CHAPTER 1

INTRODUCTION

1.1 Background

Tuberculosis (TB) is the leading cause of death due to a bacterial pathogen worldwide (Günther et al., 2022). Tuberculosis occurs frequently in densely populated areas, is more common in the lungs, and is transmitted by droplet nuclei when coughing or sneezing. TB is still a big problem, especially in Indonesia, because the incidence of this disease continues to increase every year even though diagnostic tests have been established and effective TB medication is fully available. It has resulted in Indonesia being ranked third with the most TB sufferers globally (Mathofani PE & Febriyanti R, 2019).

The correlation between diabetes mellitus and tuberculosis in humans has been known for centuries. Better sanitation, better nutrition, and less overcrowding contributed to the incidence of tuberculosis. In recent years, tuberculosis without diabetes mellitus has become a problem in low-income countries because many TB patients on treatment have elevated blood glucose levels (Baghaeil, et al. 2013).

Tuberculosis occurs in every part of the world. According to a WHO report in 2020, 87% of new Tuberculosis cases occurred in the 30 high TB burden countries. Eight countries accounted for more than two-thirds of the global total: India, Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh, and Democratic Republic of the Congo. In 2021, an estimated

10.6 million people fell ill with tuberculosis (TB) worldwide. Six million men, 3.4 million women and 1.2 million children. TB is present in all countries and age groups. However, TB is curable and preventable. Multidrug-resistant TB (MDR-TB) remains a public health crisis and security threat. Only about 1/3 of people with drug-resistant TB accessed medication in 2020. An estimated 66 million lives were saved through TB diagnosis and medication between 2000 and 2020 (WHO, 2022).

Global Tuberculosis Report states that in 2020, the TB incidence rate in Indonesia was 301, a decrease compared to the 2019 TB incidence rate of 312 out of 100,000 population. Meanwhile, the TB mortality rate in 2019 and 2020 is still the same, namely, 34 out of 100,000 residents. In 2021, the number of tuberculosis cases found was 397.377, an increase compared to all tuberculosis cases found in 2020, which were 351.936. The highest number of cases were reported from provinces with large populations, namely West Java, East Java, and Central Java. Tuberculosis cases in the three provinces account for 44% of the total tuberculosis cases in Indonesia. Treatment Coverage (TC) is the number of TB cases that are treated (get medication) and reported in a given year divided by the estimated number of incident TB cases in the same year and expressed as a percentage of 47.1% (Kemenkes RI, 2021).

Health Profile of East Java 2021 explains that the number of tuberculosis cases found was 43.247 cases, a decrease compared to all tuberculosis cases found in 2020, which were 44.A947 cases, and the number of TB cases found, consume medication and reported in 2021 is 45.08%,

Treatment Success Rate (TSR) is an indicator used to assess tuberculosis treatment (medication) in East Java as much as 90% (Dinas Kesehatan Jawa Timur, 2021).

When viewed from the highest number of case discoveries in sub-districts with large populations and statistically, TB case detection in 2020 shows a significant positive relationship with the number of residents per sub-district in Banyuwangi Regency in 2020 (Dinas Kesehatan Kabupaten Banyuwangi, 2020). The latest data from the Banyuwangi Health Service in November 2022 stated that the number of TB sufferers found and getting medication in Banyuwangi was 2,094. 84,84% success of TB medication and 15,16% failed TB medication in Banyuwangi, 18 people of drug-resistant TB patients, and 71 people died from tuberculosis. They discovered 272 cases of TB with DM in Banyuwangi. Klatak, the first public health center with the most TB sufferers, 116 people. In second place is the Singojuruh public health center with the most TB sufferers, 70 people. In third place is the Singotrunan Public Health Center, with the most TB sufferers, 68 people. (Dinas Kesehatan Kabupaten Banyuwangi, 2022). From the results of a preliminary study conducted by researchers at the Klatak Public Health Center on December 26, 2022, it was found that there were 135 tuberculosis patients undergoing medication at the Klatak Public Health Center. Meanwhile, 124 tuberculosis patients were not accompanied by diabetes mellitus at Klatak Public Health Center.

Tuberculosis (TB) is a chronic infection caused by *Mycobacterium tuberculosis* (*M.Tuberculosis*) which attacks the lung parenchyma.

Mycobacterium tuberculosis is an aerobic bacterium that often infects tissues with a high oxygen content. *M. Tuberculosis* infection can be in the form of active infection, clinically silent, or latent infection. It is estimated that a third of the world's population is infected. *M. Tuberculosis* is mostly asymptomatic and becomes Latent Tuberculosis Infection (LTBI), especially in patients with HIV/AIDS, DM, malnutrition, chemotherapy or steroids, and anti-tumor necrosis factor therapy (Novita Dewi, 2019).

