ASSESSMENT OF LIVER AND METABOLIC DISORDER AND ASSOCIATED FACTORS AMONG TUBERCULOSIS PATIENTS ATTENDING AT JIMMA TOWN PUBLIC HEALTH FACILITIES, SOUTHWEST ETHIOPIA

BY: YESUF SEID

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ASSESSMENT OF LIVER AND METABOLIC DISORDER AND ASSOCIATED RISK FACTORS AMONG TUBERCULOSIS PATIENTS ATTENDING AT JIMMA TOWN PUBLIC HEALTH FACILITIES, SOUTHWEST ETHIOPIA

ADVISORS: 1- AKLILU GETACHEW (BSc,MSc,Phd cad)

2- WAQTOLA CHENEKE (BSc, MSc,Phd cad,Asso. Prof)

ABSTRACT

Background: *Most developing countries are still suffering from diffrent infectious disease,such as tuberculosis. Patients infected with tuberculosis are more likely susceptible to metabolic disorders and liver diseases that cause,which may results non communicable disease like diabetes mellitus and derangementof hepatic biomarkers. The elevations of liver enzymes and hyperglycemia are the primary indicator of hepatic and metabolic abnormalities .However; thus, regular updated data on the studies of liver and selected metabolic disorder using liver enzymes and metabolic tests among TB patients in Ethiopia important to reduce tuberculosis associated complications,morbidities and mortalities.*

Objectives: to assess liver and metabolic disorder and associated risk factors among patients who are on anti TB Treatment at Jimma town public health facilities, South west Ethiopia from October 2020 to February 2021.

Methods and materials: It was Institutional-based cross-sectional studyconducted in Jimma.Convenient sampling technique was carried out to select 179TB patients attending at Jimma town public health facilities.The socio-demographic and other related clinical data were collected using the structured questionnaires and by reviewing patient's medical record . Five ml venous blood was collected from participants aftereach participants stay on fastingovernight. Then fasting blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma glutamyl-transferase (GGT) were measured using Humastar 100 automated analyzer.Data were analyzed using statistical package for social science version 26, while logistic regression was used to assess associated factors.

Result: *Among 179 TB patients, 45(*25.1%)*of them were found to have one or more elevated liver enzymes. The prevalence of elevated serum ALT, AST, ALP and GGT was 18.4%, 17.3%, 3.9%, and 5.6% respectively and prevalence of hyperglycemia was 7.3%. In this study, intensive phase of anti TB treatment and government employed were found significant predictors of elevated serum ALT in TB patients (P< 0.05).*

Conclusion:I*nthis study high prevalence of hyperglycemia and one or more liver enzymes increments in TB patients was found. This result indicates TB patients were more susceptible toliver enzyme disturbance .Routine assessment of serum liver enzymesand blood sugar might be beneficial for TB patients to control and follow up of liver dysfunction and metabolic disorder.Furthermore, researches that clarify causative factors and mechanisms of liver enzyme increment and metabolic disturbance in TB patients should be conducted.*

Key word; *Tuberculosis, liver function test, alanine amino transferase, aspartate amino transferase,gamma glumayn transferase, alkaline phosphatase*

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Abbreviations and acronyms

ALT	Alanine amino transferase
ALP	Alkaline phosphatase
AST	Aspartate amino transferase
ATDILI	Antituberculosis drug-induced liver injury
DILI	Drug induced liver injury
IFCC	International federation for clinical chemistry
IU/L	International unit per liter
HbsAg	Hepatitis B surface antigen
HCV	Hepatitis C virus
IRB	Institutional Review Board
GGT	Gamma Glutamy-Transferase
LFT	Liver function test
Mtd	Metabolic disorders
Mtb	Mycobacterium tuberculosis
NCEP	National Cholesterol Education Program
SOP	Standard Operating Procedure
SPSS	Statistical Package Software for Social Science
TB	Tuberculosis
WHO	World Health Organization

Operational definitions

Adherence: the extent ofstudy participants behaviour, taking medication

Adult: a person whose age is ≥18 years.

Alcohol drinking: The study participants who drink alcohol currently.

Body Mass Index (BMI): BMI is calculated by dividing the body weight in kilograms by height in meters squared (kg/m^2).

Cigaratte smoking: The study participants who actively smoke cigarette currently.

Phase of anti TB treatment Continious phase and intensive phase): refers to in Ethiopia the first line anti TB drug formulations for adults are given in a fixed dose regimen, with HRZE (75mg/150mg/400mg/275mg) for for insensive phase and HR (75mg/150mg) for continous phase.The dose based on patients weigt(17).

Diabetes mellitus:fasting plasma glucose value ≥ 126 mg/dl or RBS>200mg/dl.

Drug induced liver injuries: refers toalanine amino transferase (ALT) ≥ 5 times the upper limit of normal (5 × ULN) or ALT ≥ 3 × ULN with total bilirubin > 2 × ULN (29).

Elevated serum liver enzymes:refers to an enzyme which is above the upper limit of normal values (ULN) based on reference ranges of HUMASTAT100/200 analyzer kit(Human reagent kit); for male ALT > 40U/L, AST > 40 U/L, ALP > 129, and GGT > 60 U/L. For female ALT > 33U/L, AST> 32 U/L, ALP > 104, and GGT > 40 U/L.

Fasting blood Sugar: Glucose value after 8 hours of food abstinence.

Good medication adherence: When the participantstake anti TB drugs regularly.

Intensive phase:a patients *first phase two months* of the anti TB drugs used

Liver enzymes are enzymes include alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma glutamyl-transferase (GGT).

Poor medication adherence: When the study participants missed regular takingof anti TB drugs

Metabolic disorder; is refers to disorder of glucose (carbohydrate) metabolism (hyperglycemia)

CHAPTER ONE INTRODUCTION

1.1. Background Information

Tuberculosis (TB) is a bacterial infection caused by the acid fast bacillus mycobacterium tuberculosis. It is a chronic infectious disease resulting from many strains of mycobacteria(1).This organisms mostly affects the lungs and may also enter the blood stream and cause the infection in other organ such as kidney, brain, spine and other vital organ, this is known as extra pulmonary tuberculosis. Pulmonary (2). In the extrapulmonary tuberculosis bacteria may go in the blood stream and cause the infection in other organ such as kidney, brain, spine and other vital organ in similar ways(3).

The liver is the largest organ in the human body.It performs a number of functions essential for life(4).These functions includes receiving, processing and storage of materials absorbed from the digestive tract such as amino acids, carbohydrate, fatty acid ,cholesterol and vitamins (5).It also plays a critical role in the metabolism of drugs and xenobiotic,and may leading to a peculiar risk of toxic effects(6).

TB has effect in liver in three forms. The most common form is the diffuse hepatic involvement seen along pulmonary or miliary tuberculosis. The secondform is diffuse hepatic infiltration without recognizable pulmonary involvement. While the third and much rare form is presents as a focal/local tuberculoma or abscess(7). Tuberculosis is prooxidant state as active inflammation involves activated inflammatory cells that secrete cytokines and free radicals. There is progressive decline in plasma antioxidant activity and increasing oxidative stress causing organ damage including liver in TB patients (8,9).

Metabolic derangements are infrequent in patients with tuberculosis. The metabolic abnormalities may produce direct infection of the organ or gland by Mycobacterium tuberculosis bacteria or as a result from physiological response or as a consequence of therapy (10).

TB induces a state of secondary hyperglycemia and insulin resistance in individuals with or without a history of DM(11,12).As an infectious disease, tuberculosis increases insulin resistance and stress-induced hyperglycemia, which may lead to over diagnosis of DM during the acute phase of tuberculosis(13).

It is hypothesised that the stress experienced during a significant long-term infection (such as TB or HIV) could result in increased IR. As a result of infection with the mycobacteria, macrophages, which form a vital part of the innate immune system, are often the first line of defence against these harmful organisms(14). As is found with any infection, an increased amount of pro-inflammatory cytokines (such as IL-6 and TNF-α) is usually produced. This inflammatory attempt by the body to ward off possible pathogens such as TB might have a role to play in increasing IR, subsequently lowering insulin production and ultimately leading to hyperglycemia.This process may also be accompanied by the release of certain stress hormones such as epinephrine, cortisol and glucagon, which further impair the action of insulin (15).

The treatment of tuberculosis primarily starts with four drugs. The drugs prescribed are called as the extensive period or initial phase which lasts for two months after the continuation period in which drugs are reduced to two which endures for 4-8 months subjected condition of patients(16). These anti tuberculosis treatments though very effective. The drugs are having many side effects mainly on the liver of the patient. As compared to another treatments such antimicrobial and anticonvulsants etc. anti tuberculosis treatment is establish to be main source of drug induced hepatitis or hepatotoxicity.These drugs can cause severe adverse reactions including hepatotoxicity (17).Unfortunately almost all the chemotherapeutic agents used in tuberculosis cause hepatotoxicity by single or multiple mechanisms.The defeat of the liver is one of the main causes of the development of drug intolerance in tuberculosis due to the leading role of this organ in the system of detoxification. The frequency of toxic medicinal hepatitis is 4-16% of complications of drug therapy; it increases with the duration of drug intake(18).

With this background this study was conducted to determine liver enzymes such as alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP) and gamma-glumamyl transferase (GGT) analyzing using HUMASTAR 100 analyzer.The study was also meant to determine metabolic disorder using blood sugar test which were analyzed using using HUMASTAR 100 chemistry analyzer

1.2 Statement of Problem

Tuberculosis (TB) is one of the erliest amajor health risk, and socioeconomic burden in both developing and industrialized countries that kill approximately 2 million people annually. Worldwide it has been identified as one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS)(20).The severity of national TB epidemiology varies significantly among countries. According to WHO 2019 report ranking of regions/ countries which developed TB :South-East Asia (44%), Africa (25%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8.2%), the Americas (2.9%) and Europe (2.5%). Eight countries accounted for two- thirds of the global total: India (26%), Indonesia (8.5%), China (8.4%), the Philippines (6.0%), Pakistan (5.7%), Nigeria (4.4%), Bangladesh (3.6%) and South Africa (3.6%) (20).

WHO member countries have agreed upon an ambitious target to achieve 25% reduction in TB incidence and 75% reduction in TB mortality between 2015 and 2025, and 90% reduction in TB incidence and 95% reduction in TB mortality by 2035. This ambitious target cannot be achieved unless the escalating burden of risk factors such as diabetes and liver enzymes abnormalities is properly addressed. (21,22).

The severity of national epidemics varies widely among countries.The TB incidence rate at national level varies from less than 5 to more than 500 new and relapse cases per 100 000 population per year. In 2019, 54 countries had a low incidence of TB (<10 cases per 100 000 population per year), mostly in the WHO Region of the Americas and European Region, plus a few countries in the Eastern Mediterranean and Western Pacific regions(20).

Hepatic transaminase elevation without clinical presentation is common and benign episode following anti TB treatment, but symptomatic hepatotoxicity can be fatal without any intervention. Due to the long duration of therapy and concurrent use of multiple drugs adverse effects are regarded as the most important clinical considerations in patients undergoing anti TB

treatment. Hepetotoxity is the most serious one, which not only leads to high morbidity and mortality but also diminishes anti TB treatment effectiveness owing to non adherence(17,23,24).

TB and hyperglycemia co-morbidity is considerably an emerging public health problem and TB is the third leading cause of death among patients with non-communicable disease (NCD), particularly DM. The WHO has identefied diabetes mellitus (DM) as a global epidemic, mostly affecting low- and middle-income countries where 80% of all deaths from DM occur. Simultaneously, tuberculosis (TB) continues to be a major cause of death worldwide despite the fact that the epidemic appears to be on the verge of a decline (20).

