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Incidence and comparative analysis of adverse drug reactions in antiretroviral therapy (highly active antiretroviral therapy, HAART)

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ABSTRACT

The use of antiretroviral therapy especially use of Highly Active Antiretroviral Therapy (HAART) for HIV/AIDS patients has changed the treatment approach. The use of such therapy causes a reduction in mortality. The purpose of this study was to evaluate the adverse effects of Antiretroviral Therapy (ART) in HIV patients.

Methods

Previously reported papers related to adverse drug reactions caused by Antiretroviral Therapy during 2003 to 2017 were searched from following referred internet sources. We shortlisted 13 articles from referred sources. The evaluation of all 13 articles had been done accurately and thoroughly. The incidence of each type of adverse drug reaction (ADR) from entire reported ADRs was analyzed.

Result

A large number of ADRs (3930) were found in 2495 patients (41.52%). The large cases of ADRs (892)were related to Miscellaneous typed which include fever, change in taste, lipodystrophy, weight loss, lactic acidosis, hepatotoxicity, blurred vision and adverse effects associated with metabolic changes. The ADRs reported for Gastrointestinal System were found to be 804.Other includes ADRs related to nervous system 686, skin and subcutaneous tissues 831, and musculoskeletal system 269.

Conclusion

Various types of adverse drug reactions were observed in the current study. Adverse drug reactions are quite predictable and common but their management must be individualized. Reduction in ADRs is possible by educating the patients regarding drug toxicity and efficient Pharmacovigilance strategy.

Keywords: ADRs, Antiretroviral Therapy, Adverse reactions to antiretroviral therapy, HIV.

INTRODUCTION

HIV-1 belongs to the retrovirus family [1]. The statistical report at the end of 2016, said that 36.7 million [30.8–42.9 million] people were living with HIV and 35 million people have died with HIV, globally. The study showed that 0.8% of adults

aged 15-49 years found to be living with HIV. Sub-Sahara Africa region is the most affected with HIV (1 in every 25 adults). In 2016, 1 million people died because of AIDS-related illnesses. The vast majority of people living with HIV are located in low- and middle- income countries [2]. Food and Drug Administration (FDA)-approved more than 25 antiretroviral drugs in six classes for the treatment of HIV-infection [3]. These six classes are the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), a fusion inhibitor (FI), a CCR5 antagonist, and Integrase strand transfer inhibitors (INSTIs) [4]. Highly active antiretroviral therapy (HAART) is the current standard of care for HIV infection. The Resistance of HIV to Antiretroviral Drugs (ARV) is one of the most common causes for therapeutic failure in people infected with HIV [1]. Clinicians know the fact that adverse drug reactions are able to impart burden on healthcare systems. The combination of drugs is used for a very long time which likely to give ADRs (Adverse drug reactions). The identification of ADR profile of the drug is useful for early detection & proper management of ADRs. There is need to monitor ADRs occurred during Antiretroviral treatment in HIV patients [5, 20-22]. Objective of our study is to evaluate incidence & pattern of ADRs in HIV/AIDS patients undergoing antiretroviral treatment specially HAART (HIGHLY ACTIVE ANTIRETROVIRAL THERAPY).

MATERIAL AND METHODS

Previously reported papers related to adverse drug reactions caused by Antiretroviral Therapy during 2003 to 2017 were searched from following referred internet sources. As per the study concerned, we searched 50 articles from various sources like online journals and databases like science direct, Scopus, etc. We shortlisted 13 articles from following referred sources and informed all authors via emails. We got permissions from them for usage of data. The evaluation of all 13 articles was done accurately and thoroughly.

The observed cases of patients with at least one type of ADR were mentioned in the table. We studied the total number of ADRs reported among the 41.52% (2495/6008) reported population. We classified the adverse drug reactions in various sections which are as follows:-

Such as Gastrointestinal system covers Diarrhea, abdominal pain, constipation, Loss Appetite, dry mouth, heartburn, Nausea, vomiting, and others ADRs. Nervous system related ADRs covers Peripheral Neuropathy, and Others e.g. Insomnia, Dizziness, Headache. Skin and subcutaneous tissues system covers e.g. Allergy, nail hyperpigmentation, rash, itching, pruritis, etc. Musculoskeletal system covers ADRs like Muscle Fatigue, Body ache, Pain in legs, weakness, etc.

