ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

ASSESSMENT OF FACTORS AFFECTING ADHERENCE AND UTILIZATION OF ISONIAZID PREVENTIVE THERAPY AMONG HIV PATIENTS IN YEKATIT 12 HOSPITAL ADDIS ABABA

By

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ADDIS ABABA, ETHIOPIA

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ACRONYMS

AIDS……Acquired immune deficiency syndrome

ART……Antiretroviral therapy

CD4……Cluster of differentiation

CI……..Confidence interval

CPT……..Co-trimoxazole prophylactic therapy

CSA……Central statistics agency

EC……..Ethiopian calendar

EFY……Ethiopian fiscal year

FMOH……Federal ministry of health

HIV…… …Human immune deficiency virus

ICF……..Intensified case finding

IDU……Intravenous drug use

INH……Isoniazid

IPT……..Isoniazid preventive therapy

MDG……Millennium development goal

OR……Odds ratio

AARHB……Addis Ababa regional health bureau

TB……Tuberculosis

TST……Tuberculin skin test

UNAIDS……Joint united nations programs on HIV/AIDS

USD……United states dollar

WHO……..World health organization

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Abstract

Background: Isoniazid (INH) is given to individuals with latent infection of tuberculosis in order to prevent progression to active disease. It is important to understand factors associated with non-adherence so that high adherence can be maintained or low adherence improved since adherence to effective treatment improves health outcomes.

Objective: To assess factors affecting adherence and utilization of IPT in HIV patients and to explore the opinions of patients and health care providers about factors affecting adherence and use of INH

Methods: Participants eligible for the study 403 individuals who were HIV positives taking INH on follow up at yekatit 12 hospital randomly selected and Adherence measured by self-report of INH tablets taken for past 3, 7 and 30 days and in depth interview for recruited patients, adherence counselor and health professionals at ART clinic was done.

Results: Adherence to INH was 94% by self-report for last 7 days .The odds of adherence to INH was 7.7 [95% CI (2.6, 22.9)]times higher among those with no skin rash compared to patients with skin rash.

Conclusion: The prevalence of adherence to INH among people living with HIV in yekatit 12 hospital has a better rate of adherence than other local and African studies and the reasons for poor adherence was strongly associated with occurrence of jaundice, skin rash and seizure and rate of utilization is perceived to be low because of interrupted drug supply.

Recommendation: Availability of comprehensive care and support such as nutritional support and appointment per demand adequate time for counseling, follow up, sustainable drug supply, evaluation and treatment of side effects .

1. Introduction

1.1 Statement of the problem

Tuberculosis (TB) remains a major global health problem(1). It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immune deficiency virus (HIV). There were almost 9 million new cases in 2011 and 1.4 million TB deaths 990 000 among HIV-negative people and 430 000 HIV associated TB deaths in the same year(1). This is despite the availability of treatment that will cure most cases of TB. Short-course regimens of first-line drugs that can cure around 90% of cases have been available since the 1980s(2).

People living with HIV who are also infected with TB are much more likely to develop TB disease than those who are HIV-negative. Starting in the 1980s, the HIV epidemic led to a major upsurge in TB cases and TB mortality in many countries, which persisted throughout the 1990s and up to around 2004, especially in Southern and East Africa. In 2011, 1.1 million (13%) of the 8.7 million people who developed TB worldwide were HIV-positive, 79% of these HIV-positive TB cases were in the African Region(1).

Isoniazid is given to individuals with latent infection with *Mycobacterium tuberculosis* in order to prevent progression to active disease. Exclusion of active TB is critically important before isoniazid preventive therapy (IPT) is started. The absence of all of current cough, night sweats, fever, or weight loss can identify a subset of adolescents and adults living with HIV who have a very low probability of having TB disease that can reliably be initiated on IPT. This screening rule has a negative predictive value of 97.7% (95% CI 97.4–98.0) at 5% TB prevalence among people living with HIV (4).

Promoting research is a key component of the “Stop TB Strategy”, which includes conducting “program-based operational research” and “research on introducing new tools into practice”. the importance of program-based operational research is increasingly recognized, as exemplified through the insertion of a concise Operational Research section in the new Global Plan to Stop TB 2011-2015, and was recently identified as a major area in which global action is urgently needed(3).

The Ethiopian national guidelines for TB/HIV collaboration advised offering HIV testing to those with cough more than 2 weeks, provision of IPT to HIV positives screened negative for TB, co-trimoxazole prophylactic therapy (CPT) to co-infected patients, and regular TB screening of clients in HIV care(4) despite the recommendations there are no enough data on magnitude of adherence and utilization of IPT in Ethiopia**.**

1.2 Rationale of the study

TB mortality rate has decreased by 41% since 1990 and the world is on track to achieve the MDGs target of a 50% reduction by 2015. At country level, Cambodia demonstrates what can be achieved in a low-income and high-burden country: data shows a 45% decrease in TB prevalence since 2002. Globally, 48% of the TB patients known to be living with HIV in 2011 were started on ART; coverage needs to double to meet WHOs recommendation that all TB patients living with HIV are promptly started on ART. Kenya and Rwanda are top performers in HIV testing and provision of ART(1).

There are critical funding gaps for TB care and control(1, 2). Between 2013 and 2015 up to USD 8 billion per year is needed in low- and middle-income countries, with a funding gap of up to USD 3 billion per year. International donor funding is especially critical to sustain recent gains and make further progress in 35 low-income countries (25 in Africa), where donors provide more than 60% of current funding. There are also critical funding gaps for research and development. Governance and coordination at national and sub-national levels resource mobilization provision of general policy and program direction for the management of activities capacity-building including training ensuring coherence of communications about TB and HIV ensuring the involvement of civil society, nongovernmental and community organizations, and individuals(2).

One of the collaborative TB/HIV activities by WHO is to have 100% coverage of IPT for people living with HIV attending HIV care services among those eligible by 2015(1, 2). Ethiopia has developed guideline for clinical and programmatic management of TB, leprosy, TB/HIV in line with WHO's recommendation and policy guideline to meet the MDG's 6thtarget by 2015(5). There were 5442(8%) of HIV patients diagnosed with TB in Ethiopia in 2011 and only 30816 people living with HIV were provided with IPT during the same year(6).point estimates for HIV incident TB cases in 2011 were in the range of 27 to 41 cases per 1000 population(1).

Adherence rates for IPT varied widely from 34% to 98% from observational studies and did not directly address whether poor adherence adversely affects individual or program outcomes and a number of factors were identified to improve adherence(7). Since the implementation has gaps in scaling up the recommendation on IPT for people living with HIV evidenced by limited local and global data (5, 6, 8). Hence, the purpose of the study is to determine factors associated with adherence of IPT and its use to Influence standard of practice and implementation of existing national and global policy and guidelines on use of IPT for eligible people living with HIV.

2. Literature review

2.1 Overview of tuberculosis

TB is a major public health problem throughout the world. About a third of the world's population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease(2). According to the WHO Global TB Report 2011, there were an estimated 9 million incident cases of TB globally, in 2010, of which 1.2 million were among people living with HIV(1). About 26% of the incident TB cases occurred in Africa in 2010. The proportion of TB cases Co-infected with HIV is highest in countries in the African region; overall, the African region accounted for 82% of TB cases among people living with HIV(5) of the 22 high TB burden countries 9 are in the sub Saharan region with range of TB/HIV incident cases 23 to 390 per thousand; South Africa is the leading and Ethiopia the sixth(1).

HIV is the strongest risk factor for developing tuberculosis (TB) disease in those with latent or new Mycobacterium tuberculosis infection. The risk of developing TB is between 20 and 37 times greater in people living with HIV than among those who do not have HIV infection.

Relatively more women than men were detected to have TB in countries with a prevalence of HIV infection of more than 1%. In response to the dual epidemics of HIV and TB, the WHO has recommended 12 collaborative TB/HIV activities as part of core HIV and TB prevention, care and treatment services(7). They include interventions that reduce the morbidity and mortality from TB in people living with HIV, such as the provision of antiretroviral therapy (ART) and the Three I's for HIV/TB: intensified case-finding of TB (ICF), isoniazid preventive therapy (IPT), and infection control for TB(7).A high rate of previously undiagnosed TB is common among people living with HIV. ICF and treatment of TB among people living with HIV interrupts disease transmission by infectious cases, reduces morbidity and delays mortality. Most importantly, active screening for TB offers the opportunity to provide preventive therapy for those who do not have symptoms and signs of TB.

IPT is a key public health intervention for the prevention of TB among people living with HIV(1, 7). And has been recommended since 1998 by WHO and the Joint United Nations Program on HIV/AIDS (UNAIDS) as part of a comprehensive HIV and AIDS care strategy. It has subsequently been included in a number of WHO guidelines and recommendations. However, its implementation has been very slow and has been impeded by several barriers including lack of an accepted approach to exclude active TB disease and restricted access to isoniazid for fear of developing drug resistance(7).

By the end of 2009, globally only 85 000 people living with HIV received IPT(7).Ethiopia is one of the 22 high burden countries (1). There were an estimated 220,000 (261 per 100,000) incident cases of TB in Ethiopia in 2010. According to the same report the prevalence of TB was estimated to be 330,000 (394 per 100,000). There were an estimated 29,000 deaths (35 per 100,000) due to TB, excluding HIV related deaths, in Ethiopia during the same period. According to the 2002 EC (2009/10) health and health related indicators of the Federal MoH, tuberculosis is the second cause of death in Ethiopia. During the year 2010/11 (2003 EC), a total of 159,017 TB cases were notified in Ethiopia(5).

2.2 Burden of latent TB

The WHO estimates that one-third of the world's population is latently infected with Mycobacterium tuberculosis(9). Latent tuberculosis (TB) infection results when individuals infected with M. tuberculosis carry the organism in a latent state**,** which is characterized by slowed or intermittent metabolism and replication below the level necessary to produce clinical illness. The risk of reactivation of latent infection is low in healthy individuals but is greatly increased in individuals with immune suppression, most notably that due to HIV infection.

The greatest burden of latent TB infection is found in South-East Asia (prevalence, 46%), the Western Pacific region (32%), Africa (31%), and the Eastern Mediterranean region (27%). This finding contrasts with the much lower prevalence of latent TB infection noted in the Americas (15%) and Europe (14%). In sub-Saharan Africa, 5%–35% of the adult population is infected with HIV, and one-third to one-half of HIV-infected individuals is co-infected with M. tuberculosis.

