

Evaluation of Drug Utilization of Antiretroviral Therapy among HIV Patients in a Tertiary Care Hospital

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Abstract

Introduction: Development of acquired immunodeficiency syndrome (AIDS) following infection with human immunodeficiency virus (HIV) continues to be a major global public health concern. Guidelines and protocols have been evolved over a period of time. Drug utilization studies help to evaluate changing pattern of drug usage, adherence with treatment guidelines and rational use of medicines. We aimed to evaluate the drug use indicators and utilization of anti-retroviral drugs among adult HIV patients.

Materials and Methods: An observational, descriptive study was carried out on adult HIV patients visiting at Out Patient Department (OPD) of anti-retroviral therapy (ART) center of Medical College, Kolkata over a period of four months. The detailed data from case file was collected and recorded in a pre-designed proforma. Simple descriptive statistics was used to evaluate drug use indicators and utilization pattern of anti-retroviral drugs.

Results: A total of 548 encounters were obtained from 122 patients. Majority of them were male (53.28%), belonged to the age group of 18 to 30 years, education below primary level (62.55%), married (72.06%), non-smokers (70.49%) and did not drink alcohol (51.25%). Heterosexuality was the most common mode of acquiring the infection (90.16%). Efavirenz was most commonly prescribed (6.57%) single drug ART regimen whereas the commonest combined ART regimen was combination of zidovudine+lamivudine+nevirapine (37.6%). Lamivudine was the most commonly prescribed nucleoside reverse transcriptase inhibitor (NRTI) [87.22%]. Among the concomitant medicines prescribed, anti-tubercular drugs were the most frequent (14.23%). The commonest adverse drug reaction was anemia (5.7%). Folliculitis was the most common opportunistic infection (11.47%) followed by tuberculosis (9.84%). Average number of drugs per encounter was 3.08. Drugs were prescribed mostly in generic name (99.65%) and in oral forms (97%)

Conclusion: The results of our study suggested that the prescribing pattern was in accordance with national guidelines and reflected the changing patterns of drug usage in HIV patients. Drug use indicators reflected rational approach towards prescribing pattern.

Keywords: Antiretroviral therapy, drug utilization, HIV/AIDS

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Introduction

Human immunodeficiency virus (HIV) infection is considered as one of the most important public health issue. In 2021, global incidence and prevalence of HIV patients were 1.5 million and 38.4 million respectively. Number of the patients died of it was 650000. Among the affected people only 28.7 million had the access to antiretroviral therapy (ART) [1]. Till date 84.2 million people have become infected with HIV and 40.1 million have died from acquired immunodeficiency syndrome (AIDS) related illnesses [1]. In 2021, Indian prevalence of HIV was 2.4 million and death due to this disease was 42000. Among the affected, only 65% patients were under cover of ART [2].

Both of HIV infection and AIDS are caused by human retrovirus. The mode of transmission of the virus includes sexual contact, by blood and blood products, body secretions and from infected mothers to infants intrapartum, perinatally or via breast milk [3]. Following infection, the virus remains in the body of the infected person for his/her lifetime. With progression of time gradual depletion of CD4 T cells or helper T cells occurs. This leads to development of profound immunodeficiency associated with HIV infection or AIDS. This may eventually result in development of opportunistic infections. The infection may also affect B cells, macrophages and nerve cells leading to reduction in cellular immunity. However, development of antibodies to HIV is very few and is not effective against the disease [4].

Several classes of drugs with different mode of action are available for HIV treatment: Nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, entry inhibitors, C-C chemokine receptor type 5 (CCR5) co-receptor antagonist and HIV integrase strand transfer inhibitors.

The goal of ART is to suppress virus replication as much as possible for as long as possible. As HIV replication requires a multi-step process, using a combination of different drugs targeting different steps within the HIV life cycle provides either synergistic or additive antiviral effect, thus enhancing the efficiency by which viral replication is suppressed. The current standard of care is to administer at least three drugs simultaneously throughout the treatment period. A minimum of three antiretroviral drugs are required for effective long-term suppression of HIV replication without development of resistance. In treatment-naïve patients, a regimen containing a NNRTI plus two NRTIs is as effective as a regimen containing an additional nucleoside [5].

