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Research article

DETECTING ADVERSE DRUG REACTIONS IN HOSPITALIZED HIV/AIDS PATIENTS USING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

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ABSTRACT

Background: An estimated 33 million people are living with human immunodeficiency virus (HIV) and around 3 million people have access to highly active antiretroviral therapy (HAART) worldwide. The introduction of HAART has led to a significant reduction in AIDS-related to the morbidity and mortality. Like most medicines, antiretroviral drugs can cause side effects, but are often mild & sometimes they are more serious and can have a major impact on health or quality of life. To evaluate this study is undertaken. Methodology: This study was conducted based on the review of clinical records of adult patients obtained from the ART center. Any selected adult patient on ART who fulfilled the inclusion criteria of study subject was enrolled. Results: In the study 64.78 % of patients showed at least 1 ADR and Skin rash and anemia complaints and in other patients, ADRs were moderate and need just symptomatic treatment. Conclusion: To optimize adherence, physicians must focus on early detection and prevention of ADRs, when possible and distinguishing those that are self-limited from those that are potentially serious. Our study finding showed that there is a need for active Pharmacovigilance with intensive monitoring for ADRs by treating Physician and Pharmacist in Indian HIV patients on HAART who are illiterate, with CD4 count ≤250 cells/mm^3 with co-morbid conditions.

Key Words:- Human immunodeficiency virus (HIV), Highly active antiretroviral therapy (HAART), Adverse drug reactions.

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INTRODUCTION

Most of the people are suffering from various diseases in the day to day life worldwide, but an estimated 33 million people are suffering from HIV with Human Immunodeficiency Virus (HIV) and around 3 million people have to access to Highly Active Antiretroviral Therapy (HAART) (World health organization, 2008). India is a most populated country with over 1 billion inhabitants. It is estimated that around 2.4 million people are currently living with life-threatening disease HIV. HIV had emerged later in India than it did in many other countries (Averting HIV and AIDS, 2011).

ART is the therapy given to the HIV patients, Highly Active Antiretroviral Therapy (HAART) has led to a significant reduction in AIDS -related mortality and morbidity (Averting HIV and AIDS, 2011). The standard treatment consists of a combination of at least 3 drugs

often called **"HAART"** that suppress HIV replication (Department of AIDS Control, 2009).

A continuous high level of replication of HIV takes place in the body right from the early stages of infection. At least 10 viral particles are produced and destroyed each day. The HIV destroys CD4+ Cells, while the body produces more CD4+ cells (Adverse Effects of Antiretroviral Drugs, 2010). This balance is maintained for some years after which the rate of CD4+ destruction becomes more than that of CD4+ production. This progressive immune system damage results in susceptibility to different opportunistic infections (OI), malignancies, neurological diseases, wasting and ultimately it leads to death.

ARV drugs have low safety profile as they have the following facts:

a) they need to be taken on chronic basis

b) they are consumed by patients who are immuno-deficient

c) immune-deficient patients are more prone to develop an adverse reaction to any drug.

Hence, it is utmost important to monitor the patients closely who are on ARV drug therapy to detect the possible ADRs and to manage them appropriately so that the prescribed treatment is ensured (Naranjo *et al*., 1981). A large number of adverse drug reactions effects have been reported with all antiretroviral drugs and they occur because of the most common reason for switching or discontinuing therapy as well as medication non-adherence. The incidence of ADRs with newer antiretroviral regimens is generally declining now (less than 10%). Several factors may prone individuals to certain antiretroviral-associated ADRs viz., women seem to have a higher propensity of developing **"Steven-Johnson Syndrome"** and **"Symptomatic drug Hepatic"** events with nevirapine and high rate of lactic acidosis with NRTIS (A project of the New Mexico AIDS Education and Training Centre, 2011).

Clinicians and patients face many challenges associated with antiretroviral (ARV) therapy. These include decisions taken on the drug therapy, when to start therapy, what regimen to start with, when to change medications, and how to switch if a regimen is failing. Although clinical research should guide the selection of ARV regimens, it is important to remember that the best regimen for any individual patient is the regimen he or she is willing and able to take (Mehta U. Durrheim DN, 2008).

AIM AND OBJECTIVES: To evaluate the incidence, preventability and risk factors for adverse drug reactions (ADR's) in human immunodeficiency virus (HIV) patients using highly active antiretroviral therapy (HAART).

1. To assess the magnitude of adverse drug reactions (ADR's) and find out the factors associated with the occurrence of ADR's among patients on highly active antiretroviral therapy (HAART).

2. To assess the severity of ADR's among patients on highly active antiretroviral therapy (HAART).

3. To evaluate the incidence of ADR's among patients on highly active antiretroviral therapy (HAART).

RESEARCH METHODOLOGY:

Study design: A RETROSPECTIVE CASE-CONTROL STUDY was conducted by reviewing the clinical records of adult patients who got admitted to the ART center.

Study Subjects: Any selected adult patients on ART who fulfilled the inclusion criteria of a study subject.

Sampling technique: The patients are selected randomly from the ART unit.

Study population: A total sample size was 528 patients.

Inclusion criteria - All adult age above 16 years newly registered HIV patients on HAART therapy of either sex were included. The cases were analysed based on the parameters of Demographic details such as Age, Gender, Educational status, Family history, Weight, CD4+ cell count, Haemoglobin levels (Hb), Drugs prescribed and Incidence and Preventability of Adverse drug reaction (ADRs).

Exclusion criteria - Patients taking anti-tubercular treatment (ATT), opportunistic infections, 2ndline drugs and missing clinical record, incomplete data or those transferred to other centers or left against medical advice after they have been on ART and pregnant women were excluded from the study.

Data collection - Data was collected by reviewing the Patients case records and the following data were collected i.e.,

1) Date of the patient enrolled for ART treatment

2) The patient started using ART medication,

3) Demographic data on age, gender, education details, occupation, weight, hemoglobin levels, other available

4) Laboratory data, CD4 cell count, patient medication regimen and

5) Adverse drug reactions were clearly observed and noted on the specially designed Patient data collection form (Annexure 1).

