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Original Research Article

Study of Efficacy of Anti-Retroviral Drugs in a Tertiary Care Teaching Hospital

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Abstract: Till 2015, an estimated 36.7 million people lived with HIV (UNAIDS (2015) 'Global Report 2015') and up to 44% in 2015 are under cover of ART Programme. Highly Active Anti-Retroviral Therapy (HAART) has led to a significant reduction in AIDS related morbidity and mortality. Unfortunately, up to 25% of patients discontinue their initial HAART therapy because of opportunistic infections, Adverse Drug Reactions (ADRs) and noncompliance. According to the Annual Report 2015-16, Odisha has shown an estimated adult HIV prevalence in the range of 0.21–0.25%. In view of increasing epidemic trend in seven states of the country including Odisha, there is an urgent need to draw the attention of the policy and programme managers towards the effectiveness of the ongoing ART medication. Aim of the study was to evaluate the efficacy of ART therapy in terms of improvement in CD4 count and WAB (Working, Ambulatory, and Bedridden) status of the patients in this Centre. CD4 count was measured at 6 months interval up to 18 months in patients on ART. 48.51% patients had CD4 count between 50-200 cells/cmm at initial visit and 44.55% patients had CD4 count > 500cells/cmm at final (4^{th}) visit. Majority of patient having CD4 count >500 reflects patients improved on ART therapy. There was also a significant improvement in functional status. But, 51.48% of patients had to change to a new ART regimen for treatment failure. Therefore time to time surveillance of such patients is needed for early detection and prevention of ADRs to HAART. Further, assessment of risk factors associated with treatment failure, compliance, adverse effects and follow up of patients for a longer duration is needed to interpret the effectiveness of any ART Programme.
Keywords: HIV/AIDS, Antiretroviral treatment, Efficacy, ART Regimen, CD4 Count

INTRODUCTION:

In 2015, an estimated 36.7 million people leaved with HIV (UNAIDS (2015) 'Global Report 2015') and up to 44% in 2015 were under cover of ART Programme [1]. As per the recently released, India HIV Estimation 2015 report, 3.49 million people are living with AIDs (PLWHA) and National adult (15–49 years) HIV prevalence in India is estimated at 0.26% (0.22%–0.32%) in 2015. In 2015, adult HIV prevalence is estimated at 0.30% among males and at 0.22% among females. According to the Annual Report 2015-16, Odisha has shown an estimated adult HIV prevalence in the range of 0.21– 0.25%. In view of increasing epidemic trend in seven States of the country including Orissa, there is an urgent need to draw the attention of the policy and programme managers towards the effectiveness and compliance of ART medication. As of 17th October 2016, 528 ART centers are operational in India [2]. In 2014, worldwide 14.9 million HIV-positive people had access to ART of which almost 13.6 million people were living in low- and middle-income countries. HAART has led to a significant reduction in AIDS related morbidity and mortality. Unfortunately, up to 25% of ambulatory HIV-positive patients discontinue their initial HAART therapy because of opportunistic infections, ADRs and noncompliance. Anti-retroviral therapy (ART), aims to effectively suppress the viral replication. Successful viral suppression not only restores the immune system but also helps to halt the onset and progression of disease along with a lesser risk of getting opportunistic infections. Studies show that, with effective ART, CD4 cell count increases up to more than 50 cells /cmm within weeks after viral suppression [3]. ART medication thus enhances both quality of life and longevity. Understanding ART effectiveness within the

routine care setting is crucial to ensure quality care to people living with AIDs and prevent emergence of resistance to ARVs.

MATERIAL & METHODS:

This was an institution based observational study conducted at the Anti-retroviral therapy centre, MKCG Medical College, Berhampur. Prior permission & approval from the project Director, Odisha State AIDS Control Society and the Institutional Ethics Committee was obtained.