National AIDS Control Organization (NACO) provides various means for prevention, support, care and treatment to HIV patients in India through ART centers [6]. Adopting changing trends in medications of HIV/AIDS globally and rational use of medicines are some of the measures to treat it more effectively.

The principal aim of drug utilization studies (DUS) is to facilitate the rational use of medicines in population. DUS are important for the optimization of drug therapy.

The study of drug utilization or prescribing patterns serves a component of medical audit, which seeks monitoring, evaluation and necessary modifications in the prescribing practices to achieve rational and cost effective pharmacotherapy. These studies help to evaluate changing pattern of medication use and compliance with national guidelines [7].

Several DUS of ART among HIV patients have been conducted in India as well as across the world. These studies should periodically be conducted throughout the world. In view of this, present study was conducted to evaluate the utilization of

ART among HIV patients in a tertiary care hospital.

Materials and Methods

Following obtaining the approval from institutional ethics committee this observational, descriptive study was carried out. The study was conducted in the Regional ART Centre, Medical College, Kolkata and Department of Pharmacology of the same institute over a period of four months, from July, 2017 to October, 2017. Adult HIV patients of either sex, visiting the Out Patient Department (OPD) of this Regional ART Centre willing to participate in the study were included. An informed consent written in a language which the study participants could best understand was taken before their enrolment. The diagnosis and the treatment protocol for the patients were decided by the physician in charge of the ART centre.

Adherence was determined by asking patient about the missed doses, if any and by verifying empty package of drugs. The level of adherence was classified as >95%

if less than 3 doses missed, 80-95% if 3-12 doses missed and <80% if more than 12 doses missed [8]. The collected data were analyzed with the help of MS excel using descriptive statistics to determine drug utilization pattern and drug use indicators [8].

Following interview of the patients data regarding their demographic profile, clinical status, ART prescribed, opportunistic infections, concomitant medications used etc. were recorded in case record forms.

Results

The total number of HIV patients included in our study was 122 and the total number of encounters was 548. Mean (\pm SD) age of the study subjects was 32.02 years \pm 6.99 years (range: 18 years – 55 years). Most of the subjects were male (53.28%). HIV was found to be most prevalent in the age group of 18 to 30 years (47.81%), followed by 31 to 40 years (43.06%), 41 to 50 years (6.56%) and > 50 years (2.55%). Distribution of age of the study subjects has been shown in figure 1.

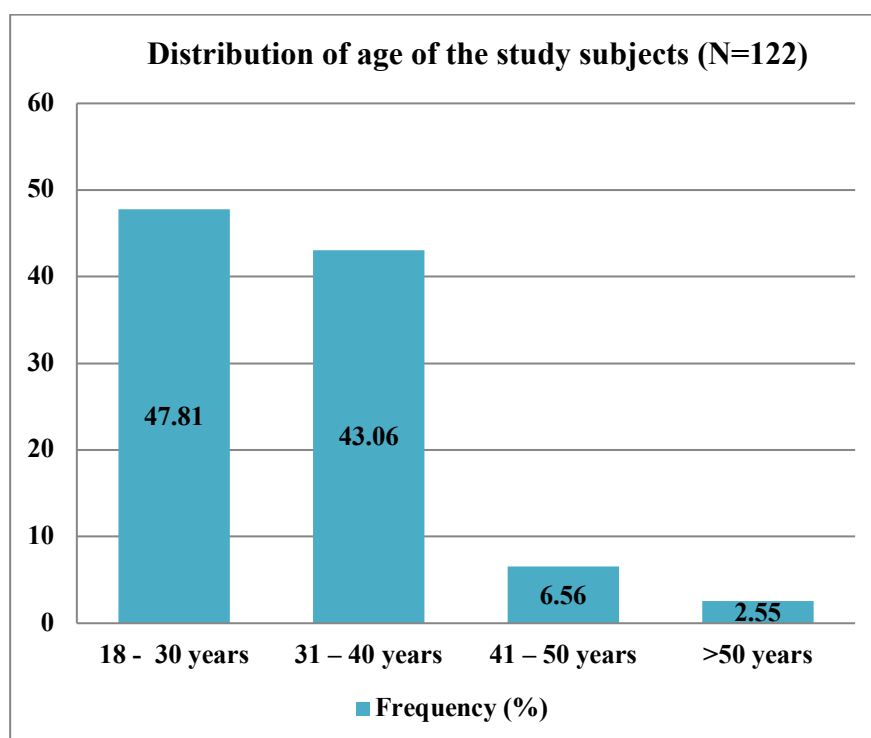


Figure 1: Distribution of age of the study subjects (N=122)

