ADDIS ABABA UNIVERSITY
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Assessment of HIV treatment outcome among mentally disordered patients at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia

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This is to certify that the thesis prepared by Nebila Ibrahim, entitled: Assessment of HIV treatment outcome among mentally disordered patients at Amanuel Mental Specialized Hospital: A retrospective cohort study, submitted in partial fulfillment of the requirements for the Degree of Master of Science in Pharmacoepidemiology and Social Pharmacy complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Chair of Department

Abstract

Assessment of HIV treatment outcome among mentally disordered patients at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia.

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Addis Ababa University, 2015

Human immunodeficiency virus infection usually leads to clinical diseases that affect almost every organ system and present with a wide range of symptoms and syndromes. Accurate assessment and diagnosis of systemic as well as central nervous system impairment requires close medical and psychiatric management. Therefore, psychiatric disorders associated with HIV/AIDS should be accurately identified and treated as its impact on health is substantial. The aim of this study was to assess the HIV treatment outcome among mentally disoredred patients following their treatment at Amanuel Mental Specialized Hospital. A retrospective study was conducted from September 2010 to August 2013 among HIV positive patients (N=337). Data on socio-demographic characteristic of patients, HIV stage based on WHO classification, the type of psychiatric disorder, medication, treatment outcome, and CD4 count were collected from patients' chart. Among the 337 study participants, 138 (40.9%) were diagnosed to have a psychiatric condition. Out of these patients, more than 70% and 90%, respectively, showed an improvement in their CD4 count and WHO class over the three years period. The adherence among the HIV infected mentally ill patients was rated to be good in 39%, fair in 47%, and poor in 67% of the patients. Compared to psychiatric patients, the adherence of non-psychiatric HIV patients to their ART medication was significantly

higher (OR = 3.06; P=0.046). Forty one percent of the study participants had opportunistic infection; of these 73.2 % were psychiatric patients. Overall, the co-occurrence of HIV and Psychiatric illness did not influence the treatment outcome. However, this does not completely exclude the attention needed to be given to these patients regarding adequate ART treatment. Therefore, further studies should be done to come up with optimum management of HIV positive patients with mental illness.

Key words: Mental illness, HIV in Ethiopia, treatment outcome and Amanuel Mental Specialized Hospital

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List of Acronyms

AIDS	Acquired immunodeficiency syndrome
AMSH	Amanuel Mental Specialized Hospital
ART	Anti-retroviral therapy
ARVDs	Anti-retroviral drugs
AZT/3TC/EFV	Zidovudine/Lamivudine/Efavirenz
AZT/3TC/NVP	Zidovudine/Lamivudine/Nevirapine
BMI	Body mass index
CMV	Cytomegalovirus
CNS	Central nervous system
DDIs	Drug-drug interactions
DSM	Diagnostic and Statistical Manual
GAD	Generalized Anxiety Disorder
HAART	Highly Active Antiretroviral Therapy
HIV	Human immunodeficiency virus
ICD	International Classification of Disease
MI	Mental illness

NNRTIs	Non- Nucleoside Reverse Transcriptase Inhibitors
NRTIs	Nucleoside Reverse Transcriptase Inhibitors
OIs	Opportunistic Infections
PJP	Pneumocystis jiroveci pneumonia
PGL	Persistent generalized Lymphadenopathy
PIs	Protease Inhibitors
SMI	Severe mental illnesses
SSRIs	Selective Serotonin Reuptake Inhibitors
TB	Tuberculosis
TLC	Total lymphocyte count
TDF/3TC/EFV	Tenofovir/ Lamivudine/Efavirenz
TDF/3TC/NVP	Tenofovir/ Lamivudine/Nevirapine
WHO	World Health Organization

1. Introduction

HIV/AIDS remains one of the leading causes of death globally (WHO, 2004). It has recently ranked to be the sixth leading cause of death (WHO, 2014). It is projected to continue as a significant cause of premature mortality. According to the joint 2011 HIV/AIDS report of WHO, UNAIDS, and UNICEF an estimated 34 million people were living with HIV/AIDS globally with 2.7 million new HIV infections in 2010. Of these, 68% were residing in sub-Saharan Africa (UNAIDS, 2011). Ethiopia is one of the seriously affected countries in sub-Saharan Africa with a large number of people (approximately 800,000) that are living with HIV/AIDS and 44,751 AIDS-related deaths (Hambisa *et al.,* 2013, Federal democratic Republic of Ethiopia, 2012).

Multiple studies document a higher prevalence of chronic diseases, such as diabetes, respiratory disease, hepatitis B and C, and HIV, in people with mental disorders compared with the general population. HIV-AIDS and viral hepatitis continue to represent major public health concerns, particularly among individuals at high risk of infection because of injection drug use, homelessness, and severe mental illness (SMI) (Goulet *et al.,* 2007).

Individuals with co-occurring mental and other disorders have higher rates of treatment compared with individuals with only one disorder, although most individuals with co-occurring disorders do not receive adequate treatment for either or both. A diagnosis of co-occurring disorders occurs when at least one disorder of each type can be established independent of the other and is not simply a cluster of symptoms resulting from the one disorder (Grella & Stein, 2006).

Understanding that HIV infection and psychiatric illness have features in common, and each is a significant risk factor for the other, optimizing and treatment of HIV infection in patients with psychiatric disorders can be achieved by giving these patients appropriate psychiatric treatment that can decrease risk behaviors, improve treatment adherence, improve quality of life, and help decrease mortality.

Therefore, this research on HIV treatment outcome in mentally ill patients would provide information for treatment centers to reduce occurrence of worsened immune response, increased HIV replication, and development of drug-resistant viral mutations so as to use the limited resources efficiently and plan for optimum HIV management. The current study assessed the HIV treatment outcome among mentally ill patients in Amanuel Mental Specialized Hospital (AMSH) between September 2010–August, 2013. In addition, this work assessed the adherence rate to ART in both patients with and without mental illness.

2 Statement of the problem

Mental illness (MI) is associated with a more rapid and harder-to-treat progression of HIV disease (Baingana *et al.*, 2005). A study done in the US in 1997 indicated that the prevalence of HIV infection among people with MI was 4.0%–22.9% (Cournos, 1997). And another study in the US in 2012 indicated that psychiatric diagnosis in HIV patients had increased to a prevalence of 20-70%, showing a high prevalence and indicating further study to address unanswered issues (Watkins *et al*., 2015). HIV prevalence data in the African psychiatric population is scarce but in 2000 an HIV prevalence study was carried out at Weskoppies Hospital, South Africa on 200 new admissions, and only 9% were found to be HIV positive. Another study conducted in 2012 in the same hospital showed an increase in prevalence to 11% (Henning *et al.*, 2012).