Selection of cases: Data of 150 patients enrolled in the ART Register from January 2014 to June 2015 was collected, as per the following inclusion & exclusion criteria:

Inclusion criteria:

- All diagnosed cases of HIV infection, cases of AIDS receiving treatment at ART centre
- Both sexes

Exclusion criteria:

- Irregularly treated cases/Lost to follow up cases
- Critically ill patients
- Children of either sex

All the data were collected in pre-designed case record form (CRF) from the patient card available at ART Centre with knowledge of senior medical officer in charge. Strict confidentiality was maintained throughout the data collection procedure. The patient's cards were followed up every six month from the starting of study up to 18 months through patient card.

Parameters for evaluation:

Demographic profile

Information about the age, gender, marital status, educational status & employment status of the patient was recorded.

Efficacy parameters:

Efficacy of the given regimen was evaluated by taking all the indicators like CD4 count, WHO Clinical Staging and WAB Status.

- CD4 count: CD4 count is an indicator of the immunity status of the patient. It is not directly related to the viral load or clinical status. But indirectly it gives information regarding patient immunity & it's susceptibility to various opportunistic infections. Normal CD4 count is > 500/cubic mm. In HIV infected individuals CD4 count keeps on dropping as the disease progresses. The antiretroviral therapy given helps in improving the CD4 count & protects the individual from opportunistic infections. According to the current guideline of WHO the ART should be started at CD4 count < 350 cubic mm. The efficacy of a regimen can be measured by taking the improvement of CD4 count in account.
- WHO Clinical Staging: In resource poor underdeveloped country with high prevalence of HIV infection there is not adequate facility to evaluate viral load or CD4 count. In these circumstances WHO clinical staging is helpful to measure the efficacy of the regimen. The WHO clinical staging is classified into four stages (I, II, III, and IV).The progression of clinical staging from lower to higher stage (IV→III→II→I) shows the efficacy of the regimen.
- WAB Status: Other scoring methods used by National AIDs Control Organization (NACO) are WAB method [4]. These are Working, Ambulatory and Bed Ridden. As the name indicates improvement of the patient from bed ridden to working is measured and it indirectly shows the efficacy of the regimen.

DATA ANALYSIS:

Data were expressed as percentage values. CD4 Count over the study period was analysed by One way ANOVA followed by Dunnett's multiple comparison test using Graph Pad Prism Version 5.0. $P < 0.05$ was considered as significant.

RESULTS:

Of the 150 patients enrolled 49 patients were lost to follow up.

Table.1 Demographic Profile

PARAMETERS	FEMALE (%)	MALE (%)
Marital status Married	41.03	82.05
Single	2.56	17.95
Widowed	51.28	0.00
Divorce	5.13	0.00
Live-in	0.00	0.00
Education Illiterate	100.00	28.21
Primary	0.00	20.50
Secondary	0.00	41.03
College	0.00	10.26
Employment Employed	2.56	84.62
Unemployed	97.44	15.38
Family history Yes	51.28	69.23
No	48.72	30.77

Table 2: Case Characteristics

REGIMEN	No.	%
STV+LMV+NVP	39	38.61
STV+LMV+EFV	8	7.92
ZDV+LMV+NVP	41	40.59
ZDV+LMV+EFV	8	7.92

STV- Stavudine, **LMV-** Lamivudine, **NVP –** Nevirapine**,** - Efavirenz

Table 3: Reasons for Change of Regimen

REASON FOR CHANGE	NUMBER	PERCENTAGE
New Onset TB	18	17.82
Side Effect	31	30.69
Previous Treatment Failure	52	51.48

Table 4: Stratification of HIV/AIDS patients basing on CD4 Count during successive visits

CD4 COUNT	1ST VISIT	2ND VISIT	3RD VISIT	4TH VISIT
<50	12(11.88%)	2(1.98%)	3(2.97%)	2(1.98%)
50-200	49(48.51%)	16(15.84%)	9(8.91%)	5(4.95%)
201-350	34(33.66)	34(33.66%)	33(32.67%)	24(23.76%)
351-500	2(1.98%)	29(28.71%)	27(26.73%)	25(24.75%)
>500	4(3.96%)	20(19.80%)	29(27.71%)	45(44.55%)
n=101				

