

A Study on the Evaluation of Adverse Drug Reactions Associated with Antiretroviral Therapy in Tertiary Care Hospital

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Abstract

Objectives: This present study was to evaluate the sociodemographic profile and adverse drug reaction in HIV patients with antiretroviral therapy in tertiary care hospital in Bihar.

Methods: A total of 200 diagnosed cases of HIV infection based on various clinical features and laboratory investigations were enrolled in this study. Socioeconomic status (SES) of the patients were assessed by Modified Kuppuswamy score. Causality assessment of the reactions was done by WHO causality assessment scale and modified Hartwig and Siegel's scale was used for severity assessment. Once the ART drug causing the drug reaction was identified, the offending agent was stopped, and the regimen was changed.

Results: Out of 200 HIV cases, most of the cases 100(50%) were in age group of 34-49 years. And 128(64%) cases were males. According to the modified Kuppuswamy scale, most of the patients 129(64.5%) were belonged in lower middle class and had 11-15 score. Out of 200 cases, 90 (45%) cases had shown adverse drug reaction with ATR. Among them cases had 41(45.55%) anaemia, 23(25.55%) nephrotoxicity, 15(16.67%) skin rashes, 7(7.78%) giddiness, 3(3.33%) peripheral neuropathy and 1(1.11%) lipodystrophy.

Conclusions: Preponderance of HIV infection was more common in lower middle class socioeconomic and middle-aged male population. Anaemia was the most common side effects with ART associated with ziduvudin based regimens.

Keywords: HIV, ART, Socioeconomic status, Age group.

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Introduction

Human immunodeficiency virus (HIV) infection is a global pandemic with 35 million people living worldwide [1]. India too has a concentrated HIV epidemic with substantial geographical variation. The

epidemic peaked in the 1990s and in 2009, there were an estimated 2.4 million (1.8–2.9 million) persons living with HIV [1,2]. Of about 36.9 million people living with HIV (PLHIV) around the world, around 15.8 million people have been receiving

antiretroviral therapy (ART) [3]. Antiretrovirals mainly suppress viral load, thus restoring the immune function. Declining costs of antiretrovirals along with the production of drugs by generic manufacturers has helped tertiary care hospital in resource-limited areas cater better antiretroviral care to HIV-seropositive population [4]. Despite showing considerable efficacy in reducing mortality and morbidity in PLHIV, ART is also associated with wide range of potential adverse effects leading to reduction in patient's quality of life and adversely affecting treatment adherence which may consequently lead to treatment failure. Adverse drug reactions (ADRs) to these medications remain a significant point of concern which may subsequently compromise the effectiveness of an ART program [5].

In India, the National AIDS Control Organization (NACO) publishes guidelines regularly, outlining the steps for diagnosis and treatment of HIV infection, the most recent ones being those published in 2013. According to these guidelines, the ideal time to start ART is before the patient presents with an opportunistic infection [6, 7]. However, the current WHO recommendation with moderate-quality evidence states that ART can be initiated in all adults living with HIV, regardless of the WHO clinical stage, at any CD4 cell count, and as a priority, ART has to be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤ 350 cells/mm³ [8]. Objectives of this study was to evaluate the sociodemographic profile and adverse drug effects in HIV patients with antiretroviral therapy in tertiary health care centre of Bihar, India.

Materials & Methods

This present study was conducted in Department of Pharmacology with the collaboration of Department of ART, Jawahar Lal Nehru Medical College,

Bhagalpur, Bihar during a period from January 2020 to November 2020. Entire subjects signed an informed consent approved by institutional ethical committee, of Jawahar Lal Nehru Medical College, Bhagalpur was sought.

A total of 200 diagnosed cases of HIV infection based on various clinical features and laboratory investigations were enrolled in this study. All the participants had age group ≥ 18 years. These data were obtained about the basic demographic details, diagnosis, duration of illness and treatment, current treatment regimen, per-capita family income, side effect due to drugs, whether the drug was stopped after the side effect and patient was treated as out-patient or was admitted in the hospital.

Socioeconomic status (SES) of the patients were assessed by Modified Kuppaswamy score. According to this Score, upper class: 26-29, upper middle class: 16-25, lower middle class: 11-15 and upper lower class: 5-10.

Drug reactions like anaemia, skin rashes, lipodystrophy and nephrotoxicity were diagnosed by routine investigations (CBC, RFT, LFT, Viral load) done during the regular follow up. Reactions like giddiness and peripheral neuropathy were described by patients during the visit. During the course, Causality assessment of the reactions was done by WHO causality assessment scale and modified Hartwig and Siegel's scale was used for severity assessment. Once the ART drug causing the drug reaction was identified, the offending agent was stopped, and the regimen was changed.

Statistical Analysis

Data was analysed by using simple statistical methods with the help of MS-Office software. All the data were tabulated, and percentages were calculated.

