ORIGINAL RESEARCH PAPER

Volume-8 | Issue-6 | June-2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY ON ADVERSE DRUG REACTIONS IN ANTIRETROVIRAL THERAPY RECIPIENTS ATTENDING ANTIRETROVIRAL CENTRE IN GOVERNMENT TERTIARY CARE HOSPITAL, HYDERABAD.

Pharmacology

Kotte Sumedha Final year MBBS, Osmania Medical College, Hyderabad, Telangana, India

Dr A B Suguna* MD., Associate Professor, Department of Pharmacology, Government Medical College, Nizamabad, Telangana, India *Corresponding Author

ABSTRACT

INTRODUCTION: Antiretroviral therapy(ART) is effective in decreasing AIDS related deaths but it is associated with many adverse drug reactions(ADRs) which are leading to non-adherence to treatment.

AIM: We sought to study ADRs, their variations with duration of treatment and also their causality and preventability.

METHODOLOGY: A retrospective study was done over a period of four months on 500 patients attending ART center at Government tertiary hospital, Hyderabad.

RESULTS: Out of 500 patients, 91% have experienced at least one type of ADR with majority affecting musculoskeletal system. A total of 1011 ADRs are reported by 455 patients. Females are found to be more susceptible to ADRs. According to causality and preventability scales, 76% of ADRs are probable and 27.2% are definitely preventable.

CONCLUSION: To improve ART medication compliance, active screening for ADRs and educating patients may help in their early detection and prevention.

KEYWORDS

Antiretroviral therapy(ART), Adverse drug reactions(ADRs), Acquired Immunodeficiency Syndrome(AIDS).

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS) remains the greatest public health concern in the world. Around 36.7 million people were living with HIV/AIDS on this planet out of which 2.1million were in India[1][2].HIV infection and AIDS are caused by human immunodeficiency virus which is a retrovirus. HIV causes initial acute viremia, infects T-lymphocytes which have CD4 markers on their cell surface, invades the cellular machinery and finally kills the T-lymphocytes. This multiplication of virus and decrease in CD4 cells progress to AIDS. It is difficult to eradicate HIV since virus becomes an integral part of the infected T cell. Thus, lifelong multidrug therapy is required for near complete suppression of HIV replication.

The introduction of antiretroviral therapy (ART) has changed the perspective of HIV infection from being a fatal disease to chronic manageable disease. An estimated 17 million people have access to these medicines at the end of 2015 and the world's most affected countries have reduced AIDS related deaths from 1.5 million in 2010 to 1.1 million in 2015[3]. ART has reduced the incidence of secondary infections, improved health and prolonged patient survival. Presently, there are five classes of drugs which act on different stages of HIV life cycle-Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs), Non-nucleoside reverse transcriptase inhibitors (NNRTIs), fusion inhibitors, integrase inhibitors and protease inhibitors. Usually combination of 3 or 4 drugs are given as treatment which constitutes Highly Active Anti Retroviral Therapy(HAART). Commonly used drugs are NRTIs like Zidovudine, Lamivudine, Tenofovir, Stavudine; NNRTIs like Efavirenz, Nevirapine; protease inhibitors like darunavir, Atazanavir and Ritronavir.

HAART has improved the prognosis of HIV infection/AIDS but at the same time posing clinical challenge with adverse drug reactions (ADRs)[4]. WHO defines adverse reaction as 'A response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for the modifications of physiological function[5]. ADRs may be caused either by the interaction of the drug with healthy cells or with virus or by the interaction with other drugs. The increased incidence of adverse drug reactions and drug toxicities are becoming one of the limiting factors for decreasing viral load as they are leading to non-adherence to treatment and also decreasing the quality of life of patients. Studies on incidence of ADR from developing and developed countries have reported incidence of ADR among patients on antiretrovirals ranging between 11% to 35.9%[6][7]. About 25% of all patients discontinue their initial ART regimens because of treatment failure, toxic effects or noncompliance[8]. ART causes short term, long term adverse reactions and toxicities. Common but mild adverse effects occurring early with most the antiretroviral regimens include cutaneous reactions, gastrointestinal effects such as bloating, nausea and diarrhea, which may be transient or may persist throughout therapy[9]. Other adverse effects include mitochondrial damage caused by NRTIs that can lead to hepatic steatosis, lactic acidosis, peripheral neuropathy and also causes anemia which is a major challenge in developing nations, NNRTIs which are mainly used in combination with NRTIs cause maculopapular rash, pruritis, fatal hepatotoxicity[10]. Adverse effects caused by other classes of drugs include allergic reactions, GI disturbances, nephrolithiasis and metabolic disorders like insulin resistance, hyperbilirubinemia, increased triglyceride and cholesterol levels[9]. Some adverse events are also caused by the interaction of NNRTIs and protease inhibitors with cytochrome P450 isoforms [11]. The severity of the adverse effects may vary with the type of regimen used for treatment, host genetics, diagnostic delays and opportunistic infections.

