COLLEGE OF EDUCATION AND BEHAVIOURAL STUDIES

SCHOOL OF PSYCHOLOGY

MEASURING ADHERENCE LEVEL TO ANTIRETROVIRAL TREATMENT AMONG ADULT PLWHA IN ZEWDITU MEMORIAL HOSPITAL ADDIS ABEBA

BY

TIRUWORK AKLIE BITEWULIGN

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR MA DEGREE IN MEASUREMENT AND EVALUATION

AUG, 2014

ADDIS ABABA, ETHIOPIA

This is to certify that this thesis prepared by Tiruwork Aklie, entitled: Measuring adherence level to antiretroviral treatment among adult PLWHA in Zewditu Memorial Hospital Addis Ababa and submitted in partial Fulfillment of the requirements for the degree of master of Art in Measurement and Evaluation complies with the regulations of the University meets the accepted standards with respect to originality and quality.

Signed by the Examining committee

Internal Examiner_____ signature_____ Date_____

External Examiner _____signature_____Date_____

Advisor_____signature_____Date_____

_____

Chair of Department or Graduates program coordinator

Acknowledgements

I want to acknowledge the following persons and institutions for their respective contributions to this thesis:

Firstly, a special gratitude goes to my supervisor Dr. Teka Zewdie for his support and encouragement. Secondly, I am indebted to my neighbor w/r. Yesunesh Teshome for her willingness and help in the statistical analysis. Thirdly, my gratitude goes to my husband Dr. Getahun Mengistu and for his idea and empowerment. Fourthly, my gratitude goes to my brother Ato Teshager Aklie for his encouraging ideas and help. Fifthly, I would like to thank Zewuditu memorial Hospital ART clinic head and manager Dr, Aster for her facilitation and help in collecting the data. Sixthly, I thank the Medical director of Zewuditu memorial Hospital and Addis Ababa regional health bureau for allowing me to conduct this research in the hospital. Finally, Zewuditu memorial Hospital ART clinic Data collectors and archive workers for their good will in assisting me in the data collection process

ABSTRACT

This study attempted to measure anti-retroviral therapy (ART) adherence level in Zewditu Memorial Hospital, Addis Ababa. Retrospective and cross-sectional sources were used. Patient self-report adherence measuring tool was used. Based on this structured Patient self-report adherence questionnaire and in a simple random sampling technique data were collected from 138 clinical records of ART patients, exit- interviews were conducted on 50 ART patients and few ART providers. Descriptive, one sample t-test, correlation, uni-variate and multivariate logistic regression analysis were used. The findings revealed mixed adherence level (clinical data perspective 95-100% adherence rate found among 95% of the sample whereas in exit interview data analysis perspective 100% perfect adherence level was found among 30 respondents, suboptimal adherence rate which ranges from 29% to 86% found among 19 individuals whereas, one individual had 0% adherence/he didn't took his ART for that week/. Waiting months on ART and regimen change were predictive factors for non-adherence behavior. Drug side effect/toxicity is a major reason for missed drug doses and regimen changing behavior. Forgetting, being busy, social stigma or discrimination, and alcohol use were the identified barriers for non- adherence behavior. Finally the study hints the necessity to design and practically implement substantive theories of behaviors based adherence interventions programmes that can promote adherence behaviors and alleviate the burdens of stigma or discrimination and drug side effects among ART patients.

Table of Contents

Page

Acknowledgments..... I

Abstract II

List of Tables III

List of Figures IV

Abbreviations V

I. INTRODUCTION..... 1

1.1. Background 2

1.2. Statement of the Problem 4

1.3. Rationales of the Study……... 4

1.4. Research Questions……5

1.5. Objectives of the study**……6**

1.6. Significances of the study……...6

1.7. Scope of the study…… ……..…….6

1.8. Limitations and delimitations of the Study……7

1.9. Operational Definitions……..7

II. LITRATURE REVIEW……8

2.1.HIV /AIDS disease progression ……8

2.2.Highly active antiretroviral therapy for HIV infection/HAART……9

2.3.HAART Adherence promoting measurement tools……...10

2.4.Factors affecting ART adherence rate……12

2.5.Outcome of highly active ant-retroviral treatment /HAART…….12

2.6.Risk of antiretroviral non – adherence……...13

2.7.Care and support for persons living with HIV/AIDS……13

2.8.Local studies on ART treatment adherence……...14

2.9.Theoretical concept…….....15

2.9.1. Cognitive model of compliance……..15

2.9.2. The theory of planned behavior (TPB)……...15

2.9.3. The health belief model (HBM)……..16

2.10. Summary of the review…….....21

III. RESEARCH DESIGN AND METHODOLOGY……..23

3.1. Research Design 23

3.2. Data source.....23

3.3. Population 24

3.4. Sample.....24

3.5. Sampling criteria 24

3.6. Sample size determination 25

3.7. Sampling procedures.....26

3.8. Data collection…….26

3.8.1. Data collection instrument…….27

3.8.2. Procedure of instrument development……...27

3.8.3. Pre-test……...28

3.8.4. Validity and reliability of instrument……28

3.9. Data analysis……29

3.10. Ethical consideration……...29

IV. DATA ANALYSIS AND RESULTS 31

4.1. Retrospective data analysis 31

4.1.1. Respondents' profile…….....31

4.1.2. Self-report adherence level from records…….33

4.1.2.1. Adherence level verses demographic factors…….34

4.1.2.2. Adherence and demographic variable association…….35

4.1.3. Regimen change and adherence behavior……....35

4.1.4. Mean distribution of weight & CD4 level……..36

4.1.4.1.Adherence clinical outcomes and demographic factors association…….38

4.1.4.1.1. Multivariate Logistic Regression analysis for significant demographic factors…….39

4.2. ART Providers based data …….41

4.2.1. Status of the providers……...41

4.2.2. Adherence monitoring interventions of the facility……..41

4.2.3. Adherence behavior promoting measures…….41

4.3. Exit interview survey……...43

4.3.1. Respondents profile……..43

4.3.2. Respondents psycho-social and economic factors……...44

4.3.3. Interviewed respondents' adherence rate……..44

4.3.4. psycho-social factors and adherence behavior……...46

4.3.5. Adherence factors…….....48

V. DISCUSSION of Major findings ……52
5.1. Discussions……52
VI. Summary, Conclusion and Recommendations……60
6.1. Summary……...60
6.2. Conclusion……62
6.3. Recommendations……..63

REFERENCES ……64

Appendix……70

List of tables **Page**

Table-1Demographicprofile of study subjects…..……..33

Table-2 Adherence rate within 6 month interval after ART initiation…….34

Table- 3 Adherence rate after 6 month ART initiation versus demographic factors……35

Table – 4Respondents' ART drug first regimen change behavior…….37

Table-5 Patients' mean Weight and CD4+ cells count every 6 months interval……..38

Table- 6 Adherence rate and clinical outcome: Six months after ART initiation……39

Table -7 Demographic and after 6 months' clinical outcomes (weight and CD-4)

associations……39

Table-8 Logistic regression parametric estimate…….41

Table -9 Profile of interviewed respondents ……44

Table -10 Respondents' adherence rate…….46

Table -11 Psycho-social factors and adherence…….48

Table -12 Adherence factors and adherence rate association from the exit interview data…..49

Table -13 Logistic regression parametric estimate…….51

LIST OF ACCRONOMIS

ART: Anti-retroviral therapy

ARV: Anti-retroviral

HBM: Health Belief Model

HIV: Human immune deficiency virus

IRB: Institutional review board

WHO: World Health Organization

AAU: Addis Ababa University

M& E: Monitoring and Evaluation

TPB: Theory of Planned Behavior

TRA: Theory of Reasoned Action

CD-4: Cluster of Differentiation -4

SD Standard deviation

COR Crud odds ratio

AOR Adjusted odds ratio

IAA : Initiative on Antiretroviral Adherence

EFMOH: Ethiopian Federal Ministry of Health

FHAPCO: Federal HIV/AIDS prevention and Control Office

HAART: Highly active anti-retroviral therapy

MEMS: Medication event monitoring system

PLWHIV: People living with HIV

UNAIDS: The Joint United Nations Programme on HIV/AIDS

EHNRI: Ethiopian Health and Nutrition Research Institute

Annexes

Anex -1 Clinical records structured questionnaires

Anex -2 ART providers' adherence promoting practice questionnaires

Anex -3 Exit interview questionnaires

Anex -4 AAU proposal clearance

Anex -5 IRB Ethical clearance

CHAPTER ONE

I. INTRODUCTION

1.1. Background of the study

Human immunodeficiency virus (HIV) is the most significant emerging infectious pathogen of the 21st century. The agent that caused acquired immunodeficiency syndrome (AIDS) was first recognized in 1981. Its epidemiology and diagnostic tests were known rapidly (Baveja, Usha & Bharat, 2004). Moreover, antiretroviral therapies that reduce the viral copies in the blood and avoid the morbidity because of the infection were discovered subsequently (Baveja, 2004); then after HIV/AIDS has been considered to be a chronic and globally spread serious illness that requires life-long treatment (Chesney, 2003).

In Ethiopia, antiretroviral treatment (ART) first became available for those who could afford it in 2003. In 2005, a free ART service was launched with financial support obtained from the Global Fund, the World Bank and the United States President's Emergency Plan for AIDS Relief (WHO, 2009).This service helps to increase the number of HIV patients who are regularly taking HAART; consequently it become highly important and desirable to address the high mortality and morbidity rates among patients who do not meticulously adhere to their HAART regimen (Johnson and Witt, 2007).

Optimal adherence to the HAART regimen, i.e. an adherence rate of greater than 95%, is an indispensable requirement for patients receiving HAART if they hope to reap the benefits of long-term treatment (Baveja, 2004). Patients at first hand need to maintain the only optimal adherence level to the requirements of HAART that will ultimately minimize treatment failures and the

interpersonal transmission of strains of HIV that may have developed a strong resistance to HAART (Johnson, 2007).

If an HIV patient on ART is not taking the ARV drugs thoroughly, i.e. if the patient is not optimally adherent to ART, the possibility of the failure of the treatment along with a deterioration in the health status of the patient and the development of a multidrug resistance to antiretroviral drugs that can be transmitted to others, is undeniably high (INRUD Ethiopia & the RPM Plus, 2007).

People diagnosed as having HIV infection and related illnesses, including AIDS, are confronted with a host of problems that call for emotional and/or practical support. Depression, isolation, hospitalization, discrimination within the community or family, financial problems and disease progression are all concerns that may have to be managed (Baveja, 2004).

In an effort to scale up and decentralize ART services in Ethiopia, there are increasing number of health facilities providing ART and similarly the number of patients getting ART services is increasing (FHAPCO, 2012). With the large number of patients on antiretroviral therapy at the health facilities, the issue of adherence is critical to both the control of the disease and effective use of the resources being devoted to AIDS treatment (WHO, 2010).

1.2. Statement of the problem.

Careful conformity to the ARV medication adherence routine is vital for patients who hope to obtain the long-term benefits of ARV medications (Beith and Johnson, 2006) yet surprisingly; adherence is not well addressed as a central component at health facilities and patient levels. If adherence is low, treatment failure will occur and the likelihood of development of resistant virus will be high. The global interest in improving access has ensured a lot of funds for ARV programs, but no one is taking the lead in the issue of adherence (UNAIDS, 2010).

In a recent meta-analysis, a pooled estimate of adherence levels study in sub-Saharan Africa reported that only 77% of people taking antiretroviral medications adhered to the regimen. Over all, in resource limited settings, there are little data on the adherence levels reached at health facilities providing routine ART services in general, (Johnson, 2007) and this is much worse in Ethiopia in particular

HIV prevalence in the overall Ethiopian population is 2.4% but the urban prevalence is 7.7% while the rural prevalence is 0.9% (EFMOH/HAPCO; 2007a). This makes urban areas a potential high yield recruitment area for ART patients to participate in research projects (EFMOH/HAPCO, Road Map 2007b:09). Ethiopian Health and Nutrition Research Institute (EHNRI, 2012) points out, in Ethiopia in general about 790,000 people were living with HIV, total annual AIDS deaths were 33,357 and ART needs total was for 246,120 patients. In Addis Ababa in particular, the total annual AIDS deaths are 4,532; moreover, 45,135 numbers of people required ART drug initiation (EHNRI, 2012). Addis Ababa is the capital city of Ethiopia and the adult prevalence rate of HIV/AIDS in this area is 9.2% (EFMOH/HAPCO, 2007a).This figure is higher than the national prevalence rate, making Addis Ababa a highly affected area in the country in particular and in sub-Saharan region in general.