Hematological system & cardiovascular systems covers ADRs like Neutropenia, Thrombocytopenia, Anemia, etc. Miscellaneous section covers ADRs like fever, Loss of smelling sensation, hearing impairment, Irregular menstrual cycle, change in taste, Hepatic: elevated liver enzymes, lactatemia, lipidostropy, hepatotoxicity, and blurred vision. In this way, the incidence rate of each type of ADRs related to ARV treatment from entire ADRs reported was analyzed and compared (Table No.:1, 2).

Table No.:1 DATA SOURCES [7-19]

Sr. No.	Country/region in which study carried out.	Total No. Of patients Registered/undergoes study(one regimen based or multi-regimen based)	Actual Number of patients with At least one type of Severe Adverse Drug Reactions/Adverse events.	No. of ADRs reported in studies
1.	Eastern India	242	45	45
2.	Manipal (India)	130	57	74
3.	Maharashtra (India)	151	109	132
4.	Delhi ,India	235	213	618
5.	Karnataka ,India	50	32	32
6.	Mangalore ,India	327	43	53

7.	Guwahati ,India	300	93	160
8.	Eastern India	610	198	330
9.	Mumbai, India	1844	222	228
10.	Philippine	59	12	12
11.	Penang ,Malaysia	743	314	425
12.	Nigeria	1237	1119	1679
13.	Lagos ,Nigeria	80	38	142
		Total No. of patients undergoes treatment/registered=**6008**	Total No. of patients with at least one type of ADR=**2495**	Total No. of ADRs occurred=**3930**

RESULTS

According to study, the total 6008 patients were registered for ARV (Antiretroviral) treatment. The total of 2495 patients from 13 studies was analyzed. We found that 2495 patients showed at least one type of ADR (Adverse drug reactions) (Table No.:2).A large number of ADRs (3930) were found in 2495 patients (41.52%). The cases of ADRs associated with Hematological system & cardiovascular systems were found to be 448. The large cases of ADRs (892)were related to Miscellaneous typed which include fever, change in taste, lipodystrophy, weight loss, lactic acidosis, hepatotoxicity, blurred vision and adverse effects associated with metabolic changes. The ADRs reported for Gastrointestinal System were found to be 804.Other includes ADRs related to nervous system 686, skin and subcutaneous tissues 831, and musculoskeletal system 269.(Table No.:3, Fig No.: 2).

Table No: 2 Incidence rate of ADR in ARV Treatment [6-18]

Total No. of patients	Total No. of patients with at least one type of ADR	Percentage (%)
6008	2495	41.52

ARV=Antiretroviral

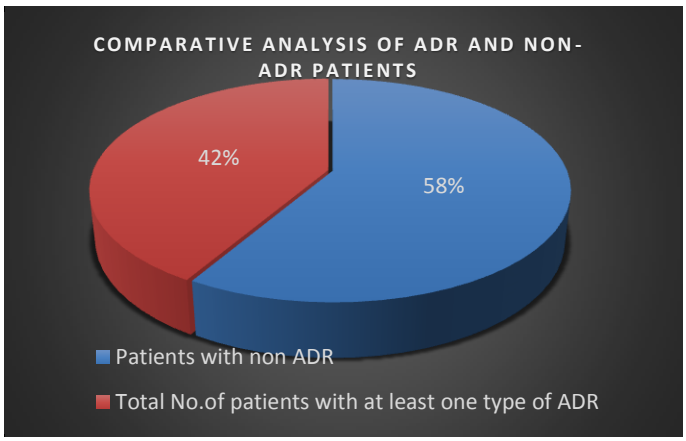

Fig No.:1 Comparative analysis of patients with ADRs and Non -ADRs. [6-18]

Table No: 3 Classification of ADRs [7-19]

Segment of ADR	**No. of ADRs reported (N=3930)**
Nausea, Vomiting, diarrhea, flatulence, dry mouth (Gastrointestinal System)	804
Peripheral Neuropathy and Others e.g. Insomnia, Dizziness, Headache (Nervous System)	686

skin and subcutaneous tissues- e.g. Allergy, pruritis ,etc.	831
musculoskeletal system- muscular weakness, etc.	269
Hematological system & cardiovascular systems- Anemia, etc.	448
Miscellaneous (fever, change in taste, lipidostropy)	892

