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Original Research Article

The study of adverse drug reactions (ADRS) of antiretroviral therapy (ART) on HIV infected persons (PLHIV) at our Art Centre, Jodhpur, Rajasthan

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Abstract: Antiretroviral drugs are successful in controlling HIV/AIDS and reducing disease progression. Antiretroviral regimens are stopped in up to 25% of all patients during their initial treatment therapy as a result of adverse drug effects, failing treatment and non adherence within the initial eight months of treatment. A pharmacovigilance surveillance system makes it possible for physicians, pharmacists and other healthcare providers to report suspected ADRs. The objective of this study was to assess the prevalence and severity of Adverse Drug Reactions (ADRs) among HIV/AIDS patients at ART centre, Jodhpur. In our study, 595 patients were included for study of ADRs of the ART for period of one year. These patients were interviewed and examined in each follow-up visits for ART related problems or Opportunistic Infections (OIs). Of the 595 patients, only 120 patients were developed total 188 ADRs. In this study, adverse drug reactions were observed to be present more in males as compared to females and majority of the patients were in the age group of 31-45 years. Incidence of ADRs was 20.16% (120/595). Most commonly encountered side effects were hematological (26.59%), gastrointestinal (20.74%), cutaneous (18.61%), neurological (8.51%) and musculoskeletal (7.97%). Causality assessment by Naranjo's scale, most of ADRs was 'possible' (62.76%). Severity assessment showed that most of the reported ADRs 11.6% were mild and 85.2% were moderate in nature while 4.2% was life threatening. This concluded that earlier ART initiation, before the development of a low CD4 cell count and opportunistic infection, may reduce the incidence of adverse effects.
Keywords: Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome, Antiretroviral Therapy, Adverse Drug Reactions, Hematological Disorders, Gastrointestinal Disorders.

INTRODUCTION

In the early 1930s, people were dying of a mysterious wasting illness in the Congo basin in Africa. By the 1960s and 1970s, the illness spread to parts of the United States, Europe and Asia – a silent new pandemic was underway even as the virus and its effects on the human host remained unknown. When the Human Immunodeficiency Virus (HIV) was first described [1] and identified [2, 3] in 1981, the illness had already spiraled out of control. Highly Active Antiretroviral Therapy (HAART; a combination of at least three drugs) for HIV-1 infection has led to substantial reductions in morbidity and mortality and many Highly Active Antiretroviral Therapy (HAART) regimens result in near-complete suppression of HIV-1 replication.

There are now 15 antiretroviral drugs available in five drug classes and so the number of possible HAART combinations is huge. Choosing between many of these combinations is, therefore, increasingly dependent upon knowledge of antiretroviral toxicities. There is evidence that potential side effects impact acceptance of offered medication and research [4] suggests that side effect concern is a primary reason for discontinuing ART among HIV positive individuals.

Antiretroviral drugs toxicity profile is not well known in developing countries. The spectrum of adverse effects related to HAART in developing countries may differ from that in developed countries because of the high prevalence of conditions such as anemia, malnutrition, and tuberculosis and frequent initial presentation with advanced HIV/AIDS disease. Therefore, it is important for a study to be carried out to assess the continuous evaluation of the benefits and harm of medicines which will help in achieving the ultimate goal of making safer and more effective treatment available to patients, as well as to help health professionals to participate in the very important

process of continuous surveillance of safety and efficacy of drugs used in clinical practice [5].

The presence of side effects is associated with non-adherence to ART. The high adherence demands associated with ART make treatment success challenging. If the effects are bad enough, some patients will begin skipping doses, or quit altogether. It is also important that healthcare providers inform their patients that some side effects will gradually dissipate over time. This will encourage patients to remain adherent at the beginning of their regimens.

When prescribing or switching one or more drugs in an ART regimen, clinicians must consider the potential for drug-drug interactions—both those that affect ART and those that ART affect on other drugs a patient is taking. The magnitude and significance of interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. When prescribing interacting drugs is necessary, clinicians should be vigilant in monitoring for therapeutic efficacy and/or concentration-related toxicities.

All antiretroviral drugs can have both short-term and long-term adverse events. The possibility of specific side effects differs from drug to drug, from drug class to drug class and from patient to patient[6]. The patient should carefully be monitored by the prescriber of ART for any possible side effects related to the combination of medications being in use. The use of routine blood tests in measuring CD4 cell counts and HIV viral load should be used as prognostic markers for disease progression. The side-effects of ART need to be differentiated from manifestations of new Opportunistic Infections (OIs) and Immune Reconstitution Inflammatory Syndrome (IRIS).

