The impact of Isoniazid Preventive Therapy (IPT) on Tuberculosis Incidence among HIV infected patients in Addis Ababa, Ethiopia

by

ANTENEH HABTEMARIAM SADE

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SUPERVISOR: DR T NEGUSSIE

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DECLARATION

I declare that **the impact of isoniazid preventive therapy (IPT) on tuberculosis incidence among HIV infected patients in Addis Ababa, Ethiopia** is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references.

_____   _____Oct 27 2012_____

SIGNATURE   **DATE**

(MR AH SADE)

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THE IMPACT OF ISONIAZID PREVENTIVE THERAPY (IPT) ON TUBERCULOSIS INCIDENCE AMONG HIV INFECTED PATIENTS IN ADDIS ABABA, ETHIOPIA

STUDENT NUMBER:　　　　**46457259**
STUDENT:　　　　　　**AH SADE**
DEGREE:　　　　　　　**MASTER OF PUBLIC HEALTH**
DEPARTMENT:　　　　　**HEALTH STUDIES, UNIVERSITY OF SOUTH AFRICA**
SUPERVISOR:　　　　　**NEGUSSIETAFFA (MD, PHD)**

ABSTRACT

Background: IPT is an effective, safe and feasible disease prevention scheme that should be administered for all PLHIV living in areas with high latent TB prevalence.

Objective: To assess the impact of isoniazid in the incidence of tuberculosis among HIV infected individuals in Addis Ababa.

Methods: A case control study design was undertaken among 489 HIV and TB infected patients in Addis Ababa from January 2008 to December 2010.

Results: Tuberculosis incidence rate among those who developed TB after completing 6-9 month isoniazid preventative therapy was17.14 PYO compared to 10.28 PYO among those who were not. Isonizide reduced the chance of developing tuberculosis among HIV infected patients (OR= 0.072; 95% CI 0.044, 0.12). Age (AOR= 0.14; 95% CI 0.03, 0.97) and sex (AOR= 1.86; 95% CI 1.02, 2.23) of the patient, CD4 count at HIV diagnosis (AOR= 0.21; 95% CI 0.13, 0.31), clinical stage of HIV illness (AOR= 1.22; 95% CI 1.09, 1.84) and past tuberculosis history (AOR = 1.97; 95% CI 1.24, 3.67) were major factors associated with tuberculosis incidence.

Conclusions: INH prophylaxis was associated with lower incidence of tuberculosis among PLHIV.

KEY CONCEPTS
IPT, Tuberculosis, Incidence, HIV, Addis Ababa

ABBREVIATIONS

AACCHB	Addis Ababa City Council Health Bureau
AIDS	Acquired Immune Deficiency Syndrome
ART	Anti Retroviral Therapy
ARV	Anti Retroviral
AU	Africa Union
CD4	Cytokine D cells
CI	Confidence Interval
EFHAPCO	Ethiopia Federal HIV/AIDS Prevention and Control Office
HIV	Human Immunodeficiency Virus
ICF	Intensified Case Finding
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
MDR-TB	Multi Drug Resistant Tuberculosis
EFMOH	Ethiopian Federal Ministry of Health
HATiP	HIV & AIDS Treatment in Practice
OI	Opportunistic Infection
OR	Odds Ratio
PLHIV	People Living with HIV
PYO	Person Years of Observation
PPD	Purified Protein Derivates

SPSS	Statistical Package for Social Sciences
TB	Tuberculosis
TST	Tuberculin Skin Test
WHO	World Health Organization

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CHAPTER 1

ORIENTATION TO THE STUDY

1.1. INTRODUCTION

Tuberculosis (TB) is the foremost opportunistic infection associated with Human Immunodeficiency Virus (HIV) infection causing a number of deaths (Balcells, Thomas, Godfrey-Faussett, and Grant 2006:744). TB and HIV have remained critical public health problems for the last three decades. HIV and TB have a synergic effect. HIV suppresses immune system and maximizes the risk of tuberculosis infection among people living with HIV (PLHIVs). Similarly, TB increases HIV replication which further causes increased viral load (Balcells et al 2006:744; Chakaya, Getahun, Granich and Havlir 2008:1). As a result, tuberculosis is the leading cause of morbidity and mortality among PLHVs (Szakacs, Wilson, Cameron, Clark, Kocheleff, Muller and McCarthy 2006:1-2; Mosimaneotsile, Mathoma, Chengeta, Nyirenda, Agizew, Tedla, Motsamai, Kilmarx, Wells and Samandari 2010:71; Eldred, Churchyard, Durovni, Godfrey-Faussett, Grant, Getahun and Chaisson 2010: S1; Mindachew, Deribew, Tessema and Biadgilign 2010:1).

Anti-retro viral therapy (ART) has been found to reduce the risk of tuberculosis infection by 64% (Golub et al 2009: 634). An observational cohort study done by Lawn and colleagues (2010:490) showed that using ART alone is associated with 67% reduction in the incidence of tuberculosis. Furthermore Lawn and colleagues described the reduction in the incidence of tuberculosis to be proportionately similar both in developed and developing countries. A study in Rio, Brazil, also found that both Isoniazid Preventive Therapy (IPT) and ART were effective in reducing tuberculosis infection independently (Golub et al 2007:1445). The effect of ART in reducing TB is further supported by Mosimaneotsile et al (2010:71) showing ART by itself reduces TB occurrence by 80% among PLHIVs. A study by Lawn (2010:2) also confirmed that ART reduces the risk of acquiring TB by more than 66% in HIV infected individuals.

IPT reduces the reactivation of latent tuberculosis infection and reduces the risk of acquiring TB by 70-90% among HIV co-infected individuals (Cohen, Lipsitch, Walensky and Murray 2006: 7042; Golub et al 2007:1441). Individuals who are not enrolled on IPT or ART are considerably at higher risk of having new tuberculosis infection and reactivation of latent tuberculosis (Akolo, Adetifa, Shepperd and Volmink 2010:2). World Health Organization (WHO) recommends use of ART and IPT combination to reduce the burden of TB among HIV infected patients (WHO 2010a:5).

In spite of its effect and evidence-based WHO recommendations, use of IPT and its integration with HIV programs is very slow in most countries as a result of fearing occurrence of adverse effects, INH resistance and lack of knowledge about IPT (Pontali, Pasticci, Matteelli, Baldlli and Migliori 2011: 1258; Padmapriyadarsini et al 2011: 854) .

1.2. BACKGROUND TO THE RESEARCH PROBLEM

Tuberculosis is one of the major opportunistic infections (OI) contributing to high morbidity and mortality among HIV sero-positive persons. The HIV pandemic has resulted in the rise of tuberculosis occurrence affecting the most economically productive age group, especially in sub-Saharan Africa countries. The condition is further fuelled by poverty, inadequate case detection, diagnosis and treatment, poorly financed health systems and the deepening impact of HIV pandemic (WHO 2007:11).

The WHO, Global Tuberculosis Control Report in 2010 showed that 9.4 million new TB cases were reported worldwide including the 1.1 million (11.7%) HIV co-infected cases. Eighty-five percent of these cases were reported in Asia and Africa: 55% and 30% respectively (WHO 2010b:5-7). The same report demonstrated that the mortality among 380,000 HIV co-infected individuals worldwide, were attributable to tuberculosis. According to Golub JE et al (2007:1446), the risk of tuberculosis recurrence in an HIV infected individual increases by 19 times due to re-infection or relapse.

According to the above report, a total of 1.6 million TB patients with known HIV status were reported, of which 47.8% were from Africa. Thirty seven percent of HIV positive persons were on ART, whilst, only 80,000 peoples were on IPT. This accounts for less than one percent of the estimated HIV co-infected persons in need of TB preventive therapy (WHO 2010b:16-18).

Out of all Africa countries, South Africa was more effective in IPT program delivery and implementation whereby in 2009 alone the country reported 23,583 HIV infected persons who have received prophylaxis for TB, and Namibia and Botswana sited in second and third (Getahun, a et al 2010:59). The WHO (2011:138-139) report indicated that South Africa took the lead in reaching 124, 049 HIV infected individuals with IPT, which accounts 79.5 percent of African coverage (WHO 2011: 138-139).

There is growing evidence on effectiveness of ART in reducing HIV related mortality (Golub et al 2007:1442; Patel et al 2008: 2; Smart 2009: 2). However, ART alone is not sufficient in controlling HIV related TB occurrence. The study by Jonathan and colleagues (2009: 632) found that treating PLHIVs with a combination of ART and IPT is more effective in reducing TB rate than using ART and IPT separately.

A prospective cohort study conducted to assess the effect of IPT, ART or both in South Africa revealed that ART only reduced the risk of TB by 64%, whereas, the blended IPT and ART had 89% impact on reduction of TB hazard (Golub et al 2009:635). Considering the convergence of TB and HIV, WHO recommended countries to combine TB and HIV collaborative activities together and acclimatize the combined 3'I' measure including: Intensive TB case finding (ICF), TB Infection control in health care settings and ART, and Isoniazid/INH preventive therapy (WHO 2010c:65; WHO 2011:1; Pontororing et al 2010:362).

IPT is an effective, safe and feasible scheme that should be administered for all PLHIV's living in areas with high latent TB prevalence (Granich et al 2010:217; Naidoo, Naidoo, Padayatchi and Karim 2011:3). TB preventive therapy has to be administered for 6 months to trim down the burden of TB on HIV infected individuals from 33 to 67% (WHO 2010a:5).

Studies in HIV infected individuals and other communities who took IPT prior to ART showed the effectiveness of INH to prevent tuberculosis (Golub et al 2009:632; 635). Clinical trials conducted to measure progress in implementing preventive measures implied that IPT use considerably reduced the incidence of TB among HIV infected persons (Date et al 2010: 253). Supporting this finding, Granich and colleagues found a significant reduction of TB incidence among HIV infected person receiving IPT (Granich et al 2010: 218). A research conducted in Brazil showed that incidence of TB among TB/HIV co-infected person who received IPT only was 1.27 per 100 Person years of Observation/PYO (Golub et al 2007:1444).

Though IPT is effective in reducing TB incidence, the duration of treatment is not well studied. A recent study from Botswana found that offering IPT continuously for 36 months is much more effective in preventing TB than short course therapy for 6 month. The study further showed that, those who received 6 months of IPT had 2.56 per 100 PYO TB risk. On the other hand, those who received the 36 month TB preventive therapy had a risk of 0.19 per 100 PYO yielding 0.08 hazard ratios (Samandari et al 2010: 1588 –1598). Samandari and his colleagues (2010:2) reported that there was a 92% decrease in TB incidence among those who continuously took INH preventive therapy.

Botswana is the only country in Africa which has a nationwide IPT program. There are controversies around its efficacy in the era of widespread ARV (Anti retro viral) therapy. The above study by Samandari et al (2010: 1596) clarified this controversy such that early ART can actually do more TB prevention than IPT provision. The current recommendation for IPT is to give IPT to purified protein derivative (PPD) positive TB patients only. Botswana is revising its national guideline to fit into this recommendation. But only few countries in sub-Saharan Africa have the necessary financial, human and infrastructural resource capacity to adopt a policy of early ART initiation for all PLHV in the near future.

In spite of the good evidence that IPT reduces incidence of TB among persons infected with HIV, access to and uptake of preventive therapy is still low (Granich, Akolo,

Gunneberg, Getahun, Williams and Williams 2010:S217; Lester, Hamilton, Charalambous, Dwadwa, Chandler, Churchyard, and Grant 2010: 45-48; Golub et al 2007:1442). The low accessibility and uptake of IPT use results from lack of standard TB screening algorithm and guidelines, shortage of IPT supply and challenges regarding competency and attitude of health care providers towards IPT (Getahun et al 2010; Lester et al 2010).

In addition, there are also widespread concerns around duration of IPT protection, INH drug toxicity/resistance and adherence to prophylaxis and inability to rule out active TB during the screening procedures (Naidoo et al 2011:2; EFMOH 2007c:19; Eldred, Churchyard, Durovni, Godfrey-Faussett, Grant, Getahun and Chaisson 2010 1-3; Golub et al 2007:1-2). These factors may affect both the perception and attitude of the policy makers, health care providers and clients towards INH prophylaxis and its implementation. A critical review of health system, political, client related and other barriers should be carried out in-order to develop nation specific strategies that are essential to foster implementation of IPT program.

Ethiopia is one of the low income countries in the horn of Africa with an area of 1.1 million square kilo meters and the population is estimated at 74 million. The country has one of the fastest growth rates at, 2.6% per year and having a total population of 73.8 million (Federal democratic republic of Ethiopia: Population census Commission 2008:8-1; EFMOH 2009:2). Nearly half of the population is female and life expectancy is relatively low at 48 due to high prevalence of HIV and other co-infections (Ethiopia Federal HIV/AIDS Prevention and Control Office/FEHAPCO 2010:6).

Ethiopia is ranked 7th among the 22 listed high burden countries. The incidence of TB in Ethiopia is estimated at 579 per 100,000 for all forms of TB and 163 per 100,000 for smear positive TB. TB accounts for 7% of deaths (EFMOH 2009:3). The sero-prevalence rate of HIV among adult TB patients is estimated from 20-50% (MOH 2007a:7).

The Government of Ethiopia introduced ART in 2003 and free ART program was started in 2003 (Kloos, Assefa, Adugna, Mulatu and HaileMariam 2007:45; MOH 2007a: v; MOH 2007b:1).

According to the 2010 country progress report, 511 health facilities were engaged in delivering the service and 53% of eligible PLHV were on treatment (EFHAPCO 2010:53). The same report showed that out of the 24,112 HIV-positive people referred for TB screening, 2,403 (10%) received IPT.

