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# EFFECT OF ADHERENCE TO ANTI-RETROVIRAL THERAPY ON CD4 T CELLS AND HIV VIRAL LOAD IN NEPALESE TERTIARY CARE HOSPITAL

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## ABSTRACT

**Background:** The purpose of this study was to analyze the study on effect of adherence to Anti-Retroviral Therapy on CD4 cells and viral load among HIV infected patients at TUTH. **Methodology:** Retrospective study was carried out in 66 patients of age ≥18 years receiving ART from Tribhuvan University Teaching Hospital, Kathmandu, Nepal. Information was noted into data collection sheet such as demographic information, medication information, CD4 T cells and Viral load count. **Results:** The majority of patients were female (50%). At entry, 95.4% and 4.5% patients had ≤350 and >350 CD4 count respectively. At baseline investigation, patients with ≤350 CD4 count decrease to 57.5% and increase >350 CD4 count-to 42.2% patients. At one year, only 36.3% patients had ≤350 CD4 count-36.3% and >350 CD4 count was observed in 63.7%. Viral load <400copies/ml found in 77.3% patients at baseline and this figure increase to 95.5% at one year whereas 22.7% patients had ≥400 copies/ml at baseline which data decrease to 4.5% patients at one year. At one month of therapy, >95% adherence was in 97% patients which gradually decrease to 81.8% patients at one year. **Conclusion:** The HIV incident was seen to be more in female than male however it was almost equal. Increase in CD4 count and reduction in viral load was seen after initiation of therapy however there was no significance relation of adherence with CD4 count and viral load suppression.

**KEYWORDS:** Human immune deficiency virus, Antiretroviral Therapy, Adherence, CD4 T cells count, viral load, WHO guideline.

## INTRODUCTION

### Background of study

On June 5, 1981, when the Centers for Disease Control reported five cases of Pneumocystis carinii pneumonia in young homosexual men in Los Angeles, few suspected it heralded a pandemic of AIDS. In 1983, a retrovirus (later named the human immunodeficiency virus, or HIV) was isolated from a patient with AIDS. In the 25 years since the first report, more than 65 million persons have been infected with HIV, and more than 25 million have died of AIDS. Worldwide, more than 40 percent of new infections among adults are in young people 15 to 24 years of age. 95% of these infections and deaths have occurred in developing countries. Sub-Saharan Africa is home to almost 64 percent of the estimated 38.6 million persons living with HIV infection. In this region, women represent 60 percent of those infected and 77 percent of newly infected persons 15 to 24 years of age.[1] Since its origin from USA in 1981, has killed an enormous number of humankind throughout the world due to wide spread of the disease and lack of medications to cure the disease.[2] The data from 2002 estimates 3000 deaths per year from the disease and about 70,000 people living with HIV.[3] The data of 2007, globally, there were an estimated 33.2 million people living with HIV/AIDS infection, an increase from 29.5 million in 2001. However, the overall number of people living with HIV increased as new infections continued to occur, the annual incidence of new HIV infections declined from an estimated 3.0 million in 2001 to an estimated 2.7 million in 2007 as increasingly available highly effective antiretroviral treatment. In Asian country, there were about 5 million people with HIV infection in 2007.[4] 12% of the global population remains as the most heavily affected by HIV&AIDS in 2010.[5]

Nepal is a small landlocked country with multicultural, geographical richness and diversity. It covers an area of 147,181 $km^2$. According to the World Bank, HIV in Nepal is extremely heterogeneous, with respect to the most-at-risk populations, geographic distribution and risk factors in different geographic regions. The overall prevalence of HIV among adult, aged 15-49 years was estimated to be 0.30%. However, World Bank report suggests that due to limitations of Nepal's public health surveillance system, the actual number of infections is could be even higher.[5] HIV/AIDS is a major public health concern in Nepal since its isolation in 1988. As August 2008, the National Centre for AIDS and STD (Sexually Transmitted Disease) Control (NCASC) in Nepal reported that there were 12415 HIV positive people.[6] And after receiving HIV that Nepal has lost /is losing a lot of population yearly from the deadly disease.[7] HIV/AIDS is recognized as a global emergency demanding

the attention on the international health agenda and one of the most important public health problems.