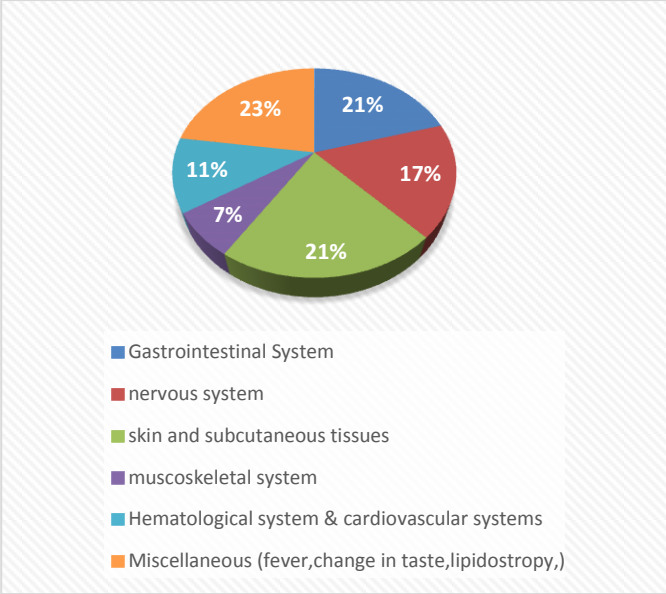

Fig No.2: ADR distribution in Antiretroviral Therapy According to study [7-19]

DISCUSSION

According to study, total 6008 patients were studied [6-18]. Total 2495 patients show at least one type of ADR. Antiretroviral drugs are having low safety profile. The ADRs related to Hematological system (11.39%) & Gastrointestinal system (21%) were found to be common. As the females are having low body weight, small body size & passes through different phases like pregnancy, menstruation phases; they were found to have large No. of ADRs. The Changes in the drugs regimen were likely to found increase in the ADRs. We found that majority of patients were treated with triple regimen which includes two NRTIs (Nucleoside Reverse Transcriptase Inhibitors) and one NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitors) or PIs(Protease Inhibitors).

AZT (zidovudine) +3TC (Lamivudine) +EFV (Efavirenz) was most common regimen. In some study, we observed that the drugs like Ritonavir, Indinavir, Saquinavir or Lopinavir were part of quadruple regimen. The hepatotoxicity found to be associated with the use of 3TC and AZT. It was also found to be common with NNRTIs. Diarrhoea was found to be linked with use of PIs. Dermatological reactions were found to be linked with use of common regimen (AZT+3TC+EFV/ NVP (NEVIRAPINE)).AZT treated patients were linked with hematological ADRs. Among hematological ADRs, anemia (Hb<7g/dl) was found to be common. We found that treatment with AZT+3TC+EFV was associated with low blood cell count. The treatment with Stavudine was reported for ADRs related to skin and skin rashes. ADRs related to nervous system were linked with use of NVP. All NNRTIs and PIs treated patients was reported for hypersensitivity and cutaneous reactions. PIs were found to cause lipodystrophy. Other drugs with ADRs, we found are- Ritonavir (hematological ADRs), Nelfinavir (utricaria), AZT(nail hyperpigmentation, hypertrichosis, Anemia, headache, myopathy, fatigue dermatological ADRs), 3TC(dermatitis), NVP (Stevens-Johnson Syndrome ,hepatotoxicity),

Stavudine (peripheral neuropathy), EFV(neuronal, hepatotoxicity, skin rash).The ADRs are avoided by rapid detection and changing drug regimen used for treatment. The study showed that there is need to monitor Antiretroviral treatment especially HAART for detection of ADRs. Proper and effective Pharmacovigilance system for ADRs can improve patients cure rate as well as patient's compliance. The patient counselling by pharmacist definitely help to reduce the incidence of ADRs.

CONCLUSION

Various types of adverse drug reactions were observed in the current study. Adverse drug reactions are quite predictable and common but their management must be individualized. Several factor will affect the management of adverse reactions. These factors are comorbid conditions, the availability of alternative regimens, the patient's other current medications, and the patient's medical history. The Antiretroviral therapy in HIV patients needs to be monitored in order to prevent Severe ADRs like hematological reactions and ultimately death of the patient. The Pharmacist has a key role in the management of adverse drug reactions. The efficient Pharmacovigilance programs will ultimately reduce the extent of ADRs in patients and provide a better quality of life.

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REFERENCES

[1]. Suraj Narayan Mali et al. HIV Drug Resistance: An Overview. International Journal of research methodology. 1(1), 2015, 72-82.

[2]. Available from: [https://www.avert.org/global-hiv-and-aids-statistics] on 02/11/2017.

[3]. Available from: [https://emedicine.medscape.com/article/1533218-overview] on 02/11/2017.

[4]. Available from: [https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/11/what-to-start] on 02/11/2017.

[5]. Languluri Reddenna et al. Highly Active Antiretroviral Therapy: Incidence of Adverse Drug Reactions. International Journal of Allied Medical Sciences and Clinical Research, 1(1), 2013, 25-30.