Ministry of health reported 12,926 new cases of tuberculosis in Addis Ababa, the capital city of Ethiopia, including 2,723 new smear positive pulmonary tuberculosis cases. The number of all forms of tuberculosis was 13, 483 (EFMOH 2008:33). There are nine public hospitals serving people infected with HIV and co-infected persons in Addis Ababa.

Similarly, Addis Ababa health bureau (AACCHB) 2010 report showed that the total number of tuberculosis cases receiving IPT in hospitals was 1349. Of the nine hospitals, Zewditu and Yekatit 12 hospitals are pioneer on starting IPT service by 2008 and eighty percent of cases were receiving IPT from these hospitals. They had 613 and 365 cases respectively (AACCHB 2010:13).

The Ethiopian TB/HIV guideline incorporates IPT as the single most important HIV preventive strategy. The initiation of IPT is based on laboratory findings, WHO clinical staging and presence or absence of contraindications. HIV infected individuals without confirmed active TB by clinical or laboratory method could be eligible for IPT. Due to high prevalence of TB in Ethiopia, all HIV–infected people with no signs or symptoms of active TB and/or negative laboratory (sputum smear or culture) result are eligible for TB preventive therapy. But, sero-positive individuals who are categorized in either WHO staging III or IV or symptomatic patients will be excluded from receiving IPT. Cognizant to this, those clients with active tuberculosis, abnormal chest X-ray, active hepatitis, known high daily alcohol consumption, prior allergy or intolerance to INH and history of close contact with Multi Drug Resistant–tuberculosis (MDR-TB) patient are not entitled to take IPT (EFMOH 2007c:18).

ART program is implemented across the country; however, the coverage of TB/HIV integration in health facilities is not optimal enough to tackle the burden of tuberculosis (EFMOH 2007b:2). Besides, the impact of IPT on reducing tuberculosis incidence among

HIV infected individuals is not well documented. Hence; this research intends to assess the impact of IPT on TB incidence among HIV infected persons in public hospitals of Addis Ababa.

1.3. RESEARCH PROBLEM

WHO recommends that IPT provision for HIV infected persons, particularly in areas where the HIV prevalence among TB patients is 5% or more (EFMOH 2007c:17). The prevalence of HIV among TB patients in Ethiopia is estimated to reach around 40-70% (Deribew, Tesfaye, Hailmichael, Negussu, Daba, Wogi, Belachew, Apers and Colebunders 2009:105; Datiko, Yassin, Chekol, Kabeto and Lindtjørn 2008:1).

A cohort study conducted in Arba-Minch Hospital, South Ethiopia, showed a TB incidence rate of 9.9 per 100 person-years of observation (PYO) which is twice more than a research finding from factory working PLHIVs in Ethiopia (Jerene 2007:43). The same study showed that PLHIVs on pre ART care had TB incidence rate of 11.1/100 PYO compared to those on ART (3.7/100 PYO). Among PLHIVs started ART, the incidence of TB decreases from first to fifth year of treatment (Jerene, Naess, and Lindtjorn 2006:3; Jerene et al 2007:45).

INH preventive therapy is cost effective, safe and feasible drug of choice to reduce the incidence of TB among HIV infected persons especially in resource limited settings (Granich et al 2010:217; Naidoo et al 2011:5; WHO 2011:16). However, several challenges associated with its implementation limit the benefit of this public health strategy in Ethiopia. These challenges are rooted in the weakness in the country's health system, societal beliefs and norms and patient knowledge, attitude and behaviour. Health resources and services are not sufficiently available and their distribution is not equitable. If available, the quality of service delivery is generally not optimal. There is a widespread misconception on INH resistance and side effects both among health workers and patients (EFMOH 2007c:19).

The knowledge about IPT effectiveness in reducing TB incidence among HIV infected persons might help in the scale up of the service. However, public health importance of INH Preventive Therapy in preventing TB occurrence among PLHIV is not well studied. The main focus of this study is to assess the helpfulness of IPT in reducing the rate of TB among PLHIV in Ethiopian context.

1.4. PURPOSE OF THE STUDY

1.4.1. Research purpose

The main purpose of this study is to assess the impact of INH preventive therapy on the incidence of tuberculosis among TB and HIV co-infected individuals in Zewditu and Yekatit 12 hospitals in Addis Ababa, Ethiopia

1.4.2. Research objectives

The specific objectives of this research were

- To compare the incidence of TB among HIV infected clients who received IPT and those who did not
- To determine the socio-demographic and behavioural factors associated with TB incidence among HIV infected patients
- To compare HIV disease related factors associated with TB infection among those who received IPT and those who did not

1.5.   SIGNIFICANCE OF THE STUDY

The findings of this study is to contribute to the existing knowledge of IPT effectiveness by comparing the incidence of TB among HIV infected persons who received INH prophylaxis and those who don't in Ethiopian context. It would also provide information on IPT program implementation and its challenges for health planners and managers.

1.6. DEFINITIONS OF TERMS

For the purpose of this specific study, the following terminologies were used.

- **Active Tuberculosis:** TB that has been confirmed by clinical and positive sputum smear or chest x-ray result suggestive of TB.
- **Cohort study:** is type of study that begins with a group of peoples who are free of disease and similar exposure status are followed for a certain period of time.
- **Defaulter:** A patient whose INH Preventive Therapy was interrupted for 2 consecutive months or more.
- **Epidemiology:** is the study of the frequency, distribution and determinates of health-related conditions and events in a specified populations, and the application of this study to the control of health problems.

- **Isoniazid preventative therapy (IPT) completed:** An HIV infected person who took Isoniazid (INH) for a course of six months without interruption with a maximum dose of 400mg/day aiming to prevent development of tuberculosis.
- **Prospective Cohort study:** is a type of cohort that starts the study with the identification of the population and the exposure status and follows them for the development of the outcome factor.

1.7. LIMITATIONS

The study is retrospective analysis of patient records. Firstly, the research will utilize secondary data abstracted from TB/HIV treatment forms, which may be incomplete. Secondly, the study will include TB/HIV co-infected individuals from selected public facilities, which may not include patients managed in private sector. Thirdly, this data is most likely to be limited to patients residing in Addis Ababa and its environs who cannot represent other patients from the rest of the country. These factors reasons may reduce the validity and generalize-ability of this study.

1.8.   OUTLINE OF THE STUDY

Chapter 1 describes the background to the research problem and the research problem, purpose and significance of the study, and limitations of the study.

Chapter 2 covers the literature review.

Chapter 3 describes the research design and methodology used.

Chapter 4 presents the data analysis and interpretation of findings including discussion

Chapter 5 concludes the study findings, discusses its limitations, and makes recommendations for practice.

1.9. CONCLUSION

Tuberculosis is the leading opportunistic infection associated with HIV infection. INH preventive therapy is effective and significantly reduces the occurrence of tuberculosis infection among HIV infected individuals. The helpfulness of IPT in reducing the rate of TB among PLHIV in Ethiopian context not well studied in Ethiopia. This chapter briefly described the background of the problem; and purpose, objectives and significance of the study and definition of terms. The researcher described the ethical considerations upheld and defined key terms.

Chapter 2 covers the literature review conducted for this study.

CHAPTER 2

LITERATURE REVIEW

2.1. INTRODUCTION

This chapter discusses the literature review on TB and HIV co-infection, including the background and history, the description, treatment and prevention of the disease which can be added to the knowledge, awareness and practices regarding TB and the programmes related to TB control.

Researchers carry out a literature review to understand and extend their knowledge of the phenomenon under study. According to Polit and Beck (2007:88- 89) literature review is intended to understand the nature and meaning of the problem under study clearly. Cognizant to this, literature review assisted the researcher in exploring the knowledge and findings regarding TB and HIV co-infection, IPT and the impact of INH preventive therapy in reducing tuberculosis incidence in an to attempt to minimize the knowledge gap in this area of public health in Ethiopia

Generally, the purpose of this literature review was to:

- Ensure that previous studies are not duplicated.
- Describe recent research developments on the subject.
- Find out the most widely accepted empirical findings in the field of study.
- Identify the available study instruments that have proven high validity and reliability.

2.2. TUBERCULOSIS

2.2.1. Global burden of Tuberculosis

Tuberculosis is a contagious airborne disease caused by *Mycobacterium tuberculosis* bacteria and transmitted when individuals with infectious TB come into in contact with healthy individuals at different settings (WHO 2010a: 6; Roeger, Feng and Castillo-Chavez 2009: 815-837; Halima 2011:1). Both HIV infected and non-infected individuals can acquire Tuberculosis, even though there is a difference in incidence. Tuberculosis (TB) is the leading opportunistic infection associated with Human Immunodeficiency Virus (HIV) infection causing a number of deaths (Balcells et al 2006:744). Specially, the burden of TB is common in people living with HIV in developing countries (Szakacs, Wilson, Cameron, Clark, Kocheleff, Muller and McCarthy 2006: 1). It is estimated that more than 2 billion people have latent TB infection worldwide, which almost accounts for 32% of the world population (WHO 2008:293; Roger et al 2009: 816).

In 2010, worldwide, there were an estimated 12 million prevalent TB cases, which is comparable to 178 cases per 100,000 populations (WHO 2011b: 5-7; 9-13). According to WHO inference, in 2010, there were 8.8 million new TB cases globally, which equates to 128 cases per 100,000 populations. TB incidence is decaling from 2004, 142 cases per 100,000 to 137 in 2009 and 128 new cases per 100,000 populations in 2010. Though there is a decrease in TB incidence, tuberculosis is still among the top three greatest causes of death among the population (WHO 2011b: 5-7; 9-13).

Despite the fact that TB is a curable disease, an estimated mortality of 1.7 million in 2009 and 1.45 million, occurred in 2010, showing a remarkable decline (Mohammed 2011:1). Out of these 1.45 million deaths, 1.1 million TB deaths were among HIV uninfected patients and 0.35 million (24.14%) deaths were HIV infected patients. The overall death rate among HIV infected and HIV uninfected TB patients also shows a decline from 26 deaths per 100,000 populations in 2009 to 15 deaths per 100,000 populations in 2010. (WHO 2011b:5-7; 9-13).

2.2.2. Burden of tuberculosis in Africa

Tuberculosis is the major cause of AIDS allied mortality among people living with HIV, accounting for 26% of all deaths and 99% of these deaths occur in developing countries. Africa a home for not more than 11% of the world population shares one third of global tuberculosis burden (Africa Union /AU 2006:1-3). Developing countries, where ninety five percent of new TB cases and ninety nine percent of death occur, are predominantly affected region (Mohammed 2011:1). .

Tuberculosis is the major burden in developing countries, especially in sub-Saharan Africa. More than two-third (34) countries have at least 300 cases per 100,000 population TB notification rates which is more than 20 times (less than 15 cases per 100, 000 population) higher than the developed world (AU 2006:2). The World Health Organization Global Tuberculosis report indicated that, of the estimated 8.8 million incident cases in 2010, 2.29 million (26%), were in Africa. The number of prevalent cases in the same reporting period was 2.5 million and mortality was 30 cases per 100, 000 populations (WHO 2011b:9-13).

According to Moore and colleagues (2007:713-719), TB accounts for up to 11% of AIDS related death worldwide and case fatality rate for TB among HIV infected patients are extremely high reaching up to 40% in sub-Saharan African countries. Besides, the rates of recurrence after the completion of treatment is up to 20 per 100 person years in sub Saharan Africa (Crampin, Mwaungulua, Mwaungulu, Mwafulirwa, Munthali, Floyd, Fine and Glynn 2010: 417).

2.2.3. Burden of TB in Ethiopia

Ethiopia is among the countries hardly affected by tuberculosis. The global WHO report estimated 0.3 million incident TB cases and 54,000 TB related mortality in Ethiopia in 2009 (WHO 2010b:5). The Ethiopian Federal Ministry of Health estimates 579 per 100,000 population occurrence of all forms of TB in the country annually (163 per 100,000 for smear positive TB) and TB accounts for 7% of deaths (EFMOH 2009:3).

The recently released Global TB Control Report (WHO 2011: 9-13) showed that the current TB prevalence rate in Ethiopia is estimated at 394 cases per 100, 000 population, more than 46% lower from the national estimate in 2009, whereas, the incidence rate was 262 cases per 100, 000 population. The same report showed a relatively higher level of death related to TB in Ethiopia which accounts 35 cases per 100, 000 populations

2.3. TB/HIV CO-INFECTION

2.3.1. TB/HIV interaction

HIV associated TB poses the majority of disease burden worldwide in general and in resource-limited settings specifically in particular (Padmapriyadarsini et al 2011:850; Pawlowski, Jansson, Sköld, Rottenberg and Källenius 2012: 1; WHO 2012: 8). Tuberculosis and HIV have synergistic biological outcome and profound effect on the immune system. The co-existence of these diseases compromises the immune system. TB is the commonest opportunistic infection occurring among immuno-compromised individuals including HIV and AIDS (Padmapriyadarsini et al 2011:850). The risk of developing tuberculosis among immuno-compromised individuals is higher than their immuno-competent counterparts. People living with HIV have 21-34 times more risk of developing TB than those without HIV infection (Pawlowski et al. 2012: 1-3). Individuals who are co-infected with HIV have 20-50% more risk of developing active form of tuberculosis than HIV negative individuals. The co-infected people are at a greater risk of dying due to late diagnosis and treatment. According to World Health Organization, 90% HIV individuals who are untreated will die within months of co-infection (Nieburg, Ramachandran and Hofler 2008: 2).

2.3.2. Epidemiology

Gao and colleague (2010:1) reported that stated that more than one-third of the 33.3 million people living with HIV (PLHIV) worldwide in 2007 were co-infected with TB approximately, and close to 80% of the live in sub-Saharan Africa.

