A SURVIVAL ANALYSIS OF HIV/AIDS PATIENTS IN THE CASE OF DEBRE BERHAN REFERRAL HOSPITAL

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ABSTRACT

This study was conducted in Debre Berhan, located 125 k.m distances from Addis Ababa capital of Ethiopia. Debre Berhan is a city in central Ethiopia and located in Amhara region. This case study focuses on the survival analysis of HIV/AIDS patients. HIV refers to human immunodeficiency virus; it is a collection of virus those most likely mutated decades ago from a virus that infected chimpanzees to a virus that infects humans. It began to spread beyond the African continent in the late 1970s and is now endemic worldwide. HIV infection leads to low levels of CD4+ T cells that in turn make the body susceptible to opportunistic infection. The introduction of ART in 1996 was a turning point for thousands of people with sophisticated health care. Retrospective fife years HIV/AIDS Disease cohort study was conducted in patients, who were undergoing Antiretroviral Therapy in the ART clinic of Debre Berhan Referral Hospital, Debre Berhan, Ethiopia, during the period of January 2013 up to January 2018 were followed up through the ART routine registered recorded up to January 2018 taken from patients chart. Survival data was recorded. The data were collected at random by using simple random sample form the patient's data card .Further from this study, we observed the following results. Survival of patient is affected by sex that means being a male's decrease survival time than being a female. In the base line regimen class taking the first has high survival time than taking the second class that means when regimen is change from first to next time of survival is decrease. Survival is affected by functional status. WHO clinical stages, that is stage1 has high survival time than others, opportunistic infection and marital status.

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Keywords: Survival Analysis, HIV/AIDS, Kaplan-Meier Plots, ART.

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INTRODUCTION

HIV refers to human immunodeficiency virus; it is a collection of virus those most likely mutated decades ago from a virus that infected chimpanzees to a virus that infects humans. It began to spread beyond the African continent in the late 1970s and is now endemic worldwide.HIV causes disease because it attacks critical immune defense cells and over time overwhelms the immune system. When HIV positive people live without treatment, HIV

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infection starts to cause symptoms in an average of eight to 10 years with opportunistic infection, opportunistic infection is caused when people have weak immune function. The period from infection to the cause of symptom is known as latent period where as the period started from symptomatic phase up to death referred to as acquired immune deficiency syndrome (AIDS) or HIV disease Sandra Gonzalez Gompf (2018). HIV infection leads to low levels of CD4+ T cells that in turn make the body susceptible to opportunistic infections. According to the UNAIDS (United Nation for International Development) report, it was estimated that 33.2 million people lived with the disease worldwide, and that AIDS killed an estimated 2.1 million people, including 330,000 children. In 2008, an estimated 33.4 million people were living with HIV/AIDS worldwide; nearly 70% of these were found in sub-Saharan Africa Sandra Gonzalez Gompf(2018).

The introduction of ART in 1996 was a turning point for thousands of people with sophisticated health care. Roughly 75% of AIDS patients in need of antiretroviral therapy (ART) in the world still have no access, and most of them live in Africa (World Health Organization 2006). This, despite the fact that the three by five initiative of the World Health Organization (WHO), as well as the resources provided by the Global Fund, greatly facilitated access to ART in all regions of the world and boosted ART programs in most of sub-Saharan Africa, where the number of persons treated was multiplied by more than eight in just 2 years [World Health Organization (WHO) 2006]. The clinical benefit of ART for AIDS patients, in terms of mortality reduction and improved quality of life, is well established but shows regional variations, with higher case fatality rates in poor countries. There are several predictors of mortality for patients on ART: viral load, CD4 count, total lymphocytes, body mass index (BMI), and adherence. Although these determinants tend to be similar across the world, there are some striking differences in their relative frequency, example, and the much lower baseline CD4 counts of patients starting ART in poor countries Isidore Sieleunou. et al.(2009).

Globally an estimated 34 million people were living with HIV at the end of 2010. United Nation for International Development and world health organization estimates since the availability of effective treatment some 2.9 million lives have been saved. About 68% of all people living with HIV resided in sub Saharan Africa, a region with only 12% of the global population in 2010. Ethiopia is the seriously affected countries in sub Saharan Africa with more than 1.3 million people living with HIV and an estimated 277,800 people requiring treatment. The overall Adult HIV prevalence was 1.4% and 1.5% in 2005 and 2011. The government of Ethiopia launched its free based ART initiative in 2003 and free initiative in 2005.peoples ever started ART were 150,136,208,784 and 268,934 respectively in 2008, 2009 and 2010. Peoples who were on ART on the same year were 109,930,152,472and 207,733 respectively. (Nurilign Abebe, 2014)

The first HIV infection in Ethiopia was reported in 1984 from stored sera which later expended as an epidemic similar to elsewhere in sub-Saharan Africa. The 2005 Demographic and Health Survey estimated national adult HIV prevalence of Ethiopia to be between 0.9%-2.1%, with infection levels highest in the Gambella (6%) and Addis Ababa (4.7%) regions.

Recent expansion of surveillance data and improved analysis has lowered the 2005 estimate drastically. Antenatal care surveillance data showed declining HIV prevalence rate in urban areas being 10.1% and stable trend in rural (1.8%). The highly vulnerable groups include young women living in urban areas, commercial sex workers and members of military and policy. In rural areas no significant gender difference in risk of infection. (Worku, Pattern and determinants of survival in, 2009). Statistics show that approximately 40 million people are currently living with HIV infection, and an estimated 40 million have died from this disease since the beginning of the epidemic. HIV has been particularly devastating in sub-Saharan Africa, which accounts for almost 70% of new HIV infections globally. However, infection rates in other countries also remain high. Sandra Gonzalez Gompf, (2018).