In low income countries like Ethiopia, where malnutrition and infectious diseases are common, the prevalence of mental disorders is shockingly high. As estimated by the World Bank, mental health problems contribute to 8.1% of the global burden of disease (Murray *et al.*, 2010). Consistent with this finding, a recent study in Ethiopia showed that MI contributes to over 12% of the burden of disease (WHO, 2009). A similar study carried out by Shibire and Alem (2006) indicated that the health problem associated with mental disorder in Ethiopia is as high as 20%. The prevalence of MIs in HIV-infected individuals is substantially higher than in the general population. Furthermore, HIV tends to be concentrated in highly vulnerable, marginalized and stigmatized population (WHO, 2011).

Adherence to a treatment regimen is profoundly important for patients with HIV infection. Worsened disease outcomes can be caused by non-adherence to HIV medication, which can lead to worsened immune response, increased HIV replication, and development of drug-resistant viral mutations. Other, less obvious, connections may also exist. Specifically, there is likely a relationship between stress, depression and immune response such that HIV infection may progress more rapidly in individuals with these symptoms (Leserman, 2003). Given the risk for worse HIV disease outcomes, treatment advocates have used the presence of a coexisting psychiatric illness as a reason to suggest more aggressive and comprehensive clinical management of HIV infection (Angelino & Treismana, 2001).

HIV infection and MI comorbidity appear to be detrimental for medication adherence (Goulet *et al.*, 2007). In addition to the problems caused by non-adherence to HIV medications, there may be equally significant difficulties caused by non-adherence to psychotropic medications. Depressive symptoms have long been linked to poor medication adherence among HIV+ persons, and treatment with antidepressant medication appears to improve antiretroviral adherence among those with a current mental health problem, especially those with more complex medication regimens (Kumar & Encinosa, 2009).

In addition, poorly controlled HIV leads to a higher likelihood of HIV transmission when individuals engage in risky behaviors. A study has showed that HIV+ individuals with comorbid bipolar disorder have significantly worse adherence to their antiretroviral medication than a comparable group of HIV+ individuals without bipolar disorder. The

proportion of persons with an ART adherence level above 90 percent was nearly twofold higher in the HIV+ persons without bipolar disorder (Moore *et al.*, 2011).

In general, psychotic disorders in individuals with HIV or AIDS are important areas with limited data and unanswered questions regarding incidence, prevalence, course, clinical features, and treatment. And aspects such as medication side-effects and DDIs are important considerations when patients are prescribed antipsychotic agents for the treatment of new-onset psychosis while concomitantly receiving HAART. Consequently, the potential for antipsychotic-induced side-effects and, overlapping toxicity between ART and antipsychotic medications should lead to a careful selection of medications (Dolder, 2004).

Given that psychiatric illness is present in almost half of HIV positive patients and that, of these patients, ~50% do not receive psychotropic medication (McDaniel *et al.*, 2000). This study attempted to assess if there were any gap in the management of HIV in psychiatric patients at AMSH. At the end, the result would help to bring an understanding whether the use of ART is beneficial in psychiatric patients with HIV.

3. Literature Review

3.1 Psychiatric disorder and HIV

Psychological disorder, also known as mental disorder, is a pattern of behavioral or psychological symptoms that impact multiple life areas and/or create distress to the person experiencing these symptoms. The classification and diagnosis is an important concern for both mental health providers and mental health clients. While there is no single, definitive definition of mental disorders, a number of different classification and diagnostic criteria have emerged. Clinicians utilize the Diagnostic and Statistical Manual of Mental Disorders (latest edition, DSM-V), published by the American Psychiatric Association, to determine whether a set of symptoms or behaviors meets the criteria for diagnosis as a psychological disorder (Whitlock and Schantz, 2008).

The International Classification of Diseases (ICD-16), published by the World Health Organization (WHO), is also frequently used. The DSM-V describes approximately 250 different psychological disorders, most of which fall under a category of similar or related disorders. In addition Psychotic disorders can be classified into primary (e.g. schizophrenia, schizoaffective disorder) or secondary (e.g. psychosis caused by a medical condition such as HIV infection) disorders (Thakker and Ward, 1998; WHO, 1995).

The human immunodeficiency virus, or HIV, is the virus that causes HIV infection. During HIV infection, the virus attacks and destroys the infection-fighting CD4 cells of the body's immune system. Loss of CD4 cells makes it difficult for the immune system to fight infections (DHHS, 2012). HIV infection usually leads to clinical diseases that affect almost every organ system and present with a wide range of symptoms and syndromes.

Accurate assessment and diagnosis of systemic as well as central nervous system (CNS) impairment requires close medical and psychiatric management, with increasing vigilance as immune competence declines and the possibility of life-threatening disorders increases. Therefore, psychiatric disorders associated with HIV/AIDS should be accurately identified and treated (WHO, 2005).

An estimated number of 249,174 adults (86% of eligible) are on ART treatment (WHO, 2006). The average life expectancy for Ethiopians is expected to further decline if the present HIV infection rates continue (Hambisa *et al.,* 2013). Globally, rapid expansion and early access to antiretroviral treatment (ART) services have resulted in a dramatic decrease in HIV-related mortality and morbidity. However, the current regimens are life-long requirement of strict compliance by patients to achieve treatment success and prevent drug resistance (Tran *et al.,* 2013).

In adults and children with HIV infection, changes in mental status or the emergence of new psychiatric or cognitive disorders requires ruling out treatable and reversible causes; medical causes are of increasing concern if CD4 counts are low or viral load has begun to rise. The more common diagnoses found in association with HIV/AIDS are dementia and the spectrum of cognitive disorders; delirium; mood disorders; substance use disorders; anxiety disorders; psychotic disorders; adjustment disorders; sleep disorders; disorders occurring in infants, children, and adolescents; and HIV-associated syndromes with psychiatric implications. Both psychopharmacologic and psychotherapeutic treatment strategies are often indicated (McDaniel *et al*., 2000).

3.2 Treatment of HIV patients with Psychiatric disorder

According to Ethiopia's regulatory authority and many other countries, management of HIV disease includes prevention and treatment of opportunistic infections (OIs) and controlling viral replication with ARVDs as Highly Active Antiretroviral Therapy (HAART). The goal of ART is to attain maximal and durable suppression of the viral replication. The effectiveness of ART is assessed by clinical observations, CD4 cell count and determination of plasma viral load. Stage of HIV disease and the degree of immune damage serve as determinants for the initiation of ART. For ART naïve patients, treatment is initiated with a combination of 3 drugs (Triple Therapy); consisting of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and a third drug from the non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) or Protease Inhibitors (PIs) (DACA, 2010).