Tuberculosis medication aims to kill the *Mycobacterium bacteria*. Anti-tuberculosis drugs used in the medication of TB are synthetic antibiotics and anti-infectives (Arimbawa & Mulyantari, 2019). Tuberculosis medication aims to cure patients, prevent death, prevent recurrence, break the chain of transmission, and prevent germ resistance to anti-tuberculosis drugs. However, anti-tuberculosis drugs are reported to have side effects such as fever, acne, gastrointestinal complaints, and hepatic dysfunction, which can increase blood glucose levels (Adriztina et al., 2014).

The National Guidebook for Health Services "Tuberculosis Control" states that anti-tuberculosis drugs are the most important component in TB medication. TB medication is one of the most efficient efforts to prevent the further spread of TB-causing bacteria (Kemenkes RI, 2020). Most of the widely consumed anti-tuberculosis drugs are hepatotoxic. Hepatotoxicity is a reaction that interferes with the function of the liver as a very important glucose buffer system. So, controlling glucose levels in the blood is very difficult. Glucose levels are a very important factor for the smooth working of the body. Glycogenesis is When blood glucose is increased due to the

digestion and absorption of carbohydrates. As much as two-thirds of all glucose absorbed from the intestine is stored in the liver as glycogen. Over the next several hours, as the blood glucose concentration and rate of secretion decrease, the liver releases glucose back into the blood. The liver reduces fluctuations in blood glucose concentration to about one-third of the fluctuations that can occur. This situation can lead to hyperglycemia (Guyton AC & Hall JE, 2011). When a TB patient has hyperglycemia, there is usually an effect that will be felt like the mouth feels dry, often thirsty, and polyuria (Ministry of Health, 2022).

TB medication is one of the most efficient efforts. The blood glucose levels of TB still have a chance to increase. Therefore, blood glucose levels can be controlled with a low-carb diet and exercise at least 3 times a week (Putra et al., 2020). In addition, Novita et al., 2018 stated in their research that health workers should conduct routine screening of TB patients to help detect diabetes and pre-diabetes earlier so that primary prevention methods can be started more quickly and effectively. Patients are advised to control glucose levels in TB patients so the medication can reach optimal. In their research, Istiqomah & Yuliyani (2022) mentioned that there are 4 pillars of DM management to control blood glucose levels: education, physical activity, diet, and pharmacological therapy.

Based on the background and problems above, the authors are interested in conducting research with the title "The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023”

1.2 Formulation of the Problem

Based on the description in the background, the problem formulation in this study, “Is there any Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023?”

1.3 The Objective of the Study

1.3.1 General Purpose

Find out the Correlation between Tuberculosis Medication and Blood Glucose Levels in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

1.3.2 Specific Aim

1) Identify Tuberculosis Medication in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.
2) Identify Blood Glucose Levels in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.
3) Analyzing The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

1.4 Expected Result

1.4.1 Theoretical

Contributing to the nursing field to develop knowledge related to tuberculosis medication with blood glucose levels can be a reference for future researchers.

1.4.2 Practical

1) Respondent

The results of this study are expected to be used as a prevention effort that can be carried out independently or in groups.

2) Research Place

Improving services to the community so that tuberculosis patients can take medication properly and understand the correlation between tuberculosis medication and blood glucose levels.

3) Researchers

Increase the knowledge and ability of researchers from the concept and theory of tuberculosis medication and blood glucose levels.

4) Other Researchers

Become a reference for future researchers or researchers who will conduct other research related to tuberculosis medication and blood glucose levels.

5) Educational Institution

Adding library materials and references as material for consideration for similar research in the future.

CHAPTER 2

LITERATURE REVIEW

2.1 Tuberculosis

2.1.1 Definition

Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*) that most often affect the lungs. Tuberculosis is curable and preventable (WHO, 2022). Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. These bacteria usually affect the lungs (pulmonary TB) and other organs (extra-pulmonary TB) (Rahman et al., 2022).

Mycobacterium tuberculosis is rod-shaped and acid-fast, often referred to as Acid-Fast Bacilli. Most TB germs are often found to infect the lung parenchyma and cause pulmonary TB disease. However, these bacteria can also infect other body organs (extra-pulmonary TB), such as the pleura, lymph nodes, bones, and other extra-pulmonary organs. (Kemenkes RI, 2020).

2.1.2 Etiology

Pulmonary tuberculosis is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* type humans, a rod-shaped bacterium with a length of 1-4/mm and a thickness of 0.3-0.6/mm. Most germs consist of fatty acids (lipids). These lipids make bacteria more resistant to acids and more resistant to chemical and physical disturbances (Budiartani, 2020)

2.1.3 Pathophysiology

Seven Steps in the Pathophysiology of Active Tuberculosis. These steps are aerosolization, macrophage phagocytosis, phagolysosome blockage and replication, TH1 response, granuloma formation, clinical manifestations, and transmission.