Data was collected from a patient past medication history chart and assessed.

The status human immunodeficiency virus-positive patients under anti-retroviral therapy for at least a period of one year and followed up by monthly visit has been determined by reviewing the patient record using the following HAART regimens in the study.

A) Stavudine, Lamivudine and Nevirapine.

B) Zidovudine, Lamivudine and Nevirapine.

C) Zidovudine, Lamivudine and Efavirenz.

D) Stavudine, Lamivudine and Efavirenz.

Statistical analysis: The prevalence of the disease was calculated by considering the ratio of a number of patients with ADRs and a total number of patients involved in the study. The incidence rate was calculated by considering the ratio of ADRs and the exposure of patients. Data were analyzed using the chi-square method for estimating the correlation between ADRs and different variables. Risk factors for the ADRs were determined at a P value <0.05 by investigating the effects of gender, age, weight, CD4+ count, concomitant drugs. All statistical calculations were performed using Epi Info version 3.5.3. A p-value of <0.05 was considered statistically significant.

RESULTS: The cases were analysed based on the parameters of Demographic details like Age, Gender, Educational status, Family history, Weight, CD4+ cell count, Haemoglobin levels (Hb), Drugs prescribed and Incidence and Preventability of Adverse drug reaction (ADRs).

1. Age and Gender: A 208 newly registered patients for the highly active antiretroviral therapy of different age groups ranging from 17 – 65 years were selected in this study. Out of these 121 Males (58.17 %) and 87 Female (41.82 %) were selected based on the inclusion criteria during the period of January 2010 to May 2011.

2. Educational status: 118 (49 %) were illiterates followed by 38 (22 %) were still 5th class, 35 (18 %) people studied 10th class and patients holding graduates degree were found to be 17 (11 %).

3. Marital Status: The Marital status of HIV/AIDS patients included for the study and the incidence was found to be SINGLE 17 (8.17 %), MARRIED 149 (71.63 %), DIVORCED 8 (3.84 %) and WIDOW 34 (16.34 %).

The overall incidence of males was high with 63.94% followed by females of 36.05 % and the maximum of HIV/AIDS patients in our study were found to be MARRIED – 149 (71.63 %) and least of them were DIVOCSED – 8 (3.84 %).

4. CD4+ Cell Counts: Our study evaluated the initial CD4+ Cell count on the 1stday of using highly active antiretroviral therapy.

The initial CD4+ cell count ≤250 cells/mcL was observed in 169 HIV patients and more in Males - 101 than in Females – 68 based on it regression analysis was identified.

5. Weight Variation: Out of patients 84 (40.38 %) were in between 41-50 kg, 39 (18.75 %) were in between 31-40 kg, 8 (3.85 %) in 21-30 kg range. The patients with an average of 45 kg were considered for the estimating the malnutrition in HIV/AIDS patient using HAART regimen.

6. haematological daTA: In the total of 208 patients 70 (33.65%) were shown Hb levels <9.5 g/dl of which 7 were <6.5 g/dl and they were categorized according to WHO grades.

7. Distribution Pattern of HAART Regimen: Majority of patients were under ZLN86 (41 %) followed by 52 (25 %) patients under ZLE, 44 (21 %) patients under SLN and 26 (13 %) patients under SLE regimens.

8. Adverse Drug Reactions to the ARV Drugs: Adverse effects have been reported with all antiretroviral drugs and among them, the most common reason for ADRs are switching or discontinuing therapy as well as medication non-adherence. The incidence of ADRs with newer antiretroviral regimens is generally declining now (less than 10 %).

Of 208 patients 71 were reported ADR's to the different ART regimens. Of 71 ADR reports the majority of reports were in ZLN regimen (46 %) followed by ZLE (21 %), SLN (20 %) and SLE (13 %).

The incidence of adverse drug reactions was very high with ZDV+LMV+NVP of 33 (46 %) to the total number prescriptions of 86 (41 %) and overall incidence for the occurrence of adverse drug reactions to the following regimen were found to be 38.33 %.

Almost all the ADRs were mild to moderate, the suspected drugs was withdrawn in 90.14 % (64/71) of ADRs and symptomatic treatment was continued to remain cases 9.85 % (7/71). Lamivudine use was observed as risk factors for ADRs like skin rash and hepatitis. Zidovudine use was identified as a risk factor for ADRs like anemia and vomiting and Stavudine were the risk factors for the peripheral neuropathy.

Table 1. Education Status

Education status	Male	Female	Total
Uneducated	60	58	118
Till 5thclass	27	11	38
Till 10th	22	13	35
Graduation	13	4	17
Total	122	86	208

Table 2. Initial CD4+ Cell Counts

CD4+ count cells/mcL	Male	Female	Total
≤250	101	68	169
≥250	21	18	39
Total	122	86	208

Table 3. CD4+ Count in ADR Patients (Case) (n=71)

CD4+ Count (Cells/mcL)	Male	Female	Total (%)
≤250	35 (49.29 %)	25 (35.21 %)	60 (84.51 %)
≥250	6 (8.45 %)	5(7.04 %)	11(15.49 %)

Table 4. CD4+ Count in Non - ADR Patients (Control) (n=137)

CD4+ Count (Cells/mcL)	Male (%)	Female (%)	Total (%)
≤250	66 (44.17 %)	43 (31.38 %)	109 (79.56 %)
≥250	15 (10.94 %)	13 (9.48 %)	28 (20.43 %)

Table 5. CD4+ Count in ADR and Non-ADR Patients: Case Vs Control (n=208)

CD4+ count (Cells/mcL)	ADR Patients	Non - ADR Patients	P - Value
≤250	60 (28.8 %)	109 (52.4 %)	0.3862
≥250	11 (5.2 %)	28 (13.4 %)	0.3874