Average duration of HIV infection was 4.62 years. Most of the subjects were married (72.06%) and majority of the subjects were non-smokers (70.49%) and did not drink alcohol (51.25%). Majority of the subjects had their education below primary level (62.55%). Most of the subjects were housewife (36.06%) followed by driver (18.03%) and daily wage workers (8.2%). Demographic characteristics of study subjects have been presented in table 1.

Table 1: Demographic characteristics of study subjects (N=122)

Parameters	Frequency (%)
Age	
Years	32.02 ± 6.99
Gender	
Male	65 (53.28)
Female	57 (46.72)
History of smoking	
Smoker	36 (29.51)
Non smoker	86 (70.49)
Alcohol intake	
Drinks	59 (48.37)
Does not drink	63 (51.63)
Duration of HIV infection	
Up to five years	71 (58.19)
More than five years	51 (41.81)
Marital status	
Married	88 (72.06)
Never married	34 (27.86)
Educational status	
Below primary level	76 (62.55)
Above primary level	46 (37.70)
Profession	
Business	6 (4.92)
Carpenter	4 (3.28)
Driver	22 (18.03)
Helper	2 (1.64)
Housewife	44 (36.06)
Labour	8 (6.56)
Laundry	2 (1.64)
LIC Agent	2 (1.64)
Mobile mechanic	2 (1.64)
Nurse	2 (1.64)
Service	8 (6.56)
Shopkeeper	4 (3.28)
Student	4 (3.28)
Tailor	2 (1.64)
Daily wage Worker	10 (8.20)

Heterosexuality was the most common mode of acquiring the infection (90.16%), followed by mother-child (9.01%) and blood transfusion (0.82%). This has been shown in table 2.

Table 2: Mode of transmission of HIV (N=122)

Mode of transmission of HIV	Frequency (%)
Heterosexuality	110 (90.16%)
Mother to child	11 (9.01%)
Blood transfusion	1 (0.82%)

Most common opportunistic infection was folliculitis (11.47%). This was followed by tuberculosis (9.84%), diarrhoea (6.56%) and scabies (4.92%). Occurrences of opportunistic infections among HIV infected patients has been presented in figure 2.