[6]. K.D.Tripathi: Essentials of Medicinal Pharmacology by Jaypee Brothers Medical Publishers,India, 2007.

[7]. Era N, Mukherjee S, Saha B, Tripathi SK. Monitoring cutaneous adverse drug reactions in patients on TDF+3TC+EFV: a single centre experience. International Journal of Basic & Clinical Pharmacology. 6, 2017, 1467-71.

[8]. Rajesh R, Vidyasagar S, Nandakumar K. Highly active antiretroviral therapy induced adverse drug reactions in Indian human immunodeficiency virus positive patients. Pharmacy Practice (Internet) 9(1), 2011, 48-55.

[9]. Patil PT, Pawar MP, Halasawadekar NR, Shinde MP, Kumbhar AV, Rathod MS. Current pattern of adverse drug reactions to anti-retroviral therapy in an antiretroviral therapy centre attached to a government medical college of Maharashtra, India: a retrospective study. International Journal of Basic &Clinical Pharmacology, 5, 2016, 2438-43.

[10]. Nagpal M, Tayal V, Kumar S, Gupta V.,Adverse drug reactions to antiretroviral therapy in aids patients at a tertiary care hospital in India: A prospective observational study.Indian Journal of Medical Sciences, 64, 2010, 245-52.

[11]. Rajesh R, Sudha V, Varma DM, Soika S.Association between medication adherence outcomes and adverse reactions to highly active antiretroviral therapy in India human immunodeficiency virus positive patients, J Young Pharmacist 4, 2012, 250-60

[12]. Jha AK, Gadgade A, Shenoy AK, Chowta MN, Ramapuram JT. Evaluation of adverse drug reactions in HIV positive patients in a tertiary care hospital. Perspectives in Clinical Research . January-March 6, 2015, 34-8.

[13]. LIHITE RJ et al., A study on adverse drug reactions in hiv infected patients at haart centre of tertiary care hospital in Guwahati, India, Asian Journal of Pharmaceutical and Clinical Research, 6(2), 2013, 102-104.

[14]. Mukherjee S, Era N,Saha B, Tripathi SK. Adverse drug reaction monitoring in patients on antiretroviral therapy in a tertiary care hospital in Eastern India. Indian Journal of Pharmacology, 49, 2017, 223-8.

[15]. Anwikar, S. R., et al. HAART induced adverse drug reactions: a retrospective analysis at a tertiary referral health care center in India. International Journal of Risk & Safety in Medicine 23(3), 2011, 163-169.

[16]. Roman, Arthur Dessi & Leyritana, Katerina & Tenorio, Allan & Lim, Jodor..High Rates of Adverse Drug Reactions to Nevirapine in Filipino HIV Patients, 428, 2011. Available from- [https://www.researchgate.net/publication/267912288_High_Rates_of_Adverse_Drug_Reactions_to_Nevirapine_in_Filipino_HIV_Patients]

[17]. Khan, K., Khan, A. H., Sulaiman, S. A., Soo, C. T., & Akhtar, A. Adverse drug reactions in HIV/AIDS patients at a tertiary care hospital in Penang, Malaysia ,Japanese journal of infectious diseases, 69(1), 2016, 56-59.

[18]. Agu, Kenneth A., and Azuka C. Oparah. Adverse drug reactions to antiretroviral therapy: Results from spontaneous reporting system in Nigeria. Perspectives in clinical research 4(2), 2013, 117.

[19]. Oshikoya K. A., et al. "Adverse events in HIV-infected children on antiretroviral therapy at a teaching hospital in Lagos, Nigeria: a retrospective study." Advances in Pharmacoepidemiology &Drug Safety, 1(4), 2012, 1000117.

[20]. Max B, Sherer R. Management of the adverse effects of antiretroviral therapy and medication adherence. Clinical Infectious Diseases. 30(2), 2000, S96-116.

[21]. Divakar B, Mistry SD, Kantharia ND, Mamtarani. The study of adverse drug reactions (ADR's) in HIV patients taking highly active antiretroviral therapy in ART centre, NCH, Surat, India. International Journal of Medical and Pharmaceutical Sciences. 03, 2012, 9-18.

[22]. Patel NM, Vaniya HV, Agrawal JM, Balat JD, Singh AP, Trivedi HR. Adverse drug reaction monitoring on antiretroviral therapy in human immunodeficiency virus patients in a tertiary care hospital. International Journal of Basic & Clinical Pharmacology. 4, 2015, 907-11.

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