The most effective regimen will fail if the patient does not take the medication as prescribed or refuses to take it at all. Consequently all things being equal, the most important factors influencing adherence are patient-related (Chesney, 2000). Moreover, in all settings, maintaining high treatment adherence for a life-long condition is a considerable challenge (Gill, Hamer, Simon, et al., 2005). It is challenging, because patients need almost perfect adherence of at least 95% to keep viral load at undetectable levels as long as possible and to maintain the functionality of the immune system.

In a study done by Markos & his colleagues (2008) at Yirgalem Hospital, adherence level for patients who missed ARV treatment drug doses was 88.7%. Failure to achieve high levels of patient adherence in ART programs will lead to an increase in the rates of treatment failure and an increase in demand for second-line treatment, which is currently ten times more expensive than first-line treatment (Johnson, 2007).

According to Yimenu's (2009) study done on factors influencing anti- retroviral therapy in Ethiopia, the optimal self- reported adherence level (greater than or equal to 95% adherence rate) were reported by only 80.2% of the total sample. The few existing reports and studies indicated that, the presence of non-adherence behavior among PLWHAV in this country which may cause treatment failure and increases the likelihood of drug resistant HIV transmission among the community which is dangerous for the population as a whole.

1.3. Rationale of the Study

Nowadays, the global response for HIV/AIDS related issues charted a new way towards UNAIDS' vision of zero discrimination, zero new HIV infections, and zero AIDS-related deaths to the effective HIV prevention, treatment, care and support (UNAIDS, 2010). To move equally with these international philosophies, countries like Ethiopia, need more research and work to avoid treatment failure and drug resistance associated factors, like measuring adherence to antiretroviral treatment at both level of patient behavior and health facilities.

At Zewditu Memorial Hospital, routinely ART drug adherence level is measured by patients' missed dose recall self- report with the notion of; if a patient missed <= 2 doses of ART drugs within 30 doses, the adherence level of a patient will be Good (G) which is equivalent to better than 95% adherence ; if he or she missed three to five doses, the adherence level will be Fair (F),

which mean his /her adherence is between 85–94% whereas, if a patient missed >=6 doses, the patient will be leveled as poorly adhered (P) which is equivalent to less than 85% adherence.

However, in Zewditu hospital ART clinic, there are about 18,000 enrolled HIV patients (including children). Among these currently, about 6500 adult patients are taking ARV treatment. As observed at the ART clinic in 2012/13, 9 months' report, about 30 PLWHA were reported to have died.

Furthermore, it is known that Zewditu Memorial Hospital is one of the first HIV/AIDS counseling and treatment center in Ethiopia. In spite of large number of people living with HIV/AIDs enrolled and getting treatment service, research on ART treatment adherence measurement level of the site has not been yet done. Therefore, to fill this gap, this study was conducted focusing on the measurement of ART drug adherence level.

1.4. Research questions

This study attempts to answer the following questions.

1. What is the level of ART drug adherence rate of patients enrolled in the Zewditu Memorial hospital?
2. What individual-level factors are associated with ART non-adherence?
3. What are the current adherence promoting mechanisms in the facility?
4. Which are the household and community factors that affect patients' ART adherence behavior?
5. What are the medical or treatment related factors that contribute to ART non-adherence behavior?
6. What are the ART non-adherence predictive factors?

1.5. Research objectives

1.5.1. General objective of the study

The objective of this study is to measure the ART adherence level among people living with HIV/AIDS at Zewditu memorial Hospital.

1.5.2. Specific objectives

1. To measure the patients' ART adherence level.
2. To evaluate the extent of adherence promoting interventions of the facility.
3. To assess antiretroviral treatment and patient related behavioral factors for non-adherence.

1.6. Significance of the study

The failure to adhere to the given HAART regimen causes the occurrence of treatment failure and resistance to ART drugs which is dangerous both for individuals and the community at large (Beith, 2006). In Ethiopia studies in terms of health behavioral theories are very few. Hence, this study may fill this gap and add something important to improve treatment adherence rate.

This study may provide data to guide the ART providers and policy makers in improving the adherence levels by promoting adherence and designing interventional adherence guide tools so that the patients and the community at large may benefit. This study could also provide data to a future well designed nationwide study on adherence level of ART.

1.7. Scope of the study

The research was conducted at Zewditu Memorial Hospital, Addis Ababa. In the hospital, 18000 patients were enrolled for ART service by the end of February, 2014. Adult patients on ART during February 2014 were the target population of this study provided that they had started ART from one to 24 months (Feb, 2012 to Feb, 2014)

1.8. Limitations and delimitations of the study

The following limitations of the study are recognized: Part of the data was retrospective in design. This has its own limitation. Clinical adherence indicators; CD-4 count and weight were not fully documented in the facility log books and it has own difficulty in assessing adherence of clinical indicators. Given that the data extracted from routine records are likely to contain some errors and missing outs, the problems of adherence are likely to be underestimated. The sample taken from only one facility is not representative of the whole of Addis Ababa and cannot be used to make inferences to the other health facilities and regions of the country. However, inferences made from the sample might be applicable to ART patients in the selected similar health facilities. There was financial and time constraint to maximize exit interview respondents so that, the sample size was small.

1.9. Operational definitions

Adherence

It refers to the ability of the patient to develop and follow forever plan on his/her psycho-social and socio-economic behavioral factor to bring attitudinal change to benefit from life - long ART drug and build endless curiosity to improve his /her health quality, weight and CD4 level (Markos, 2008).

Stigma: The operational definition applicable to this study is a person's or groups' undesirable feelings towards HIV patients (Negash, 2011).

Factor

It is anything that affects how a patient takes or adheres to his/her antiretroviral drugs (Sendagala, 2010).

CHAPTER TWO

2. Literature review

This section provides a review of conceptual, theoretical and empirical studies, which are related to ART adherence level and core adherence promotional indicators in health facilities. It begins with essential psycho-social health behaviors concepts and theories that explained the nature of the patient behavior related to non-adherence problems. The second section discuses local studies conducted on adherence related issue and the third section of the review provides a summary the review.

2.1. HIV /AIDS disease progression

HIV/AIDS pandemic is emerging as one of the most serious health problems of the century. It has been discovered in USA, a highly industrially developed nation. However, the problem has widely spread to developing nations, eliminating millions of the working forces and children; hence the focus is shifting fast from developed nations to developing countries (Yimenu, 2009). Various epidemiological studies have shown that the rate of disease progression varies substantially depending on various viral, host and environmental factors, treatment intervention and prophylaxis strategies (Gourevitch, 1996). In spite of that, its disease progression from seropositive to the development of AIDS is shorter in Africa than industrialized countries (Pantako & his colleagues, 1995).

Moreover, HIV infected women were found to be at an increased risk of death. Gender differences in disease progression in males and females are not due to differences in the natural history of disease, but were related to access to care, socio-economic factors or difference with respect to

access for antiretroviral treatment and prophylaxis for different opportunistic infections (Baveja, 2004).

2.2. Highly active antiretroviral therapy for HIV infection /HAART/

With several antiretroviral drugs approved for use, management of HIV infection is getting increasingly complex. HAARTs are potent but have serious side effects, drug interactions and problems of adherence (Baveja, 2004). The toxicities, drug –drug interactions and the pill burdens affect negatively to the adherence which needed to be kept close to 100% more than any illness so far faced in the history of mankind.

HIV replicates very rapidly and up to 10 billion virus particles are produced per day. This is responsible for progressive immune system damage in infected persons (Pantako, 1995). In the absence of effective inhibition of viral load, patients suffer progressive immunologic damage and develop opportunistic infections. For effective inhibition, powerful drugs need to be used in combination to achieve synergism. Moreover, replication of virus is highly error-prone, which leads to development of mutations, thereby conferring drug resistance (Baveja, 2004) which might be worsened and compounded by poor adherence.

CDC update recommendations (CDC, 1996) point out that the inherent ability of HIV to develop drug resistance is the major obstacle for long-term success of antiretroviral therapy. The amount of free viral copies/ml of plasma can be quantified/determined using viral load assays. Viral load indicates the magnitude of HIV replication in the blood. It also serves as an independent predictor for disease progression (CDC, 2002). In conformity with adherence, Baveja (2004) wrote some ART therapy principles that are needed to be implemented in every ART service. These are: health providers need to notice and maintain the goal of maximal therapy, monitor routine viral load and

CD4 counts markers, build optimum drugs schedules and dosages usage behaviors among the patient, notice any change, and ongoing adherence counseling.

2.3. HAART Adherence promoting measurement tools

Although HAART has given hope to people who are living with HIV, even if it plays a significant role in improving their quality of life, it requires near-perfect adherence behavior among the patient to obtain the benefits of ART drugs. Such benefits include the maintenance of the maximum possible rate of viral suppression as long as the regimen is being taken as prescribed (Chesney, 2003). Successful viral control and prevention of ARVS drugs resistance requires near perfect levels of adherence (Steel, Nwokike, & Joshi, 2007). In addition, adherence to ART means taking the ARV medications prescribed at the “right time”, the “right doses” and in the “right way”. Adherence is “not a single event” rather a “dynamic process” that needs to be addressed during every follow-up meeting with patients who are on an ART schedule (Steel, 2007).

The study done by Bell and his colleagues (2007) recommends that health providers need to be equipped with routine quantitative adherence rate measurement skills. Adherence to ART can be calculated by dividing the number of doses taken in specific period by the number of prescribed/dispensed doses that should be taken during a similar specific period (Bell, 2007 & Chesney, 2006). Adherence to ARV treatment could be also measured objectively by different measuring tools like electronic medical devices to measure serum level drugs directly and medication event monitoring system (MEMS) caps that are equipped with microprocessors that record the times and dates of bottle openings (Chesney, 2006). But MEMS caps can either underestimate or overestimate adherence rate because patients can open the cap and then take more than one dose after a single opening and then results underestimation of the adherence rate to ART

or else the patient can open the cap but not take any tablet at all that leads an overestimation of ART adherence rate. Even though MEMS might be one of the best methods of objectively measuring adherence rates, it is not commonly used in Africa because of the financial constraints.

Other methods that are used to measure HAART adherence rates include subjective reporting methods such as self-reporting, pill counts, and records of pharmacy refills. The self-reporting of HAART adherence rates is the method that is most commonly used in order to obtain the required data (Chalker, Andualem, Gitau, et. al., 2011).

The INRUD-IAA & Chalker (2011) field study on standardized adherence measures tool (tool they used had validity tested by Ross (2010) approaches, done in low-resource settings examine and indicate four categories of indicators for adherence to ARV medicines and treatment defaulting which are: Self-reported adherence from exit interviews, counting days supplied by medicine, Patient attendance and Pill counts and self-reports in clinic records. Thus, they produced valid and reliable concurrent and predictive self-report, pill counting and VAS (visual analogue scale). Finally WHO suggest self-report, pill counting and VAS as a measurement tool for resource – limiting settings (Steel, 2007).

Self - report adherence measures has commonly been used by most studies. Berg and Arnston (1969) had also confirmed the validity of self-reported assessments However, there is no single gold standard for assessment of adherence that is currently regarded as the best method for measuring adherence to HAART because it is a complex issue that is not easily reducible (Berg, 1969).

2.4. Factors affecting ART adherence rate

According to Chesney (2003) study result, adherence to HAART can be affected by ARV regimen characteristics, patient-specific factors, provider-patient relationships, and various characteristics of the health care system itself. According to EHNRI (2012) report patient factors such as age, gender and substance abuse are also non-adherence behavior determinants. Complexities surrounding the act of drug dosing, pill burdens, side effects and special food requirements of the treatment are some of the non-adherence treatment factors (Gill, 2005). Chesney's (2006) study result suggests that adherence to ART must take into consideration a variety of social, cultural, economic and personal factors. Although numerous studies have shown that adherence to HAART is not optimal in many patients, the social, psychological, clinical and behavioral factors that are associated with it have not yet been fully explored or explained (Gifford, Bormann, Shively et al., 2000).

The research taken by Deribe and his colleagues (2008) in Jimma University Specialized Hospital in Southwest Ethiopia reported that, the reasons for missing their appointments included a loss of hope in the efficacy of the medication, lack of food, the debilitating effects of mental illness, a belief in the power of holy water to achieve what ART could not, the fact that they did not have the money required for transport, and the effect of various other illnesses.

2.5. Outcome of highly active ant-retroviral treatment /HAART/

The goal of antiretroviral therapy is to suppress the serum viral load of an individual to be below detection limits which is less than 20 copies/ml. If an individual who is taking his/her treatment with maximum optimum schedule and dosage, incidence of opportunistic infections upon him/her will decrease. In additions, if CD4- cell counts consistently show improvement, remains above

250/ml for three months or more, chemoprophylaxis for opportunistic infections can also discontinued. This shows the immune system of an individual is building up, and the patient may not develop opportunistic infections (El-sadr, Burman, Grant, et al., 2000). Also it provides good quality of life this means there is a reduction in morbidity or hospitalizations of an individual (Baveja, 2004).