Table 5: WAB Status at successive visit

WAB STATUS	1ST VISIT	2ND VISIT	3RD VISIT	4TH VISIT
W	75(74.26%)	88(87.13%)	96(95.05%)	96(95.05%)
A	26(25.74%)	13(12.87%)	05(4.95%)	05(4.95%)
B	0	0	0	0
n = 101				

W: able to perform usual work in or out of the house, harvest, go to school**, A:** able to perform activities of daily living but not able to work/go to school/play **B**: not able to perform activities of daily living**. Reference: Patient card, NACO.**

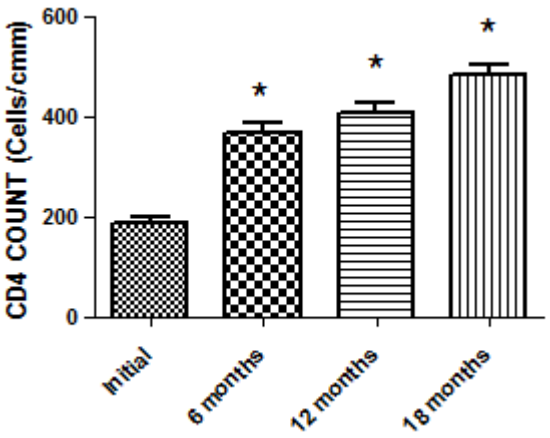

Fig-1: CD4 count of HIV patients during successive visits

DISCUSSION:

From January 2014 through June 2015, 150 patients started first-line ART; Among the 150 patients enrolled 49 patients were lost to follow up so data of 101 patients were analysed. The study was undertaken to observe the demographic profile of people living with HIV/AIDS, to delineate the various regimens prescribed at this ART centre and study the efficacy of the given regimen among them. Evaluation of the efficacy of the regimen was measured in terms of improved CD4 count & WHO clinical staging and WAB Status of the patients.

Demographic profile showed that 58.52% were male patients whereas 41.17% were females. 43.79% patients were in the age group of 35-44 years, followed by 39.86% in the age group of 25-34 year. Majority of the males were of the age group >44 years (87.5%) and most of the females were from the age group 15-24 years (77.78%). Marital statuses revealed that majority of patients were married. 82.05% male patients are married whereas 41.02% female patients were found to be married. Another important finding from this study was that around 51.28 % of the cases were found to be widowed females and 5.13% were divorced.[Table- 1] All the female patients were not only illiterate so also unemployed. 69.23% male patients had a positive family history.

An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI). [5]. The study showed that ART effectiveness was higher for NNRTI-based regimens. These findings corroborate results from various other studies that demonstrate greater effectiveness of NNRTI-based regimens [6-8]. Four different regimens SLN [Stavudine + Lamivudine + Nevirapine], ZLN [Zidovudine + Lamivudine + Nevirapine], SLE [Stavudine + Lamivudine + Efavirenz], ZLE [Zidovudine + Lamivudine + Efavirenz] were used in this hospital setting. [Table-2] But unfortunately, 80.19% of patients had to be changed to a new regimen from the initial regimen. The most common reason being previous treatment failure (51.48%). [Table-3] According to the "Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection 2016" a successful ART requires all medications to be taken as prescribed [9].

Efficacy assessment: In resource limited settings where facilities like viral m-RNA load assessment are not feasible, absolute CD4 count, clinical staging and WAB status are important indicators of measurement efficacy of ART regimen. Therefore in this study these parameters were taken into account for evaluation of the given ART regimen.