Consequently, the World Health Organization has recently identified DM as a neglected, important and reemerging risk factor for TB (1).While studies prior to 1950s could not distinguish between coincidence or association between TB and DM, Union Against TB and Lung Disease Union have acknowledged the need for international guidelines on the joint management and control of TB and DM and have published a provisional collaborative framework for the care and control of both diseases (25).

In sub-Saharan Africa, a systematic review and meta-analysis of observational studies revealed that the prevalence of diabetes mellitus among tuberculosis patients was 9.0%.The highest prevalence was found in Nigeria 15% followed by Tanzania 11% and then Ethiopia 10%. Besides, the prevalence of diabetes mellitus among HIV infected TB patients was(8.9% which is slightly higher than HIV uninfected 7.7% TB patients(26).

A study conducted in Ethiopia ,Hawassa Adare Hospital Pulmonary Tuberculosis and Associated Factors Among Diabetic Patients showed the prevalence of 5.3% and a number of risk factors were observed like underweight, had more than 10 years duration with DM, Alcohol drinking habit and history of contact with TB were the factors positively associated with pulmonary TB infection (27).

Despite different literatures from several countries showed that abnormal levels of liver enzymes and metabolic disorder were important for diagnosis, treatment,prognosis,drugresponse and evaluation of tuberculosis severity.Therefore this study was primarly focus to evaluate lever enzyme disorder, metabolic disorder and factors associated with liver enzymes and metabolic

among tuberculosis patients on anti TB treatment at Jimma town health facilities,south west Ethiopia.

1.3. RATIONALE OF THE STUDY

The reason selecting this topic is that TB is one of the factors for the development of liver impairment and metabolic disorder and a public health problem as well as a socioeconomic Challenge.WHO and union against tuberculosis and lung disease is recommend assessment of liver enzymes monitoring and blood glucose level for the patient on anti TB treatment. However, the magnitude of elevated liver enzymes among TB patients in Ethiopia, particularly in Jimma is unknown. So the aim of this study is to assess the liver and metabolic disorder and associated factors.

1.4. Significance of the study

Tuberculosis is one of the risk factors for the development of liver impairment and metabolic disturbance. The initial and most important indicators in assessing liver injury is the measuring level of serum ALT, AST, ALP and GGT. However, the magnitude ofliver and metabolic disorder among TB patients in Ethiopia, particularly in Jimma is unknown.Therefore, this study is aimed to assess the prevalence of liver enzymes elevations and metabolic disorder and associated risk factors among TB patients attending Jimma town public health facilities.

The finding of the study may be used for health care policymakers to develop strategies to reduce morbidity and mortality of TB patients from TB-associated liver disease and metabolic disturbance and also to create awareness among TB patients and health care professionals to take care of liver function impairment due to Tuberculosis . Furthermore, it may be used as a baseline reference for other researchers those have interest to conduct similar or related studies.

CHAPTER TWO: LITERATURE REVIEW AND CONCEPTUAL FRAMEWORK

2.1. LITERATURE REVIEW

Tuberculosis is a major cause of preventable infectious disease and death in the world. Timely diagnosis and proper chemotherapy are the mainstays of treatment.Disturbances in liver function and structure in patients with tuberculosis can be a consequence of the effect of tuberculosis intoxication, hypoxemia, antituberculosis drugs, concomitant diseases, tuberculosis lesion of the hepatobiliary system. The effect of tuberculosis intoxication affects the enzymatic, protein-synthetic, coagulation, excretory functions of the liver which causes a decrease in the volume flow of the organ and a slowing of the elimination of drug substances. Common forms of tuberculosis can be accompanied by hepato- megaly (28).

The hepatotoxic side effect of anti tuberculosis treatment (ATT) has been under extensive discussion and studies to confirm their frequency and outcome in patients, all over the world. However, it is a surprising fact that most of this research work has been done in the west and in the more developed nations.As defined as based on international expert working group consensus statement DILI was defined as peak amino tarnsferase (ALT) ≥ 5 times the upper limit of normal (5xULN) or ALT≥ 3 × ULN wuth total blirubin > 2 × ULN(29).

According to a study conducted in Europe anti-tuberculosis chemotherapy is associated with abnormalities in liver function tests in 10–25% of patients. Clinical hepatitis develops in about 3%, though estimates vary, and in these patients there is likely to be significant morbidity and mortality. On the basis of reported cases of tuberculosis, 160 patients in England and Wales can be expected to develop drug-induced hepatitis due to anti-tuberculosis therapy each year (30).

A study was conducted in Ireland on predictors of hepatotoxicity among patients treated with antituberculous on medication on a total of 170 (62%) male and 105 (38%) female patients with active TB with a mean age of 44 years. A total of 15 patients (6%) required their medication to be stopped or altered as a consequence of hepatotoxicity (31).

A study conducted in Taiwan on the role of regular liver function monitoring in antituberculosis drug-induced liver injury from a total of 1062 patients were included, and of them 469 (44.2%) received regular liver function monitoring (good monitoring group).Antituberculosis drug-induced liver injury ATLI was recognized in 100 (9.4%) patients. The good monitoring group detected more ATLI cases early compared with the poor monitoring group (14.7% vs 5.2%, and 21.4 vs 61.6 days, $p < 0.01$), with a lower peak serum alanine aminotransferase (276.1 vs 507.1 IU/L, $p = 0.05$)(32).

Another study conducted in Thailand on characteristics and risk factors for antituberculosis drug-induced liver injury in a cohort of patients with cirrhosis in a tertiary referral university teaching hospital showed that (9.4%) patients developedantituberculosis drug-induced liver injury with the median duration from ATD initiation of 14 days (range: 6–66). All the 6 patients who developed ATDILI received 3 hepatotoxic ATDs (isoniazid, rifampin, and pyrazinamide) and had child–turcotte–pugh class B cirrhosis. The patients with ATDILI were found to have a higher percentage of human immunodeficiency virus (HIV) infection than patients without ATDILI (50% vs. 8.6%; $P = 0.02$ (33).

A prospective study conducted in India on abnormal liver function test patterns in patients receiving anti tuberculosis therapy levels incomparison between before treatment and 2 months treatment showed a significant increase in the level of AST, ALT, and ALP, viz., 51.6±3.92, 42.7±3.21, and 129±3.2 (U/L), respectively, as compared to pre-treatment levels(34).

Another study conducted at Rims, Ranchi in India on changes in liver enzymes (ALT & AST) with antitubercular treatment in newly diagnosed sputum smear positive patients showed that the baseline enzyme levels before therapy was within normal limits. Mean ALT level was 19.28±4.7IU/ltr while mean AST level was20.20±5.6 IU/L.After 1 month of treatment most of the patients showed increase in liver enzymes, but were mostly asymptomatic with <3 fold elevation of serum transaminases. Mean ALT level at 2month was 64.10±31.8 IU/L while mean AST level 48.42±12.0 IU/L. Thus at the end of intensive phase of treatment serum transaminase levels were in increasing trend. Mean ALT level at 3 month was 51.32±14.9IU/L while mean AST level 40.60±8.8U/L.There was a decrease in transaminase level in continuation phase of treatment. This shows the additive effect of multidrug therapy(35).

Another study conducted in Pakistan on derangement in liver enzymes among patients undergoing anti tuberculosis therapy showed that 12 patients had deranged liver function test while 102 patients had normal liver function test after 4 weeks of treatment while 10 patients had deranged LFTs and 104 patients had normal LFTs after 8 weeks of treatment(36).A cross sectional study conducted in Iran on risk factors and pattern of changes in liver enzymes among the patients with anti-tuberculosis drug-induced hepatitis showed 5.5% cases had drug-induced hepatotoxicity (37).

Astudy was conducted in Egypt on evaluation of drug induced liver injury in tuberculosis and hepatitis co infection by liver fibrosis index score on 195 tuberculosis patients, age (19-61) years old. Of those, 62% (non hepatitis) were control, 31% Hepatitis C virus(HCV), 5% Hepatitis B (HBV), 2% were both HepatitisB and C(HB-C). Average baseline fibrosis indices in groups respectively were 0.81, 1.41, 0.70, and 1.47. Overall drug induced liver injury (DILI) was 7%, 31%, 30%, 75%respectively(38).

Astudy was conducted in Ethiopia on among 103 HIV-Positive and 94 negative Patients, all patients were evaluated for different risk factors and monitored biochemically and clinically for development ofdrug induced hepatotoxicity (DIH). Sub-clinical hepatotoxicity was observed in 17.3% of the patients and 8 out of the 197 (4.1%) developed clinical hepatotoxicity (39).

In Ethiopia study conductedon incidence of atni-tuberculosis drug induced hepato toxicity and associated risk factors among tuberculosis patients in Dawuro zone showed that the incidence of DIH was 8%(40). Other research carried out on anti-tuberculosis drug induced hepatotoxicity among TB/HIV co-infected patients at Jimma University Hospitalrevealed that incidence of anti-TB drug induced hepatotoxicity was 11.5%(41)

Other research carried out DM among TB patients the systematic review revealed that there is a high burden of DM among TB patients at global level, the prevalence was 16% ,the highest prevalence was observed in the studied countries of Asia, North America and Oceania (42).Another study conducted in Europe Co morbidity TB-DM TB net Prevalence Survey and Case-Control Among TB patients, DM prevalence overall was 10.7% and ranged from 4.4% in Greece to 28.5% in the United Kingdom (43) .Another study conducted in Georgia the prevalence of co-morbid DM among patients with TB disease,11.4% (44).

A study conducted in India showed that, the prevalence of diabetes among TB patients was 15.29% among them 8.23% were known DM cases and 7.06% were newly diagnosed cases (45). Among diagnosed cases of tuberculosis registered at a tuberculosis unit of Bhopal city, Madhya Pradesh,15.4% were found to have DM and 11.3% had previous diagnosis of DM; 4.09% were newly diagnosed (46). Another study conducted among admitted cases in a tertiary care hospital of North India indicated that a significant proportion of diabetic patients had coexistent tuberculosis 65.5%. In addition, the double burden of tuberculosis and diabetes prevalence of diabetes mellitus in tuberculosis prevalence of diabetes among TB patients was found to be 24.5% of which 18.5% were known DM cases and 5.9% were newly diagnosed (47).

A study in Laos,Maho sot Hospital diabetes mellitus among tuberculosis patients admitted to the pulmonary-tuberculosis ward 24.12% had DM, of which 68(75%) previously diagnosed, 31.25% new diagnosis at TB diagnosis(48). Another study conducted in Sri Lanka to assess the prevalence of DM among TB patients was 22.5 %(49).

A community-based study conducted in china on hyperglycemia associated with increased risk of patient develop pulmonary tuberculosis was 26.5 %(50). Another study conducted to assess the change in blood glucose levels in tuberculosis patients before and during anti-tuberculosis treatment patients without diabetes mellitus (DM) whose initial Fasting blood glucose (FBG)< 6.1 mmol/L, over 90% maintained FBG < 6.1 mmol/L during treatment and no patient developed DM. patients without DM and initial FBG between 6.1 and 6.9 mmol/L, over half had FBG < 6.1 mmol/L during treatment and no patient had DM at the end of treatment (51).

In sub-Saharan Africa, a systematic review and meta-analysis of observational studies revealed that the prevalence of diabetes mellitus among tuberculosis patients was 9.0%.The highest prevalence was found in Nigeria 15% followed by Tanzania 11% and then Ethiopia 10%. Besides, the prevalence of diabetes mellitus among HIV infected TB patients was(8.9% which is slightly higher than HIV uninfected 7.7% TB patients (52).

A study conducted in Cape Town, South Africa the prevalence and determinants of active tuberculosis among diabetes patients among DM patients screened, the active TB prevalence was 3.0% prevalent TB cases, 53.9% had no TB symptoms, and 61.5% were HIV–1 co–infected (53).