1) Aerosolization is the beginning and the end of the cycle of tuberculosis pathophysiology. Aerosolization occurs when a person with active tuberculosis forcefully expires through actions such as coughing.
2) A susceptible person who breathes in the aerosolized *Mycobacterium tuberculosis* and droplets small enough to reach the alveolar sacs (shown in the first magnification) will encounter macrophages, dendritic cells, and monocytes. The macrophages will phagocytose the bacteria (shown in the second magnification) and attempt to destroy the invader. Dendritic cells will migrate to lymph nodes to activate T-helper cells.
3) *M. tuberculosis* prevents phagolysosome fusion, avoids destruction, begins replicating, and releases DNA, RNA, proteases, and lipids. Additionally, the macrophages will release cytokines and vascular endothelial growth factor (VEGF). The VEGF will trigger angiogenesis and increase vascularization of the lesion. The cytokines will initiate the innate response and recruit natural killer (NK) cells, dendritic cells (DC), neutrophils, and macrophages in different forms.

4) The T-helper cell response will involve the migration of TH1, Tregs, and B cells primed in the germinal center. These cells will combine to form the granuloma.
5) The granuloma is a prison to block off the bacteria from spreading systemically.
6) Later, or at present, immune compromise prevents the granuloma from containing the bacteria. The bacteria will spread and multiply in multiple clinical manifestations.
7) During this phase, the bacteria can be aerosolized by the original susceptible, now infected host and begin the cycle anew.

It was adapted from "Granuloma" by BioRender.com (2021) in a journal article (Maison, 2022).

2.1.4 Tuberculosis Transmission

The transmission source is positive acid-resistant bacilli TB patients through the sputum droplets they secrete. The transmission source is actively infected people (active TB sufferers). When coughing or sneezing, these sufferers spread germs into the air as droplets (sputum splashes). Droplets containing germs can survive in air at room temperature for several hours. A person can become infected if these droplets are inhaled into the respiratory tract. After TB germs enter the human body through breathing, TB germs can spread from the lungs to other body parts, namely through the circulatory system, lymphatic system, respiratory tract, or spread directly to other body parts (Simamora, 2021).

2.1.5 Classification

There are several classifications of tuberculosis, including (Menteri Kesehatan Republik Indonesia, 2016)

1) Classification based on the anatomical location of the disease:
   a. Pulmonary tuberculosis

      TB located in the lung parenchyma is considered pulmonary TB because of lesions in the lung tissue. Patients who suffer from pulmonary TB and extra pulmonary TB are classified as lung TB patients.

   b. Extra pulmonary tuberculosis

      TB occurs in organs other than the lungs, for example, pleura, lymph nodes, stomach, urinary tract, skin, joints, lining of the brain, and bones.

      The diagnosis of extra-pulmonary TB can be established based on the bacteriological or clinical examination results. The diagnosis of extra-pulmonary TB must be pursued bacteriologically by finding *Mycobacterium tuberculosis*.

2) Classification based on previous medical history:
   a. New tuberculosis patients

      Patients who had never previously received TB treatment or taken anti-tuberculosis drugs for less than 1 month (< of 28 doses).

b. Patients who have been treated for tuberculosis

Patients previously taking anti-tuberculosis drugs for 1 month or more (≥ 28 doses). Classification based on the results of the last TB treatment:

a) Relapsed patient: TB patients who have been declared cured or have received complete treatment and are currently diagnosed with TB based on the results of bacteriological or clinical examination (due to true relapse or due to reinfection).

b) Patients are treated again after failure: previously treated TB patients who failed the last treatment.

c) Treated patients returning after discontinuation of treatment: patients who have been treated and declared lost to follow-up.

d) Other: TB patients who have received previous treatment but the results of previous treatment are unknown.

3) Classification based on drug sensitivity test results:

The grouping of patients here is based on the results of the sensitivity test of the *Mycobacterium tuberculosis* test sample to anti-tuberculosis drugs and can be in the form of:

a. Mono-resistant (MR TB): *Mycobacterium tuberculosis* is resistant to only one type of first-line anti-TB drug.

b. Polyresistant (PR TB): *Mycobacterium tuberculosis* is resistant to more than one type of first-line anti-TB drugs besides Isoniazid and Rifampicin simultaneously.
c. Multi-drug resistant (MDR TB): *Mycobacterium tuberculosis* is resistant to Isoniazid and Rifampicin simultaneously, with or without other first-line TB resistance.
d. Extensive drug resistance (XDR TB): MDR TB, which is also *Mycobacterium tuberculosis*, is resistant to one of the fluoroquinolone anti-TB drugs and at least one second-line anti-tuberculosis drug (Kanamycin, Kapreomycin, and Amikacin).
e. Rifampicin Resistance (RR TB): *Mycobacterium tuberculosis* is resistant to rifampicin with or without resistance to other anti-TB drugs detected using the genotyping method (molecular rapid test) or the phenotyping method (conventional).