There is a gap in awareness and training about drug safety monitoring especially in the field of ART. Most of the time ADRs are not reported by the patients, because of misinterpretation as manifestations of disease itself. So monitoring ADRs is the call of hour for better surveillance on ADRs due to ART. So the present study is conducted to know the different types of ADRs, their variations with the duration of treatment and to assess their causality and preventability.

METHODOLOGY

STUDY DESIGN:

A retrospective hospital based observational study on Adverse Drug Reactions was conducted on 500 HIV infected patients receiving antiretroviral therapy using a pre-designed and pre-structured questionnaire at ART center of Government tertiary hospital located in Hyderabad for a period of four months. The data was collected through questionnaire and the follow up of patients was not done.

INCLUSION CRITERIA:

1. Patients between the ages 18 to 60 years who are antiretroviral therapy recipients at Government tertiary health care centre, Hyderabad are included.
2. Patients who have given consent.

EXCLUSION CRITERIA:

1. Patients below the age of 18 years and above 60 years are excluded.
2. Patients who are not willing to participate in the study.
3. Adverse drug reactions caused by non-antiretroviral drugs are excluded

DATA COLLECTION PROCEDURE:

The subjects for the study were selected from the patients attending the ART centre by using systemic random sampling technique i.e. every 5th patient(Based on ART center OP statistics) attending the ART on a

particular day were included in the study. The subjects were explained clearly about the study and the consent was obtained from the subjects who were willing to participate in the study by using a consent form. The subjects who have given their consent were educated about the adverse drug reactions, their manifestations and were encouraged to declare the adverse reactions suffered by them during the course of antiretroviral therapy and the data related to documented adverse reactions were also collected from their ART treatment books. This data was collected from the eligible subjects using a questionnaire. The data collected from the ART treatment books and the questionnaires include patient's socio-demographic details such as age; sex; occupation and clinical information such as personal history; family history; drug history; history of secondary infections associated with HIV infection; date of start of ART; ART regimen used for treatment; type of the adverse effects reported after the start of the ART regimen their onset, all the drugs received prior to the onset of reaction; Health care provider decision whether to change the regimen or not; drugs used to relieve the adverse effect. The adverse effects of ART drugs were recognized by the WHO definition for adverse reactions and were differentiated from those caused by other drugs by considering relevant details. Causality of ADRs was assessed by Naranjo's causality scale[19] and preventability was assessed by modified criteria of Schumock and Thornton's preventability scale[20].

DATA ANALYSIS:

The data collected from the ART books through questionnaire was entered in MS excel 2013 spreadsheet and analyzed.

ETHICAL CONSIDERATIONS:

The study was approved by the institutional main ethical committee. Informed consent was obtained from the patients who were included in the study through consent form.

RESULTS

The data was collected from 500 patients who are taking antiretroviral therapy. Out of the 500 patients, 455(91%) have suffered atleast one type of ADR during their course of treatment while 55 (9%) have never had an adverse drug reaction. Out of the 455 patients who presented with adverse drug reactions; 73(16%) patients are between the age group of 18 to 31 years, 262(57%) are between 32 to 45 years and 120(27%) are between 46 to 60 years and 197(43%) are males and 258(57%) are females.