Between1990 and 2005, the incidence of TB increased at an average rate of 7.0% per year in countries where there was a high prevalence of HIV infection among adults(5%), but it increased at an average rate of only 1.3%per year in countries where the prevalence of HIV infection among adults was low (5%)(1).

HIV infection is the major risk factor contributing to the growing burden of TB globally, Particularly in countries in sub-Saharan Africa(9).Tuberculin skin test (TST) relies on a competent immune response to identify people with latent Mycobacterium tuberculosis infection. Studies in people living with HIV demonstrate that IPT is more effective in people with a positive TST than in those with a negative test(10). In addition, the use of TST could reduce the number of patients receiving IPT and the numbers needed to treat to prevent one case of active TB. However, in resource-constrained settings, operational challenges to the implementation of TST are significant impediments for access to IPT. People living with HIV who are TST negative should be assessed on a case-by-case basis for their individual risk of TB exposure and the added advantage of the provision of IPT (e.g. health-care workers, prisoners, miners and others who live in a high TB transmission setting)(7).

2.3 Drug resistance

Concerns about the risk for development of isoniazid resistant tuberculosis may hinder its widespread implementation. A systematic review of data showed IPT is a safe, low-cost Intervention that has the potential to reduce illness and death caused by TB, especially among HIV-infected persons. The main cause of anti-tuberculosis drug resistance is inadequate treatment of active TB. Therefore, any risk for a small increase in the incidence of isoniazid resistance attributable to wider use of IPT needs to be weighed against its benefit in reducing TB incidence(8).Worldwide, 3.7% of new cases and 20% of previously treated cases were estimated to have MDR-TB. India, China, the Russian Federation and South Africa have almost 60% of the world's cases of MDR-TB.

The highest proportions of TB patients with MDR-TB are in Eastern Europe and central Asia(1). Ethiopia had 212 laboratory confirmed cases of MDR-TB and 199 patients were started on MDR-TB treatment(6).Factors associated with development of MDR/XDR-TB is said to be poor adherence, inappropriate dosing of anti TB and weak policy on collaborative TB/HIV programs(1).

If IPT does increase the risk for isoniazid-resistant TB, one might argue that combination regimens should be used. Combination regimens have similar efficacy to isoniazid alone among HIV-infected persons and are shorter, but these regimens generally have more adverse effects, are more expensive, and risk promoting resistance to rifampin(11).

IPT substantially reduces the risk for active TB disease in persons whose tuberculin skin test is positive. In accordance with WHO policy, ongoing surveillance for isoniazid resistance is required among populations in which this intervention is widely implemented(11).

2.4 Adherence to INH

Non-adherence and loss to follow-up in a clinical trial threatens the validity of conclusions about the intervention. The Botswana Isoniazid Preventive Therapy (IPT) clinical trial was a double-blinded, randomized, placebo-controlled clinical trial to determine whether isoniazid taken daily for 36 months was more effective in protecting against tuberculosis (TB) in HIV-infected adults compared to the standard-of-care in which isoniazid was taken daily for six months. It was reported that participants receiving 36 months of IPT had half the risk of TB compared to participants receiving the 6-month regimen, Generally speaking, patients are less adherent to treatment when they feel well, such as when taking prophylactic treatment, than they are for a symptomatic condition(12).

Based upon the pharmacy refill criterion for adherence from the Botswana clinical trial(i.e.,>=80% attendance to study medication refill visits), despite a prolonged 36-month period of prophylaxis, participants in the trial had a78% adherence rate which is similar to the 69–86% rates reported by other clinical trials that provided 6 months of IPT. Using the urine isoniazid metabolite criterion as an assessment of adherence, participants in the 36-month Botswana study had a 74–80% adherence rate which is comparable to the 45–80% rates reported in two other IPT clinical trials of shorter duration(12). In a Brazilian study physicians are substantially more compliant with HIV monitoring and PCP prophylaxis than with TB prophylaxis guidelines(13).

2.5 Toxicity

Most drugs cause liver injury infrequently. These reactions are considered idiosyncratic, occurring at therapeutic doses from 1 in every 1000 patients to 1 in every 100,000 patients, with a pattern that is consistent for each drug and for each drug class. Idiosyncratic reactions are characterized by a variable delay or latency period, ranging from 5 to 90 days from the initial ingestion of the drug, and are frequently fatal if the drug is continued once the reaction has begun. In contrast, with a drug such as isoniazid, mild injury may disappear despite continued use(14).Even with this risk, the benefits of IPT outweigh the risk of liver damage for people living with HIV.

Client monitoring and education can decrease the risk of a severe adverse event. The degree of monitoring that is feasible depends on the setting and ranges from educating clients on symptoms and self-monitoring to monthly check-ups at a health facility. Two recent studies of IPT for HIV patients in the U.S. reported rates of liver damage of 0.1 percent and 0.3 percent respectively. One hospitalization and no deaths were reported across data that included over 14,000 patients In both studies, monitoring for potential liver damage included monthly clinical monitoring by a nurse and was required for continued treatment. Patients were also counseled about potential symptoms and side effects at these monthly sessions(8, 15).

2.6 Duration and effectiveness

In a randomized, double-blind, placebo-controlled trial from Botswana 36 months' isoniazid prophylaxis was more effective for prevention of tuberculosis than was 6-month prophylaxis in individuals with HIV infection, and chiefly benefited those who were tuberculin skin test positive. Increasing use of antiretroviral therapy conferred a progressively greater reduction in the risk of tuberculosis and was additive to the protective effect of isoniazid preventive treatment(16). In a different study a trial based analysis from southern India demonstrated that a six-month course of isoniazid-based preventive therapy for HIV-infected individuals decreased TB incidence, increased overall life expectancy and was cost-effective. These findings were robust across wide variations in parameters including adherence, prevalence of drug-resistant TB, drug toxicity, and costs(10).

The thirty-six month regimen may be considered more cost-effective than the six month regimen in the best case scenario when efficacy was significantly greater than the six-month regimen, only marginal costs of IPT medications were considered in the case of co-localized TB/HIV care, and ART was initiated earlier(10)**.**Pooled data from 3586 patients suggested that 4-month rifampin therapy was associated with a significant reduction in the risk of non-completion (RR for random-effects model, 0.53; 95% CI, 0.44–0.63).

Non completion rates were lower among patients who received 4-month rifampin therapy (range, 8.6%–28.4%), compared with non-completion rates among patients who received 9-month isoniazid therapy (range, 24.1%–47.4%). Also, rates of hepatotoxicity (defined as grade 3 or 4 liver failure leading to drug discontinuation) were lower for patients who received 4-month rifampin therapy (range, 0%–0.7%), compared with the corresponding rates for patients who received 9-month isoniazid therapy (range, 1.4%–5.2%), and rifampin was associated with significant reduction in the risk of hepatotoxicity (RR for fixed-effects model, 0.12; 95% CI, 0.05–0.30).Given the lack of solid evidence on tuberculosis reactivation rates in this arm, 6 to 9 months INH therapy remains the standard of care(17).

2.7 TB screening tool and risk of active TB

Report from individual participant data meta-analysis of observational studies the absence of all of current cough, fever, night sweats, and weight loss can identify a subset of people living with HIV who have low probability of having TB disease. This screening rule was superior over other candidate rules in eight of the nine studies included. It was demonstrated that the negative predictive value of the rule was high across a range of TB disease prevalence estimates and across different population subsets, including those with low and high CD4 count, and those drawn from clinical and community settings and South African miners(18).

These screening questions are likely to be acceptable to practitioners, because they are symptoms classically associated with TB disease. Under diagnosis and delayed diagnosis of TB contribute to excess mortality among people living with HIV. Similarly, concerns about the ability to reliably rule out active TB before initiating IPT have been a major barrier for wider use of this intervention. In the absence of a rapid and effective TB diagnostic tool available at the point-of-care, simple clinical algorithms must be used to screen people living with HIV for TB, dividing them into those in whom active TB is excluded and those who require further evaluation(18).

A study from eight outpatient clinics in Cambodia, Thailand, and Vietnam screening for tuberculosis should include asking questions about a combination of symptoms rather than only about chronic cough. It is likely that antiretroviral therapy and isoniazid preventive therapy can be started safely in people whose screening for all three symptoms is negative, whereas diagnosis in most others will require mycobacterial culture(19).

A study from Spain showed that isoniazid preventive therapy provides a long-term benefit in HIV-infected patients (0.61 per 100 patient-years), with a cumulative probability of TB <5% Three years after isoniazid in the HIV population at highest risk for TB (IDUs with positive TSTs). Which is consistent with previous reports and support that the use of isoniazid provides >90% drop in TB incidence. It is not known whether development of TB after prophylaxis is secondary to reactivation of a latent infection or to a newly acquired infection. It has been suggested that isoniazid cannot eradicate the whole population of M. tuberculosis. Thus, despite isoniazid chemoprophylaxis, cases of active TB could be anticipated in long-term surviving HIV-infected patients with progressive immune suppression(20).

The burgeoning problem of the occurrence of TB soon after the initiation of ART and unrecognized active disease with the risk of subsequent transmission has focused attention on Isoniazid in addition to ART which decreased the risk of TB to 0.80 cases per 100 person-years, compared with 4.01 cases per 100 person-years in those receiving neither treatment, with the greatest benefit of dual therapy realized by patients with the most severe immune suppression(21).

Fifteen years after WHO recommended IPT for all people living with HIV, less than 1 percent of those living with HIV received IPT. Supportive policy for IPT exists in 84 countries, yet few are implementing IPT programs. Health systems face several challenges to IPT implementation. Understanding how to address these challenges can open opportunities for the creation of successful programs(8).

Ethiopia has had mechanisms for TB/HIV collaborative activities since 2002. However, no published account has defined the role of these collaborative efforts in strengthening linkages between HIV and TB management units at the point of care level, this supports The rates of HIV testing and linkage to co-trimoxazole prophylactic therapy being higher than screening HIV positives for TB, initiation of IPT, referral, linkages, and TB diagnostic capacity(4).

In summary, TB remains a major global health problem(1). In 2011 there were 430,000 HIV associated TB deaths. INH is given to individuals with latent infection with TB in order to prevent progression to active disease(1, 7).

The Ethiopian national guideline for TB/HIV collaboration recommends TB screening and provision of IPT(5). Multiple factors affect implementation of IPT program in different ways including; burden of latent TB in resource limited settings, HIV infection being the strongest risk factor for TB disease, fear of INH resistance, drug toxicity and efficacy, physician adherence to implementation of policy and guidelines. Patient related factors such as fear of side effect, pill burden, believe in efficacy and level of information(7).