Another cross-sectional study was conducted at a TB clinic in Cape Town (South Africa)on overlap of tuberculosis,diabetes and HIV, diabetes was associated with TB (OR 2.4, 95% CI 1.3–

4.3; p=0.005),with 14% population-attributable risk fraction ,the association in HIV-1-infected individuals 2.4,%. A high prevalence of impaired glucose regulation 65.2% among TB cases and a significant association with TB 2.3,% (54).

A study conducted inNigeria the clinical profile of diabetes mellitus in tuberculosis DM/TB comorbidity was 12.3% (55). Another nationwide population-based study in Egypt Screening for DM among 1435 TB patients' with no history of DM detected 30 new cases of DM, with a case detection rate of 2.09% (56). A study conducted in Ghana the prevalence of DM among TB cases was 9.4% (57).

Across-sectional study screening tuberculosis patients for diabetes mellitus in a routine program setting in Kampala, Uganda among TB patients registered, 88.0% were screened with random blood glucose (RBG). Of those with RBG ≥6.1mmol/l, 83.3% were screened with FBG. In total, 2.3% patients were diagnosed with DM and 71.8% of them were newly diagnosed. (58).A study conducted in Nairobi and Kiambu countries in Kenya among TB and TB/DM co morbidity DM prevalence Glycated haemoglobin (HbA1c>6%) among TB infected patients was 37.2%(59).

In Ethiopia different studies were conducted at different regions. A cross sectional study conducted in South-Eastern Amhara Region the prevalence of DM was estimated to be 8.3% being a pulmonary TB case 1.69%, and having a family history of DM was 4.54% (60). A cross-sectional study conducted in Dessie referral hospital on smear positive pulmonary tuberculosis patients the prevalence of smear positive PTB was 6.2% and a number of risk factors were observed in other population in our country like ages, urban residence, history of TB , contact with TB patients in the family and long duration of DM that were independently associated with the development of active TB in people living with DM (61).

A study done in Hawassa Adare Hospital pulmonary tuberculosis and associated factors among diabetic patients the prevalence was 5.3% and a number of risk factors were observed like underweight, had more than 10 years duration with DM, alcohol drinking habit and history of contact with TB were the factors positively associated with pulmonary TB infection (27).

Another study conducted in Diredawa Eastern Ethiopia among adult tuberculosis patients the prevalence of diabetes mellitus was 13.5% and age 26-40 (AOR=6,95%CI: 1.28,27.5), age≥41(AOR=9,95%CI:(1.9,44.4)),andfamilyhistoryofdiabetes(AOR=3.14,95%CI:(1.23,8.02)we refoundtohaveasignificantassociationwithdiabetes mellitus(62).Even though different studies

were conducted nationally and internationally giving due attention to this dual problem almost all of them were conductedwhich couldn't represent the present status but the present study is assessment of serum liver and metabolic inJimma, south west part of Ethiopia.

2.2. Conceptual frame work

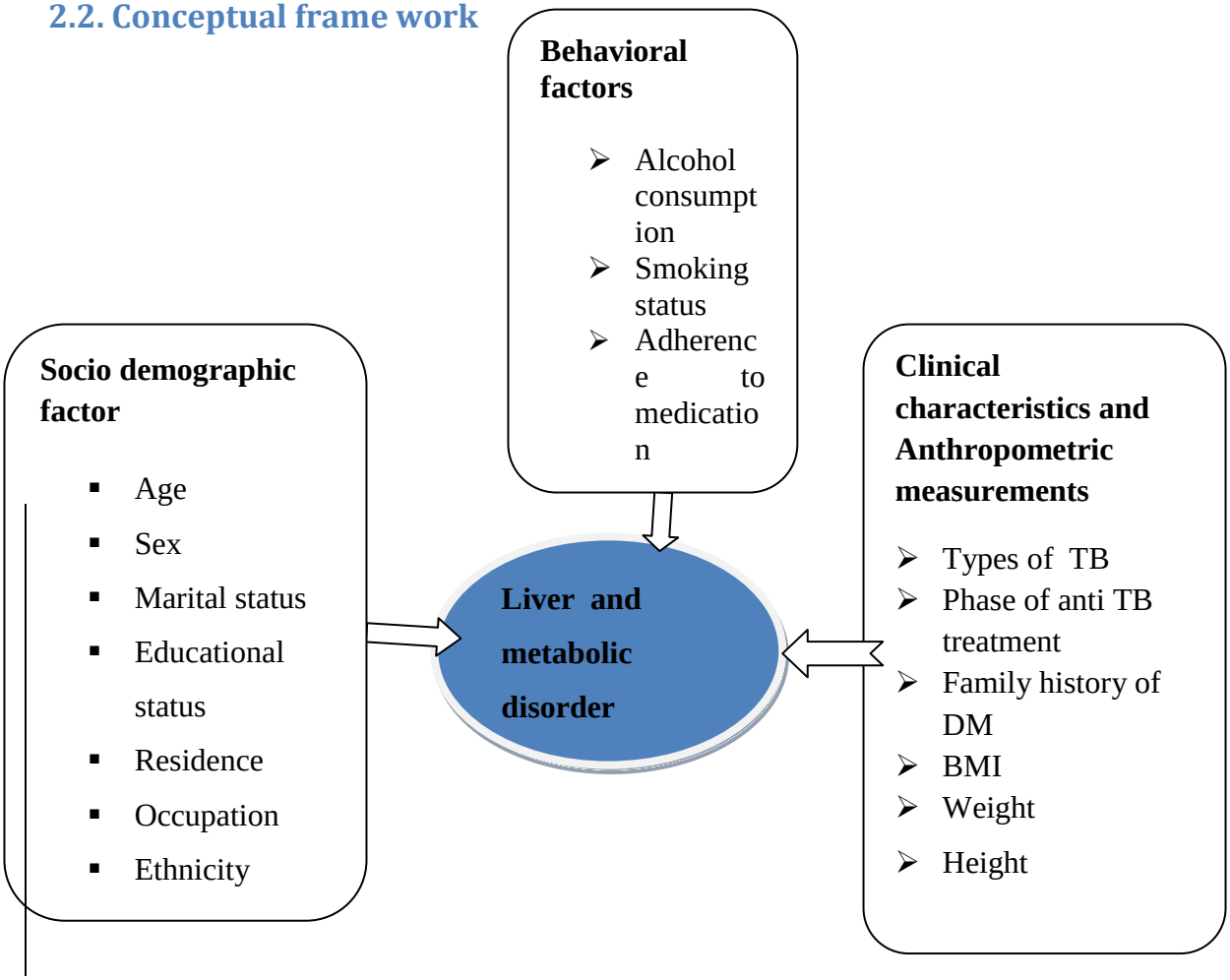

Figure 21: conceptual frame work that indicates liver and metabolic disorder associated with different variable

CHAPTERTHREE: OBJECTIVES OF THE STUDY

3.1. General objective

To assess prevalence and associated risk factors of liver and among TB Patients on treatment at Jimma town health facilities,south west Ethiopiafrom October 2020 to February 2021.

3.2.Specific Objectives

- To determine prevalence of hyperglycemia among patients with tuberculosis in Jimma town public health facilities, Jimma, Ethiopia from October 2020 to February 2021
- To determine prevalence of ALT, AST, ALPand GGT elevation among TB patientsin Jimma town public health facilities, Jimma, Ethiopia from October 2020 to February 2021
- To identify factors associated with elevation of ALT, AST, ALP,GGT and hyperglycemia among TB patientsin Jimma town public health facilities, Jimma, Ethiopia from October 2020 to February 2021

CHAPTER FOUR: METHOD AND MATERIAL

4.1. Study Area and Setting

The study was conducted inJimma town public health facilities at Jimma medical center,Jimma health center one,Jimma health center two and mendera kochi health center,from October 2020 to February 2021.Jimma is found oromia region located in south west direction 352 km from capital Addis Ababa.

Jimma medical center was established 1937 by Italian invenders for the service of solidoers.After the withdrawal of the colonial occupants, it has been governed under the Ethiopian government by the name of Ras Desta Damtew Hospital and later Jimma Hospital "during Dergue regime and currently renamed as Jimma University Medical Center. It is the only teaching and referral hospital in the southwestern part of the country, providing services for approximately 18,000 inpatient, 160,000 outpatient attendants, 11,000 emergency cases and 4500 deliveries in a year coming to the hospital from the catchment population of about 15 million people. The hospital has many chronic follow-up clinics for both pediatric and adult patients. The hospital has a directed observed treatment short course (DOTS) clinic where TB patients are treated and monitored according to the national guideline. All patients information, s and services given to TB patients vising the clinical have been registered on a TB log book available inthis clinic.

Jimma health center one,two and mendera kochi health centers found in Jimma city serving about 75000 people living in the town and serounding cutchment area in the town.The health centers had a directed observed treatment short course (DOTS) clinic where TB patients are treated and monitored according to the national guideline. All patients information, s and services given to TB patients visiting the clinical have been registered on a TB log book available inthis clinic.

4.2. Study design and time of the study

Institutional-based cross-sectional study design was conducted.

4.3. Source population

All patients attending those health facilities during the study period were source population.

4.4. Study Population

All TB patients who visiting selected health facilities and fulfilling the inclusion criteria were used as the study population

4.5. Sample size and sampling technique

The sample size was calculated using single-population proportion formula, with the following assumptions:

The estimated proportion (p=0.135%)was taken from reviewed literature, a study conducted at Diredewa to which the prevalence of DM among TB patients was 13.5%(60). Whereas margin of error (d=0.05), 95% confidence interval (CI), Zα/2 = the standard normal value for 95% confidence interval (1.96) and n=total sample size

$$n = \frac{(Z\alpha/2)^2 P(1-P)}{d^2}$$

$$n = \frac{(1.96)^2 * 0.135 (1-0.135)}{(0.05)^2}$$

n = 179

There were one Hospital and three health centers providing TB treatment in Jimma town at the time of study.Samples were taken from each Hospital and Health centers according to their patient load after determining 'k' from total study population and sample size. Hence: K= n/N=179/300=0.6. Where n= 179, N is total of TB patients all health facilities that on anti TB treatment N=H1+H2+H3+H4 n=n1+n2+n3+n4

$n_i =$ Ni* K, where Ni=number of patients on anti TB at the respective Hospital

Table.1. Shows sampling technique of TB patients attending at jimma town public health facilities from October2020 to January 2021 south west Ethiopia

S.NO	Hospital(Health facilities)	No of source population (patient on anti TB)	Final sample size from respective Hospital and health centers
1	Jimma medical center(H_1)	167	100
2	Jimma Health center one($H_{2)}$	59	36
3	Jimma Health center two(H_3)	42	25
4	Mendera kochi Health center(H_4)	29	18
	Total	300	179

Convenient sampling technique was implemented and the samples were taken consecutively until the quota given for the respective health facility is attained. A total of 179 TB patients those fulfill inclusion criteriawere included in this study.

4.6. Inclusion and exclusion criteria

4.6.1. Inclusion criteria

All selected inmates those willing to participate in the study were included in the study.Ages of between 18-65 years old were included after their consents approved.

4.6.2. Exclusion criteria

Individuals whowere known DM cases, HIV positive patients,hadhistory of liver disease or clinical evidence of acute hepatitis,subjects sero positive for HBsAg and HCV antibodieswere excluded . Patients who refused to participate or not signed informed consent form and who failed to fast for the next appointmentwere exclude from the study.

