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# SPECTRUM OF ANTIRETROVIRAL (ART) REGIMEN CHANGE AND CONTRIBUTING FACTOR AMONG ADULT HIV/AIDS PATIENT AT NEDJO GENERAL HOSPITAL,NEDJO TOWN, WEST WOLLEGA ZONE, OROMIA REGIONAL STATE, ETHIOPIA

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## ABSTRACT

**Background:** Human Immune Virus (HIV) is responsible for a worldwide pandemic and it is the cause of Acquired Immune Deficiency Syndrome (AIDS). According to latest statistics 33.4 million individuals worldwide are living with HIV, of which 15.7 million (47%) are women and 2.1 million (6.3%) are children under 15 years. In addition there are 2.7 million new infections and 2.0 million deaths from AIDS worldwide. **Objective:** To determine the reason and contributing factors of anti-retroviral regimen changes among patients on anti-retroviral therapy in ART clinic of Nedjo General Hospital. **Method:** A retrospective cross-sectional study was done using patient information sheet and physician diagnosis chart from January 1, 2008 to May, 2018. **Result & Conclusion:** Patients that changed their regimen were included in the study to identify the reasons for change and descriptive statistics were generated by calculating manually & using excels for figures. Out of 116 patients, 56% were females and 79.3% were in the age group 20-39. 47.4% were WHO clinical stage III patients and 50% of patients had missed their CD4 count. In 72.4% of patients initial treatment regimen was modified after six months, while, in 8.6% and 6 % of patient's initial regimen was modified less than a month and within two to three month time respectively ,the most common initial regimens were D4T/3TC/NVP (50%), AZT/3TC/NVP (21.5%) and D4T/3TC/EFV (12.9%) The main reasons for modification of therapy were toxicity (53.4%), new drug (25%), treatment failure (9.5%), new TB (6.9%), stock out (1.7%), and pregnancy (0.9%) respectively. The main toxicity observed was peripheral neuropathy (51.6%) followed by rash (19.4%) and anemia (12.9%). Among toxicities observed 43.5% were due to D4T/3TC/NVP, and the remaining 24.2 %, 16.1 %, 8.1 %, 4.8 %, 1.6 % and 1.6 % were due to AZT/3TC/NVP, D4T/3TC/EFV, AZT/3TC/EFV, TDF/3TC/EFV, TDF/3TC/NVP, and TDF/3TC/LPVr respectively. D4T containing regimens accounted for 100% of the peripheral neuropathy observed, while NVP containing regimens accounted for 99.9% of the rashes reported and AZT containing regimens accounted for 100% of the Anemia observed. Toxicity was the main reason for initial regimen modification, D4T based regimens had high incidence of peripheral neuropathy.

**KEYWORD:** Nedjo General Hospital, Regimen change, Contributing Factor, Antiretroviral therapy.

## INTRODUCTION

Human Immune Virus (HIV) is responsible for a worldwide pandemic and it is the cause of Acquired Immune Deficiency Syndrome (AIDS).[1] According to latest statistics 33.4 million individuals worldwide are living with HIV, of which 15.7 million (47%) are women and 2.1 million (6.3%) are children under 15 years. In addition there are 2.7 million new infections and 2.0 million deaths from AIDS worldwide, albeit recent improvements in access to Antiretroviral Therapy (ART). About 22 million people have died from the HIV/AIDS worldwide since the beginning of the pandemic in the early 80s The proportion of females infected is becoming increasingly significant, with 55% of the infection from Sub-Sahara Africa in 1999 being attributed to women.[2]

Sub-Sahara Africa remains the region most heavily affected by HIV. 1.9 million People living in sub-Sahara Africa become newly infected with HIV, bringing the total number of people living with HIV to 22.4 million.

Moreover an estimated 1.4 million AIDS related deaths occur in sub-Sahara Africa. But the rate of new HIV infections and death has slightly declined as a result of improved access to ART.[3]

In Kenya, already more than 2 million people are estimated to have been infected from 1985 when the first case of AIDS was reported.[4]

The HIV/AIDS epidemic in Ethiopia continues to pose a threat to the lives of its people. According to the single point estimate in 2007, 977,394 people are living with the virus in Ethiopia. Resulting, a prevalence rate of 2.1% (1.7% among males and 2.6% among females;

7.7% urban and 0.9% rural areas) for a total estimated population of 73 million. The number of new infections is 125,528 including 14,147 HIV positive births of which females' account 57.4%.[5]