It is important to understand factors associated with non-adherence so that high adherence can be maintained or low adherence improved since adherence to effective treatment improves health outcomes(12).

This study will answer the question what factors are affecting adherence and use of IPT at facility level by setting a hypothesis; factors affecting adherence and utilization of IPT are similar across all people living with HIV by using a study framework adopted for the purpose of this study.

2.8. Conceptual framework

Determinants of adherence adopted for this study were considering the interaction between the following variables and outcome on adherence, disease characteristic: latent or active tuberculosis. Treatment variables: toxicity, efficacy, use of other medications including ART, duration and dosing. Clinical setting: staff proficiency, clinic distance from home. Patient variables: socio-demography, previous treatment for tuberculosis and behavioral factors such as use of alcohol, cigarette, Khat, and patient provider relationship(22). (Annex 2 for schematic presentation).

4. Objectives

4.1 General objective

To assess factors affecting adherence and utilization of IPT in HIV patients

4.2 Specific objective

4.2.1 To measure the magnitude of adherence among HIV patients who are taking INH

4.2.2 To determine factors associated with adherence to use of INH

4.2.3 To explore the opinions of patients and health care providers about factors affecting Adherence and utilization of INH

5. Methods and materials

5.1 Study area

Addis Ababa lies at an altitude of 2,300 meters and is a grassland biome, located at 9°1′48″North38°44′24″East.The city lies at the foot of Mount Entoto. From its lowest point, around Bole International Airport, at 2,326 meters above sea level in the Southern periphery, the city rises to over 3,000 meters in the Entoto Mountains to the North. Addis Ababa has a Subtropical highland climate. The city has a complex mix of highland climate zones, with temperature differences of up to 10°C, depending on elevation and prevailing wind patterns(23).

Based on the 2000 EC figures from the Central Statistical Agency (CSA) of Ethiopia, Addis Ababa has an estimated total population of 3,147,000 consisting of 1,511,000 men and 1,636,000 women. The city is divided into 10 administrative sub cities and 99 districts. With an estimated area of 530.14 square kilometer, this chartered city has a density of 5,607.96 people per square kilometer According to the 2000 (EFY) Health and Health Related Indicators publication by FMoH. Addis Ababa has 33 Hospitals, 28 Health Centers and 35 Health Posts(23).

Yekatit 12 hospital is one of the regional referral hospitals under the auspices Addis Ababa city administration health bureau. It gives service for 600 people per day as an outpatient and has 280 beds for inpatient. HIV clinic is one of the nine Departments for service in the hospital it has 5000 clients ever enrolled for HIV care and treatment, which has been providing antiretroviral therapy since 2005. Since the study hospital is among the largest number of service providers for people living with HIV we selected for doing research on assessment of factors affecting adherence and utilization of isoniazid preventive therapy among HIV patients.

5.2 Study design

Facility based cross sectional study on people living with HIV and to complement findings on quantitative results qualitative study using in depth interview were used.

5.3 Source population

HIV positive individuals of age above 15 who were ever enrolled to HIV care, treatment and support at the study hospital without active TB and who were on IPT and on follow up during the study period**.**

5.4 Study population

The study population were sample adults who were receiving IPT, attending follow up visit and full filling the inclusion criteria during the study August 07 to October, 03, 2013.

5.4.1 Inclusion criteria

Participants aged 15 years and above

HIV positive and receiving INH for prevention of tuberculosis for at least one month before the initiation of the study

5.4.2 Exclusion criteria

Individuals who were seriously ill and unable to respond

5.5 Sample size and sampling technique

The sample size is determined by assuming stabilized adherence prevalence rate 50%, giving any particular out come to be with 5% marginal error and 95% confidence interval of certainty (alpha = 0.05), and 5% allowance for abstains and refusal was considered. Based on this assumption, the actual sample size for the study was computed using single population proportion formula as indicated below

$N = (Z_{\alpha/2})^2 P (1-P)/d^2$

Where N=sample size

$Z_{\alpha/2}$= critical value 1.96

P= assume stabilized adherence prevalence rate of 50%

D= precision (marginal error) =0.05

Thus sample size was calculated as

N = (1.96)2 X (0.5) X (0.5)/ (0.05)2 = 384

Non response rate 5% + 384

Total=403

For the qualitative study participants who were eligible selected randomly, 02 health care providers giving service in HIV clinic purposely selected and one of them were ART clinic's focal person and there was no physician assigned to the clinic since few months earlier than data collection and one peer counselor who was the only one available for the adult ART clinic were used for in depth interview. Total sample size of 09 of which 06 were eligible participants determined when saturation of ideas were achieved.

5.6 Sampling procedure

All HIV positive individuals attending HIV Clinic of the study hospital and who fulfilled the entry criteria were identified from the average daily visit of 50 to 60 patients who came for regular clinical follow up and were randomly selected until they were 12 which was the required number of study participants for the day in two months of study period.

For the qualitative study 06 eligible participant were selected, health care providers with minimum work experience of 2 years in HIV clinic and a peer counselor with minimum counseling experience of 2 years were selected and sample size was determined on saturation of ideas.

5.7 Data collection

Questionnaire developed based on the format from demographic health survey (DHS)(24). Originally developed in English then translated to Amharic and back translated to English by a different translator who was blinded to the original questionnaire to check for its consistency.

Three data collectors were selected from a different facility qualified in bachelor of health science and experience of minimum three years in HIV clinic (two health officers and one nurse).One field supervisor qualified in doctor of medicine was selected from the same facility.

Training using lecture and demonstration on data collection procedure and supervision was given for two days.

Questionnaire was pretested at different facility involving enumerators and supervisor and data was collected at the study hospital**.** Draft of data collection guideline was developed and Data collection procedure was stipulated between data collectors, supervisor and principal investigator which serve for the study period.

Face to face interview technique was used. An average of 3 to 4 participants per enumerator total of 9 to 12 daily for two months from august 07 to October 03 2013 was duration of interview. For non-respondents random sampling for next participant was applied.

Data collection for in depth interview was done by the principal investigator using open ended questionnaire and tape recorder during the study period. Each in depth interview took 20 to 30 minutes. Duration of interview days was determined by saturation of ideas during data collection period. In depth interview was transcribed by graduate with bachelor of Amharic language and translated by graduate with bachelor of English language.

5.8 Measurement

The outcome (dependent) variable was self-reported adherence to IPT in the last 3, 7, and 30 days. Independent variables were socio-demography status such as sex and age, travel time to clinic, ART and other medications use, knowledge about IPT, belief on effectiveness of INH, report of side effects; nausea, vomiting, jaundice as liver toxicity, skin rash, and numbness as peripheral neuropathy and seizure, knowledge and interpersonal communication skill of health care provider, dosing, duration and frequency of INH, previous treatment of tuberculosis, use of any other of the following; *khat* (Catha Edulis), alcohol and cigarette and compliance on clinical appointments.

Screening tool for measuring level of adherence was using percent of pill taken which is calculated as ratio of pill taken to pill prescribed over the past 3, 7, and 30 days. Adherence level 80% and above considered adherent and < 80% as non-adherent(25).

5.9 Data quality assurance

Questionnaire was pretested at menellik II hospital which had similar service to study area on HIV care and support in Addis Ababa was chosen and important findings were used to modify questionnaire. Investigator and supervisor had a day to day visit to review questionnaires' completeness, accuracy and consistency and corrective discussion was undertaken with research team members on gaps identified. A reminding remark was given during each morning by supervisor on how to minimize errors and timely corrective actions were taken.

5.10 Data cleaning and analysis

After data collection, the data was coded on pre-arranged coding sheet by the investigator and the corresponding code number was written at each questionnaire margin and data entry was done using Epinfo version 3.5.3. Template scheme for data entry was developed and pre tested for ranges, skipping patterns and allowed legal values. Any error was identified before analysis by revising entered data and original data's code number and statistical commands. SPSS version 16 for data analysis was used and EndNote X2 for reference citation.

During analysis for response rates with yes or no, one point was given for positive response and zero point for negative response. Each variable from socio-demography, behavioral factors and service utilization had univariate analysis using percentages.

Analysis of the outcome variables were being adherent or non-adherent and measurement scales used was percentages. Outcome variables as adherent coded 1 and non-adherent coded as 0 were dichotomized for INH tablet taken for last 3, 7 and 30 days.

Frequency distributions in tables and graphical presentations were presented. Moreover, the overall association between the different factors and the outcome variables was done using chi-square test at a p value of <5%.

Age, educational level, monthly expenditure, time to reach the clinic walking in minutes were the characteristics considered to be associated with the variables of interest.

Multivariate binary logistic regression analysis was used to assess the strength and significance of association between the covariates and the outcome variables of interest. Significance level was decided when a p-value <0.05 was obtained at each level of analysis. All variables found statistically significant at the bivariate level was entered in the multivariate models for each dichotomy outcome of INH taken last 3, 7 and 30 days were used.

The qualitative data was first transcribed word for word and then translated to English language. The English version was exported into Open Code software version 3.6.2.0. The software was used for coding and categorization. Thematic content analysis was used. Moreover, some verbatim were used in the report to better reveal the opinions and perceptions of key informant interviewees.

5.11 Ethical consideration

Ethical clearance was obtained from both research ethics committees of school of public health Addis Ababa University and Addis Ababa city administration health bureau.

In this study, the risk of unintended health outcome is negligible since it is only interview to fill questionnaire. And the only risk is only taking few minutes for interview.

Verbal consent was taken after explaining the stated risk. For each study participant explanation about the purpose and importance of the study was given. There was no denial of health service for refusal.

Each participant told it is strictly confidential and privacy during interview will be maintained.

Each participant told the right to refuse, ask any question that is not clear and to discontinue Interview any time in between for any inconveniences.

5.12 Dissemination and utilization of data

The study findings will be disseminated to relevant authorities who deserve the results; Yekatit 12 Hospital, Addis Ababa city government regional health bureau and FMOH. Publication in a scientific journal shall also be considered.

6. Results

6.1 Socio demographic characteristics of the respondents

In this study a total of 403 people living with HIV taking INH prophylaxis at Yekatit 12 hospital Addis Ababa Ethiopia were participated and all eligible individuals responded to the question.

Out of the 403 respondents 149 (37%) and 245 (63.03%) were men and women respectively. The majority were in the age range of 35 to 44 [N 176 (43.7%)] followed by 25 to 34 [119 (29.5%)] and those in the age range 45 to 54 [77 (19.1%)]. The two ends of the age range 15 to 24 were 8 (2%) and those age of 55 and above were 23 (5.7%) the mean age was 38.8 and standard deviation (SD) of 9.3 (table 1).