Different treatment regimens used by patients included in the study are

- Zidovudine+Lamivudine+Nevirapine[ZLN]
- Tenofovir+Lamivudine+Efavirenz[TLE]
- Zidovudine+Lamivudine+Efavirenz[ZLE]
- Stavudine+Lamivudine+Nevirapine[SLN]
- Tenofovir+Lamivudine+Nevirapine[TLN]
- Didanosine+Lamivudine+Nevirapine[ddl/L/N]
- Zidovudine+Lamivudine[ZL]
- Virocomb+Efavirenz
- Zidovudine+Nevirapine[ZN]
- Tenofovir+Nevirapine[TN]
- Abacavir+Lamivudine+Lopinavir/Ritonavir[ABC/3TC/LPV/RTV]
- Zidovudine+Lamivudine+Lopinavir/Ritonavir[ZL/LPV/r] r=Ritonavir in small dose
- Tenofovir+Lamivudine+Atazanavir/Ritronavir[TL/ATV/RTV] Tenofovir+lamivudine+Lopinavir/Ritonavir [TL/LPV/r]
- Tenofovir+Lamivudine+Atazanavir[TL/ATV]
- Nevirapine[NVP]
- Zidovudine[AZT]

Table No. 1: Distribution of patients based on duration of treatment

Sl.No.	Duration	Male	Female	Total
1.	Less than 1 year	12(3%)	23(5%)	35(8%)
2.	1-5 years	80(18%)	121(27%)	201(44%)
3.	6-10 years	76(17%)	82(18%)	158(35%)
4.	11-15 years	27(6%)	24(5%)	51(11%)
5	16-20 years	2(0.4%)	8(1.6%)	10(2%)
Total		198	258	455

Observation: Out of the 455 patients, 8% have been under ART for less than one year, 44% - 1-5 years, 35% - between 6-10years,11% - between 11-15 years and 2% - between 16-20 years

Table No. 2: Distribution of the patients based on the regimens used for the treatment

Sl.No.	Regimen	Male	Female	Total
1.	ZLN	106(23%)	116(26%)	222(49%)
2.	TLE	79(17%)	119(26%)	198(43%)
3.	ZLE	8(2%)	13(2.85%)	21(5%)
4.	TL ATV/RTV	1(0.2%)	6(1.3%)	7(1.6%)
5.	TL RTV/LPV	2(0.4%)	1(0.2%)	3(0.6%)
6.	ZL	0	1(0.2%)	1(0.2%)
7.	NVP	0	1(0.2%)	1(0.2%)
8.	A L/L/R	0	1(0.2%)	1(0.2%)
9.	TL ATV	1(0.2%)	0	1(0.2%)
Total		**197**	**258**	**455**

Observation: The present regimens used by the patients who reported ADRs are ZLN(49%), TLE(43%), ZLE(5%), TL/ATV/ RTV(1.6%), TL/RTV/LPV(0.6%), ZL(0.2%), NVP(0.2%), ABC/3TC/LPV/ RTV (0.2%), TL/ATV(0.2%)

Table No. 3: Total number of reported adverse drug reactions

No of ADRs	Male	Female
1011	417(41%)	594(59%)

Observation: Total ADRs reported by the patients are 1011, Out of which 41% are reported by males and 59% are reported by females.

Table No. 4: Association of regimen with the percentage of ADRs

Sl. No.	Regimen	No of ADRs
1.	ZLN	456(45%)
2.	TLE	399(39%)
3.	ZLE	83(8%)
4.	SLN	13(3%)
5.	TL ATV/RTV	14(3%)
6.	TL RTV/LPV	8(2%)
7.	TLN	10(2%)
8.	ZL	6(1%)
9.	NVP	3(0.6%)
10.	TL ATV	4(0.8%)
11.	Virocomb, EFV	5(1%)
12.	ZN	1(0.2%)
13.	Virocomb, NVP	3(0.6%)
14.	AZT	2(0.4%)
15.	TN	1(0.2%)

Observation: Out of 1011 ADRs reported, more adverse reactions i.e;45% are due to ZLN, then 39% are due to TLE, 8% due to ZLE,3% are due to SLN,3% due to TL ATV/RTV,2% due to TL RTV/LPV and TLN,1 % due to ZLN,Virocomb/EFV;0.8% due to TL ATV;0.6% due to NVP, Virocomb/NVP;0.4% due to AZT;0.2% due to ZN, TN