Several authors have reported bone marrow suppression as the adverse effects of ART which causes anemia and/or neutropenia by Zidovudine (AZT). The morbilliform eruption is the most common type of reaction after HIV treatment. Risk factors for lipodystrophy in patients on Nucleoside Reverse Transcriptase Inhibitors (NRTI) include accelerated age, abnormal lipid profile prior to therapy, and low CD4 cell [7] Ritonavir-containing regimens have been associated with increased incidence of dyslipidemia [8]. All NRTIs are neurotoxic to a varying degree and in a dose-dependent manner. Tenofovir (TDF) most often has been reported to cause proximal renal tubulopathy, e.g., Fanconi syndrome, other related nephrotoxicities, including diabetes insipidus, calcium and phosphorus dysregulation with bone disease[9], and reduction in glomerular function have also been reported [10]. Stevens–Johnson Syndrome (SJS**)** and Toxic Epidermal Necrolysis (TEN) are rare, severe cutaneous reaction caused by antiretroviral agents.

In addition, if only known adverse reactions are reported, unexpected adverse reactions will not be identified. Previously unrecognized adverse reactions are always found when using new medicines. It is important to identify them, understand their importance, determine their incidence and identify the risk factors as quickly as possible [11]. When confidence in medicine safety is lost, patients may stop taking their ART medicines leading to failure of therapy and possible development of drug resistant viral strains thus reduced medicine efficacy. In recent years, many studies have been carried out on ADRs of ART in western countries. But in India, there are less number of studies going on so there is need to evaluate the current scenario on side effects of ART. In this study we are assessing prevalence and severity of Adverse Drug Reactions (ADRs) among HIV/AIDS patients in western Rajasthan.

MATERIALS AND METHODS

Study Area:

A prospective cross sectional observational study was conducted in Department of Pharmacology and in ART centre under the Department of Medicine, Dr. S.N. Medical College, Jodhpur, Rajasthan for the period of 12 months from July 2014-June 2015. The aim of the study was to investigate whether patients in Jodhpur, a important part of Western Rajasthan, who were on Antiretroviral drugs (ARVs) developed various adverse drugs reactions. Clinical examination and laboratory biomarker tests were used to assess these ADRs. These biomarkers were tested at different intervals: before initiation of ARVs (baseline), six months and twelve months. Any significant change was noted in accordance with the NACO-2013 Guidelines.

Study Population:

All newly diagnosed PLHIV (both male and female) who are eligible for initiation of ART and those who are already on ART (either 1st line/alternate 1st line/2nd line ART), total 627 patients were included in this study as per NACO guidelines. Out of 627 patients, 595 (94.89%) were still continuing either AZT or TDF based ART and were regular visitors at the ART center while remaining 32 (05.10%) lost to follow-up(LFU) were excluded from this study.

Inclusion criteria:

- Adults i.e. > 18 years of age were included.
- Patients who were on ART for at least 1 month were included.

Exclusion criteria:

- Patients younger than 18 years.
- Pregnant women.

- All HIV/AIDS patients who were defaulter on 1st line ART
- All HIV/AIDS patients who were transferred out of the ART centre.
- All HIV/AIDS patients who died or Lost to follow-up(LFU)during the study period

Data Collection and Data Analysis:

Both primary (of patient interview and examination) and secondary (of patient cards) data sources were used. Baseline laboratory investigations such as hemoglobin (Hb), total counts, differential counts, erythrocyte sedimentation rate, urine analysis, serum Venereal Disease Research Laboratory (VDRL) test, serum Hepatitis B Surface Antigen (HBsAg), Mantoux test (MT), liver function tests (LFTs), renal function tests (RFTs), lipid profile and blood sugar were carried out in each patient to rule out any opportunistic infection or specific contraindication to any drug. X-ray of the chest and ultrasonography of the abdomen were done in all cases to determine the focus of TB. CD4 count was done every six months or more frequently if clinically indicated.

Variance:

The dependent variable was presence of ART Adverse Effect, while the independent variables were socio-demographic characters: Age, sex, educational status, CD4, co-morbid diseases, concomitant medications. Causality of ADRs will be assessed by Naranjo's algorithm scale and Severity of ADRs is to be assessed by Modified Hartwig & Siegel Scale.