The majority of respondents 162 (40.2%) were married, 98 (24.3%) widowed, 79 (19.6%) separated, 41 (10.2%) single, and 23 (5.7%) were divorced (table 1).

Most [362 (89.8%)] respondents attained formal school and 41 (10.2%) never been to formal school among the group who attended formal school the majority 153 (42.3%) went to high school while 113 (31.2%) went to college and the rest 96 (26.5%) attended primary school with. Orthodox Christianity followers were 265 (65.8%), Muslims 30 (7.4%), Catholics 12 (3%), Protestant 94 (23.2%) and other religion followers were 2 (0.5%) (table1).
Amhara ethnicity were the majority 179 (44.4%), Oromo 106 (26.3%), Tigre 76 (18.9%) and others were 42 (10.4%) (table1).

Unemployed were 55 (13.6%), housewives were 136 (33.7%) followed by private employees 95 (23.6%), civil servant 78 (19.3%), daily laborers 45 (11.2%), traders 24 (6%) and others 25 (6.2%)

Among 403 respondents, 58 (14.4%) did not know their monthly expenditure, 70 (17.4%) had less than a thousand birr, 192 (47.6%) between one and three thousand birr and the remaining 83 (20.6%) had three thousand and more birr for monthly expenditure with mean value of 1800.5, SD 1000.96(table 1).

Most 204 (50.6%) responded between one hour and ninety minutes walking to reach to the clinic, 128 (31.8%) took less than one hour, and the 71 (17.6%) had to travel ninety minutes and more minutes and the mean value was 69.6, SD 34.56 (table 1).

Table 1 Socio demographic characteristic of respondents at Yekatit 12 hospital Addis Ababa Ethiopia October 2013

Variables		Number (n=403)	Percentage (%)
Sex :	Male	149	36.97
	Female	254	63.03
Age in group:	15-24	8	2
	25-34	119	29.5
	35-44	176	43.7
	45-54	77	19.1
	>= 55	23	5.7
	Mean +_ SD		38.8 +_ 9.3
Marital status:	Single	41	10.2
	Married	162	40.2
	Divorced	23	5.7
	Widowed	98	24.3
	Separated	79	19.6
Level of education:	Never been to school	41	10.2
	1-8	96	26.5
	9-12	153	42.3
	College	113	31.25
Religion :	Orthodox	265	65.8
	Muslim	30	7.4
	Catholic	12	3
	Protestant	94	23.2
	*Others	2	0.5
Ethnicity :	Amhara	179	44.4
	Oromo	106	26.3
	Tigre	76	18.9
	**Others	42	10.4
Occupation:	Civil servant	78	19.3
	Private employee	95	23.6
	Trader	24	6
	Daily laborer	45	11.2
	Unemployed	136	33.7
	***Others	25	6.2
Monthly expenditure:	Do not know	58	14.4
	< 1000 Br	70	17.4
	1000-3000 Br	192	47.6
	>= 3000 Br	83	20.6

How long takes to the clinic:	< 60 minutes	128	31.8
	60-120 minutes	204	50.6
	>= 120 minutes	71	17.6
	Mean +_ SD		69.6 +_ 34.56

*jeouva witness

**Wolayta, Sidama, Harari, Agew

***handcraft, broker

6.2 Factors related to service utilization

From the total of 403 respondents 374 (93.1%) and 28 (6.9%) were initiated on ART and ART naïve respectively. Among those initiated on ART 363 (90.1%) were on first line regimen and 12 (3%) on second line regimen. The duration of ART in the majority was between one and five year 195 (52.1%) followed by those taking between six and ten years were 151 (40.4%) and the least were those taking ART for eleven years and more 28 (7.5%) with mean duration and SD of 5.23 +_ 3.45.

Medications were prescribed for other chronic medical illnesses and/or preventive therapy additional to INH and ART for 105 (26.1%) respondents and the rest 298 (73.9%) did not receive prescriptions.

Cotrimoxazole preventive therapy for opportunistic infections were the most prescribed additional medication 101 (96.2%), followed by treatment for diabetes 03 (2.85%) and one was on treatment for Hypertension.

Participants were asked to rate their opinion on once daily INH use 358 (88.8%) rated satisfactory and the rest 45 (11.2%) said it is not satisfactory. INH use for six months was rated as satisfactory by 331 (82.1%) while 72 (17.9%) said not satisfactory. Participants believe in efficacy of INH preventing TB was strong in 337 (83.6%) respondents, weak in 26 (6.5%) and no believe in 40 (9.9%).

The level of self -assessment of participant's knowledge about INH was rated as satisfactory in 329 (81.6%) and not satisfactory in 74 (18.4%). The interaction between health care providers and respondents were satisfactory 378 (93.8%) and not satisfactory 25 (6.2%). The health care provider's explanation on INH was rated similar to respondent's interaction with care providers.

Nutritional support was provided only for 18 (4.5%) respondents and 385 (95.5%) did not receive any. Regular peer counseling was given for 56 (13.9%) and 347 (86.1%) was not given. Appointment per demand for next visit and treatment for other illnesses were provided for 101 (25.1%) and 250 (62%) while 302 (74.9%) and 153 (38%) were not provided respectively.

The number of INH prescribed during a single visit was high 211 (52.4%) for thirty days compared to sixty to ninety days 150 (37.2%) and 120 to 180 days 42 (10.4%) combined with mean value of 55.5 +_ 32.6.

6.3 Behavioral factors

Alcohol use was the most common 20 (5%), followed by khat use 11 (2.7%) and smoking cigarette was 5 (1.2%) (table3) and the result did not show the magnitude of alcohol, khat or cigarette use. Previous treatment for tuberculosis was 119 (29.5%) and 284 (70.5%) never been treated for TB.

There were 10 (2.7%) respondents who discontinue ART for more than one month otherwise the majority 364 (97.3%) were adherent to their medication. Some of the reasons why they discontinued ART for more than one month includes the majority went to holy water 6 (60%), due to sickness 2 (20%) and the remaining 2 (10%) each said felt healthy and lack of support.

Most of the respondents 395 (98%) came on their regular clinical appointments and 321 (79.7%) felt comfortable to take INH while others watch them taking and the rest 82 (20.3%) did not feel comfortable.

6.4 Factors related to use of INH

INH related common side effects were reported in 142 times and vomiting was the most common 93 (65.5%), skin rash 33 (23.2%), jaundice or yellowish discoloration of the eyes 8 (5.6%) and the least reported were seizure or abnormal body movement and numbness each accounting 4 (2.8%) respondents. When they had one or more of the above symptoms only 350 (86.8%) continued taking INH and 53 (13.2%) discontinued for variable duration of day and it showed that most who had vomiting were continued taking INH.

The number of INH tablets taken during the past 3, 7 and 30 days were asked to assess level of Adherence and 18 (4.5%) took zero to 1 INH tablet which is less than 80% adherent and 385 (95.5%) took 2 to 3 INH tablets considered 80% and above as adherent for past 3 days. Over the past 7 days 24 (6%) took zero to 4 INH tablets and 379 (94%) took 5 to 7 tablets the former considered as less than 80% adherent and the later 80% and above adherent. And over all for the last 30 days 22 (5.5%) took zero to 23 INH tablets and 381 (94.5%) took 24 to 30 INH tablets with the former considered as less than 80% adherent and the later 80% and above, and 368 (91.3%) of those who were considered adherent for past 30 days took all 30 INH tablets.

The reasons for missing to take INH who were considered non adherent 34 (64.2%) was sickness 29 (54.7%), fear to take and forgot to take each 2 (3.8%) and no supply 1 (1.9%) among 53 (13.2%) respondents who missed INH tablets.

Table 2 Variables related to service utilization, behavior and use of INH in Yekatit 12 hospital October 2013

Service utilization variable	**N = 403**		**Percentage (%)**
Once daily INH	Satisfactory	358	88.8
	Not satisfactory	45	11.2
INH for six months	Satisfactory	331	82
	Not satisfactory	72	18
Belief in efficacy of INH	No belief	26	6.5
	Weak	40	9.9
	Strong	337	83.6
Self-assessment of INH knowledge	Satisfactory	329	81.6
	Not satisfactory	74	18.4
Interaction with health care workers	Satisfactory	378	93.8
	Not satisfactory	25	6.2
Health care workers explanation of INH	Satisfactory	378	93.8
	Non satisfactory	25	6.2
Nutritional support	18		4.5
Regular peer counseling	56		13.9
Appointment per demand	101		25.1
Treatment for other illnesses	250		62
Variables related to behavioral factors	**n=36**		
Alcohol	20		5
Khat	11		2.7
Smoking cigarette	5		1.2
Variables related to use of INH	**n=142**		
Vomiting	93		65.5
Skin rash	33		23.2
Jaundice	8		5.6
Numbness	4		2.8
Seizure	4		2.8
Common reasons for missing INH	**n= 34**		

Sickness	29	54.7
Fear to take	2	3.8
Forgot to take	2	3.8
No supply	1	1.9
Adherence less than 80%	**Number of days INH taken**	Adherence level (#(%))
18(4.5%)	Past 3 days	385(95.5%)
24(6%)	Past 7 days	379(94%)
22(5.5%)	Past 30 days	381(94.5%)

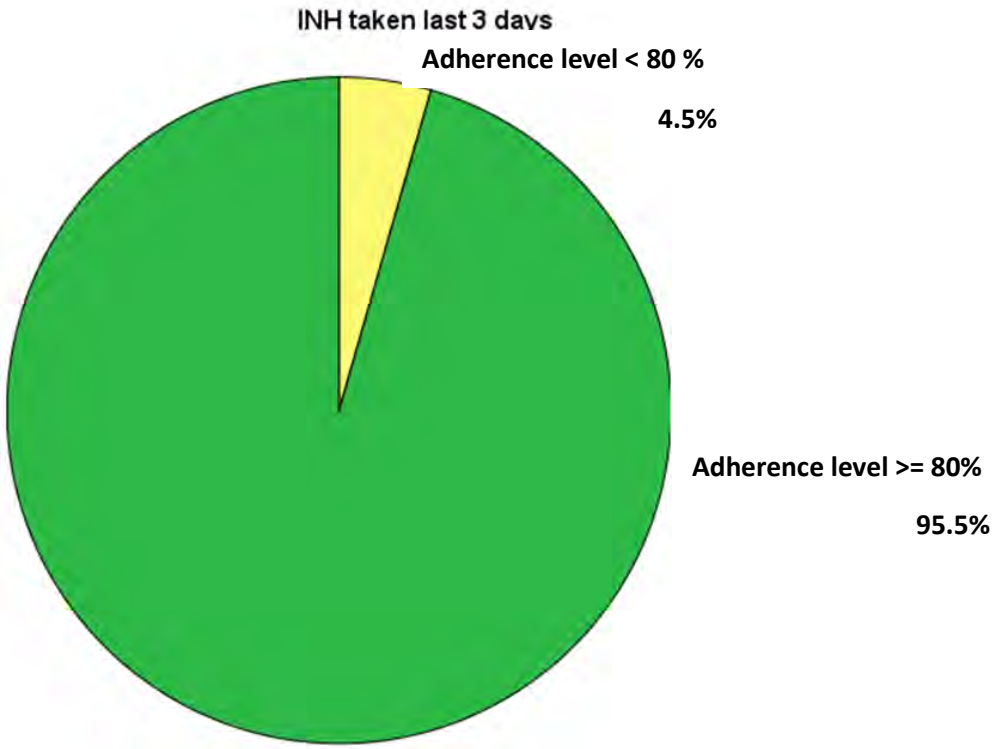

Chart 1: Adherence Level of INH taken in last 3 days in Yekatit 12 Hospital, October 2013