Table No. 5: Percentage of ADRs reported in relation to duration of treatment

Sl.No.	Duration	ADRs
1.	Less than 1 year	219(22%)
2.	1-5 years	415(41%)
3.	6-10 years	274(27%)
4.	11-15 years	71(7%)
5.	16-20 years	32(3%)
Total		1011

Observation: Most of the patients who reported to have suffered from ADRs have been under ART for 1 to 5 years but more ADRs were reported in the first few months of initiation of their treatment.

Most commonly used regimen by the patients are ZLN, TLE and ZLE. These three regimens account for 93% of the reported ADRs.

Table No. 6: Percentage of ADRs reported by ZLN in relation to duration of treatment

Sl.No.	Duration	ADRs
1.	Less than 1 year	67(15%)
2.	1-5 years	138(30%)
3.	6-10 years	177(39%)
4.	11-15 years	52(11%)
5.	16-20 years	22(5%)
Total		456(100%)

Observation: Out of the 456 ADRs reported by ZLN regimen,15% were reported within 1 year of start of regimen;30% were between 1 to 5 years;39% were between 6 to 10 years;11% were between 11 to 15 years of treatment and 5% were between 16 to 20 years of treatment.

Table No. 7: Percentage of ADRs caused by TLE in relation to duration of treatment

Sl. No.	Duration	No. of ADRs
1.	Less than 1 year	105(26%)
2.	1-5 years	238(60%)
3.	6-10 years	51(13%)
4.	11-15 years	5(1%)
Total		399(100%)

Observation: Out of the 399 ADRs reported by patients TLE regimen, majority of ADRs i.e. 60% were during 1 to 5 years of treatment.

Table No. 8: Percentage of ADRs caused by ZLE in relation to duration of treatment

Sl. No.	Duration	No. of ADRs
1.	Less than 1 year	26(31%)
2.	1-5 years	25(30%)
3.	6-10 years	32(39%)
Total		83(100%)

Observation: Out of 83 ADRs reported by patients on ZLE regimen, majority of ADRs were noted during 6 to 10 years of treatment.

Table No. 9: Organ systems involved in different types of adverse drug reactions and their incidence