CD4 count [10, 11] is most important laboratory indicator of how a patient's immune system is working and is the strongest predictor [12] of HIV progression. Current HIV treatment guidelines recommend that HIV care provider need to perform a CD4 test every 3 to 6 months from starting ART to assess the response to treatment. Regular CD4 testing improves health outcomes in PLWHA by permitting monitoring of their immune function, decide when to initiate ART, assess immunologic response to ART, and assess the need for initiation or discontinuation of prophylaxis for opportunistic infections [13]. During the study the CD4 count was recorded and it was found that during first visit or starting of therapy, maximum number of cases were in the range of 50-200 (48.51%) followed by 33.66% cases in 201-350. At the end of study period i.e., 18months from starting of therapy 44.55% patients were in the range of >500. [Table-4, Fig 1]

According to the WHO, advanced HIV/AIDS disease is defined for surveillance purposes as any clinical stage-3 or stage-4 disease or any clinical stage with a CD4 count greater than 350 per cubic mm, and this information can be used to calculate the burden of disease and the demand for antiretroviral therapy [9]. Patient's overall health and whether or not he/she is receiving antiretroviral therapy is a factor to decide how frequently CD4 count needs to be estimated. Untreated patients who have CD4 cell counts higher than 500 are usually tested once every six to 12 months. Individuals who have CD4 counts between 350 and 500 are usually tested about once every three to six months.

The clinical staging is one parameter to measure efficacy of the regimen. Majority of cases were in stage II (49.01%) followed by stage III (26.14%) in first visit. In second visit the percentage went upto 61.43% for stage I. In third visit the number went up to 84.96% and in last visit it was 92.15%. WAB status is used to record the functional capability of the patient to do day to day function. Accordingly it is scored as W-Working, A-Ambulatory, B -Bedridden. During the study no patient was found as bedridden. The score W kept on increasing from 74.26% to 95.05% from starting of therapy to end of study period. Whereas the score A came down from 25.74% to 4.95%. [Table-5]

CONCLUSION:

Though the study reveals an improvement in CD4 count and clinical status of patients under study, change in ART Regimen in majority of patients from 1st line regimen is a matter of concern. Further, identification of risk factors associated with treatment failure, compliance, adverse effects and evaluation of patients for a longer duration is needed to interpret the effectiveness of the ART Programme. The authors believe that the data collected from this study will be an important source of information to the ART Personnel and health planners to help them to cater further interventional steps that will address the local needs.

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REFERENCES:

1. National Aids Control Organisation. (n.d.). Retrieved January 13, 2017, from http://naco.gov.in/treatment.
2. "HIV and AIDS in India." *AVERT*. N.P., n.d. Web. 13 Jan. 2017.
3. Allison A. 2008. HIV Laboratory Monitoring, available from: http://www.aidsalliance.org/publications.
4. ART-Patient Treatment Record. National AIDS Control Organization (NACO), Ministry of Health and Family Welfare, Government of India. 2007 Feb.
5. Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. African journal of medical practice/African Academy of Sciences. 1998; 5(2):79.
6. Bartlett JA, Fath MJ, Demasi R, Hermes A, Quinn J, Mondou E, Rousseau F. An updated systematic overview of triple combination therapy in antiretroviral-naive HIV-infected adults. Aids. 2006 Oct 24; 20(16):2051-64.
7. Taniguchi T, Grubb JR, Nurutdinova D, Önen NF, Shacham E, Donovan M, Overton ET. Efavirenz outperforms boosted atazanavir among treatment-naive HIV-1-infected persons in routine clinical care. Journal of the International Association of Providers of AIDS Care (JIAPAC). 2013 Mar; 12(2):138-41.
8. Riddler SA, Haubrich R, DiRienzo AG, Peeples L, Powderly WG, Klingman KL, Garren KW, George T, Rooney JF, Brizz B, Lalloo UG. Class-sparing regimens for initial treatment of HIV-1 infection. New England Journal of Medicine. 2008 May 15; 358(20):2095-106.
9. "Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection." World Health Organization. World Health Organization, n.d. Web. 13 Jan. 2017.
10. World Health Organization. Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for surveillance: African region. Switzerland: World Health Organization; 2005.
11. Sharma B. Drug Resistance in HIV-1: Genetic and Molecular Bases, Mechanisms and Strategies to Combat the Issue. Biochem Anal Biochem. 2015; 4:e153.
12. Simone E Langford, Jintanat Ananworanich, David A Cooper AIDS Res Ther. 2007; 4: 11. Published online 2007 May 14
13. Ford MA, Spicer CM. Indicators Related to Continuous HIV Care and Access to Supportive Services. 2012.