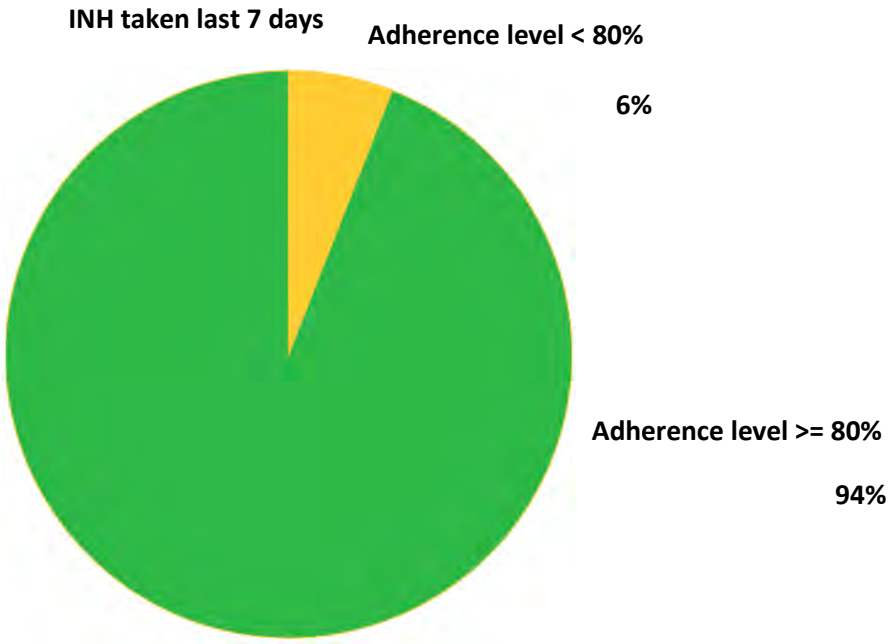

Chart 2: Adherence level of INH taken in last 7 days in Yekatit 12 Hospital, October 2013

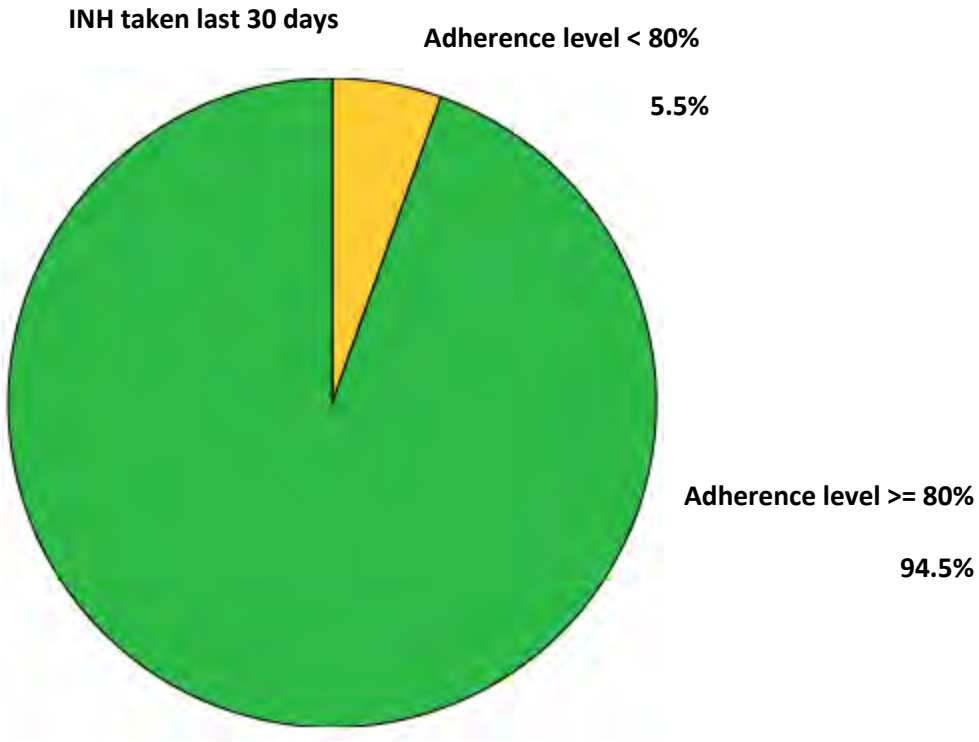

Chart 3: Adherence level of INH taken in last 30 days in Yekatit 12, October 2013

6.5 Multivariate association between characteristics of patients and INH

The chi-square test between independent variables: sex, age, marital status, religion, ethnicity, level of school, type of occupation, monthly expenditure in Birr, time to reach to the clinic walking in minutes, whether on ART or not, the type of ART regimen, duration of ART, reason to discontinue ART for more than one month, taking other medications, Khat, alcohol or cigarette use, feeling comfortable to take INH while others watching, regularly coming to the clinic per appointment, , nutritional care, peer counseling, vomiting and numbness and outcome variables as adherent or non-adherent for INH taken last 3, 7 and 30 days had no statistically significant association.

Statistically significant associations between independent variables: previous treatment for TB, appointment per patients' demand, jaundice, skin rash and seizure and outcome variables as adherent or non-adherent for INH taken last 3, 7 and 30 days from the bivariate analysis were used for multivariate binary logistic regression.

Multiple binary logistic regression models were used for INH taken last 3, 7 and 30 days to observe the odds of change for a unit change from predictor variable.

The odds of adherence to INH taken for last 3 days (*for practical purpose 2 tablets and above was taken adherent*) was 169.8, 95% CI (23, 1250) times higher among those patients who did not have jaundice compared to those who developed jaundice. Similarly the odds of adherence for to INH last 3 days was 23.9, 66.4 and 4.5 [95% CI (6, 95.4), (4.9, 908) and (1.2, 17.1)] times higher among those who did not have skin rash, seizure and appointment per patients' demand compared to those who developed skin rash and seizure and having appointment per patients' demand respectively (table 3).

Table 3 the association of side effects, previous TB treatment and appointment per demand with INH adherence for last 3 days in Yekatit 12 hospital October 2013.

Variable		INH adherence last 3 days Yes (%)	No (%)	Crude unadjusted OR (95% CI)	Adjusted OR (95% CI)
Jaundice	No	383(95)	12(3)	95.8(17.5, 524.2)	169.8(23, 1250)
	Yes	2(o.5)	6(1.5)	1.0	1.0
Skin rash	No	358(88.8)	12(3)	6.6(2.3, 19.0)	23(6, 95.4)
	Yes	27(6.7)	6(1.5)	1.0	1.0
Seizure	No	382(94.8)	17(4.2)	7.5(0.7, 75.8)	66.4(4.9, 908)
	Yes	3(0.7)	1(0.25)	1.0	1.0
Previous TB treatment	No	276(68.5)	8(2)	3.2(1.2, 8.2)	2.44(0.7, 8.8)
	Yes	109(27%)	10(2.5)	1.0	1.0
Appointment per demand	No	294(73)	8(2)	4(1.6, 10.5)	4.5(1.2, 17.1)
	Yes	91(22.5)	10(2.5)	1.0	1.0

The odds of adherence to INH for the last 7 days was 104, 7.7 and 34.8 [95% CI (18.7, 582.6), (2.6, 22.9) and (4.4, 272.6)] times higher among those patients who did not have jaundice, skin rash and seizure compared to those who developed jaundice, skin rash and seizure respectively (table 4).

Table 4 the association of side effects with INH adherence for last 7 days in Yekatit 12 hospital October 2013.

Variables		INH adherence last 7 days Yes (%)	No (%)	Crude unadjusted OR (95% CI)	Adjusted OR (95% CI)
Jaundice	No	377(93.5)	18(4.5)	62.8(11.8, 333.3)	104(18.7, 582.6)
	Yes	2(0.5)	6(1.5)	1.0	1.0
Skin rash	No	352(87.3)	18(4.5)	4.4(1.6, 11.9)	7.7(2.6, 22.9)
	Yes	27(6.7)	6(1.5)	1.0	1.0
Seizure	No	377(93.5)	22(5.5)	17.1(2.3, 127.5)	34.8(4.4, 272.6)
	Yes	2(0.5)	2(0.5)	1.0	1.0

The odds of adherence to INH for the last 30 days was 131, 11.8 and 14.6 [95% CI (22.9, 753), (3.9, 35) and (1.4, 156)] times higher among those patients who did not have jaundice, skin rash and seizure compared to those who developed jaundice, skin rash and seizure respectively (table 5).

Table 5 the association of side effects with INH adherence for last 30 days in Yekatit 12 hospital October 2013.

Variables		INH adherence last 30 days Yes (%)	No (%)	Crude unadjusted OR (95% CI)	Adjusted OR (95% CI)
Jaundice	No	379(94)	16(4)	71(13.3, 380)	131(22.9, 753)
	Yes	2(0.5)	6(1.5)	1.0	1.0
Skin rash	No	355(88.1)	15(3.7)	6.4(2.4, 17)	11.8(3.9, 35)
	Yes	26(6.5)	7(1.7)	1.0	1.0
Seizure	No	378(93.8)	21(5.2)	6(0.6, 60.2)	14.6(1.4, 156)
	Yes	3(0.7)	1(0.3)	1.0	1.0

6.6 Findings from the qualitative study

A total of 12 respondents for in depth interview were interviewed. Three of whom were males and six females and eligible for the quantitative study, one peer counselor who was the only available for the adult ART clinic and two nurses working at ART clinic one of them was focal person for the clinic.