Practice guideline for the treatment of patients with HIV/AIDS implies that the rational choice of psychotropic medications must also include critical considerations of adherence (Fong *et al.,* 2003). Adherence to a treatment regimen is profoundly important for patients with HIV infection. Research has demonstrated that less than 95% adherence to antiretroviral medications results in the development of viral resistance which leads to further progression of the disease and also psychiatric disorder (Slade, 2002). Furthermore, studies indicate that advancements in the treatment of psychiatric disorders are limited by non-adherence, which steal power from even the most beneficial medications. According to the study done in a Tertiary Care Hospital, Karachi, Pakistan patients with comorbidity were less adherent as compared to patients without comorbidity (Taj *et al.,* 2008).

However when HIV and psychiatric disorders occur together, the development of a psychiatric treatment plan for patients with HIV infection requires thoughtful and comprehensive consideration of the biopsychosocial context of the illness. Adherence is of utmost concern with antiretroviral treatment because the regimens are so unforgiving; even minor deviations from the prescribed regimen can result in viral resistance and permanent loss of efficacy for existing medications. Psychiatrists can play an important role in the promotion of patient adherence, since comorbid psychiatric disorders (e.g., substance abuse or depression) have been shown to adversely affect patient compliance with a complicated treatment regimen. The management of disturbances in mood, such as major depression or mania, for patients with HIV infection may not be similar to that for other patients with medical comorbidity (Sebit *et al.,* 2003).

Choice of an antidepressant or mood-stabilizing agent may be influenced by the antiretroviral regimen in place, and dose adjustments may be necessary if drug-drug interactions (DDIs) are likely (McDaniel *et al*., 2000). A wide array of antidepressant agents is effective in the treatment of HIV-associated major depression, including newer agents such as the selective serotonin reuptake inhibitors (SSRIs) and medications such as psychostimulants and testosterone. Psychotherapy, particularly interpersonal psychotherapy, either alone or in combination with antidepressant agents, is also an effective treatment for HIV-related depression. Mania associated with HIV infection, particularly late in the course of HIV disease, may be difficult to treat; however, treatment studies suggest that traditional Anti manic agents are effective and tolerated (McDaniel *et al.,* 2000; Rosenberg *et al.,* 2010).

For patients who are taking PIs, benzodiazepines are generally contraindicated because of DDIs. Thus, benzodiazepines should be given only as a short-term intervention in most instances. Psychotic symptoms in late-stage HIV infection are generally managed with atypical antipsychotic medications at the lowest effective dose, since standard neuroleptic medications have been associated with severe and difficult-to-treat extrapyramidal side effects. Adjustment disorders may require treatment with psychotherapy or medication to prevent progression to a more severe psychiatric disturbance (Rosenberg *et al.,* 2010).

HIV-associated syndromes with psychiatric implications encompass wasting syndrome, fatigue, pain, and sexual dysfunction. Wasting syndrome has been effectively treated with testosterone (or its derivatives), growth hormone, and thalidomide. Psychostimulants are one of the main interventions used for fatigue. Chronic pain from peripheral neuropathy is often treated with tricyclic antidepressants and anticonvulsant medications, but published treatment studies of pain syndromes in patients with HIV infection have not supported their use. The challenge in the management when both HIV and psychiatry occur together indicates that their prescription should be carefully looked into before dispensing to the patients to optimize treatment outcome (McDaniel *et al.,* 2000).

3.3 Factors affecting HIV treatment outcome

Without treatment, the vast majority of HIV-infected individuals will eventually develop progressive immunosuppression (as evident by CD4 count depletion), leading to AIDS-defining illnesses and premature death. The primary goal of ART is to prevent HIV-associated morbidity and mortality. This goal is best accomplished by using effective ART to maximally inhibit HIV replication so that plasma HIV RNA levels (viral load) remain below that detectable by commercially available assays (Meintjes *et al.*, 2014).

Durable viral suppression improves immune function and quality of life, lowers the risk of both AIDS-defining and non-AIDS-defining complications, and prolongs life. Furthermore, high plasma HIV RNA is a major risk factor for HIV transmission and use of effective ART can reduce viremia and transmission of HIV to sexual partners. Modeling studies suggest that the expanded use of ART may result in lower incidence and, eventually, prevalence of HIV on a community or population level. Thus, a secondary goal of ART is to reduce the risk of HIV transmission (Beard, 2009).Different studies from different countries reported that WHO clinical staging, viral load, age, gender, CD4 cell count, total lymphocyte count (TLC), body mass index (BMI), ART adherence, and baseline hemoglobin level were determinants of mortality. Even though studies had identified these determinants of mortality, they are so many other variables with context and dynamic across time with advancement of care and treatments as many years are being spent on HAART (Hambisa *et al.*, 2013).

The treatment outcome could be measured using biomedical outcomes, impacts of ART on patients' economic activities, quality of life, and other non-biomedical outcomes.

Clinical outcome can be measured by patients CD4 count, patients' plasma HIV RNA and the presence of opportunistic infections (Oyugi *et al.,* 2004). Furthermore, findings suggest that the economic benefits of ART are an important addition to the fundamental benefits of survival and reduced morbidity. Estimates from studies conducted in Kenya, with assumptions about various parameters such as the return to education, can be used to calculate the value of employment and education gains enabled by antiretroviral therapy. These calculations as well as a recent analysis of the Global Fund for AIDS, Tuberculosis, and Malaria have shown positive returns on investment in antiretroviral therapy programs. Money spent on financing treatment programs is thus likely to provide substantial economic returns to individuals, households, and employers in HIV-affected countries (Resch *et al.,* 2011; Thirumurthy *et al.,* 2008).

At the most basic level, ART leads to a dramatic improvement in the survival and health of HIV-infected people who have progressed to the latter stages of the disease. In principle, this improvement in health status and functional capacity should be accompanied by a greater ability to do productive work. Considerable evidence now shows that this is indeed the case (Augustyn *et al.,* 2012). Two early studies conducted in Kenya focused on populations of patients who were primarily engaged in subsistence or estate agriculture. Both studies showed that within twelve months of initiating antiretroviral therapy, patients were working in excess of 30 percent more (as measured in hours or days worked) than they had before starting ART. The increase in employment levels as a result of ART would be even greater if the likelihood of reduced employment levels in the absence of ART were used as the relevant comparison (Thirumurthy, Goldstein & Zivin, 2008).