Medical and epidemiological studies are mostly conducted with an interest in measuring the occurrence of an outcome event. Studies conducting survival analysis, however, are focused toward measuring time to event or outcome. Time to event could vary from time to fatal event that is death, or time to occurrence of a clinical endpoint such as disease, or attainment of a biochemical marker. Survival analysis studies originated with the publication of John Graunt's Weekly Bills of Mortality in London. First life table was prepared by Healy. Survival analysis is also known as lifetime data analysis, time to event analysis, reliability and event history analysis depending on focus and stream where it is used. However, survival analysis is plagued by problem of censoring in design of clinical trials which renders routine methods of determination of central tendency redundant in computation of average survival time. The present essay attempts to highlight different methods of survival analysis used to estimate time to event in studies based on individual patient level data in the presence of censoring. (Shankar Prinja, 2010).Censoring is said to be present when information on time to outcome event is not available for all study participants. Participant is said to be censored when information on time to event is not available due to loss to follow-up or non-occurrence of outcome event before the trial end. Broadly classifying two types of censoring are encountered, that is point and interval censoring. Point censoring is said to occur when despite continuous monitoring of outcome event, the patient is lost to follow up or the event does not occur within the study duration. It is also known as right censoring which can be either end-of-study censoring or loss-to-follow-up censoring. An individual is said to be left censored if the patient had been on risk for disease for a period before entering the study. However, left censoring is usually not a problem in clinical trials, since starting point is defined by an event such as entry of patient in trial, randomization or occurrence of a procedure or treatment (Shankar Prinja, 2010).

STATEMENT OF THE PROBLEM

To find the Survival estimates from the collected data can be analysis by using Kaplan-Meier plot and some other descriptive statistics with different variables that are involved in this study. The analysis of survival data can be done by a non- parametric Kaplan and Meir method. Survival data is differed from other statistical data in that survival data is often

censored. To overcome this problem in easy was researchers use and develop different types of methods of analysis.

This study is designed to answer the following questions:

- Does patients survival is associated with their age and number of CD4+?
- Does patient's survival depend on the place where they live?
- Are individuals with different educational level having different survival time in the ART treatment?

OBJECTIVE

- **General Objective**

The general objective of this study is to apply survival analysis of HIV patients who follow in the ART.

- **Specific Objectives**
  - To identifying factors that affect survival of HIV/AIDS patients who were in ART clinic.
  - To compare adequacy of models for survival data.
  - To asses time to death of HIV/AIDS patients.

SIGNIFICANCE OF THE STUDY

The outcome of this study is providing information about the survival time or the most influential covariate that have significant impact on survival of HIV patients during treatment. This study is look at a time to death and other host factors that may play a role in fastening as well as slowing of the death of the patient with important impact to antiretroviral therapy has had in disease progression. The study tries to identify death extent of patients under these significant factors at different time during their care. Findings are help in making a decision as to which model to apply under specified conditions defined by predictor variables.

LIMITATIONS OF THE STUDY

- The study was restricted to adult's patients and results cannot be applicable to infants and Children since their regimen class is different.
- The study presumed that all deaths are caused by HIV infection only; it does not include death due to natural case or due to other disease.
- Parts of information on individuals are missed because of censored observation.

DATA AND METHODOLOGY

- **Study Area**

Location of Debre Berhan or Birhan, formerly spelled Debra-Berhan or Bernam, is a city and woreda in central Ethiopia. Located in the Semien Shewa Zone of the Amhara Region, about 120 kilometers north east of Addis Ababa on the paved highway to Dessie, the town has a latitude and longitude of 9°41'N 39°32'ECoordinates: 9°41'N 39°32'E and an elevation of 2,840 meters. It was an early capital of Ethiopia and afterwards, with Ankober and Angolalla, was one of the capitals of the kingdom of Shewa. Today, it is the administrative center of the Semien Shewa Zone of the Amhara Region. Debre Birhan is located in Ethiopia (Amhara region) and time zone Africa/Addis Ababa. Places in the near are Debre Sīna, Abomsa and Fichē.

- **Demography**

Based on the 2007 national census conducted by the Central Statistical Agency of Ethiopia (CSA), Debre Berhan town has a total population of 65,231, of whom 31,668 are men and 33,563 women. The majority of the inhabitants practiced Ethiopian Orthodox Christianity, with 94.12% reporting that as their religion, while 3.32% of the population said they were Muslim and 2.15% were Protestants. The 1994 national census reported a total population for Debre Berhan of 38,717 in 8,906 households, of whom 17,918 were men and 20,799 were women. The five largest ethnic groups reported in the town were the Amhara (90.12%), the Oromo (3.94%), the Tigrayan (1.81%), the Gurage (1.6%), and the Argobba (1.2%); all other ethnic groups made up 1.33% of the population. Amharic was spoken as a first language by 93.81%, Oromiffa was spoken by 3.04%, and 1.5% spoke Tigrinya: the remaining 1.65% spoke all other primary languages reported. The majority of the inhabitant's practiced Ethiopian Orthodox Christianity, with 94.59% reporting that as their religion, while 4.05% were Muslim, and 1.02% Protestant.

DATA SOURCE AND STUDY DESIGN

Retrospective five years HIV/AIDS Disease cohort study was conducted in patients, who were undergoing Antiretroviral Therapy in the ART clinic of Debre Berhan Referral Hospital, Debre Berhan, Ethiopia, during the period of January 2013 up to January 2018 were followed up through the ART routine registered recorded up to January 2018 taken from patients chart. Survival data was recorded. By random as using simple random sample form the patients data card (Chart). This study used secondary data, which was collected from both ART database and the Medical chart of HIV positive patients started to ART. The patients ART database and medical chart includes the patient intake forms, follow up cards and followed up records which are adopted by Federal Ministry of Health (FMOH) to be uniformly used by ART clinics to early identify and document laboratory, clinical and epidemiological variables. The database is on establishment as it is known from ICT experts. Based on the records the variables which are important for this study such as baseline CD4+ cell counts of patients, sex, age, marital status, baseline weight, religion, functional status, Educational level, Opportunistic illness, WHO clinical stage, regimen class, the time patients initiated ART, the time to loss to follow up(if any) and censoring status are collected using patients identification number or laboratory code, but no contact with individual patients. As we said before, part of the data was collected from the ART data base, and it was collected by the ART data base ICT experts, and the manually entered data was collected by ART Nurse working in the ART clinic and Card Clerk working together. The data was recorded in a list format by taking the necessary variables. The data includes both qualitative and quantitative variables for survival data characteristics was extracted from the patients chart which contains epidemiological, laboratory and clinical information of all HIV patients under ART follow-up including a detailed anti-retro-viral therapy history.

STUDY POPULATION

The study population was included HIV positive adults whose age is started from 16 and above initiated ART treatment in the Debre Berhan Referral Hospital. All patients who have initiated to ART and their baseline CD4 cell count, baseline weight who started first line regiment class was included in the study population, while patient started ART with their age is less than 16 years old and patient who starts ART before January 2013 and after January 2018 are not included in the study population. All patients who fulfill the inclusion criteria were included in the study. When the data is recording from medical charts Identification numbers were used to each individual patients to make it easy to identify individuals visiting profile by keeping patients medical secrete. Legal permission Latter was taken from Department of statistics of the Debre Berhan University to make it legal.