The remarkable increase in access to life-saving ART continued in 2012. Fully 1.6 million more people were receiving ART in low- and middle-income countries at the end of 2012, compared with a year earlier – the largest annual increase ever – with the greatest contribution coming from the WHO African Region. The 300 000 people who were receiving ART in low-and middle-income countries in 2002 increased to 9.7 million in 2012.(22) Since beginning of Highly Active Antiretroviral Therapy (HAART) in 1996, there have been dramatic declines in morbidity and mortality due to HIV. But these advancements were not without a cost in terms of drug resistance and side effects.[6]

A concern about these negative effects has lead to a more conservative approach to the timing of initiation of therapy and to clinical trials of intermittent therapy in an attempt to decrease the total exposure to drugs over time. ART brings a complex series of choices; when to initiate therapy, what regimen to use, which class of drugs to use, when to change therapy, and which alternative drugs to use.[7]

According to the Standard Treatment Guideline of Ethiopia; the criteria for initiating ART for adults and adolescents are; 1) if CD4 testing is available (a) WHO stage IV disease irrespective of CD4 cell count. (b) WHO stage III disease with CD4 cell counts below 350/mm3. 2) If CD4 testing unavailable; WHO stage III and IV disease irrespective of total lymphocyte count or WHO stage II diseases with a total lymphocyte count bellow 1200/mm3.[8]

Accordingly, the first line ARV regimen in Ethiopia include a triple therapy, two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one Protease Inhibitor (PI), if this is not possible, a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) or else a triple therapy of three NRTIs. Based on the guideline, common ART regimens in Ethiopia are; TDF/3TC/EFV, AZT/3TC/EFV, AZT/3TC/NVP, D4T/3TC/NVP or D4T/3TC/EFV.[9]

There are many factors that lead to the ineffectiveness of Antiretroviral (ARVs) and change in the combinations. Rationale for treatment switch may be; either pre-emptive (risk of long term toxicity, poor adherence, desire for pregnancy, a sub-optimal regimen, co-morbidity, etc.), when virological suppression is usually retained or reactive to virological rebound or (because of resistance or poor adherence) or an established acute and/or chronic toxicity.[10]

Toxicity or Adverse Drug Reaction (ADR) starting from simple rash up to life threatening adverse effects like hepatotoxicity, mitochondrial damage and bone marrow toxicity, create adherence and compliance problems.[11]

After the introduction of ART, the overall AIDS related morbidity and mortality have been markedly decreased. But it is still high in sub-Saharan Africa. Africa is the region most affected by virus. The HIV/AIDS epidemics spreading through the countries of sub-Saharan Africa. Africa's HIV/AIDS epidemic has had important effects on society, economics, and politics in the continent.[3]

According to single point estimate in 2007 based on AIDS in Ethiopia 6$^{th}$ report, it was estimated there were 977,394 people living with the virus, and of these 258,264 require ART. From this data we can understand that how HIV is a major problem.[13]

There are many factors that lead to the ineffectiveness of ARVs and lead to change in the combination. Rational for treatment switch may be; either pre-emptive (because the risk of long term toxicity, poor adherence, a desire for pregnancy, a sub-optimal regimen, co morbidity, etc) when virological suppression is usually retained or reactive to virological rebound or (because of resistance or poor adherence) or an established acute and/or chronic toxicity.[10]

Toxicity or ADR create adherence problems and affect patients` willingness to take drugs. Starting from simple rash up to life threatening adverse effects like hepatptoxicity, mitochondrial damage and bone marrow toxicity.[13]

Except a study conducted in tertiary care Hospital in southern part of Ethiopia (Woldmedhin and Wabe, 2012), the pattern of modification of ART regimen and factors responsible for the modification are not well studied and data on modification of HAART are scarce in Ethiopia. Furthermore, no study focuses on modification of ART regimen in primary care hospitals which are fundamental in the health delivery system, serving a catchment area of 250,000 populations (Meseret Wube and Andualem, 2013).

Thus, ART brings a complex series of choices; when to initiate therapy, what regimen to use, which class of drugs to use, when to change therapy, and which alternative drugs to use. Therefore, the aim of this study was to assess reasons for initial ART regimen change in Nedjo General Hospital. This study would provide a valuable assistance to the concerned organizations especially for health facilities in handling the causes for switching and making the possible amendment.

This study also can potentially provide a long term strategic approach to initial and subsequent decision regarding ART. Moreover, the result would be of paramount importance for being as a baseline for further study.