Studies that observed treated patients over a longer period of time, up to three years after the initiation of treatment, confirmed that initial employment increases were sustained. In South Africa, employment rates among treated patients rose from 27 percent to 42 percent in the three years after the patients began ART (Rosen *et al.,* 2010). In India, the percentage of patients who were employed rose from 28 percent to 65 percent in a two-year period (Thirumurthy *et al.,* 2011).Two comprehensive reviews of these and many other studies suggest that the findings described above can be generalized to various settings, such as countries with high and low prevalence of HIV/AIDS and rural and urban areas (Beard, 2009).

4. Objective

4.1 General objective

- To assess HIV treatment outcome among mentally disordered patients at Amanuel Mental Specialized Hospital, Addis Ababa, Ethiopia.

4.2 Specific objective

- To compare the CD4 cell count among HIV positive patients with and without mental illness.
- To compare the occurrence of OIs among HIV positive patients with and without mental illness.
- To look into WHO classification of HIV clinical stages and the change over the course of the study period.
- To compare adherence to HIV treatment among both mentally ill and not mentally ill patients.

5. Methods

5.1 Study Setting

The study was conducted at Amanuel Mental Specialized Hospital. The hospital was established in 1930, to serve as a general hospital for the native Ethiopians during the short Italian regime. The structure of the hospital was not initially made to serve as a mental hospital and it was only after 1956 E.C that the hospital was named mental treatment hospital. After 1997 E.C, the hospital has been recognized as a specialized mental hospital. This hospital is the first of its kind situated in Addis Ketema subcity, Addis Ababa, the capital city of Ethiopia. The hospital has a 300 bed capacity. Of these, 277 are for inpatients and 23 are emergency beds. There is also a large outpatient service, with around 115,000 treated each year. The hospital service focuses on improving mental health of its clients. In addition the hospital has Anti-Retroviral treatment (ART) clinic which is run by two nurses for refill and one general practitioner. The clinic on average sees 40 patients per day.

5.2 Study Design

A retrospective cohort study of HIV treatment outcomes in mentally ill patients treated in the hospital in a three year period (September 2010 to August 2013) was conducted. In the ART clinic, there were two group of patients; HIV positive patients with no mental illness and HIV positive patients with concomitant mental illness.

5.3 Source and Study Population

The source population included all patients treated in AMSH during the period from September 2010 to August 2013. The study population consists of all HIV-positive patients treated at AMSH during the study period. Patients with age less than 18 years old, Patients with incomplete 3 year data and pregnant women were excluded from the study.

5.4 Sample size and Sampling procedure

All HIV positive patients treated in the Hospital during the three year period were included in the study. The sample was divided into two groups as HIV patients with mental illness and HIV patients with no mental illness.

Records of 429 HIV patients that were treated during the study period were obtained from the ART Clinic. Out of these, 337 HIV patients were included in the study because of lack of significant amount of information in the 92 charts. The cohort groups were divided after reviewing their charts for the presence of mental illness.

5.5 Data collection

5.5.1 Instrument and data collectors

Data extraction tool was designed to collect relevant data regarding patient characteristics and treatment outcome from patients' chart, in such a way that all relevant variables were collected so as to meet the intended objectives. Data on socio demographic characteristic of patients, HIV stage based on WHO clinical classification, the type of psychiatric disorder, medication, treatment outcomes such as CD4 count/ viral load were collected from patients' charts. Four nurses working in the hospital extracted data from the charts using the extraction form.

5.5.2 Data quality assurance

The prepared data extraction tool was pre tested in 5% of the sample and data collectors were trained to familiarize them with the data abstraction format. The completeness of the data collected was supervised by the principal investigator.

5.5.3 Data Entry and Analysis procedures

Data were entered into Epi-Info 2007 and exported to SPSS version 16.0 for analysis. Descriptive statistics (frequencies, tables, percentages, means, and standard deviation) were used to describe socio-demographic (age, sex, regional status) and clinical variables (medication profile, adherence distribution, psychiatric condition, and measures of treatment outcomes i.e. presence of opportunistic infection, change in CD4 count, adherence to ART and change in WHO class). An exploratory univariate analysis was done in order to select candidate variables for the multivariate analysis. A variable was considered a candidate if it showed marginal association ($p<0.25$) or if it is clinically

important. Multivariate logistic regression analysis was done with the identified candidate independent variables ($p< 0.05$) to check for confounding factors.

5.5.4 Study variables

Dependent variable: Presence of opportunistic infection at least once, change in CD4 count, adherence to ART and change in WHO clinical stage over the 3 years.

Independent variables: Presence of psychiatric illness, age, gender and weight

5.5.5 Operational definition

Treatment outcome in HIV positive patients- the treatment outcome is measured by the patients CD4 counts, WHO classification of clinical staging, adherence to ART and the occurrence of OIs at least once over three years.

WHO HIV/AIDs staging class assessment definition: In this study WHO class, is said to have increased when the patients' WHO staging assessment in a 3 year time interval increases from one class to the other, then the patient's condition has worsened. The WHO class staging is said to have decreased if the patients WHO staging assessment in a 3 year time interval shows improvement and results in a lesser WHO class stage than the previously assessed one and when the WHO class staging shows no change in a time interval then the patient shows no improvement.

CD4 count assessment definition: if the patients CD4 count increases over the 3 year time interval then the patient is improving, if the patient shows a decrease in the CD4 count then the patient is worsening. And when the CD4 count is the same then the patient is not progressing.

WHO staging: Clinical stages are categorized as 1 through 4, progressing from primary HIV infection to advanced HIV/AIDS. Staging is based on clinical findings that guide the diagnosis, evaluation, and management of HIV/AIDS. New or recurrent stage 4 events may suggest failure of response to treatment; new or recurrent stage 2 or stage 3 events may suggest an inadequate response to treatment, potentially because of poor adherence.

Adherence: is classified as good, fair and poor based on the number of doses missed as shown in Table 1.

Table 1 Classification of Adherence indicated in the HIV CARE/ART follow up form

Class	**%**	**Missed Doses**	
		of 30 doses	of 60 doses
G(good)	95%	< 2 doses	<3 doses
F(fair)	85-94%	3-5 doses	3-9 doses
P(poor)	<85%	6 doses	>9 doses

(HIV CARE/ART FOLLOW-UP FORM)

5.6 Ethical consideration

Ethical clearance was obtained from the ethics review committee of the School of Pharmacy, Addis Ababa University as well as Amanuel Mental Specialized Hospital ethical review committee. In view of the fact that the data collectors are already employed and working in the hospital, there will not be any ethical breach that would occur as a result of conducting this research. Furthermore confidentiality of the information obtained in the course of the study was secured by not using personal identifiers.