2.1.6 Signs and Symptoms

Based on the Regulation of the Minister of the Republic of Indonesia concerning Tuberculosis Control, the signs and symptoms of tuberculosis are: (Menteri Kesehatan Republik Indonesia, 2016)

1) Coughing up phlegm for 2 weeks or more
2) Cough followed by phlegm mixed with blood
3) Cough up blood
4) Difficulty breathing

5) Weak
6) Decreased appetite
7) Weight loss
8) Night sweats without physical activity
9) Chills for more than a month.

2.1.7 Tuberculosis Diagnosis

Diagnosis of TB is determined based on complaints, history, clinical examination, laboratory tests, and other supporting examinations. (Menteri Kesehatan Republik Indonesia, 2016)

1) Complain and Anamnesis Result

   Complaints submitted by patients and detailed interviews based on patient complaints. Clinical examination based on symptoms and signs of tuberculosis.

2) Laboratory Examination

   a. Bacteriological Examination

      Sputum examination serves not only to make a diagnosis but also to determine the potential for transmission and assess the success of treatment. Sputum examination for diagnosis is carried out by collecting 2 sputum test samples, which are collected in the form of current sputum and sputum in the morning:

a) Current: Sputum collection in health facilities.

b) Morning: Sputum is collected in the morning immediately after waking up. It can be done at the patient's home or in the inpatient ward when the patient is hospitalized.

b. TB Molecular Rapid Test Examination

Molecular rapid test examination using the Xpert MTB/RIF method. Molecular rapid tests are diagnostic tools but cannot be used to evaluate treatment outcomes.

c. Culture Examination

To identify Mycobacterium tuberculosis, culture examination can be done with solid media (Lowenstein-Jensen) and liquid media (Mycobacteria Growth Indicator Tube). The examination is carried out in a quality-controlled laboratory facility.

3) Other Supporting Examinations

a. Chest X-ray examination

b. Histopathological examination of cases treated with extra-pulmonary TB.

4) Drug Sensitivity Test

The drug sensitivity test aims to determine whether *Mycobacterium tuberculosis* is resistant to anti-tuberculosis drugs. Drug sensitivity testing must be conducted in a laboratory that has passed the Quality Assurance (QA) test and received national and international certificates.

2.2 Tuberculosis Medication

2.2.1 Definition

Tuberculosis medication aims to cure patients, prevent death, prevent recurrence, break the chain of transmission, and prevent germ resistance to anti-tuberculosis. Anti-tuberculosis drugs used for tuberculosis are classified into the first and the second (Novita Dewi, 2019).

In the medication of pulmonary TB, the patient must swallow all the drugs given as recommended with the direct supervision of a Drug Swallowing Supervisor to prevent drug resistance (Ariyani et al., 2018).

2.2.2 Category of Anti-Tuberculosis Drugs

Based on data from Menteri Kesehatan Republik Indonesia, 2016 there are 2 categories of anti-tuberculosis drugs :

1) Category one (intensive stage 1-2 months) :

   Anti-tuberculosis drugs are rifampicin, isoniazid, pyrazinamide, ethambutol, and streptomycin (Menteri Kesehatan Republik Indonesia, 2016).

2) Category two (advanced stage 2-6 months)

Table 2.1 Category 2 of Anti-Tuberculosis Drugs

Group	Class	Type of Medication
A	Florokuinolon	• Levofloksasin (Lfx) • Moksifloksasin (Mfx) • Gatifloksasin (Gfx)*
B	Second-line (category two)	• Kanamycin (Km) • Amikacin (Am)*

	injectable anti-tuberculosis drug	• Capreomycin (Cm) • Streptomycin (S)**	
C	Second-line (category two) oral anti-tuberculosis drug	• Etionamid (Eto)/Protionamid (Pto)* • Sikloserin (Cs) /Terizidon (Trd)* • Clofazimin (Cfz) • Linezolid (Lzd)	
D	D1	First-line (category one) anti-tuberculosis drug	• Pyrazinamide (Z) • Ethambutol (E) • Isoniazid (H) high dose
	D2	New anti-tuberculosis drug	• Bedaquiline (Bdq) • Delamanid (Dlm)* • Pretonamid (PA-824)*
	D3	Additional anti-tuberculosis drug	• Para-aminosalicylic acid (PAS) • Imipenem-cilastatin (Ipm)* • Meropenem (Mpm)* • Amoxicillin clavulanate (Amx-Clv)* • Thioacetazone (T)*

(Source: Menteri Kesehatan Republik Indonesia, 2016)

Description :
*Not provided by the program
**Excludes second-line injectable drugs, but can be given under certain conditions and not provided by the program.