## 2. METHODOLOGY

### 2.1 Study setting

The study was conducted in Nedjo General Hospital (NGH), Nedjo town, Western Wollega zone, Oromia region, western Ethiopia which is found at 506 km from Addis Ababa. According to the central statistical Agency of 2013 G.C, the current population size of Nedjo is 24,400. The dominant ethnic group is Oromo. The town has governmental and private organizations/ service providers to the community such as Government Hospital and Health center, elementary, Junior Secondary and preparatory schools and colleges. Telephone, electric, banks, post office, private pharmacy, clinics, drug vendors, etc are from the most prominent mentionable services provided in Nedjo town(Central statistical authority 2000. Statistical abstract 1999. Addis Ababa Ethiopia CSA).

NGH has many departments and wards like Outpatient department (OPD), medical ward, gynecology and obstetrics ward, pediatrics ward and surgical ward. It delivers diversified health services and clinics including the emergency services, eye clinic, dental clinic, mother and child health (MCH), psychiatry clinic, laboratory, X-ray, and follow up of chronic disease like TB and HIV AIDS. The Hospital possesses outpatient, inpatient, emergency and ART pharmacies.

### 2.2 Study Design and Period

A retrospective cross sectional study was done by reviewing patient information sheet from January 1, 2008 to May, 2018.

### 2.3 Source Population

All patient information sheets of HIV/AIDS patients who take ART in Nedjo General Hospital from January 1, 2008 to May, 2018.

### 2.4 Study Population

The study population was patient information sheet of HIV/AIDS patients who had undergone switching ART regimen in Nedjo General Hospital.

### 2.5 Inclusion and Exclusion Criteria

#### 2.5.1 Inclusion criteria

All HIV/AIDS patients who are on ART drugs and are undergone spectrum of therapeutic change in Nedjo General Hospital Hospital. .Patients change only initial regimen.

#### 2.5.2 Exclusion criteria

Those patients who undergone regimen change more than one times. All HIV/AIDS patients on ART drugs who are less than 18 years old.

### 2.6 Study variable

#### 2.6.1 Dependant Variables

Change of regimen
Prevalence of regimen change

#### 2.6.2 Independent Variables

Age Sex
Type of initial regimen Pregnancy
Co morbidity

### 2.7 Sample size and sampling technique

No sampling technique was done because all patients who had changed their initial regimen from January 1, 2008 to December 31, 2012 were included

### 2.8 Data collection process

Data was collected using data collection format. A well-structured data collection format containing the variables to be measured are designed, developed and utilized by the principal investigator.

### 2.9 Data analysis and presentation

The data's were categorized and analyzed manually using calculator for statistical analysis. The result was interpreted and presented using tables and figures.

### 2.10 Quality assurance

The clarity and completeness checkup of data collection formats was under taken before the actual data collection and data clearing was done every day, formats with insufficient information was excluded from the study to avoid error. Then collected data was processed and retained cautiously in the line of its objective.

### 2.11 Ethical consideration

A formal letter was written from college of medical & health science, department of pharmacy of Wollega University to Nedjo General Hospital in order to get permission to conduct the study. The confidentiality of patients is secured throughout the study periods without writing full patient names by using codes.

### 2.12 Operational definition

**Anti Retroviral Therapy:** Treatment that suppresses or stops a retrovirus. One of the retrovirus is the human immunodeficiency virus (HIV) that causes AIDS.

**Drug Side effect**: any unwanted effect of a pharmaciteutical product occurring in doses normally used by a patient which is related to pharmacologic property of the drug.

**Highly active antiretroviral therapy:** a combination of drugs including NRTIs, NNRTIs and Protease inhibitors.

**Regimen**: a drug or combination of drug used for one course of treatment.

**Regimen change:** In this study, regimen change refers to change in either of the following: dose, frequency and/or change or modification of one or more drugs used in the possible combinations of either of first line drugs used in ART. It also includes a change of entire regimen within first line or from first line to second line.

**Treatment Failure:** can be defined as a suboptimal response to therapy. It is often associated with virologic failure, immunologic failure and/or clinical progression (**STG FOR PRIMARY HOSPITALS 2010).**

**Immunological failure:** is fall of CD4 count to baseline (or below) or 50% fall from on-treatment peak value or persistent CD4level below 100 cells/mm3 **(STG FOR PRIMARY HOSPITALS 2010).**

**Clinical failure:** is either occurrence of new or recurrent stage4 condition like TB, candidacies, pneumonia, herpes simplex, toxoplasmosis, etc. **(STG FOR PRIMARY HOSPITALS 2010).**

### 2.13 Limitation of the Study

The findings of this study should be interpreted with some limitations. These include, lack of appropriately filled patient information sheet, and the retrospective study might not allow for a direct investigation of causal relationship between the factors studied and the outcome of interest. The study collected the main reasons as reported by physician for modification of treatment, but reasons for modification are often interrelated.