Antiretroviral drugs have become the cornerstone of care and treatment for HIV infected people. Antiretroviral regimens improve survival rates and lower the incidence of opportunistic infections of HIV infected people.[6] In 1986, Zidovudine was developed as a first drug therapy for HIV/AIDS, and then the newer drugs such as NRTIs, NNRTIs and PIs were also developed. Though, none of them offer the complete treatment of the disease.[2] After the development of Antiretroviral therapy the disease condition has been moved to chronic condition as ARTs have increased the lifespan of HIV/AIDS patient without complete disease cure. In 2003 the government of Nepal started giving free ARV drugs in a public hospital and National guidelines for ARV treatment were developed in 2004 from Teku hospital. Now the ART service and counseling for HIV patients are free of cost through different ART centre and sub-centre. WHO recommended ART eligibility to patients with CD4, below 350cells/$mm^3$.[5]

Over the last decade, treatment of HIV with mono, dual or triple regimen of highly active antiretroviral therapy (HAART) has led to a stark decrease in HIV morbidity and mortality. Development of opportunistic infection and decrease of CD4 T cell count has ratcheted down since HAART has been employed for the management of HIV progression and it has precisely reduced the development of AIDS increasing the quality of life of HIV patients.[8] Although treatment for AIDS and HIV exit to decelerate the virus progressing, still there is not exact known cause.

Regarding the treatment with medications, adherence is defined as a patient's ability to follow a treatment plan, take medications at prescribed times and frequencies, and follow restrictions regarding food and other medications. Adherence is a primary determinant of the effectiveness of treatment and also considered as a major predictor of the survival of individuals living with HIV/AIDS infection >95% adherence is required in ART in order to prevent the emergence of resistant viral strains. Practically, this degree of adherence requires a patient on a twice-daily regimen to not miss or substantially delay more than 3 doses of antiretroviral medications per month. Adherence to antiretroviral therapy (ART) has been strongly correlated with HIV durable viral suppression, reduced destruction of CD4 cells.[5] Incomplete adherence is <95%.

Virological failure is >400 copies/ml HIV virus[9] and is currently associated with suboptimal adherence(<95%)[5,10] and/or suboptimal ART regimen.[11] Hence, the strict adherence to HAART and proper dosing of the ART is believed to maintenance of virological suppression. However, adherence and resistance relationship is quite complex.[12] Adherence program shows that significant reduction in viral load and improved CD4 counts.[13]

National Antiretroviral therapy guidelines developed by National centre for AIDS and STD control (NCASC) has suggested NRTIs, NNRTIs and PIS combination for the treatment of HIV where most drug regimen contains 2 NRTIS with either of PIS and NNRTIS. Though the most common drug regimen used is Zidovudine, Lamivudine and Nevirapine, there is a sometimes changed medication as per the drug toxicity, physiological changes and conditions and patient such as pregnant, children etc.[7]

**WHO clinical stage of HIV/AIDs**

**Clinical stage 1**

- Persistent generalized lymphadenopathy (PGL).
- Performance scale 1: Asymptomatic, normal activity.

**Clinical stage 2**

- Weight loss<10% of body weight.
- Unexplained chronic diarrhea >1 month.
- Unexplained prolonged fever (intermittent or constant) >1 month.
- Oral candidacies, within the past year.
- Several bacterial infections (e.g. pneumonia, pyomyositis) and /or performance scale 2, symptomatic, normal activities.

**Clinical stage 3**

- Weight loss >10% of body weight.
- Unexplained chronic diarrhea >1 month.
- Unexplained prolonged fever (intermittent or constant) >1 month.
- Oral candidacies, within the past year.
- Several bacterial infections (e.g. pneumonia, pyomyositis) and /or performance scale 3: bed-ridden < 50% of the day during the last month.

**Clinical stage 4**

- Pneumocystic carinii pneumonia.
- Toxoplasmosis of the brain.
- Crytoporidiosis, disease of an organ other than liver, spleen or lymphnodes.
- Herpes simplex virus (HSV) infection,
- Progressive multifocal Leuko-encephalopathy (PML).
- Candidiacies of the esophagus, trachea, bronchi or lungs.
- Atypical mycobacteriosis disseminated.
- Non Typhoid Salmonella septicemia.
- Extra pulmonary tuberculosis.
- Lymphoma.
- Kaposis sarcoma (KS).
- HIV encephalopathy.