2.6. Risk of antiretroviral non - adherence

In spite of aggressive therapy, a significant number of patients exposed for ART, develop treatment failures. One of the major causes of antiretroviral therapy failure is insufficient drug exposure due to poor adherence. And detectable virus in the plasma of a patient who is on HAART indicates virological failure. This is commonly associated with emergence of drug specific resistance (Baveja, 2004). In addition to virological failure, immunologic and clinical failure can occur in an individual who is on HAART (Kaufmann, Pantaleo, Meylan, 1998). The emergence of HIV drug resistance (HIVDR) is of increasing concern in countries where ART and ARV prophylaxis is widely used, and represents a potential impairment to the achievement of long-term success in treatment outcomes.

2.7. Care and support for persons living with HIV/AIDS

As much as possible the victim needs to obtain continuous physical and psychological care and support from the community, family and government agencies to provide an extended fruitful life. During the lifetime of an HIV patient, all the possible places of care provision (at home or at hospital) must be made complementary to each other. (Baveja, 2004) .Facilities will be expected to develop an M&E system, capable of informing a full evaluation of HIV care, including ART and regimen component.

2.8. **Local studies on ART treatment adherence**

With rapidly expanding access to ARVs in resource-poor settings, it will be vital to monitor adherence and to identify interventions that can encourage sustained adherence. Accurate assessment of adherence is critical to maximize clinical efficacy and minimize the potential population risks associated with drug resistance. However, no validated approaches exist to measure adherence, especially in low resource settings with potentially poor data availability. Moreover, no studies have validated whether routine self-reported data in medical or pharmacy records are predictive of clinical outcomes (Ross, Pierre, Fahg, & Hailu, 2010).

There are some studies on this topic in Ethiopia at different place, different periods, and different subjects and most of them suggested the need for research into objective measures of adherence as well as longitudinal studies on adherence behavior because strict adherence to treatment is a long-term process and not a one-time activity.

Study conducted by Alemayehu, and Kifle, (2008) in the ART unit of Jimma University Specialized Hospital, the Self-reported dose adherence rate was 94.3%. Similarly, Yimenu's, (2009) study in Adama Hospital on adherence related research showed that, out of the total number of respondents, 19.8% respondents took their HIV medications < 95% of the time, while 80.2% of the respondents took their HAART medications for >95% within the 30 days preceding the study period. In general, the patients' adherence is promising. However, in contrast with the above research results, a study by Markos & his colleagues (2008) on adherence to ART in PLWAS at Yirgalem Hospital, the adherence level for patients who missed doses in the study was found 88.7%. Moreover, survey study by Johnson & Witt (2007) on adherence to ART Practices in Resource-Constrained Settings in Ethiopia, Kenya, Rwanda, Tanzania, and Uganda indicated that health care facilities in countries were rarely monitor adherence levels. And they reported also the

presence of difficulty to analyzing the effectiveness of adherence promotion measures especially in Ethiopia.

2.9. Theoretical concept

Studies on life-long drug adherence behaviors have been influenced by cognitive based theories such as human belief model, planned behavior and Cognitive model of compliance theories.

2.9.1. Cognitive model of compliance

It draws attention to the importance of the relationship between patient and healthcare providers; it points out a host of other factors such as social support, the disruptive nature of adherence on daily lifestyle, and the patients' beliefs and attitudes in the effectiveness of the medications adherence (Ogden, 2004).

2.9.2. The theory of planned behavior (TPB)

It is an extension of the Theory of Reasoned Action (TRA) (Nejad, Werth, & Greenword, 2005). This theory postulates that an individual's behavior is determined by one's intention, which in turn is determined by 3 main predictors: attitudes; subjective norms; and, perceived behavior control. Attitudes in TRA refer to an individual's beliefs about the outcomes of his/her behavior and an evaluation of the importance of such an outcome. Subjective norms refers to social pressure, that is, expectation of approval or disapproval of such an action by significant others. Behavioral control is an individual's belief in the availability of the requisite resources to accomplish an action such as information, abilities, dependence or independence from others etc. As an extension, TPB has four principal areas: attitudes towards behavior; subjective norms; perceived behavioral control; and socio-demographic variables. Thus, Treatment seeking behavior can be used as an

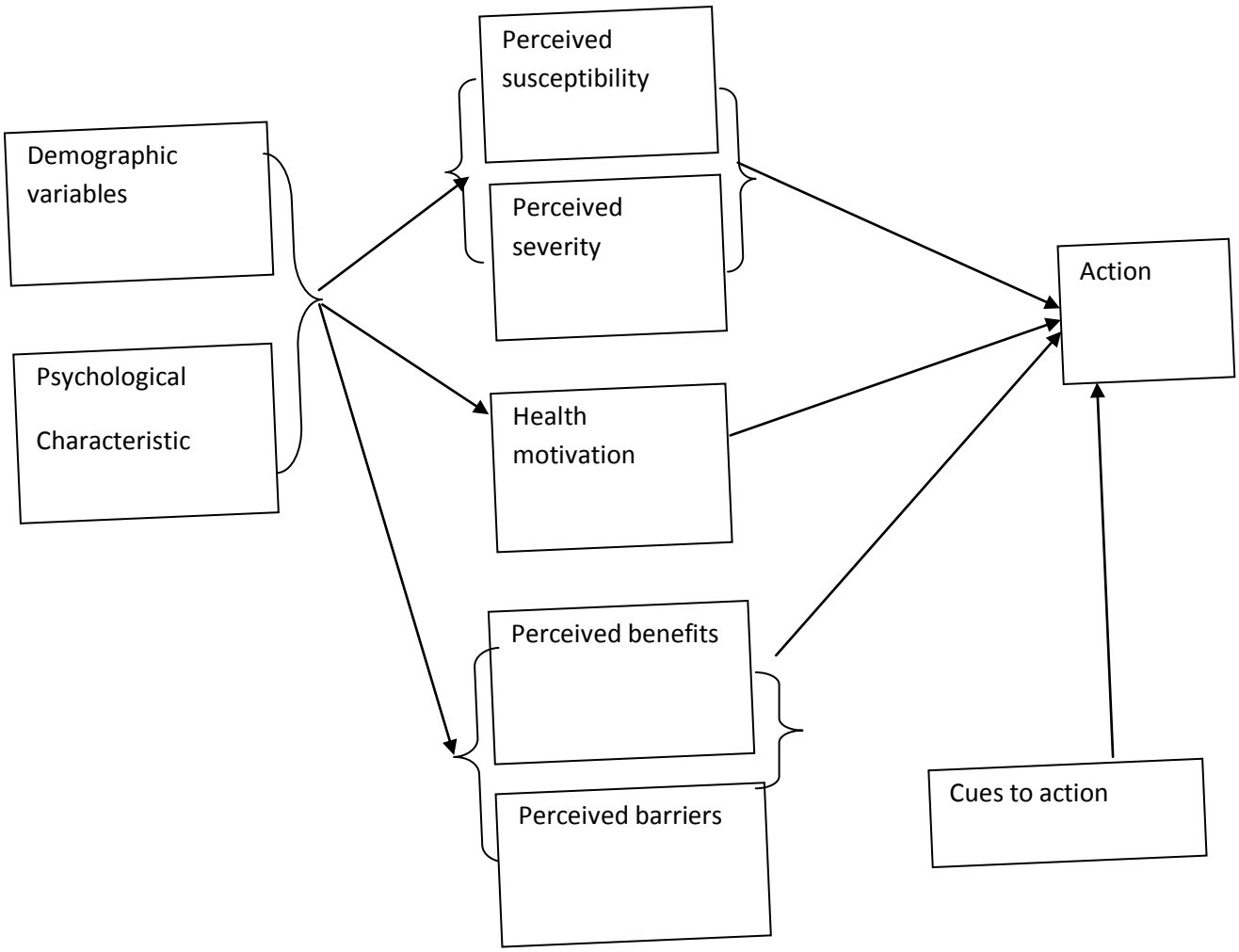
indicator of a patient's willingness to preserve life, and is crucial to personal, societal and national development.

2.9.3. The health belief model (HBM)

This model was developed in the 1950s' work by Rosenstock with an intention to predict which individuals would or would not take specific actions to avoid illness (Rosenstock, Stretcher & Becker, 1988). Since then, the HBM has been adapted to explore a variety of long- and short-term health behaviors. The dimensions of the HBM are perceived susceptibility, perceived severity, perceived benefits and perceived barriers. The HBM proposes that in order for an individual to take action to avoid a disease, he/she has to be susceptible to a disease.

The HBM is used in health behavior that can be grouped into 3 main categories: Preventative health behaviors, sick role behaviors, and clinical use (Nejad, 2005). With reference to the concepts introduced about the HBM, adherence can be taken to be a desired health related action or behavior that can be influenced by the perceptions, beliefs and cues to action of an individual. If these perceptions and beliefs are not re-enforced or addressed they may lead to non-adherence. Therefore, the HBM provides an important framework for understanding the psychosocial factors that may contribute to medication adherence. The next framework illustrated below is developed and adapted from the HBM to give a deeper understanding of related concepts of the study phenomena.

Figure2: The Health belief Model



Source: Stretcher & Rosenstock, 1997

Health Belief Model: Major Concepts of HBM based on six key concepts

Concept	Definition	Application
Perceived Susceptibility	One's belief of the chances of getting a condition	• Define population(s) at risk and their risk levels • Personalize risk based on a person's traits or behaviors • Heighten perceived susceptibility if too low
Perceived Severity	One's belief of how serious a condition and its consequences are	• Specify and describe consequences of the risk and the condition
Perceived Benefits	One's belief in the efficacy of the advised action to reduce risk or seriousness of impact	• Define action to take — how, where, when • Clarify the positive effects to expected • Describe evidence of effectiveness
Perceived Barriers	One's belief in the tangible and psychological costs of the advised behavior	• Identify and reduce barriers through reassurance, incentives, and assistance
Cues to Action	Strategies to activate "readiness"	• Provide how-to information • Promote awareness • Provide reminders
Self-Efficacy	Confidence in one's ability to take action	• Provide training, guidance, and positive reinforcement

Source: **http://recapp.etr.org/, Viewed 4/5/2014**

The Health Belief Model is a framework for motivating people to take positive health actions that uses the desire to avoid a negative health consequence as the prime motivation (**http://recapp.etr.org/, Viewed 4/5/2014**). For example, HIV is a negative health consequence, and the desire to avoid HIV can be used to motivate sexually active people into practicing safe sex. Similarly, the perceived threat of a heart attack can be used to motivate a person with high blood pressure into exercising more often. The health belief model assumes that a person will adopt appropriate health behaviors if they feel the consequences are severe and feel personally vulnerable. A person's ability to adopt the change will depend on the relative balance of barriers to implementation versus the benefits of change. This "decision balance" construct is a common construct in many behavioral theories (Rosenstock, 1988).

With reference to the concepts introduced about the HBM, ART drug Adherence can be taken to be a desired health related action or psychological behaviors that can be influenced by the perceptions, beliefs and cues to action of an individual in order for an individual to take action to avoid a non-adherence behavior.

HBM in ART adherence notion.

1. Perceived susceptibility - This refers to a person's subjective perception of the risk of non adherence behavior to life -long ART treatment. There is wide variation in a person's feelings of personal vulnerability to HIV.
2. Perceived severity - This refers to a person's feelings on the seriousness of non-adherence's clinical outcomes like treatment failure and expose to drug resistance virus strain (or leaving the illness or disease untreated). There is wide variation in a person's feelings of severity, and often a person considers the medical consequences (e.g., death, disability) and social consequences (e.g., family life, social relationships) when evaluating the severity.

3. Perceived benefits - This refers to a person's perception of the effectiveness of ART drug adherence and available understand to reduce the threat of non-adherence behavior consequences. The course of action a person takes in preventing non adherence behavior relies on consideration and evaluation of both perceived susceptibility and perceived benefit, such that the person would accept the recommended action if it was perceived as beneficial.

4. Perceived barriers - This refers to a person's feelings on the obstacles to performing a recommended health action. There is wide variation in a person's feelings of barriers, or impediments, which lead to a cost/benefit analysis. The person weighs the effectiveness of the ART drug adherence actions against the perceptions that it may be expensive, dangerous (e.g., side effects, meal balance), unpleasant (e.g., adverse effect), stigma or social inconvenient.