2.2.3 Dose of Anti-Tuberculosis Drugs

Siberian, 2019 states the dose of anti-tuberculosis drugs in his research as follows:

1) Isoniazid: 5 mg/kg BW, maximum 300 mg. 10 mg/kg 3 times a week, 15 mg/kg 2 times a week, or 300 mg/day for intermittent adults: 600 mg/time.
2) Rifampicin: 10 mg/kg BW, maximum 600 mg 2 to 3 times a week or B>60 kg: 600 mg, BW 40-60 KG: 450. BW <40 kg: 300 mg, intermittent dose 60 mg/kg.
3) Pyrazinamide: intensive phase 25 mg/kg BW, 35 mg/kg BW 3 times a week, 500 mg/kg BW 2 times a week or BW> 60 kg: 1500 mg, BW 40-60 KG: 100 mg, BW < 40:750 mg.
4) Ethambutol: intensive phase 20 mg/kg BW, continuation phase 15 mg/kg BW, 30 mg/kg BW 3 times a week, 45 mg/kg BW 2 times a week, or BW> 60 kg.
5) Streptomycin: 15 mg/kg BW or BW> 60 kg: 100 mg, BW 40/60 kg: 750 mg, BW < 40 kg: according to BW.

2.2.4 Side Effect

The side effect of tuberculosis medication is : (Masdidik, 2020)

1) Isoniazid

The most common and mild side effects of isoniazid are nausea, vomiting, and epigastric pain. However, there are some side effects from other TB drugs, isoniazid, such as:

a. Acne
b. Changes in behavior: May experience dizziness or headaches, difficulty sleeping, euphoria, agitation, and feelings of anxiety.
c. Arthralgia: Although rare, arthralgia can occur in some cases.
d. Fever
e. Hepatic Dysfunction
f. Seizures

2) Rifampicin

Rifampicin-type TB drugs' side effects range from mild to adverse side effects. Check out what side effects are caused by using this rifampicin drug.

a. Gastrointestinal complaints, such as nausea, anorexia, and abdominal pain
b. Remove body fluids, such as tears, sweat, and urine
c. Skin reactions: Pruritus, with or without erythema
d. Flu Syndrome

3) Pyrazinamide

Pyrazinamide is a nicotinic acid derivative. The TB drug pyrazinamide has a molecular structure similar to the drug isoniazid.

a. Gastrointestinal symptoms: Nausea, vomiting and anorexia
b. Hyperuricemia and arthralgia
c. Exanthema and pruritus
d. Skin infection (Dermatitis)

4) Streptomycin

   a. Pain at the injection site
   b. Impaired balance and hearing
   c. Anaphylactic shock
   d. Anemia
   e. Agranulocytosis
   f. Thrombocytopenia

5) Ethambutol

   However, if the dose of ethambutol exceeds 15 mg/kg body weight, some side effects will appear.

   a. Gout
   b. Retrobulbar Neuritis
   c. Hypersensitivity, such as itching, skin rash, fever
   d. Gastrointestinal symptoms, such as nausea, vomiting, abdominal pain, and hepatotoxicity
   e. Hematological symptoms, such as eosinophilia, neutropenia, and thrombocytopenia
   f. Cardiovascular symptoms, such as myocarditis and pericarditis
   g. Neurological symptoms, such as headache, dizziness, and mental confusion
   h. Pulmonary infiltrate (rare)

2.2.5 Factors Affecting Medication

A person's actions that affect tuberculosis medication are influenced by 3 factors (Wulandari, 2015)

1) Predisposing factors

   Factors that precede a person's behavior that will encourage behavior, namely knowledge, attitudes, beliefs, values, and perceptions that encourage a person or group to take action.

2) Enabling factors

   Factors that motivate individuals or groups to take action include the physical environment, availability of health facilities and facilities, ease of reaching health facilities, service time, and ease of transportation.

3) Reinforce factors

   Including the attitude and support of family, friends, teachers, employers, health care providers, leaders and decision makers.

2.3 Blood Glucose Level

2.3.1 Definition

Blood glucose level is the glucose concentration in the blood expressed in mg/dl (Simamora, 2021). Glucose is the most important carbohydrate; most carbohydrates in food are absorbed into the bloodstream as glucose and other sugars are converted to glucose in the liver (Agustina, 2017).

2.3.2 Risk Factor

According to Notoatmodjo (2009) in Aritonang, 2020 the factors causing an increase in blood glucose levels (hyperglycemia) are:

1) Education

Education is an effort to persuade or teach people to want to take action to maintain or overcome problems and improve their health. This education is very important so that the patient's behavior in controlling blood glucose levels remains stable.

2) Knowledge

Patients can control blood glucose levels well based on knowledge about the disease, the signs and symptoms, and the treatment.