6. Results

6.1 Background Characteristics

Majority of the participants were females 205 (60.8%). The mean age of the participants was 37.44 ± 9.46 years. The minimum age was 20 and the maximum was 71 years. Majority of the participants were from Addis Ababa 289 (85.8%) followed by Oromia Region 26 (7.7%), SNNPR 11 (3.3%), Amhara 10 (3.0%) and Tigray region 1 (0.3%) [Table 2].

6.2 Substance use profile of the study participants

Thirty six patients had history of Khat use; of these 13 (36.1%) had psychiatric problem. Regarding alcohol use, 38 (11.3) of HIV patients had history of alcohol consumption; of these 21 (55.2) were having psychiatric problems (Table 2).

6.3 Psychiatric diagnosis of the study participants

Of the 337 study participants, 138 (40.9%) were diagnosed to have had a psychiatric condition, of these 94 (68.1%) were females. The majority were diagnosed to have schizophrenia 29 (21.0%). The overall psychiatric condition diagnosed among the participants is depicted in Table 2.

Table 2: Background characteristics of study participants at Amanuel Mental Specialized Hospital, September 2010-August 2013.

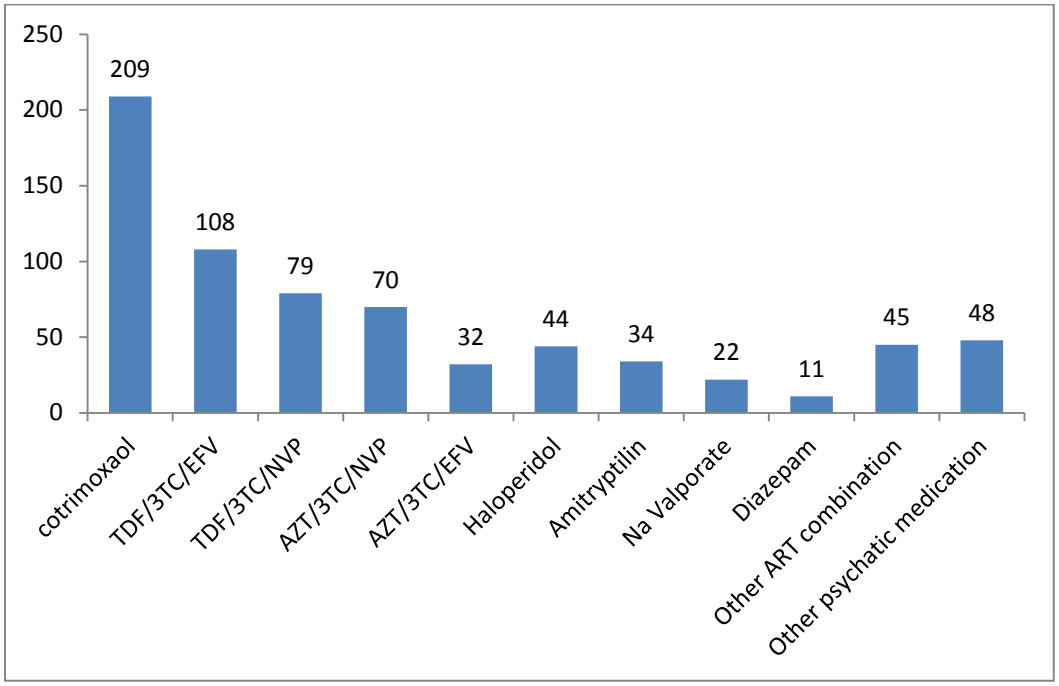
Characteristics		Number (%) of Psychiatric Patient (n=138)	Number (%) of Non Psychiatric Patient (n=199)
Sex	Male	44 (31.9)	88 (44.2)
	Female	94 (68.1)	111(55.8)
Age in years	18-24	4 (2.8)	9 (4.5)
	25-44	112 (81.2)	152 (76.4)
	45-64	20 (14.5)	36 (18.1)
	≥ 65	2 (1.4)	2 (1.0)
Region	Addis Ababa	117 (84.8)	172 (86.4)
	Out of Addis Ababa	21(15.2)	27 (13.6)
Khat Use	Yes	13 (9.4)	23 (11.6)
	No	125 (90.5)	176 (88.4)
Alcohol Use	Yes	21 (15.2)	17 (8.5)
	No	117 (84.8)	182 (91.5)
Primary psychiatric conditions	Schizophrenia	29	
	Psychosis	28	
	Bipolar & Mania	14	
	Depression & Mood	26	
	GAD and Anxiety	9	
	Psychosis + bipolar	3	
	Psychosis + Depression/mood	2	
	Others	27	

n=337

6.4 Medication Profile

Medication profile of the patients was reviewed and the most common prescribed non-ART medication was found to be Cotrimoxazol followed by Haloperidol and the most common ART medication prescribed was found to be TDF/3TC/EFV followed by TDF/3TC/NVP (Figure 1).

Figure 1 Medications used by HIV positive patients at AMSH, September 2010-August 2013.



- Other ART medication: TDF/3TC/ABC, D4T/3TC/EFV, D4T/3TC/NVP, AZT/3TC/Kaletra and TDF/3TC/Kaletra
- Other psychiatric medication: Artane, Bromazepam, Carbamezapam, Chlorpromazine, Clonazepam, Diazepam, Imipramine, Olanzepam, Phenobarbitone, Pheneytion, Promethazin, Risperidone and Sertraline

6.5 Measures of treatment outcome

6.5.1 WHO clinical stage classification and CD4 count

Worsening of WHO staging over the 3 years was observed in 2 (0.6%, n=335) participants, which were non psychiatric patients. In 24 (11.3 %) non-psychiatric patients and 12 (9.6%) psychiatric patients the WHO class had neither improved nor worsened. In addition, the WHO class showed an improvement in 125 (92%) psychiatric patient and 173 (87%) non-psychiatric patients.

Regarding CD4 count of the study subjects, 59 (18.2%) patients' CD4 count were found to be worsened over time. Among one hundred thirty three psychiatric patients for which CD4 count information was available, 104 (78.2%) patients' CD4 count increased showing improvement, 24 (18%) patients' CD4 count decreased, and 5 (3.8%) had shown no change. Initial and final clinical characteristics of the patients are depicted in Table 3 and 4.

Table 3: Distribution of participants by initial clinical characteristics at Amanuel Mental Specialized Hospital, September 2010-August 2013.

Characteristic		Psychiatric patient	Non Psychiatric Patient
Mean weight in Kg (SD)		53.8 (± 9.5)	55.9 (±10.7)
Mean CD4 count (SD)		241.13 (±166.1)	241.34 (±171.7)
WHO class (N=336)	Primary HIV	0	1 (0.5)
	Class 1	13 (9.4)	39 (19.6)
	Class 2	36 (26.3)	65 (32.7)
	Class 3	68 (49.6)	80 (40.2)
	Class 4	20 (14.6)	14 (7.03)

n=337

Table 4: Distribution of participants by Final clinical characteristics at Amanuel Mental Specialized Hospital, September 2010-August 2013.