## 3. RESULTS

### Demographic Characteristics

The mean age of patients was 39 years. Majority of the patients (79.3%) were in the age range of 20-39 years majority (56 %) of the patients were females, as shown in *Table 1*.

**Table 1: Age and Sex distribution of the HIV/AIDS patients who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**

| *Demographic characteristics* | | Frequency | % |
|---|---|---|---|
| **Age group** | | | |
| 20-24 | | 11 | 9.5 |
| 25-29 | | 24 | 20.7 |
| 30-34 | | 37 | 31.9 |
| 35-39 | | 20 | 17.2 |
| 40-44 | | 12 | 10.3 |
| 45-49 | | 6 | 5.2 |
| 50-54 | | 3 | 2.6 |
| 55-59 | | 2 | 1.7 |
| ≥65 | | 1 | 0.9) |
| Sex | Female | 65 | 56 |
| | Male | 51 | 44 |

### WHO Clinical Stage and CD4 Count

A majority of the patients 47.4 % of patients were WHO clinical stage III, while 11.2 % were WHO clinical stage IV as depicted in *Fig- 1.* Most patients (50 %) the initial CD4 count was not recorded and (41.4%) had CD4 count bellow 350 cells/mm3, illustrated in *Fig-2.*

**Table 2: Initial WHO clinical stage study population in Nedjo General Hospital from January 1, 2008 to May, 2018.**

| WHO stage | Frequency | % |
|---|---|---|
| I | 34 | 29.3 |
| II | 14 | 12.1 |
| III | 55 | 47.4 |
| IV | 13 | 11.2 |

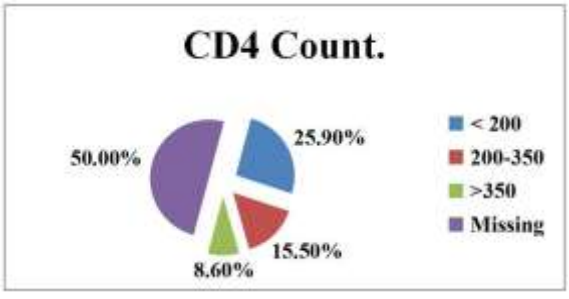


**Fig 2: CD4 count of HIV/AIDS patients who changed their initial regimen in Nedjo hospital, January 1, 2008 to May, 2018.**

### Antiretroviral Treatment Regimens and Causes of Change

A majority (50 %) of the patients were on D4T/3TC/NVP at the beginning of the antiretroviral

treatment and the rest were on AZT/3TC/NVP (21.5%), D4T/3TC/EFV (12.9 %), AZT/3TC/EFV (10.3 %), TDF/3TC/EFV (3.4 %), TDF/3TC/NVP and TDF/3TC/LPV/r (0.9%) as shown in *Table 3.*

The main reasons for modification of treatment regimen were toxicity/side effects (53.4 %), new drug available (27.5 %), and treatment failure (9.5 %) [Clinical 5.2 %, immunological 4.3 %], new TB (6.9 %), stock out (1.7 %), and pregnancy (0.9 %) as shown in *Table 3 or Fig-3.*

**Table 3: Common reasons for modification by first treatment regimens of HIV/AIDS patients, who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**

| *Initial regimens* | Reasons | | | | | |
|---|---|---|---|---|---|---|
| | **Toxicities N(%)** | **Pregnancy N(%)** | **New drug N(%)** | **Treatment failure N(%)** | **New TB N(%)** | **Stock out N(%)** |
| D4T/3TC/NVP | 27 (43.5) | - | 29 (90.6) | 1(9) | 1(12.5) | - |
| D4T/3TC/EFV | 10 (16.1) | - | 3(9.4) | 2(18.2) | - | - |
| AZT/3TC/EFV | 5 (8.1) | 1(100) | - | 6(54.5) | - | - |
| AZT/3TC/NVP | 15 (24.2) | - | - | 2(18.2) | 7(87.5) | 1(50) |
| TDF/3TC/NVP | 1 (1.6) | - | - | - | - | - |
| TDF/3TC/EFV | 3 (4.8) | - | - | - | - | 1(50) |
| TDF/3TC/LPV/r | 1 (1.6) | - | - | - | - | - |