Interviewees who were candidate clients said "*TB is a major disease and transmitted from person to person through cough, sputum, sharing cups and cold exposure*" and they believed INH is important for prevention of TB with more emphasis from those who had been treated for TB previously. Interviewees said they were not informed about side effects of INH and adequate information on its use and they reported "*during INH use alcohol use is forbidden*" and none of them said they had fear of INH to their health.

The opinion of a female peer counselor was: "i do not counsel clients on INH together with counseling for ART adherence since i do not have adequate information and the nurses did not inform me because they are busy at the clinic and she thought the nurses will tell clients more during initiation of INH". The counselor also was not started on INH because she thinks she has pill burden from ART drugs for herself and fear of INH since she heard some clients saying "it has vomiting, jaundice and allergy to skin".

The opinion from in depth interview of the two female nurses at ART clinic one also works as focal person to the clinic was based on their general view on INH, how frequently they initiate INH, factors affecting its utilization and adherence as well as important issues to emphasize on IPT program.

They have not seen clients developing active TB while on INH and after completion of INH and they rarely saw side effects of INH. Based on their experience most do not discontinue INH and even after completion some said it‟s good to take INH.

Both nurses said the ART clinic is busy and they are less motivated to initiate INH and besides no one has told them formally the details of IPT except a little about the prescription. Clients who stop INH will not stop ART but the converse is different those who are ART defaulters will stop INH too but they do all the possible to assess their ART adherence before initiating INH otherwise to their observation defaulters had skin rash as common side effect to stop taking INH.

Patients might say I will take it and will not start when reach their home and will resist to be initiated with different reasons such as I have pill burden and weak believe on its prevention for TB.

The problem for poor adherence are the initial prescription is for one month and they lose motivation to come on the next month for refill since their ART refill is usually for three months they demand same day appointment and the other complain and reason to stop INH was gastric pain, forgot to take and went to holy water.

When they had doctor visits they miss the next refill and the doctors do not know that the patient was on INH missing the record on the chart and generally doctors do not initiate INH and they do not encourage nurses to do it either and no patient ever asked to be initiated on INH even when they heard about its use.

Because of interrupted supply of either INH alone or both INH and pyridoxine the nurses usually were reluctant to initiate IPT also there is no one responsible monitoring and evaluating the program no training for nurses regarding IPT and recently partners who were trying to support the program before now phased out and the regional health bureau is currently responsible and so far no one had yet said about IPT.

7. Discussion

In this study we tried to assess factors affecting the rate of adherence and utilization of INH among people living with HIV at Yekatit 12 hospital based on self-reported adherence and its determinants also to complement findings from in depth interview. Since the methods were easy, readiness to get the desired information, identify patients at risk of poor adherence and cheap.

The study showed prevalence of adherence to INH taken for past 7 days prior to the date of response was 379(94%), 3 days prior 385(95.5%) and 30 days prior 381(94.5%) which was comparative across the three different days. Similar cross sectional study in Ethiopia showed adherence rate of 86.5% over past 7 days(25) and the Botswana three year case control study in eight public health clinics also showed 78% of adherence despite a prolonged 36 month period of prophylaxis(12) and another cross sectional study from rural south Africa adherence rate at 6 months of completion of IPT was 47%(26).

An operational assessment in Uganda for adherence to IPT showed 62%(27). Randomized trial from Thailand to see the effect of tuberculin skin test (TST) positive or not on adherence to IPT among HIV infected individuals showed 81.8% and 73.9% adherence respectively which was acceptable rate(28)and similar study from Tanzania showed 87% of adherence(29).

Observational studies compiled by WHO showed over all adherence rates of 34% to 98%(7).The current studies‟ prevalence of adherence close to the upper limit of WHO‟s report and higher than other studies could be due to the mean number of INH tablets prescribed was 55.5 which was less than the duration of 2 months compared to the other studies who completed 6 months to 3 years of prescribed INH.

The other possible reason was the report of side effects attributed to use of INH from other studies was considered in general than the current studies approach which tried to see each possible reported side effect and its association with adherence such as vomiting was reported most commonly than other side effects but had no statistical significance on adherence to INH for last 3, 7 or 30 days also those studies were done few years after IPT program implementation and scale up where by clients‟ adherence could be low for a relatively new program compared to the current study after increased awareness through counseling and increased knowledge which is complemented by the result from qualitative study patients awareness on the importance of INH and TB and HIV association and its severity despite providers‟ opinion on factors affecting utilization of INH such as inconsistent supply, limited monitoring and evaluation system, busy clinic, lack of time for counseling and lack of training to health care providers.

The common reasons for missed tablets in this study were experiencing one or more side effects, forgot to take, fear to take and no supply of INH at dispensary which is consistent reason from local studies.

The frequency of respondents less than the age of 44 is 75% with mean age of 38.8 which could be the reason why there was low rate of comorbidities because of younger age population and prescription of other medications [26%] and out of which cotrimoxazole preventive therapy was 96%.

The view of participants rated as satisfactory on dosing and duration of INH, their self-assessment of knowledge on INH, interaction with health care providers and believe in efficacy of INH rated as strong was above 80% a consistent finding with a study done for patients‟ beliefs about prescribed medicines and their role in adherence to treatment, most patients (89%) believed that their prescribed medication was necessary for maintaining health(30)which showed medication beliefs were more powerful predictors of reported adherence than the clinical and socio demographic factors, accounting for 19% of the explained variance in adherence(30).

The chi-square test between adherence to INH for last 3, 7 and 30 days and sex has no statistical significance unlike the case from Botswana trial men are poorly adherent than women(12).

Feeling comfortable to take INH while others were watching and coming to the clinic regularly per appointment were not statistically significant unlike study from Addis Ababa, Ethiopia which showed 6 times and 4 times likely to adhere to IPT respectively(25), however in our study having appointment per patients‟ demand had 4.5 times higher adherence to INH for last 3 days.

The odds of adherence to INH for last 3 days were 169.8, 23.9, and 66.4 times higher among those patients who did not have jaundice, skin rash and seizure respectively with similar higher odds of adherence to INH for last 7 and 30 days despite small number of observations which was seen on wide CI there seem to be strong association between not reporting those side effects and maintained good adherence unlike other studies who analyzed only self-reported side effects attributed to INH as one variable which did not show whether patients‟ poor adherence were due to headache, abdominal cramp, numbness or vomiting where the later was reported more frequently 65.5% in this study but did not have association with level of adherence. Immunogenetic differences contributing to the development of hepatitis induced by anti-tuberculous drugs have been suggested and disputed. Different backgrounds among the patient groups can create confounding factors, such as comorbidity (e.g., HIV infection or hepatitis A, B, or C virus infection)(31).

Apart from increasing hepatotoxicity with increasing age for isoniazid unlike in our study majority being young individuals, information on possible contributing causes of liver injury induced by anti-tuberculous drugs is conflicting or speculative(31).

Both jaundice and skin rash were not reported statistically significant before the current study affecting adherence in neither the Ethiopian nor other African studies probably because of study design difference specifically looking for occurrence of side effects.

The wide range of 95% confidence interval in jaundice, skin rash and seizure could be explained by small sample size and few number of occurrences significantly affecting adherence this findings could be confounded by the potential toxicity to occur due to either the ART regimen or cotrimoxazole since 96% of respondents are taking the later and/or since it is self-reported compliant patients might be preoccupied by potential side effects and attributes for non-genuine complains or one might have been dealing with a different disease conditions with same complaints and clinical presentation or it could be searching for a medical reason to discontinue INH and minimize blame by the health care providers for non-adherence.

The opinion of clients on INH is more or less similar regarding their knowledge about TB and IPT where most emphasized more on poorly told about INH and its potential side effects which is an idea complemented by the nurses opinion that since they are less courageous to initiate INH because of; busy ART clinic, repeated shortage of either INH or pyridoxine supply, physicians were reluctant to initiate or motivate stuff nurses on utilization of IPT which is supported by qualitative study from brazil there was a poor adherence for detection and treatment of latent tuberculosis infection among HIV-infected patients by physicians in Rio de janeiro(13) although the above stated prevalence of adherence for the current study showed the highest rate than similar local and African studies.

Lack of training on INH and no one showing responsibility for monitoring the program are the commonly mentioned reasons for low prescription rate. Care providers opinion for factors affecting adherence and utilization of IPT also depends on clients‟ believe for imaginary idea of prevention with a potentially toxic drug, pill burden, prescription only for one month and lack of trust when the supply is inconsistent after initiation for few months which is partly consistent with a systematic review of qualitative studies Patient choice in taking treatment is framed by the physiological and psychological impacts of the disease and also by the social and cultural structures in which the person is immersed(32).

Patient motivation and willingness, and the effect of incentives on treatment taking, have received some attention. However, it remains unclear whether the incentive, or the attention received by the patient, serves as the primary source of motivation(32). Caution should therefore be exercised when attributing adherence solely to „personal motivation “, because not only can important influences be ignored, but this factor is difficult to modify or even operationalize(32).
WHO suggests providing IPT as a core component of HIV preventive care should be the responsibility of national AIDS programs and HIV service providers(4) like the nurses opinion for a need to have support monitoring and evaluation.

8. Strength and limitations of the study

The strength of this study is it involved a relatively larger sample size than the other local studies, had included qualitative study method to explore and complement the quantitative study also in an intention to generate hypothesis for future study designs.

The study also tried to look for additional factors affecting adherence to IPT than other local studies regarding occurrence of side effects and availability of other comprehensive care and support.

There are also a number of limitations of this study since there is no a “gold standard” for assessment of adherence, we used self-reported adherence which might introduce recall bias.

The fact that it is a cross sectional study we cannot generate cause effect relationship between the dependent and independent variables.

The study is done in a single center where by diversity of population could have been missed for comparison, since there was no INH supply few months prior to data collection most respondents were eligible for the study at the end of one month which could mask the true adherence level if they were taking more than few months to completion at 6 months and it has a limited generalizability for other public health facilities.

9. Conclusion

The association of factors affecting adherence and utilization of INH among people living with HIV in yekatit 12 hospital has a better rate of adherence than other local and African studies and the reasons for poor adherence was strongly associated with occurrence of jaundice, skin rash and seizure.

The quantitative study findings were complemented by the qualitative study finding on possible other factors affecting adherence and utilization of IPT such as lack of appointment per demand, lack of training, busy clinic and non-sustainable drug supply.