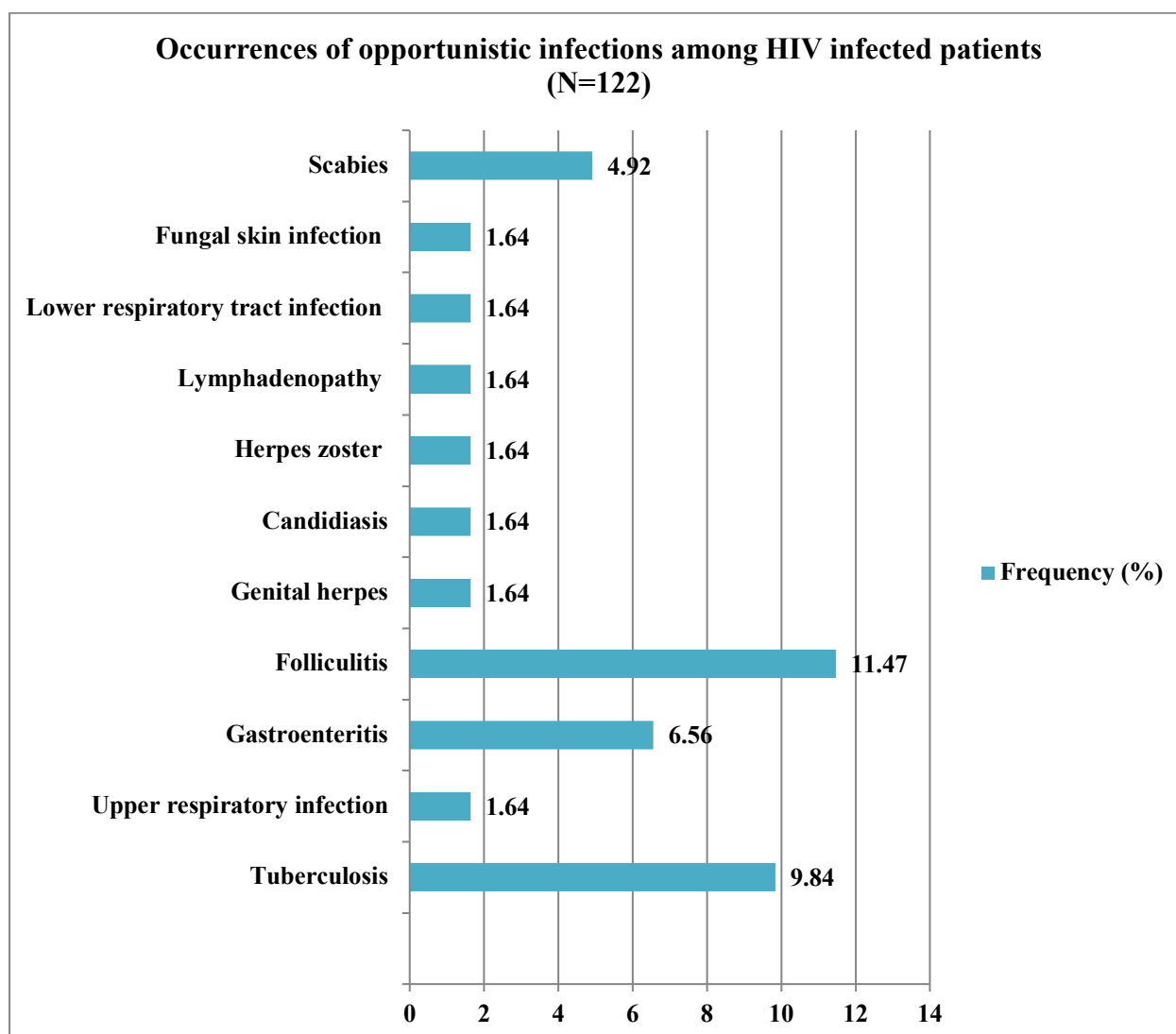


Figure 2: Occurrences of opportunistic infections among HIV infected patients (N=122)

ART was prescribed as single drugs as well as combination regimens. Among the single drug regimen efavirenz was most commonly prescribed (6.57%) followed by nevirapine (3.65%). On the other hand most commonly prescribed combination ART regimen was zidovudine + lamivudine + nevirapine (37.6%) followed by tenofovir + lamivudine + efavirenz (24.08%). Different ART regimens prescribed has been presented in figure 3.