4.7. Variables

4.7.1. Dependent variables

- Eleveted serum liver enzymes (AST,ALT,GGT and ALP) and Fasting Blood Sugar

4.7.2 Independent variables

- Socio demographic (Age ,Sex ,Residence,Educational status,marital status, Smoking ,Alcohol consumption)
- Clinical check list
    - Tuberculosis type
    - Phase of anti-TB treatment
    - Family history of DM
    - Medication adherence to anti-TB
- Anthropometric (BMI ,Height ,Weight)

4.8. Data collection and measurements

4.8.1. Socio-demographic, Behavioral and Clinical Data

Data were collected by trained data collectors under supervision of principal investigator via structuredquestionnaire. The first part of questionnaire involves socio-demographic characteristics of patient's such as age, sex, occupation, educational status, marital status and residence of participants. The second part includes about life style of patients such as alcohol consumption, habit of cigarate smoking,family history of diabetes and adherence to medication. The third part involves types of tuberculosis,phase of treatment were collected by review of medical card and history of liver disease were collected by face to face interview.

4.8.2 Anthropometrical Measurements

Weight and height were measured by using a digital weighing machine and height scale respectively. BMI was calculated as weight divided by heightsquare in meters. During the height measurement, the study participant's shoes and any hats or hair ornaments were removed. With the subject looking straight ahead, the projection was placed at the crown of the head and with the reader's eye at the level of the headpiece. Then the height was taken in meter.The WHO definition of obesity is based on various categorical cut-points based on the body mass index (BMI) of weight-for-height: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2) and overweight (25.0–29.9 kg/m^2) (63).

4.8.3. Laboratory Analysis and Biochemical Test

The study participants were asked for informed consent to be interviewed and to give blood sample. About 5 mL blood was drawn with gel separator tube from each study participant who was fasting overnight to determine the levels ofALT,AST,GGT,ALPin IU/L andfasting blood glucose in milligram per deciliter.The results of fasting blood glucose and liver enzymes were reported immediately to the physician.

Serum of all individuals were screened for HBsAg by using Onsite HBsAg rapid test cassette and for anti-HCV by using HCV rapid test Cassette in order to exclude patients those infected with hepatis B virus, and hepatitis C virus.None of study partcipants positive for HCVab butfor HBVsAg two patients positive.The two patients was excluded from our study and replace it.

Biochemical tests such as fasting blood glucose (FBS), serum alanine aminotransferase activity (ALT), serum aspartate aminotransferase activity (AST), serum alkaline phosphatase activity(ALP), and serum gamma-glutamyltransferase activity (GGT) were analyzed by HUMA STAR100/200 automated clinical chemistry analyzer according to the manufacturer's instruction and laboratory standard operation procedures.

Serum glucose: was analyzed on the HUMA STAR100/200 clinical chemistry analyzer, using the glucose oxidase (GOD) method. Glucose is oxidized by glucose oxidase to gluconate and hydrogen peroxide. Phenol + 4-AAP + hydrogen peroxide, in the presence of peroxidase, produce a quinoneimine dye that is measured at 500nm. The absorbance at 500nm is proportional to the concentration of glucose in the sample.

Serum ALT activity: was measured by an enzymatic rate method. In the reaction, ALT catalyzes the reversible transamination of L-alanine and α-ketoglutarate to pyruvate and L-glutamate. The pyruvate is then reduced to lactate in the presence of lactate dehydrogenase (LDH) with the concurrent oxidation of NADH to NAD. The catalytic activity of alanine aminotransferase is determined by measurements of the rate of NADH oxidation in reaction. The system monitors the rate of change in absorbance at 340 nm over a fixed time interval. The rate of change in absorbance is directly proportional to the ALT activity in the sample.

Serum AST activity: was also measured by an enzymatic rate method on HUMA STAR100/200

analyzer in which AST reversibly catalyzes the reaction of aspartic acid with alpha-ketoglutarate to yield oxaloacetate and glutamate in presence of co-factor B6 (pyridoxal phosphate). The resulting oxaloacetate is then catalyzed with malate dehydrogenase, which converts the oxaloacetate to malate. NADH is converted to NAD, the rate of change in absorbance at 340 nm over a fixed time interval is recorded.

Serum ALP activity: was determined by measuring the rate of hydrolysis ofρ-Nitrophenyl phosphate to ρ-nitrophenol and inorganic phosphate.The rate at which the ρ-Nitrophenyl phosphate is hydrolyzed, measured at 405 nm, is directly proportional to the ALP activity.

Serum GGT activity: was determined by modified kinetic method in which GGT catalyzes the transfer of the glutamyl group from gamma-glutamyl-3-carboxy-4-nitroanilide to glycylglycine and 5-amino-2-nitrobenzoate. The change in absorbance at 410/480 nm is due to theformation of 5-amino-2-nitrobenzoate and is directly proportional to the GGT activity in the sample.

4.9. Data qualitymanagement

Data quality of questionnaire, laboratory investigation and anthropometric measurements were assured by following mechanism, checking consistence of questionnaire meaning as English version translated to Amharic then to Afaan Oromo and Amharic and back translation to English by language expert. Training was given for data collectors.

To maintain quality of laboratory data daily maintenance of clinical chemistry analyzer was done, standard operating procedures were followed during specimen collection and processing of sample, daily quality controls were done for fasting blood glucose,ALT,AST,GGT and ALPtests beforerunning patient sample.Expiration date for all reagents were checked, calibration was done for new reagent lot number and all the laboratory process was supervised by principal investigators. To keep quality of anthropometric measurements calibrated weight and height measuring instrument was used. Furthermore data were entered in epidata version 3.1, which improve data quality.

4.10. Statistical analysis

The collected data were reviewed and checked for completeness and consistency by principal investigators on daily bases at the spot during the data collection time. After filtered and checked for their completeness, data were entered to epi-info version 7 and exported to excel then to SPSS. SPSS version 26was used to analyze recorded data. Mean ± SD were used to summarize continuous variables, whereas frequencies and percentages were used to express categorical variables. Binary logistic regression was computed to assess statistical association via calculating odds ratio to see the association of independent variables and dependent variables, and the significance of statistical association was assured or tested using 95% confidence interval and P-value (<0.05),during multivariable analysis model fitness has been checked by Hosmer Lemeshow model fitness

4.11. Ethical consideration

Ethical clearance was obtained from the Institutional review Board of faculty Health Sciences, Jimma University(IRB000135/2020).Letter of cooperation was written from Jimma university research coordination office to JMC and health facility focal person.Then permission was obtained from the clinical directors of JMC andthe focal person of health facility.Data collectors were trained on how to approach the study participants, and on the contents of the study. Participation in the study was based on each participant's willingness. Voluntarily informed written and signed consent was taken from each participant after explanation of the study purpose, risks, benefits and rights given to them and they were declare with their signatures.The purpose, benefit and method of the study were clearly explained to participant with the language they can understand. All of participants were informed that, their response would be kept confidential. To ensure confidentiality of data, study participants were identified using codes and unauthorized persons were not able to access the collected data. In addition, the clinical specimen collected during the study period wasused for the stated objectives only. The study participants' result was reported to the physician for proper management as necessary**.**

4.12. Result dissemination plan

The findings will be presented to Jimma University, Faculty of Health Science, School of Medical Laboratory Sciences. It will also be disseminated through publication on peer reviewed scientific journals and presented on scientific conferences. The study finding and recommendation will be given toconcerned body. The copy of the result will be submitted to Jimma University Faculty of Health Sciences.

Chapter Five: Results

5.1. Socio-demographic, anthropometric, and clinical characteristics

Among 179 adult TB confirmed patients enrolled in this study, 93 (51.7%) were males and 86(47.8%) were females. The age group ranged from 20-67 with mean age of 43 years.About 122 (68.2%) of participants were from urban, and 57(31.8%) were from rural. The majority of the participants were Oromo by their ethnicityand background 101(56.4%). From a religious point of view, Islam, Orthodox and protestant constituted 84(56.8%), 40 (27%) and 23(15.5%) respectively. Regarding marital status, majority were married (58.7%) followed by single (37.4%). Regarding their educational background majority of the participants, 72(40%) were from primarily school (1-8) and 9(5%) attended their education up to college and university level. About 141 (78.8%) of study participants were non alcohol consumer (Table:2**)**.

Table 2:Sociodemographic characteristics of TB patients attending at jimma town public health facilities from October2020 to January 2021 south west Ethiopia

Variables	**Category**	**Frequency N**	**Percentage (%)**
Age in years	<25	56	31.3%
	25-34	66	36.8%
	35-45	31	17.4%
	46-54	12	6.7%
	>55	14	7.8%
Sex	Male	93	51.9%
	Female	86	48.1%
Educational level	No formal education	36	20.1%
	Primary(1-8)	72	40.2%
	Secondary (9-12)	62	34.6%
	Diploma and above	9	5.1%
Marital status	Single	67	37.4%
	Married	105	58.7%
	Divorced	7	3.9%
Residence	Urban	122	68.2%
	Rural	57	31.8%
Occupation	Farmer	45	25.1%
	Merchant	71	39.7%
	Government	28	15.6%

	employed	35	19.6%
	Other		
Religion	Muslim	99	55.3%
	Orthodox	52	29.1%
	Protestant	27	15.1%
	Others	1	0.5%
Ethnicity	Oromo	101	56.4%
	Amahara	53	29.6%
	Dawuro	16	8.9%
	Gurage	8	4.5%
	Others	1	0.6%
Smoking status	No	149	83.2%
	Yes	30	16.8%
Alcohol consumed	Yes	38	21.2%
	No	141	78.8%

Ninety one of study participants (50.6%) were pulmonary TB patients whereas the remaining 88(49.24%) were extra pulmonary TB patients. Majority of the study participants 111 (62%) was on intensive phase of treatment. Family history of diabetes were reported in 13 (7.3%). Medication adherence of anti TB were good for 74 (41.3%) and poor for 105 (58.7%) .The calculated BMI revealed that majority of the participants 90(50.3%) had BMI in the normal range (18.5-24.9 Kg/m²)(Table 3).

Table 3: Clinical and Behavioral Characteristics of TB patients attending at Jimma town public health facilitiesfrom October2020 to January 2021 south west Ethiopia

Variables	Category	Frequency	Percentages %
Types of tuberculosis	Pulmonary TB	91	50.6%
	Extra pulmonary TB	88	49.4%
Phase of anti TB	Intensive phase	111	62%
	Continuous phase	68	38%
Adherence to medication	Good	74	41.3%
	Poor	105	58.7%
BMI	<18.5kg/m2	77	43%
	18.5-24.9kg/m2	90	50.3%
	>25kg/m2		

		12	6.7%
Family history of DM	Yes	20	11.2%
	No	159	88.8%

Kg/m²- kilogram per meter square,

From 179 TB patients, 45 (25.1%) of participants were found to have one or more elevated liver enzymes. The Mean ±SD was 37.8±17for ALT, 35.7±15.4for AST, 289.7±94.5 for ALP, and 31.8±16.2for GGT. The elevated serum ALT activity among TB patients was 18.4% (n=33)with organ-specfic prevalence of 10.6% (n=19) in pulmonary TB and 7.8% (n=14) in extra pulmonary TB. The elevated serum GGT activity was 6.1% (n=11) in pulmonary TB and1.2% (n=2) in extra pulmonary TB. The elevated serum ALP activity was 7(3.9%). In 31 (17.3%) of TB patients both serum ALT and AST activities were elevated while in 7(3.9%) of participants both serum ALP and GGT activities were elevated.None of our study participants devlop drug induce liver injury .The overall eleveted blood glucose among study participants was (7.4%) .Hyper glycemia was higher in patients with pulmonary TB, 6.8 % than in patients with extra pulmonary 0.6%(Table 4).