Performance scale 4: bed ridden, 50% of the day during the last month

[HIV wasting syndrome: weight loss 10% of body weight plus eight unexplained chronic diarrhea (>1 month) and unexplained prolonged fever (>1 month)].

[HIV encephalopathy: clinical findings of disabling cognitive and / or motor dysfunction interfering with activities of daily living progressing over weeks to months in the absence of a concurrent illness or condition other than HIV infection that could explain the findings.].

## MATERIAL AND METHOD

### Study design

It is a retrospective study on HIV/AIDs patients over 2.5 years from April 2013. The data of HIV-infected patient's which available on ART centre of TUTH who received ART and having at least 3 CD4 T cells count report and 2 viral load report data was reviewed for adherence, CD4 T cells count and viral load in order to asses relationship between adherence and CD4 T cells s well as adherence and viral load over one year of therapy during the period of survey. The information regarding antiretroviral regimen and their proper use, different measure of laboratory report were recorded and these core indicators like proper use and laboratory report was evaluated based on indicator.

**Adherence CD4 T cells and viral load monitoring indicators**

- Adherence report made at ART centre through recommended method such as self report was recorded.
- At the same period, various laboratory indicators like Viral load, CD4 T cells count, opportunistic infection was observed.
- Different type of treatment failures like clinical, immunologic and virologic (<400 copies/ml) recorded on the patient's data was recorded.

**Type of study**

Retrospective.

**Study variables**

**Dependent variable**

- Stage of infection and use of ARV drugs.
- Laboratory findings(CD4 T cells, viral load etc).
- Adherence to medication.

**Independent variable**

- Socio-demographic variables.
- Age, gender.

**Study site and its Justification**

This study was carried out at Tribhubhan University Teaching Hospital (TUTH), ART centre Kathmandu, Nepal. The study was carried out for six months.

**Sampling Techniques**

The sampling technique was purposive sampling. Data collection was done by the principal investigator and all those whom fall in the inclusion criteria was taken for the study during the data collection period.

**Criteria for sample selection**

**Inclusion criteria**: HIV/AIDS patients above 18 years of age taking Anti Retroviral therapy from April 2013 to November 2015.

**Exclusion criteria**: Pregnant women, Neonates and Children <18.

**Collection tool**

HIV related history contained data of patient and laboratory findings/data sheet by using questionnaire.

**Plan for data management and analysis**

Data entry, checking, compiling and editing was done manually and data analysis was done as per the objectives of the study. Data analysis was done 20.0 version of statistical package for social sciences (SPSS) software. The age, sex, adherence status, antiretroviral regimen, CD4 T cells status and viral load status were shown in frequency and percentage. Effect of adherence on CD4 T cells and viral load, relation between CD4 cell count and viral load was done by using chi- square test, p value <0.5 was considered at a level of significance.

**Ethical consideration**

Ethical clearance was taken from IOM, TUTH, MMC, Department of Pharmacy and Tribhuvan University Institute of Medicine Institutional Review Board, Maharajgunj, Kathmandu, Nepal.

**IRB reference no.** 135(6-11-E)$^2$/073/074.

**RESULTS**

**Demographic studies**

**Table: 1 Demographic studies.**

| Characteristics | Frequency(N=66) | Percent% |
|---|---|---|
| **Sex** | | |
| Male | 32 | 48.5 |
| Female | 33 | 50.0 |
| TG | 1 | 1.5 |
| **Age group** | | |
| 18-27 | 9 | 13.6 |
| 28-37 | 29 | 43.9 |
| 38-47 | 22 | 33.3 |
| 48-57 | 4 | 6.1 |
| 58-67 | 2 | 3.0 |

Out of 66 patients 48.5% were male whereas 50.0% were female and 1.5% was TG. Among these patients the greatest number of patients was in the age group of 28-37 i.e 43.9%, followed by age group 38-37 covered 33.3% of patients. Likewise, group of 18-27 years covers 13.6% patient. The least percentage 9.1% of patients was found above 48 years.