Characteristic		Psychiatric patient	Non Psychiatric Patient
Mean weight in Kg (SD)		55.0 (± 9.5)	58.3 (±12.0)
Mean CD4 count (n=325) (SD)		350.5 (±212.2)	372.9 (±214.2)
WHO class (N= 335)	Primary HIV	9 (6.6)	37 (18.6)
	Class 1	58 (42.6)	73 (36.7)
	Class 2	56 (41.2)	71 (35.7)
	Class 3	13 (9.5)	18 (9.0)
	Class 4	-	-

n=337

6.5.2 Opportunistic Infections

The presence of opportunistic infections was assessed among the study participants and it was found that 138 (41%) patients had opportunistic infection among which 101 (73.2%) were psychiatric patients.

The highly prevalent opportunistic infections identified in the current sample were pulmonary TB and extra pulmonary-TB. Specific opportunistic infection present in the study participants is depicted in Table 5.

Table 5 Opportunistic infections in HIV positive patients at AMSH, September 2010- August 2013.

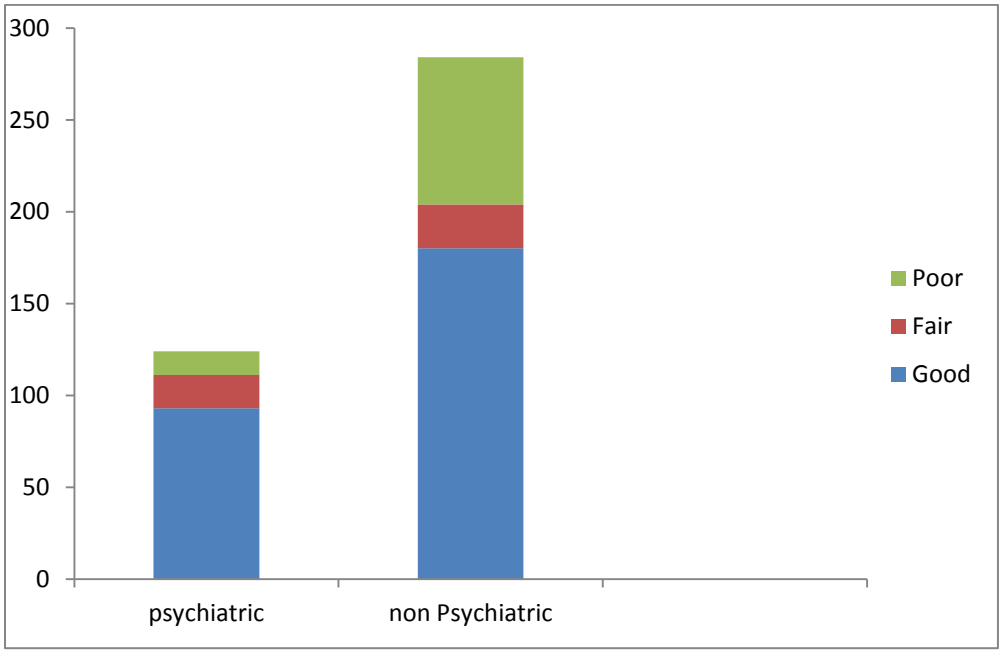
Disease	Number	Percent
Pulmonary TB	102	30.3
TB-Extrapulmanary	74	22.0
Recurrent Upper Respiratory Tract Infections	59	17.5
Fever	55	16.3
Herpes Simplex	41	12.2
Pneumonia (Recurrent)	41	12.2
Diarrhea	40	11.9
Candidiasis	28	8.3
Candidiasis(Oropharyngeal)	20	5.9
Minor Mucocutaneous Manifestation	14	4.2
Salmonella Septicemia	13	3.9
Mycosis	12	3.6
Others*	37	8.1

*Others include: Cryptococal Infections, Cryptococal Meningitis, Kaposis Sarcoma, Encephalopathy, Pneumocystis carinii Pneumonia, PGL, and Taxoplamosis. These infections were included in the others category for individually having less than 5% frequency.

6.5.3 Adherence profile

As shown in Figure 2, the overall adherence of the study participants on ART medication was assessed to be good in 262 (77.7%) of the patients among which 101 (38.5%) were psychiatric patients'. However, adherence was identified to be fair in 34 (10.1%) and poor in 15 (4.5%) of the study participants. Among these latter patients, 16 (47.1%) and 10 (66.7%) were psychiatric patients, respectively. Univariate logistic regression analysis comparing adherence (coded as 1for Good and 0 for fair and poor) with presence of psychiatric condition revealed that non-psychiatric patients significantly adhered to their ART medication (Adjusted odds ratio = 3.06 (1.02, 9.18); P = 0.046) as compared with psychiatric patients. The change in CD4 count and weight were compared with the adherence profile and it was found that both CD4 count and weight decreased in those that had lower adherence. Similarly, Opportunistic infection was more common in non-adherent patients compared to the adherent ones.

Figure 2 Adherence Vs Psychiatric condition in HIV positive patients in AMSH, September 2010-August 2013.



6.6 Factors associated with HIV treatment outcome in mentally ill patients

The possible association between HIV treatment outcomes (Occurrence of OIs, change in WHO clinical staging, and change in CD4 count) and adherence to ART with independent variables (such as age, sex, psychiatric diagnosis, and weight) were explored using multivariate logistic regression. Univariate analysis for the selection of candidate variable for the multivariate logistic regression model identified all four variables to be included as independent variables for the four models because they meet either the marginal association rule or the clinical importance rule.

Using occurrence of OIs as dependent variable, age (P = 0.09), adherence (P = 0.13), and psychiatric diagnosis (P = 0.18) showed marginal association. Gender and weight failed to meet the first rule of marginal association with the occurrence of OIs but were deemed clinically important to be included in the final analysis. Regarding the selection of candidate variables for identification of potential predictors for change in WHO class, only psychiatric diagnosis (P = 0.21) was selected because it showed marginal association while age, gender, adherence, and weight were selected because of their clinical importance. Univariate analysis with CD4 count change as a dependent variable identified all of the five independent variables to be selected for the final analysis; age (P = 0.06) and weight (P = 0.02) meet the first rule of marginal association; psychiatric diagnosis, adherence, and age meet the second rule of clinical importance. Using adherence as dependent variables, all variables were selected for the final analysis.

Multivariate logistic regression analysis revealed that occurrence of OI significantly differed by psychiatric diagnosis, where psychiatric patients with HIV showed more occurrence of OIs compared with non-psychiatric patients with HIV (Table 6).