STUDY VARIABLES

In the case of Statistical study the type of model is used for data analysis is base on the nature and measurement scale of response variable. Since our focus is time to death of a patient we have a single response variable, it is survival time of a patient on the ART. The interest of the study is survival analysis; the data have the nature of time-to-event, from the time started medication in the ART clinic to the occurrence of an event (or occurrence of death).

RESPONSE VARIABLE

Time-to-event of interest: "Survival-time" is defined as the number of years or months from the date of enrollment to ART until one of the events of "death", "lost to follow-up", "dropped out", "stopped", "transferred out to other health care centers" are occurred. This implies that the survival data. As we know survival data has different types of censoring in this study the data is with the "right censored observation". This was computed as the time difference between the events occurred and the time of the ART started (initiated).

EXPLANATORY VARIABLES

Independent/explanatory variables are: Baseline age, baseline CD4+ count, time (in months), sex of the patient, marital status of a patient at a baseline, WHO clinical stage, regimen class of the patient, weight of the patient at a baseline, Religion of a patient, Educational level of a patient, opportunistic illness of a patient, Censoring status of a patient and functional status of a patient are the explanatory variables used to meet the objective of this study. Baseline age, baseline CD4, weight, time and survival time of a patient are continuous variables.

Sex of the patient is the first categorical covariate with two levels: Male and Female. The second categorical covariate is marital status having three levels: Married, Single and Others (include Widowed and Divorced). Single represents Never Married. The third categorical covariate is (WHO) Clinical Stage which is classified into four as I, II, III and IV; where stage I indicates asymptomatic disease, Stage II indicates mild disease, Stage III indicates advanced disease and Stage IV indicates sever disease. Therefore; the disease severity increases from Stage I to Stage IV. The fourth categorical covariate is Functional Status

of a patient with three categories: Working, Ambulatory and Bedridden. Working patients are those patients who can able to work day-to-day activities while ambulatory patients are those patients who can able to work sometimes but, bedridden patients cannot able to do their work due to the disease. The other categorical covariate is ART regimen class of a patient which have five categories: AZT-3TC-EFV, AZT-3TC-NVP, TDF-3TC-NVP, ABC-3TC-NVP and TDF-3TC-EFV the other categorical co-variate is Residence of a patient it is categorized in to two Rural, Urban , the other the categorical covariate is educational level of a patient it is categorized in to four category Not educated, primary, secondary, tertiary, The final categorical variable is Censoring Status, which is the time-to-event interest of a patient with two categories: Censored and Death. Age is measured in years and time in months.

Table1: Variables Used in this Study

S. No.	Variables	Category	Code
1	Sex	Female Male	0,1
2	Age	16-25, 26-35, 36-45,46-55,56-65 and >55	1, 2, 3, 4, 5, and 6
3	Marital status	single, married and other	0, 1, 2
4	Education level	no education, primary, Secondary and tertiary school level	0,1,2,3
5	Religion	orthodox, Muslim and protestant	0, 1, 2
6	Residence	rural and urban	0, 1
7	Functional status	working and others	0, 1
8	Opportunistic illness	yes and no	0, 1
9	WHO clinical stages	Stage1, Stage2, Stage3 and Stage4	0,1,2,3
10	Regimen class	AZT-3TC-NVP, AZT-3TC-EFV, TDF-3TC-EFV or NVP, ABC-3TC- NVP	0,1,2,3,4
11	Time in month	time in month	-----------
12	Base line CD4 cell count	baseline CD4 in ml/cube	------------
13	Baselineweigh	Baseline weight in kilogram	

CLINICAL AND OPERATIONAL DEFINITION OF SOME CO-VARIATES

- **Educational Level of Patients:** patients were classified based on educated as not educated, primary, secondary and tertiary, to identify which part of population are affected highly in this disease.

- **Baseline CD4 Cell Count:** is the number of CD4 cell in the patients T-cell. Since T-cells are defender of the body from foreign enemy.

- **Baseline Weight:** is weight of patients at the beginning of ART.

- **Survival Time:** is the time of patient they live in the follow up of ART clinic.

- **Functional Status:** patient's population is classified based on their functional status to identify which one is highly in number working, ambulatory or bed reddens.

- **WHO Clinical Status of Patients:** there are four WHO clinical stages; in these stages patients has different status. In WHO clinical stages patients' health status and type of medicine they take are different.

- **Regimen Class:** is the class of patients based on the type of medicine they use, there are two regimen class first line and second line regimen. First line for adult is different from for child.

- **Residence:** the residence of patients is two types Urban and Rural. Urban mean place is city, Rural is place is country side.

Religion of patients is three Muslim, orthodox and protestant. Religion is the belief of patients. In the following sections and subsections the method used for the study will be presented

STATISTICAL DATA ANALYSIS

- **Descriptive Data Analysis**

It is a technique to visualize the patterns of data relative to researcher interests. Since Descriptive data analysis can serve to discover as much of the information regarding raw data as possible, plotting, numeric, tabular are used to carefully examine the data. For a plot Kaplan-Meier estimation is applied .In order to address the objectives of the study, in this section results obtained from K-M method will be presented.

- **The General RMesult of the Data Set**

This study used five year's adult HIV/AIDS patient population of Debre Berhan Referral Hospital. During the study period (January 2012 to January 2018), a total number of 1130 HIV patients were on Antiretroviral treatment (ART). Debre Berhan Referral Hospital, this Hospital start in 1993 in Ethiopian colander, from the beginning of the hospital up to know, the patient population of Debre Berhan Referral Hospital ART clinic were 3755 from this total population 1130 of the patients were registered in the five years (2013 to 2018) of study period. In those five years patient 741 of them were females, 388 of them were males,1061 orthodox,19 muslim,49 protestant,16 of the total population live in urban area, 1020 of total population are live in rural area, 780 of them are alive,117 died due to HIV/AIDS, 190 of them dropout due to unknown reason,45 of them were transfer out to the other health care, 958 working, 154 ambulatory,17 bed redden,154 are not educated,563 are primary school education,332 secondary school education,80 tertiary or higher education,394 single,417 maried,318 are divorce and widowed,161 have no opportunistic infection,968 are HIV/AIDS with opportunistic infection,495 are in the first WHO clinical stage,254 are in the second WHO clinical stage,321 are in the third WHO clinical stage,58 are in the fourth WHO clinical stage. Finally, after exclude all the non- eligible HIV infected (positive) patients, for this study 1036 Adult HIV infected patients were included.