Table 4: Mean value of the biochemical parameters in TB patients attending at jimma town public health facilitiesfrom October2020 to January 2021 south west Ethiopia

Biochemical parameters	Mean **±SD**	**Reference range**	TB prients with abnormal reference range	
ALT	37.8±17	0-45U/L(M)	33(18.4%)	19(10.6%) (PTB)
		0-35U/L(F)		14(7.8%) (EPTB)
AST	35.7±15.4	0-35U/L(M)	31(17.3%)	17(9.4%) (PTB)
		0-31U/l (F)		14(7.82%) (EPTB)
ALP	289.7±94.5	89-306U/L(M)	7(3.9%)	
		64-306U/L(F)		
GGT	31.8±16.2	0-55U/L	10(5.6%)	8(4.4%) (PTB)
				2(1.1%) (PTB)

FBS	95.3±30.73	>126mg/dl	13(7.3%)	6.1 %(PTB) 1.2%(EPTB)

5.3. Factors associated elevated serum liver enzymes among study participants

In this study, it was found that being male, pulmonary TB, intensive phase of anti TB treatment and government employed were significant predictors of elevated serum ALT in TB patients (P< 0.05). Male tuberculosispatients were 3.37 times (AOR=3.37, 95% CI: 1.164-9.78) more likely to have elevated serum ALT activity than those from females. On the other hand, the prevalence of elevated ALT was significantly higher in patients who have Pulmonary TB than those who have extra pulmonary TB patients (elevated ALT: 9.2% in pulmonary TB patients and 8.1% in extra pulmonary TB patients. In addition, in the intensive treatment phase of patients were 3.52 times (AOR=3.52, 95% CI: 1.154, 10.736) more likely to have elevated ALT than in the continuous treatment phase patients.

We observed that elevated AST was positively associated with living in the urban area: AOR=2.38, 95% CI: 1.02, 5.54, p=0.04. The prevalence of elevated AST was significantly higher in patients who are alcohol consumer (AOR=5.585, 95% CI: 0.809, 38.552, p=0.081) than in patients non alcohol consuming . Moreover, participants who have pulmonary TB were 8.43 times (AOR=8.43, 95% CI: 1.69-41.89, p=0.01) more likely to have elevated AST than those extra pulmonary TB patients.

This study showed that Urban recidence, age group of 25-34,merchant of occupation,intensive phase of treatment ,pulmonary TB, were significant predictors of elevated serum GGT in tuberculosis patients (p<0.05). Patients in age group of 25-34 were 4.4 times (AOR=4.41, 95% CI: 0.799,1.482, p=0.065) more reasonably to have elevated GGT. Urban residences were 0.011 times (AOR=0.011,95%CI: 0.000, .776) more likely to have elevated serum GGT than rural residents. Moreover, patients of merchant occupation were 0.001 times(AOR= 0.001,95% CI:0.000, .614). In addition, intensive treatment phase TB patients were 0.042times (AOR=0.042, 95% CI: 1.47-7.545) more likely to have elevated GGT than continuous treatment phase of TB patients(Table 5).

Table 5:Association between demographic, clinical characteristics and elevated ALT and AST in TB patients attending TB Jimma town Public health facilities, 2020.

Variables		ALT				AST		
		categories	COR(95% CI)	AOR(95 % CI)	P-Value	COR(95 % CI)	AOR(95% CI)	P-Value
Age	<25	60(33.5 %)	2.395(0.523,10.960)	0.397(0.253, 0.623)	0.260	2.202(.432,11.228)	0.169(0.019,1.494)	0.342
	25-34	32(17.8 %)	10.313(6.009, 17.702)	0.400(0.155, 1.031)	0.479	.875(.198, 3.865)	0.056(0.008,0.417)	0.860
	35-44	10(5.5%)	0.598 (0.144,2.485)	0.225(0.107, 0.477)	0.148	2.660(.554, 12.770)	0.155(0.027,0.884)	0.222
	45-54	15(8.3%)	2.777(0.697,11.072)	0.239(0.114, 0.502)	0.187	1.707(.227, 12.833)	0050(0.012,0.209)	0.603
	>55	62(34.6 %)	3.174(.571, 17.648)					
Gender	Male	94(52.5 %)	0.41(0.075-2.232)	3.376(1.164, 9.786)	0.025	2.416(.819, 7.129)	2.938(0.036,242.25)	0.110
	Female	85(47.4 %)	1			1		
Residence	Urban	131(73.1 %)	1.586(0.382,6.583)	3.391(0.766-15.0)	0.526	0.965(0.412-2.26)	2.38(1.02,5.54)	0.04
	Rural	48(26.8 %)	1			1		
Marital status	Single	67(37.4 %)	0.954(0.318-2.86)	0.336(0.168,0.670)	0.999	4.131(.000, .000)	0.210(0.017,2.520)	0.999
	Married	109(60.8 %)	4.45(1.389-14.44)	0.140(0.025,0.786)	0.999	1.196(.000, .000)	0.998(0.027,36.927)	0.999
	Divorced	3(1.6%)	1			1		
Occupation	Farmer	45(25.1 %)	0.398(.068, 2.328)	0.777(0.366,1.652)	0.307	1.199(.204, 7.051)	0.379(0.043,3.334)	0.841
	Merchant	92(51.3 %)	0.543(.106, 2.794)	0.530(0.267,1.052)	0.465	0.397(.063, 2.510)	0.336(0.033,3.381)	0.326
	Government employed	10(5.5%)	0.138(0.015, 1.242)	0.668(0.350,1.276)	0.077	0.179(.018, 1.739)	0.309(0.036,2.672)	0.138
	Other							
Educational levels	No formal education	36(20.1 %)	0.200(.013, 3.165)	2.645(0.913-7.66)	0.073	0.508(.034, 7.648)	0.344(0.101,1.167)	0.625

	Primary(1-8)	63(35.1%)	0.324(.025, 4.212)	1.503(0.601-3.76)	0.389	0.246(.020, 3.009)	0.093 (0.051, 0.172)	0.272
	Secondary (9-12)	68(37.9%)	0.276(.023, 3.324)	3.14(1.003-9.84)	0.311	0.879(.078, 9.905)	0.105 (0.063,0.173)	0.917
	Diploma and above	12(6.7%)	1	1	1	1	1	
Smoking status	No	155(86.5%)	1			1		
	Yes	24(13.4%)	1.765(.430, 7.236)	0.321(0.203, 0.507)	0.430	1.302(.314, 5.395)	0.105 (0.063,0.173)	0.716
Alcohol consumed	Yes	39(21.7%)	0.710(.145, 3.480)	0.178 (0.111, 0.287)	0.673	1.846(0.339-10)	5.585(0.809, 38.552)	0.041
	No	140(78.2%)	1			1		
Types of tuberculosis	Pulmonary TB	93(51.9%)	9.79(1.3,73.51)	1.67(0.134-3.1)	0.03	4.45(1.389-14.44)	8.43(1.69,41.89)	0.01
	Extra pulmonary TB	86(48.04%)	1			1		
Phase of anti TB	Intensive phase	112(62.5%)	0.965(0.412-2.26)	3.520(1.154,10.736)	0.027	2.546(.786, 8.250)		0.119
	Continuous phase	67(37.4%)	1			1		
Adherence to medication	Good	77(43%)						
	Poor	102(56.9%)	0.506(.188, 1.364)	0.072(0.042, 0.125)	0.178	2.339(.851, 6.429)	3.59(1.078,11.951)	0.100
BMI	<18.5kg/m2	77(42.8%)	1.269(.189, 8.532	3.213(1.433,7.201)	0.807	1.037(.197, 5.454)	0.91(0.044,18.838)	0.966
	18.5-24.9kg/m2	90(50%)	617(.250, 10.352)	0.388(0.187 ,0.805)	0.617	0.382(.076, 1.934)	4.83(1.628,14.351)	0.245
	>24.9kg/m2	12(6.7%)	1			1		
Family history of DM	Yes	16(8.9%)	1			1		
	No	163(91%)	0.419(.063, 2.798)	0.155(0.048,0.499)	0.369	0.294(.025, 3.408)	0.128(0.075, 0.220)	0.328

COR=Crude Odds Ratio, CI=Confidence Interval,*AOR: adjusted odd ratio*

Table 6: Association between demographic, clinical characteristics and elevated ALP and GGT in TB patients attending jimma town Public health facilities, 2020.

Variables		ALP categories	COR(95% CI)	AOR(95% CI)	P-Value	GGT COR(95% CI)	AOR(95% CI)	P-Value
Age	<25	60(33.5%)	0.916(.081, 10.400)	1.286(0.419-3.941)	0.944	1.846(0.339-10)	0.94(0.342-2.583	0.99
	25-34	32(17.8%)	6.913(.962, 49.653)	1.667(0.437-6.358)	0.055	1.46(0.28, 7.65)	4.411(0.799,1.482)	0.035
	35-44	10(5.5%)	0.439(.015, 12.985)	1.924(0.635-5.831)	0.634	7.099(.183, 275.965)	0.8(0.265-2.415)	0.294
	45-54	15(8.3%)	0.000(.000, .000)	0.9(0.148-5.489)	0.998	1.395(.033, 59.743		0.862
	>55	62(34.6%)						
Gender	Male	94(52.5%)	3.598(.477, 27.142)	1.067(0.573-1.987)	0.214	12.986(.379,445.104)	1.717(0.83-3.552)	0.155
	Female	85(47.4%)						
Residence	Urban	131(73.1%)	1.187(.123, 11.473)	1.538(0.722-3.279)	0.882	1.78(0.678-4.677)	0.011(0.000, .776)	0.038
	Rural	48(26.8%)						
Religion	Muslim	99(55.3%)	0.000(.000, .000)	1.508 (0.182-12.517)	0.998	0.014(.000, .000)	1.08 (0.505-2.308)	1.000
	Orthodox	52(29.1%)	0.000(.000, .000)	1.649 (0.839-3.24)	0.999	0.401(.000, .000)	1.013 (0.991-1.035)	1.000
	Protestant	27(15.1%)	0.000(.000, .000)	0.933 (0.503-1.729)	1.000	0.098(.000, .000)	0.646 (0.115-3.62)	1.000
	Others	1(0.5%)						
Marital status	Single	67(37.4%)	3.617(.000, .000)	0.511 (0.125-2.08)	0.999	1.465(.000, .000)	1.379 (0.448-4.24)	0.999
	Married	109(60.8%)	2.271(.000, .000)	0.617 (0.124-3.07)	0.999	2.333(.000, .000)	0.646 (0.115-3.62)	0.999
	Divorced	3(1.6%)						
Occupation	Farmer	45(25.1%)	3.233(.186, 56.303)	1.93(0.29,1.92)	0.421	0.044(.000, 4.320)	0.75(0.29,1.92)	0.182