System involved	ADRs	Frequency (%)
Skin and its appendages (10.1%)	Rashes with itching	59(6%)
	Hyperpigmented macules	3(0.3%)
	Erythematous rash	2(0.2%)
	Papular itchy rash in seborrheic areas	1(0.1%)
	Photosensitive lichenoid eruption	1(0.1%)
	Hyperkeratotic papules	1(0.1%)
	Acne	3(0.3%)
	Pigmentation of skin	15(1.5%)
	Pigmentation of nails	2(0.2%)
	Pruritis	6(0.6%)
	Hair fall	2(0.2%)
	Profuse sweating	4(0.4%)
	Skin-dryness	1(0.1%)
GIT (17.1%)	Dryness of mouth	3(0.3%)
	Acidity	36(4%)
	Gastritis	3(0.3%)
	Nausea	29(3%)
	Vomiting	47(5%)
	Diarrhea	16(2%)
	Constipation	5(0.5%)
	Flatulence	4(0.4%)
	Dysphagia	4(0.4%)
	Pancreatitis	1(0.1%)
	(increased serum amylase levels)	7(0.7%)
	Jaundice	
	Mild splenomegaly	1(0.1%)
Respiratory (1.3%)	Dyspnea	10(1%)
	Chest pain	3(0.3%)
CVS (1.5%)	Hypotension	3(0.3%)
	Hypertension	10(1%)
	Pedal edema	2(0.2%)
Blood (4%)	Anemia	40(4%)
Genitourinary (1.5%)	Burning micturition	10(1%)
	Polyuria	1(0.1%)
	Urinary incontinence	1(0.1%)
	Renal calculi	2(0.2%)
	Cystitis	1(0.1%)
Endocrine (2.4%)	Irregular menstrual cycles	11(1%)
	Menorrhagia	3(0.3%)
	Increased blood sugar levels	8(1%)
	Gynecomastia	1(0.1%)
Central Nervous System (8.1%)	Peripheral neuropathy	3(0.3%)
	Altered sensorium	1(0.1%)
	Numbness of limbs	66(6.5%)
	Tingling sensation of limbs	2(0.2%)
	Paresthesia	4(0.4%)
	Resting tremors	1(0.1%)
	Hallucinations	1(0.1%)
	Irritability	3(0.3%)
	Neurofibroma	1(0.1%)
MusculoSkeletal system (24.4%)	Joint pains	62(6%)
	Pain in limbs	76(7.5%)
	Fatigue	66(6.5%)
	Myalgia	2(0.2%)
	Back pain	21(2%)
	Pain in the neck muscles	11(1%)
	Cervical Spondylosis	2(0.2%)
	Swelling of legs	6(0.6%)
	Difficulty in walking	2(0.2%)
	Osteoporosis	1(0.1%)
	Ganglion on hand	1(0.1%)
Adipose tissue (7.1%)	Swelling on the back(buffalo hump)	12(1%)
	Facial lipoatrophy	39(4%)
	Lipodystrophy	20(2%)
	Increase in triglyceride levels	1(0.1%)
Sensory system (2.7%)	Decreased vision	13(1%)
	Impaired hearing	3(0.3%)
	Tinnitus	1(0.1%)
	Itching of eyes with lacrimation	5(0.5%)
	Burning sensation of feet	6(0.6%)
	Loss of vision of one eye	2(0.2%)
Others (21.9%)	Body pains	17(2%)
	Loss of appetite	33(3%)
	Increase in appetite	2(0.2%)
	Malaise	1(0.1%)
	Headache	58(6%)
	Disturbed sleep patterns	41 (4%)
	Dizziness	59(6%)
	Swelling of jaw	5(0.5%)

Table No. 10: Causality assessment of adverse drug reactions

Causality Assessment	No of ADRs
Possible ADRs	768(76%)
Probable ADRs	243(24%)

Observation: Causality of the ADRs is assessed by Naranjo's causality scale. According to that scale 76% of ADRs are possible and 24% are probable ADRs.

Table No. 11: Preventability assessment of adverse drug reactions

Preventability	ADRs
Definitely preventable	275(27.2%)
Probably preventable	324(32%)
Not preventable	412(40.8%)

Observation: Preventability was assessed by Schumonk and Thornton preventability scale. According to that scale 27.2% of ADRs are Definitely preventable, 32% Probably preventable, 40.8% Not preventable

DISCUSSION

An observational study was conducted on 500 patients attending the Antiretroviral Therapy Center (ART) in Hyderabad to know the adverse drug reactions caused by antiretroviral therapy. ART has emerged as a ray of hope to the patients living with HIV infection and AIDS, many new drugs are being discovered which are increasing the life expectancy of the HIV infected patients but at the same time it is accompanied by marked increase in short term and long term adverse events which range from mild to life threatening effects.

This study was done on 500 patients, out of them 91% have suffered from atleast one type of adverse drug reaction. This is in line with the study conducted in India[12], where 90.6% of population experienced ADRs and it is high when compared to a study done in Ethiopia[21] which showed that 70.8% of patients suffered with ADRs. This may be because the study in Ethiopia considered the data from the patients who have been under ART since 3 years and this difference may also be

due to regional pharmacogenetic variations. Further, 1011 ADRs are reported by 455 patients. This is in line with 454 ADRs experienced by 217 patients in a study conducted in South Africa[22] and is less when compared to 618 ADRs reported by 213 patients in other study conducted by Manish Nagpal, Vandana Tayal, Suresh kumar and Usha Gupta[12]

In this study, majority of the patients who reported ADRs belonged to age group 32-45 years as they constituted the major subject group on random selection. A study conducted in South Africa[22] showed that more ADRs were in patients above 31 years. Further, this study observed that females are more susceptible to ADRs than males. This is in line with the study in Kenya[23] and by Patel NM[17] which revealed that 68% of ADRs are found in women and is in contrast to the study conducted in India by Kumar[16] which showed that 53% of total ADRs are reported by males.