The data set of this study consists survival time of patient in the ART clinic from start up to occurrence of an event with the minimum value 1 month, the maximum value is 61 month and first quartile of survival time is 7, third quartile of survival time is 40, median of survival time is 20, mean of survival time is 23. Whereas the weight of patients has minimum value 13 maximum value 89, first quartile 46, third quartile 59, and mean and median are equal that is 52. Age at baseline of patient has minimum 16, maximum 71, median of age is 32.00, mean of age is 34.02, first quartile of age is 27 and third quartile of age is 40.The patient of the data contains 691

females, 345 males. The patients based on functional status working 936, 86 ambulatory, 14 beds redden. Patients WHO Clinical stage found in stage I 463 stages II 224 stage III 300 and stage IV 49 patients (881 Patients with opportunistic infection 155 patients without opportunistic infection). In the Regimen class of patients 95 patients use AZT-3TC-NVP, 33 patients use AZT-3TC-EFV, 834 patients use TDF-3TC-EFV, 71 patients use TDF-3TC-NVP, and 3 patients only use ABC-3TC-NVP. 151 patients are not educated, 495 and 310 patients are primary and secondary level of education, 80 patients are higher education. 301 patients are single, 417 married and 318 patients include divorced and widowed. 968 Patients are orthodox, 19 Muslim, 49 protestant. 16 patients live in rural, 1020 patients live in urban area.

- **Results of Descriptive Statistics**

When we see based on survival time, among total of 1036 study subjects 77 were died during the first 12 months, 39 deaths occurred within the first three months after initiation of ART. Another 21 died in the following three months of follow up; that is a total of 60 deaths occurred within six months. In the last six months, 17 patients died; the total of 12 months death makes the remaining 5.79787% of the total. When we come to the sex of patients, among the total of 691 females 65 of them were died whereas among the total of 345 males patients 48 of them were died. When we see the patient population based on age with age group in to six from 16 to 25 censored 213,17 death, from 26 to 35 censored 455 death 39 death, from 36 to 45 censored 239, death 37, from 46 to 55 censored observations were 77 with 10 death, in the age of greater than or equal to 66 the censored observation were 7 with 2 death. The patient population in the case of Functional status the large number of patients were working group, it consists 935 with 96 death and 839 censored observation, the other group is ambulatory 75 censored 11 death observation, the last one is bed redden it has total of 14 with 8 censored 6 death.

Table 2: Baseline Demographic and Clinical Characteristics

	censoring status		
Sex	Censored	Death	Total
Females	626	65	691
Males	296	48	344
Age group			
16-25	196	17	213
26-35	415	39	454
36-45	205	34	239
46-55	67	10	77
56-65	34	11	45
>66	5	2	7
Functional status			
Working	839	96	935
Ambulatory	75	11	86
Bed redden	8	6	14
WHO clinical stage			
Stage I	441	21	462
Stage II	191	33	224
Stage III	248	52	300

Stage IV	42	7	49
Opportunistic infection			
No	41	113	154
Yes	881		881
Regiment class			
AZT-3TC-NVP	87	8	95
AZT-3TC-EFV	31	2	33
TDF-3TC-EFV	748	86	834
TDF-3TC-NVP	53	17	70
ABC-3TC-NVP	3	0	3
educational status			
No Education	133	18	151
Primary school level	439	55	494
Secondary school level	280	30	310
Tertiary (higher education)	70	10	80
Marital status			
Single	281	20	301
Married	370	46	416
Other	271	47	316
Religion			
Orthodox	660	207	967
Muslim	18	1	19
Protestant	44	5	49
Residence			
Rural	14	2	16
Urban	908	111	1019
Total	922	113	1035

The patient population in the case of WHO clinical Status, stage I contains 441 censored, 21 death, 462 total observation, stage II contains 224 total 191 censored 33 death, in stage III among total of 300 observation 248 censored, 52 death , the final stage which is stage IV consists 42 censored, 7 death and 49 total observation . The patient population in the case of opportunistic infection among total of 1036 observation 881 were with opportunistic infection but there were no death 154 observation were without opportunistic infection with the total of event is occurred in this part that is 113 death. The population in the case of marital status, among total of 301 singles 281were censored 20 were died, among 416 married subjects 370 were censored 46 were died, among total of 318 other group (divorced and widowed) 271 were censored 47 were died. The patient population has three kinds of religions, those are orthodox with total 967,660 were censored, 107 were died, the second is Muslim with 1 death observation and 18 censored a total of19, the third is protestant with total of 49 and 5 death 44 censored. In the referral hospital there are five kinds of regimen classes, among total of 1035 observation 95 of them were used AZT-3TC-NVP, from the 8 death, 87 censored, the second regimen is AZT-3TC-EFV it consists 31 censored 2 deaths with 33 total users. the third regimen class is TDF-3TC-EFV it contains 748 censored, 86 death, 834 total observation, this class holds the largest number of users, the fourth class is TDF-3TC-NVP with 53 censored,17 death,70 total population, the last one is ABC-3TC-NVP it has 3 total users with no death observation. the patient population based on educational level there were 151 illiterate with 133 censored, 18 death, 494 were primary school level with 439 censored, 55 death, 310 were secondary school level of education with 270 censored and 30 death, the other is tertiary or higher education level of patients who were 80 with 10 death and 70 censored observation. When we see subjects based on residence 16 observations only live in rural with 14 censored, 2 death whereas 908 censored, 111 death totally 1019 observations live in urban area.