**Status of CD4 T cells count**

**Table: 2 CD4 T cells count**

| Characteristics | Frequency(n=66) | Percent% |
|---|---|---|
| **CD4 count before ART** | | |
| 0-100 | 28 | 42.4 |
| 101-200 | 12 | 18.2 |
| 201-350 | 23 | 34.8 |
| 351-500 | 2 | 3.0 |
| >500 | 1 | 1.5 |
| **CD4 count at baseline** | | |
| 0-100 | 9 | 13.6 |
| 101-200 | 15 | 22.7 |
| 201-350 | 14 | 21.2 |
| 351-500 | 12 | 18.2 |
| >500 | 16 | 24.2 |
| **CD4 count at one year** | | |
| 0-100 | 2 | 3.0 |
| 101-200 | 8 | 12.1 |
| 201-350 | 14 | 21.2 |
| 351-500 | 17 | 25.8 |
| >500 | 25 | 37.9 |

Out of 66 patients, at the initiation of ART, the highest percentage of patient start ART with CD4 from 0-100 where 28(42.4%) patients fall. 12(18.2%) had CD4 count 101-200. 201-350 CD4 count covers 23 (34.8%) and 3(4.5%) patients were started ART >350 CD4 counts. Overall, 95.4% had ≤350 CD4 T cells counts whereas 4.5% had >350 CD4 counts.

Similarly, at six month investigation, 9(13.6%) patients had CD4 counts 0-100. 15(22.7%) had CD4 count 101-200. 14(21.2%) patients fall under CD4 202-350. >350 CD4 count was observed for 28(42.2%) patients. Likewise, at one year investigation, 2(3%) patients had CD4 counts 0-100. 8(12.1%) had CD4 count 101-200. 14(21.2%) patients fall under CD4 202-350. >350 CD4 count was observed for 42(63.7%) patients.

**Status of viral load**

**Table: 3 Viral load count**

| Characteristics | Frequency (n=66) | Percent% |
|---|---|---|
| **Viral load at baseline** | | |
| <400 | 51 | 77.3 |
| 400-10,000 | 12 | 18.2 |
| >10,000 | 3 | 4.5 |
| **Viral load at one year** | | |
| <400 | 63 | 95.5 |
| 400-10,000 | 2 | 3 |
| >10,000 | 1 | 1.5 |

Of 66 participants, at six month viral load investigation, 51(77.3%) patients had viral load <400 copies/ml, 18.2% patient had still viral load in between 400-10,000 copies/ml and 4.5% had viral load ≥10, 000 copies/ml.

In one year viral load investigation, 63(95.5%) patients had viral load <400coppies/ml, 3% patients had viral load in between 400-10,000coppies/ml and 1.5% had viral load ≥10, 000coppies/ml.

**Status of adherence**

**Table 4: Status of adherence.**

| Characteristics | Frequency(n=66) | Percent% |
|---|---|---|
| **Adherence in 1 month** | | |
| >95% | 64 | 97.0 |
| (80-95)% | 1 | 1.5 |
| <80% | 1 | 1.5 |
| **Adherence in 6 month** | | |
| >95% | 56 | 84.8 |
| 80-95% | 2 | 3.0 |
| <80% | 8 | 12.1 |
| **Adherence in 1 year** | | |
| >95% | 54 | 81.8 |
| 80-95% | 6 | 9.1 |
| <80% | 6 | 9.1 |

The one month of initiation of ART among 66 patients, >95% adherence was observed in the largest percentage of patients i.e. 97% (64) and adherence ≤95% was observed in 3% (2) patients.

Within six month of adherence monitoring, >95% adherence was observed in the largest percentage of patients i.e 84.8% (56) and ≤95% was observed in 15.1% (10).

Within one year of initiation of ART, >95% adherence was observed in the largest percentage of patients i.e 81.8% (54). And adherence ≤95% was observed in 18.2% (12) patients.