All side effects reported to be related to use of INH may not necessarily affect adherence and utilization of IPT

10. Recommendation

Increase provider‟s knowledge on IPT through training and monitoring and evaluation

Availability of comprehensive care and support such as nutritional support and appointment per demand adequate time for counseling, follow up, sustainable drug supply, evaluation and treatment of side effects

Conducting program based operational research and research on introducing new tools into practice for future plan in line with the global plan to stop TB is highly desired.

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Annexes

Annex 1: Quantitative survey questionnaire English version

Part one

Information sheet

Addis Ababa University College of health sciences school of public health

Questionnaire on assessment of factors affecting adherence and utilization of isoniazid preventive therapy among HIV patients in yekatit 12 hospital

Greetings!

My name is _____ I am part of the research team from Addis Ababa University, College of health sciences, school of public Health. The aim of the research is to assess factors affecting adherence and utilization of isoniazid preventive therapy among HIV patients in yekatit 12 Hospital Addis Ababa. You are chosen randomly to participate in the study and your genuine responses will help to see the truth and find solutions. If you have any questions regarding the study you can contact the principal investigator by the following address.

Yitagesu Getachew

Mobile; 0913-54-41-63

Email; Yitsami@yahoo.com

Thank you very much

Part two

Consent form

Your participation in this study is having only few minutes of face to face interview and there is no need to put your name on the questionnaire, no individual response will be reported and it is highly confidential. You will not be denied of any service for refusal in participation. It is your full right to participate or refuse in the study, you also have the right to discontinue interview any time in between for any inconveniencies. But your honest participation will have a great contribution to make a difference in the quality of service, so please take a few minute to answer the questions we hope you will participate in the survey since your views are important. If there is anything that is not clear please don't hesitate to ask the facilitator for clarification.

At this time, do you want to ask me anything about the survey?

May I begin the interview now?

Yes_____ signature of participant _____

No_____ signature of participant _____

If the participant is illiterate:

Yes _____ Signature of third person _____

No _____ Signature of third person _____

Thank you very much

Signature of Interviewer _____ questionnaire number_____

Date of interview_____ signature of supervisor_____

Part three

	Baseline characteristics		
No	**Questions**	**Categories**	**code**
101	Sex	Male_____ Female_____	/----/
	In what month and year were you born?	____/_____	
102	How old were you at your last birthday?	_____	/----/
103	What is your current marital status?	Single Married Divorced Widowed Separated	/----/
104	Have you ever attended school?	Yes No	/----/
105	What is the highest level of school you attended?	_____	/----/
106	What is your religion?	Orthodox Muslim Protestant Catholic Other, please specify_____	/----/
107	What is your ethnicity?	_____	
108	What is your occupation?	_____	/----/
109	How much is your monthly expenditure?	_____ birr	/----/
110	How long it takes you to get to the clinic?	_____in minutes	/----/

Variables related to use of INH

No	Questions	Category	code
201	When were you started on INH?	___/___/___	/----/
202	Which one did you experience?	Vomiting Jaundice Numbness Seizure Skin rash None of them	/----/
203	When you had one or more of the above, did you continue taking INH?	Yes No	/----/
204	Are you taking ART?	Yes No	/----/
205	If yes to above question, what is the ART regimen?	First line regimen Second line regimen	/----/
206	How long have you been taking the above regimen?	_____	
207	Have you ever discontinued ART use more than one month?	Yes No	/----/
208	If yes to above question, why did you discontinue?	_____	
209	Are you taking medications other than INH and ART?	Yes No If yes, please specify_____	/----/
210	Have you ever been treated for tuberculosis?	Yes No	/----/
211	Do you use one of the following?	Khat Alcohol Cigarette No use	/----/
212	How do you see the frequency of INH (once daily)?	Poor Very good Satisfactory Excellent Good	/----/
213	How do you see the duration of INH (6 months)?	Poor Very good Satisfactory Excellent Good	/----/
214	What is Your Belief in efficacy of INH?	No belief Very strong Weak Excellent Strong	/----/
215		Poor Very good Satisfactory Excellent	/----/

	How is the level of your knowledge about INH?	Good	
216	How is your interaction with health care workers in ART clinic?	Poor Satisfactory Very good Good Excellent	/----/
217	How is the health care provider's knowledge, interpersonal skills and willingness to explain about INH?	Poor Very good Satisfactory Excellent Good	/----/
218	Do you regularly come on clinical appointments?	Yes No	/----/
219	Do you feel comfortable to take INH in front of others?	Yes No	
220	Do you get the following care and support services from the facility?	Nutritional support Regular peer counseling Appointment per your demand Treatment for other illnesses No extra care and support	/----/
221	How many tablets of INH were prescribed and how many of it you took for the following days?	Prescribed tablets ____ Taken_____ last 3 days _____ last 7 days _____ last 30 days	/----/
222	What is the reason for missing to take INH?	_____	

Annex 2: In depth interview guide English version

Similar information sheet and consent form will be used from the quantitative questionnaire.

Part one

The part of baseline characteristic from structured questionnaire for quantitative method will be used.

Part two

Section of interview for patients and peer counselors

1/ what do you know about tuberculosis?

2/ why INH is important for persons infected with HIV?

3/ what information did you get about INH before you are started?

4/ do you fear INH will harm your health?

5/ how are you taking the medication?

6/ what do you say about knowledge and communication skill of the health care Provider who started you on INH?

Section of interview for health care provider and focal person

Sex___ age___ profession_____ year of experience in HIV clinic_____

1/ what is your view about INH?

2/ how frequently you initiate an individual on INH?

3/ how is the utilization and what factors are affecting adherence of INH?

4/ what are the issues you want to emphasize on IPT program?

Annex 3: Quantitative survey questionnaire Amharic version

ክፍል አንድ

□ቅላላ መረጃ

በአዲስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌ□ □ሕብረተሰብ ጤና ት/ት ቤት በ የከቲት 12 ሆስፒተል በ ኤች አይ ቪ ቫይረስ የተጠቁ ህመምተኞችን የቲቢ መከላከያ አይ ኤን ኤች መድኀኒት አጠቃቀምን ተጽኖ የሚያደርጉ ምክንያቶችን ለማጥናት የተዘጋጀ መጠይቅ

ሰላም አኔ----------አባላለሁ በ አዲስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌጅ የሕብረተሰብ ጠና ት/ት ቤት የጥናት ቡድን አባል ነኝ፤ርሶ በዚህ ጥናት አንዲሳተፉ በአጋጣሚ ተመርጠዋል □ርሶ በጥናቱ መሳተፍ ያለውን አውነት ና መፍትሄ ለማግኘት በጣም ጠቃሚ ነው፤፤ ጥናቱን አስመልክቶ ማንኛውንም አይነት ጥያቄ መጠየቅ ከፈለጉ የጥናት ቡድን መሪውን በሚከተለው አድራሻ ማ□ኘት ይችላሉ፤፤

□ታዙ ቴታቸው

ሞባ□ል ስል□ 0913 54 41 63

ኢሜል yitsami@yahoo.com

አመሰግናለሁ

የሚስጢር አጠባበቅ ስምምነት

□ህ መ□□ቅ ጥቂት □ቂቃ ይወስዳል በዚህ መጠይቅ የርሶ ስም አይጻፍም መረጃውም ለሌላ ሰው ወይም ድርጅት አይሰጥም ያልገባዎትን ጥያቄ መጠየቅ ይችላሉ በማንኛውም ሰአት በፈለጉት ምክንያት ጥያቄውን ማቋረጥ ይችላሉ፤፤ ነገር ግን የርሶ ተሳትፎ ለጠና አሰጣጥ ጥራት ተጨማሪ ግብአት ከፍተኛ አስተዋጸ አለወ ስለሆነም በጥናቱ ተሳተኝ አንደሚሆኑ ተስፋ አለኝ፤፤

ጥያቄ አለዎት?

ወደ ጥያቄና መልስ ል□ባ ?

አዎ---------- የተሳታፊ ፊርማ_____

□ስም---------- የተሳታፊ ፊርማ _____

ተሳታፊው ማንበብና መጻፍ ካልቻሉ፤

አዎ_____ የምስክር ፊርማ _____

□ስም_____ የምስክር ፊርማ_____

አመሰግናለሁ

□□ጸቂ ኝርማ----------

□መ□□ቅ ቁ□ር----------

□ተቆ□□ሪ ኝርማ----------

ቀን----------

□አ ል ሶስት

□ዞ□ጸቂ□· አ□ቃላ□ □ማህበራዊአ ኮኖሚያዊ መረጃ መጠይቅ

ቁ□ር	□ጸቄ	አማራ□ መልስ	ኮት
101	□ታ	ወንድ_____ ሴት_____	/----/
	የትውልድ ወርና ዘመን ?	____/_____	
102	ባለፈው ልደቶ አድሜዎ ስንት ነበር ?	_____	/----/
103	ወቅተዊ የጋብቻ ሁኔተ ?	ያላገባ/ች ያገባ/ች የተፋተ/ች ባል/ሚስት የሞተበት ተለያይተው የሚኖሩ	/----/
104	ትምህርት ተምረዋል ?	አዎ □ስም	/----/
105	ከፍተኛው የትምርት ደረጃዎ ስንት ነው ?	_____	/----/
106	ሀይማኖትዎ ምንድን ነው ?	ኦርቶዶክስ ሙስሊም ፕረተስተንት ከቶሊክ ሌላ □ካለ□_____	/----/
107	ብሄረሰብ ?	_____	
108	ስራ ?	_____	/----/
109	የ አንድ ወር ወጪዎ ምን ያህል ነው ?	_____ ብር	/----/
110	ወደ ሆስፒተል ለመድረስ ምን ያህል ይፈጅቦተል ?	_____በ □ቂቃ	/----/