3) Food intake (Diet)

Blood glucose levels are partly reflected in what is eaten, and therefore, when eating, it is necessary to have a balanced diet. Maintaining blood glucose levels close to normal can be done with a balanced food intake. Different foods can have different effects on blood glucose levels. Important factors in carbohydrate diet to increase blood sugar levels:

a. Fiber content in food
b. Digestive process
c. How to cook
d. Effect of glucose intolerance

4) Physical activity

The benefits of physical activity have long been known as an effort to control blood glucose levels.

5) Medication

Medication is one of the influencing factors because taking medication can stabilize or control blood glucose levels.

6) Disease or stress

In patients with stress, it can change their diet, physical activity, and medication, leading to hyperglycemia.

2.3.3 Classification

Simamora, 2021 mentions that blood glucose levels are classified into :

1) Hyperglycemia

It can occur due to excessive intake of carbohydrates and glucose. Some signs and symptoms of hyperglycemia are increased thirst, headache, difficulty concentrating, blurred vision, increased frequency of urination, fatigue, weakness, and weight loss.

2) Hypoglycemia

It can occur due to insufficient intake of carbohydrates and glucose. Some signs and symptoms of hypoglycemia are impaired consciousness, vision, memory, sweating, tremors, palpitations, tachycardia, restlessness, paleness, chills, nervousness, and hunger.

2.3.4 Blood Glucose Level Test

Blood glucose level test, according to Simamora (2021) :

1) Patient Preparation
    a. Glycemic Index

       Checking blood glucose at any time of day regardless of the last meal eaten and the condition of the person's body.

    b. Fasting Blood Glucose

       A fasting blood glucose check is a blood glucose check that is done after the patient has fasted for 8-10 hours.

    c. Blood Glucose 2 Hours Post Prandial

       Blood glucose examination 2 hours postprandial is calculated 2 hours after the patient eats.

2) Blood Glucose Test with Glucometer
    a. Make sure the glucometer is clean and ready to use.
    b. Remove the glucose test strips from the container, then close the container tightly again. Test strips can be damaged when exposed to moisture.
    c. Wash hands with soap and warm water, then dry.
    d. Do not use alcohol because it can dry out the skin.
    e. Massage your hands so that blood collects in your fingers.
    f. Use the lancet to prick the finger.
    g. Press the base of the finger to circulate the blood onto the glucose test strip.
    h. Place the strip into the glucometer.

i. After a few seconds, some blood glucose levels will appear.

j. Record the results of the examination.

k. Discard the lancet and test strip in the trash.

2.3.5 Normal Value of Blood Glucose Levels

Budiartani, 2020 mentions that the value of blood glucose levels in the blood can be calculated in several ways and different criteria. The following table classifies blood glucose levels is:

Table 2.2 Glycemic Index and Fasting Blood Glucose

Examination	Low	Normal	High
Fasting Blood Glucose (mg/dl)	≤ 75	74 - 106	≥ 107
Glycemic Index (mg/dl)	≤ 59	60 - 139	≥ 140

(Source: PERKENI Diabetes Melitus in Indonesia, 2015)
(Source: Nugraha & Badrawi, 2018)

Table 2.3 Glycemic Index and Fasting Blood Glucose

Examination	Not DM	Uncertain DM	DM
Fasting Blood Glucose (capillary blood)	<90	90-109	≥110
Glycemic Index (capillary blood)	<90	100-199	≥200

(Source: Aritonang, 2020)

2.4 Correlation Between Tuberculosis Medication and Blood Glucose Level

One of the medications in tuberculosis patients is Isoniazid (INH). The activity of this drug is highly dependent on the rate of its acetylation reaction. The speed of isoniazid acetylation (N-acetylation) shows a difference in ability, which is divided into 2 types, namely fast and slow acetylator types. The function of the acetylation reaction is for the detoxification process and converting the drug/mother compound into its inactive metabolite compounds, which are more polar in nature, so they are easily excreted. INH administration does not have to be done repeatedly/at high frequency because INH metabolism is slow, so INH can have a constant effect for a long time after being taken. The ability of INH to be excreted in the inactive form of acetyl isoniazid is slow. Medications metabolized in the inactive form of acetyl isoniazid slowly can increase the toxic effects caused by INH even more. In addition, individuals with the slow acetylator type are more prone to experience side effects of INH in peripheral neuropathy due to vitamin B6 deficiency. INH will inhibit the use of vitamin B6 and will increase the excretion of B6. The essential amino acid tryptophan is usually not used if the body is deficient in vitamin B6 (pyridoxine). Instead, it turns into a substance known as Xanthurenic acid. This acid increases and damages the pancreas, raising blood glucose levels (Agustina, 2017).

Based on research by Nagar et al., 2014, screening TB patients for DM is a feasible, effective, and comprehensive approach that can lead to improved care, better patient outcomes, and decreased possibility of elevated blood glucose levels.