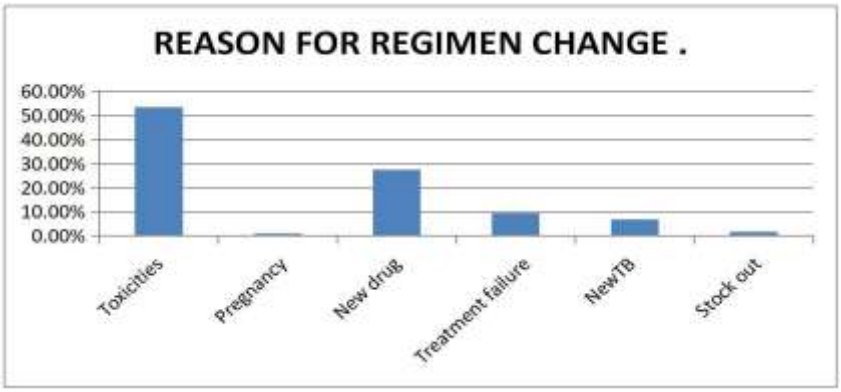


**Fig. 3: Common reasons for modification by first treatment regimens of HIV/AIDS patients who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**

From all toxicity reported, peripheral neuropathy accounted 51.6 % being the most common followed by rash (19.4 %) and Anemia (12.9 %) as depicted in *Fig-4.*

Among toxicities observed 43.5% were due to D4T/3TC/NVP, and the remaining 24.2 %, 16.1 %, 8.1 %, 4.8 %, 1.6 % and 1.6 % were due to AZT/3TC/NVP, D4T/3TC/EFV, AZT/3TC/EFV, TDF/3TC/EFV, TDF/3TC/NVP, and TDF/3TC/LPVr respectively. D4T containing regimens accounted for 100% of the peripheral neuropathy observed, while NVP containing regimens accounted for 99.9% of the rashes reported and AZT containing regimens accounted for 100% of the Anemia observed (*Table 3*).

**Table 4: Toxicities reported as reason for initial treatment regimen change by first treatment regimen of HIV/AIDS patients who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**

| *Toxicities* | Initial Regimens | | | | | | |
|---|---|---|---|---|---|---|---|
| | **D4T/3TC/NVP N (%)** | **D4T/3TC/EFV N (%)** | **AZT/3TC/EFV N (%)** | **AZT/3TC/NVP N (%)** | **TDF/3TC/NVP N (%)** | **TDF/3TC/EFV N (%)** | **TDF/3TC/LPV/r N (%)** |
| Nausea | - | - | - | 2(100) | - | - | - |
| P. neuropathy | 22(68.7) | 10(31.3) | - | - | - | - | - |
| Numbness/tingling | 3(100) | - | - | - | - | - | - |
| Diarrhea | - | - | - | - | - | 1(100) | - |
| Lipoatrophy | 1(100) | - | - | - | - | - | - |
| Anemia | - | - | 4(50) | 3(37.5) | - | - | 1(12.5) |
| Rash | 1(8.3) | - | - | 10(83.3) | 1(8.3) | - | - |
| Jaundice | - | - | - | - | - | - | - |
| Anxiety/night mare | - | - | 1(33.3) | - | - | 2(66.6) | - |

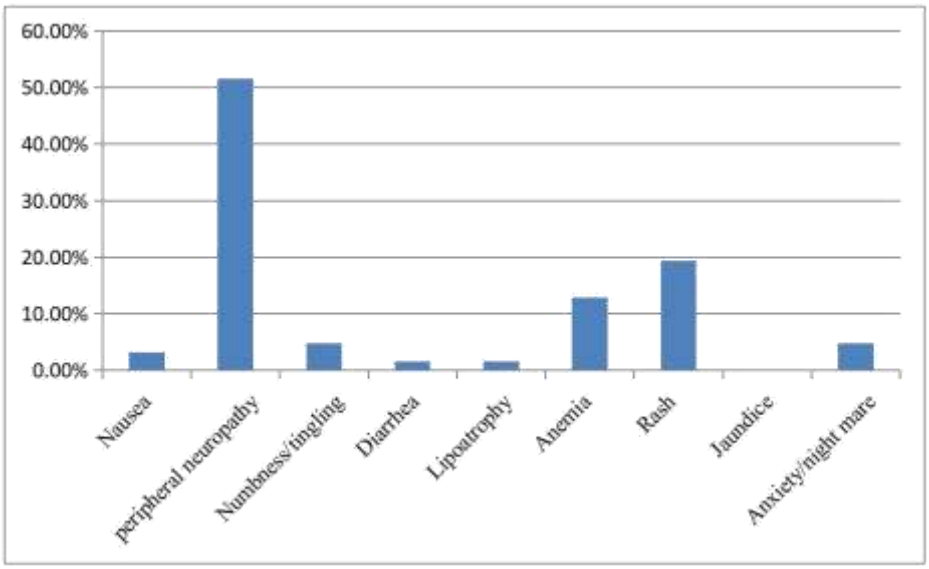


**Fig. 4: Toxicities reported as a reason for initial treatment change in Nedjo General Hospital, January 1, 2008 to May, 2018**.