Observations

A total of 200 diagnosed cases of HIV were included in this study. Most of the cases

100(50%) were in age group of 34-49 years. And 128(64%) HIV cases were males.

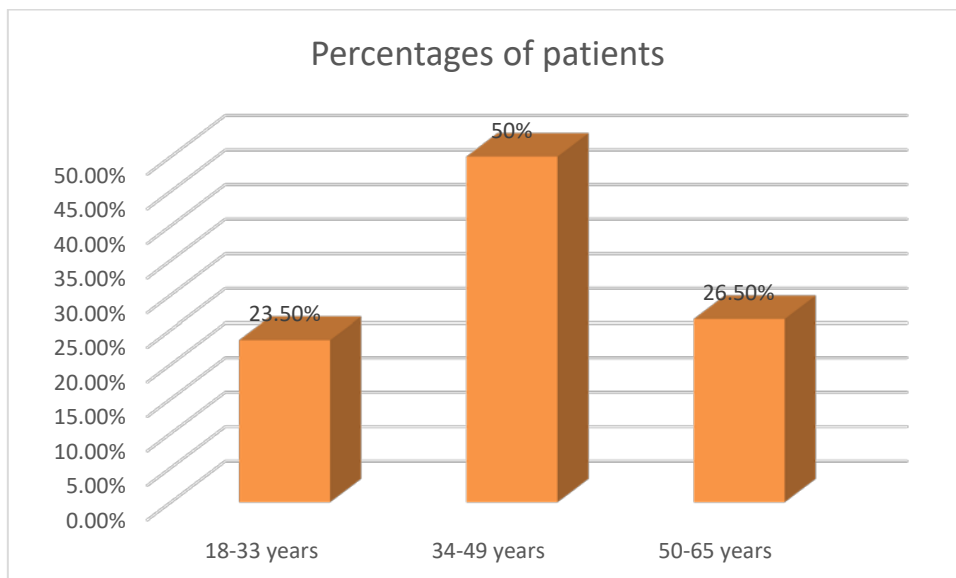


Figure 1: Age wise distributions of the patients.

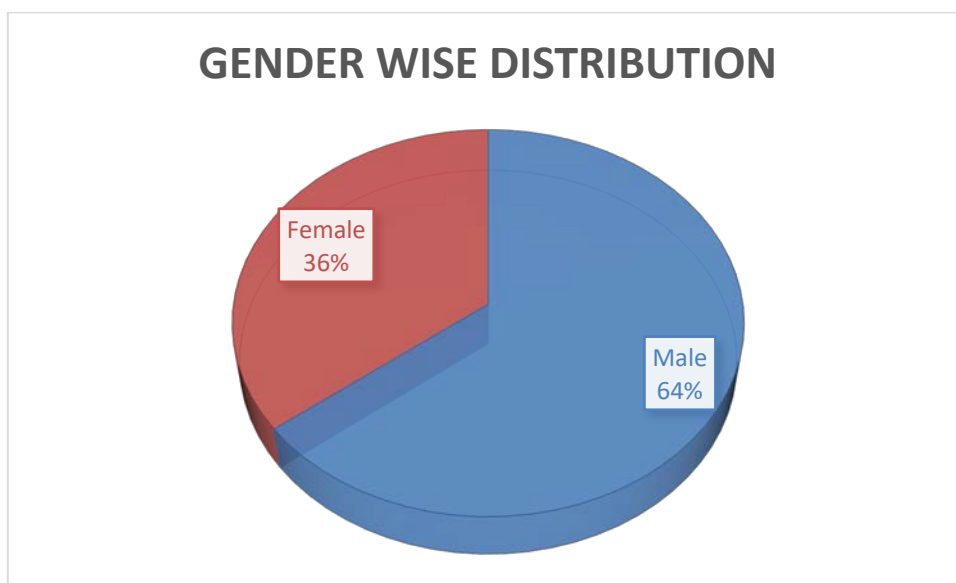


Figure 2: Gender wise distributions of the patients.

Table 3: Showing the socioeconomic status of the patients.

Modified Kuppuswamy score.	No. of patients	Percentages
26-29	0	0
16-25	0	0
11-15	5	2.5%
5-10	129	64.5%
>5	66	33%

On the basis of modified Kuppuswamy scale, most of the patients 129(64.5%) were belonged in lower middle class and had 11-15 score.

Table 4: Adverse drug reaction

ADR	No. of patients	Percentages
Anaemia	41	45.55%
Giddiness	7	7.78%
Peripheral neuropathy	3	3.33%
Lipodystrophy	1	1.11%
Skin rashes	15	16.67%
Nephrotoxicity	23	25.55%
Total	90	100%

Out of 200 cases, 90 (45%) cases had shown adverse drug reaction with ATR. Among them cases had 41(45.55%) anaemia, 23(25.55%) nephrotoxicity, 15(16.67%) skin rashes, 7(7.78%) giddiness, 3(3.33%) peripheral neuropathy and 1(1.11%) lipodystrophy.