Table 3: World Health Organization Stages with Other Covariate

sex of patient	WHO clinical stage of patients				Total
	Stage I	Stage I I	Stage III	Stage IV	
Females	339	148	176	28	691
Males	123	76	124	21	344
Total population	462	224	300	49	1035
Functional status					
Working	444	204	255	32	935
Ambulatory	17	18	41	10	86
Bed redden	1	2	4	7	14
Total	462	224	300	49	1035
opportunistic infection of patients					
No	39	43	64	8	154
Yes	423	181	226	41	881
Total	462	224	300	49	1035
Regimen Class					
AZT-3TC-NVP	45	28	19	3	95
AZT-3TC-EFV	7	10	16	0	33
TDF-3TC-EFV	385	161	243	45	834
TDF-3TC-NVP	24	24	21	1	70
ABC-3TC-NVP	1	1	1	0	3
Total	462	224	300	49	1035
Educational level					
No education	57	34	48	12	151
Primary school level	220	110	143	21	494
Secondary school level	145	69	83	13	310
Tertiary (higher education)	40	11	26	3	80
Total	462	224	300	49	1035
Marital status					
Single	138	62	83	18	301
Married	178	89	132	17	416
Others	146	73	85	14	318
Total	462	224	300	49	1035
Religion					
Orthodox	433	212	278	44	967
Muslim	9	4	4	2	19
Protestant	20	8	18	3	49
Total	462	224	300	49	1035
Residence					
Rural	5	6	5		16
Urban	457	218	295	49	1019
Total	462	224	300	49	1035
Age group					
16-25	105	58	42	8	213
26-35	231	85	121	17	454
36-45	86	50	85	18	239
46-55	26	15	31	5	77
56-65	11	15	18	1	45
>66	3	1	3	0	7
Total	462	224	300	49	1035

Table 3 shows that the patients number in each clinical stage with respect to the other factor such as sex, age, functional status, WHO clinical status, educational level, marital status, religion, and residence of patients. number of females in stage I were 339 in stage II 148 in stage III 176 in stage IV 28 and total female patients were 691. In the other hand 123 male patients were in stage I, 76 in stage II,124 in stage III,21 in stage IV and totally 344 males patient and total of male and females in stage I462, stage II 224, stage III 300, stage IV 49 and total 1035. The age of patients that is 16-25 contain 231 in stageI,85 in stage II,121 in stage III,17 in stage IV and total 454, age group 26-35 is contain stage I 86, stage II 50,stage III 85, stageIV18 and total 239, the next one is age group 36-45 stage I 26,stage II 15 stage II 31 stage IV 5 and total 77, the other age group is 46-55 it has in stage I stage 11stage III stage IV and the total . The clinical stage of patient is explained as follows, in the four stage females 339 in stage I, 148 stage III 178 stage IV 28 total females 691, stage I 123, stage II 76, stage III 124, stage IV 21 the total of 344 males and the total males and females in each stages were stage I, stage II, stage III, stage IV were 462,224,300, 49 respectively. The grand total of the population is 1035. The observation based on functional status were three starts from working these were in stage I 444, stage II 204, stage III 255, stage IV 32,955 second one is ambulatory stage I 17, stage II 18, stage III 41, stage IV 10, 86total within group, the last one bed redden in this group stage I 1, stage II 2, stage III 4, stage IV 7, 14 total within group the total within group , total observation in each stage were stage I 462,stage II 224, stage III 300, stage IV 49. The grand total 1035. The patients with or without opportunistic infection in each clinical stages were stage I 39, stage II 43, stage III 64, stage IV 8, the total of 154 patients were without opportunistic infection .the other one patients with opportunistic infection were stage I 423, stage II 181, stage III 226, stage IV 41, the total of 881 patients were with opportunistic infection, the total of patients in each stages were stage I 462, stage II224, stage III 300, stage IV 49, grand total 1035. The Regimen class of patients which they take in the ART were five kinds these were AZT-3TC-NVP the user of these drug were stage I 45, stage II 28, stage III 19, stage IV 3 and the total of 95 patients were used, the second one AZT-3TC-EFV the user of these drug were stage I 7,stage II 10,stage III 16, stage IV no users, the total of 33 patients were user of this drug. The third one is TDF-3TC-EFV the user of this drug were 385 in stage I, 161 stage II,243 in stage III, 45 in stage IV and total of 834 patients were use this drug. The fourth one is TDF-3TC-NVP it is used by 24 patients in stage I,24 in stage II, 21 in stage III,1 patient in stage IV the total of 70 patients were user of this drug, the last one ABC-3TC-NVP it is used by 1 in stage I, 1 in stage II, 1 in stage III, no user in stage IV, the total of 3 patients were the user of this drug. those all drugs in each stages holds 462 in stage I, 224 in stage II, 300 in stage III, 49 in stage IV the grand total were 1035. When we see observation based on educational level there were four levels the first one is patients who were not educated, tis portion consists of 57 in stage I, 34 in stage II,48 in stage III,12 in stage IV, the total of 151 patients were not educated, the other portion which contains patients with primary school level those were 220 in stage I,110 in stage II, 143 in stage III, 21 in stage IV, the total of 494 patients were primary school level of education. Secondary school educated patients were 145 in stage I, 69 in stage II, 83 in stage III, 13 in stage IV, the total of 310 patients were secondary education level, the patient who were in higher level of education in stage I 40, stage II 11, stage III 26, stage IV 3, the total of 80 patients. The total of patients in

each WHO clinical stages is similar from the above. Among the total of 1036 observation, 301 were single, 138 in stage I, 62 in stage II, 83 in stage II, 18 in stage IV. Among 416 married patients 178 were in stage I, 89 in stage II, 132 in stage III, 17 in stage IV and the total of 416 patients were married. The other portion of patient population is other it includes divorce and widowed who were 146 in stage I, 73 in stage II, 85 in stage III, 14 in stage IV, total 318. Patients were classified based on religion as orthodox 433 in stage I, 212 in stage II, 278 in stage III, 44 in stage IV, total 967, Muslim 9 in stage I , 4 stage II, 4 in stage III,2 in stage IV ,total 19, protestant 20 in stage I, 8 in stage II, 18, in stage III, 3 in stage IV, total 49 were included. There were two places where patients live Rural 5 in stage I, 6 in stage II, 5 in stage III, no patient in stage IV, total 16 were in rural area. Urban 457 in stage I, 218 in stage II, 295 in stage III, 49 in stage IV, a total of 1019 patients were live in urban area.

The age group of patients 16 to 25 were 105 in stage I,58 in stage II, 42 in stage III,8 in stage IV in this age group the total of 213 patients were included. The next age group is 26 to 35 in this group 231 were in stage I, 85 were in stage II, 121 were in stage III,17 were in stage IV, in this group 454 patients were includes. In the age group 36 to 45 in stage I 86, in stage II 50, in stage III 85, in stage IV 18, this contains total of 239 patients. In the age group 46 to 55 in stage I 26, in stage II, 15, in stage III 31, in stage IV 5, total of 77 patients were included. In the age group 56 to 65 stages I 11, stage II 15, stage III 18, stage IV 1 and total of 45 patients included. In the age group 66 in stage I 3, in stage II 1, in stage III 3, in stage IV no patients and the total of 7 patients were included.