5. Cue to action - This is the stimulus needed to trigger the decision-making process to accept a recommended drug adherence action e.g., advice from others, reminding from family member, diary, Phone call, etc.).

6. Self-efficacy - This refers to the level of a person's confidence in his or her ability to successfully perform ART adherence behavior. Self-efficacy is a construct in many behavioral theories as it directly relates to whether a person performs the desired behavior.

In general, if these perceptions and beliefs are not re-enforced or addressed they may lead to non-adherence. Therefore, the HBM provides an important framework for understanding the psychosocial factors that may contribute to medication adherence. The next framework illustrated below is developed and adapted from the HBM to give a deeper understanding of related concepts of the study phenomena.

2.10. Summary of the review

In terms of ART, such different cognitive based psychosocial theories help to understand adherence behavior in detail. In this case adherence is not just a single Ordinary concept but rather multidimensional.

Furthermore, every patient has his or her own unique experience with ART and they face difficulties at large and it is a product of their individual, social, financial, cultural and health service component. For this reason, this study focus on patient-related factors, such as forgetfulness, motivation, substance abuse, psychological illness, stigma, drug out of stock, patient ran out of pills or lost pills, travelling problems, inability to pay, alcohol use, depression, fasting, changed regimen, age, sex, education level, marital status, patient and health providers relationship, adherence knowledge of patient, and adherence information need to be considered as non-adherence factors.

To obtain optimal ART adherence among PLHWAs, the patient himself, Health providers and communities should take endless action against non-adherence behavior of an individual. Trust worthy relationship between Patients and health providers is also essential adherence strengthening factors (Melissa, 2008). These show that, adherence is a process, not a single event, and adherence supports should be integrated.

However, several studies clarify the absence of gold standard adherence assessment methods as a whole and local studies were almost old and their findings did not show optimal adherence level. Studies also suggested the need for research on objective ART adherence measures as well as longitudinal studies on adherence behavior. And the most sub-Saharan Africa ART adherence research works have been using self-reported adherence measuring tool. And others like medical or pharmacy records, pill count, visual analogue, and pill identification test are recommended as well

subjective drug adherence measuring systems in resource limited countries.In general, assessment of psychosocial, socio-economic and treatment factors provides an important framework for understanding the adherence behavior of a client.

CAHAPTER THREE

3. Research methods and procedures

In order to achieve the objectives of this study, both quantitative and qualitative methods were used. The study data were obtained from the self-report individual clinical records, exit-interview and ART providers. The following sections describe and discuss each of the following components of the research method: the population, sample and sample size, method of data collection and data analysis.

3.1. Research Design

By large a retrospective cohort study design on a total of 138 adult ART cohort people and a cross-sectional exit-interview on 50 randomly sampled adult PLWHA who are on ART and 8 health providers of the study site were used.

3.2. Data source

For the purpose of this study the investigator used both retrospective and cross-sectional data: retrospective data were collected from randomly selected routine clinical records of individuals' charts, log books and designed formats. The cross-sectional primary data were collected from randomly selected adult PLHWAs', who came to attend Zewditu Memorial Hospital's ART clinic and from health care providers. Quantitative data by large and few qualitative data were used to measure ART adherence rate; to assess association of patient, treatment and community related factors of non adherence behavior and monitor current ART adherence promoting experience of the facility to enhance patients' drug adherence behavior.

3.3. Population

In Zewditu Memorial Hospital a total of 18,000 people had been enrolled for HIV care, support and treatment, 6,500 of these are adults put on ART regimen. Of this, 920 (study population) were on ARV treatment from Feb, 2012 to Feb, 2014 (one months before data collection of this study) were the target population of this study. Thus, the target population for a retrospective cohort study design consisted of all adult HIV patients who are 18 and above years of age and initiated to ARV treatment from Feb, 2012 to Feb, 2014. Moreover for the cross-sectional data ART provider health workers and ART experienced adult people who came to revisit the ART clinic who were 18 years and above were used in the exit interview.

3.4. Sample

Based on simple random sampling technique the study sample was 196 among this,138 adult patients were on ART for less than or equal to 24 months prior to data collection, 8 ART providers and 50 exit interviewees on ART who came to revisit at the time of 5 consecutive dates of data collection.

3.5. Sampling criteria

Each member of the study sample had to fulfill the following inclusion criteria:

1. Participants had to be on ART experience for > = one month and ≤ 24 months after ART initiation for retrospective cohort study.
2. Participants had to be on ART and who are ≥ 18 years old,
3. They have at least one adherence self- report in medical records,
4. The exit interviewee participants had to be willing to give their informed consent.
5. The exit interviewee participants have to speak either Amharic or English because the questionnaires were prepared both in English and Amharic versions

6. The exit interview participants also had to be at least 18 years old and who were on ART at list for one month before data collection dates.

Each member of the study sample had to fulfill the following exclusive criteria:

1. All ART patients who were recently transferred in from the children cohort to adult cohort.
2. All ART patients who had taken the ARV medications for less than one month at the time of data collection.
3. All ART patients who were less than 18 years old.

3.6. Sample size determination.

The sample size depends up on the magnitude of the difference we are trying to detect, the variability of the interest, the type of statistical procedure we are using, the seriousness of the errors we might make, and the cost involved in sampling. Thus, in order to estimate how large the size of the sample should be, single point proportion estimate formula was used. $N = P (1- P)* (Z \alpha_{/2})^2 /d^2$ where P is the anticipated adherence proportion; for the purpose of this study the least adherence report in Ethiopia in Yirgalm Hospital by Markos (2008), 88% is taken as anticipated adherence proportion. If p =0.88, d is the precision required on either side of the proportion (d = 0.05), and confidence interval is 95% (the cut- off value of the normal distribution z=1.96), n1 = unadjusted sample size, n_{final}= adjusted sample size and N = total target population which is 926

$n1 = p (1- p)* (z \alpha_{/2})^2 /d^2$

$n1= 0.88(1- 0.88) (1.96)2/.05^2$

n1 = 162 (unadjusted sample size)

To get adjusted sample size use formula $n_{final}= n1_{/ (1+n1/N)}$

$n_{final =} 162/(1+162/926) = 138.$

The adjusted sample obtained in this calculation is used to collect the retrospective data of the research. To strength the data and to obtain statistical significant result additional 50 self - report exit interview participants and 8 samples of ART providers interviewed to monitor the mechanism they are using to promote adherence in practice.

3.7. Sampling procedures

The simple random sampling method was used to select the total number of patients that were required for the study. Each of the participant's clinical follow up record was thus randomly selected. This means that each individual in the population has an equal chance of being selected for the sample. In order to achieve this, a sampling frame that consists of the complete list of the whole 920 study populations sampling frame had been taken from the database of the unit, and the sample was selected in a lottery method of random numbering technique with scientific calculator. In addition, interview participants were informed about the nature, scope and purpose of the study during their routine attendance at the clinic before they were invited to give their informed consent before participating in the study.

3.8. Data collection

The data were collected by the principal investigator assisted by five trained and supervised data collectors who are working at the data base and archive staff of Zewditu Memorial Hospital ART clinic. Using prepared structured and pretested questionnaires data were collected by interviewing patients and care providers and from charts, log books and designed filled up formats used by the ART clinic.

3.8.1. Data collection instrument

The questionnaire used in this study was extracted and adapted from WHO and MSH recommended adherence self report measuring tool (WHO, 2011). The instrument is part of adherence measurement indicators used by International Network for Rational Use of Drugs (INRUD) and national HIV/AIDS programs in 2006. It is used to assess adherence intervention in five East African countries Ethiopia, Kenya, Rwanda, Tanzania, and Uganda (Johnson, 2007) that began the five-year Initiative on Antiretroviral Adherence (IAA) and to develop practical interventions to improve adherence to ART in routine treatment settings. Hence it is previously validated, used and proven to be effective and recommended in the African region and resource poor settings.

WHO and MSH report (2011) suggested clinical information from patient self-reported clinical data and pharmacy records were important indicators to prove non-adherence. Thus, selected questionnaires of the suggested patient self-report adherence measurement tools were used for the retrospective cohort in this study. According to Chesney (2003), self – report behavioral questions were relatively inexpensive and simple to apply, and were sufficiently sensitive enough to collect the kind of data required in the study.

3.8.2. Procedure of instrument development

The principal investigator used a modified version of the world wide health management promoting program questionnaire, which reflected the specific situation in Ethiopia and that was originally compiled by Johnson (2007). The investigator adopted part of the strengthening health programs adherence monitoring and promoting worldwide practice assessment questionnaires. The first draft was reviewed by experts in this field; those are a statistician, a medical person and a

research advisor. After incorporating their comment the instruments were pre-tested. Finally the original questionnaires were revised based on the given comments and the pretest result and the questionnaires were well structured in order to avoid ambiguity; interviewers were trained to ask questions in a uniform way.

3.8.3. Pre-testing

The researcher gave a questionnaire to a research advisor and ART adherence measurement experts, who were a clinician (MD), a research expert (MPH graduating student, MA in Management & BA in Statistics) and two others (data collectors) in order to obtain their comments about the length, suitability and content of the questionnaire. For secondary data collection, the data collectors undertook a pre-test with 10 follow up records from the ART clinic which were not included in the final study. This pre-test of the instrument was done in order to find out whether there were any problems with in the data collectors in the ambiguity of meanings or limitations in the response categories of instrument. The comments of the subjects who took part in the pre-test were used to finalize the structured questionnaire.

3.8.4. Validity and reliability of the instrument

Validated self-report adherence measures in resource-poor settings are limited (Dan, Erica & Susannah, 2011). Reliability in measurement implies consistency and precision lack of reliability implies inconsistency and imprecision, both of which are equated with measurement error (Myer & Karim, 2007). Validity of research instrument means the extent to which it is accurate and reliable for measuring what it is supposed to measure (WHO, 2009). In other words, validity is the degree to which all the accumulated evidence supports the intended interpretation of measurement tool for the proposed purpose (Ross, 2010). Content validity is a descriptive indication (not given

as a statistic) of the extent to which the content of the test covers all aspects of the attribute or trait of interest and internal consistency is the extent to which all test items measure the same construct. The data collection instruments of this study were adopted from national patient self-reported adherence clinical information recording format suggested by WHO and MSH (2011) and based on this previous similar study were done in five East African countries including Ethiopia (Johnson, 2007). In addition, a researcher integrated the given comments by an advisor (PhD), a research expert (MPH graduating student, MA in Management & BA in Statistics) and two data collectors to maintain internal consistency (reliability) and content validity of the data collection instruments. The INRUD-IAA & Chalker (2011) field study on standardized adherence measuring tool and the tool they used had previous validity taste by Ross (2010) with 95% cut- off, sensitivity of 0.85 and specificity of 0 .75 (Meyer, Summery, Lentsoane & et al., (2012). In addition the reliability of the extracted questionnaires is 0.722.

3.9. Data Analysis

For the statistical analysis procedures the Statistical Package for the Social Sciences (SPSS version 20) computer software was used. Descriptive, t-test, uni-variant, correlation, binomial and multi-variant logistic regression models were used to analyze the outcome variable.

3.10. Ethical consideration

Information obtained from patient interview and clinical data has been anonymous and confidential. All data and information collected from each had been handled only by the investigator. This was done to avoid loss of confidentiality of their personal information and to make sure that there has not been any risk or harm to study participants as a result of their

enrolment and participation in the study. Participants were free not to participate in the study and this has no influence to the care they were given for.

Furthermore, prior to the beginning of the study, the final version of the study protocol was submitted and ethical clearance was obtained from the local IRB of Addis Ababa health Bureau and AAU. Permission for conducting the study had been secured from the medical director and the head of the selected facility respectively.

CHAPTER FOUR

4. Result

This chapter is devoted to the explanation of some selected demographic, psycho-social and socio-economic factors and adherence facility interventions. The data analysis and interpretations of this study resulted from three groups of data source (from 138 subjects clinical records, 50 exit interviewed respondents and 8 ART providers). These combinations data were done to strengthen the results of the complicated nature of adherence for ART.

4.1. Retrospective data analysis

4.1.1. Respondents' profile

As illustrated in table -1 below, a total of 138 Zewditu Memorial Hospital ART clinic PLWHAs' clinical records were assessed for the retrospective data and the profiles of the total 138 respondents are summarized. 0f which 59 (42.8%) and 79 (57.2%) were male and female patients, respectively. The age range of the participants was between 20 – 66 years. The mean and the median age of the whole respondents were found to be 36.5 and 35, respectively with the standard deviation of 9.4. And 33 (23.93%) respondents were in the age group of 20-29, 59 (42.8%) were in the age group of 30-39, 123 (89.1%) of the study subjects were less than 50 years of age.