Statistical Analysis:

The data was entered Microsoft Excel and analyzed using Statistical Package for the Social Sciences Software (SPSS 17.0). The data was presented in the form of mean ±S.D, percentages and ratio. P value <0.05 was considered significant. The number of ADRs observed and the prescribed drugs with which these ADRs were seen were also expressed in percentages.

Ethical Clearance:

Ethical clearance was requested and approval was obtained from National AIDS Control Organization (NACO), Ministry of Health and Family Welfare, Government of India and Institutional Ethics Committee, Dr. S.N. Medical College, Jodhpur, Rajasthan. Participants were also assured that all the information used in the study would remain confidential.

RESULTS

A total 627 patients were registered for study of ADRs of the HAART at the ART center, Jodhpur from July 2014 to June 2015. Out of 627 patients, 595 (94.89%) were still continuing either AZT or TDF based ARV and were regular visitors at the ART center while remaining 32 (05.10%) lost to follow-up(LFU) were excluded from this study. Of the 595 patients, only 120 patients were developed total 188 ADRs. Incidence of ADRs were 20.16% (120/595).Exactly, 55% (66/120) of study subjects who manifested a reaction had one ADR, 33.33% (40/120) had two, while 11.66% (14/120) had three different types of ADRs within the study period. At the start of the study, 79.66% patients were categorized in I and II WHO clinical stage where as only 20.34% patients were categorized in III and IV stage. Similarly, 85% of the patients were categorized under Working (W) functional status and only 15% under Ambulatory (A) and Bed ridden (B).

Total 120 patients were enrolled for the study those developed various types of ADRs. 62.5% were males and 37.5% were females. In our study, majority of the ADRs were observed in males 121(64.37%) as compared to females 67(35.63%).58.33% of the patients were in age group of 30-45 yrs, 28.33% of patients in age group of 18-30 yrs and 13.33% patients were above 45 yrs of age. Maximum number of ADRs was developed in 31-45 yrs 102(54.25%) Age group, while least in >45yrs 35(18.61%).

As per the distribution of various organ systems affected by ADRs, 50 (26.59%) ADRs were related to hematological system, 39 (20.74%) ADRs were related to gastrointestinal, 35 (18.61%) ADRs were related to cutaneous, 16 (8.85%) ADRs were related to central nervous system, 15 (7.97%) ADRs were related to musculoskeletal system, 8 (4.25%) ADRs were related to metabolic abnormalities and 6 (3.19%) ADRs were belonged to cardiovascular system, 4 (2.12%) ADRs were related to Liver, 3 (1.59%) ADRs were belonged to psychiatric, 2 (1.06%) ADRs were related immune restoration (IRIS) and 10 (5.31%) ADRs were related to others systems (Table 1).

The most commonly reported ADRs were (15.95%) anemia, (8.51%) gastritis, (6.38%) rashes, (5.85%) nausea/vomiting, (5.31%) itching, (4.25%) leucopenia, (3.72%) macrocytosis and (3.19%) diarrhea(Table 1). Most of ADRs were observed during 1st six month of ART short term/medium term e.g. nausea/vomiting, anemia, rashes, itching, diarrhea etc. Those were developed after six month is long term ADRs e.g. nail pigmentation, lipodystrophy, hyperlipidemia etc. In this study maximum number of ADRs were due to Zidovudine + Lamivudine + Nevirapine (AZT+3TC+NVP) based regimen 52.65% and least were due to Tenofovir + Lamivudine + Atazanavir/ Ritonavir (TDF+3TC+ATV/r) based regimen 02.65 %(Table 2).

According to Naranjo Causality Assessment Scale, 118 (62.76%) ADRs were found to be possible and 70 (37.24%) ADRs were probable. Based on the Modified Hartwig & Siegel Scale for Severity Assessment, 20 ADRs were mild, 160 ADRs were moderate and 8 ADRs were severe in nature.