Among the 1011 ADRs, 45% are caused by ZLN regimen as this regimen is commonly used by patients who were included in the study, but more ADRs are reported by patients using ZLE regimen (83 ADRs are reported by 21 patients on ZLE). This is in contrast to the study in Ethiopia which showed that more ADRs are caused by SLN[21] and other study in Nigeria[24] found that TLE caused more ADRs, this difference arised since SLN and TLE are more commonly prescribed in Ethiopian and Nigerian studies respectively.

In this study, about 41% of ADRs are observed in the patients who have been using ART since 1 to 5 years as they constitute the majority of patients included in study under random selection, relatively more ADRs are observed to occur in the first year of commencement of treatment i.e. about 22% of ADRs. Patients who have been using ART for many years have reportedly suffered from various ADRs during the first year of ART and these ADRs are playing decisive role for the adherence to regimens. This is a similar finding with the study conducted by Rajesh[18] which showed that 91% of ADRs are caused within one year of treatment; other study conducted in Kenya[23] also showed that more ADRs are caused during first year of treatment and other study conducted by Eluwa et al.[15] also showed that most of the ADRs occurred within 12 to 24 months of treatment and there are no studies till date which showed the occurrence of ADRs within 6 to 20 years of use of ART and their association with different regimens. In this study 27% of ADRs occurred within 6-10 years; 7% within 11-15 years of treatment and 3% within 16-20 years of treatment. This difference is because of the short term and long term ADRs caused by the regimens. Long terms effects are due to the toxic accumulation of drug in the body.

Most commonly used regimens in the study are ZLN, TLE and ZLE. There is difference in the occurrence of ADRs in the course of treatment. Majority of ADRs caused by ZLN & ZLE regimen are within 6 to 10 years of treatment and by TLE regimen is within 1 to 5 years. For all the regimens, the early adverse events are rashes, pruritis, nausea, vomiting with abdominal pain. TLE and ZLN caused dysphagia in two patients within 2 months of starting the regimen. Other early adverse effects are pigmentation of skin, loss of appetite, disturbed sleep patterns. It is observed ZLN caused dryness of mouth, anemia, blurred vision, neuropathy, improper digestion, burning micturition, facial lipoatrophy, lump at the back, lipodystrophic syndrome after one year of treatment. And one reported renal calculi after a year of starting the regimen. Irregular menstrual cycles, altered sensorium, numbness of limbs, myalgia, joint pains, changes in blood sugar level and blood pressure levels are noted after 6 years of use of ZLN. Tinnitus, impaired hearing was reported by 2 patients using ZLN regimen and patient was diagnosed with mild splenomegaly after 10 years of treatment. Gynecomastia was found to be caused by Nevirapine based regimens. Adverse reactions caused by TLE within one year of treatment are peripheral neuropathy, acute pancreatitis, swelling on neck, hair loss, swelling and stiffness of joints, weight loss, dizziness, pigmentation of skin, paresthesia and some neuropsychiatric problems like anxiety, hallucinations. One patient reported neurofibroma, irritability after one year of start of TLE regimen. Peripheral neuropathy progressing to difficulty in walking and facial lipoatrophy is observed as the long-term side effects caused by this regimen. As other regimens, ZLE caused nodules on skin with itching as an early adverse reaction. Peripheral neuropathy, facial lipoatrophy and anemia are observed after two years of regimen. Resting tremors is reported as a long-term side effect observed after 6 years of initiation of treatment with ZLE and TLN. Anemia is also caused by SLN, ZN, ZE regimens. Peripheral neuropathy is caused by SLN, ddl/L/N. Resting tremors, dizziness are also caused by TLN. Polyarthralgia, urinary incontinence is reported in patients using second line regimens. Mild adverse reactions like fatigue, joint pains, dizziness, pain in neck muscles, pain in limbs and generalized weakness with back pain and headache are caused by almost every regimen but the onset of these varied with the duration of start of treatment.