In relation to participants' level of education, 29 (21%) were illiterate, 21 (15%) were primary school completed, 58 (42%) were high school completed, and 26 (18.8%) were graduates. Concerning the marital status the majority 61(44.2%) were married, 41(29.7%) were single, 16 (11.6%) were widowed and 17 (12.3%) were divorced.

Table-1: Demographic profile of study subjects, Zewditu memorial hospital, March 2014 (N= 138)

Age in the ten year interval (n=138)	Number	Per-cent
20-29	33	23.9
30-39	59	42.8
40-49	31	22.5
50-59	14	10.1
>=60	1	0.7
Sex of respondents(n=138)		
Male	59	42.8
Female	79	57.2
Marital status (n=138)		
Single	41	29.7
Married	61	44.2
Widowed	16	11.6
Divorce	17	12.3
Unknown	3	2.2
Education level (n=138)		
illiterate	29	21
Primary school completed	21	15.2
Secondary school completed	58	42
Colleges diploma or certificate	4	2.9
Degree and above	26	18.8
Final status(n=138; alive, drop out/lost, transfer to another hospital or died)		
Alive	86	62.3
Dropped out/lost	35	25.4
Died	12	8.7
Transferred out to another hospital	5	3.6

With respect to the current status of the patients, the 86(62.30%) were alive, 35(25.4%) dropped out/ lost from clinical follow up, 12 (8.7%) were reported to be dead and 5(3.6%) were transferred out to another hospital. With respect to participants' occupation the employed and unemployed participants were equally proportionate with 42(30.4%), while more than one third of the participants 54 (39.1%) occupational status were unknown

4.1.2. Self-report adherence level from records

PLWHAs' self – reported ARVs treatment drugs adherence rate were scrutinized every six months intervals from adherence records after the initiation of ART.

Table-2: Adherence rate with in 6 month interval after ART initiation, Zewditu Memorial Hospital, March 2014 (N= 138)

ART adherence rate	6 month after treatment (n = 138)		12 month after ARVs (n = 108)		18 months after ARVs (n = 77)		24 months after ARVs (n = 31)	
	No. of participant	percent	No. of participant	percent	No. of participant	percent	No. of participant	percent
Good	**128**	**92.8**	**102**	**94.4**	**74**	**96.1**	**31**	**96.8**
Fair	2	1.4	1	0.9	-	-	30	96.8
Poor	8	5.8	5	4.6	3	3.9	1	3.2

Thus, as illustrated in the above table, after 6 months ART treatment were found 138 participants and out of which 128 (92.8%) had good adherence while, 2 were fairly adhered and 8 were poorly adhered. After 12 months of ART treatment were found 108 participants and out of which 102 (94.4 %) had good adherence, 1 respondent were fairly adhered and 5 were poorly adhered. After 18 months of ART treatment were found 77 participants and out of which 74 (96.1%) had good adherence record, while, 3 (3.9%) had poor adherence record. Finally, after 24 months of ART

initiation there were total 31 participants and out of which 30 (96.8%) had good adherence record and only 1 (3.3%) had poor adherence record.

4.1.2.1. Adherence level verses demographic factors

In the descriptive statistics from the total 138 individuals, after 6 month treatment the majority 128 (92%) of participants had good (optimal) adherence level while, 8 had poor adherence rate and only 2 individuals had fair adherence record. To see demographic status of the patient versus their adherence status, only the first 6 month adherence status after ART initiation were taken..

Table- 3: adherence rate after 6 month ART initiation versus demographic factors (Zewditu Memorial Hospital, March 2014 (N= 138)

Variables		Optimally (Good) adhered participants (n = 128)		Fairly adhered participants (n =2)	Poorly adhered participants (n =8)
		No. of participants	Percent	No. of participants	No. of participants
Sex	Female	73	57	3	5
	Male	55	43	1	1
Age	20-35	67	52.3	1	4
	36-66	61	47.7	1	4
Highest level of education completed	Illiterate	28	21.9	-	1
	Primary school	20	15.6	1	-
	High school	53	41.4	-	5
	Some college	3	2.3	1	-
	Degree and above	24	18.8	-	2
Occupation status	Employed	39	30.5	1	2
	Unemployed	40	31.2	1	1
	Not known	49	38.3	-	5
Marital status	Single	36	28.2	1	4
	Married	57	44.5	-	4
	Divorced	17	13.3	-	-
	Widowed	15	11.7	1	-
	Not known	3	2.3	-	-
ART Regimen change	Yes	39	30.5	1	2
	No	89	69.5	1	6
Final status of the patient	Alive	82	64	2	2
	Transfer out to another clinic	5	3.9	-	-
	Lost/droop out	33	25.8	-	2
	died	8	6.3	-	4

As described in table 3 above, from optimally adhered 128 participants; 57% were females, 52% were n the age group of 20- 35, 41.4% were secondary school completed, 45% were married, 70% had not changed their first prescribed ART regimen, 64% were alive.

Whereas, from non - optimally adhered 10 participants, after 6 months of treatment initiation; 6 of them were females and from which 5 each had poor adherence record, secondary school complete and single, 6 individuals were not exposed to drug regimen change, 4 individuals have died.

4.1.2.2. Adherence and demographic variable association

In this study, association of demographic factors, regimen change behavior and clinical outcomes with respect to adherence behaviors was done based on the participants' first 6 months drug adherence level after ART treatment.

Thus, in the bi-variant non- parametric correlation test with 95% confidence interval the participants' sex, age, education, marital status and occupation had no association with the first 6 months ART treatment adherence level with the spearman's rho correlation coefficient of ($r = -0.48$, $p=0.575$), ($r= -0.078$, $p=0.365$), ($r = -0.085$, $p=0.324$), ($r = 0.035$, $p=0.682$) and ($r= 0.011$, $p=0.894$) respectively.

4.1.3. Regimen change and adherence behavior

According to table 4 below, the individuals' clinical records out total 138, in 42(30.4%) the ART drug regimen was changed or substituted, where as 96 (69.6%) patients were on the first prescribed ART drugs regimen. The identified reasons for regimen change were drug toxicity/side effect42.9%), pregnancy, new onset tuberculosis, new combined drug availability, clinical and immunological treatment failures. In non-parametric statistics with spearman's rho correlation

there was no association between drug regimen change and adherence behavior (95% CI, r = 0.004, P >0.05).

Table – 4; Respondents' ART drug first regimen change behavior, Zewditu Memorial Hospital, March 2014 (N= 138)

Did patients' ART drug first regimen Changed /substituted? (n=138)	Number	Pre-cent
No	96	69.6
Yes	42	30.4
Explained reasons for drug regimen change/substitution(n=42)		
Drug Toxicity/side effect	18	42.9
Pregnancy	3	7.1
New drug availability	7	16.7
Due to new onset Tuberculosis	3	7.1
Clinical failure	6	14.3
Immunological failure	5	11.9

4.1.4. Mean distribution of weight & CD4 level

The six months interval after treatment mean weight and CD4 distribution of participants were examined. Thus, as illustrated in the table 5 below, the samples mean weight distribution in kilograms & Standard deviation; at base line of ARVs initiation, after 6 ,12. 18, 24 were 58.297 $\pm$ 12.62, 59.27 $\pm$ 13.14, 60.54 $\pm$ 12.73, 60$\pm$ 12.46 and 67.70$\pm$.14.00 respectively.

Table-5. patients' mean Weight and CD4+ cells count every 6 months interval, Zewditu Memorial Hospital, March 2014 (N= 138)

Variable	Base line of ART initiation	6month after treatment	12 month after ARVs	18 months after ARVs	24 months after ARVs
Weight in kg					
Median Mean	56 58.297 for **n=138**	58 59.27 **for n=138**	58.54 60.54 **for n= 108**	60 60.63 **For n=78**	60 61.70 **For n=27**
S.D.	12.62	13.14	12.73	12.46	14.00
CD4 level in cell/mm^3					
Median	**for n=138** 136	For **n=83** 259	for **n= 55** 339	For **n=21** 308	for **n=3** 457

In addition, median CD4+ cells count at base line of ARVs initiation, after 6, 12, 18 and 24 months of ARVs treatment were 136, 259, 339, 308 and 457 respectively. The number of patients in each month was not equal. This is because all of them were not started on ARV at the same month and some died, lost or dropped out from the clinical follow-up or transfer out or was not done due to financial reasons.

As illustrated in the above table – 5, in the first 6 months after ARV initiation, the median weight and CD4+ increment were 2 kg and 123 cell/mm^3 CD4 cells respectively

Table- 6 Adherence rate and clinical outcome: Six months after ART initiation, Zewditu Memorial Hospital, March 2014 (N= 138)

Clinical outcomes after 6 months of ART initiation	after 6 months ART initiation adherence rate	
	Spearman's rho correlation coefficient with 95%CI	P-value
Weight of the patient	- 0.187	0.091
CD-4 cell count of the patient	- 0.041	0.637

In spearman's rho correlation test at 95% confidence interval , after 6 months of ART, adherence of respondent had no significant association with CD-4+ cell count and weight measurement of the respondents with (95%CI, r= -0.187, p = 0.091) and (95% CI, r= -0.041, p = 0.637) respectively,

4.1.4.1. Adherence clinical outcomes and demographic factors association

CD-4+ cell count and weight increment after ART treatment initiation are the clinical predictors of optimal adherence rate. Thus, identifying the associative demographic factors of clinical outcomes is the other side of adherence factors assessment.

Table -7, Demographic and after 6 months' clinical outcomes (weight and CD-4) associations, Zewditu Memorial Hospital, March 2014 (N= 138)

Demographic variables	**Weight after 6 month treatment**		**CD-4 after 6 month treatment**	
	Spearman's rho correlation coefficient with 95%CI	**P-value**	Spearman's rho correlation coefficient with 95%CI	**P-value**
Sex	-0.30	0.000	-0.196	0.865
Age	0.23	0.007	0.132	0.225
Occupation	-0.196	0.021	-0.029	0.794
Education	0.152	0.074	-0.120	0.279
Marital status	-0.153	0.073	0.022	0.845
Final health status	0.057	0.506	-0.660	0.553
Regimen change	-0.007	0.936	0.058	0.660

The above table showed, sex, age, occupation, education, marital status, health status and regimen change variables had no association with the after 6 months treatment CD-4 cell count (Adherence outcome), at 95% CI, spearman's rho correlation coefficient of (r = -0.196, P= 0.865), (r = 0.132, P= 0.225) and),(r = -0.029, P=0.794), (-0.120, P = 0.279), (r = 0.022, P=0.845), (r = -0.660, P= 0.553), (r = 0.058, 0.660) respectively.

Whereas, only sex, age and occupation had significant association with patient weight after 6 month treatment, with spearman's rho correlation coefficient at 95%CI (r = -0.30, P=0.000), (r = 0.23, P = 0.007) and (r = -0.196, P= 0.021) respectively. While, education, marital status, final health status and regimen change have no significant association with weight after 6 months of treatment with spearman's rho correlation coefficient (r = 0.152, P=0.074),(r = -0.153, P = 0.073), (r = 0.057, P=0.506), (r = -0.007,, P= 0.936) respective.

4.1.4.1.1. Multivariate Logistic Regression analysis for significant demographic factors

The uni-variate associations were observed without controlling the effect of other confounding factors it is very difficult to conclude whether the observed statistically significant association was because of the existing causal relationship between the given independent variables and the adherence outcomes. Since both the dependent and independent variable coded to dichotomous and multivariate logistic regression analysis was used. The dichotomous dependent variables is respondents' weight after 6 months of treatment which was coded based on respondents' median weight (59kg) and then weight categorized as (31-59 or 60-92)kg and independent variables are having age within 20-35 or 36-60 years (was coded based on age median were 35), male or female

sex and employed or unemployed. To this end, logistic regression models were run to analyze the net association of factors into the model on the dependent variables.

In logistic regression, the coefficient β represents the increase or decrease in the log odds of occurrences of adherence behavior with a unit of change in the independent variable controlling for the possible confounding effect of all other variables.

The term Exp (β) represents the multiplication estimates in the odds of an event for a unit of change in the independent variable holding the effect of all other predictors constant.