Table 1:- Organ system wise distribution of ADRs

ADRs	NUMBER OF ADRS(n=188)(Percentage)	SEX	
		MALE	FEMALE
Hematological	**50(26.59)**	**37**	**13**
Anemia	30	23	7
Leucopenia	8	7	1
Macrocytosis	7	4	3
Thrombocytopenia	5	3	2
Gastrointestinal	**39(20.74)**	**24**	**15**
Gastritis	16	11	5
Nausea/Vomiting	11	6	5
Diarrhea	6	4	2
Abdominal pain	2	1	1
Anorexia	1	-	1
Flatulence	1	1	-
Dyspepsia	1	-	1
Gastric intolerance	1	1	-
Cutaneous	**35(18.61)**	**16**	**19**
Rash(Grade I,II,III)	12	4	8
Rash(Grade IV/SJS/TEN)	2	1	1
Itching	10	4	6
Maculopapular Rash	4	1	3
Nail pigmentation	1	1	-
Oral pigmentation	1	1	-
Hair loss	2	2	-
Erythema	1	1	-
Acne form skin eruption	1	-	1
Urticaria	1	1	-
Neurological	**16(8.51)**	**10**	**6**
Insomnia	4	2	2
Headache	4	2	2
Giddiness	2	1	1
Tingling sensation	2	2	0
Numbness	1	-	1
Drowsiness	1	1	-
Peripheral neuropathy	1	1	-
Vivid dreams	1	1	-
Musculoskeletal	**15(7.97)**	**10**	**5**
Parasthesia of legs	4	3	1
Body ache	3	2	1
Myalgia	3	2	1
Arthalgia	2	1	1
Leg weakness	1	1	-
Muscle cramps	1	1	-
Osteoporosis	1	-	1
Metabolic	**8(4.25)**	**7**	**1**
Hyperlipidemia	5	4	1
Lypodystrophy	2	2	-
Lactic acidosis	1	1	-
Cardiovascular	**6(3.19)**	**4**	**2**
Palpitation	4	3	1
Moderate increase in BP	1	1	-
Chest pain	1	1	-
Hepatic toxicity	**4(2.12)**	**3**	**1**
Abnormal LFT	2	1	1
Fatty change	1	1	-
Jaundice	1	1	-
Psychiatric disorders	**3(1.59)**	**2**	**1**
Confusion	1	1	-
Anxiety	1	-	1
Depression	1	1	-
IRIS	**2(1.06)**	**1**	**1**
Others	**10(5.31)**	**7**	**3**
TOTAL	**188(100%)**	**121(**64.37%)	**67(**35.63%)

Table 2:- Adverse drug reaction (ADR) profile of cases on ART

ADRs	NUMBER OF ADRS(n=188)(Percentage)	AZT+3TC +NVP	AZT+3TC +EFV	TDF+3TC +NVP	TDF+3TC+ EFV	AZT+3T C+ATV/r	TDF+3T C+ ATV/r
Hematological	50(26.59)	36	12	-	-	2	-
Gastrointestinal	39	18	13	6	-	2	-
Cutaneous	35	23	2	10	-	-	-
Neurological	16	2	6	2	6	-	-
Musculoskeletal	15	8	2	1	1	1	2
Metabolic	8	4	1	-	-	2	1
Cardiovascular	6	3	-	1	1	1	-
Hepatic toxicity	4	1	1	1	-	-	1
Psychiatric disorders	3	-	2	-	1	-	-
IRIS	2	1	-	1	-	-	-
Others	10	3	2	2	1	1	1
TOTAL	188(100%)	99(52.65%)	41(21.80%)	24()	10(12.76%)	9(4.78%)	5(2.65%)

[Zidovudine+Lamivudine+Nevirapine (AZT+3TC+NVP) ; Zidovudine+Lamivudine +Efavirenz (AZT+3TC+EFV) ; Tenofovir+ Lamivudine + Nevirapine (TDF+3TC+NVP) ; Tenofovir+ Lamivudine +Efavirenz (TDF+3TC+EFV) ; Zodovudine+Lamivudine+Atazanavir/Ritonavir (AZT+3TC+ATV/r) ; Tenofovir+Lamivudine+Atazanavir/Ritonavir (TDF+3TC+ATV/r)]

DISCUSSION

In our study, the prevalence of ADRs was high in males (64.37%) as compared to female (35.63%) patients. In contrast to this finding, Rajesh *et al.;* has found high prevalence of ADRs in females, when compared to males [12]. The reasons for these sex differences in adverse drug reactions might be due to differences between men and women in body mass index and fat composition, hormonal effects on drug metabolism, or genetic constitutional differences on the levels of various enzymes.

The Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI), nevirapine is also responsible for more frequent side effects in women than in men. Nevirapine related rash has been observed in 6.38% of women but only in 3.19% of men, and nevirapine-associated itching is also more common in women.

We have observed lesser incidence of ADRs to ART (20.16%) than reported by Rajesh *et al.;* (43.85%) [12] and Ghate *et al.;* (35.32%) [13] Respectively. These variations in the incidence rate of ADRs may be because of concurrent medications used for treating opportunistic infections and other co-morbid conditions which may results in increase of ADRs incidences.