According to World Health Organization report (2010:7), the HIV-prevalence among TB incident cases is 12% globally. The least co-infection rate is reported from the eastern Mediterranean region which is 1.6% and 37% reported as the highest. A recent hospital based retrospective cross-sectional analyses study in Dar es Salaam, Tanzania showed that more than 90% of TB patients were also co-infected with HIV. Contrary to this, a study done in mainland China showed that only 0.9% of HIV sero-prevalence among TB patients (Geo et al 2010:2).

In the case of Ethiopia, there is a dearth of information regarding TB/HIV co-infection. According to Jeren (2007:7), TB/HIV co-infection rate of Ethiopia is about 45% among sputum-smear-positive pulmonary TB patients. In 2009, the global tuberculosis control report indicated that HIV sero-prevalence among TB cases was 12%, which equals the global co-infection rate. A cross-sectional study conducted to evaluate the TB/HIV collaborative activities at the capital city of Ethiopia in Addis Ababa (2012:1-6) showed that, 24% of TB patients were HIV sero- positive. The same report showed that among HIV infected individuals who participated in an exit interview, 52.1% were co-infected with tuberculosis in the past 3 years after learning their HIV sero status (Kassa, Jerene, Assefa, Teka, Aseffa and Deribew 2012: 1-6).

2.4.   COLLABORATIVE TB/HIV ACTIVITIES

The collaborative TB/HIV activities policy was formulated by World Health Organization in 2004 to provide well established framework for countries in their response to HIV-related TB. The recently updated collaborative TB/HIV activities policy recommends national programmes and other stakeholders to incorporate TB/HIV activities into routine HIV prevention package. The aim of collaborative TB/HIV activities is to reduce the dual burden of TB and HIV in people living with the disease or at risk of disease. In order to achieve this goal, WHO TB/HIV collaborative activities were made to scale up the three 'I's - intensified TB case-finding (ICF), Isoniazid preventive therapy and TB Infection control in health-care facilities and congregate settings (WHO 2012:14-30).

2.4.1. Isoniazid preventive therapy (IPT)

WHO and International Union against TB and Lung Disease (IUTLD) recommended the use of IPT in reducing TB among HIV infected persons since 1993, which was further revised and strengthened in 1998. In 2004 the TB/HIV collaborative activities were introduced. INH preventive therapy is given to those with latent tuberculosis infection in order to prevent development to active disease. Isoniazid preventive therapy (IPT) is a daily self-administered therapy for at least 6 months for all eligible PLHIVs (EFMOH 2007c:18). IPT should be initiated based on the WHO clinical staging, laboratory and clinical findings, and presence or absence of contra-indications (EFMOH 2007c:18). It could be mandatory to exclude active, which is a major challenge for health care providers, from of tuberculosis before prescribing IPT.

Studies showed that IPT is effective and safe preventive method that reduces the incidence of TB and death among HIV infected people. WHO strongly suggest patients living with HIV should be screened for active TB, should not have current cough, fever, weight loss or night sweats; and adolescents and adults living with HIV with unknown or positive tuberculin skin test (TST) status should obtain at least 6 months of IPT. IPT should be accessible to persons on ART, PLHIV's with-out considering the extent of immunosuppression, and also to those who have formerly been treated for TB and pregnant women. Before the administration of IPT exclusion of active TB and absence of present cough, night sweats, fever, or weight loss should be made (WHO 2012: 24).

2.4.5. Current IPT Program Practices

2.4.2.1. Global

According to the global TB control (WHO 2010:18), in 2009 around 80, 000 HIV positive people were provided with IPT, which accounts for less than 1% of the estimated number of eligible people living with HIV.

Afterward, in 2010, the global number of HIV positive individuals without active TB who enrolled on IPT was estimated at 180,000, which is seven times significant to the level achieved in 2005 and three-fold in 2008. High burden countries contributed to more than ninety four percent to this figure and of which eighty nine percent (160,000) of individuals were from Africa. WHO classified forty-one countries as high burden countries, 29 of which are from Africa continent (WHO 2010:18).

2.4.2.2. Ethiopia

The Ethiopian and WHO TB/HIV implementation collaborative activities guideline recommends IPT for people living with HIV with unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB, those who screened with a clinical algorithm; those who do not present with any one of the symptoms of current cough, fever, weight loss or night sweats (EFMOH 2007c: 17-18; WHO 2012:23). The Ethiopian guideline recommends a self-administered Isoniazid at a dose of 5mg/kg with a maximum dose of 300mg/day for six months (EFMOH 2007c:18; Marais, Zyl, Schaaf, Aardt, Gie, Beyers 2006: 762-764; Mindachew et al 2011: 1).

In 2005 the number of HIV infected person who were provided with IPT were only 1983 and 2403 in 2009 (WHO 2010). A recently released report by WHO (2011:62) states that of 43, 837 HIV infected individuals screened for TB, 6,636 were enrolled on IPT in 2010 in the whole Ethiopia. IPT is an integral part of the routine HIV and TB prevention package in most health care setting (EFMOH 2007c:18).

2.4.5. Scientific Consensus on IPT

Providing ART and IPT helps in reducing the effect of tuberculosis among people infected with HIV. Though ART is the major strategy to reduce opportunistic infections including TB, studies suggest that using IPT together with ART will have strong impact on reducing TB recurrence and activation. However, using ART and IPT among HIV-infected patients with positive TST, reduced the risk of TB infection by 90% (WHO 2012: 24).

Effective Anti-retroviral therapy (ART) reduces TB incidence significantly among HIV infected individuals. A study from South Africa has shown that ART reduces the incidence of TB by two-third among HIV infected individuals (Lawn 2010: 2; Golub 2007:1441-1442; Patel et al 2008: 57-508). The world health organization on its TB/HIV collaborative activities policy states that ART risk of TB by the population-based risk of PLHIV by 27% to 80% and TB recurrence rate by 50%. A recent clinical trial conducted in Botswana, also, found that early initiation of ART alone reduce the risk of TB by 80% (WHO 2012: 24). Despite the fact that ART is increasingly becoming accessible and successful in reducing HIV related deaths, tuberculosis remains the leading cause of mortality and morbidity among PLHIV and an intimidation for countries (Charalambous, Grant, Innes, Hoffmann, Dowdeswell, Pienaar,Fielding and Churchyard 2010: S5; Cohen, Lipsitch, Walensky and Murray. 2006: 7042 , Pawlowski et al 2012:2).

A prospective cohort study by Golub et al (2009: 631) showed that using a combination of ART and IPT among PLHIVs is more effective in reducing latent TB infection than using discretely. Jonathan and colleagues' study showed that the rate of TB infection was reduced in PLHIVs who were on either IPT or ART (Golub et al 2009:631; 635; Nieburg et al 2008:2). These findings were further supported by Mosimaneotsile and colleagues study illustrated that providing IPT together with ART may lessen the incidence of TB by additional 58-76% (Mosimaneotsile et al 2010: 71).

Studies suggest that TB preventive therapy is not only effective against TB incidence, it also reduces rate of mortality related to TB. A study from South Africa has revealed that the death rate within the first three months after the instigation of ART among those who were not on IPT (20.15 PYO) was higher compared to those on IPT (6.65 PYO) (Charalambous et al 2010:S9-S10). Similarly, a randomized control trial study by Zar and colleagues (2006: 1-7) also showed that a death rate of 5.9% among PLHIV's who took IPT and 21.3% among those who don't receive.

A randomized controlled trial study conducted in 2006 showed that the incidence of tuberculosis among the INH group (3.8%) was lower than in the placebo group (9.9%) using intention to treat analysis. Besides, the same research pointed out that the rate of death among children infected with HIV and grouped under INH was lower than that of the placebo group (Zar et al 2006:1). A similar finding was reported by Golub and colleagues in 2009, IPT independently reduces TB incidence by 70-90% in peoples infected with HIV (Golub et al 2007: 1441). Supporting this finding, Padmapriyadarsini and colleagues found that taking IPT daily for six months reduces the rate of TB by more-than 67% among HIV infected individuals (Padmapriyadarsini et al 2011: 854).

Despite the fact that IPT is effective in reducing tuberculosis, different studies showed individuals who received continuous IPT had better outcome than those who took for short-term. A study by Samandari and colleagues found that PLHIVs who received continuous IPT had 92% reduction in TB incidence. Supporting this finding, a study from Botswana revealed that providing a daily based IPT for 36 months is much more effective in reducing incidence of TB among HIV infected persons than 6 months do. The same study showed that those PLHIV's who received 36 months IPT had a risk of only 0.19 per 100 PYO, whilst, those who took 6 months of IPT had 2.56 per 100 PYO tuberculosis risk (Samandari et al 2010: 1588).

2.4.5. Concerns Related to IPT

Despite the availability of policies and recommendations and significant evidence that IPT reduces incidence of tuberculosis (TB) in HIV-infected individuals, the utilization of IPT is still lower than expected due to diverse arguments. The uptake and delivery of INH preventive therapy is disappointingly slow in most countries. Lack of standard operating procedures, guidelines and screening algorithms, lack of health care provider capacity in providing the service, and shortage of preventive therapy supplies contributes to the low availability and poor uptake of IPT (Granich et al 2010:S216; Lester et al 2010:S45-S48; Golub et al 2007:1441; Eldred et al 2010: S1; Gao et al 2010: 1-2; Mosimaneotsile et al 2010: 71).

Furthermore, there is a wide spread concern regarding side effects, complexity to rule-out active TB case and duration of IPT protection. INH drug toxicity, poor adherence to IPT, fear of INH resistance and patient driving factors including pill burden, non-adherence, economic status and unfamiliarity about IPT are also contributing factors for low delivery and uptake of IPT (Zanoni, Phungula, Zanoni, France and Feene 2011: 50; EFMOH 2007c:19, Eldred et al 2010:S1; Golub et al 2007:1441-1442; WHO 2008:23-24; Lester et al 2010: S45–S48).

INH preventive therapy when used to treat latent TB infection doesn't promote INH resistance. A study done in Addis Ababa, Ethiopia, found that the most-important cause for INH preventive therapy failure is poor adherence (Mindachew et al 2011:2). The study by Padmapriyadarsini et al (2011: 850-865) also indicated that there is no study on IPT that reported greater INH resistance rate exclusively attributable to IPT.

Besides, a cluster randomized trial conducted by Grant and colleagues (2010:S29-S36) showed that the low performance of IPT program has been primarily due to fear of adverse effects. Among 24, 221 study participants, 61 (0.25%) developed mild-to-moderate degree of hyper-sensitivity, 50 (0.21%) peripheral neuropathy, 17 (0.07%) hepatotoxicity and 4 (0.05%) had convulsion. It was clear that the risk of INH prophylaxis related adverse effect particularly hepatotoxicity, was very low (Grant et al 2010: S29-S36).

2.4.5. IPT recommendation

IPT is recommended for HIV infected individuals without active TB infection. The Ethiopian TB/HIV guideline recommends IPT for all Individuals who are HIV infected, including pregnancy, except for individuals with any one or more of the following conditions. A person with active tuberculosis, symptoms compatible with tuberculosis, even if the diagnosis of TB cannot be confirmed, abnormal chest X-ray, diagnosis and treatment of TB in the past 3 years and cases where poor treatment prognosis is expected (i.e.) - terminally ill AIDS patients, history of poor compliance with treatment, active hepatitis, known or reported high daily alcohol consumption, prior allergy or intolerance to isoniazid, and history of close contact with MDR-TB patient are not eligible and should not receive IPT (EFMOH 2007c :18; WHO 2008:23-24).

CHAPTER 3

RESEARCH DESIGN AND METHODOLOGY

3.1. INTRODUCTION

In this chapter, the study design and data collection method will be discussed in detail, covering population and sampling, the instrument, data collection and analysis, ethical considerations and issues around study reliability and validity.

3.2. RESEARCH DESIGN

Polit and Beck describe research design as the overall plan for obtaining answers to the questions being studied and for handling some of the difficulties encountered during the research process (Polit and Beck 2008:49; 730). The choice of study design determines how the researcher samples the population, collects measurements and analyses the data. A quantitative, descriptive study case control study design was chosen for this study. The main purpose was to assess the impact of INH preventive therapy on the incidence of tuberculosis among TB and HIV co-infected individuals in Addis Ababa, Ethiopia.

3.2.1. Quantitative studies

Broadly speaking, quantitative studies is a type of empirical research that focuses on numeric information that results from structured measurement of occurrences and that is analyzed using statistical procedures. Besides quantitative methods are formal, objective, systematic procedure in which numerical data are used to obtain information about the reality. Quantitative researchers' uses data in numeric form (Polit and Beck 2008: 15-16; 33; Bruce, Pope and Stanistreet 2008: 1-7).

This study collected quantitative data of HIV infected and TB patients who were enrolled on IPT and those who were not using patient record reviews.

3.2.2. Descriptive Study

Descriptive study designs observes, classify, count and describes characteristics of a condition without affecting its natural occurrence (Polit and Beck 2008:20; 192).

In this study the researcher compared HIV infected TB patients who were enrolled on IPT with those patients who did not take IPT for occurrence of TB disease.

3.2.3. Case-control studies

Case-control design is the simplest and most commonly used study design that involves and looks the relationship between a "case" and a "control" (Polit and Beck 2008: 190; 712; Joubert and Ehrlich 2007:82-85; 313). The researches begin from the outcome or cases, could be disease, and backwardly looks the disparity in exposure. The exposure is occurred or started in the past and prior to disease onset. Case-control studies help in describing and realizing the outcome of interest or cause of a disease, determining the effect of events or interventions and investigation of disease outbreaks (Joubert and Ehrlich 2007:82- 85; 226; 313; Bruce et al 2008: 257- 305).