**Duration of Initial Antiretroviral Treatment before Regimen Change**

In 72.4% of patients initial treatment regimen was modified after six months, while, in 8.6% and 6 % of patient's initial regimen was modified less than a month and within two to three month time respectively *Fig -5*. Of the patients who changed their initial regimen after six months 63.1% and 16.6% were on D4T/3TC/NVP and D4T/3TC/EFV respectively as shown in table-5.

**Table 5: Weeks on initial antiretroviral treatment by treatment regimen of HIV/AIDS patients who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**

| *Initial Regimens* | Number of the patient stayed weeks on initial ART regimen | | | | | |
|---|---|---|---|---|---|---|
| | < 4 N(%) | 4-8 N(%) | 8-12 N(%) | 12-16 N(%) | 16-20 N(%) | >24 N(%) |
| D4T/3TC/NVP | 3(30) | 1(16.6) | - | - | 1(25) | 53(63.1) |
| D4T/3TC/EFV | - | - | - | - | 1(25) | 14(16.6) |
| AZT/3TC/EFV | - | 1(16.6) | 1(14.3) | 1(20) | 1(25) | 8(9.5) |
| AZT/3TC/NVP | 5(50) | 3(50) | 6(85.7) | 3(60) | - | 8(9.5) |
| TDF/3TC/NVP | - | 1(16.6) | - | - | - | - |
| TDF/3TC/EFV | 2(20) | - | - | - | 1(25) | 1(1.2) |
| TDF/3TC/LPV/r | - | - | - | 1(20) | - | - |

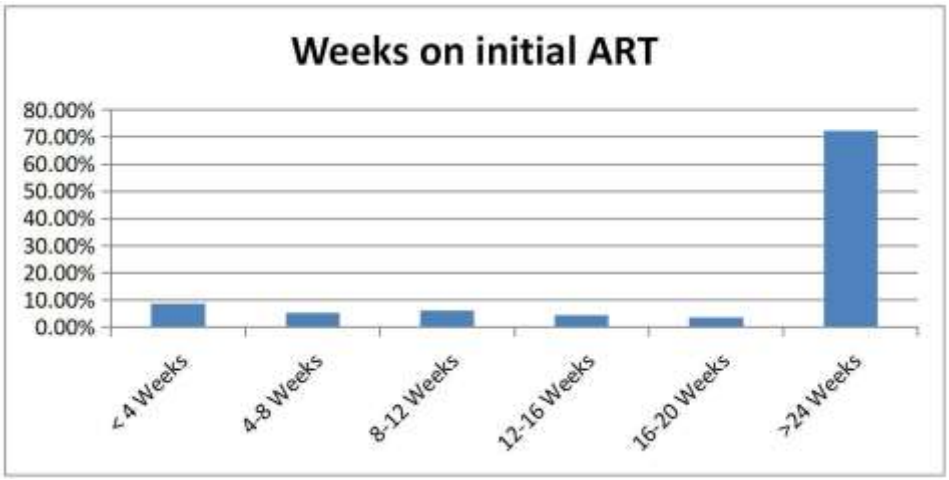


**Fig. 5: Percentage of HIV/AIDS patients on initial ART regimen per duration of therapy before switching in Nedjo hospital, January 1, 2008 to May, 2018.**

Among the initial regimen changes after six months of therapy 41.9% and 37.2% were due toxicity and new drug available respectively as shown in Tabel-6.

**Table 6: Common reasons for modification by duration of initial regimen of HIV/AIDS patients who changed their initial regimen Nedjo General Hospital from January 1, 2008 to May, 2018.**
[3]

| ***Reasons*** | **Number of the patient stayed weeks on initial ART regimen** | | | | | |
|---|---|---|---|---|---|---|
| | **< 4 N(%)** | **4-8 N(%)** | **8-12 N(%)** | **12-16 N(%)** | **16-20 N(%)** | **>24 N(%)** |
| Toxicities | 9(14.5) | 5(8.1) | 7(11.2) | - | 5(8.1) | 36(58.1) |
| Pregnancy | - | - | - | - | - | 1(100) |
| New drug | - | - | - | - | - | 32(100) |
| Treatment failure | - | - | - | - | - | 11(100) |
| New TB | 1(12.5) | 1(12.5) | 1(12.5) | - | - | 5(62.5) |
| | | | | | | |
| Stock out | - | - | 1(50) | - | - | 1(50) |
| | | | | | | |