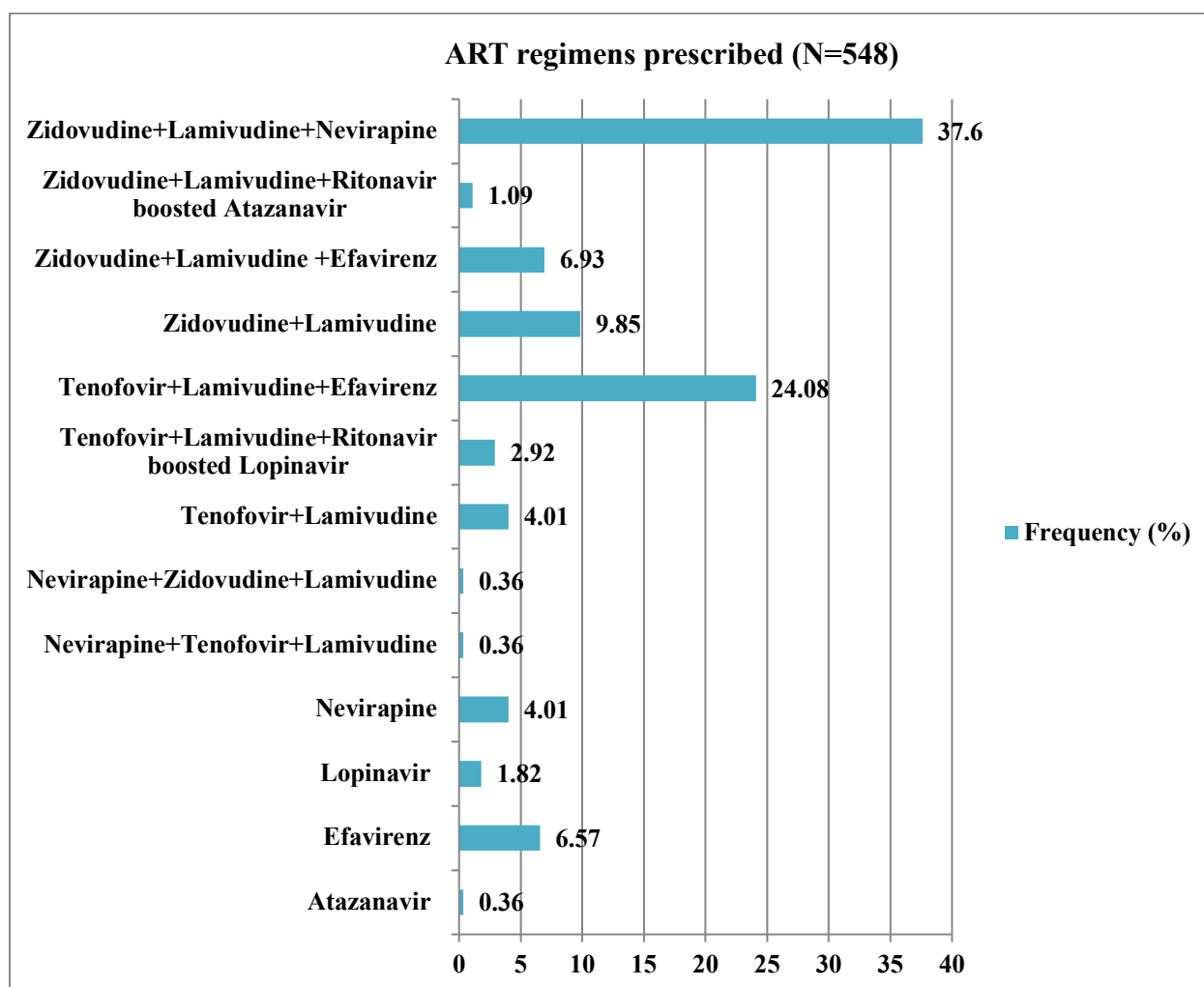


Figure 3: Different ART regimens prescribed (N=548)

Most commonly prescribed anti-retroviral drug was lamivudine (87.22%) followed by zidovudine (55.83%) and nevirapine (41.97%). The least prescribed anti retroviral drug was atazanavir (1.45%). Ritonavir was used as a booster to lopinavir in tenofovir + lamivudine + lopinavir combination therapy (2.92%) and to atazanavir in zidovudine + lamivudine + atazanavir combination (1.09%). Different antiretroviral drugs prescribed have been presented in table 3.

Table 3: Different antiretroviral drug prescribed (N=548)

Antiretroviral drug	Frequency (%)
Atazanavir	8 (1.45)
Efavirenz	206 (37.59)
Lopinavir	26 (4.74)
Nevirapine	232 (42.33)
Tenofovir	172 (31.38)
Lamivudine	478 (87.22)
Zidovudine	306 (55.83)
Ritonavir	22 (4.01)

Prescribing pattern of different subclass of antiretroviral agents was NRTIs (58.07%) followed by NNRTIs (32.44%) and PIs (4.14%).

Besides ART, concomitant medicines were also prescribed. Among them anti-tubercular drugs were the most frequent (14.23%) followed by azithromycin and cotrimoxazole (5.47% in each case). Table 4 presents the concomitant drugs prescribed in the study.

Table 4: Concomitant drugs prescribed (N=548)

Drugs prescribed	Frequency (%)
Antitubercular drugs	78 (14.23)
Azithromycin	30 (5.47)
Cotrimoxazole	30 (5.47)
Metronidazole	6 (1.09)
Pyridoxine	26 (4.74)
Atrovastatin + Fenofibrate	4 (0.73)
Calcium	4 (0.73)
Cetzine	4 (0.73)
Famotidine	4 (0.73)
Fenofibrate	26 (4.74)
Paracetamol	4 (0.73)
Iron	6 (1.09)
ONDEM	2 (0.36)
Cough Syr.	6 (1.09)
Tonoferon	4 (0.73)
Vitamin B complex	8 (1.45)

Average number of drugs per encounter was 3.08. Most of the drugs were prescribed in generic name (99.65%), route of administration was oral (97%). Percentage of encounters where an antibiotic was prescribed was 25.18%. World Health Organization (WHO) drug use indicators have been presented in table 5.