Case control study design was employed in this study to assess the impact of TB preventive therapy on TB incidence. In this study, HIV infected TB patients who were receiving TB preventive therapy selected from hospitals were named as cases, whereas, HIV infected TB patients without prior IPT exposure from the same hospital were taken as controls.

3.3. STUDY POPULATION AND SAMPLE

3.3.1. Study Population

Study population is the total set of persons (or objects) having common characteristics from which the sample is essentially selected (Polit and Beck 2008: 727). Polit and Beck (2008:50; 289) population is refers to the aggregate or total members possess specific attributes which a researcher is interested in studying. The population may consist of events, places, objects, animals, or individuals (Burns & Grove 2005:342).

In most researches, two populations are illustrated, the target population and the accessible population.

The study population in this study consisted of all HIV infected TB patents aged 14 years and older in Addis Ababa followed up in the Zewditu and Yekatit 12 hospitals between January 2008 and December 2010.

3.3.2. Inclusion and exclusion criteria's

3.3.2.1. Inclusion criteria

Those HIV Infected TB patients who received Isoniazid therapy from January 2008 to December 2010 at Zewditu and Yekatit 12 hospital and were eligible to participate in the study.

3.3.2.2. Exclusion criteria

- HIV infected individuals who were on ART,

- TB patients with no HIV diagnosis,

- HIV infected persons with unknown IPT start and end date

- HIV infected persons with prevalent TB diagnosis at the time of HIV diagnosis

- Due to similarity of many HIV allied infections like Pneumocystis carinii pneumonia, viral and bacterial pneumonias, the study was limited to HIV Infected TB patients who are aged 14 and over.

3.3.3. Sampling frame

Polit and Beck (2008: 296; 731) and De Vos and colleagues (2007:194) describe sampling frame as a listing of the elements of the population from which the sample will be selected (Joubert and Ehrlich 2007: 94-95).

The sampling frame of this study was a list of HIV infected individuals who were diagnosed and/or followed up at Zewditu and Yekatit 12 hospitals in Addis Ababa between January 2008 and December 2010 period.

3.3.4. Study Area and Period

This study was carried out at the capital city of Ethiopia, Addis Ababa. Addis Ababa is the most populous and chartered city of Ethiopia with a total population of 2.8 millions contributing 3.7% to the nation population (Federal democratic republic of Ethiopia: Population census Commission 2008:10). There are nine public hospitals serving people infected with HIV and co-infected persons in Addis Ababa.

Zeweditu hospital and Yekatit 12 hospitals are the two general hospitals in Addis Ababa most used for TB/HIV treatment since 2008.

The study was conducted from May to October 2012.

3.3.6. Sampling

Polit and Beck (2008: 291; 731) and De Vos and colleagues (2007:194) concurs that sampling is the way of choosing a section of the population who will be studied to represent the whole population (Joubert & Ehrlich 2007: 190; 94-105).

This study reviewed a record of 489 HIV and TB infected patients. Some were enrolled on IPT and others were not.

3.3.6. Sample size

The sample size was calculated by using two sample proportion formula using Epi-Info version 3.3 for windows. The calculation was based on the assumption of 0.05 alpha level, study power of 80%, 1: 2 case-to-control ratio and 2.0 desired OR level. The proportion of controls with exposure (IPT) was assumed 70% and 30% for cases. Using Epi-Info sample size calculator, 148 cases and 295 controls were estimated to give sample size of 443. A

10% was added on this sample size to adjust for incomplete patient records. The final sample size became 489 (163 cases and 326 controls).

The list of all HIV infected TB patients who received IPT or not, was extracted from the ART and TB entry and follow-up register. In order to get the required number of participants, the investigator used computer generated table of random numbers to take a sample of patient ID numbers from the register. Simple random sampling is a technique in which elements are selected for the study in a random manner in-order to get representative sample (Joubert and Ehrlich 2007: 95-97). All the elements had the same possibility to being included for the case and control group.

3.4. RESEARCH ASSISTANT

At the beginning, discussion was made with the ART clinic heads for the selection of nurses who had an experience and training on ART/TB formats. Permission was given to use the nurses for data abstraction during off-duty days. The nurses worked in ART program and were familiar with TB/HIV and ART data collection forms. The nurses were well acquainted with the current knowledge of ART and TB infection and treatment guidelines and the current Ministry of Health ART/TB intake and follow-up forms. One day training was given for data abstractors before the start of data collection process. The principal investigator took the responsibility of quality assurance and quality control for the study.

3.5. THE INSTRUMENT

A questionnaire is a printed document with a list of questions designed to gain information on a certain variables (Joubert and Ehrlich 2007:106-116). Similarly, Polit and Beck (2008:729; 236) argues that questionnaire is a technique of gathering information from participants using a list of questions in a written format.

A structured data collection checklist was developed containing closed-ended questions. The national ART and TB entry and follow up form, the national TB/HIV guideline and exiting literature on TB/HIV were the basis for the development of data abstraction tool used in the study. The TB/HIV collaborative activity and ART unit were consulted for review of the tool.

The tool comprised of 6 sections, namely:

Section 1: Socio-demographic characteristics

Section 2: Baseline clinical, laboratory and treatment information

Section 3: Social condition of patients

Section 4: Health education, knowledge and risk behaviours

Section 5: Follow-up information

Section 6: Information on TB treatment outcome

Before the actual data collection procedure took place, data collection checklist was piloted in Black Lion Hospital, which was in the same region as study areas, and suitable modifications were made afterwards.

3.6. DATA COLLECTION

Polit and Beck (2008:716) defines data collection as a methodical information gathering technique which helps assembling of appropriate information to the focus of study and applied to address a research problem.

In this study, data was collected using data abstraction checklist. The checklist was piloted before the actual data collection procedure took place. Piloting was used to identify gaps in the data collection instrument and correct formatting and TB/HIV variable related errors.

Each HIV infected TB patient normally has uniquely identifiable ID number which appears on the ART/TB intake and follow-up cards. Each-day after the patient received medication and/or counselling services, data entry clerks transfer the updated information into an electronic database.

PLHIVs where were followed at pre-ART clinic, diagnosed with active TB and/or who received IPT during the period of January 2008 and December 2010 were identified and listed (using clinic IDs) and samples were drawn randomly. Patients with the selected ID numbers were identified, printed and passed over to hospital registrar, which was responsible to identify and provide data abstractors with the individual patient records.

The data collectors were responsible to abstract data from patient records, while quality assurance and quality control was made by principal investigator.

3.7. DATA ANALYSIS

Collected quantitative data need analysis and interpretation with the intention to be able to answer the study questions and the testing of study assumption using those data. De Vos et al (2007:218) and Polit and Beck (2008:716) explain data analysis as is a systematic organization, classifying, manipulating and eventually summarizing and synthesis of study data. Data analyses give outline to the study, elicit meaning from research data and help in drawing conclusion about the study population (De Vos et al 2007:217-219; Polit and Beck 2008: 716).

The principal investigator assessed the abstracted data for completeness and carried out data cleaning and a statistician was consulted during data processing and analysis. Data was entered into SPSS version 16.0. Data was described using graphs, tables, charts and diagrams and statistical associations were calculated using analytic tests including odds ratio and chi-square test.

3.8. RELIABILITY AND VALIDITY

3.8.1. Reliability

Reliability helps to assess the quality and adequacy of quantitative instruments. Dyson and Brown (2006:112-128) and Polit and Beck (2008:43; 416-428) describe reliability shortly as the stability, repeatability and regularity of information obtained in a study.

It is important to ensure the reliability of the instrument. The ability of an instrument is considered reliable when it measures the target attribute consistently and accurately and provide the same result again and again (Dyson and Brown 2006:112- 128; Joubert and Ehrlich 2007: 116-122).

To ensure the reliability of the instrument, current national ART/TB intake and follow-up forms were used to guide its development. Close-ended questions were used. Experienced TB and ART clinic staff were used as data abstractors. Data collection checklist was piloted to identify gaps in the tool and they were corrected before actual data collection.

3.8.2. Validity

Validity concerns the soundness and rationality of the study's evidence or it measures the ability of the data collection tool to measure what it is intended to measure (Polit and Beck 2008: 43; 416-428; Joubert and Ehrlich 2007: 116-122).
 Joubert and Ehrlich (2007: 120-121) and Polit and Beck (2008:423) define face validity as the degree to which the measurement creates a sense to the interviewer or individuals who have understanding on the subject matter or those who are familiar with the language and culture. Whereas, content validity described as the extent to which instrument has a suitable contents for the subject being measured.

The quality of data was, also, ensured starting from the development of appropriate data collection checklist up to the data entry and analysis process. The researcher used already existing ART and TB intake and follow-up format to develop the questionnaire which maintains the validity. Besides, In order to improve the validity of the study and instrument, the researcher defined terms and contextualized for the specific research. Furthermore, the instrument was developed to answer the study questions according to the research objectives and existing literatures.

An extensive literature review was conducted in order to ascertain the content validity for data abstraction tool. All formats were checked for completeness and uniformity to ensure

both the content and face validity. Pre-testing and continuous supervision maximized the quality of data.

3.9. ETHICAL CONSIDERATIONS

Polit and Beck (2008: 717) define ethics as "a system of moral values that is concerned with the degree to which research procedures adhere to professional, legal, and social obligations to the study participants". Implementation of a research that violates the ethical principle is immoral and unethical. Though, this research purely uses secondary data from follow up and entry forms, the ethical protocol were strictly followed.

3.9.1. Ethical Permission

Before the start of data collection, the investigator was obtained ethical clearance from the Higher Degrees Committee of the Department of Health Studies of the University of South Africa (annexure A). Then, permission to undertake the study was achieved from the ethical committee of city government of Addis Ababa city council health bureau. The necessary information about the study was offered to the Addis Ababa city council health bureau, hospital officials and health personnel's in the ART clinic.

3.9.2 Informed Consent

During this retrospective study, the researcher had no direct contact with participants. Hence, there was no need to develop an informed consent. After securing ethical clearance from the health bureau, authorization letter was written from Addis Ababa City Administration Health Bureau to Zewditu and Yekatit 12 Hospital Managements. This helped to get permission to use the data from the hospitals.

3.9.3. Protecting the Right of the Participants

3.9.3.1. Anonymity

Anonymity is a way of protecting the privacy of study participants. The investigator cannot associate participants or individuals with the information offered in a study with maintained its anonymity (Polit and Beck 2008: 149; 711; Joubert and Ehrlich 2007:32).

No personal identification (ID) of individual patient (name, address and telephone numbers, etc.) was collected rather anonymous ART identification numbers were used. The information collected form participants were not linked to either the participants or the institution. The researcher followed the same principle while reports and findings were published.

3.9.3.2. Confidentiality

Polit and Beck (2008:714) explain confidentiality as protecting the privacy of prospective participants in a study. Therefore, the information that is collected is not allied with individuals participating in the study and by no means publicly disclosed. This study employed a retrospective institution based record review and all information was collected in protected and confidential way.

ART nurses working at TB/HIV clinics were recruited for data abstraction and supervision. This guaranteed confidentiality of patient data because that is part and parcel of their daily responsibility. Besides, no third person had access to the data other than the study team. Computers used for data analysis were password protected.

3.9.3.3. Beneficence

Beneficence imposes the researcher to reduce harm and maximize benefits on the study participants (Polit and Beck 2008:170). The result of the study gave highlight about IPT effectiveness in the prevention of tuberculosis. The result may encourage expansion of the service at all level and improve the attitude of practitioners that will improve the utilization of INH prophylaxis by the participants; thus, the participants will have better quality of life.

The findings of this study would help in providing information on program implementation and its challenges for health planners and managers to strengthen and expand IPT services at all facility level. This indirectly may help HIV infected individuals to have access to and utilization of TB prophylaxis at health facilities of their vicinity.

3.9.3.4. Non-maleficience

Non-maleficience inculcates the investigator not to harm others deliberately (Joubert and Ehrlich 2007:33). Since the study didn't involve clinical trial, no potential harm or risks were foreseen. The researcher utilized neither direct contact with the participants nor any kind of procedures during the conducting the study. Therefore, the study had no emotional, social or physical harm to the participants.

3.9.4. Protecting the Rights of the Institution

The proposal was submitted to the research and ethical committee of the University of South Africa for ethical clearance. Then permission to collect data was sought from Addis Ababa health bureau and medical directors of the hospitals. All facet of the research was disclosed to the health bureau, the management of the hospital and then to the ART clinic head and staffs. Discussion on the objective and methodology was made with Addis Ababa Health bureau ethical clearance committee, hospital disease prevention and control core process owner and ART nurse data collectors. No information was given to third party without the permission of Addis Ababa Health bureau and the Hospital. Permission will be requested form Addis Ababa Health Bureau to publish the research finding.

3.9.5. Human right

This research employed a retrospective institution based record review and all information was collected in protected and confidential way. Merely, ART nurses were recruited for data collection and supervision, this guaranteed confidentiality. Besides, no third person had access for the data without the permission of the hospital or health bureau.

3.10.SUMMARY

The chapter dealt with research methodology incorporating the research design, study population, sample, the instrument and researcher/data collector, data collection and analysis and ethical standards that directed the study. Data was collected from HIV infected TB patients who were on IPT and those HIV infected TB patients who were under follow up between January 2008 to December 2010 at Zewditu and Yekatit 12 hospital.

In the next chapter, the results of the study will be presented.

CHAPTER 4

ANALYSIS AND INTERPRETATION

4.1. INTRODUCTION

This chapter included the overall research findings and presented as data analysis and interpretation, including discussion of study findings and their programmatic implications.