**Antiretroviral regimen**

**Table 5: Antiretroviral regimen**

| Characteristics | Frequency(n=66) | Percent% |
|---|---|---|
| ZDV/3TC + NVP | 11 | 16.7 |
| ZDV/3TC + EFV | 8 | 12.1 |
| TDF/3TC +EFV | 45 | 68.2 |
| TDF/3TC + NVP | 1 | 1.5 |
| ABC/3TC + EFV | 1 | 1.5 |

Out of 66 subjects, the most frequently used Antiretroviral combination was TDF/3TC+EFV i.e. 68.2% (45) patients. ZDV/3TC+NVP combination was prescribed for 16.7% (11) patients. For 12.1% (8) patients, ZDV/3TC +EFV were prescribed. Two combinations TDF/3TC+NVP and ABC/3TC +EFV were used for 1.5% and 1.5% of patient respectively.

**Association between baseline CD4 T cells count and Adherence**

**Table 6: Association between baseline CD4 T cells count and Adherence.**

| Characteristics | | Adherence | | P value |
|---|---|---|---|---|
| **CD4 count** | >95% | 80-95% | <80% | |
| 0-100 | 8(12.1%) | 0(0.0%) | 1(1.5%) | |
| 101-200 | 12(18.2%) | 1(1.5%) | 2(3.0%) | |
| 201-350 | 13(19.7%) | 1(1.5%) | 0(0.0%) | 0.730 |
| 351-500 | 10(15.2%) | 0(0.0%) | 2(3.0%) | |
| >500 | 13(19.7%) | 0(0.0%) | 3(3.0%) | |

Out of 66 HIV infected patients who were used ART, the baseline CD4 T cell count and adherence is shown in the Table 8. CD4 T cells count 0-100 was observed in 8(12.1%) patient when adherence was >95% and 1(1.5%) patient when adherence was ≤95%. 101-200 CD4 T cells count was observed in 12(18.2%) patients when adherence was >95% and 3(4.5%) patient when adherence was ≤95%. 13(19.7%) patient had CD4 T cells count 201-350 when adherence was >95% and 1(1.5%) patients had the same CD4 level when adherence was ≤95%. >350 CD4 T cell was observed in 23(34.9%) when adherence was >95% and 5(8.5%) patients when adherence was ≤95%. Overall, >95% adherence was observed in 56(84.8%) patients, 80-95% adherence was in 2(3%) patients and 8(12.1%) patient had adherence <80%. Also 9(13.6%) patients had CD4 T cell count 0-100, 15(22.7 %) patient had CD4 T cells 101-200, CD4 T cell 201-350 was observed in 14(21.2%) patients, and >350 CD4 T cell was observed in 28 (42.4%) patients. It has p=0.730.

**Association between one year CD4 T cells count and Adherence**

**Table 7: Association between one year CD4 T cells count and Adherence.**

| Characteristics | | Adherence | | P value |
|---|---|---|---|---|
| CD4 cells count | >95% | 80-95% | <80% | |
| 0-100 | 1(1.5%) | 0(0.0%) | 1(1.5%) | |
| 101-200 | 8(12.1%) | 0(0.0%) | 0(0.0%) | |
| 201-350 | 11(16.7%) | 2(3.0%) | 1(1.5%) | 0.346 |
| 351-500 | 13(19.7%) | 1(1.5%) | 3(4.5%) | |
| >500 | 21(31.8%) | 3(4.5%) | 1(1.5%) | |

Out of 66 HIV infected patients who were on ART, one year CD4 T cell count and adherence shown in the Table 9. CD4 T cells count 0-100 was observed in 1(1.5%) patient when adherence was >95% and 1(1.5%) patient when adherence was ≤95%. CD4 T cells count 101-200 was observed in 8(12.1%) patient when adherence was >95%. 11(16.7%) patient had CD4 T cells count 201-350 when adherence was >95% and 3(4.5%) patients had the same CD4 level when adherence was ≤95%. >350 CD4 T cell was observed in 34(51.5%) when adherence was >95% and 8(12%) when adherence was ≤95%. Overall, >95% adherence was observed in 54(81.8%) patients, 80-95% adherence was in 6(9.1%) patients and 6(9.1%) patient had adherence <80%. Also 2(3%) patients had CD4 T cell count 0-100, 8(12.1 %) patient had CD4 T cells 101-200, CD4 T cell 201-350 was observed in 11(31.8%) patients, and >350 CD4 T cell was observed in 42 (63.7%) patients. It has p =0.346.