It was observed from patients ART books that dechallenging was done for 98 patients (21%) because of the occurrence of severe adverse reactions. This is high when compared to the study by Nagpal[12] where dechallenging was done in 17.4% of patients. Further in this study more ADRs are seen to effect musculoskeletal system i.e.; 24.4% of ADRs, next gastrointestinal disorders this is in contrast with other the study conducted in India[18] which showed that more ADRs are hematological and other study conducted by Shet et al.[13] and Nagpal et al.[12] found that majority of ADRs belong to gastrointestinal tract. This difference is because long term adverse effects up to 15 to 20 years were not considered in those studies. The most common ADRs found in this study are mild events like headache, pain in the limbs, Numbness of limbs, joint pains and rashes. Anemia accounts for 4% of the total ADRs.

Causality of the ADRs is assessed by Naranjo's causality scale. It is found that 76% of ADRs are possible and 24% are probable ADRs. This is in line with the study conducted in Guwahati, India[25] where majority(63.75%) ADRs are possible and in the other study conducted by Kumar, Majhee and Gari[14] ,revealed that 86.80% possible, 9.64% probable and 1.52% definite, but this is contrast to the study conducted by Rajesh et al.[18] which showed that majority (63.5%) of ADRs are probable.

Preventability of ADRs is assessed by Schumonk and Thornton preventability scale. It is observed that 27.2% of ADRs are definitely preventable,32% probably preventable and 40.8% not preventable This is nearly in line with the study conducted by Bhuvana[26] where only 41.2% of ADRs are not preventable and with other study by Kumar[16] revealed that 21.82% ADRs were definitely preventable, 37.06% probably preventable, and 41.12% not preventable.

CONCLUSION

Adverse drug reactions are found to be very high among the patients undergoing antiretroviral therapy, 91% of the sample has experienced at least one adverse drug reaction during the course of treatment. Multiple adverse reactions are reported, most of them caused mild to moderate manifestations but a few are life-threatening. Most of the ADRs are leading to decreased adherence to treatment so active screening for the ADRs at ART centers along with proper counseling of patients regarding effects of ADRs and also educating patients about ADRs will help in the early detection of the adverse reactions which in turn can significantly improve the quality of life among the ART recipients. The antiretroviral therapy involving the combination of 3 or 4 drugs which can cause severe adverse drug reactions is the only currently available effective treatment to improve the life span of HIV infected persons, so there is need for clinical research to develop efficient medications with less adverse drug reactions.

REFERENCES

1. UNAIDS (20170. Fact sheet–Latest statistics on the status of the AIDS epidemic - UNAIDS. www.unaids.org. Archived from the original on July 13, 2017. Retrieved July 21, 2017.
2. NACO (2015). Annual report 2015-16.
3. Joint United Nations Programme on HIV/AIDS (2016). AIDS scorecards: overview: UNAIDS report on the global AIDS update 2016.UNAIDS.
4. Sanjay Fotedar [et al.] (2016). Adverse drug reactions of antiretroviral therapy(ART) in people living with HIV/AIDS (PLHI). International Journal of Current Research 8 (09), pp. 38217-38221.
5. WHO (1972). International drug monitoring: The role of national centers. Report of a WHO meeting. World Health Organ Tech Rep Ser. - 1972, pp. 498;1-25.
6. Patrice , S [et al.] (2010). Early versus standard antiretroviral therapy for HIV infected adults in Haiti. N Engl J Med-2010, pp. 363, 257-265.
7. Bonfanti, P [et al.] (2000). Incidence of adverse reactions in HIV patients treated with protease inhibitors: a cohort study. JAIDS 23, pp. 236-245.
8. Crun, N F [et al.] (2006). Comparisons of causes of death and mortality rates among HIV-Infected persons: Analysis of the pre early and late HAART eras. J Acquir Immune Defic Syndr 41, pp. 194-200.
9. Carr, A and Cooper, D.A. (2000). Adverse effects of antiretroviral therapy. Lancet 356, pp. 1423- 30.
10. Rita Kumari [et al.] (2017). An assessment of adverse drug reaction patterns among HIV positive patients receiving antiretroviral therapy. International Journal of Pharmacological Research 7 (04), pp. 88-93.
11. Hardman, Joel H and Limbird, Lee E (2001). The pharmacological basis of therapeutics. In. Stephen Raffanti, David W Haas. Goodman and Gilman's. Antiretroviral agents