The specific objectives for this study were to:

- To compare the incidence of TB among HIV infected clients who received IPT and those who did not
- To determine the socio-demographic and behavioural factors associated with TB incidence among HIV infected patients.
- To compare HIV disease related factors associated with TB infection among those who received IPT and those who did not

The tool was divided into six sub-sections, while, in-order to answer the study objectives the data was analysed including the following sections:

Section 1: Socio-demographic and social characteristics

Section 2: Social factors

Section 2: Baseline clinical and laboratory information

4.2. DATA MANAGEMENT AND ANALYSIS

The sample size consisted of 489 HIV patients co-infected with TB: 163 were receiving INH prophylaxis and the remaining 326 were not. Data was abstracted from registers by trained nurses who had experience working in TB and HIV. Quality of data was monitored by supervisors and the principal invigilator. Data was entered and analysed using SPSS for windows version 16.

4.3. RESULTS

The following sections discuss data analysis in the context of the study's research objectives and to answer the question according to the order in the questionnaire.

4.3.1. Socio-demographic Characteristics

The socio-demographic factors included age, sex, and marital status, level of education, and religion.

4.3.1.1 Sex

A total of 489 patient records were reviewed and majority were females 285 (58.3%). Among those who were receiving IPT, 49 (30.1%) were males and 114 (69.9%) were females (OR=2.11; 95% CI 1.42, 3.14). Among the 326 patients who didn't take IPT, 155 (47.5%) patients were males (Table 4.1)

4.3.1.2 Age

The mean age of patients who were on IPT was 33.76 years with a standard deviation (SD) of 8.20. It was 37.31 years (SD=8.45) for those who were not receiving INH prophylaxis (OR=0.048; 95% CI 0.004, 0.52). Those who developed tuberculosis and who were not on INH were on average 4 years older than those who were on IPT (p<0.001) (Table 4.1).

4.3.1.3 Marital Status

About 50% of both patient groups (those receiving INH prophylaxis and those who did not) were living in marital union. A quarter of patients receiving INH prophylaxis were never married compared to a fifth of those who did not. There was no statistically significant difference between the two groups regarding marital status (Table 4.1).

4.3.1.4 Educational status

About 40% of both groups had secondary education, and less than a quarter of them went to tertiary level education. There was no statistically significant difference in educational status between those who were receiving IPT and those who did not (Table 4.1).

4.3.1.5 Religion

Of the overall study participants, 80.4% were followers of Orthodox Christianity. Protestant Christians and Muslims constituted 11.7% and 6.1% respectively. There was no statistically significant difference between those who were taking INH and those who did not with regards to religion (Table 4.1).

Table 4.1: Socio-demographic characteristics of patients, Addis Ababa, Ethiopia (n=489)

Variable		INH Prophylaxis		OR; 95% CI	X^2 (p value)
		Yes: 163(100%)	No: 326(100%)		
Sex	Male [R]	49 (30.1%)	155 (47.5%)	1.0	
	Female	114 (69.9%)	171 (52.5%)	2.11; (1.42, 3.14)	
Age	<20 [R]	6 (3.7%)	1 (0.3%)	1.0	
	20-24	10 (6.1 %)	9 (2.8 %)	0.19; (0.019, 1.85)	
	25-34	77(47.3 %)	115 (35.3 %)	0.11; (0.013, 0.95)	X^2= 26.37 (p=0.001)
	35-44	52 (31.9 %)	138 (42.3 %)	0.06; (0.007, 0.54)	
	45-54	18 (11 %)	63(19.3 %)	0.05; (0.005, 0.42)	
Marital Status	Never Married [R]	46 (28.2%)	66 (20.2%)	1.0	
	Married	82 (50.3%)	165 (50.6%)	2.09; (1.03, 4.26)	
	Separated	8 (4.9%)	7 (2.1%)	1.49; (0.77, 2.89)	X^2= 10.86 (p=0.028)
	Divorced	13 (8.0%)	46 (14.1%)	3.43; (1.05, 11.17)	
	Widowed	14 (8.6%)	42 (12.9%)	0.85; (0.36, 2.01)	
Educational status	No education [R]	14 (8.6%)	26 (8.0%)	1.0	
	Primary	45 (27.6%)	109 (33.4%)	0.77; (0.37, 1.60)	
	Secondary	63 (38.7%)	139 (42.6%)	0.84; (0.41, 1.72)	X^2= 6.48 (p=0.09)
	Tertiary	41 (25.2%)	52 (16.0%)	1.46; (0.68,, 3.16)	
Religion	Orthodox [R]	133 (81.6%)	260 (79.8%)	1.0	
	Protestant	17 (10.4%)	40 (12.3%)	0.84; (0.37, 1.88)	
	Muslim	9 (5.5%)	21 (6.4%)	0.83; (0.45, 1.52)	X^2=1.01 (p=0.798)
	Catholic	4 (2.5%)	5 (1.5%)	1.56; (0.41, 5.92)	
Occupational status	Jobless [R]	78 (47.9%)	129 (39.6%)	1.0	
	Go'vtal Employee	49 (30.1%)	78 (23.9%)	1.04; (0.66, 1.64)	X^2 = 16.08 (p=0.007)
	Day Labourer	20 (12.3%)	82 (25.2%)	0.40; (0.23, 0.71)	
	Merchant	16 (9.8%)	29 (8.9%)	0.91; (0.47, 1.79)	

R: stands for reference variable

4.3.1.6 Occupational status

Occupation wise, 42.3% (207/489) of the patients were jobless 26% were employee of governmental organizations and 20.9% were daily labourers (Table 4.1).

4.3.2 SOCIAL FACTORS

4.3.2.1.Living Home

Table 4.2: Number of living rooms and number of people per household, Addis Ababa,Ethiopia 2012 (n=489)

Variable		INH Prophylaxis		OR; (95% CI)	X^2 (p value)
		Yes: 163(100%)	No: 326(100%)		
Number of rooms	**1-3[R]**	134 (82.2%)	288 (88.3%)	1.0	X^2= 8.06 (p=0.045)
	4-6	25 (15.3%)	29 (8.9%)	1.96; (1.10, 3.49)	
	7-9	4 (2.5%)	4 (1.2%)	2.46; (0.60, 10.20)	
	≥10	0 (0%)	5 (1.5%)	0.00; (0.00, 0.00)	
People per room	**1-3[R]**	127 (77.9%)	229 (70.2%)	1	X^2= 4.96 (p=0.18)
	4-6	34 (20.9%)	84 (25.8%)	0.68; (0.43, 1.09)	
	7-9	2 (1.2%)	10 (3.1%)	0.34; (0.07, 1.59)	
	≥10	0 (0%)	3 (0.9%)	0.84; (0.00, 1.34)	

R: Stands for reference category

Out of the 489 patients, 422 (86.3%) were living in houses which had rooms ranging from 1 to 3 and only five (0.2%) individual had living rooms greater or equal to ten rooms. Of those who lived in house with 1-3 rooms, 134 (81.6%) were provided IPT and 288 (88.9%) were non IPT groups (Table 4.2).

Regarding number of people per room, 356 (72.8%) patients were living in rooms shared by up to three other individuals. About a quarter of them (118) had 1 to 3 rooms and the numbers of people living in these rooms were range from 4 to 6 (Table 4.2). There was no statistically significant difference in the number of peoples living in a room between those who were enrolled on IPT and those who did not (Table 4.2).

4.3.3. BASELINE CLINICAL AND LABORATORY FACTORS

4.3.1.1 Tuberculosis incidence

Among those who were receiving Isoniazid, 23 (13.6%) developed tuberculosis while on INH therapy. Out of 326 participants who were not on INH, 225 (69.2%) of them had confirmed tuberculosis. The analysis revealed that the TB incidence rate among those who developed TB after completing isoniazid was significantly lesser when compared to those who were not on isoniazid (OR= 0.072; 95% CI 0.044, 0.12) (table 4.3). This association persisted even after controlling for confounders using logistic regression analysis (AOR=12.1; 95% CI 4.54, 32.02).

Table 4.3: Tuberculosis incidence among INH and Non-INH groups in Addis Ababa, Ethiopia 2012 (n=489)

		TB	No TB	Total	OR (95% CI)
INH prophylaxis	**YES**	23 (14.1%)	140 (85.9%)	163	
	NO	225 (69.0%)	101 (31.0%)	326	**OR= 0.072; (95% CI 0.044, 0.12)**
	TOTAL	248 (50.7%)	241 (49.3%)	489	

4.3.3.4.CD4 Result

The figure below (Figure 4.1) shows the level of CD4 count during HIV diagnosis among TB co-infected HIV patients who were on INH and compared with those who were not. Less than one-third (7 out of 23) of those who developed TB while taking INH and more than ninety percent (209 out of 225) of those who didn't receive INH had CD4 count less than 350 cells per µL at HIV diagnosis. Having CD4 count less than 350 cells per µL at diagnosis of HIV was strongly associated with the group who was not put on INH prophylaxis and hence were at more risk of TB infection (OR = 0.02; 95% CI 0.006, 0.065).
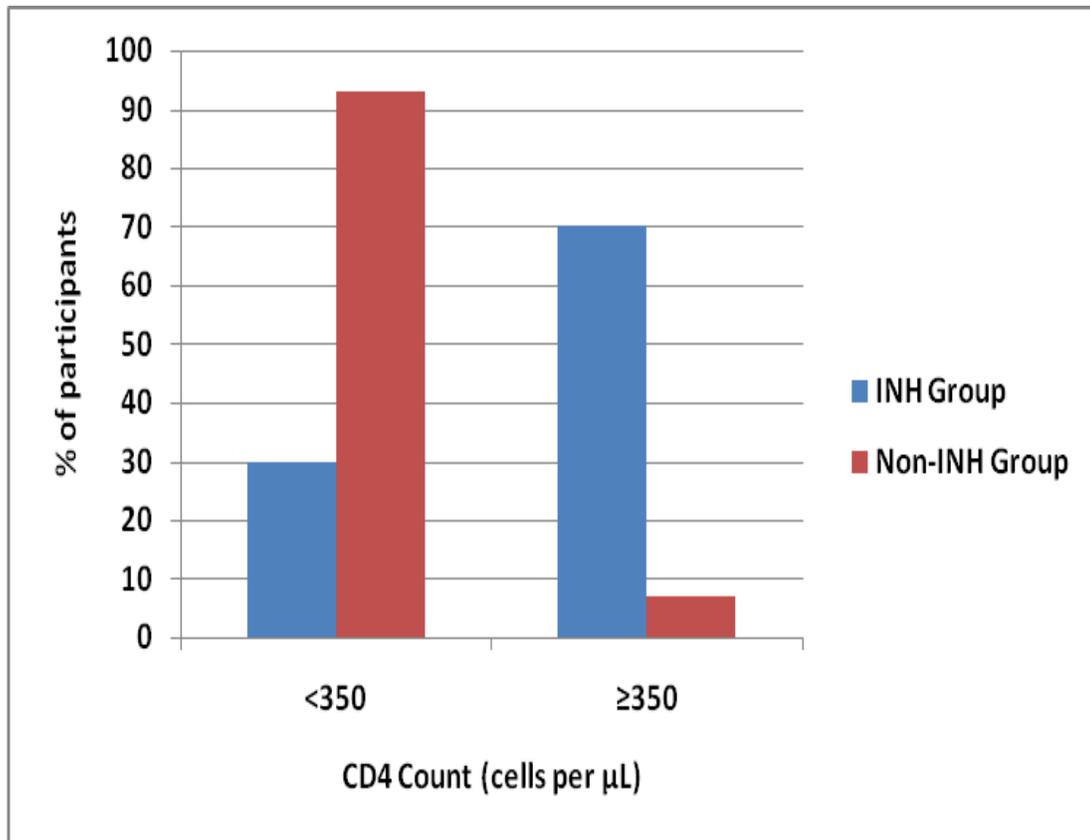
Figure 4.1: CD4 count at HIV diagnosis among patients who developed TB infection while on INH prophylaxis and those not on INH, Addis Ababa, Ethiopia 2012.

The percentage of TB infected patients with CD4 counts < 350 cells per µL at HIV diagnosis reduced by 38.3% during the six months of follow up period among those who were not put on INH (Figure 4.2).
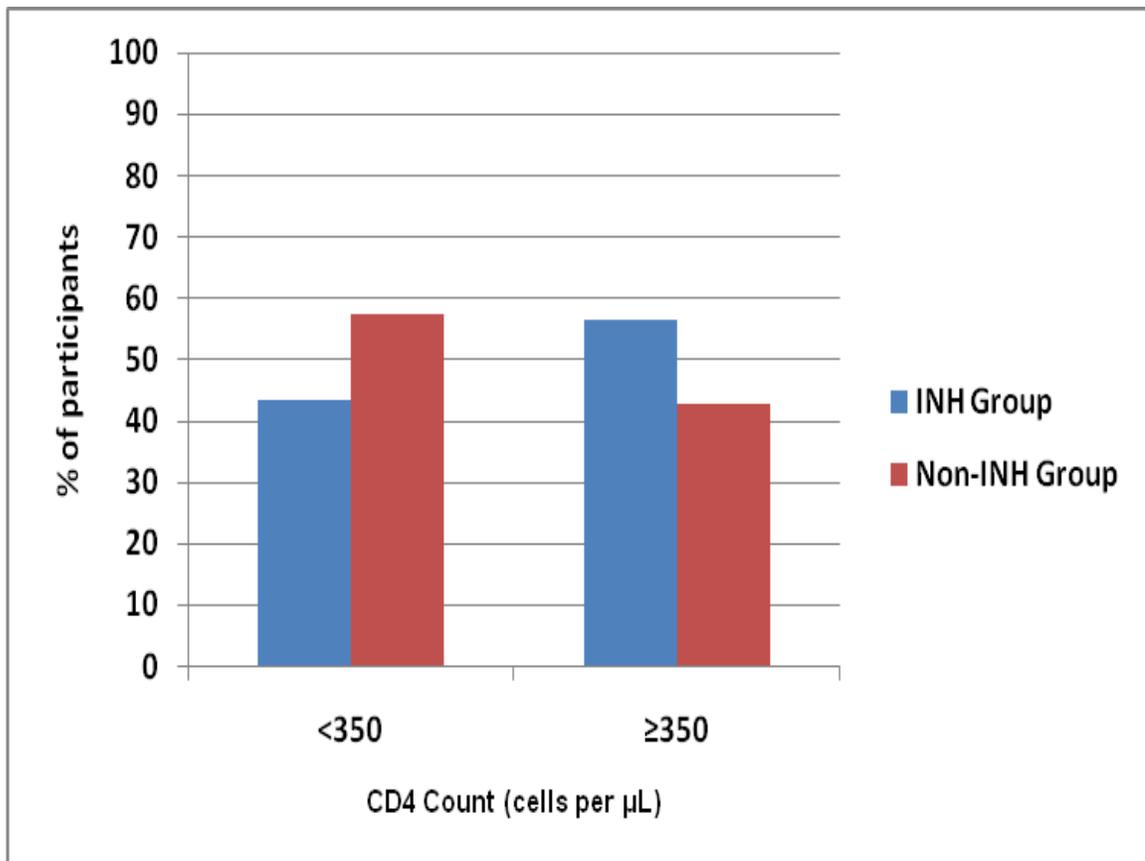
Figure 4.2: CD4 count of INH and Non-INH groups after six months of follow-up in Addis Ababa, Ethiopia 2012.