**Association between baseline Viral Load and Adherence**

**Table 8: Association between baseline Viral Load and Adherence.**

| Characteristics | | Adherence | | P value |
|---|---|---|---|---|
| Viral load | >95% | 80-95% | <80% | |
| <400 | 42(63.6%) | 1(1.5%) | 8(12.1%) | 0.415 |
| 400- 10,000 | 11(16.7%) | 1(1.5%) | 0(0.0%) | |
| >10,000 | 3(4.5%) | 0(0.0%) | 0(0.0%) | |

Out of 66 patient, 42 (63.6%) patient had viral load < 400 copies/ml, 11(16.7%) patients had viral load 400-10,000 copies/ml and >10,000 viral load was observed in 3(4.5%) patients when adherence was >95%. When adherence was ≤95%, Viral load <400 copies/ml was observed in 9(13.6%) patient and 1(1.5%) patient had 400-10,000 copies/ml viral load. Overall, 56(84.8%) had adherence >95% and 51(77.3%) had <400 copies/ml viral load. 10(15.1%) patients had ≤95% adherence and had viral load in 15(22.7%) patients. It has p value 0.415.

**Association between one year Viral Load and Adherence**

**Table 9: Association between one year Viral Load and Adherence**

| Characteristics | | Adherence | | P value |
|---|---|---|---|---|
| **Viral load** | **>95%** | **80-95%** | **<80%** | |
| <400 | 52(78.8%) | 6(9.1%) | 5(7.6%) | |
| 400- 10,000 | 1(1.5%) | 0(0.0%) | 1(1.5%) | 0.349 |
| >10,000 | 1(1.5%) | 0(0.0%) | 0(0.0%) | |

Of 66 patients, 52 (78.8%) patients had viral load <400 copies/ml, 1(1.5%) patient had 400-10,000 copies/ml viral load and 1(1.5%) patient had >10,000 copies/ml when adherence was >95%. Viral load was <400coppies/ml was observed in 11(16.7%) patients and Viral load 400-10,000 copies/ml was observed for 1(1.5%) patient when adherence was ≤95%. It has p value 0.349.

## DISCUSSION

### Age distribution

The study of age distribution among HIV infected patients is shown in Table 1, in which greatest number of patients was of age group 28-37 years (43.9%). Though the age group division was not similar to that of study conducted by Mary B Cauldbeck et al which showed that 50% patients were age group 30-40.[14] Audrey E. Pettifor et al, explained that older (25–35 years) age group had more than one sexual partner and also engaging in commercial sex worker.[15] However the finding of MARCIA G.ORY et al, revealed that younger people were more prone to infection than older people.[16]

### Gender distribution

The variation in gender among HIV infected patients is shown in Table 1. Though the majority of patients were female (50%), no vast difference was found between male and female. Our result was similar to the study of Gina M. Wingood et al, which predicted that number of male and female will be equal by the year 2000, Since women the fastest growing gender with AIDs. Women are more liable to infect with HIV than men because the risk of acquiring HIV from a single act of intercourse is 8 times as high from men to women than women to men and another reason is female specific biological characteristics such as sex during menstruation, using oral contraceptive etc.[17,18]

**Status of CD4 T cells count over one year**

The status of CD4 count before ART initiation, at baseline and in one year is shown in Table 2. Our study showed the majority of patient started ART in the late stage of HIV infection (CD4 <100cell/mm$^3$) i.e.42.4% and ≤350 CD4 count was observed in 95.4% patients. The baseline CD4 level >350 was observed in 42.2% which was increased by 4.5% from initiation of therapy. The study of Kaufmann GR et al, supports our result, which defined that individuals with larger decreases in the CD4 T cell count before ART initiation had larger increases in the CD4 T cell count during the first 6 months of ART. CD4 T cell changes during first 3–6 months of ART reflect the capacity of the immune system to replenish depleted CD4 T lymphocytes.[19] While ≤350 CD4 count was observed in 57.5% patients. >350 cell/mm$^3$ CD4 T cells was observed in 63.7% patient at one year while ≤350 CD4 T cells count was observed in 36.3% patient which was lower than baseline and initiation. Therefore our finding points that CD4 T cells increase within a year and no matter how much CD4 was at entry. In contrast to our result, the study conducted by Gilbert R. Kaufmann et al, which showed that CD4 T cell counts seemed to reach a plateau after the first 2–3 years of ART. And also they noted that approximately two-thirds of patients had reached a CD4 T cell count >500 cells/ml but that the remaining one-third showed impaired CD4 T cell recovery. Therefore, these CD4 T cell count variation may be because of Older age, lower baseline CD4 T cell Count and longer duration of HIV infection were significantly associated with a CD4 T cell count <500 cells/ml at 5 years.[19]