	Merchant	92(51.3%)	1.383(.120, 15.928)	0.32(0.09,1.15)	0.795	0.001(0.000, .614)	0.648(0.328-1.281)	0.034
	Government employed	10(5.5%)	28.204(1.050,757.907)	0.56(0.20,1.151)	0.86 (0.48,1.57)	7.772(.075,805.527)	0.61(0.29,1.29)	0.386
	Other							
Educational levels	No formal education	36(20.1%)	9.43(3.88, 22.94)	1.78(0.678-4.677)	0.032	1.036(.005, 204.292)	0.66(0.33,1.31)	0.989
	Primary(1-8)	63(35.1%)	3.33(1.47-7.545)	0.954(0.318-2.86)	0.032	8.792(.093, 834.853)	0.75(0.39,1.43)	0.349
	Secondary (9-12)	68(37.9%)	6.139(.134, 282.297)	0.42(0.10,1.72)	0.035	1.628(.002, 1.257)	0.53(0.13,2.10)	0.886
	Diploma and above	12(6.7%)						
Smoking status	No	155(86.5%)						
	Yes	24(13.4%)	16.548(0.885,309.501)	0.47(0.12,1.84)	0.060	0.267(.018, 3.998)	0.85(0.37,1.93)	0.339
Alcohol consumed	Yes	39(21.7%)						
	No	140(78.2%)	0.188 (.010, 3.564)	0.90(0.07,11.00)	0.266	0.135(.003, 6.861)	1.05(0.10,11.01)	0.318
Types of tuberculosis	Pulmonary TB	93(51.9%)	2.854(.483, 16.881)	0.82(0.31,2.10)	0.248	70.210(1.265, 3.897)	1.49(0.206-10.8)	0.038
	Extra pulmonary TB	86(48.04%)						
Phase of anti TB	Intensive phase	112(62.5%)	0.512(.106, 2.467)	1.15(0.53,2.60)	0.404	0.020(0.000, .865)	3.33(1.47-7.545)	0.042
	Continuous phase	67(37.4%)						
Adherence to medication	Good	77(43%)	2.524(.443, 14.384)	0.47(0.12,1.84)	0.297	41.121(.431, 3.920)	1.03(0.22,4.70)	0.110
	Poor	102(56.9%)						
BMI	<18.5kg/m2	77(42.%)	2.686(.000, .000)	1.21(0.41,3.57)	0.998	27.972(.020, 3.927)	1.46(0.73,2.92)	0.368
	18.5-24.9kg/m2	90(50%)	8.945(.000, .000)	0.85(0.37,1.93)	0.999	0.828(.001, 1.290)	1.46(0.73,2.92)	0.960

	>25 kg/m2	12(6.7%)						
Family history of DM	Yes	16(8.9%)						
	No	163(91.06 %)	4.154(.263, 65.588)	1.15(0.53,2 .60)	0.31 2	0.049(.000, 11.325)	0.61(0.33,1 .72)	0.142

COR=Crude Odds Ratio, CI=Confidence Interval,*AOR: adjusted odd ratio*

5.4. Magnitude of hyperglycemia among study participants

The overall prevalence of hyperglycemia was7.4%.None of the participants know their hyperglycemic status previously. In this study, age group of 45-54,cigarate smoker, being were significant predictors of elevated serum hyperglycemia in TB patients (P< 0.05).Tuberculosis patients in the age group of 45-54 were 5.5 times (AOR=5.57, 95% CI: 1.093-28.369) more likely to have elevated hyperglycemia than other age groups. Moreover, patients who smoke cigarettes were 4 times (AOR=4, 95% CI: 1.62,9.91) more likely to have hyperglycemia than non smokers. On the other hand, the prevalence of hyperglycemia was significantly higher in patients who under weight and normal weight than those who have over weight.

Table 7: Association between demographic, clinical characteristics and elevated hyperglycemia in TB patients attending TB jimmatown Public health facilities, 2020.

Variables		**FBS**			
		categories	**COR(95% CI)**	**AOR(95%CI)**	**P-Value**
Age	<25	60(33.5%)	1.640(.419, 6.416)	0.79(0.21,3.0)	0.477
	25-34	32(17.8%)	0.966(.285, 3.275)	0.91(0.41,2.0)	0.955
	35-44	10(5.5%)	1.511(.431, 5.298)	0.56(0.81,1.8)	0.519
	45-54	15(8.3%)	0.42(0.18, 1.02)	5.570(1.093,28.39)	0.039
	>55	62(34.6%)			

Gender	Male	94(52.5%)	1.12(0.34, 3.68)	2.74(1.07,7.02)	0.036
	Female	85(47.4%)			
Residence	Urban	131(73.1%)	1.350(.348, 5.233)	1.03(0.46,2.3)	0.664
	Rural	48(26.8%)			
Marital status	Single	67(37.4%)	1.168(.086, 15.832)	1.63(0.46,5.8)	0.907
	Married	109(60.8%)	4.314(.332, 56.099)	0.96(0.19,4.6)	0.264
	Divorced	3(1.6%)			
Occupation	Farmer	45(25.1%)	0.585(.115, 2.971)	1.12(0.49,2.6)	0.518
	Merchant	92(51.3%)	0.577(.145, 2.289)	1.14(0.5,2.4)	0.434
	Government employed	10(5.5%)	1.024(.171, 6.151)	0.91(0.26,1.4)	0.979
	Other				
Educational levels	No formal education	36(20.1%)	3.930(.264, 58.581)	0.61(0.18,2.0)	0.321
	Primary(1-8)	63(35.1%)	5.883(.451, 76.800)	0.32(0.07,1.3)	0.176
	Secondary (9-12)	68(37.9%)	6.889(.566, 83.781)	1.47(0.28,7.8)	0.130
	Diploma and above	12(6.7%)			
Smoking status	No	155(86.5%)			
	Yes	24(13.4%)	2.46(0.64, 9.49)	4(1.62,9.91)	0.003
Alcohol consumed	Yes	39(21.7%)			
	No	140(78.2%)	1.095(.261, 4.600)	0.45(0.08,2.3)	0.901
Types of tuberculosis	Pulmonary TB	93(51.9%)	1.504(.623, 3.628)	1.64(0.71,3.77)	0.364
	Extra pulmonary TB	86(48.04%)			
Phase of	Intensive phase	112(62.5%)	0.790(.333, 1.879)	0.55(0.94,3.3)	0 .594

anti TB	Continuous phase	67(37.4%)			
Adherence to medication	Good	77(43%)			
	Poor	102(56.9%)	1.427(.599, 3.401)	0.76(0.4,1.61)	0.422
BMI	<18.5kg/m2	77(42.8%)	0.13(0.01, 1.32)	0.150(.030, .745)	0.020
	18.5-24.9kg/m2	90(50%)	0.11(0.01, 1.04)	0.091(.019, .437)	0.003
	>25kg/m2	12(6.7%)			
Family history of DM	Yes	16(8.9%)			
	No	163(91.06%)	0.442(.089, 2.204)	0.43(0.08,2.0)	0.319

COR=Crude Odds Ratio, CI=Confidence Interval,*AOR: adjusted odd ratio*

6. Discussion

Monitoring hepatic function is a very important measure in TB patients who are on anti-tubercular therapy. This allows early detection of any hepatic injury and thus permits withdrawal of potentially hepatotoxic drugs before serious life threatening manifestations develop.The national institute for health and clinical excellence (NICE) guidelines suggest monitoring of liver function in patients with coexisting liver disease, abnormal liver functions at baseline, or a history of alcohol misuse or drugs(64). The WHO recommends monitoring of liver functions in patients with pre-existing liver disease. Testing for the presence of transient hyperglycemia by measuring the FBG level detects patients with tuberculosis who have a higher risk of an adverse outcome of tuberculosis and allows management of hyperglycemia, but the impact of such an intervention on tuberculosis outcome needs to be confirmed.This study assessed serum Liver enzymes and selected metabolic disorder and associated factors among TB patients who are anti TB treatment at Jimma town public health facilties Jimma, Ethiopia.One hospital and three health centers providing TB service were included in the study.

Over all, 45(25.1%) of TB patients had atleast one or more impaired liver enzymes.This result is in agreement with the study conducted inEurope10-25% (30).It washigher than studies done in Taiwan in which 9.4% of TB patients had drug induced liver injury (32). It was also higher than study done in Iran the risk factors and pattern of changes in liver enzymes among the patients with anti-tuberculosis in which 5.5% drug- induced hepatitis(37).The variation may be due to differences in methodologies, genetic,living satandard and sample size.

The Mean ±SD of liver enzymes was 37.8±17for ALT, 35.7±15.4for AST, 289.7±94.5 for ALP, and 31.8±16.2for GGT. The most abnormal serum concentration of liver enzymes observed in our study was ALT; 18.4%, AST; 17.3%, ALP; 3.9% and GGT; 5.6%.

More ever the results of our study revealed that, patients on urban recidence, age group of 25-34,merchant of occupation,intensive phase of treatment, pulmonary TB, were significant predictors of elevated serum GGT.The factors likecigarette smoker, were 16.54 times (AOR=16.54, 95% CI ;(0.885, 309.501) than non smoker.

Our study has also showed that, overall, 7.3% of TB patients have hyperglycemia.This findingwas slightly comparable with study done with previous study conducted in Europe

10.7%(43),India8.23% and 4.09% (43,44), sub-Saharan Africa 9% (52), Nigeria 12.3%(55), Ghana 9.4% (57),Ethiopia Dessie 6.2% and Dire dawa 13.5%(61,62).However, the prevalence of hyperglycemia was less than study done in Europe United Kingdom in wich 28.5% (43), Sri Lanka 22.5%(49), China 26.5% (50) and Nairobi Kenya which was 37.2% (59).The variation may be due to differences in methodologies, genetic,living satandard and sample size.

6.1. LIMITATIONS

The nature of cross-sectional study design by itself is the main limitation due to its inability to show longitudinal temporal relationships between the two variables. A single fasting serum specimen was analyzed which lead to over/under estimation of the hyperglycemia and impaired liver enzymes values of the study participants. There might be recall bias as study participants could forget to give accurate information. For instance, when they were infected and when they started anti TBduration of infection, which was taken as a date when confirmed TB positive, might not exactly indicate the actual duration of infection

6.2. Conclusion

We conclude that there washigh prevalence of one or more liver enzymes and metabolic disorders among TB patients in our study area. Elevated serum ALT was more frequently found among TB patients who have Pulmonary TB and intensive treatment phase of patients. Elevation of serum AST activity was significantly associated with living in the urban area and patients who werealcohol consumed. Elevation of serum GGT activity in TB patients was positively and significantly associated with urban residences, intensive phase of treatment and pulmonary TB. Elevated serum fasting blood glucose was more frequently found patients in the age group of 45-54 and significantly associated with cigarette smoker.

6.3. Recommendation

Based on the above research finding the following recommendation is forwarded.Routine assessment of serum liver enzymes and metabolic dis orders might be beneficial for TB patients

to control and follow up liver dysfunction and metabolicdisorders due to infection and treatment side effects with tuberculosis.

Metabolic and liver abnormalities inpulmonary tuberculosis is common and may be as valuable aids in patient's clinical management.

Patients should be monitored for their marked change of liver enzymes, metabolic and other risk factors at the time of diagnosis, treatment and follow up.

Large observational studies are required to establish aposible role of TB in liver and metabolic alteration and its effect on the rest of biochemical values by using appropriate sample size.

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Annex- I Information Sheet

English version

The title of the project: Assessment **of Serum Liver Enzymes and Selected Metabolic StatusandAssociated Risk FactorsamongTuberculosis Patients atJimma town health facilities,SouthwestEthiopia**

Name of Principal Investigator: YESUF SEID

Name of Advisors: 1. AKLILU GETACHEW

2. WAQTOLA CHENEKE

This information sheet is prepared to explain the research project that you are asked to review and approve. The main aim of this research project is to determine liver enzymes and selected metabolic disorders among TB patients at Jimma town public health facilities. The research includes a final year (clinical laboratory science) CLS graduate student and two senior advisors from Jimma University, Institute of health Faculty of Health Sciences School of Medical Laboratory Science.

Procedure:

This study uses cross-sectional study design, through face-face interview using structured questionnaire. Permission will be asked from the JMC Hospital chronic care center and Jimmatown publichealth facilities focal person.

Risk and/or Discomfort:

Except small pain to give 5ml blood samples and dedication of time for responding the questioner, there is no any risk or discomfort that you will face by participating in this research.

Any personal information registered in registration books will not be copied and transferred to other bodies. Every piece of information will be kept confidentially using coding system.

Benefits:

There may benefit for policy maker and chronic care center specifically to these TB patients participating in this research. Based on the findings of the research, generally it will help to

design effective and appropriate management follow-up for impairments of livels of liver enzymes and metabolic disorders of TB patients to prevent from complication.