Table 6. Haematological Data

Haematology	Grade 1	Grade 2	Grade 3	Grade 4
Haemoglobin levels	**8.0 – 9.5 g/dl**	**7.0 – 7.9 g/dl**	**6.5 – 6.9 g/dl**	**<6.5 g/dl**
Males	31	6	1	3
Females	23	2	0	4

Table 7. Incidences of Adverse Drug Reactions to Individual HAART Regimen

NACO HAART regimen implicated in ADRs (n=71)		Number of prescriptions n=71(%)	Number of ADRs n=105 (%)	Incidence of ADRs n=105 (%)	P -value
Regimen I	Zidovudine + Lamivudine + Nevirapine	33 (46.47 %)	38 (53.52 %)	36.19	0.4166
Regimem I (a)	Stavudine + Lamivudine + Nevirapine	14 (19.71 %)	28 (39.43 %)	26.66	
Regimen II	Zidovudine + Lamivudine + Efavirenz	15 (21.12 %)	20 (28.16 %)	19.04	
Regimen II (a)	Stavudine + Lamivudine + Efavirenz	9 (12.67 %)	19 (26.76 %)	18.09	

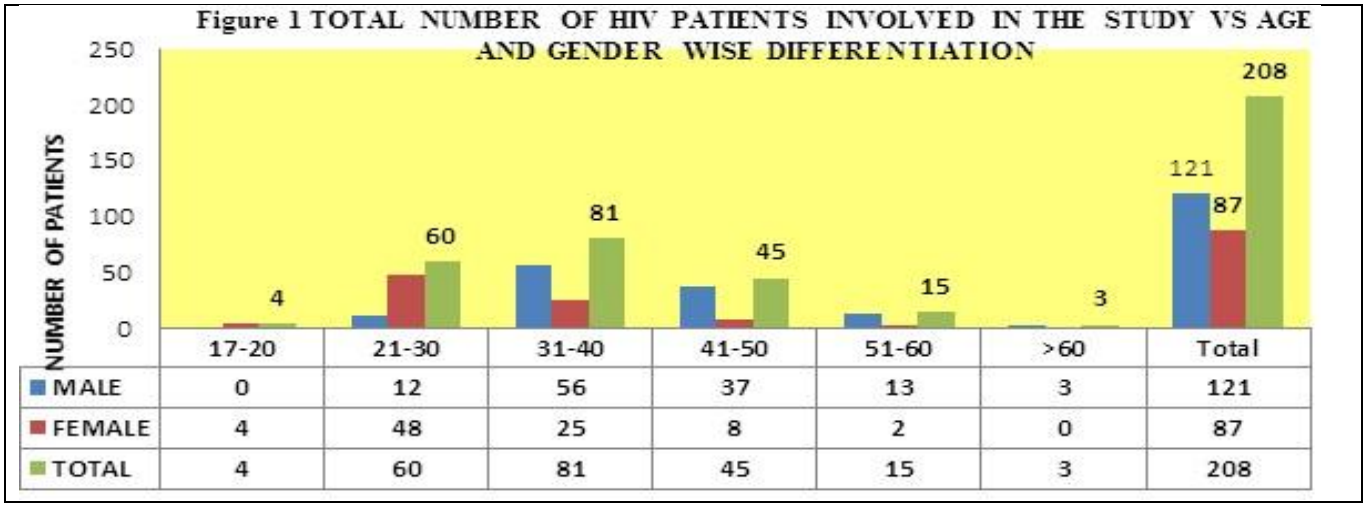
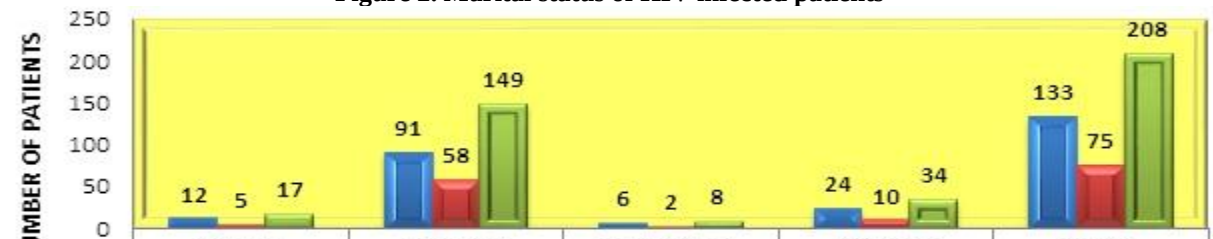