The likelihood of developing an adverse drug reaction was highest in the first six months of commencing antiretroviral therapy. In our study most of ADRs were also observed during 1st six month of ART (86.18%) e.g. nausea/vomiting, anemia, rashes, itching, diarrhea etc. Those were developed after six month was long term ADRs e.g. nail pigmentation, lipodystrophy, hyperlipidemia etc.

In this study, regimens used were Zidovudine + Lamivudine + Nevirapine (46.66%), followed by Tenofovir + Lamivudine + Nevirapine (33.33%), Zidovudine + Lamivudine Efavirenz (7.5 %%), Tenofovir + Lamivudine + Atazanavir/ Ritonavir (5.83%), Zodovudine + Lamivudine + Atazanavir/ Ritonavir (4.16%) and Tenofovir + Lamivudine + Efavirenz (2.50%). So, 80% of the cases used Nevirapine based regimen. It was also seen that most of the ADRs (65.42%) were reported from regimen ZDV+3TC+NVP and TDF+3TC+NVP consisting of zidovudine and nevirapine. Rajesh et al. has also found that those patients who received regimen containing zidovudine and nevirapine were reported maximum number of ADRs [12]. In our study most commonly encountered side effects were hematological (26.59%), gastrointestinal (20.74%), cutaneous (18.61%), neurological (8.51%) and musculoskeletal (7.97%).

Zidovudine causes bone marrow suppression leading to anemia and thrombocytopenia. Increased prevalence of anemia was seen in our patients, though anemia was more prevalent among males (12.23%) than females (3.27%). Agarwal *et al.;* reported high incidence of zidovudine-induced anemia in HIV infected patients in eastern India [14]. Another study by Kumar swamy *et al.;* has shown peripheral neuropathy, anemia and nail hyper pigmentation as the most common side effects [15] Headache and anemia were highest in patients who received AZT+3TC+NVP regimen.

Anemia was seen in 16% of the cases; grade IV anemia was seen in 3.4% cases as compared to 34%

in an old study by Van Leeuwen *et al.;* [16]. In cases with grade IV anemia (Hb < 6.5 g/dl), AZT was replaced by TDF and the remaining cases were managed conservatively with iron and folic acid supplementation. Currently, all patients who received d4T-based regimens are gradually being switched to AZT-based and TDF-based regimens.

The most common gastrointestinal ADR was gastritis (8.51%) in the present study and most of them occurred before the 4th month of treatment. In a study by O.Brien et al., GI events were mentioned as the most common reason (4.4%) for a patient to discontinue ART due to ADRs[17]. Maniar *et al.;* reported abdominal pain and diarrhea in 0.7 and 0.2% of their cases, respectively, while they were observed in 1.06 and 3.19% of our cases, respectively [18].

In our study, gastrointestinal and cutaneous were 2nd and 3rd most common ADRs. Similarly, in the study of Khalili *et al.;* [19] gastrointestinal toxicity was most prominent with incidence rate of 63.7% whereas Singh *et al.;* [20] have found skin related toxicity with the incidence rate of 15.83%. Nevirapine was used in 80% of our regimens so it was high risk factor for gastritis.

Nevirapine was commonly used in our patients, thereby, explaining the increased dermatological adverse drug effects, like skin rashes and itching seen in our patients. The common adverse effects of NNRTIs are rash and hepatitis. Gangar *et al.;* [21] were the first to suggest a trend toward a higher frequency of rash among women taking nevirapine than among men. Three additional studies provide further support of this sex difference [22].

Our findings show that the rates of skin rash (9.57%) were similar to those found in Blantyre, Malawi [23]. Steven Johnson Syndrome (SJS) is the most severe medical emergency which is seen with nevirapine use. In our study, we have found one case of SJS due to nevirapine where the patients was having diffuse, exfoliating exanthema with generalized bulbous eruptions all over the body. This drug also caused fever and hepatitis which constituted 1.8% each. Chen *et al.;* have induced skin rashes by the use of nevirapine in rats and determined that the 12-hydroxylation metabolic pathway is responsible for the rashes [24].

CNS side effects were common among patients on efavirenz based regimens (AZT/3TC/EFV, TDF/3TC/EFV). In our study, efavirenz use was observed as a risk factor for insomnia, parasthesia, nightmares, drowsiness, giddiness and depression. Subbaraman *et al.;* have also reported similar kinds of ADRs with the efavirenz use[5]. Weight loss could be due to efavirenz. It can be also explained by the primary disease or concomitant opportunistic infections.