Incentives/Payment for Participating:

There was no incentive or payment to be gained by taking part in this project. Persons to contact:

If you have any question or want to know more information you can contact through the address below the following individuals.

Investigator: YESUF SEID Tel.0917337642 Email:yesjiren @gmail.com

Advisors: 1. Mr. AKLILU GETACHEW Tel: +251911743331 Email: - akeachew.2@gmail.com

2. Mr. WAQTOLA CHENEKA Tel: +2517804412 Email: -waqtolachalt@yahoo.com

School of Medical laboratory science

Jimma University

ANNEX-II

UUNKAA ODEEFFANNOO HIRMAATAA (AFAAN OROMOO VERSION)

Mata duree Qoranna:

Sakanta'insa dhibe tiruu fi dhibee sukaara dhiga kesatti argamu fi sababoota isaaf saaxilan hordoftoota dhibee TB qaban walkaati gageefamu Magaala Jimma, Itoophiyaati.

Kaayyoo qoranna kana:

sakatta'iinsa dhibee tiruu fi dhibee sukaara yeroo hordooftoota dhibee TB barbaachisoofi kan dagatame keessaa isa tokkoo dha.

Kaayyoo guddaan qorannoo kanaa dhibe tiruu fi dhibesukaaraa fi haalota isaaf saaxilan nama baasan hordoftoota dhibee TB ta,anmagaala Jimma Itoophiyaa keessatti maal akka fakkaatu gamaggamuu dha. Qorannoon kun firii hamma baayina sukaara jiruu fi sababoota dhibe tiru dhigaa saaxilan nama baasan waliin kan dhufuu fi kun immoo qamni ilaalatu tarkaanfiiwwan barbaachisaa ta'an akka fudhataniif gargaaru danda'a.

Adeemsa fi yeroo fudhatu:

Dhibe tiruuft,anif dhibesukaara fi sababoota isaaf saaxil nama baasan hordoftoota qoricha dhibee TB fudhachaa jiran kan fedhii qabaachuu isaanif mallatteessan hundi qoranna kannarratti ni hirmaatu. Ragaalee kana sassaabuuf daqiiqa 5-10 fudhachuu danda'a.

Miidhaa fi bu'aa :

Rakkoon addaa dhukkubsattota qorannoo irratti hirmaatan mudatu hin jiru. Akkasumas qorannoo kana irratti hirmaachuf rakkoon dhabbata fayya keessan mudatu hin jiru. Garuu yeroo saamudni dhiigaa dhukkubsattoota irraa fuudhamu lilmoon gogaa isaanii xiqqoo uruu dandeessi.

Dhukkubsattoota cooma dhigaa keessatti hanga hin barbaachif ni argatu . Qorannoon kuni dhibe tiru fi sababoota isaaf saaxil nama baasan hordoftoota qoricha TB magaala Jimmaa Itoophiyaa beekuuf gargaaru danda'a. Firiin qorannichaas dhabbata keessaniif, hojjattoota keessaniif, warren qajeelfamoota fayyaa naannichaa baasanii fi ministeera eegumsa fayyaa biyyoolessaa kan isin gargaaruf jireenya dhukkubsattota fooyyessuuf sababoota adda bahan irratti hojjachuuf ragaa baay'ee barbaachisaa ta,a.

Iccitii:

Odeeffannoon isin irraa funaanaman kan itti fayyadamu garee qorannoo gaggeessu qofa. Namoota biroof hin kennamu.Ragaaleen funaanaman yeroo qorannichi dhume gaggeessaa qorannichaatin saanduqa furtuu qabu keessatti itti cufamee olkaayama.

Mirga:

Isin mirga qorannicha keessatti hirmaachuu diduu fi yeroo barbaaddan qorannoo keessaa of baasuu qabdu. Qorannoo kana keessatti hirmaachuu diduu keessaniif hin adabamtani; akkasumas yaala fi deeggarsa barbaachisaa ogeessota fayyaan kennamu hin dhabdani.

Teessoo:

Qorannaa kana ilaalchisee waan ifa isinii hin taanee yoo jiraate yeroo kamiiyyuu gaafachuu mirgaa ni qabdu. Yeroo barbaaddan gaafii ykn yaada biraa yoo qabaatan teesson armaan gadii kana fayyadamuu ni dandeessu.

Investigator:YESUF SEIDTel.0917337642Email:yesjiren@gmail.com

Advisors: 1. Mr. AKLILU GETACHEW Tel: +251911743331 Email: - akeachew.2@gmail.com

2.Mr.WAQTOLA CHENEKA Tel: +251917804412Email: -waqtolachalt@yahoo.com

School of Medical laboratory science Jimma university

ANNEX- III

ለጥናቱተሳታፊዎችየሚሰጥመረጃ (AMHARIC VERSION INFORMATION SHEET)

የጥናቱርዕስ፤በጅማ ከተማ የመንግስት የህክምና ተቃማት ላይ የTB መድሃኒት በምወስዱ ክትትላቸዉን የሚያደርጉት ህሙማንን የጉበት ኢንዛይም እና የሱኺር መጠንና ተያያዥነት ያላቸዉ መንስኤዎች በጅማ ከተማ የመንግስት ህክምና ተቃማት ላይ ማጥናት ጅማ፣ኢትዮጵያ።

ተመራማሪ፡የሱፍሰይድ

አማካሪ፡ 1. አክሊሉጌታቸው

2. ዋቅቶላጨነቀ

የተቋሙ ስም፡-ጅማዩ ኒቨርሲቲ፣ጤና ኢንስቲትዩት፣ሜዲካል ላቦራቶሪ ትምህርት ክፍል ወጪውን የሚሸፍነው ተቋም፡- ጅማዩኒቨርሲቲ

መግቢያ፡ይህ የማብራሪያ ቅፅ አሁን እርስዎ እንዲሳተፉ የምንጠይቀዎትን ምርምር ጥናት የሚያብራራነው።በዚህጥናት ለመሰሳተፍ ከመወሰንዎ በፊት ይህንን ቅፅ መረጃ ሰብሳቢዎቹ በሚያነቡበት ጊዜ በጥሞና በማድመጥ ጥያቄ ካለዎት በመጠየቅ ትክክለኛዉን መልስ ይመልሱ።በዚህ ጥናት መሳተፍ ከጀመሩ በኃላ በማንኛውም ጊዜጥያቄ ካለዎት መጠየቅይችላሉ።

የጥናቱ ዓላማ፡በጅማ ከተማ የመንግስት ህክምና ተቋም ላይ የሚከታተሉ የTB ህመምተኞች የጉበት ኢንዛይም እና የስኳረ መጠን እና ተያያዥ የሆኑትን ችግሮችን ለማጥናት፣ጅማ፣ደቡብምዕራብኢትዮጵያ።

የጥናቱ ሂደት፡ይህን ጥናት ለማካሄድ የደም ናሙና በመውሰድ የላብራቶሪ ምርመራማደርግነው።

ከጥናቱ ጋር የተያያዘ ጉዳት/አለመመቸት፡እርስዎ በዚህ ጥናት ውስጥ በመሳተፈዎ ለከፋ ጉዳት የሚጋለጡበት ሁኔታ አይኖርም።ደም በሚወሰድበት ወቅት አነስተኛ ህመም ሊሰማወት ይችላል።እንዲሁም የመቅላት፣እና የማበጥ ሁኔታ ደም ከተወሰደበት ቦታ ላታይ ይይችላል።ነገርግን እነዚህ ሁኔታዎች የከፋ ጉዳት የሚያስከትሉ አይደሉም።

በጥናቱ የመሳተፍ ጥቅም፡በዝህ ጥናት ዉስጥ በመሳተፎ በጥሬ ገንዘብ የሚደረግ ካሳ ክፍያ አይኖርም።ነገርግን የምርመራዉ ዉጤት በወቅቱ የሚሰጥ ሲሆን በምርመራዉ ዉጤት መሰረት የህክምና እርዳታ እንዲያገኙ ይጠቆማል።

የጥናቱ ተሳታፊ ድርሻ፡በዚህ ጥናት ለመሳተፍ ፍቃደኛ ከሆኑ ከጤናዎ ሁኔታ ጋር የተያያዙና ሌሎች የግል መረጃዎችን እንዲሰጡ ይጠየቃሉ።በመቀጠልም የሰዉነት ክብደተዎን እና 5 ሚሊ መጠን ያለው የደም ናሙና ለተጠቀሰዉ ዓላማ እንድን ወስድ ይጠየቃሉ።

የጥናቱ ተሳታፊዉ መብት፡በጥናቱ ላይ ለመሳተፍ ባይስማሙ ምንም አይነት ቅጣት የማያስከትል ሲሆን ማንኛውም እርሰዎ ሊያገኙ የሚገባውን ህክምናና ተያያዥ መብት የማያሳጣ መሆኑን እናረጋግጣለን።

የጥናቱ መረጃዎች ምስጥራዊነት፡እርሰዎን በተመለከተ የምንናገኘውን መረጃ በጥናቱ ወቅትም ሆነከዚያ በኃላ ባሉት ጊዜያት እንዲሁም ከጥናቱ የተገኘው መረጃ ሚስጥራዊነት የሚጠበቅ ሲሆን መረጃዎቹም የሚያዙት በስም ሳይሆን በልዩ ኮድነው።ይኸው መረጃ በጥንቃቄ የሚያዝና የተፈቀደለት ተመራማሪ እና ለህክምና ባለሙያዉ ብቻ ይህም እጅግ አስፈላጊ በሆነ ጊዜ ብቻ ካልሆነ በስተቀር ለሌላ ለማንም ሰው አይሰጥም።ማንኛውም ከርስዎ ጋር የተያያዘ ውጤት በልዩ ኮድ ብቻ የሚያዝ ሲሆን ውጤቱም ለሳይንሳዊ ዓላማ ብቻ ስም በማይገልፅ ሁኔታ እንዲታተም ይደረጋል።

ስለጥናቱ መረጃ ማግኘት ቢፈልጉ፡ጥናቱን በተመለከተ ግልጽ ያልሆነ ማንኛዉንም ጥያቄ ካለዎት ነፃሆነው ከዚህ በታች ባለው አድራሻ መጠየቅይችላሉ።

የሱፍ ሰይድ Tel: 09-17-33-76-42

Email: yesjiren@gmail.com

Jimma, Ethiopia

ANNEX-IV

CONSENT FORM

I confirm that, as I give consent to participate in the study, it is with a clear understanding of the objectives and conditions of the study and with recognition of my right to withdraw from the study if I change my idea. I have been given the necessary information about the research. I have also been assured that I can withdraw my consent at any time without penalty or loss of benefits. The proposal is explained to me in the appropriate language I understand. I_____ do here by give consent to Dr. /Mr. /Mrs. /Miss _____to include me in the proposed research.

Participant code _____

Participant (signature) _____date_____

Name of the data collector_____

Data collector (signature) _____date_____

GUCA WALIIGALTEE (AFAAN OROMOO VERSION)

Qorannicha irratti hirmaachuuf waliigaluun koo kaayyoo fi haala qorannichaa haala ifaa ta'een hubachuu fi yaada kiyya yoon jijjiire mirga addaan kutuu qabaachuu koo hubachuu nan mirkaneessa, odeeffannoo waa'ee qorannichaa ilaalchisee naaf kennamee jira. Yeroon barbaade adabbii fi tajaajila dhabuu tokko malee qorannicha keessaa bahuu akkan dandahu naaf himameera, qorannichi afaanin ani hubadhuun naaf ibsame.

Ani _____ Dr. /Mr. /Mrs. /Miss _____qorannoo yaadame keessatti hirmaachuf waliigaleera.