Figure 2. Marital status of HIV infected patients



	SINGLE	MARRIED	DIVOURSED	WIDOW	TOTAL
MALE	12	91	6	24	133
FEMALE	5	58	2	10	75
TOTAL	17	149	8	34	208

Figure 3. Comparison of CD4+ according to gender and cell count

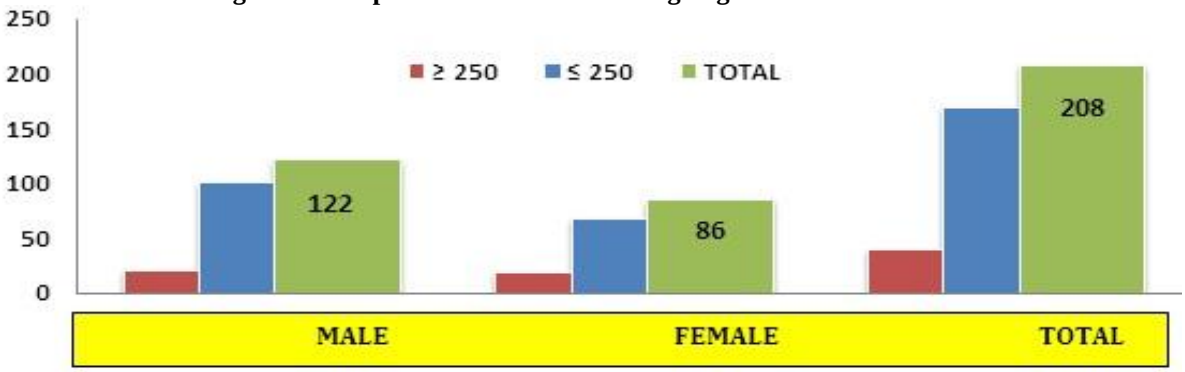


Figure 4. Number of patients v/s weight

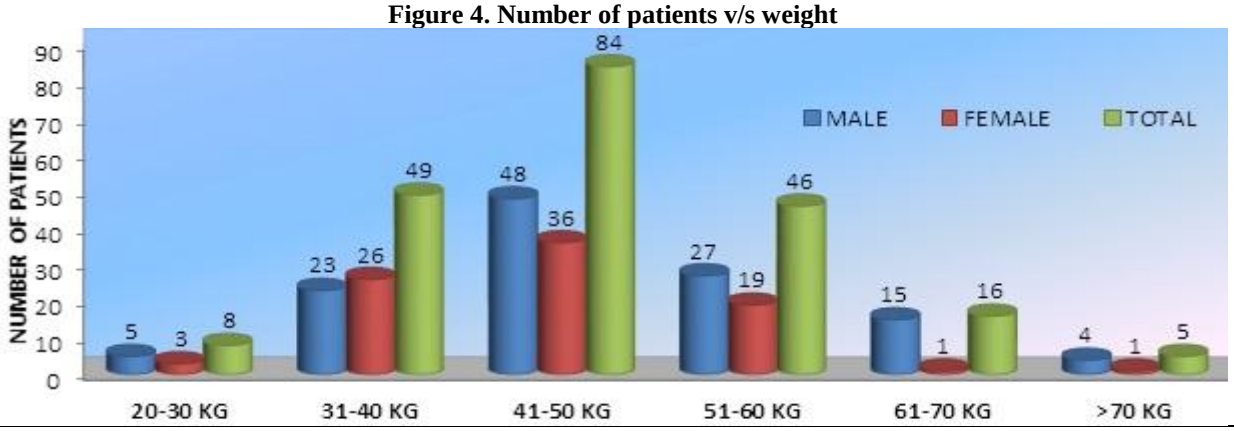


Figure 5. Distribution pattern of haart regimen

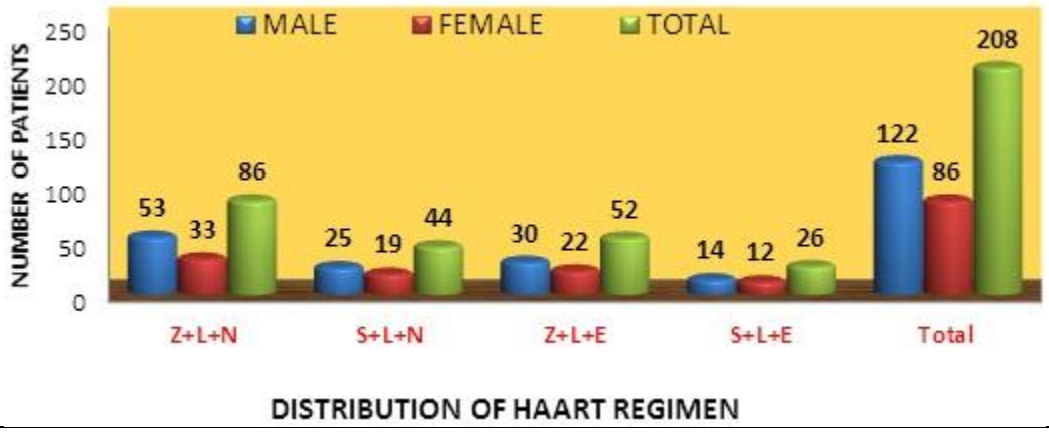


Figure 6. Art regimen implicating in adverse drug reactions art regime implicated in adverse drug reactions