Table-8. Logistic regression parametric estimate, Zewditu Memorial Hospital, March 2014 (N= 138)

Variable	Sig.	Crud odds ratio	95%CI		Sig.	Adjusted odds ratio	95%CI	
			Lower border	Upper border			Lower border	Upper border
Sex	0.005	0.342	0.161	0.726				
• Male	0.001	0.287	0.141	0.582	0.005	2.226	1.378	6.214
• Female	0.029	1.810				1		
Age	0.223	1.605	0.750	3.433				
• 20-35	0.007	0.391	0.197	0.778	0.223	0.627	0.291	1.333
• 36-66	0.142	1.444				1		
Occupation	0.830	0.494	0.220	1.097				
• Emplo yed	0.023	2.375	1.128	4.998	0.083	2.025	0.912	4.498
• Unemp loyed	0.068	0.684						

As illustrated in the above table, with uni-variat logistic model only male sex had significant effect on after 6 month ART initiation weight gain (good adherence outcome) with (COR 0.287, 95%CI, P=0.001). With further multivariate logistic model male sex had 2.226 times more likely hood than female sex effect on after 6 month ART initiation weight gain (good adherence outcome) with (OR of 2.226, P=0.005).

4.2. ART Providers based data

4.2.1. Status of the providers

Eight ART providers were randomly sampled and asked with structured questionnaires about their adherence promoting practice and the available adherence promoting facility. From 8 health providers, 1 respondent was person in charge of ART clinic, 2 were ART physicians, 1 was a health officer and 4 were ART nurses.

4.2.2. Adherence monitoring interventions of the facility

Zewditu Memorial Hospital ART drug adherence monitoring interventions were examined. All of the respondents stated the presence of routine CD4 cell count and patient self-report adherence measurement system; the medication calendar checking system and clinicians' subjective adherence judgment system were also explained by 7 and 6 of the 8 respondents respectively.

While, all of the respondents clarified the absence of all routine Viral load & routine lymphocyte count test, pill count, Visual analogue system, pill identification test, directly observed treatment observation of treatment at patients' home and at health facility.

4.2.3. Adherence behavior promoting measures

As stated by all 8 respondents, patient counseling both before and after ART treatment has influenced the required adherence promoting practice of the site, and above half of the respondents explained that patient support person/ care partners were required to observe treatment adherence of patient behavior. on the contrary, all of the 8 respondents have assured that, both social support (like home visitors, food support and day care); adherence promoting devise like pill box, memory cup, diary, and adherence reminder phone calls were not used at the facility at all; besides 7

respondents assured the absence of community - based health worker/volunteers adherence promoting techniques at health facility.

From qualitative approach study, 7 respondents explained that, if the patient did not attend his/her clinical follow-up, the clinic has used patient's phone call system to check whether a patient has died, has dropped out/lost from the clinic follow-up.

4.3. Exit interview survey

4.3.1. Respondents profile

The total sampled respondents of exit interview were 50 and out of which 32 respondents were female. The age range of the participants was between the age group of 20 – 63 year. In general, 6 respondents were in the age group of 20-29, 17 were in the age group of 30-39, 20 were in the age group of 40-49, while 7 were within age group of 50-63 years age group. The mean and the median age of the exit interview respondents were found to be 39.84 and 40, respectively with the standard deviation 9.49.

Table 9, Profile of interviewed respondents Zewditu Memorial Hospital, March 2014 (N= 50)

Profile	number	Per-cent
Sex of the respondents(n=50)		
Male	18	36
female	32	64
Age of respondents(50)		
20-29	6	12
30-39	17	34
40-49	20	40
>=50	7	14
Working normal activities(n=50)		
Yes	41	82
No	9	18
Occupation of the respondents(50)		
Public employed	9	18
Private employed	18	36
house maid	11	22
Retired	3	6
Unemployed	9	18
knowledge about number of drug doses per day(50)		
Yes	48	96
No	2	4

As illustrated in the above table – 6, from the total 50 participants' 18 individual were private employee, 9 were public employee, 11 were maids, 9 were unemployed and 3 were retired.

Consequently, the majority 41 respondents were able to perform their daily normal activity, while 9 respondents were not able to do their daily normal activity in comfortable way.

When we see the respondents' level of knowledge about their daily number of ARVs doses adherence, the majority 48 respondents had enough knowledge in their prescribed daily drug dose, and while 2 respondents had no enough knowledge about their daily number of ARVs doses.

4.3.2. Respondents psycho-social and economic factors

In relation to the patient and ART providers' relationship, 35 patients had very well and 14 had poor relationship with the health providers. The mean waiting months on ART were 53.12 $\pm$ 35.29, transport cost from home to clinic was 6.68 $\pm$ 3.26 Birr) time lapsed to come from home to clinic was 74.20 $\pm$ 36.09 minutes, and hospital waiting time at day of interview was 93 $\pm$ 30.59 minutes and the mean number of missed ARV drugs within a week recall time was 1.24 $\pm$ 1.7 doses.

4.3.3. Interviewed respondents' adherence rate.

Adherence rate calculation from self-report missed doses

Different periods of adherence recall measurement may be used like four-day, one-week, one-month or most-recent recall of missing a dose commonly (HPCICRH, 2004). Adherence to ART can be calculated by dividing the number of doses taken in specific period by the number of prescribed/dispensed doses that should be taken during a similar specific period (Bell, 2007). Based on this the patients self report adherence rate in this study was calculated with a week adherence recall period.

$$\% \text{ Adherence over last 7 days} = \frac{(\#\text{Doses should have taken} - \#\text{ missed doses})}{\#\text{ Doses should have taken}} * 100$$

In this study the investigator used a 7 days recall missed doses patient self- report adherence measuring tool and as illustrated in table - 6 below. Of the total 50 respondents, 30(60%) have practiced perfect adherence behavior; whereas, 20(40%) respondents practiced 1-7 dose misses in a week. Consequently, among those 20 non- optimally adhered respondents' 8 were who missed 1-2 number of drug doses per week, whereas the majority 12 participants missed 3-7 doses per a week.

In the 7 days recall self-report adherence rate calculation that illustrated in the above table, 1 individual has an extreme poor adherence rate (who was out of his home for a week without his ART drugs) whereas calculated adherence rate in a 7 days recall self- report is ranges from 29% to 86% had seen in 19 individuals.

Table -10.Respondents' adherence rate Zewditu Memorial Hospital, March 2014 (N= 50)

Questions.	number	Adherence rate (dose taken in a week / doses prescribed in a week)* 100
Number of missed ARVs doses in recent week at the time of interview(n=50)	N=50	Adherence in %
Respondents had not missed their drug dose	30	(7-0/7)*100= 100
Respondents had missed doses	20	
1 dose missed per week	2	(7-1/7)*100 = 86%
2 doses missed per week	6	(7-2/7)*100 = 71.43%
3 doses missed per week	5	(7-3/7)*100 = 57.14
4 doses missed per week	2	(7-4/7)*100 = 43%
5 doses missed per week	4	(7-5/7)*100 = 29%
7 doses missed per week	1	(7-7/7)*100= 0% adherence

4.3.4. psycho-social factors and adherence behavior

The possible somatic and psycho - social factors that can influence individuals' adherence behavior were assed using structured questionnaires. Thus as shown in table - 11 below, the reasons for missed dose behavior as stated by 20 respondents were drug toxicity/side effect in 40%, stigma/ discrimination in 15%, forgot/being busy, being out of the home, too ill, fasting and alcohols/substance abuse.

From the total 50 exit-interviewed respondents 32 (64%) had got the ARVs drug regimen change/substitutions. The major reasons for drug regimen change / substitutions were drug toxicity/side effect in 14 (43.8%) and availability of new combined drug in 9 (28.2%) followed by pregnancy, new combined drug availability, the occurrence of new tuberculosis and immunological treatment failure.

Table -11, Psycho-social factors and adherence, Zewditu Memorial Hospital, March 2014 (N= 50)

questions	number	Per-cent
Investigated possible Reason for missed dose (n=20)		
Forgot/busy	8	40
stigma	3	15
Drug toxicity	2	10
Too ill	2	10
fasting	2	4
Alcohol/ substance abuse	2	10
Being Out of home	1	5
Did the respondents face ARVs regimen Change/substitution?(n=50)		
Yes	32	64
No	18	36
Investigated Possible reason for regimen change(n=32)		
Drug toxicity/ side effect	14	43.8
Availability of new drug	9	28.2
pregnancy	4	12.5
Immunological problem	4	12.5
Occurrence of new tuberculosis	1	2

At the time of the pilot interview, several health services complains were raised by the patients and questionnaire was revised and modified to include service related issues. Based on this, ART health service problems of the site were: ART follow-up card loss sated by 17 respondents,

absence of regular CD4 cell count and viral load test at the site stated by 15 respondents and 8 patients were worried and frustrated of future ART drug shortage rumors.

4.3.5. Adherence factors

Association of the patient variables including socio-demographic factors (age, gender, occupation, ability to do normal activity) , socio-economic factors (time lapsed in minutes from home to clinic, transport cost from home to clinic) and treatment related factors (clinic waiting time in minutes, waiting months on ART, regimen change and patient & health providers relationship) were tested with dependent variable of dichotomously coded number of missed doses (self- report adherence behavior).

Table -12. Adherence factors and adherence rate association from the exit interview data Zewditu Memorial Hospital, March 2014 (N= 50)

ART adherence Factors		Spearman's rho correlation coefficient with 95% CI	P-value
Socio-demographic factors	age	-0.202	0.159
	gender	0.017	0.907
	occupation	0.180	0.210
	Pt' ability to do normal activity	-0.170	0.238
Economic factors	Time in minute from their home to clinic	-0.098	0.497
	Transport cost from home to clinic	-0.236	0.317
Treatment related factors	Hospital waiting time in minute	-0.178	0.216
	Waiting months on ART	-0.134	0.574
	Art first regimen change	-0.370	0.008
	Patient and health providers relationship	-0.360	0.011

Thus, based on non-parametric spearman's rho correlation associations, socio-demographic factors (age, gender, occupation and ability to do normal activity) had no significant association with self-reported adherence behavior with (r = - 0.202, p = 0.159), (r= 0.017,p = 0.907), (r = 0.180, p= 0.210) and (r = -0.170, p= 0.238) respectively.

Socio-economic factors (time in mint. from home to clinic, transport cost from home to clinic) have no significant association with self-reported adherence behavior with (95% CI, r =-0.098, p= 0.497) and (r = -0.236, p = 0.317) respectively

Treatment related factors (waiting time in the hospital and patient & health providers relationship) have not significant association with self-reported non-adherence behavior at (r = - 0.178, p= 0.216) and (r = -0.134, p= 0.574) respectively; while waiting months on ART and Regimen change have significant association with self-reported non-adherence behavior with (r = -0.37, p= 0.008) and (r = -0.36, p= 0.011).

After testing the association of the above variables with adherence behavior, the variables that have significant association with the dependent variables were checked using the uni-variate and multivariate regression model to identify whether the association has net effect or not on dependent variables. In this case both the dependent and independent variables were coded dichotomously and multivariate logistic regression analysis was used. The dichotomous dependent variables is number of missed dose (no missed or 1-7 doses missed) of self - report adherence behavior measures, Independent variables were ART drug regimen change or not and waiting months on ART coded as (2 - 24 months or above 24 months). To this end, logistic regression

models were run to analyze the net effect of each of the predictors entered into the model on the dependent variables.

Table -13: Logistic regression parametric estimate Zewditu Memorial Hospital, March 2014 (N= 50)

Variable	Sig.	Crud odds ratio	95%CI		Sig.	Adjusted odds ratio	95%CI	
			Lower border	Upper border			Lower border	Upper border
Months on ART • <24 months • >24 months	0.008 0.011 0.010	0.137 4.929 1	0.032 1.439	0.593 16.884	0.008	7.3021 1	1.685	31.640
Regimen change • Yes • No	0.011 0.017 0.011	0.117 5.667 1	0.023 1.369	0.607 23.462	0.011	8.553 1	1.646	44.431

Using multivariate logistic regression analysis the adjusted odds ratio showed that both these factors have significant effect as:

Those with regimen change are 9 times more at risk to miss doses (non-adherence behavior) compared to those without regimen change with (AOR 8.553.95%, CI = (1.646-44431), p=0.011).

Those waited for < 24 months on ART are 7 times more at risk to non- adherence behavior compared to those waited for > 24 months on ART with (AOR = 7.3021, 95%CI=1.685-31.640), p= 0.008). This might be the result of behavioral adaptation of events from experience.

.

CHAPTER FIVE

5. Discussion of major findings

The main purposes of this study were to measure the self reported ART adherence rates, non-adherence rates of adult patients on ART and identify adherence associated factors and current adherence promoting systems of the facility. Self reported adherence was measured on treatment experienced patients' aged 18 and older years at the Zewditu Memorial Hospital. The results were used to make recommendations addressing behavioral barriers of ART adherence

Adherence rate Determination in Zewditu Memorial Hospital

From clinical record data analysis perspective, the 6 months interval of AR adherence rates were separately computed. The 6, 12, 18 and 24 months optimal adherence rate ranges from 95-100% were found in 93.4%, 94.4%, 96.1% and 96.7% respectively (on average 95%) of the sampled population of the study which is greater than 88.7% adherence rate reported from a cross sectional study conducted in Yirgalem Hospital by Endrias, (2008).