Koodii hirmaataa _____

Mallatoo hirmaataa _____guyyaa_____

Maqaa nama raga funaanuu_____

Mallatoo nama raga funaanuu _____guyyaa_____

Consent Form (Amharic Version)

ከላይ የተፃፈውን የመረጃ ቅፅ አንብቤ የጥናቱ ዓላማና ጥቅም በግልጽ ተረድቻለሁ በማንኛውም ጊዜ ከጥናቱ ያለምንም ችግርና መንገላታት መውጣት እንደምንችል ተገልፆልኛል።ከዚህም በተጨማሪም የጥናቱን ዓላማ በሚገባኝ ቋንቋተረድቻለሁ።በዚህ መሠረት ያለጥናት ቡድኑ አባላት ተፅዕኖ በሙሉ ፈቃደኝነት በዚህ ጥናት ውስጥ በመሣተፍ የሚጠበቅብኝን አስተዋፅዎ ለማበርከት በፊርማዬአረጋግጣለሁ።

የተሳታፊው የሚስጥርቁጥር ----------

የተሳታፊው ፊርማ ----------ቀን ----------

የመረጃ ሰብሳቢው ስም ---------- የመረጃ ሰብሳቢው ፊርማ ----------

-ቀን ----------

ANNEX-V

English version questionnaire

This questionnaire is prepared to assess the serum liver enzymes and associated factors among TB patients attending JMC in 2020.

Card No/ID_____

Part I. Socio-demographic characteristics

Instruction: for the following question circle one from the given choices/write on given space

SN	Questions	Choices	Remark
1.	Gender	1. Male 2. Female	
2.	Age		
3.	Place of residence	1. Urban 2. Rural	
4.	Marital status	1. Single 2. Married 3. Divorced 4. Widowed /Widower	
5.	Educational level	1. No formal education 2. Primary school 3. Secondary school 4. College/ University	

6.	Religion	1. Muslim 2. Orthodox	
		3.Protestant 4.Others,specify_____	
7	Smoking habit	1. yes 2. No	
8	Ethnicity	1. Oromo 2. Amara 3. Kefa 4. Gurage 5. Dawuro 6. Other, specify _____	
9	Occupational status	1. Farmer 2. Merchant 3. Government/private employed 4. Unemployed	
10	Doyou drink alcohol?	1.Yes 2.No	If no skip to Q11
	If yes for Q11 how much do you drink per day in average?	----------ml	
11	Family history of DM:	1. Yes 2. No	

Clinical data

12	Type of TB	1. PTB 2. Extra pulmonary TP	
13	Phase of anti TB	1. Intensive phase 2. Continuous phase	
14	Do you sometimes forget to take your medications?	1. Yes 2. No	
	Were there any days when you did not take your medications due to other reasons rather than forgetting?	1. Yes 2. No	
	Have you ever cut back or stopped taking your medications without telling your doctor, because you felt worse when you took it?	1. Yes 2. No	

Anthropometrics measurements

15.Height (m)_____

16.Weight (Kg)_____

BMI (Kg/m2)_____

This is the end of the questions .Thank for your participation!

Laboratory measurements

- FBS (mg/dl)_____
- ALT (IU/L)_____
- AST (IU/L)_____
- ALP (IU/L)_____
- *GGT* (IU/L)_____

ANNEX-VI

Afan oromo version questioner

Guyyaa gaaffii fi deebii_____

Guca Gaaffiilee Afan Oromootin qophaa'e

Gamaaggama haala fayumaa tiruu fi shukaaraf haalota saaxilan wal qabatanin dhukubsatoota TB tataajjila qorichaa hordoofira jiranif kan qophaa'e.

Lakofsa kodi hirmaata _____

Kutaa I: Ibsa Eenyummaa

Lakk.	Gaafilee	Filannoo	Yaada
1.	Saala	1. Dhiira 2. Dhalaa	
2	Umrii (Waggaan)		
3	Iddoo jireenya	1. Magaalaa 2. Baadiyyaa	
4	Haala gaa'ilaa	1. Kan hin fuune/heerumne 2. Kan fuudhe/heerumte 3. Kan wal hiikan 4. Gursummaa	
5	Sadarkaa barnoota	1. Kan hin baranne	

		2. Dubbisuu fi barreessuu 3. Sadarkaa tokkoffaa 4. Sadarkaa lammaffaa 5. Kollajjii/ Yuuniversiitii	
6	Amantaa	1. Musliima 2. Ortoodooksii 3. Piroteestaantii 4. kaatoolikii 5. Kan biraa _____	
7	Sabummaa	1. Oromoo 2. Amaaraa 3. Guraagee 4. Tigree 5. Kan biraa----------	
8	Haala hojii	1. Qotee bulaa 2. Daldaalaa 3. Hojjetaa Mootummaa/dhuunfaa 4. Haadha manaa 5. Kan biraa (ibsi) _____	
9	Tamboo hinxuxuu?	1. Eyee 2. Lakki	
10	Dhugaatti alkoli ni dhugdu?	1, Eyee 2,Lakki	Yoowan lakii jedhan gara gaafi 11 itti darbi
	guyaatti hagam dhugdu	_____ml	
11	Maatti kessa namni	1. Eyee	

	dhukuba sukaara qabu jira?	2. Lakki	

Kutaa II: Odeeffannoo wal'aansaa

12	Garee dukkuba TB	1. PTB 2. EPTB	
13	Erga qoricha fudhachu egaltan hagami ?	1. Ji,aa 3 2. Ji,aa 3 olii	
14	Qoricha oso hin fudhatin dagatani bektu	1. Eeye 2.Lakki	Yoowan lakii jedhan gara gaafi 14 itti darbi
	Qoricha daganaan ala guyaan osohin fudhatin oltan jira?	1. Eyee 2.Lakki	
	Qoricha adaan hinkutu ajaja doktori malee sababa isinitti toludidef jecha	1. Eyee 2.Lakki	

Kutaa III: Safara qaama fi dhiibbaa dhiigaa

3. Dheerina (m)_____
4. Ulfaatina (Kg)_____ BMI (Kg/m2)_____

Kutaa IV: Qorannoo Laaboraatorii

18. FBS (mg/dl)_____

19. ALT (IU/L)_____

20. AST (IU/L)_____

21. ALP (IU/L)_____

22. GGT (IU/L)_____

Xummurame!

Hirmaannaa keessaniif galatoomaa!

Maqaa nama odeeffannoo funaanuu_____ mallattoo_____guyyaa_____

ANNEX- VII

Amharic version questioner

በጅማ ከተማ ለTB ህሙማን ተከታታይ በደማቸዉ አላስፈላጊ የስካር እና የጉበት ኢኒዛይም ዳሰሳ መጠይቅ

መጠይቅ ውድ ተሳታፊ ቀጥሎያለውን መጠይቅ ለሞምላት ስለተባበሩን እናመሰግናለን፡

የመጠይቁ መለያ ቁጥር_____

ክፍል 1.የማህበራዊና ስን-ህዝብ ባህሪያት

ተ.ቁ	ጥያቄዎች	አማራጮች	አስተያየት
1.	ፆታ	1. ወንድ 2. ሴት	
2	ዕድሜ	በዓመት	
3	አድራሻ	1. ከተማ 2. ገጠር	
4	የጋቢቻ ሁኔታ	1. ያላገባ/ች 2. ያገባ/ች	
5	የትምህርት ደረጃ	1. ሚደበኛ ትምህርት ያልተሚ/ች 2. ሚማማብና ሚጻፍ 3. አንደኛ ደረጃ 4. ሁለተኛ ደረጃ 5. ኮለጅ/ዩኒቨርሲቲ	
6	ሀይሞት	1. ማላሊም 2. ኦርቶዶክስ 3. ፕሮቴስታንት 4. ካቶልክ 5. ለላ ከሆኔ ይጡቀሱ----------	
7	ብሔር	1. ኦሮሞ 2. አማራ 3. ጉራጌ 4. ትግሬ 5. ለላ ከሆኔ ይጡቀሱ----------	
8	ሥራ	1. አርሶአደር 2. ነጋዴ 3. መንግስት ሰራተኛ 4. የግል ሰራተኛ 5. ያልተቀጠረ 6. የቤት እማቴት	
9	ሲጋራየ ሜጩል ምድአለብዎት	1.አዎ□2. የለብኝም□	

10	የ ሚያ ሰ ክ ር ማስጥይጣስሉ	1.አ ዎ □ 2.የ ለ ብኝ ም□	
	ሜ ል ሶ አ አ ዎ ን ከ ሆነ በ ቀ ን ምን ያ ህ ል ይጣጣሉ	----------ሚ ኒ	
11	ቤ ተ ሰ ቦ ውስ ጥ የ ስ ኪ ረ ህ ሙም ተ ሙም ሰ ውነ በ ረ	1.አ ዎ □ 2.የ ለ ብኝ ም□	

ክፍል 2. የ ህ ክ ምና ማ ከ ረ ጀ

12	የ TB በ ሽ ታ አ ይነ ት	1. PTB□ 2. EPTB□	
13	ለ ምን ያ ህ ል ጊ ዜ TB ሞድ ህ ኒ ት ተ ጠቅ ሞ ል ?	1. ለ 3 ወር □ 2. ከ 3ወር በ ላ ይ□	
14	የ TB ሜ ዲ ኒ ት ሳ ይወስ ዱት ረ ስ ታ ዎ የ ወ ቃ ሉ	1. አ ዎ□ አ ላ ወ ቅ ም□	
	በ ሚ ክ ነ ት ሞ ጂ ን ት ሰ ወስ ዱ ቀ ረ ተ ወ የ ወ ቀ ሉ	1. አ ዎ□ 2 አ ይ ደ ለ ም□	
	ሃ ክ ም ሰ የ ማ ክ ሩ ሞ ጂ ን ት አ ቆ ረ ጡ የ ወ ቃ	1. አ ዎ□ 2 አ ይ ደ ለ ም□	

ክፍል 3. የ ሰ ዎ ነ ት ል ኬ ት

1. ቁ መ ት (ሜ.)_____

ክ ብ ደ ት (ክ.ግ)_____

. B.M.I. (Kg/m2) _____

ክፍል 4.የ ላ ቦ ራ ቶ ሪ ዉ ጤ ት

1. FBS (mg/dl)_____
2. ALT (IU/L)_____
3. AST (IU/L)_____
4. ALP (IU/L)_____
5. GGT (IU/L)_____

ስ ለ ት ብ ብ ሩ እ ና ማ ስ ታ ወ ሻ ለ ን !

Name of data collector_____ sign_____ date _____

Annex IX: Declaration

Declaration Form

I, the undersigned, hereby declare that this MSc thesis is my original work, and has never been presented for any degree in Jimma University or any other institutions of higher learning in Ethiopia. I also declare the duly acknowledgement of all material sources used for this thesis.

Name of the student: Yesuf Seid (MSc candidate)

Signature: _____ Date of submission: _____/_____/_____

Approval of the advisors

This research thesis will be approved by the supervision of university advisors:

External Examiner:Mistire Wolde (Bsc,Msc,PhD)

Signature: _____ Date of submission: _____/_____/_____

Internal Examiner: Mr Sintayehu Asaye (Bsc,Msc)

Signature: _____ Date of submission: _____/_____/_____

1. Name of 1st advisor: Mr. Aklilu Getachew (BSc, MSc,PhD candidate)

Signature: _____ Date of submission: _____/_____/_____

2. Name of 2nd advisor: Mr. Waqtola Cheneke (BSc, MSc, PhD cand,Asso. Prof in CLS)

Signature: _____ Date of submission: _____/_____/_____

Name of School head: Kedir; Abdela(BSc, MSc,MBS)

Signature: _____ Date of submission: _____/_____/_____