4.3.3.3. WHO clinical stage of patients

Concerning the WHO clinical staging of HIV/AIDS disease, more than half (52.9%) of those who developed tuberculosis and about two-fifth of patients who were on INH had stage four clinical staging at HIV diagnosis (Figure 4.3; Figure 4.4).

None of patients who developed TB infection while on INH prophylaxis were in WHO clinical stage 4 at the time of HIV diagnosis compared to 52.9% of those who developed TB infection and were not put on INH prophylaxis (OR 3.01; 95% CI 1.44, 6.25).
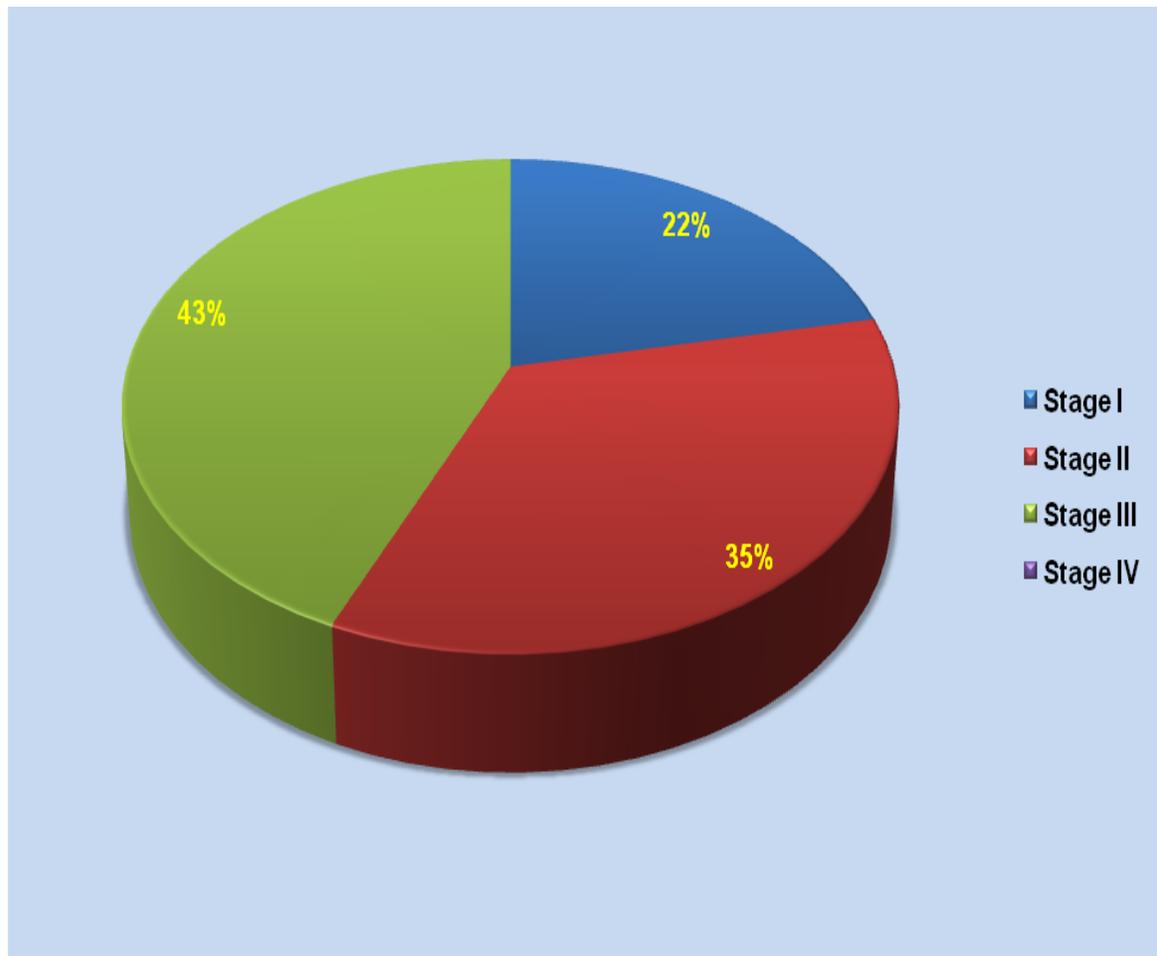
Figure 4.3: WHO clinical staging during HIV diagnosis among tuberculosis co-infected patients who were on INH in Addis Ababa, Ethiopia 2012

The analysis on entry clinical stage showed that, almost equal proportions (44%) of those who developed tuberculosis while receiving isoniazid and those who did not were categorized at stage three. Only six patients among those who were not enrolled on INH therapy and four from co-infected patients who were on INH were categorized either in stage one or two (Figure 4.3; Figure 4.4).

Patients who developed TB without receiving INH had higher odds of being at advanced stage of HIV infection than those who developed TB while receiving INH (OR=0.24; 95% CI 0.075, 0.78).
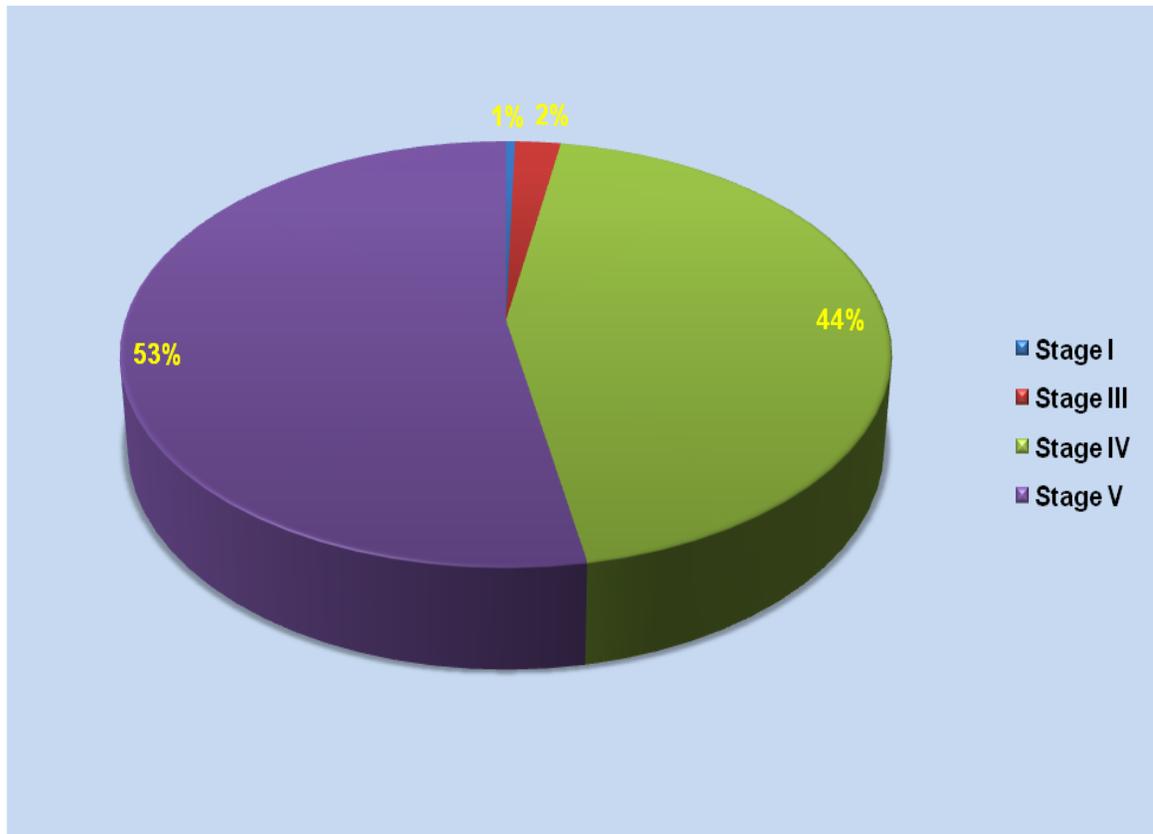
Figure 4.4: WHO clinical stage at HIV diagnosis among TB co-infected patients who were not on INH in Addis Ababa, Ethiopia 2012

4.3.3.4.ASSOCIATED FACTORS

Table 4.4: Association of tuberculosis infection with socio-demographic, TB/HIV/AIDS outcomes and behavioural factors in Addis Ababa, Ethiopia 2012 (n=489)

| Variable	OR; (95% CI)	X^2	p value	AOR; (95% CI)
Socio-demographic Factors				
Age	0.046; (0.003, 0.51)*	26.3	0.001	0.14; (0.03, 0.97)*
Sex	2.08; (1.39, 3.13)*	-	-	1.86; (1.02, 2.23)*
Marital Status[+]	1.0	-	-	1.0
Educational status	0.98; (0.46, 2.07)	5.86	0.12	0.93; (0.73, 1.17)
Religion	3.74; (0.77, 18.23)	3.97	0.27	0.88; (0.68, 1.13)
Occupation	1.01; (0.062, 16.36)	1.21	0.94	1.04; (0.86, 1.25)
TB/HIV/AIDS outcome Related factors				
CD4 result				
During HIV diagnosis	0.18; (0.12, 0.29)*	-	-	0.21; (0.13, 0.31)*
After 6 months	1.18 (0.83, 1.69)	-	-	0.99; (0.67, 1.46)
WHO clinical staging	0.104; (0.023, 0.47)*	14.69	0.002	1.22; (1.09, 1.84)*
Previous History of TB	2.31; (1.44, 5.22) *	11.91	0.035	1.98; (1.20, 4.83)*
Previous TB R_x Outcome	1.09 (0.36, 3.14)	7.56	0.059	0.95 (0.20, 3.43)
Behavioural Factors				
Tobacco	1.00; (0.85, 1.19)	0.001	0.97	0.97; (0.80, 1.17)
Alcohol	0.73; (0.60, 0.90)*	9.50	0.002	0.82; (0.66, 1.01)
Soft Drugs	0.83; (0.70, 0.98)*	4.73	0.03	0.90; (0.75, 1.08)
Hard Drugs	1.13; (0.83, 1.55)	0.60	0.44	1.16; (0.83, 1.61)
Social Factors				
Peoples per room	1.06; (0.67, 1.69)	1.50	0.68	2.12; (0.79, 4.90)

* show the presence of association; [+] indicates the reference and comparison variable

As shown in table 4.4, age (OR= 0.046; 95% CI 0.003, 0.51) and sex (OR=2.08; 95% CI 1.39, 3.13) had significant association with tuberculosis incidence. Both age (AOR= 0.14; 95% CI 0.03, 0.97) and sex (AOR= 1.86; 95% CI 1.02, 2.23) remained statistically significant during multivariate analysis.

CD4 count at HIV diagnosis (OR= 0.18; 95% CI 0.12, 0.29) and WHO clinical staging (OR 0.104; 95% CI 0.023, 0.47) were also associated with incidence of tuberculosis. Both CD4 count during HIV diagnosis (AOR= 0.21; 95% CI 0.13, 0.31) and WHO clinical staging (AOR= 1.22; 95% CI 1.09, 1.84) remained significantly associated with TB incidence at multivariate analysis.

Pervious history of tuberculosis (OR= 2.31; 95% CI 1.44, 5.22) was significantly associated with tuberculosis incidence. This significance also continued in controlled analysis with a P value of 0.035. However, previous tuberculosis treatment outcome (OR= 1.09; 95% CI 0.36, 3.14) was not significantly associated with tuberculosis infection (p= 0.059).

Among the behavioural risk factors, alcohol (OR= 0.73; 95% CI 0.60, 0.90) and use of stimulant drugs (e.g. Khat, Shisha...etc) (OR= 0.83; 95% CI 0.70, 0.98) were associated with incidence of tuberculosis on the bivariate analysis. But, in controlled multivariate analysis, this association remained statistically insignificant.

In general, age (AOR= 0.14; 95% CI 0.03, 0.97) and sex (AOR= 1.86; 95% CI 1.02, 2.23) of the patient, CD4 count at HIV diagnosis (AOR= 0.21; 95% CI 0.13, 0.31), WHO clinical stage at HIV diagnosis (AOR= 1.22; 95% CI 1.09, 1.84) and previous history of tuberculosis (AOR = 1.97; 95% CI 1.24, 3.67) were the major factors associated with tuberculosis incidence.