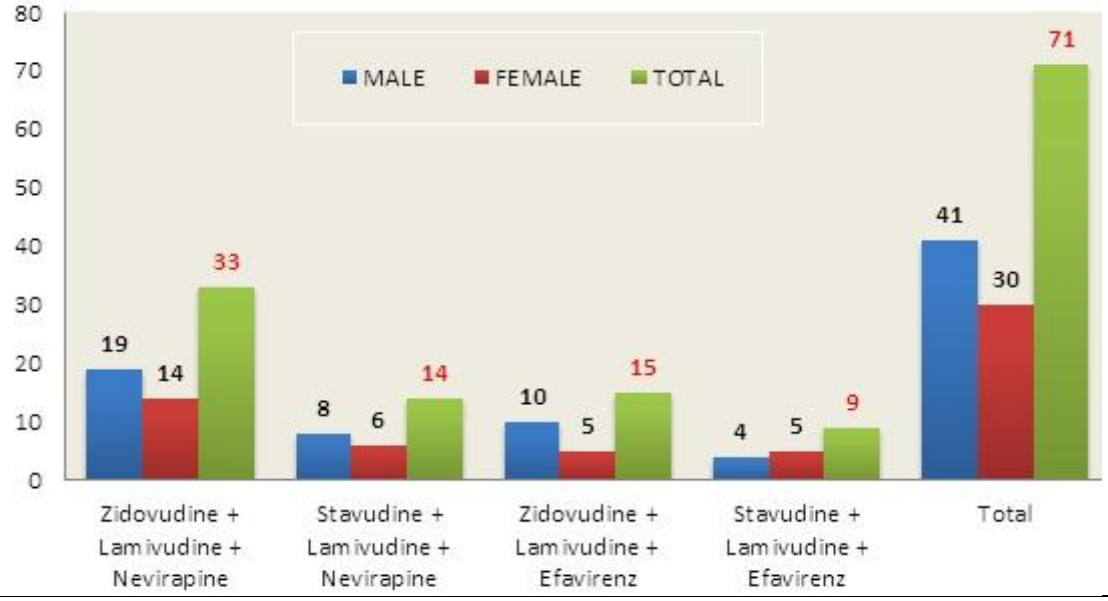


Figure 7. HAART regimen implicated adverse drug reaction

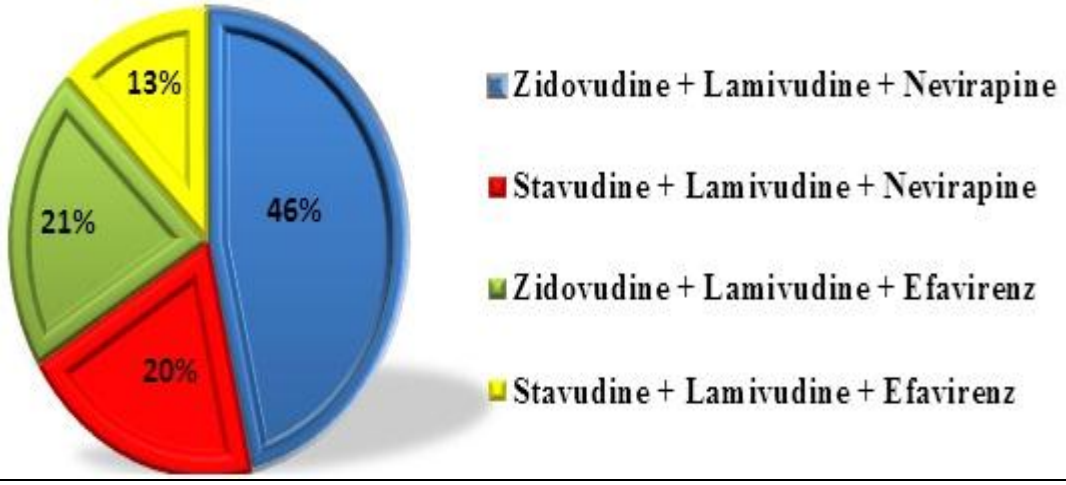


Figure 8. Number of adverse drug reactions vs % of patients

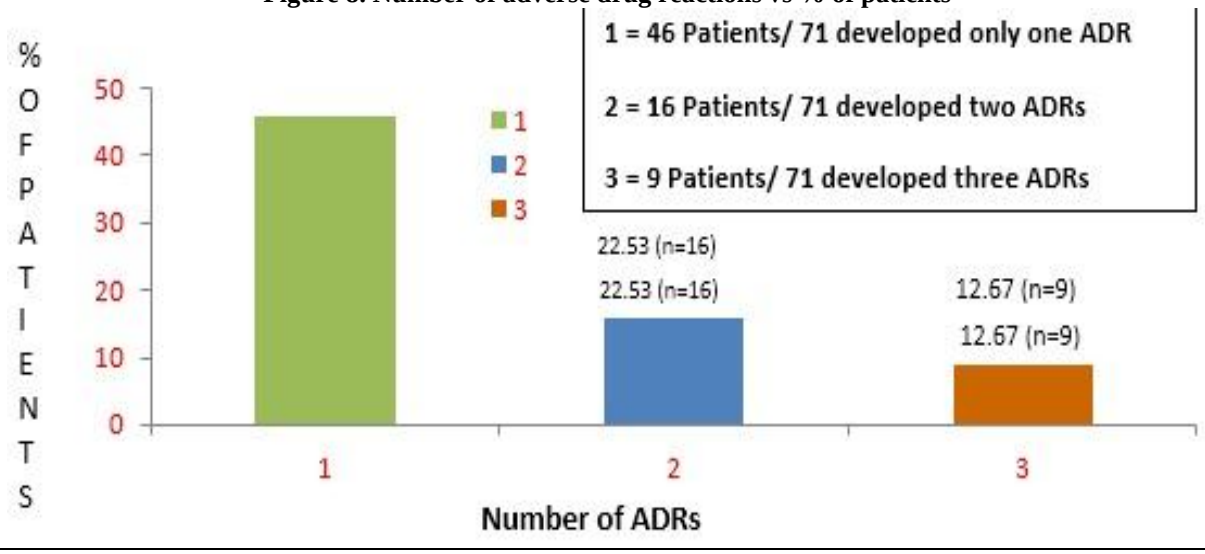


Figure 9. List of adverse drug reactions observed