Table 4: Opportunistic Infection with other Covariates

age of patients	opportunistic infection of patients		Total
	No	Yes	
16-25	27	186	213
26-35	55	399	454
36-45	42	197	239
46-55	12	65	77
56-65	16	29	45
≥66	2	5	7
Total	154	881	1035
Sex			
Females	89	602	691
Males	65	279	344
Total	154	881	1035
Functional status			
Working	132	803	935
Ambulatory	15	71	85
Bed redden	7	7	14
Total	154	881	1035
Residence			

Rural	3	13	16
Urban	151	868	1019
Total	154	881	1035
Religion			
Orthodox	145	822	967
Muslim	2	17	19
Protestant	7	42	49
Total	154	881	1035
educational status			
no education	25	125	151
Primary school level	76	418	494
Secondary school level	40	427	310
Tertiary (higher education)	13	67	80
Total	154	881	1035
Marital status			
Single	37	264	301
Married	56	360	416
Others	61	257	318
Total	154	881	1035

From Table 4 shows that the number of patients with or without opportunistic infection in each covariate and in their classification is explained as: Patients in age group 16-25 were without opportunistic infection 27, with opportunistic infection 186, total for both with and without opportunistic infection were 213 in this age group. In age group 26-35 patients without opportunistic infection 55, with opportunistic infection399, total 454 patients were in this age group. In age group 36-45 patients without opportunistic infection were 42, patients with opportunistic infection were 197, the total of 239 patients were in this age group in the age group 46-55 patients without opportunistic infection were 12, patients with opportunistic infection were 65, the total of 77 patients were in this age group. In the age group 56-65 patients without opportunistic infection were 16, patients with opportunistic infection were 29, the total of 45 patients were in this age group. From the total of 7 patients in age group 66 patients without opportunistic infection were 2, patients with opportunistic infection were 5. Opportunistic infection based on sex were 89 females patients without opportunistcinfection,602 females patients were with opportunistic infection , a total of 691female patients were included. From total 344 male patients 65 of them were without opportunistic infection, 279 were with opportunistic infection. The total patients without opportunistic infection were 154, with opportunistic infection were 881, grand total were 1035. Working patients without opportunistic infection were 132, working patients with opportunistic infection were 803, the total of 935 patients was working, 85 patients were ambulatory, 71 without opportunistic infection, 15 without opportunistic infection. In the Bed redden of the patients were 14, 7 of the without opportunistic infection, 7 of them were with opportunistic infection. Patients were classified based on residence as Rural who were 16 from this 3 were without opportunistic infection, 13 were with opportunistic infection. The total of 1019 patients were live in urban area, 151 were without opportunistic infection.868 of them with opportunistic infection.

Patients based on religion classified as orthodox 145 without opportunistic infection, 822 with opportunistic infection, totally 967 patients were orthodox. Muslim a total of 19 Muslims were included in these 2 without opportunistic infection, 17 with opportunistic infection. The last one is protestant it contains 7 without opportunistic infection, 42 with opportunistic infection., the total of 49 patients were protestant.

The educational level of patients with respect to opportunistic infection explained as; among total of 1036 patients 151 patients were illiterate from these 25 without opportunistic infection 125 with opportunistic infection. From the 494 primary school level patients 76 of them without opportunistic infection, 418 were with opportunistic infection. From the 310 secondary school level patients 40 of them without opportunistic infection, 427 were with opportunistic infection. From the 80 higher education level of patients 13 of them without opportunistic infection, 67 were with opportunistic infection. Patients marital status holds 57 single patients without opportunistic infection,264 single with opportunistic infection, total of 301 single patients. From the total of 416 married patients 56 were without opportunistic infection, 360 were with opportunistic infection. In other group or divorced and widowed group 61 were without opportunistic infection 257 were with opportunistic infection, a total of 318 patients were in other group.

Tables 5: The Regimen Class of Patients

Sex	Regimen Class of patients					Total
	AZT-3TC-NVP	AZT-3TC-EFV	TDF-3TC-EFV	TDF-3TC-NVP	ABC-3TC-NVP	
Females	57	21	553	57	3	691
Males	38	12	281	13	0	344
Total	95	33	834	70	3	1035
Age						
16-25	24	14	160	13	2	213
26-35	42	11	366	34	1	454
36-45	19	6	1999	15	0	239
46-55	6	1	65	5	0	77
56-65	4	1	37	3	0	45
≥66	0	0	7	0	0	7
Total	96	33	834	70	3	1035
Functional status						
Working	87	31	752	63	2	9335
Ambulatory	8	1	70	8	1	86
Bed redden	0	1	12	1	0	14

Total	95	33	834	70	3	1035
Educational level						
No Education	9	4	131	7	0	151
Primary school level	46	17	394	35	2	494
Secondary school level	32	8	244	26	0	310
Tertiary (higher) edu	8	4	65	2	1	80
Total	95	33	834	70	3	1035
Marital status						
Single	27	11	239	22	2	301
Married	36	13	340	27	1	416
Others	33	9	255	21	0	318
Total	95	33	834	70	3	1035
Religion						
Orthodox	86	31	784	63	3	967
Muslim	2	0	14	3	0	19
Protestant	7	2	36	4	0	49
Total	95	33	834	70	3	1035
Residence						
Rural	3	1	9	3	0	16
Urban	92	32	825	67	3	1019
Total	95	33	834	70	3	1035