Table 4.5: Association of tuberculosis infection with socio-demographic, TB/HIV/AIDS outcomes and behavioural factors of **Non-INH** group, Addis Ababa, Ethiopia 2012 (n-489)

Variable	OR; (95% CI)	X^2	p value	AOR; (95% CI)
Socio-demographic Factors				
Age	0.26; (0.08, 0.93)*	13.72	0.034	0.69; (0.31, 0.92)*
Sex	0.57; (0.13, 0.99)*	-	-	2.01; (1.23, 4.46)*
Marital Status [+]	1.0	-	-	1.0
Educational status	0.16; (0.06, 0.54) *	22.83	0.0021	1.93; (1.43, 3.76)*
Religion	18.25; (1.41, 35.75)	3.81	0.14	0.81; (0.59, 1.11)
Occupation	0.16; (0.02, 0.74) *	8.88	0.035	2.25; (1.41, 3.60)*
TB/HIV/AIDS outcome Related factors				
CD4 result				
During HIV diagnosis	0.22; (0.081, 0.73)*	-	-	1.92; (1.18, 6.71)*
After 6 months	1.21 (0.69, 2.11)	-	-	0.78; (0.48, 1.28)
WHO clinical staging	0.10; (0.04, 0.88)*	10.73	0.011	1.91; (1.11, 5.29)*
Previous History of TB	2.11; (1.89, 3.72)*	13.22	0.004	2.50; (2.00, 4.08)*
Previous TB R_x Outcome	0.94; (0.43; 2.97)	4.31	0.32	1.08; (0.86, 3.31)
Behavioural Factors				
Tobacco	0.35; (0.084, 3.26)	0.77	0.54	1.04; (0.83, 1.30)
Alcohol	0.38; (0.09, 0.79)*	7.08	0.048	0.83; (0.64, 1.07)
Soft Drugs	0.17; (0.097, 0.62)*	9.00	0.0021	0.96; (0.56, 1.21)
Hard Drugs	1.16; (0.23, 5.36)	1.07	0.69	1.28; (0.86, 2.61)
Social Factors				
Peoples per room	2.12; (0.92; 5.11)	5.89	0.67	1.37; (0.76, 1.93)

show the presence of association; [+] indicate the reference and comparison variable

The bivariate and multivariate analysis done to determine HIV disease related factors associated with TB infection among those who did not received IPT showed that age, sex, educational and occupational status from socio-demographic variables, and CD4 result during HIV diagnosis and WHO clinical staging from HIV/AIDS related factors had an association with tuberculosis infection among non-INH HIV infected tuberculosis patients. The bivariate analysis of socio-demographic variables showed that age (OR=0.26; 95%CI 0.08, 0.93), sex (OR=0.57; 95% CI 0.13, 0.99), educational status (OR=0.16; 95%CI 0.06, 0.54) and occupation (OR=0.16; 95%CI 0.02, 0.74) were shown to be statistically significant with tuberculosis infection among non-INH receiving HIV infected tuberculosis patients.

The multivariate analysis showed that the age, sex, educational and occupational status variables remained statistically significant (AOR=0.69; 95% CI 0.31, 0.92), (AOR=2.01; 95% CI 1.23, 4.46), (AOR=1.93; 95% CI 1.43, 3.76), (AOR= 2.25; 95% CI 1.41, 3.60) respectively. (Table 4.5)

In the bivariate analysis, CD4 result during HIV diagnosis (OR=0.22; 95% CI 0.081, 0.73) and WHO clinical staging (OR= 0.10; 95% CI 0.04, 0.88) were also significantly associated with tuberculosis infection among HIV infected tuberculosis infection. After controlling for possible confounders by multivariate analysis this association continued to be significant (AOR=1.92; 95% CI 1.18, 6.71) and (AOR= 1.91; 95% CI 1.11, 5.29) accordingly. (Table 4.5)

As shown in Table 4.5, previous history of tuberculosis was shown to be significantly associated with tuberculosis incidence (OR= 2.11; 95% CI 1.89, 3.72). Nevertheless, previous tuberculosis treatment outcome was not significantly associated with tuberculosis infection among TB patients who were not put on INH (OR= 0.94; 95% CI 0.43, 2.97). (Table 4.5)

The analysis of behavioural factors showed that alcohol (OR= 0.38; 95% CI 0.09, 0.79) and using soft drugs (OR= 0.17; 95% CI 0.097, 0.62) was shown to be statistically significant with tuberculosis infection. However, the multivariate analysis done with controlling for other variables this association was found to be insignificant (AOR= 0.83; 95% CI 0.64, 1.07), (AOR= 0.96; 95% CI 0.56, 1.21) correspondingly. (Table 4.5)

Table 4.6: Association of tuberculosis infection with socio-demographic, HIV/AIDS outcomes and behavioural factors among INH group in Addis Ababa, Ethiopia 2012 (n=489)

Variable	OR; (95% CI)	X^2	F test	AOR; (95% CI)
Socio-demographic Factors				
Age	0.25; (0.01, 0.91)*	9.19	0.0025	1.21; (1.01,3.46)*
Sex	7.28; (1.50, 35.54)*		0.0003	0.24; (0.08, 0.71)*
Marital Status+	1.0	-	-	1.0
Educational status	3.22; (0.08, 26.97)	2.91	0.67	1.01; (0.56,1.83)
Religion	0.063; (0.003,1.53)	1.16	0.09	0.86; (0.42, 1.77)
Occupation	1.40; (0.16, 12.30)	2.94	0.081	0.98; (0.60, 1.59)
HIV/AIDS outcome related factors				
CD4 result				
During HIV diagnosis	0.25; (0.08, 0.78)*	-	0.046	0.30; (0.12,0.97)*
After 6 months	0.71; (0.18, 2.85)	-	0.54	1.23; (0.46, 3.27)
WHO clinical staging	0.14; (0.003, 0.68)*	14.09	0.011	1.51; (1.02, 2.29)*
Previous History of TB	2.62; (1.27, 5.93)*	8.61	0.0069	2.12; (1.09, 4.99)*
Previous TB R_x Outcome	0.56; (0.12; 2.74)	6.98	0.39	0.87; (0.41, 1.78)
Behavioural Factors				
Tobacco	2.46; (0.028, 37.18)	0.86	0.53	0.96; (0.55, 1.70)
Alcohol	2.15; (0.22, 20.89)		0.048	0.97; (0.53, 1.77)
Soft Drugs	2.02; (0.27, 15.07)	1.78	0.21	1.07; (0.69, 1.67)
Hard Drugs	1.62; (0.58, 4.53)	0.67	0.58	0.61; (0.12, 3.03)
Social Factors				
Peoples per room	1.24; (0.26, 6.52)	7.21	0.86	0.89; (0.60, 1.79)

* show the presence of association; + show reference and comparison variable

The bivariate analysis of socio-demographic variables, age (OR= 0.25; 95% CI 0.01, 0.91) and sex (OR= 7.28; 95% CI 1.50, 35.54) were associated with tuberculosis infection among HIV infected patients who received INH. The association between tuberculosis infection and socio-demographic variables, age and sex, was found to be significantly associated at p<0.005 and p<0.001 respectively. (Table 4.6)

Regarding HIV/AIDS outcome related factors, CD4 result during HIV diagnosis with an OR 0.25; 95% CI (0.08 to 0.78) and WHO clinical HIV/AIDS staging with an odds of 0.14; 95% CI (0.003 to 0.68) was significantly associated with tuberculosis infection.

Similarly, CD4 result during HIV diagnosis (p<0.05) and WHO clinical staging of patients (p<0.05) was statistically associated with tuberculosis infection of INH receiving HIV infected patients. (Table 4.6)

As shown in table 4.6, history of tuberculosis had a significant association with tuberculosis incidence (p<0.05). However, previous TB treatment outcome, behavioural factors including tobacco smoking, alcohol and use of soft and hard drugs did not show significant association with tuberculosis infection among HIV infected patients who were receiving INH.

4.4. SUMMARY

This chapter presented the research findings as data analysis and interpretation. The study revealed that patients who were put on INH prophylaxis had lower chances of developing tuberculosis than patients who were not receiving INH prophylaxis. Sex and age, CD4 count at HIV diagnosis, WHO clinical staging and previous history of tuberculosis were significantly associated with tuberculosis incidence in both groups of patients.

Bivariate and multivariate analysis conducted in the absence of INH prophylaxis among HIV infected patients showed that in addition to the aforementioned four variables educational and occupational status had also a significant role in tuberculosis incidence. However, the factors associated with tuberculosis infection among those who received isoniazid was similar to the overall listed variables.

The next chapter will talk about these findings and conclusions and make recommendations based on these findings.

CHAPTER 5

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1. INTRODUCTION

Chapter five presents the discussion, conclusion and recommendations part of the study made by the researcher. The discussion section will largely focus on interpretation of the research findings by considering the research objectives. Besides, it will compare and contrast the research findings with existing literatures.

5.2. DISCUSSION OF FINDINGS

The researcher set out three specific objectives for this specific study. The objectives compared the incidence of TB among HIV infected clients who received IPT and those who did not, determined the socio-demographic and behavioural factors associated with TB incidence among HIV infected patients and compared HIV disease related factors associated with TB infection among those who received IPT and those who did not. The outline of the discussion section follows these objectives. Recommendations were made on issues of key concern based on the study findings.

The key finding of this study is the fact that tuberculosis incidence among those who received isoniazid prophylaxis was much lesser than those who didn't receive Isonizide therapy. A prospective cohort done in South Africa found that HIV infected adults who were not under INH therapy had a higher degree of tuberculosis incidence than those who were receiving INH, which was similar to the present study finding (Golub et al 2009:631; 634).

This study showed that INH prophylaxis reduced tuberculosis risk by 0.07 (by almost 40%) which was comparable to the study done in Rio de Janeiro, Brazil (Golub et al 2007:1).

A study done by Frigati and colleagues proved that those HIV infected persons who didn't enrol on INH had a greater tuberculosis incidence when compared to those who received the INH therapy which was similar to our finding (Frigati, Kranzer, Cotton, Schaaf, Lombard and Zar 2011:498-499). This finding also compares with a study result from South Africa (33%) (Charalambous et al 2010: S6). But lower than studies conducted in Rio de Janeiro, Brazil (70-90%) and a study by Padmapriyadarsini and colleagues which showed 67% overall reduction (Golub et al 2007: 1441; Padmapriyadarsini et al 2011: 854).

Age, sex, CD4 count at the time of HIV diagnosis, WHO clinical staging and previous history of tuberculosis were important socio-demographic and behavioural factors associated with TB incidence among HIV infected individuals. Similarly, a study done among HIV infected individuals in Denmark identified that age, sex and CD4 count at HIV diagnosis were risk factors associated with tuberculosis (Taarnhøj et al 2011: 3-7). A study by Nicholas et al (2011: 313-315) also found sex, CD4 count and clinical staging to have significant association with tuberculosis risk.

In this study, young HIV infected patients had a greater chance to be infected by tuberculosis than those who were at older stage. This finding is similar to a study done among Danish HIV patients which found patients at the lower age category to have greater risk for tuberculosis (p<0.036) (Taarnhøj, Engsig, Ravn, Johansen, Larsen, Røge, Andersen and Obel 2011: 3-7).

HIV infected female patients who were on INH were more prone to develop tuberculosis than their male counterpart in our study. Similarly, a study done in Nigeria found statistically significant association between female by sex and tuberculosis infection (p=0<0.05).

This study also found that majority of females who were receiving INH prophylaxis had higher CD4 count and less advanced WHO clinical stage. In contrast, among those who were not on INH, being female increased the risk of developing tuberculosis which was similar to study finding in South Africa (Komati et al 2011: 1851- 1853) and Nigerian study (Nicholas et al 2011: 313- 315).

Patients who had CD4 counts less than 350 cells per µL during HIV diagnosis had 78% more likely to develop tuberculosis than those who had CD4 counts greater than 350 cells per µL. This finding was similar to a study done in Tanzania which showed that CD4 count depletion exacerbates the development of active tuberculosis. CD4 depletion, in turn, contributes to the worsening of clinical staging, which further contributes to the progression of severe forms of diseases (Andersen, Range, Changalucha, PrayGod, Kidola, Faurholt-Jepsen, Krarup, Grewal and Friis 2012: 3-6; Taarnhøj et al 2011:3-7; Stephanus Komati, S, Shaw, PA, Stubbs, N, Mathibedi, MJ, Malan, L, Sangweni, P, Metcalf, JA, Masur, H and Hassim, S 2011: 1851- 1853).

A multicohort study done in eight sub-Saharan African countries found that those individuals who had higher CD4 counts were less (30%) likely to develop tuberculosis than those who had lower counts (Nicholas, Sabapathy, Ferreyra, Varaine and Pujades-Rodr´ıguez 2011: 313-315). Furthermore, the by Taarnhøj and colleagues in Denmark cited above showed that lower CD4 count at HIV diagnosis was associated with increased risk of tuberculosis infection (Taarnhøj et al 2011: 3-7).

Clinical stage was identified as one of the risk factors for tuberculosis in this study. Being at WHO clinical stage four was positively associated with tuberculosis incidence when compared to those who were at other stages, this finding was comparable to study in Dar es Salaam, Tanzania (Ngowi, Mfinanga, Bruun and Morkve 2008: 1-7). Ngowi et al (2008: 3-5) identified clinical stage as risk factor and as the clinical stage increases the risk of tuberculosis infection also increases. Ngowi and colleagues (2008:3-5) found that the risk of tuberculosis among stage four HIV infected TB patients was 70 times more than those at stage one.