Table 5: WHO drug use indicators

Prescribing indicator	Value
Average number of drugs prescribed per encounter	3.08
Percentage of encounters where an antibiotic was prescribed	25.18%
Percentage of encounters where an injection was the route of administration	2%
Percentage of drugs prescribed by generic name	99.65 %
Percentage of drugs prescribed from the Essential Drugs List	93.65%

Adverse drug reactions (ADR) were also observed during ART therapy. Anemia was the most common adverse drug reaction (5.7%) followed by rash (4.0%) and peripheral neuropathy (1.6%). ADRs noticed in the study have been presented in table 6.

Table 6: Adverse drug reaction (N=122)

Adverse drug reaction	Frequency (%)
Anaemia	7 (5.7)
Rashes	5 (4.0)
Peripheral neuropathy	2 (1.6)

More than 95% therapeutic adherence was shown by 85.53% of the patients, followed by adherence of 80% - 95% which was shown by 10.44% patients. Level of adherence has been shown in table 7.

Table 7: Level of adherence (N=122)

Level of adherence	Frequency (%)
>95%	104 (85.53)
80% - 95%	13 (10.44)
<80%	5 (4.03)

Discussion

Majority of subjects in our study belonged to the age group of 18-40 years (mean age 32.02 years). This is in similarity with other studies where higher prevalence of HIV was found among these economically productive and sexually active group [9-12]. Majority of the patients were males (53.28%). Similar higher HIV seropositivity among male was seen in other studies [9-11].

We found HIV more prevalent among the subjects with lower educational level, i.e. below primary level (62.55%). Same finding was also seen in a study from Uganda [13]. This may support the fact that higher educational level is associated with reduced HIV prevalence. We found most of the patients were married (72.06%) which is consistent with other studies [14,15].

In our study all the patients received ART irrespective of their CD4 count unlike the older studies [13]. Previously initiation of antiretroviral drugs was done only on patients having CD4 count less than 350cells/mm³. However according to recent guidelines all patients diagnosed with HIV infection should be given antiretroviral drugs irrespective of their CD4 count.

In our study we found ART regimen both as a single drug as well as combination therapy. As per WHO recommendation, first line ART should contain one NNRTI with two NRTIs. These recommendations were adopted in national guidelines for ART 2013 [8]. Thus NNRTI remained second most commonly prescribed antiretroviral drugs in this study followed by PIs. NRTI remains the mainstay of ART and most preferred drugs and prescribed in our study like various other studies [16,17].

PIs based regimens were not prescribed compared to regimens based on NRTI as PIs were more prone for drug interactions, intolerance or adverse effects, more complex dosing schedule, toxicities and had higher cost [18, 19]. In our study majority of patients (94.17%) were on non PI based regimen. This finding is in accordance with other studies [9,12].

We found the most commonly prescribed NRTI and NNRTI were lamivudine (87.22%) and nevirapine (42.33%) respectively. This is similar to the findings in other studies [9,10,18,20]. Higher usage of lamivudine may reflect its good safety profile and ability to restore susceptibility to zidovudine and tenofovir [19].

In this study, the most common ART regime prescribed was the combination of zidovudine with lamivudine and nevirapine (37.60%) followed by tenofovir with lamivudine and efavirenz (24.08%), zidovudine with lamivudine (9.85%) and zidovudine with lamivudine and efavirenz (6.93%). The national guidelines for antiretroviral therapy 2013 by NACO recommend zidovudine with lamivudine and nevirapine as the first choice [8]. The findings are similar to the findings in other studies [11,13]. However these findings are not similar to the findings in other studies where the most common ART regimen prescribed was the combination of tenofovir with lamivudine and efavirenz (76.96%) followed by abacavir with lamivudine and efavirenz (8.7%) [21]. Usage of tenofovir (31.38%) and efavirenz (37.59%) was higher compared to previous similar study [9,10,13]. Both of tenofovir and efavirenz have convenient dosage schedule. This changing trend of increased uses of tenofovir and efavirenz was also seen in other countries [16,17]. The most

commonly prescribed PI in this study was ritonavir boosted lopinavir (2.92%), which was similar to the other studies [9,22].