Table 5: ART drugs cause adverse reactions

*Classes	ART Drugs	Types of ADR	Treatment
NRTI	Zidovudine	Anaemia	Stopped
NNRTI	Efavirenz	Giddiness	Stopped
PI	Atazanavir	Peripheral neuropathy	Stopped
NRTI	Stavudine	Lipodystrophy, peripheral neuropathy	Stopped
NNRTI	Nevirapine	Skin rash	Stopped
NTRTI	Tenofovir	Nephrotoxicity	Stopped

*Various classes of anti-retroviral drugs – NRTI – Nucleoside Reverse Transcriptase Inhibitors; NNRTI – Nonnucleoside Reverse Transcriptase Inhibitors; PI – Protease Inhibitors; NTRTI – Nucleotide Reverse Transcriptase Inhibitors.

During the treatment, various ART drugs like Zidovudine, Efavirenz, Atazanavir, Stavudine, Nevirapine and Tenofovir were found to be associated with adverse reactions. Anaemia being the most common drug reaction was associated with the zidovudine-based regimen. Tenofovir was associated with the development of nephrotoxicity. Skin rashes were observed with nevirapine use. Efavirenz was associated with giddiness. Atazanavir and Stavudine were associated with peripheral neuropathy. Case of lipodystrophy with stavudine use was reported only in 1(1.11%) patients.

Discussions

ADRs account for considerable mortality and morbidity besides having immense economic impact on patients, health-care providers and society. Most of the ADRs are preventable. The incidence of ADRs among patients on antiretrovirals from both

developing and developed countries ranges between 11% and 35.9% [9,10] with incidence being as high as 54% coexistent with opportunistic infection [5].

In this present study, prevalence of HIV was greatly seen in age group of 34-49 years. Males 128(64%) were more preponderance than females 72(36%). Anti-retroviral therapy (ART) has improved the prognosis for people living with HIV-infection/acquired immunodeficiency syndrome (AIDS) (PLHA). There has been reduction in mortality with increased use of potent antiretroviral drugs generally administered in a combination of three or four agents [11]. Most of the drugs available and approved for use in highly active antiretroviral therapy (HAART) have some or the other adverse effects. Serious side effects are more varied with nucleoside analogs (zidovudine, didanosine, stavudine, lamivudine, tenofovir, etc.)

including mitochondrial damage that can lead to lactic acidosis as well as peripheral neuropathy and pancreatitis. HAART therapy has also been associated with lipodystrophy syndrome of hyperlipidemia and fat redistribution [12]. Among the other side effects are fatigue, malaise, nausea, anemia, and hepatotoxicity. Non-nucleoside inhibitors, nevirapine and efavirenz are used in combination with nucleoside analogs for the treatment of HIV and are associated with the development of a maculopapular rash, dizziness, feeling of lightheadedness [11,12].

In this present study, prevalence of adverse drug reaction was seen in 90(45%) HIV cases. Anaemia has been reported as the most common side effect with ART [16]. In this study, anaemia 41(45.55%) was the most common adverse drug effect associated with Zidovudine regimen. Prescription in majority of the patients and zidovudine being a myelosuppressive drug is known to cause anaemia within 3 months of initiating therapy. This could be reason for high incidence of anaemia in this study. These results are comparable with previously reported studies [13,14].

Nephrotoxicity 23(25.55%) and skin rashes 15(16.67%) were associated with tenofovir and nevirapine respectively. Lipodystrophy was seen in 1(1.11%) patients. Stavudine associated lipodystrophy is common and is a multifactorial due to endocrine and metabolic abnormalities [14,15]. In concurrence to our report, 2.3% incidence has been recorded in earlier study [16].

Numerous reports have documented rash with ART therapy mainly with nevirapine [17]. Drug hypersensitivity in form of rash occur with HAART therapy usually in first 6 weeks of therapy [15]. Nevirapine, delavirdine and efavirenz, abacavir, amprenavir cause rashes frequently due to hypersensitivity which usually resolve spontaneously [17]. In this present study, Peripheral neuropathy was seen in 3(3.33%) cases. Peripheral neuropathy is

mainly seen with atazanavir and stavudine [18]. These inhibit nerve growth factor and result in neuropathy 1.3–22.3% of prevalence has been documented [19, 20].

The success of the anti-retroviral treatment is highly dependent on the motivation of HIV positive individuals to adhere to complex ART [11] regimens. Unfortunately, up to 25% of patients discontinue their initial HAART regimen because of toxic effects, noncompliance or [12] treatment failure within the rest 8 months of therapy. The occurrence of [21] side effects can vary dramatically among different people. Continuous evaluation needs to be done for the benefit of ART help to achieve the ultimate goal of making safer and more effective treatment to the [22,23] patients.

Conclusions

This present study concluded that the Preponderance of HIV infection was more common in middle-aged male and lower middle class socioeconomic population. Anaemia was the most common side effects with ART associated with ziduvudin based regimens.

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