Table 5 shows that number of patient population in each regimen class with respect to other covariates and their classification. Regimen class of patients, patients was classified based on the regimen they used. There were five types of regimens used in the hospital. That is AZT-3TC-NVP in this 57 user were females, 38 males, the total of 95 patients were used this drug. AZT-3TC-EFV were the second it is used by 21 females, 12 male patients, total of 33 patients were user of this drug. The next one is TDF-3TC-EFV it was used by 553 female, 281 male patients, the total of 834 patients were user of this drug. The fourth one is TDF-3TC-NVP it was used by 57 females, 281 male patients, total of 70 patients were user of this drug. The last one was ABC-3TC-NVP it was used by 3 females only. on the bases of age group 16-25 was contain 24 AZT-3TC-NVP users, 14 were used AZT-3TC-EFV,160 were used TDF-3TC-EFV, 13 were used TDF-3TC-NVP, 2 were used ABC-3TC-NVP, total of 213 patients were in age group 16-25. The second age group is 26-35 it contains 42 AZT-3TC-NVP users, 11 AZT-3TC-EFV users, 366 TDF-3TC-EFV users, 34 TDF-3TC-NVP users, 1 ABC-3TC-NVP user, total of 454 patients were in this age group. In the age group 36-45 there were 19 AZT-3TC-NVP users, 6 AZT-3TC-EFV users,199 were TDF-3TC-EFV users, 15 were TDF-3TC-NVP users, in this age group there was no ABC-3TC-NVP users, total of 239 patients were in this age group. In the age group 46-55 AZT-3TC-NVP was used by 6 patients, AZT-3TC-EFV was used by 1 patient only, TDF-3TC-EFV used by 65 patients, TDF-3TC-NVP was used by 5 patients, ABC-3TC-NVP this drug has no user in this age group, total of 77 patients were in the age group. In the

age group 56-65 AZT-3TC-NVP was used by 4 patients, AZT-3TC-EFV was used by 1 patient only, TDF-3TC-EFV used by 37 patients, TDF-3TC-NVP was used by 3 patients, ABC-3TC-NVP this drug had no user in this age group, total of 45 patients were in this age group. In the age group 66 AZT-3TC-NVP had no user, AZT-3TC-EFV had no user, TDF-3TC-EFV used by 7 patients, TDF-3TC-NVP had no user , ABC-3TC-NVP this drug has no user in this age group, total of 7 patients were in the age group.

Descriptive Statistics for Continuous Variables

Table 6: Descriptive Statistics for Continuous Variables

Variables	Mean	Std. Err.	[95% Conf. Interval]	
Age	34.02027	0 .3178348	33.3966	34.64394
Time	23.74807	0 .5637235	22.6419	24.85424
BWt	52.8083	0 .3306018	52.15957	53.45703
BSCD4	361.1216	7.80169	345.8127	376.4306

From this table 6 . all four variables (Age, Time, BWt, and BSCD4) means are lie between 95% confidence interval, but standard error for Base line CD4 cell count is higher than others SEs.

Descriptive statistics by using Kaplan-Meier plot.
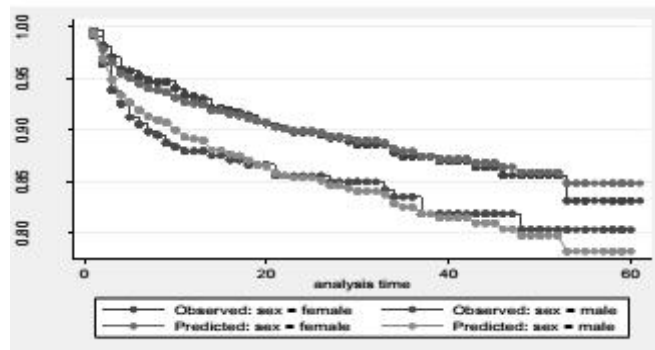
Figure 1: The Kaplan Meier survival estimates by sex
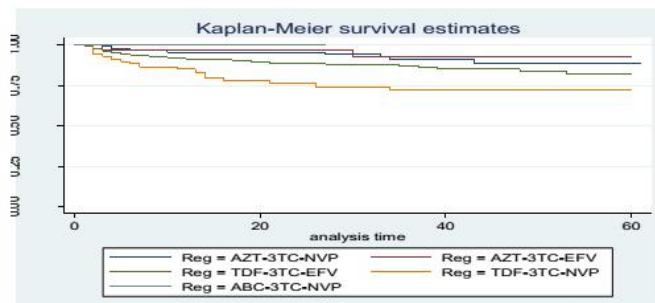
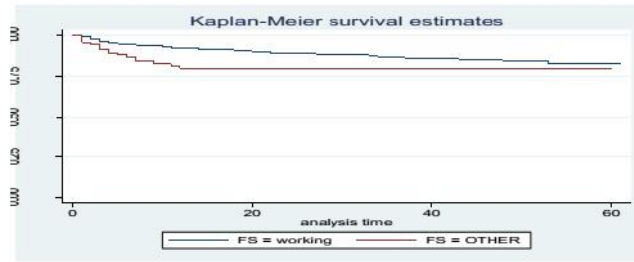Figure 2: Survival by Regimen class

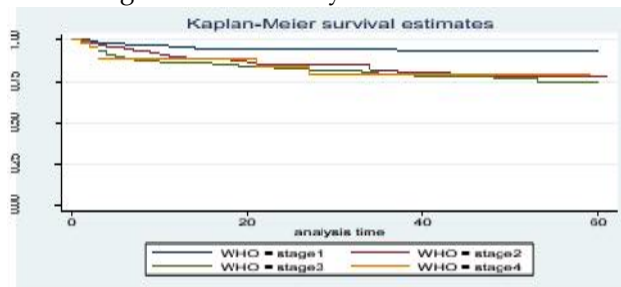Figure 3: Survival by functional status
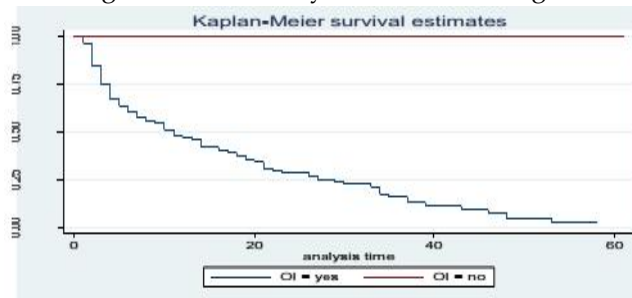

Figure 4: Survival by WHO clinical stages

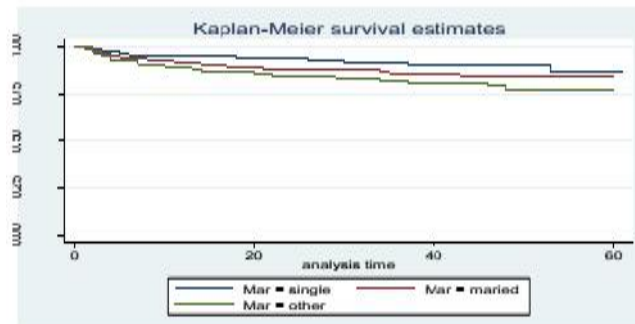Figure 5: Survival by opportunistic infection

Figure 6: Survival by marital status

In the figure1, it shows the trend among sex for female, the observed and predicted are go in same direction from 0 to 55. Then there was a little devotion but in the case of male there is fluctuation in there line. On the other hand survival of patient is affected by sex that means being a male's decrease survival time than being a female. From figure 2, above it shows that survival is affected by regimen class. In the base line regimen class taking the first has high survival time than taking the second class that means when regimen is change from

first to next time of survival is decrease. In figure 3, that survival is affected by functional status in other word being working increase survival time of patients. Figure 4 show that survival is affected by WHO clinical stages that are stage1 has high survival time than others. In figure5 survival time is affected by opportunistic infection. Survival of patient with opportunistic infection is less than that of without opportunistic infection. From the figure 6 we can observe that survival is affected by marital status. That is being single increase survival time than being married, being married decrease survival tome than being other such as divorced, or widowed.