(10th Ed.). McGrawHil, pp. 1349-1373.
12. Nagpal, M; Tayal, V; Kumar, S and Gupta, U (2010). Adverse drug reactions to antiretroviral therapy in aids patients at a tertiary care hospital in India: A prospective observational study. Indian J Med Sci. 64, pp. 245-52.
13. Shet, A; Antony, J; Arumugam, K; Kumar, Dodderi S; Rodrigues, R and DeCosta, A (2014). Influence of Adverse Drug Reactions on Treatment Success: Prospective Cohort Analysis of HIV-Infected Individuals Initiating First-Line Antiretroviral Therapy in India. PLoS ONE9(3), e91028.
14. Oumar, A [et al.] (2017).Adverse Drug Reactions to Antiretroviral Therapy (ART):Prospective Study in HIV Infected Adults in Sikasso (Mali). J Pharmacovigil 5, p. 228. doi:10.4172/2329-6887.1000228.
15. Eluwa [et al.] (2012). Adverse drug reactions to antiretroviral therapy (ARVs): incidence, type and risk factors in Nigeria. BMC Clinical Pharmacology 12, p.7.
16. Kumar, A; Majhee, L and Gari, M. (2017). Causality, severity and preventability assessment of adverse drug reactions in patients received anti-retroviral therapy in a tertiary care hospital: A retrospective study. Natl J Physiol Pharm Pharmacol 7(2), pp. 178-182.
17. Patel, N M; Vaniya, H V, Agrawal, J M; Balat, J D; Singh, A P and Trivedi, H R (2015). Adverse drug reaction monitoring on antiretroviral therapy in human immunodeficiency virus patients in a tertiary care hospital. Int J Basic Clin Pharmacol 4, pp. 907-11.
18. Rajesh, R [et al.] (2014). Evaluating the effects of combination antiretroviral therapy regimens and the development of adverse drug reactions in Indian human immunodeficiency virus positive patients. Saudi J Health Sci 3, pp.107-17.
19. Naranjo, CA [et al.] (1981). A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 30(2), pp. 239-45.
20. Schumock, G T and Thornton, J P (1992). Focusing on the preventability of adverse drug reactions. Hosp Pharm. 27(6), p. 538.
21. Ramanjireddy, Tatiparthi and Yitagesu, Mamo (2014). Prevalence of ADRs and Associated factors of antiretroviral therapy on HIV positive adults at Jush. Indian Journal of Pharmacy Practice 7 (4).
22. Masenyetse, Lieketseng J ; Manda, Samuel O M and Mwambi, Henry G.(2015). An assessment of adverse drug reactions among HIV positive patients receiving antiretroviral treatment in South Africa. AIDS Research and Therapy 12, p. 6.
23. Nderitu, F. W.; Gikonyo, N.K. and K.A. Sinei, K.A. (2013). Detection and management of adverse drug reactions related to antiretroviral drugs among HIV/AIDS patients in Kiambu Sub-Country,Kenya. East Cent. Afr. J. Pharm. Sci. 16.
24. Agu, KA; Oparah, AC and Ochei, U M (2012). Improving Monitoring and Reporting of Adverse Drug Reactions (ADRs) in HIV positive patients on Antiretroviral Therapy (ART) in Nigeria. J Basic Clin Pharm. 3(2), pp. 299–313.
25. Kiran Reddy ,A V; Lihite, Ratan J.; Lahkar, Mangala; Urmi Choudhury and Baruah, Swaroop K. (2013). A study on adverse drug reactions in hiv infected patients at a art centre of tertiary care hospital in Guwahati, India. Asian J Pharm Clin Res 6 (Suppl 2), pp. 100-102.
26. Bhuvana, K.B, Hema, N. G. and Sangeetha (2014). A prospective observational study of adverse drug reactions to antiretroviral therapy: type and risk factors in a tertiary care teaching hospital. Int J Basic Clin Pharmacol. 3(2), pp. 380-384.