Lactic acidosis and proximal myopathy were also reported in our study. Lactic acidosis is one of the most serious presentations of Nucleoside analogue Reverse Transcriptase Inhibitor (NRTI) associated mitochondrial toxicity. Although this complication is rare, the associated mortality rate may be high. Lactic acidosis is one of the established adverse effects of stavudine [25, 26]. In our case it was only in one patient who had taken stavudine previously but now he was on AZT regimen. According to a study conducted by Agu *et al.* stavudine based regimens have lesser ADRs as compared to Zidovudine based regimen, commonest being peripheral neuropathy and skin rash [27].

Dyslipidemias were seen in a small number of patients in the present study. In contrast to the earlier reports[28], number of patients who had hypertriglyceridemia was more in males compared to females.

With regard to the level of education, 51.67% (n=120) patients were literate and 48.33% were illiterate and these finding were more or less similar to a study finding of Joshi *et al.;* [29]. Participants with educational status of preparatory school level were at less risk of ADRs compared to those who attained a primary school level of education. It may be inferred that higher educational level offered some protection of ADR due to proper understanding of ARV adherence.

Patients on ATT were at higher risk of developing adverse effects as compared to patients on co-trimoxazole. Such over lapping toxicities could be serious and challenging in the management of patients with TB-HIV co-infection. So in these cases IRIS was observed (1.06%).All cases were managed conservatively and ART was continued.

Our results were in agreement that associations do exist between various co-morbidities like diabetes mellitus, malaria, hypertension, anemia, asthma, epilepsy, TB and ADRs. There is the possibility that when these predictors present in a patient they might interact resulting in a reduced severity of a ADRs or amplify its effects.

Causality assessments, according to Naranjo's scale, revealed 37.24% ADRs were 'probable' and 62.76% were 'possible'. Most of the reported ADRs 11.6% were mild and 85.2% were moderate in nature while 4.2% was life threatening. This suggests good tolerance level to ARVs in general.

Lastly, in our study we found that ADRs to ART were 20.16% and most common ADRs was

anemia (16%).We are in strong agreement with existing literature and also we have conducted a systematic approach towards detection of early ADRs, an adequate adherence and complete laboratory investigations profile optimally.

CONCLUSION

Adverse drug reactions on HAART in HIV patients are common and show wide variations. HAART effectively restores the immune system and lowers the viral load in patients with HIV/AIDS. Thus, with the widespread introduction of highly active antiretroviral therapy (HAART), the pattern and prevalence drug reactions are different and expected to change. Although adverse reactions are common and often predictable, their management must be individualized. Several factors could affect the management of adverse reactions, including co-morbid conditions; the patient's other current medications, the availability of alternative regimens, and the patient's history of medication intolerance. The purpose of our study was to evaluate the HIV/AIDS patients who were on HAART for management of AIDS and to study the changing pattern of the various drug reactions in the HAART era.

Incidence of ADRs in our study was 20.16% (120/595). Of the 595 patients, only 120 patients were developed total 188 ADRs. In our study, most commonly reported ADRs were (15.95%) anemia, (8.51%) gastritis, (6.38%) rashes, (5.85%) nausea/vomiting, (5.31%) itching, (4.25%) leucopenia, (3.72%) macrocytosis and (3.19%) diarrhea. In this study maximum number of ADRs were due to Zidovudine + Lamivudine + Nevirapine (AZT+3TC+NVP) based regimen 52.65% and least were due to Tenofovir + Lamivudine + Atazanavir/ Ritonavir (TDF+3TC+ATV/r) based regimen 02.65%.

In this study, most of ADRs were possible (62.76%) and moderate (85.20%) in nature. Low level of education, drug abuse, associated co-morbidities and concomitant medication were risk factors for ADRs. Most of ADRs (86.18%) were developed first six month of initiation of HAART.

So careful implementation of protocols designed for regular screening of patients, especially during the initial months of therapy, may detect adverse reactions earlier and help prevent serious or life-threatening consequences. Early initiation of ART at CD4 levels higher than 200cells/cmm reduces mortality, immune-depression and also improve outcome of ART treatment. In addition, patients and/or supportive family members or adherence monitors can be educated about adverse effects and taught to recognize them for early management to be instituted.

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