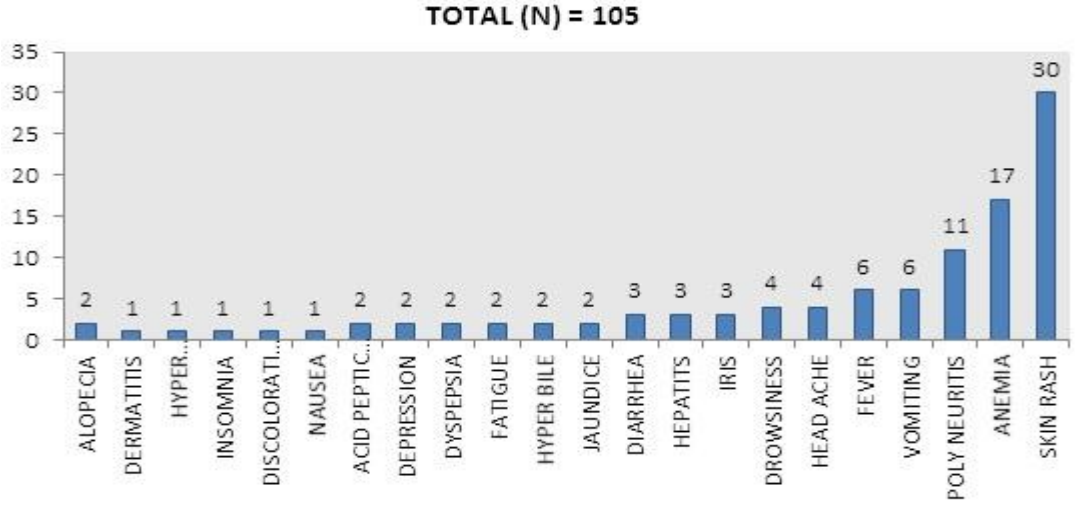


Figure 10. Incidences of ADRS to HAART

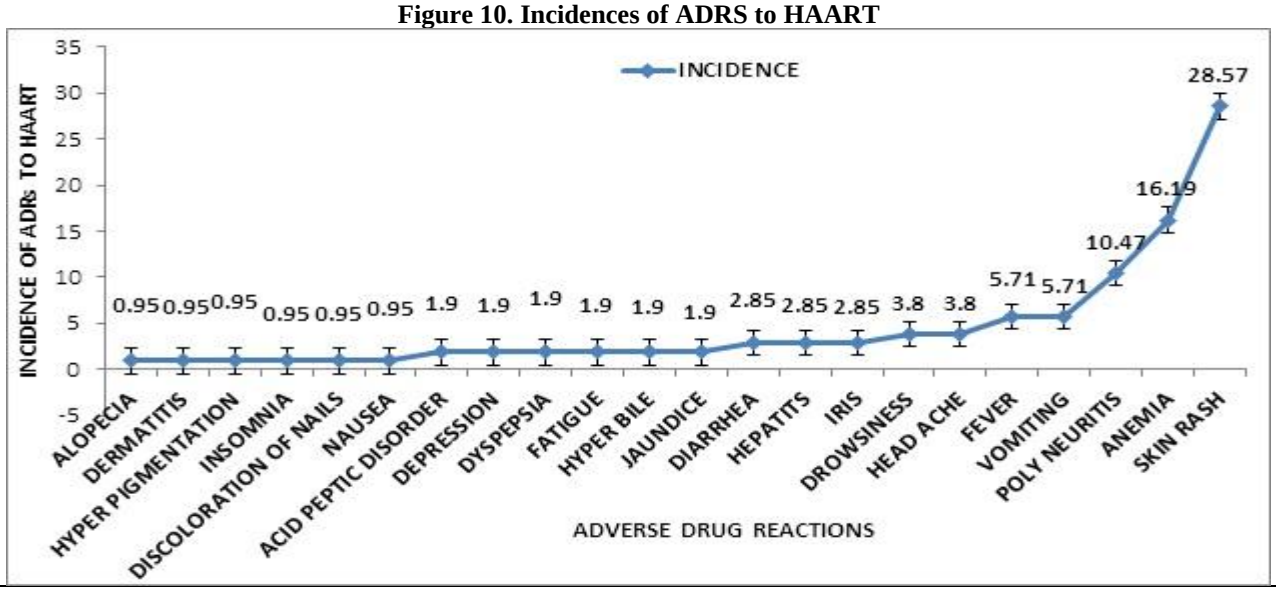


Figure 11. Organ systems affected due to HAART

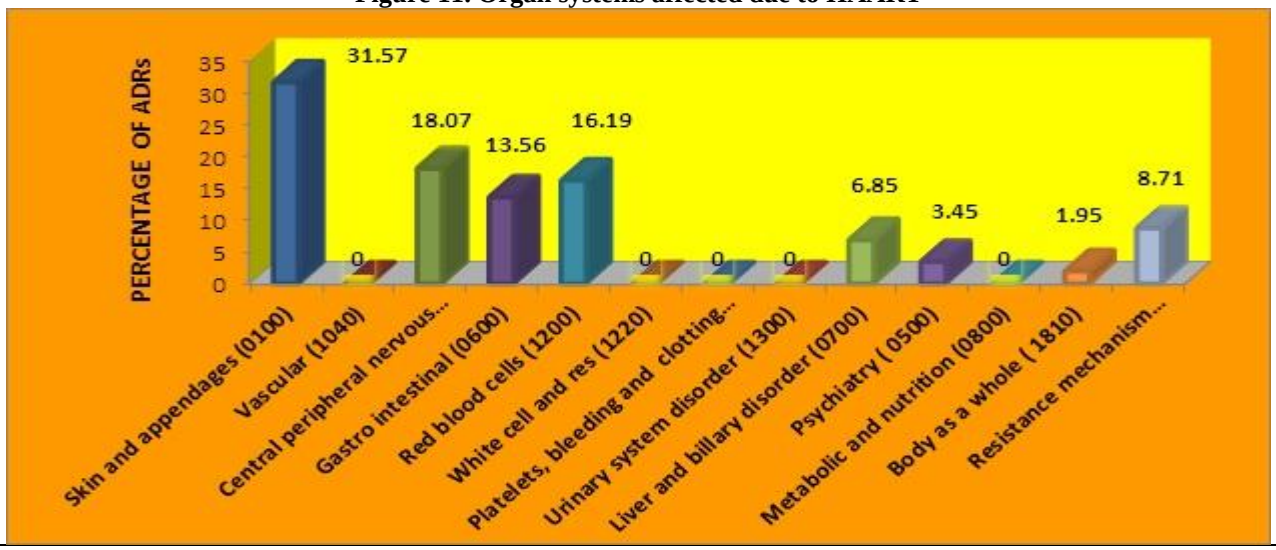
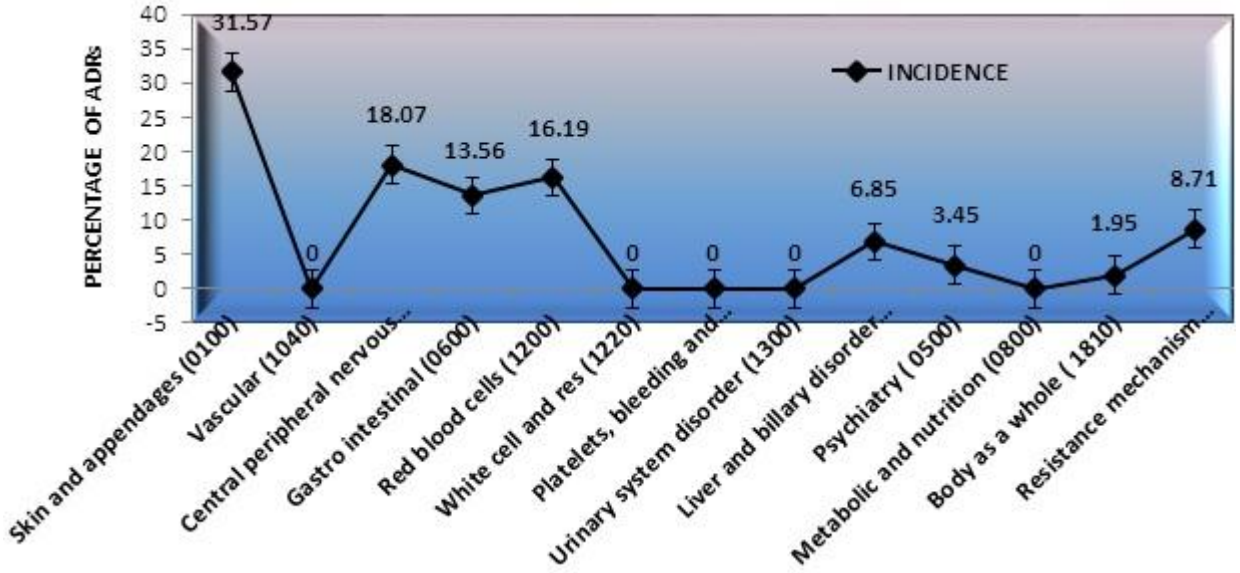