From the exit interviews perspectives, a week recall self- reported ART drug adherence rate was computed on 50 respondents and perfect optimal adherence rate (100%) was found among 30 respondents while, non-optimal adherence rate were found among 20 respondents. From the non-adherence respondents, adherence rate ranging from 29% to 86% (suboptimal) were found among 19 individuals of the sampled population. This is similar to the study done by Vreeman and his colleagues (2008) that the majority of the studies in developing countries reported adherence levels of 75% (ranging from 45- 100%). Extremely poor adherence rate per week or no adherence rate of 100% was found in one individual (he didn't take his drug for the whole week). This concurs with

other findings noted by Vanhove and his colleagues (1996) stating the dangerous consequences of missed doses of ART with evidences of increasing viral load after missing only two days dosing and the development of mutant viral strains that are resistant to ART drugs.

Generally, this study found mixed adherence rate result from the two different data sources (clinical record data compared to exit interview data) with big differences which showed ART providers' subjective judgment based overestimated good adherence from ART providers' clinical recoding system. Patients need to maintain forever optimal ART drug adherence practice /behavior/ to get full benefit of the highly potent ART drugs. Thus health providers or the facility could measure adherence rate strictly with additional adherence measuring aids like pill count, pill identification test, visual analogue test or otherwise other validated techniques that suits resource poor setting like ours.

Socio-demographic adherence factors

From the retrospective data perspective;

Above half of the respondent (57%) were female, 43.% were in the age group of 30-39, 42% were high school complete and 44% respondents were married and the mean and the median age of the respondents were found to be *36.5 and 35*, respectively with the standard deviation of 9.4. This is similar to the study done by Bavejas' (2004) that there was gender difference of disease progression in females which could be influenced by socio-economic factors. It is obvious that HIV/AIDS affects the reproductive and productive age group most.

The majority 62% of the participants were alive. In relation to non-adherence behavior and its consequences of drug resistance and treatment failure the documented 25% lost/ dropped and about 9% death of patients were not too small and ignorable. In this regard patients lost/droop out

from clinical follow-up are an indication of dissatisfaction in health care system of the hospital This is supported by the study of Chesney which indicated dissatisfaction with prior experience in the health care system has been associated with non-adherence behavior like lost from follow-up (2000).

From the exit interview perspective;

The majority 64% of the respondents were female, 40% were in the age group of 40-49, the mean and the median age of the exit interview respondents were found to be 40 each. More than two third of the respondents (36%) were private employee, the majority (82%) of the respondents were able to perform their daily normal activity, 71% of the respondents experienced a very good relationship among ART providers. As recommended by Melissa and Watt (2008) trustworthy relationship between patients and health providers is also an essential adherence strengthening factors and maintaining good relationship between patients and health provides is logically necessary to promote long lasting drug adherence behavior of patients. However in this study 30% of the sample population practiced poor relationship with their health providers which lack therapeutic alliance where both parties work towards improving the health of the patient.

Thus in one sample statistics at 95% the sample mean distribution of the respondents' waiting months on ART, transport cost from home to clinic, amount of minute used from their home to clinic, hospital waiting minute at the time of interview and number of missed ARVs drugs with a week recall were 53.12 with Stand deviation of 35.29, 6.68birr with Stand deviation of 3.26, 74.20 minute with Stand deviation of 36.09, 93 minute with Stand deviation of 30.59 and 1.24 doses with Stand deviation of 1.7 respectively. This is similar to the study done in Tanzania (Mshana,

Wamoyi, Busza, et al., 2006) and these socioeconomic costs may have implications not only for day to day adherence but also losses to follow up.

Non- adherence factors' and Adherence associations

Study review by Ross (2010) reported that patients generally maintained high rates of adherence to therapy in the first six to nine months of treatment. Similarly in this research the first six months of treatment adherence level association with key patient and treatment related factors association were done.

Patient related factors:

The written document suggests that such demographic information is not necessarily predictive of antiretroviral adherence but rather identifies particular populations that may benefit more extensively from targeted interventions (Platt, Tippy & Turk, 1994). Parallel to this, bi-variate non-parametric correlation test of the participants' sex, age, education, marital status and occupation have showed no association with the first 6 months of ART treatment adherence level.

In clinical record data analysis, the majority 92% had after 6 month treatment good (optimal) adherence rate. More than half of this (57%) were females. More than half (52%) were found in the age group of 20- 35. The majority (41%) were secondary school complete. The majorities (45%) were married; and most of them (70%) were not exposed to regimen changed/substitution. More than half (64%) of the respondents were alive.

From the exit interview perspective, patient and health providers relationship and patient knowledge about drug dosage has no significant association with adherence behavior. Other studies in the contrary showed significance and the importance of the relationship between patient

and health care providers (Ogden; 2004) and good relationship is therapeutic alliance where two parties work in one goal to improve patients' health status. This can be due to the relatively low sample size in this study.

Socio-economic factors (time from home to clinic, transport cost from home to clinic) of the respondents had no significant association with self-reported adherence behavior.

The self-reported missed dose behavior was seen among 20 interviewed respondents. Forgetting/being busy and social-stigma/ discrimination were considered as the major reasons for missed dose behavior. In this regard scholars had similar note; Stigma was an important determinant of non-adherence in settings of sub-Saharan countries (Nachega, Knowlton, Deluca, et al; 2006). And being busy or simply forgetting, changes in daily routine and being away from home were the main reasons for non-adherence elsewhere (Markos, et al ; 2008).

Treatment related factors:

Waiting time in the hospital for revisit and patient & health providers relationship had no significant association with self-reported non-adherence behavior; The first prescribed drug regimen change/substitution were documented among 30% and 64% of respondents from clinical records and the exit interview respondents data analysis respectively. And in both perspectives the major reasons for regimen change was drug toxicity/side effect which is in line with another study (Gill, 2005).

With multivariate analysis, those with first line ART drug regimen change are 9 times more likely to miss doses (non-adherence behavior) compared to those without regimen change with (AOR 8.553.95%, p=0.011). This is similar to the study done in Yirgalem hospital that showed multivariate analysis result of ART medication adverse effect were over 6 times more likely to be

non-adherent than those without medication adverse effect (Markos, et al; 2008). This study has noted that the major reason for ART drug regimen change was drug toxicity/side effect.

With multivariate analysis, those waited for < 24 months on ART are 7 times more likely to have non- adherence behavior compared to those waited for > 24 months on ART with (AOR = 7.3021, 95%, p= 0.008). This could be the result of behavioral change which is associated with adaptation of events that let the patients who waited for more than 24 months on ART to adhere with their lifelong treatment and this is in line with another study that noted the presence of significant dosing fluctuation in 50% of patients during the first two months of treatment (Melbourne, Geletko, et al., 1999).

The qualitative study of ART service problem at the site has found that, revisiting follow-up card loss were stated by 34% of interviewed respondents and absence of regular CD-4 cell count and viral load test were stated by 30% of the respondents. In addition to this, 8 patients stated their frustration from information which indicated future ART drug shortage. This implies frustration and dissatisfaction. Studies suggested that dissatisfaction experience in the health care system has been associated with non-adherence behaviors (Chesney, 2000). Similarly, another study noted the importance of non- frustrated status of patients' to be associated positive HAART adherence behavioral skills (Yimenu, 2009)

Clinical outcome and demographic factors

Both after 6 month of ART initiation weight and CD-4 count had no significant relationship with treatment adherence rate of the respondents. In contrary to this result, a study conducted by Ross (2010) noted that the clinical outcomes (weight and CD-4 cell count) increments have clear association self-reported adherence predictors like increments in CD4 counts and weight. This

difference might be due to low sample size, different setting, and retrospective design of the data in this study or due to the over estimation of the self reported adherence level registered by ART providers.

With optimal adherence rates, studies have demonstrated that ART can suppress the viral load to undetectable levels, boost the immune system by increasing the number of CD-4 cells, and improve the quality of life of PLWHAS (Erlen, 2006).

Thus, respondents' sex, age, occupation, education, marital status, final health status and regimen change have no association with after 6 months treatment CD-4 cell count (adherence outcome). Education, marital status, final health status and regimen change have no significant association with respondents' weight after 6 months treatment

While, in non-parametric correlation analysis sex, age and occupation were significantly associated with respondents' weight after 6 months of treatment with Spearman's rho correlation coefficient of ($r = -0.30$, $P=0.000$), ($r = 0.23$, $P= 0.007$) and ($r = -0.196$, $P= 0.021$) respectively; with multivariate logistic model male sex had twice more likely hood effect on after 6 month ART initiation weight gain than female sex with (OR of 2.226, P=0.005).

Weight gain and increase in CD-4 level after treatment are considerable clinical outcomes of adherence (WHO, 2004). In this study the data were taken from routine clinical records, there might be random errors of providers' recording system that leads such underestimated relationship

Assessment of adherence promoting interventions

To achieve the third objective of this research sampled ART physicians, a person in charge of the service and ART nurses were asked about adherence promoting facilities through structured interview questionnaires.

The majority of the respondent 87.5% reported that routine CD4 cell count and patient self-report adherence measurement system are their usual adherence monitoring systems, the majority 75% of respondents also reported that medication calendar checking system and clinicians' subjective adherence judgment system along with self - report adherence are their adherence monitoring mechanisms.

The Ethiopian Ministry of Health Guideline for implementation of antiretroviral therapy in Ethiopia (Vreeman, 2008) stated that the facilities' primary role is to provide ART services, including referring PLWHA to local community support groups and the primary role of the community is to provide prevention, care and support, including efforts to reduce stigma and improve adherence Such system will include a two-way recommendation system between clinical service delivery sites and community, and home-based care and support program. In contrary, this study found that adherence monitoring interventions like routine viral load & routine lymphocyte test, pill count, visual analogue system, pill identification test, directly observed treatment observation of treatment at patients' home and at health facility and using numerical adherence rate calculation were not completely applicable in Zewditu Memorial Hospital ART clinic.

In relation to assessment of adherence promoting practice of the site, the majorities reported that patient counseling before and after ART treatment are the stated required adherence promoting practice of the site, and above half of the respondents have explained patient support person/ care partners are required to observe treatment adherence patient behavior. On the contrary, social support (like home visitors, food support and day care); adherence promoting devise like pill box, memory cup, diary, and adherence reminder phone calls and community - based health worker/volunteers adherence promoting techniques are not used in the facility at all. In this regard

studies point out using a higher number of adherence aids may possibly result in higher levels of adherence (http:aidsinfo.nih.gov/guidelines, 2014 view).

Other authors (Chesney, 2006) also recommended that adherence interventions should involve a combination of self- report, visual analogue scale (VAS), pill identification test (PIT), pill count categories produce better adherence results than an intervention that only includes one category. A multi-method approach that combines feasible self –reporting and reasonable objective measures is the current state-of-the-art in measurement of adherence behavior.

CHAPTER SIX

6. Summary, Conclusion and Recommendations

6.1. Summary

Anti-retroviral drug non- adherence behavior and its consequences need great concern at a national level in general and at each health facility level in particular. Zewditu Memorial Hospital ART clinic encompassed from lower to higher classes of people living with HIV/AIDS. It provides anti-retroviral treatment and care service for a large number of infected persons. The study population comprised adult PLWHIV initiated on anti-retroviral treatment for the last one to twenty four months. The total number of the study population was 196 selected by simple random sampling technique. For data collection pretested structured questionnaire was administered. The collected data were tabulated, analyzed and interpreted.

The aim of this study was to measure ART adherence level of adult PLWHIV and to identify patient related psycho-social and socio-economic factors at Zewuditu Memorial Hospital ART clinic.

The data analysis and interpretations of this study resulted from three groups of data source (from patient clinical records, self- reported exit interviewee respondents and few ART providers). These data source combinations were used to strengthen the results of the complicated nature of adherence for ART. A descriptive analysis was made to obtain a general picture of ART drug non-adherence behavior and the risks of non-adherence behavior of the patients. Logistic regression analysis was also performed to identify the strength of association of variables with the 6- month ART initiations adherence behavior.