Uncharacteristically, occurrence of OIs was significantly higher in patents with good adherence practice. Other HIV treatment outcome indicators (change in WHO class and change in CD4 count), however, did not show significant difference by presence or absence of psychiatric conditions (P > 0.05) [Table 7 and 8].

Table 6: Factors associated with occurrence of OIs among HIV patients at Amanuel Mental Specialized Hospital, Addis Ababa, September 2010- August 2013.

Independent Variables	Presence of OI		Adjusted Odd Ratio	Sig	95% CI
	0	1			
Gender					
Male	42	90			
Female	62	143	1.05	0.86	(0.62, 1.78)
Age					
18-24	3	10			
25-44	89	175	0.76	0.70	(0.19, 3.10)
45-64	12	44	1.62	0.54	(0.34,7.64)
>65	0	4	~0	0.99	-
Weight					
Weight loss	34	71			
No Change	8	28	1.69	0.27	(0.67,4.27)
Weight Gain	60	131	1.03	0.92	(0.59, 1.79)
Psychiatric Diagnosis					
Absence	67	132			
Presence	37	101	**1.70**	**0.05**	(0.99, 2.88)
Adherence					
Good	77	185			
Fair	9	25	1.26	0.58	(0.55, 2.87)
Poor	8	7	**0.34**	**0.05**	(0.11, 0.99)

Table 7: Factors associated with CD4 count among HIV patients at AMSH, Addis Ababa, (September 2010- August 2013)

Independent Variables	Improvement in CD4 count		Adjusted Odd Ratio	Sig	95% CI
	0	1			
Gender					
Male	27	102			
Female	39	157	1.26	0.47	(0.68, 2.32)
Age					
18-24	1	12			
25-44	59	193	0.42	0.42	(0.05, 3.48)
45-64	5	51	1.52	0.72	(0.15, 15.3)
>65	1	3	0.37	0.54	(0.02, 8.65)
Weight					
Weight loss	25	75			
No Change	11	22	0.69	0.42	(0.28, 1.70)
Weight Gain	29	159	1.95	0.05	(1.01, 3.76)
Psychiatric Diagnosis					
Absence	37	155			
Presence	29	104	0.85	0.59	(0.47, 1.54)
Adherence					
Poor	2	12			
Good	50	207	0.61	0.54	(0.13, 2.97)
Fair	8	24	0.39	0.29	(0.07, 2.28)

Table 8: Factors associated with WHO clinical staging among HIV patients at AMSH, Addis Ababa, (September 2010- August 2013)

Independent Variables	Improvement in WHO class		Adjusted Odd Ratio	Sig	95% CI
	0	1			
Gender					
Male	17	115			
Female	21	184	1.18	0.68	(0.54, 2.58)
Age					
18-24	0	13			
25-44	30	234	~0	0.99	-
45-64	8	48	~0	0.99	-
>65	0	4	~0	0.99	-
Weight					
Weight loss	15	90			
No Change	5	31	0.83	0.76	(0.26, 2.70)
Weight Gain	18	173	1.14	0.76	(0.49, 2.70)
Psychiatric Diagnosis					
Absence	26	173			
Presence	12	126	2.07	0.10	(0.80, 4.88)
Adherence					
Poor	2	13			
Good	28	234	1.55	0.59	(0.32, 7.61)
Fair	1	33	5.76	0.17	(0.46, 71.3)

7. Discussion

This study is a retrospective cohort study designed to assess HIV treatment outcome among mentally disoredred patients at Amanuel Mental Specialized Hospital. Assessment and management of mental disorders is integral to an effective HIV/AIDS intervention program.

The socio-demographic factors of gender, age, marital status, education, and income have consistently been identified as important factors in explaining the variability in the prevalence of depression and other psychiatric illnesses and level of adherence. The mean age of the study participants was 37.44 ± 9.46; this was similar to the study done by Sayad et al.,(2007) and Sarana et al.,(2008) in which the mean age was 34.26±7.4 and median age was 36 years, respectively. This study found a female preponderance 60.8%, which is consistent with the UNAIDS/WHO global report stating that unlike women in other regions of the world, African women are considerably more likely at least 1.4 times to be infected with HIV than men (Sayad *et al.,* 2007).

Majority of the participants were from Addis Ababa 289 (85.8%) this is because the hospital is located in Addis Ababa. Majority of the study participants 138 (40.9%) were diagnosed to have a psychiatric condition this is consistent with the study done by *Himelhoch et al.,* (2009) this is because HIV patients have more risk to develop psychiatric condition also psychiatric disorders increase the risk of acquiring HIV (Angelino, 2008).This however may also be due to the fact that the study was done in a mental hospital.

Apart from psychological impact, HIV infection has direct effects on the central nervous system, and causes neuropsychiatric complications including HIV encephalopathy, depression, mania, cognitive disorder and frank dementia, often in combination (WHO, 2008). Recent literature has demonstrated that psychiatric patients, particularly those with a diagnosis of schizophrenia, may be at high risk for HIV infection. People with schizophrenia are more likely to engage in risky behaviors that transmit the HIV virus than the general population and as a result there is an increased prevalence of HIV infection in this group (Gray *et al.*, 2002). This study showed that among the mentally ill study participants the majority were diagnosed to have schizophrenia 29 (21.0%).

In this study the WHO clinical staging classification was one of the indicators used to assess HIV treatment outcome. Out of the 337 study participants, 335 had WHO clinical staging recorded. The WHO clinical staging has shown an improvement in 125 (92%) of psychiatric patients and 173 (87 %) non-psychaitric patients. From the total study participants the WHO clinical stage has worsened in only 2 (0.6%) patients, both of which were non-psychiatric. The finding of this study is contrary to the common expectation.

CD4 count is the most important indicator of the degree of immune deficiency in HIV-positive patients (Ray *et al.,* 2006). In this study, out of 337 study participants 133 psychiatric patients had CD4 count recorded, 104 (78.2%) patients CD4 count increased showing improvement, 24 (18%) patients CD4 count decreased and 5 (3.8%) had showed no change. The finding of this study is contrary to the normally expected. This might be due to the close follow up of the study participants in Amanuel mental specialized hospital since most of them are inpatients.

Psychiatric illness can be an important factor determining the adherence to treatment of HIV infection. Those with mental illness can have difficulty in adhering to the medication routine; consistent with these, the current study found a significant difference (P=0.046), patients without psychiatric conditions were found to be more adherent. Similarly, In a sample of 310 patients on HAART, Sarna *et al*. (2008) found that patients with severe depression were four times more likely to report lower adherence to treatment. In this study, 77.7% of the study participants showed good adherence rate, among which 38.5 % were with psychiatric illness. However, in 4.5% the adherence was found to be poor and among them the majority 66.7% is psychiatric patients. The adherence might be rated as good since most of the psychiatric patients are in patients where the physician follows their treatment where missed doses are minimized. Considering that HIV and Psychiatric conditions co-occur together frequently issues concerning treatment outcome should not be taken lightly.