2.5 Synthesize Table

Table 2.4 Synthesize The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis

No.	Author	Study Design & Sample	Analysis Data	Variable and Measurement	Result	Conclusion
1.	Arimbawa & Mulyantari, 2019 Title: Correlation of Type and Duration of Pulmonary Drug Administration to blood glucose levels in Sanglah	1. This type of research is analytic observational with a cross-sectional time approach 2. n = 38	1. Data analysis was performed using SPSS software version 20.0 for Windows. 2. The chi-square test was used to determine the correlation between tb medication and blood glucose	1. Tuberculosis medication used the observation sheet from medical records as an instrument. 2. Blood Glucose Levels from the medical	1. There is a positive correlation between the duration of administration of tuberculosis medication and blood glucose concentration in tuberculosis patients at Sanglah General Hospital, with a correlation coefficient (r) of 0.536.	1. This study showed a significant positive correlation between blood glucose levels and the duration of tuberculosis medication therapy. 2. The analysis results in this study found no correlation between the use of category I and II tuberculosis

	General Hospital for the 2015-2016 period		levels (nominal variable) 3. The correlation test was used to determine the correlation between the duration of TB medication and blood glucose levels.	record as an instrument.	2. There was no significant correlation between the types of tuberculosis medication and blood glucose levels in tuberculosis patients at Sanglah General Hospital, with a p-value of 0.133	medication on blood glucose levels.
2.	Lin et al., 2017 Title: The change in blood glucose levels in tuberculosis patients	1. Prospective cohort observational study 2. n = 266 TB patients	Comparisons of baseline characteristics between TB patients with stable or unstable FBG using the chi-square test with odds ratios	1.Tuberculosis treatment uses a questionnaire as an instrument. 2. Blood glucose	Of the 232 patients without diabetes mellitus (DM) with initial FBG < 6.1 mmol/L, more than 90% maintained FBG < 6.1 mmol/L during	TB patients who do not have DM based on FBG measurements do not develop DM during anti-TB treatment. Those newly diagnosed with DM on screening generally maintain their

	before and during anti-tuberculosis treatment in China.		(ORs) and their 95% confidence intervals.	levels used data were received and cross-checked by staff.	treatment, and none developed DM.	DM status with high FBG and need to be better managed.
3.	Nagar et al., 2014 Title: A study to assess the blood glucose level among diagnosed cases of tuberculosis registered at a tuberculosis unit of Bhopal	1. It was a cross-sectional study. 2. n = 220	Data were entered in Microsoft Excel 2007 and analyzed using Epi Info 7. Continuous variables were summarized as frequency, mean, and standard error and categorical variables were analyzed using x^2-analysis; $p < 0.05$	Tuberculosis and blood glucose levels used an observation sheet (medical record) for the instrument.	From 260 subjects enrolled in this study, complete details and blood glucose values were available for 220 subjects. Of the 220 subjects, 34 (15.4%) were found to have DM and, 25 (11.3%) had a previous diagnosis of DM, 9 (4.09%) were newly diagnosed. The prevalence of DM	The results of this study echo the need to increase awareness of DM screening in TB patients. The study findings point to a high prevalence of DM in patients with TB in Bhopal and that many patients with DM may need to be made aware of their glucose status. Screening patients with TB for DM is a feasible,

	City, Madhya Pradesh, India		was considered statistically significant.		among patients with TB was significantly higher among males aged 450 years and with pulmonary TB.	effective, and comprehensive approach that can improve care and patient outcomes.
4.	Rahman et al., 2022 Title: The Impact of Blood Glucose Levels on Acid-Fast Bacteria Conversion in Tuberculosis Patients with DM	1. This research is descriptive-analytical with a retrospective cohort approach. 2. n = 49	Descriptive-analytical with a retrospective cohort approach	The data are taken as data from TB patients with DM at the Pulmonary Hospital of North Sumatera Province from July 2018-September 2019	Of all participants with increased blood glucose levels, 4 (7.3%) had AFB conversion, while 6 (2.7%) had no conversion. In those with decreased blood sugar, 32 (28.7%) had AFB conversion, while 7 (10.3%) did not, with a p-value of 0.014.	There is a significant correlation between the effect of blood glucose levels on acid-fast bacteria conversion.

5.	Siburian, 2019 Title: Description Of Blood Glucose Levels In Outpatient Tuberculosis Patients In Medan Lung Special Hospital	1. This research is descriptive 2. n = 30	Analytic descriptive method with qualitative analysis.	1. The instrument for blood glucose level collection using a glucometer test 2. Data related to TB sufferers used the observation sheet from medical records as an instrument	Based on the results of research on examining blood glucose levels in outpatient TB patients at the Special Pulmonary Hospital with a descriptive method of 30 samples, it was found that blood glucose levels increased by 17 samples (57%) and normal blood glucose levels by 13 samples (43%)	From the research results, it is known that the overall average blood glucose level in TB patients has an increase in blood glucose levels in tuberculosis patients, which is influenced by insulin metabolism, Where TB patients can be susceptible to DM. The risk of developing active tuberculosis occurs through two processes, starting with initial exposure to mycobacterial infection and subsequent development.