This study found that history of tuberculosis and previous treatment outcome had significant association with tuberculosis infection.

Those HIV infected TB patients who had previous history of tuberculosis had more chance of tuberculosis re-infection when compared to those who had no history. Komati et al (2011: 1851- 1853) found that previous history of tuberculosis was related with increased risk of tuberculosis, which was comparable to this study.

Educational and occupational status of the patient was factors associated with tuberculosis among those who were not on isoniazid therapy. There is a dearth of studies on risk factors of tuberculosis among HIV infected peoples who were not on INH. However, a study conducted in South-west Ethiopia found that educational and occupational status of HIV infected patients was independently associated (Taha, Deribew, Tessema, Assegid, Duchateau and Colebunders 2011: 131- 139). A nested case-control study in Hunan province, China, similarly found that a low level of educational status was significantly associated with development of tuberculosis in peoples living with HIV (Chen, Yang, Chen, Tan, Bai, Zhang, Liu, Li G 2010:151-154).

5.3. CONCLUSION

INH prophylaxis has long been recommended by WHO as cost-effective public health measure to prevent TB among HIV infected individuals. Likewise, other studies conducted in different parts of the world found that INH prophylaxis to be effective in reducing tuberculosis infection among HIV infected patients. Nonetheless, the implementation of INH preventive therapy has remained very low in most developing countries including Ethiopia. The recent increase in the coverage of ART among PLHIV, which in itself results in significant reduction of TB incidence, has limited the potential target group of PLHIV who benefit from INH prophylaxis. The debate among the scientific community and decision makers on the most effective use of isoniazid preventative therapy will therefore continue for some time to come.

This study that age, sex, CD4 counts, clinical stage and previous history of the patient were associated with tuberculosis infection. This underlines the need regular screening of TB infection for all PLHIV and early initiation of ART particularly among those with lower CD4 counts and previous history of TB as per the national TB/HIV guideline.

5.4. RECOMMENDATION

Based on the study findings, the researcher makes the following recommendations:

4. **Ministry of Health**

   4.9. Development of appropriate and easily understandable IPT guidelines for Health Managers and health professionals.

   4.9. Conduct more prospective studies to identify PLHIV who will most benefit from INH prophylaxis.

   4.9. Conducting TB/HIV service utilization and implementation assessments at all stages of the health care system.

   4.9. Including IPT as an integral part of TB/HIV planning, reporting and monitoring and evaluation.

   4.9. Increasing access and availability of IPT medications at all stages of TB/HIV service provision facilities.

5. **Addis Ababa city council health bureau**

   - Intensified health education on the risk of TB infection among PLHIV.

   - Widespread implementation of regular TB screening for all PLHIV at each clinical visit.

   - Encourage use of INH prophylaxis for all PLHIV who do not have active TB and are not yet eligible for ART initiation according to the national ART guideline.

   - Active TB/HIV integration at all levels to improve identification of TB infection among PLHIV and initiation of ART among TB patients receiving anti-TB treatment.

   - Regular and continues follow up of health facilities to assess the implementation of the guidelines.

➢ **PLHIV and family/community members**

   - PLHIVs should take prescribed medication on time and correctly without discontinuation

   - Family and community members should help PLHIVs in taking prescribed Isoniazid medication.

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PERMISSION LETTER TO CONDUCT RESEARCH

Sade, Anteneh Habtemariam

Addis Ababa

Addis Ababa City Administration counsel

Health Bureau

Addis Ababa

RE: PERMISSION TO CONDUCT RESEARCH

Dear Sir/Madam,

I am a registered MPH student at the University of South Africa (UNISA) conducting study for the partial fulfilment of Masters Degree in public health. I secured the necessary ethical clearance from University of South Africa, Department of health studies ethical.

The main purpose of the study is to measure the impact of Isoniazid preventive therapy on the incidence of tuberculosis among TB/HIV co-infected infected individuals at Zewiditu and Yekatit 12 hospitals in Addis Ababa, Ethiopia. The study requires secondary data on TB and HIV from January 2008 to December 2010 from ART clinic and TB Unit.

It is my hope that the findings from this study will assist in understanding the impact of INH prophylaxis in the prevention of tuberculosis among HIV infected persons.

I shall be very delighted if you can grant me the permission to carry out the study. If you have any queries or clarification, please do not hesitate to contact me.

Regards

DATA COLLECTION FORM

INTRODUCTION

This questionnaire form is intended to assess the impact of isoniazid preventive therapy on tuberculosis incidence among HIV infected patients. The study is being conducted at Zeweditu and Yekatit 12 hospital in Addis Ababa, Ethiopia. The information will be collected through reviewing secondary data in the ART clinic. The privacy and confidentiality will strictly be secured throughout the research process. All the information will be numbered and coded and the names and identification address will not be used during the review and analysis. If the report of results is published, only information about the general group will appear. This information is intended to contribute to the existing knowledge of IPT effectiveness by comparing the incidence of TB among HIV infected persons receiving INH prophylaxis and those don't taking in Ethiopian context. Besides, it will provide information on program implementation and its challenges for health planners and managers to strengthen IPT services. Moreover it will have a paramount importance to curb the horizon of the disease.

Date of review _____ Day _____ Month _____ Year

Name of the reviewer _____ Signature of the reviewer _____

Time started _____ Time ended _____

Name of the supervisor _____Signature of the supervisor_____

Date_____

Total number of records reviewed_____

Reviewed patient card number from_____ to_____

Result

    a) Completed_____

    b) Incomplete_____

    c) Excluded_____

Action taken for the incomplete data (please use additional blank paper if the space provided is not enough)   _____

_____

STANDARDIZED QUESTIONNAIRE

Part I: Baseline information (to be filled from ART clinic intake form)

SECTION 1: SOCIO DEMIOGRAPHIC CHARACTERSTICS

NO	QUESTIONNAIRE/VARIABLE	CODING CATEGORIES	Remark
101	Age	-----------------------------------	
102	Sex	1. Male 2. Female	
103	Marital Status	1. Never Married 2. Married 3. Separated 4. Divorced 99. Widowed	
104	Educational status	1. No education 2. Primary 3. Secondary 4. Tertiary	
105	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 99. Other (Specify) ------------------	
106	Occupational status	1. Farmer 2. Merchant 3. Go'vt employee 4. Non-go'vtal org employee 5. Day labourer 6. Jobless Other (specify)-------------------	
107	Region	1. Tigray 2. Afar 3. Amhara 4. Oromiya 5. Somiali 6. Benishangul Gumuz 7. SNNPR	

		8. Gambella	
		9. Harar	
		10. Addis Ababa	
		11. Dire Dawa	

SECTION 2: BASELINE CLINICAL, LABORATORY AND TREATMENT INFORMATION

NO	QUESTIONNAIRE/VARIABLE	CODING CATEGORIES	
201	Past opportunistic infection	1. TB 2. PCP 3. Cryptococcal meningitis 4. Kaposi Sarcoma 5. Oral candidiasis 6. Toxoplasmosis 7. Herpes zoster 8. Other (specify)	
202	Screened for HIV/TB smear	1. Yes_____ 2. No_____	
203	If "yes" to Q 202	Date_____/____/____	
204	If "**yes**" to Q 202, result	1. Not determined 2. Negative 3. Positive 4. Positive +1 5. Positive +2 6. Positive +3 7. Unknown	
205	TB treatment	1. Yes 2. No	
206	If "yes" to Q 205, treatment completed	1. Yes 2. No	
207	If "**yes**" to Q 205	1. Date started____/____/_____ 2. Date Completed _____/____/____	
208	If "**yes**" to Q 205, regimen	1. Not determined 2. 2SRHZ/6EH 3. 2HRZES/1HRZE/5HRE 4. 2HRZE/6EH	

209	Post treatment smear	1. Sputum smear positive ___/__/___ 2. Sputum smear negative___/__/___	
210	HIV test	1. Yes 2. No	
211	If "yes" to Q 210, date	Date ___/___/____	
212	CD4 test	1. Yes, Date___/____/____ Result_____ 2. No	
213	INH	1. Yes 2. No	
214	Symptoms screened	1. Chronic cough 2. Night sweets 3. Dyspnea 4. Weight loss >10% 5. Fever > 1 month	
215	Physical examination		
	Lymph nodes	1. Normal 2. Abnormal	
	Chest	1. Normal 2. Abnormal	
216	If "**yes**" to Q 213,	1. Starting date ____/____/___ 2. Completion date __/___/____ 3. Discontinuation ____/___/___	
217	WHO clinical stage of HIV disease	1. Stage I (___/____/___) 2. Stage II (___/____/___) 3. Stage III (___/____/___) 4. Stage IV (____/____/___) DD/MM/ YY	
218	Did the patient evaluated for TB/cough	1. Yes 2. No	
219	If "**yes**" to Q. 217	1. TB sputum smear result 2. Chest X ray result_____	
220	Did the patient need prophylactic medications	1. Yes 2. No	
221	INH prophylaxis	1. Start date____/_____/_____ 2. Discontinue____/___/_____	

SECTION 3: SOCIAL CONDITION

NO	QUESTIONNAIRE/VARIABLE	CODING CATEGORIES	REMARK
301	Employment status	1. Working full time 2. Working part time 3. Not working/studying due to illness 4. Unemployed 5. Other specify_____	
302	Living home	1. Number of rooms_____ 2. Number of people in the household _____	
303	Religious/supportive care	1. Yes 2. No	
304	If "yes" to Q 303, religious conviction	a. Muslim b. Orthodox c. Protestant d. Catholic e. Other specify_____	
305	If "yes" to Q 303, community support/HIV support group	1. Yes 2. No	
306	Did anyone else know about your HIV status		
	Family	1. Wife/husband 2. Own child (ren) 3. Parent(s) 4. Brothers (s)/ Sister(s)	
	Other	1. Relatives 2. Friends	
307	Spouse condition		
	1. Condition of the wife/husband	a. Healthy b. Chronic ill c. Dead d. Unknown	
	2. HIV tested (result)	a. Not asked b. Negative c. Positive d. Unknown	

	3. TB (result)	a. Not asked	
		b. Negative	
		c. Positive	
		d. Unknown	
	4. Was/is on TB treatment	a. Yes	
		b. No	

SECTION 4: HEALTH EDUCATION, KNOWLEDGE AND RISK BEHAVIORS (to be filled from ART Adherence counselling form)

NO	QUESTIONNAIRE/VARIABLE	CODING CATEGORIES	
401	Attended HIV related health education session/s in the past	1. Yes 2. No	
402	Attended HIV related counselling session/s in the past	1. Yes 2. No	
403	Understanding of HIV disease	1. NA 2. − 3. + 4. ++ 5. +++	
404	Understanding of HIV transmission	1. NA 2. − 3. + 4. ++ 5. +++	
405	Understanding of prophylaxis and treatment of OIs	1. NA 2. − 3. + 4. ++ 5. +++	
406	Addiction		
	a) Tobacco	1. NA 2. − 3. + 4. ++ 5. +++	

b) Alcohol	1. NA 2. – 3. + 4. ++ 5. +++	
c) Soft drugs (e.g. Chat, Shisha, pills.. etc)	1. NA 2. – 3. + 4. ++ 5. +++	
d) Hard drug (e.g. cocaine, morphine, IV drugs...)	1. NA 2. – 3. + 4. ++ 5. +++	

PART II: FOLLOW UP INFORMATION (USE HIV CARE/ART FOLLOW UP FORM, ART and PRE ART REGISTER)

SECTION 5: FOLLOW UP INFORMATION

NO	QUESTIONNAIRE	CODING CATEGORIES	REMARK
501	Date confirmed HIV+	_____/_____/_____	
502	Type of HIV test	1. Rapid test 2. ELISA	
503	WHO staging	3. Stage I 4. Stage II 5. Stage III 6. Stage IV	
504	TB screened	1. Yes 2. No	
505	If "yes" to 504, result	1. Positive 2. Negative	
506	TB prophylaxis	1. Yes Drug_____ duration_____ 2. No	

507	Opportunistic infections	1. Pulmonary TB 2. Extra pulmonary TB	
508	TB treatment	3. Yes 4. No	
509	CD4 (mm^3)/TCL	_____ date_____	
510	ALT/AST	_____date_____	

PART III: TB TREATMENT OUTCOME (USE TB REGISTER)

SECTION 6: TB TREATMENT SUCCESS INFORMATION

NO	QUESTIONNAIRE	CODING CATEGORIES	REMARK
601	Initial diagnostic AFB result	1. Positive 2. Negative 3. Not done	
602	Classification of the patient	1. Smear positive PTB 2. Smear negative PTB 3. EPTB 4. Other (specify)_____	
603	Category of the patient	1. New 2. Relapse 3. Failure 4. Defaulter 5. Transfer in 6. Other (specify)_____	
604	Treatment given during the intensive phase	1. 2SRHZ 2. 2HRZES 3. 2HRZE 4. Other (specify)_____	
605	Dose of the drug during the intensive phase	_____	
606	Sputum smear result during the 2nd month of treatment	1. Positive 2. Negative	
607	Drug given during the continuation phase	1. 6EH 2. 1HRZE/5HRE 3. Other (specify)_____	

608	Dose of the drug during the continuation phase	_____	
609	Is AFB done on the 5th and 7th/11th	1. Yes 2. No (skip to 611)	
610	If " yes" to Q **609** the result	1. Positive 2. Negative	
611	Treatment outcome of the patient	1. Cured 2. Treatment completed 3. Died 4. Treatment failure 5. Defaulter 6. Transfer out 7. Other(specify)_____	
612	Completeness of the registration form	1. Complete 2. Incomplete	