## 4. DISCUSSION

A majority of the patients, 72.9 % of the patients in this study were on D4T based regimens, D4T/3TC/NVP (50 %) and D4T/3TC/EFV (12.9 %) While the rest were on AZT/3TC/NVP (21.5%), AZT/3TC/EFV (10.3 %), TDF/3TC/EFV (3.4 %), TDF/3TC/NVP and TDF/3TC/LPV/r (0.9%) each. The result of this study was not consistent with the studies done in Southern India (Kumarasamy *et al.*, 2006), Malawi (Bartlett and Shao, 2009), Cote d'Ivoire (Mess *et al*., 2010) , southern Ethiopia (Woldmedhin and Wabe, 2012) and Addis Ababa (YOHANNES T. JIMA,2013) where D4T/3TC/NVP accounts for 63%, 64.9%, 58% , 54.70% and 10 % respectively. Difference in WHO clinical stage, contraindications, co morbid situations, drug-drug interaction due to co morbidities and stock status could be the possible factors that might have contributed to the variation.

New drug available (27.5 % ) , and treatment failure(9.5 %) were the second and the third causes of ART regimen switching, opposite to the studies in Uganda (Kiguba, 2007) and Southern India (Kumarasamy *et al.*, 2006), Addis Ababa (YOHANNES T. JIMA,2013), southern Ethiopia (Woldmedhin and Wabe, 2012), and Nekemte (Meseret Wube, Andualem,2013).

From all toxicities, peripheral neuropathy was the most common reason for modification, similar to studies in Addis Abeba (YOHANNES T. JIMA, 2013) ,*and* southern Ethiopia (Woldmedhin and Wabe, 2012),but opposite to studies in Southern India (Kumarasamy *et al*., 2006),Colorado(Wanchu AJ, Pareek S, and Banbery P,2006) ,and Nekemte (Meseret Wube, Andualem,2013). D4T containing regimens accounted for 100% of the peripheral neuropathy observed, This is most probably due to the reason that most of the patients in this study were on D4T-based regimen of D4T/3TC/NVP and D4T/3TC/EFV, were initially with advanced HIV infection, and increased duration of ART are also significantly associated with peripheral neuropathy (van Griensven *et al.*, 2007).

Rash and anemia were second and third most causes for modification. Rash was mainly due NVP containing regimen AZT/3TC/NVP (83.3%),D4T/3TC/NVP (8.3 %),and TDF/3TC/NVP(8.3%) regimens which coincides with a study that stipulates the mechanism of NV P induced skin rash (Popovic *et al.*, 2006).

Anemia were seen in 50%, 37.5%, and 12.5% of the patients on AZT/3TC/EFV, AZT/3TC/NVP and, TDF/3TC/LPV/r respectively. Unlike the Peru's study, Study done in Peru reported anemia as a main reason for discontinuation, and associated this finding with the use of standard 600 mg ZDV in low weight patients (Bangsberg *et al.*, 2006), in this study, was likely to be due to lack of adequate baseline anemia assessment and the fact that no close monitoring of anemia at the study site.

CNS toxicities were the fourth causes for modification. Anxiety/ nightmares and Numbness/tingling were seen in 4.8%, 3.2% and 1.6% of the patients on D4T/3TC/EFV, TDF/3TC/EFV, and AZT/3TC/EFV respectively. Which may be due to EFV and studies show that EFV is associated with CNS toxicity, moreover, a CYP2B6 allelic variant is more common in African-Americans which is associated with significantly greater EFV plasma exposure (Haas *et al.*, 2004).

Availability of new drug was the second major reason for modifying ART drugs in this study, Unlike to the studies in Uganda (Kiguba, 2007) and Southern India (Kumarasamy *et al.*, 2006), Addis Abeba (YOHANNES T. JIMA,2013), southern Ethiopia (Woldmedhin and Wabe, 2012), and Nekemte (Meseret Wube, Andualem,2013).This was likely to be due to the remarkable increase in access to life-saving ART continued in 2012. Fully 1.6 million more people were receiving ART in low- and middle-income countries at the end of 2012, compared with a year earlier – the largest annual increase ever – with the greatest contribution coming from the WHO African Region(Journal of Glob Health Action.2010).

9.5% of patients changed their initial regimen due to treatment failure which occurred in patients on AZT/3TC/EFV(54.5%), AZT/3TC/NVP(18.2%), D4T/3TC/EFV(18.2%), and D4T/3TC/NVP(9%).This may be explained by differences in primary resistance to NRTIs or NNRTIs containing regimens (Dorrucci *et al*., 2001).