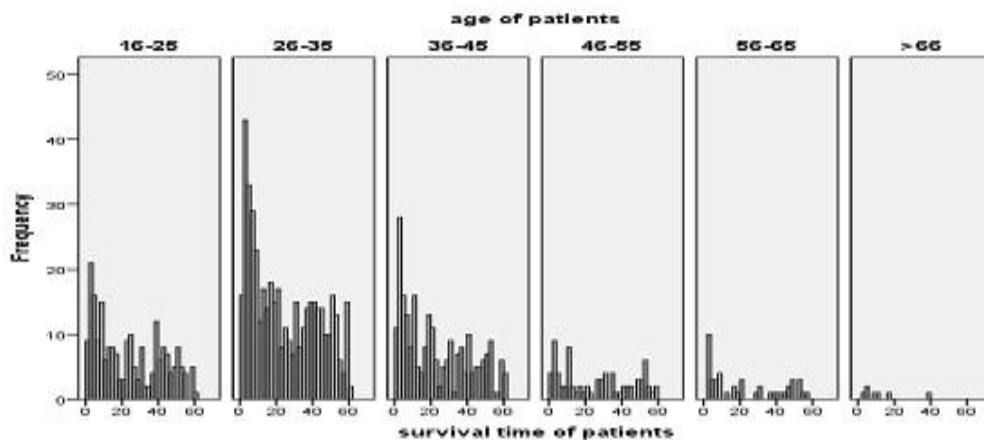- **Plots for age in group and un grouped**

Fig 7: A. Histogram for age group

In the fig 7the category shows the age of patients in group two is contain highest number of patients from the other group which is 26-35 age groups. It followed by age group three then group one, in this graph age group six contains smallest number of observation.
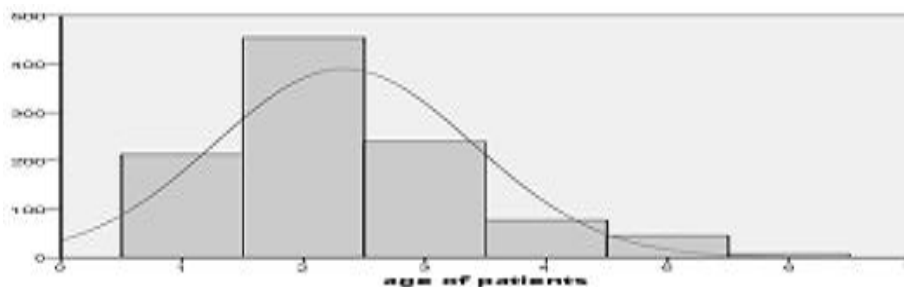
- **Histogram for age of patients**

Fig 7. A. Histogram for age group

Age is approximately normally distributed, the histogram shows the age distribution of the HIV-infected patients on ART, and the curve shows an asymmetrical distribution of age. The median age of the patients at start of anti retro-viral treatment was 32 years, and the age ranged from 16 to 71 years with 34.02 mean and 27 first, 40 third quartile respectively. Most of the patients were in age of greater than 32 years.

CONCLUSION

Survival data are unique in that the research questions, to answer whether the event has occurred in the period of follow ups and when it has took place. Censoring is the common process to handle the incomplete observation of failure times and it requires some specific statistical models to analysis the given data. Here, the analysis involved with an estimation method by using Kaplan-Meier (K.M). This method estimates the unadjusted probability of survival beyond a certain time point and also this K.M plot is useful to estimate the survival function. Further from this study, we observed the following results. Survival of patient is affected by sex that means being a male's decrease survival time than being a female. In the base line regimen class taking the first has high survival time than taking the second class that means when regimen is change from first to next time of survival is decrease. Survival is affected by functional status. WHO clinical stage that is stage 1 has high survival time than others, opportunistic infection and marital status.

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ACRONOMY

➢ AIDS - Acquired Immune Deficiency Syndrome: Commonly refers to the advanced stage of HIV illness, when the CD4 count falls under 200. It started as the CDC case definition term when patients presented AIDS defining illnesses.

➢ Antiretroviral - Refers to drugs used against retroviruses, commonly anti-HIV drugs

➢ ART - Treating people living with HIV to lower their viral load and hence decrease their infectiousness

➢ ARMS-Adaptive Rejection Sampling Algorithm used to sample parameters sequentially from their univariate full conditional distributions.

➢ CD4 - A receptor on the surface of cells that HIV attaches to the cells involved in cell-mediated immunity known as T-lymphocytes have the CD4 marker. Other cells, including some in the brain have the same marker and are the targets of HIV.

➢ Baseline CD4 count - Represents the count of the cells with CD4 receptor in circulation. Disease progression {when disease gets worse) at the beginning of ART.

➢ HAART - Highly Active Antiretroviral Therapy {Treatment with a combination of at least three different ARVs.

➢ HIV- Human Immunodeficiency Virus- The virus that causes AIDS. There are two different types HIV-1 and HIV-2. Worldwide HIV-1 is the most common type.

➢ Regimen class - medicine or medicines formulated for a specific illness or disease with different type in each class.

➢ Viral load -The mount of viruses in the blood circulation. The viral load in HIV infection directly correlates with the degree of immune suppression.

➢ WHO clinical stages of AIDS {Classification of the stages of HIV-associated clinical disease where stage1 indicates asymptomatic disease, stage2 indicates mild disease, stage3 indicates advanced disease and stage4 indicates severe disease.

➢ Ambulatory - An individual able to do activities for day to day life activity.

➢ Bed-ridden - An individual unable to carry out day to day activity and he/she follow their treatment by getting bed in hospital.

➢ Working - An individual able to perform his/hers work as healthy person.

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