Figure 12. Organ systems affected due to ADRS to HAART (who-art codes)



DISCUSSION

As the HIV rife is entering its 3rd decade, over 60 million people have been infected by the virus, nearly 25 million have died and as of December 2016, 33 million people globally were living with HIV. The eradication of the HIV infections can't be achieved with available antiretroviral (ARV) regimens.

The primary goals of Initiating Highly Active Antiretroviral Therapy are to

- Reduce HIV- associated mortality and prolong the duration and quality of survival,
- Restore and preserve immunologic function,
- Maximally and durably suppress plasma HIV viral load
- Prevent HIV transmission (Mehta *et al*., 2008)

In our study, the majority of ADRs to HAART were observed under the age group 31 - 40 years. This may be due to a large number of new HIV positive patients treating with HAART at our hospital. A finding of ADRs observed in adults, similar to another study (Melmol KL, 1971). However, another study has reported a large percentage of ADRs in geriatric and pediatric populations (Alternative 1st Line ART operational guidelines, 2010).

During the study, 64.78 % of patients showed at least one ADR and switched to another drug regimen was done in 90 % of the patients. Skin rash and anemia complaints were the most prevalent reported ADRs in our study; most ADRs were moderate and need just symptomatic treatment in few patients. Skin rash adverse effects were reported more with Nevirapine containing HAART regimen. Anemia occurred in patients received zidovudine-containing regimens were graded according to the NACO criteria. Majority of cases Grade I anemia [Hemoglobin (Hb) 8.0 - 9.5 g/dl] was observed with Zidovudine. Skin rash developed by 28.57 % (30/105) people taking Nevirapine. The side effect is much more common in males than females in our study. As the patients frequently complaints about the skin rash which is uncomfortable. Mild rash occurs with no other related symptoms and resolves over days or weeks. The moderate rash may be accompanied by systemic symptoms (eg; fever, LFT abnormalities, and myalgia). Life-threatening rashes like Stevens-Johnson syndrome associated with pain, mucous membrane involvement, fever, LFT changes, and myalgias can be fatal (Peter *et al*., 2003).

In our study Hepatitis 2.85 % (3/105), jaundice 1.90 (2/105) and hyperbilirubinemia 1.90 (2/105) were also associated with nevirapine and efavirenz and the elevated levels of bile, ALT, AST, and bilirubin levels according to the NACO grades of clinical and laboratory toxicities. Red blood cells adverse effects 16.19 % (17/105) to be more with zidovudine-containing HAART regimen, an improvement in Hb level were observed on discontinuation of zidovudine similar to the finding reported by Koduri and Parekh. In our study patients initiated on a zidovudine-containing regimen only if they had they have the Hb levels was more than 10.5 g/dl at baseline, thereby avoiding the occurrence of zidovudine-induced anemia. However, we observed a highly significant association between the zidovudine and anemia which is similar to other studies (Scarsella *et al*., 1999).

Peripheral neuropathy was observed in patients who were on the stavudine-containing regimen for more than 4 months. In 10.47 % (11/105) of these cases, stavudine was discontinued and the patient recovered. However, a few patients who took zidovudine therapy also suffered with peripheral neuropathy, followed by Fever [5.71 % (6/105)] and also finding in our study supported that stavudine as a risk factor for the peripheral

neuropathy which is also suggestive from Scarsella et al (1999). Vomiting 5.71 (6/105) was a common ADR followed by nausea 0.95% (1/105), diarrhea 2.85 % (3/105), dyspepsia 1.90 % (2/105), fatigue 1.90 (2/105), hyperpigmentation of skin 0.95% (1/105) and discoloration of nails1.90 % (2/105) were observed among patients who were on regimens containing zidovudine. Majority of the patients experienced vomiting after injection of the drug. Patients receiving a zidovudine-containing regimen had the greater risk of vomiting similar to that observed in an Iranian study (Khalili *et al*., 2009).