The WHO has encouraged countries to transition away from first-line ART containing stavudine for its well-recognized toxicities like lipodystrophy, lactic acidosis, and peripheral neuropathy. This recommendation was solidified in the ART guidelines 2010 by WHO, stating that “countries should take steps to progressively reduce the use of stavudine in first-line regimens.” As a replacement of stavudine, the WHO and other expert bodies recommended first line adult ART that utilized an NRTI backbone of either zidovudine or tenofovir [16,23,24]. These recommendations were adopted in national ART guideline 2013 by NACO [8]. Thus our study showed decrease in usage of stavudine based regimens compared to previous studies. These findings are also in consonance with recommendation by guidelines and changing trend of usage of NRTIs in other countries [16,17].

Antibacterial agents were the second most common class of drugs prescribed in our study (25.17%). The most common antibacterial agent used was antitubercular drugs (14.23%) followed by co-trimoxazole and azithromycin (5.47% in each case). This is not similar to the other studies where co-trimoxazole was found to be the most frequently prescribed antibacterial agents followed by antitubercular drugs [9,25,26]. Use of co-trimoxazole is justifiable as it is recommended for chemoprophylaxis against pneumocystis jiroveci infection frequently found in HIV patients. Besides tuberculosis (TB) is the leading opportunistic disease and cause of death in HIV patients [27,28]. Thus considering the high rates of TB-HIV co infection, higher usage of antitubercular agents is justifiable.

In our study 8.19% patients developed ADRs and the commonest ADR reported was anemia. Similar finding was observed by Mukherjee *et al* [29]. Opportunistic

infections are one of the major problems in HIV patients. In this study, among all opportunistic infections, dermatological infection in the form of folliculitis was found to be the most common (11.47%) followed by tuberculosis (9.84%), gastroenteritis (6.56%) and scabies (4.92%). However, in other studies tuberculosis was the most common opportunistic infections [13,15,27,28].

The efficacy of ART in suppressing viral replication and delaying progress of AIDS is the result of strict adherence to the treatment. To avoid development of antiretroviral drug resistance optimal adherence to the recommended regimens should be >95% [8]. We found optimal adherence of >95% was achieved in majority of cases (85.53%). This finding is similar to the findings of other Indian studies [9,30]. Factors explaining this good adherence include providing treatment as well as medications free of cost. Besides good drug procurement and distribution practices in this ART centre avoided disruption of drug supply. These points have been shown to be a significant cause of drug resistance and ART failure in Uganda [31]. Another important point in this regard is that the patients were adequately counselled for improving treatment adherence by counselors in this ART centre. Counseling is considered as an important factor for improving adherence to antiretroviral therapy in HIV positive patients [32].

The average number of drugs in a prescription is an important indicator for the standard of prescribing. The average number of drugs prescribed per prescription in our study was 3.08. The study of prescribing pattern in OPD in tertiary care teaching hospital conducted in central India showed 2.38 drugs per prescription [33]. Also in other studies, average number of drugs per encounter was 4.26 which were more than our study [9]. In our study most of the drugs were prescribed in oral formulation (97%) followed by injectable (2%). This is a far

below and favourable figure in comparison to that set forth by WHO in this concern i.e. < 10% [33]. In this study, 99.65% % drugs were prescribed by generic name. The drugs prescribed from National List of Essential Medicines 2015 were 93.65% [34]. These parameters indicate rational prescription practices. Use of drugs from the essential drug list should be promoted for optimal use of limited financial resources, to have acceptable safety and to satisfy the health needs of the majority of the population [35].

Conclusion

Our study provides a baseline data regarding the demographic profile, prescribing pattern of ART, ADRs and opportunistic infections in HIV positive patients registered at our ART center. Anti-retroviral drugs prescribed in our study were in accordance with national guidelines. This also reflects the rational approach to prescribing pattern of anti-retroviral drugs.

Authors' Contributions

Preparation of the protocol was done by Alak Kumar Das. Collection of data was done by Shreyoshree Mandal. Statistical analysis was done by Jinia Ghosh and Alak Kumar Das. Preparation of the manuscript was done by Jinia Ghosh, Manab Nandy and Alak Kumar Das.

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