**Status of viral load over one year**

The status of viral load shown is in Table 3. The majority of patient had viral load <400copies/ml, 77.3% in baseline viral load investigation. This value increased to 95.5% patient at one year. Our data support by the study of The study conducted by Gilbert R. Kaufmann et al, and Kaufmann GR et al, larger decrease in the plasma HIV-1 RNA load during the first 3 months of ART and during the first 6months.[19, 20] However the study of Wong JK et al, and McNabb J et al shows that magnitude of HIV virus reduction in patients with suppression of HIV RNA levels beyond 6 months has not been determined.[10,21]

**Status of adherence over one year**

The status of adherence over one year is shown in Table 4. The largest group, 97% of patient had adherence >95% (level above 95% is taken to be adherent i.e. missing one medication in twenty is acceptable[14]) in the one month adherence monitoring. However the study

conducted by Gretchen L. Birbeck et al, revealed that the adherence rates was good for 59.2% cases, where good means there is no documented adherence problem, in this finding adherence to ART seems lower.[22] At six month of ART initiation, 84.8% patients had >95% adherence to therapy. Though the value was high, this value was lower than one month adherence and was not similar to the study conducted by Alemayehu Amberbir et al, which showed that the rate of dose adherence in the study area was 96% at baseline.[23] The majority of patient having adherence >95% at one year is found in 81.8% patients and this value was also lesser than one month and baseline report of adherence. In our result, the changing pattern of adherence within a year was supported by the finding of Alemayehu Amberbir et al, which showed that self reported adherence rate was high in the study area. The study showed that adherence is a dynamic process which changes overtime and cannot reliably be predicted by a few patient characteristics that are assumed to vary with time.[23] Also the study conducted by Patrick O Erah et al, adherence is dependent on medication adverse effects and level of education of patients. confidentiality, occupational factors and stigmatization were the major reasons accounting for non-adherence.[24]

**Antiretroviral regimen**

The status of antiretroviral regimen is shown in Table 5. The frequently used antiretroviral regimen is TDF/3TC +EFV which are used by 68.2% patients. However the study conducted M. C. Marazzi et al, which showed that the common combinations prescribed were AZT + 3TC + NVP or d4t + 3TC + NVP.[13] Similarly the study of Sharada et al which showed that the most common regimen was Zidovudine, Lamivudine and Nevirapine.[25] Another finding of Nagalingeswaran Kumarasamy et al, which revealed that the most common first-line regimens were Stavudine + Lamivudine + nevirapine) (63%), Zidovudine + 3TC + NVP (19%), d4T + 3TC+ efavirenz (9%), and AZT +3TC +EFV (4**%)**.[26]

**Association of baseline and one year adherence with baseline and one year CD4 T cells respectively**

The association between baseline and one year CD4 T cell and baseline and one year adherence respectively is shown in Table 6 and 7 respectively. Regarding the association between baseline CD4 T cells and baseline adherence, our study showed that in >95% adherence, 50% patients had CD4 ≤350 and 34.9% patients had CD4 T cells ≥350. Similarly in adherence ≤95%, 7.5% patients had ≤350 CD4 T cells and 7.5% patients had CD4 count >350. Our study depicted that there is no significance relationship between CD4 T cells count

and adherence level (P =0.730). However, the study conducted by M. C. Marazzi et al, showed that the adherence program was confirmed by a relevant increase of CD4 counts.[13] In contrast to our result, the study conducted by Ajay K. et al, showed that low adherence and CD4 cell were independently associated with an increased viral rebound with clinically significant resistance. Therefore Clinicians and patients must set high adherence goals to avoid the development of resistance.[27] That means adherence has role to prevent HIV infection through increasing CD4 T cells.