The occurrence of a depression headache 3.80 % (3/105), drowsiness 3.80 % (3/105), depression 1.90 (2/105), alopecia 0.95% (1/105), insomnia 0.95 % (1/105) was highly associated with efavirenz therapy. The occurrence of this ADR was can be minimized by administering the efavirenz once a day at night. Our study observations were similar to the study by Fumaz et al. (2005)

In our study patients complained ADRs of dermatitis 0.95 % (1/105), acid peptic disorder 1.90 % (2/105) the reason of these ADRs are not clearly known and immune reconstitution inflammatory syndrome (IRIS) was observed within the first six months of HAART. In three patients [3.80 % (3/105)] IRIS manifested as TB. Our study findings are similar to a South African study wherein most IRIS cases (41 %) manifested as T.B.(Marc *et al*., 2003)

The majority of the ADRs were predictable as they were common (incidence≥1/10) and very common incidence ≥1/10 (Mallon *et al*., 2003). The preventive measures for ADRs were prescribed and administered to patients: like common instructions were given to avoid ADRs by providing medication counseling to each patient. The finding of the study showed that the most common causes of ADRs to highly active antiretroviral therapy cessation in these patients were due to cutaneous like Skin rash, dermatitis, hyperpigmentation, discoloration of nails with nevirapine and efavirenz. Hematological ADRs like anemia with Zidovudine and polyneuritis ADR was observed in patients using Stavudine therapy (Le Beller *et al*., 2003).

CONCLUSION

It is the 1st study on a large group of population designed to study the incidence of ADRs in HIV positive patients using antiretroviral therapy in Indian population. None of the socio-demographic variables, the initial clinical and laboratory state data were significantly associated with the development of ADRs which needs to be confirmed with the further prospective study.

Highly active antiretroviral therapy with zidovudine + lamivudine + nevirapine (53/105), zidovudine + lamivudine + efavirenz (37/105) and stavudine + lamivudine + nevirapine (30/105) is a predictor of ADRs. Antiretroviral therapy is effective for HIV treatment but also increasingly complex. The pharmacist should be able to detect the ADRs and do the minor change in the patient's disease state or development for the safety and any other new symptoms should not be ignored. The culture of reporting ADRs should be inculcated. All ART centers should have a pharmacovigilance cell. All ADRs reported should be analyzed as per WHO guidelines of causal assessment. Our study finding showed that there is a need of active Pharmacovigilance center with intensive monitoring of ADRs by the Pharmacist in Indian HIV positive patients who are illiterate, poor with CD4+ count ≤250 cells/mm^3 with co-morbid conditions.

REFERENCES

A project of the New Mexico AIDS Education and Training Centre, National Library of Medicine /AIDS Info Net/Fact Sheets/number 404/January 12, 2011. URL: http://www.aidsinfonet.org

Alternative 1st Line ART operational guidelines by NACO, Ministry of Health and family welfare, Government of India, 2010, 8 - 9.

Averting HIV and AIDS [home page on the internet]. 2008 November 26 [cited 2009 January 5]. Available from: URL: http://www.avert.org

Averting HIV and AIDS 2011 May 12 [cited 2009 January 5] URL: http://www.avert.org

Department of AIDS Control, NACO, Ministry of Health & Family welfare Annual Report 2009 - 10, Chapter 2 Current Epidemiological Situations of HIV/AIDS, Page no. 4 - 6.

Fumaz CR. Munoz –Moreno JA, Molto J. Long-term neuropsychiatric disorders on efavirenz – based approaches: quality of life, psychological issue and adherence. *Journal of Acquired Immune Deficit Syndrome*, 38 (5), 2005, 607 - 610.

Ian McNicholl, Pharm.D, BCPS, University of California San Francisco. Adverse Effects of Antiretroviral Drugs July 2010.

Incidence of Anemias among HIV-infected patients treated with highly active antiretroviral therapy. *HIV Medicine*, 8 (8), 2007, 483 - 490.

Khalili, D-ashti - Khavidaki S, Mohtaz M, Etaghani A, Almasi F. Antiretroviral induced adverse drug reactions in Iranian human immunodeficiency virus positive patients. *Pharmacoepidemiology Drug Safety*, 18 (9), 2009, 848 - 857.

Le Beller C, Thomas L, Weiss L, Gonzalez Canali G, Le Louet H; Self reporting Adverse Drug Reactions (ADRs) by HIV-1-Infected patients: A 6 months experience of a pilot study. *Antiviral Therapeutics*, 8 (Suppl.1), 2003, abstract no. 873.

Mallon PW, Miller J, Copper DA, Carr A, et al. A prospective evaluation of effects of antiretroviral therapy on the body complications in HIV – 1 infected men starting therapy. *AIDS*, 17 (7), 2003, 971-979.

Marc A. RIEDL, M D and Adrian M. Casillas MD. Adverse Drug Reactions: Types and Treatment Options, *Am Fam Physician*, 68(9), 2003, 1781-1791.

Max B, Sheerer R. Management of the adverse effects of antiretroviral therapy and medication adherence. *Clinical infections Disorders*, 30, 2000, S 96 - 116.

Mehta U. Durrheim DN, Blockman M. Kredo T, Gounden R, Barnes KI. Adverse drug reactions in adult medical Inpatients in South African Hospital serving a community with a high HIV/AIDS Prevalence: prospective observational study. *Br J Clinical Pharmacology*, 65 (3), 2008, 396 - 406.

Melmol KL. A preventable drug reaction - cause and cures. *N Engl J Med*, 284 (24), 1971, 1361 - 1368.

Naranjo CA, Busto U, Sellers EM. A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology Therapeutics*, 30 (2), 1981, 239 - 245.

Peter J. Pilfer, MD, Associate Professor of Medicine, Albay Medical College, Long-Term Toxicities associated with HIV and Antiretroviral Therapy. *HEPP Report*, June 2003, 6(6).

Scarsella A. Coodley G, Shaltit P. Stavudine - associated Peripheral neuropathy in Zidovudine-native patients. *Journal of Neurology*, 246 (3), 1999, 211 - 217.

World health organization [home page on the internet]. 2008 URL: http://www.who.int/en

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