	□ አይ ኤን ኤች መድሀኒትን የተመለከተ መጠይቅ		
ቁ□ር	□ጸቁ	አማራ□ መልስ	ኮት
201	መቼ ነው አይ ኤን ኤች የጀመሩት ?	___/___/___	/----/
202	ከሚከተለወ ⸗ያጋጠሞት ችግር ?	ማስመለስ የ አይን ቢጫ መሆን መደንዘዝ □ሚ□ል ህመም □ቆ□ ሽአታ ችግር አላጋጠመኝም	/----/
203	ከላይ የተጠቀሡት ችግሮች አያሉ አይ ኤን ኤች መ□ሰት ቀ□ሉ ?	አዎ □ለም	/----/
204	የ ጸረ ኤች አይ ቪ መድሀኒት ይወስዳሉ ?	አዎ □ለም	/----/
205	ከላይ ለተጠየቀወ ⸗□ጸቁ መልሱ አዎ ከሆነ አይነቱ ምንድን ነው ?	□መ□መሪጸ □ረጽ ሁለተኛ □ረጽ	/----/
206	ከላይ የሚወስዱትን መድሀኒት ለምን ያህል ጊ□ አየወሰዱነው ?	_____	
207	የ ጸረ ኤች አይ ቪ መድሀኒት ከ አንድ ወር በላይ አቋርጠው ያውቃሉ ?	አዎ □ለም	/----/
208	ከላይ ለተጠየቀወ ⸗□ጸቁ መልሱ አዎ ከሆነ ለምን አቋረጡ ?	_____	
209	ከ ጸረ ኤች አይ ቪ መድሀኒት ና አይ ኤን ኤች በተጨማሪ ሌላ መድሀኒት ይወስዳሉ ?	አዎ □ለም አዎ ከሆነ ይገለጽ_____	/----/
210	ለ ቲቢ ተ□መ□ ጸ□ቃሉ ?	አዎ □ለም	/----/
211	ከሚከተሉት የሚጠቀሙት የቱን ነው ?	ጫት አልኮል መጠጥ ሲ.ፉ.ራ ምንም አልጠቀምም	/----/
212	አይ ኤን ኤች በቀን አንድ መውሰት ክንዴት ነው ?	□ሩ አይደለም፤በ□ም □ሩ ነው፤ ምንም አይል፤ክ□□ በ□ም □ሩ ነው፤ □ሩ ነው፤	/----/
213	አይ ኤን ኤች ለ ስድስት ወር መውሰድ አንዴት ነው ?	□ሩ አይደለምበጣም ጥሩ ነው፤ ምንም አይል፤ክ□□ በ□ም □ሩ ነው፤ □ሩ ነወ፤	/----/
214	በ አይ ኤን ኤች ላይ ያለዎት ዕምነት አንዴት ነው ?	□ሩ አይደለም፤በጣም ጥሩ ነው፤ ምንም አይል፤ክ□□ በ□ም □ሩ ነው፤	/----/

		□ሩ ነው።	

215	ስለ አይ ኤን ኤች ያለዎት ዕ□ቀት ዕንዴት ነው ?	□ሩ አይደለም።በጣም ጥሩ ነው። ምንም አይል።ክ□□ በ□ም □ሩ ነው። □ሩ ነው።	/----/
216	በ ኤ አር ቲ ክፍል ከሚገኙ □□ና ባለሙያዎች ጋር ያለዎት መግባባት ዕንዴት ነው ?	□ሩ አይደለም።በጣም ጥሩ ነው። ምንም አይል።ክ□□ በ□ም □ሩ ነው። □ሩ ነው።	/----/
217	የጤና ባለሙጸ□/□ ዕውቀት።የመግባባት ክህሎት ና ስለ አይ ኤን ኤች ለማብራራት ያለው/ላትፈቃደኝነት ዕንዴት ነው ?	□ሩ አይደለም።በጣም ጥሩ ነው። ምንም አይል።ዕጅግ በጣም ጥሩ ነው። □ሩ ነው።	/----/
218	ዘወትር በቀጠሮ ዕለት ክትትል ያደር.ጋሉ ?	አዎ □ለም	/----/
219	በሌሎች ሰዎች ፊት አይ ኤን ኤች ቢወስዱ □ስ □ሎታል ?	አዎ □ለም	
220	በሆስ□ተሉ □ስ□ □ሚጸዮት የጤና ድጋፍና ዕንክብከቤ ?	□ም□ብ ትፉአ የአቻ ለአቻ ምክር አገልግሎት በተመችዎ ጊዜ ቀጠሮ መውሰድ ለተጨማሪ ህመም ህክምና ምንም ተፊ ማሪ ትፉአ □ለም	/----/
221	ምን ያህል የ አይ ኤን ኤች ኪኒን ተዘዘሎት ? ከተዘዘሎት ኪኒን መከከል ምን ያህሉን ለሚከተሉት ቀናት ወሰዱ ?	የተዘዘሎት ኪኒን ____ የወሰዱት ኪኒን_____ ላለፉት 3 ቀናት _____ ላለፉት 7ቀናት _____ ላለፉት 30ቀናት	/----/
222	የ አይ ኤን ኤች ኪኒን ሳይወስዱ የቀሩበት ምክንያት ምንድን ነው ?	----------	

Annex 4: In depth interview guide Amharic version

ተመመሳሳይ የጠቅላላ መረጃ ና የሚስማጢር አ□ባበቅ □ርም ከቀደመው መ□□ቅ □□ሰ□ል

ክፍል አንድ

አጠቃላይ የማሕበራዊ ኢኮኖሚያዊ መጠይቅ ከቀደመው መ□□ቅ □□ሰ□ል

ክፍል ሁለት

ለህሙማን/አቻ ለአቻ የምክር አገልግሎት ሰጪዎች የቀረበ መጠይቅ

1/ስለ ቲቢ በሽተ ምን ያውቃሉ ?

2/ አይ ኤን ኤች ለ ኤች አይ ቪ ተማሚዎች ምን ይጠቅማል ?

3/ አይ ኤን ኤች ከመጀመርዎት በፊት ምን አይነት መረጃ አግኝተዋል ?

4/ አይ ኤን ኤች ለጠናዎት አደጋ ያለው □መስል- ተል ?

5/ አይ ኤን ኤች የሚወስዱት ዕንዴት ነው ?

6/ የአይ ኤን ኤች መድሀኒት ሲጀምሩ □□.ና ባለሙያው/ዋ የዕውቀት፤የመግባባት ና የማስረዳት ደረጃ ዕንዴት ነበር ? ምን አስተያየት አለዎት ?

ለጤና ባለሙጸ □ቀረበ መ□□ቅ

□ታ..... ክትሜ..... በ ኤች አይ ቪ ክሊኒ□ □ስራ ልምት.....

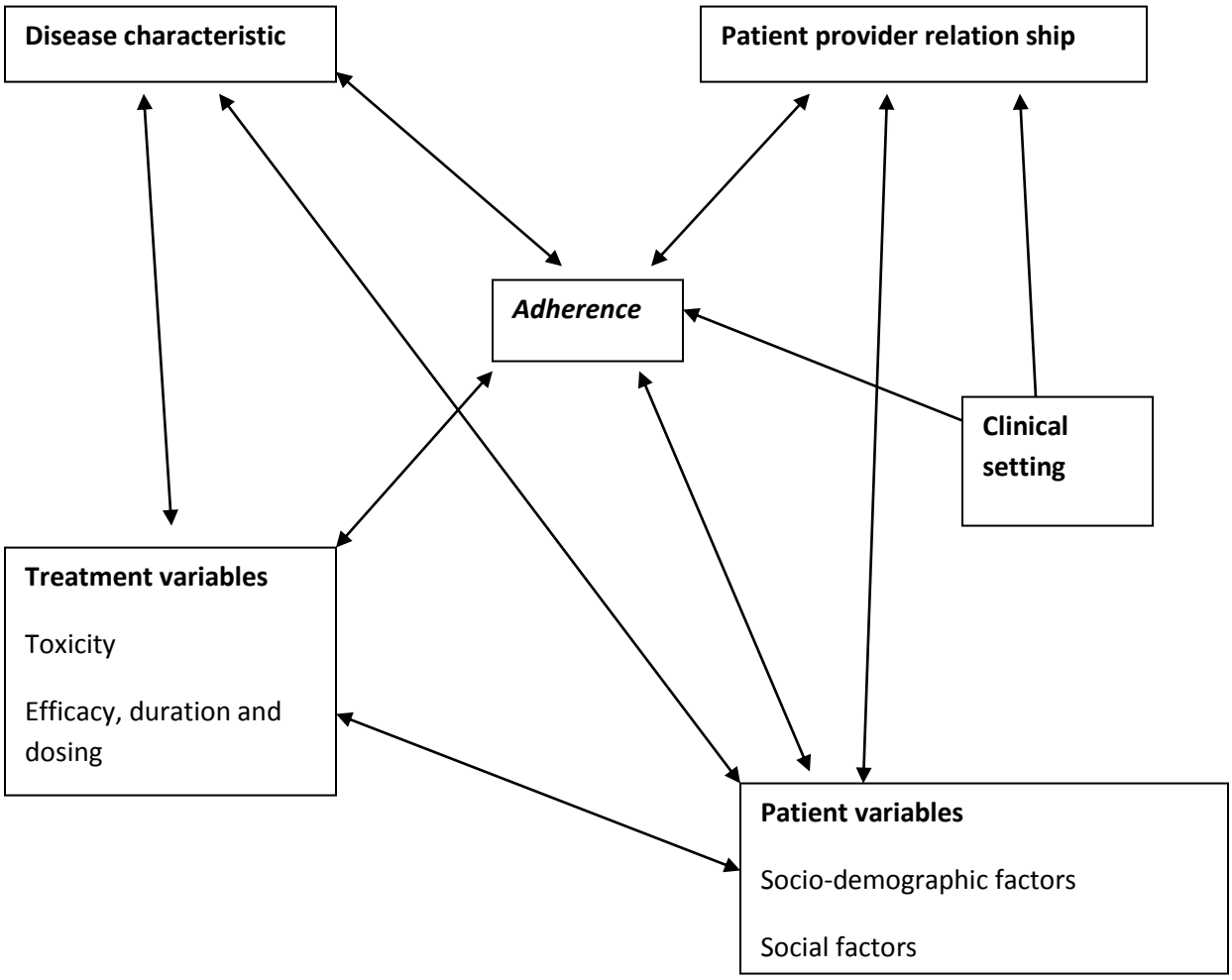
1/ ስለ አይ ኤን ኤች ያለዎት አስተያየት ?

2/ ምን ያህል ጊዘ ለህሙማን አይ ኤን ኤች ጸስ□ምራሉ ?

3/ አይ ኤን ኤች ለመጀመር፤ሳያቀሩጠ ለመውሰድ ተጽዕኖ የሚያደርጉ ነገሮች ምንድን ናቸው ?

4/ በ አይ ኤን ኤች ፕሮግራም ዙሪያ አጽንዎት መስጠት የሚፈልጉት ጉዳይ ?

Annex 5: Conceptual frame work for determinants of adherence



DECLARATION

I the undersigned, declare that this is my original work, has never been presented in this or any other university and that all the source materials used for the thesis has been duly acknowledged.

Name _____

Signature _____

Place _____

Date of submission _____

This thesis has been submitted for examination with my approval as a university advisor.

Name Dr Wubegzier Mekonnen

Signature _____

Date _____