The adherence level findings showed mixed results of both optimal and suboptimal findings and are similar to those reported by other studies in the resource poor countries. Among the demographic factors, female gender was associated with greater ART adherence levels. Age, education, marital status and occupation did not have any association with the first 6 months of ART treatment adherence. The respondents' weight and CD4 cell count increased after 6 months of treatment. Waiting months on ART and regimen change have significant association with self-reported non-adherence behavior. Drug side effect/toxicity was a major reason for missed drug doses and regimen changing behavior. Forgetting/being busy and social stigma/discrimination and alcohol use were also identified barriers for adherence behavior. Patient and health providers' relationship and patient knowledge about drug dosage have no significant association with adherence behavior. Patient counseling before and after ART treatment, patient support person/care partners are adherence promoting practice of the site. Whereas, social support (like home visitors, food support and day care); devices like pill box, memory cup, diary, and adherence reminder phone calls and community - based health worker/volunteers are not used in the site at all. To improve ART adherence it is necessary to design and implement practically sound adherence intervention programs that can promote adherence behaviors of the individuals and can alleviate the burdens of stigma/discrimination and drug side effect among ART patients. High level of adherence is the means to alleviate the potential danger of drug resistance that emanate from low level of adherence

6.2. CONCLUSION

The data collected from records, patient interview and treatment providers' interview showed suboptimal adherence, inadequate usage of adherence assessment tools, low or non-existing adherence promoting facilities and possible danger of recruiting drug resistance strains in the ART users. Moreover the CD4 count, viral load determination and weight measurement were not done as per care givers standard protocol. Regimen changes were high and frequent, subjecting patients and the nation to more toxic and expensive drugs and leaving no reserve or second line regimen for the future.

6.3. **RECOMMENDATIONS**

- Health provider's accurate adherence assessment is critical to maximize ART drug effectiveness and minimize the potential population risks associated with drug resistance.
- Clinical adherence core indicators like CD-4 count, viral load and patients' weight should be monitored in a regular manner and documented.
- To promote adherence among patients, as recommended by Steel G. (2008), regimen change decisions made by health providers should be based on valid and reliable adherence measurement like viral load and CD-4 (readiness with revised CD-4cell count and viral load test results) assessment.
- Health service problem like prolonged patient waiting time in the hospital, visiting card loss, regular CD4 cell count and viral load test shortage of the site need be managed.
- To improve adherence a multidisciplinary interventions effort like health care providers good approach, social support, family and friends networks might be employed considerably.
- Future research efforts should include interventions to improve adherence in Ethiopia and should be based on substantive theories of behaviors.
- It is necessary to design and implement practically sound adherence promoting interventions (more adherence aids).
- As this study was conducted only at a single hospital, it is important to further study ART adherence levels at all hospitals.

Lists of references

AIDS Institute, New York Department of Health. Criteria for the MedicalCare of Children and Adolescents with HIV Infection, CHAPTER 15, Antiretroviral Therapy and Clinical Trials. http://www.health.state.ny.us/nysdoh/aids/manuals/children/ped1_5.htm

Baveja, R., Usha, k., & Bharat, B.(2004) Diagnosis and Management of HIV/AIDS gold standard book.*A clinical perspective*, pp 16-347

Bell, DJ., Kapitao, Y., Sikwese, R., van Oosterhout, JJ., & Lalloo, DG. (2007). J Acquir Immune DeficSyndr Aug. 15;45(5):560 -3

Beith, A., and Johnson, A.(2006)*Interventions to Improve Adherence to Antiretroviral Therapy:A Review of the Evidence.* Submitted to the U.S. Agency for International Development by theRational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences forHealth

Berg, K.M. and Arnston, J.H.(1969) practical and conceptual challenges in measuring antiretroviral adherence, Journal of Acqired ImmuneDeficiency Syndromes, Vol. 43, no. 1, pp. 80-81.

CDC (2002), Guidelines for Using Antiretroviral Agents among HIV-Infected Adults and Adolescents. Recommendation for the panel on clinical practices for Treatment of HIV.MMWR, 51: 4-5

CDC updates (1996), Provisional Public Health Service Recommendations for Chemoprophylaxis after Occupational Exposure to HIV.MMWR, 45: 468-472.

Chalker, J., Andualem, T., Gitau, L., Ntaganira, J., Waako, P., Obua, C., &Ross-Degnan, (2011), INRUD IAA. Measuring Adherence to Antiretroviral Treatment.

Chesney, MA. (2000), Factors Affecting Adherence to Antiretroviral Therapy. Clinical Infect Dis. Jun, 30 Suppl, 2:S171-6.

Chesney, MA. (2003), Adherence to HAART regimens. *AIDS Patient Care and STDs, 17(4):169-177*.)

Chesney, MA. (2006), Tthe Elusive Gold Standard. Future Perspectives for HIV Adherence Assessment and Intervention. *J Acquir Immune DeficSyndr*. 43 : 151 -154,

Dan, K., Erica, A. H., Susannah, F. E., Mohamed, B. B., Brima, K., Thomas, P. (2011), 6th international conference on HIV Treatment and Prevention Adherence, May 22-24, Miami,Giordano1, 5.

El-sadr, WM., Burman, WJ. Grant, LB., et al.(2000). Discontinuation of Prophylaxis for Mycobacterium Avium Complex Disease in HIV Infected Patients who have a Response to Antiretroviral Therapy. *Terry Beirn Community Programs for Clinical Research on AIDS*.NEngl J Med; 342: 1085- 1092.

Ethiopian Federal Ministry of health HIV/AIDS prevention and control office (2007a). *Single point HIV prevalence estimate*. [Online] Available from: http://www.etharc.org/aidsineth/publications/singlepointprev_2007.pdf (accessed 14 June 2014).

Ethiopian Federal Ministry of Health HIV/AIDS Prevention and Control Office. 2007b. *Accelerated access to HIV/AIDS prevention, care and treatment in Ethiopia: road map 2007-2008/10.*

Ethiopian Health and Nutrition Research Institute (2012).HIV Related Estimates and Projections for Ethiopia –Federal Ministry of Health, Addis Ababa, p5-17.

Erlen, J., & Meyers, M.(2006). A Qualitative Study of Persons who are100% Adherent to Antiretroviral Therapy. AIDS Care 18(2):140-148.

FHAPCO (2012).Country progress report on response to HIV/AIDS. Planning, Monitoring and Evaluation Directorate of the Federal HIV/AIDS Prevention and Control Office.

Gill, C., Hamer, DH. Simon, JL., et al. (2005). No Room for Complacency about Adherence to Antiretroviral Therapy in Sub-Saharan Africa. AIDS;19:1243–1249

Gourevitch, MN. (1996). The Epidemiology of HIV and AIDS. *Med Clin North AM*, 80(6): 1223-38

Gifford, Al., Bormann, JE., Shively, MJ., Wright, BC., Richman, DD., & Bozzette,S.(2000). Predictors of Self-reported Adherence and Plasma HIV Concentrations in Patients on Multidrug Antiretroviral regimen, 23:386-95

Hogan D, Salomon J et al (2005); Prevention & treatment ofHIV/AIDS in resource limited settings. Bulletin ofWHO. Vol.83, No 2 Geneva Feb 2005.

Horizons/Population Council, International Centre for Reproductive Health and Coast Province General Hospital, Mombasa–Kenya,(2004). Adherence to Antiretroviral Therapy in Adults, *A Guide for Trainers*. Nairobi:Population Council. Printed in India by Mosaic Books.

http:aidsinfo.nih.gov/guidelines/htm1/1/adult-and-adolescent-ARVguidelines/30/adherence-t…4/1/2014

Johnson, A., & Witt, H. (2007). Adherence to ART Practices in Resource- Constrained Settings. Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health. E-mail: rpmplus@msh.org).

Kaufmann, D., Pantaleo, G., Meylan, P. (1998). Extended Benefit of Protease Inhibitor Containing Combination Therapy through a Dissociated

Markos, E, Worku, A & Davey, G. 2008.Adherence to ART in PLWHA at Yirgalem Hospital, South Ethiopia.*The Ethiopian Journal of Health Development* 22(2):

Melissa H. W. (2008). Understanding Patients' Adherence to Antiretroviral Therapy.*A Mixed-Methods Study in Arusha, Tanzania*(Melbourne KM, Geletko SM, Brown SL, Willey-Lessne C, Chase S, Fisher A (1999). Medication Adherence in Patients With HIV Infection: A Comparison of Two Measurement Methods. AIDS Reader, 9 (5): 329-338).

Mshana, G.H., Wamoyi, J., Busza, J., et al. (2006). Barriers to Accessing Antiretroviral Therapyin kisesa, Tanzania.a Qualitative Study of Early Rural Referrals to the National Program, *AIDS patient careand STDs*, vol. 20. No.9, pp.649-657,view at publisher.

Myer &Karim (2007).Measuring Adherence to Antiretroviral Treatment, Pp.156.

Nachega JB, Knowlton AR, Deluca A, et al (2006).Treatment supporter to improve adherence to antiretroviral therapy in HIV-infected South African adults. A qualitative study.43 :S127–S133.

Negash, T., (2011).Personal Factors Influencing Patients' Anti-Retroviral Treatment Adherence in Addis Ababa, Ethiopia.

Nejad, L., Werth, E., &Greenword, K.M. (2005).Comparison of the Health Belief Model and the Theory of Planned Behavior in the prediction of Dieting and Fasting Behaviour.*E-journal of appliedPsychology*, Social section.1(1):63-74;

Ogden, J. (2004). Doctor Patient Communication and then Role of Patient Beliefs in Health Psychology: A Textbook: London: Open University Press

Orrell, C. (2005). Antiretroviral Adherence in Resource- poor Setting, *Current HIV AIDS reports*, vol.2, no.4. Pp.171-176,

Pantako, G., et al. (1995).Studies in Subjects with Long Term Non Progressive HIV Infection. *N Engl J Med*, 332: 209-16

Platt, F.W., Tippy, P.K. & Turk, D.C. (1994), October 30). Helping patients adhere to the regimen. Patient Care, 43-52.

Rosenstock, I.M., Stretcher, V.J., & Becker, M.H.(1988). Social learning theory and the health belief theory.Health Education Quarterly, 15, 175-183 **http://recapp.etr.org/recapp/index.cfm?fuseaction=pages.TheoriesDetail&PageID=13.Viewed 4/22/2014.**

Ross, D., Pierre, J., Fahg, Z., Hailu, T., &Lillian, G. (2010). Measure Adherence to Antiretroviral Treatment in Resource- poor Settings. *The Clinical Validity of key Indicators*, BMC Health Services Research10:42 http://www.biomedcentral.com/1472-6963/10/42

Sendagala, S., (2010).Factors affecting the Adherence to Anti-retro viral therapy by HIV Positive Patients Treated in a Community Based HIV/AIDS care program in rural Uganda.A case of Tororodisctrict.

Shirley, D., Stanley, W., & Daniel, C. (2004).Statistics for Research.John Wiley & Sons, Inc. publication, Hoboken, New Jersey, third edition. Pp.29

Steel, G., Nwokike, J., & Joshi, M. (2007).Development of a Multimethod Tool to Measure ART Adherence in Resource-Constrained Settings.The South Africa Experience. Submitted to the U.S. Agency for International Development by the Rational Pharmaceutical Management Plus Program. Arlington, VA: Management Sciences for Health

Stretcher, V.J., & Rosenstock, I.M.(1997).The Health Belief Model.In Glanz K., Lewis F.M., &Rimer, B.K., (EDS.), Health Behavior & Health Education: Theory, Research & Practice. San Francisco. Jossey-Bass.

Susana, U. (2004).Essentials of Psychological Testing.*Published by John Wiley& Sons, Inc.*, Hoboken, New Jersey,PP: 117-151

UNAIDS (2010). UNAIDS Report On The Global AIDS Epidemic. P-9.

Vanhove, G., Schapiro, J., Winters, MA.,Merigan, TC. &Blaschke, TF. (1996). Patient adherence and drug failure in protease inhibitor monotherapy (letter). JAMA, 276:1955-1956).

viremia(2101). CD4 T-cell Response in 12 worlds AIDS Conference, Geneva. Ab. No. 1

Vreeman, R.C., Wiehe, S.E., Pearce, E.C. &Nyandiko, W. M.(2008). a systematic review of pediatric adherence to antiretroviral therapy inlow-and middil- income countries, pediatric infectious disease journal, vol. 27, no. 8, pp. 686-691.

WHO & MSH (2011). How to Investigate Adherence to Antiretroviral Treatment: *An Indicator-Based Approach*.

WHO (2004).Adherence to HIV Treatment Regimens.Recommendations for Best Practices APHA – www.apha.org/ppp/hiv - Juneversion.

WHO (2009). Progress Report Towards Universal Access: *Scaling up Priority HIV/AIDS Interventions in the Health Sector*:

WHO (2010) Towards universal access: scaling up priority HIV/AIDS interventions in the health sector: progress report 2010," In: WHO, editor. Geneva, Switzerland.

Yimenu, W.D (2009). Factors Affecting Antiretroviral Therapy Adherence in Ethiopia, Master of Public Health. University of South Africa, Pp, 143