chennebault J, Lafeuillade A, Raffi F. Peripheral neuropathy during stavudine-didanosine antiretroviral therapy: Neuropathy on stavudine-didanosine. HIV Med. 2001 Apr;2(2):92–6.
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