Regarding the association between one year CD4 and adherence, our study showed that in >95% adherence, 30.35% patients had CD4 ≤350 and 51.5% patients had CD4 ≥350. 6% patient had CD4 ≤350 and ≥350 CD4 is observed in 12% patients when adherence was ≤95%. CD4 T cells count was not significantly associated with adherence (p =0.346.). The study conducted by Adrina Ammassari et al, supported our finding, there was inconsistent findings regarding the relationship of adherence and CD4 T cells. Also their study supported that some studies have documented better adherence in person with higher CD4 T cell counts however the direct effect of this association still has to be clarified in terms of question for instance, do patients with less advance (not late stage) HIV disease adhere better because of fewer HIV related symptoms or do person adhere worse fail to achieve viral suppression and immunological recovery ?.[28] However strong relationship between CD4 and adherence was found in study conducted by Evan Wood et al, which showed that the gains in CD4 cell count were observed among adherent patients. Their data also suggested that previous studies showing that CD4 cell counts <350 cells/mm3 may preclude a CD4 cell count response may have been confounded by patient non-adherence.[29]

**Association of baseline and one year adherence with baseline and one year viral load respectively**

The association between baseline and one year viral load and baseline and one year adherence respectively is shown in Table 8 and 9 respectively. Regarding the association between six month viral load and adherence, our data showed that <400 copies/ml viral load was observed in 63.6% patients and 21.2% patient had ≥400coppies/ml viral load when adherence was >95%. <400coppies/ml viral load is observed in 13.6% patient and ≥400 copies/ml viral load is observed in 1.5% patients when adherence is ≤95%.

Regarding the association between one year viral load and one year adherence, our data showed that <400coppies/ml viral load is observed in 78.8% patients when adherence is

>95%. This result was almost in accordance with the study conducted by Catherine Orrell et al, in which for those who were >95% adherent at One year 73.4% had a viral load of <400copies/ml.[9] 3% patients had viral load ≥400 copies/ml when adherence was >95%. When adherence was ≤ 95%, viral load <400coppies/ml was observed in 16.7% patients and ≥ 400coppies/ml viral load was observed in 1.5% patient. Our study shows that there is not significance relation between adherence and viral load (p=0.349). In contrary to our findings, the findings of JoCarol McNabb et al, adherence was significantly associated with virologic success: lower virus loads were associated with a rate of adherence of >80%. JoCarol McNabb et al, also suggest that although non adherence predicted virologic failure, virologic success was not always predicted by adherence: 27.5% of 40 subjects with suboptimal adherence rates (<90%) had complete virologic suppression. The relationship between adherence and viral load was not dependent on the study month.[10] Therefore suggestion from this study and other study is that we could not predict adherence and viral suppression always with good adherence.

## CONCLUSION

In our study, majority of patients were female among which younger age groups were more prone to HIV infection falling under productive age group which also affect country's economy. The largest group of patients started ART when CD4 T cells was 0-100 (late stage) which ultimately leads to increase barriers to HIV care. Delays in HIV care have serious health implications because opportunities to prevent further transmission through effective treatment with antiretroviral drugs are lost. Initiating treatment for HIV disease at an advanced stage leads to worse treatment outcomes than treatment started earlier and late stage also threats to success of therapy. Patients having >350 CD4 count was increased from baseline to one year of ART initiation and few patients had CD4 ≤350, which reflects that there was relatively good increment of CD4 T cell count over one year of treatment. Similarly, the patients having viral load >400 copies/ml was increased from baseline to one year, whereas patients having ≤400 copies/ml was decreased from baseline to one year, which reflects that there was relatively good viral suppression over one year of treatment and was the indicator of virologic success and it is necessary for survival on HIV infection. There was no significant association of adherence on improved CD4 T cells and reduced viral load in patients although increase in CD4 cells count and decrease in viral load along with good adherence after ART initiation was observed in majority of patients. In this study, TDF/3TC +EFV were the most frequently prescribed ART regimen.

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