The current study initially predicted that psychiatric patients with HIV will have poor control of HIV (as evidenced by presence of OI, change in CD4 count, and change in WHO clinical staging) compared with non-psychiatric patients with HIV. This prediction emanate from another prediction that psychiatric patients with HIV might poorly adhere to their ART medications. Multivariate analysis showed only the occurrence of OIs to differ across psychiatric diagnosis, with change in CD4 count and WHO class showing no difference. The change in only one treatment outcome is not a strong suggestion to ascertain the influence of presence of psychiatric illness on HIV treatment. This discrepancy between the prediction and the actual observation might be explained by the close follow up of these patients and tight control of drug intake including ART

medications as the majority of the psychiatric patients were inpatients. This might have influenced the adherence issue that might have been observed if the patients were left to make decision on their medication intake.

8. Limitation of the study

This study suffers all the limitations of a retrospective study (relevant variables may not be available in the original records, and attrition problems may be serious due to loss of records, incomplete records or difficulties in tracing or locating all of the original population for further study). In addition, since the study was done in a major mental health institute of the country, the result may not be representative to the overall practice of the country. Furthermore, only patients that were registered on the ART unit log book were included.

9. Conclusion

Coexistence of HIV infection with mental illness has great impact on treatment of patients. This hospital-based study in Amanuel mental specialized hospital showed that more than one third of the study participants were both HIV infected and mentally ill. Treatment outcome of the study participants was measured by the CD4 count, OI, and WHO classification. In majority of the study participants, WHO class staging has showed improvement indicating the study participants are showing improvement. OIs occur in almost half of the participants and CD4 count has improved in majority of the participants. Overall, the factors used for the assessment of HIV treatment outcome (the occurrence of OIs, change in WHO class staging and Change in CD4 count) were not influenced by presence of psychiatric illness.

10. Recommendation

Based on the findings of this study it is recommended that:

- Prepare treatment guideline regarding the proper management of HIV infected mentally ill patients.
- Proper documentation of patient information in the Hospital.
- A series of awareness creation forums to be organized to health care professionals about the proper management of mentally ill HIV patients.
- Further study to be done on how HIV patients' viral load is affected when psychiatric condition co-exists.

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12. Appendices

Annex I: Data abstraction form

Addis Ababa University

College of Health Sciences

Data Extraction Form from Charts of HIV Patients Treated at Amanuel Mental Specialized Hospital.

I. Patients Related Information

1. Card No. _____
2. Age _____
3. Sex _____
4. Marital status _____
5. Level of Education_____
6. Occupation_____
7. Address_____

II. Clinical Status

8. Psychiatric Diagnosis

   8.1 Yes 8.2 No

9. If yes to Q. 8, Diagnosis

   9.1 Schizophrenia 9.2 Bipolar Disorder

   9.3 Depressive Disorder 9.4 Others _____

10. Date of Diagnosis_____
11. Psychotropic Medications 11.1_____

    11.2_____

    11.3_____

12. Side effects of psychotropic medications, Specify

13. Date of HIV diagnosis_____
14. Start of ART_____

15. ART drugs 15.1_____

15.2_____

15.3_____

15.4_____

16. Side effects of ART, Specify

17. Patients baseline weight_____

18. Patients latest weight_____

19. Patients Initial CD4 level_____

20. Patients latest CD4 level_____

21. Initial WHO clinical staging_____

21.1 Primary HIV infection

21.2 Clinical Stage 1

21.3 Clinical Stage 2

21.4 Clinical Stage 3

21.5 Clinical Stage 4

22. Final WHO clinical Staging _____

23. Patients Hemoglobin_____

24. Is there any occurrence Opportunistic illness?

24.1 Yes 24.2 No

25. If Yes specify

26. Is TB test done

26.1 Yes 26.2 No

27. Is the patient on Anti- TB treatment?

27.1 Yes 27.2 No

28. Was there any progress recorded regarding the psychiatric disorder?

28.1 Yes 28.2 No

29. If Yes

29.1 No change 29.2 Improved 29.3 Relapsed

30. Was there any shift in their first-line medication of psychotropic medication?

30.1. Yes 30.2 No

31. Why?

32. Was there any shift in their first-line medication of ARVs?

32.1 Yes 32.2 No

33. Why?

34. The status of ART refill?

34.1 Good 34.2 Fair 34.3 Poor

35. Does the patient have history of khat use?

35.1 Yes 35.2 No

36. Does the patient have history of alcohol abuse?

36.1 Yes 36.2 No

Thank You

Annex II: WHO Clinical classification guideline

Table 2. WHO Clinical Staging of HIV/AIDS for Adults and Adolescents	
Clinical Stage	Clinical Conditions or Symptoms
Primary HIV Infection	• Asymptomatic • Acute retroviral syndrome
Clinical Stage 1	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory infections (sinusitis, tonsillitis, otitis media, and pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruptions • Seborrheic dermatitis • Fungal nail infections
Clinical Stage 3	• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhea for >1 month • Unexplained persistent fever for >1 month (>37.6°C, intermittent or constant) • Persistent oral candidiasis (thrush) • Oral hairy leukoplakia • Pulmonary tuberculosis (current) • Severe presumed bacterial infections (e.g., pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia) • Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis • Unexplained anemia (hemoglobin <8 g/dL) • Neutropenia (neutrophils <500 cells/µL) • Chronic thrombocytopenia (platelets <50,000 cells/µL)
Clinical Stage 4	• HIV wasting syndrome, as defined by the CDC (see Table 1, above) • *Pneumocystis* pneumonia

	• Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital, or anorectal site for >1 month or visceral herpes at any site) • Esophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis • HIV encephalopathy • Cryptococcosis, extrapulmonary (including meningitis) • Disseminated nontuberculosis mycobacteria infection • Progressive multifocal leukoencephalopathy • Candida of the trachea, bronchi, or lungs • Chronic cryptosporidiosis (with diarrhea) • Chronic isosporiasis • Disseminated mycosis (e.g., histoplasmosis, coccidioidomycosis, penicilliosis) • Recurrent nontyphoidal *Salmonella* bacteremia • Lymphoma (cerebral or B-cell non-Hodgkin) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis • Symptomatic HIV-associated nephropathy • Symptomatic HIV-associated cardiomyopathy • Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)