Co-morbidities in patients with advanced disease and concurrent treatments for opportunistic diseases may affect antiretroviral tolerance and thereby increase risk of toxicities (Cesar *et al.*, 2010). 6.9% of the patients changed their regimen due to tuberculosis and it was the only co morbidity reported in this study which is consistent with the study in Cote d'Ivoire (Mess *et al.*, 2010) and hospitals in southern Ethiopia (Alemu and Sebastian, 2010; Woldmedhin and Wabe, 2012). 87.5%, 12.5% of the patients on AZT/3TC/NVP and D4T/3TC/NVP were switched. The most probable reason being over lapping drug toxicity of NVP with anti TB drugs and potential for drug interaction as TB drugs like rifampine is enzyme inducers.

Contrary to studies in Southern India (Kumarasamy *et al*., 2006) and Uganda (Kiguba, 2007) cost was not a major reason for ART regimen change because ARV drugs are provided to patients free of cost. Despite the cost free service stock out problems accounted 1.7% of the treatment regimen Change which is a result of poor pharmaceutical stock management system either at the hospital or national level.

Unlike the studies in Cote d'Ivoire (Mess *et al*, 2010), Addis Ababa (YOHANNES T.JIMA, 2013), Nekemte (Meseret Wube, Andualem, 2013), and southern Ethiopia (Alemu and Sebastian, 2010; Woldmedhin and Wabe, 2012), Pregnancy didn't account for the lion's share for regimen switch in this study. Only 0.9% of patients changed their initial regimen due to Pregnancy which occurred in patients on AZT/3TC/EFV. This switch was due to the recommendation of the Ethiopian guideline to avoid teratogenic effect of EFV in pregnant women during the first trimester. Contrary to the recommendation of the guideline, current studies reveal no increased risk of overall birth defects in women exposed to EFV during the first trimester of pregnancy (Ford *et al.*, 2010).

A noticeable link was observed between common reasons for Modifications of regimen and initial regimen. Similarly, toxicities like peripheral neuropathy, rash and anemia were associated with respective initial regimen. However, weeks of stay on initial regimen had no important association with initial regimen rather weeks of stay on initial regimen had important association with respect to common reasons for regimen changes because the longer stay the higher probability of regimen change. This was consistent with the findings reported in the Addis Ababa (YOHANNES T.JIMA, 2013), and southern Ethiopia (Alemu and Sebastian, 2010; Woldmedhin and Wabe, 2012).

## 5. CONCLUSION AND RECOMMENDATIONS

### 5.1 Conclusion

The result of this study indicated toxicity as the main reason for modification of initial ARV drugs among the study population. Peripheral neuropathy was the leading cause for modification of HAART, D4T containing regimens accounted for 100% of the peripheral neuropathy observed, while NVP containing regimens accounted for 99.9% of the rashes reported and AZT containing regimens accounted for 100% of the Anemia observed. While new drug, treatment failure, new TB, stock out and, pregnancy, were the rest reasons for initial antiretroviral regimen changes in this study. Majority (72.4%) of patients their initial treatment regimen was modified after six months, of the patients who changed their initial regimen after six months 63.1% and 16.6% were on D4T/3TC/NVP and D4T/3TC/EFV respectively. Tuberculosis was the only co-morbidity disease reported in this study and all patients who switched were due to occurrence of tuberculosis after starting ARV drugs on NVP based regimen.

### 5.2 Recommendations

Proper clinical recording, and there had to be sufficient qualitative and well-effective laboratory equipment. Updating ART guidelines as pharmacotherapy is dynamic and improvements in pharmaceutical procurement and stock management systems at hospital or national level, As much as possible, clinicians should stick to the national antiretroviral drug use guidelines for the management and follow up of patients receiving HAART are recommended.

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## ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| ABC | Abacavir |
| ADR | Adverse drug reaction |
| AEs | Adverse effects |
| AIDS | Acquired immunodeficiency syndrome |
| ART | Antiretroviral therapy |
| ARV | Antiretroviral |
| AZT /ZDV | Zidovudine |
| DDI | Didanosin |
| EFV | Efavirenz |
| HAART | Highly active antiretroviral therapy |
| HIV | Human immune virus |
| D4T | Stavudine |
| NNRTI | Non- nucleoside reverse transcriptase inhibitor |
| NRTI | Nucleoside reverses transcriptase inhibitor |
| OI | Opportunistic infection |
| PI | Protease inhibitor |

| | |
|---|---|
| PLWHA | People living with HIV/AIDS |
| TDF/ TFV | Tenofovir |
| TB | Tuberculosis |
| 3TC | Lamivudines |
| WHO | World health organization |
| G.C | Gregorian calendar. |

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