CHAPTER 3

CONCEPTUAL FRAMEWORK & HYPOTHESIS

3.1 Conceptual Framework

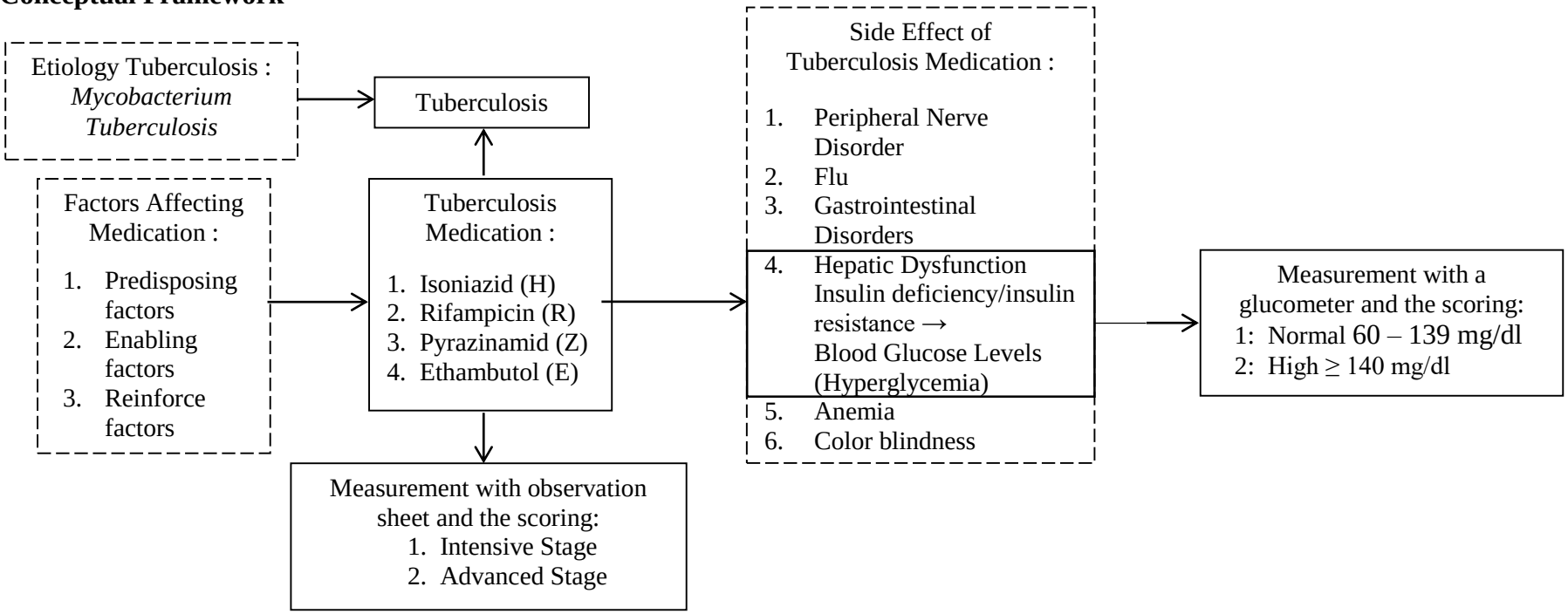

Figure 3.1 Conceptual Framework of The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

3.2 Hypothesis

The hypothesis is a statement of assumptions about the correlation between two or more variables expected to answer a question in research (Kumar, 2019).

The hypothesis in this study is that there is a correlation between tuberculosis medication and blood glucose levels in patients with tuberculosis at Klatak Public Health Center Banyuwangi 2023.

CHAPTER 4

RESEARCH METHODS

4.1 Research Design

Research design is essential because it allows maximum control of several factors that can affect the accuracy of a result. The term research design is used in two ways: first, the research design is a research strategy in identifying problems before planning the final data collection, and second, the research design is used to determine the research structure to be carried out (Nursalam, 2020).

Research design is a reflection of the researchers' ideas. It helps prevent frustration by tying the research together through a structured plan showing how all the main parts of the research work together to try to answer the research question (Asenahabi, 2019).

Researchers can also use research design as a guide in planning and conducting research to achieve a goal or answer a research question. Therefore, selecting and implementing research designs is very important to improve the quality of research, and the results can be utilized (Nursalam, 2020).

In this study, the researchers used a cross-sectional research design, which emphasizes the time of measurement/observation of independent and dependent variable data only once at that time (Nursalam, 2020).

4.2 Framework

The framework is a work chart of the research design that will be carried out, including who will be studied (research subject) and the variables that influence the research (Aziz Alimul H, 2016).

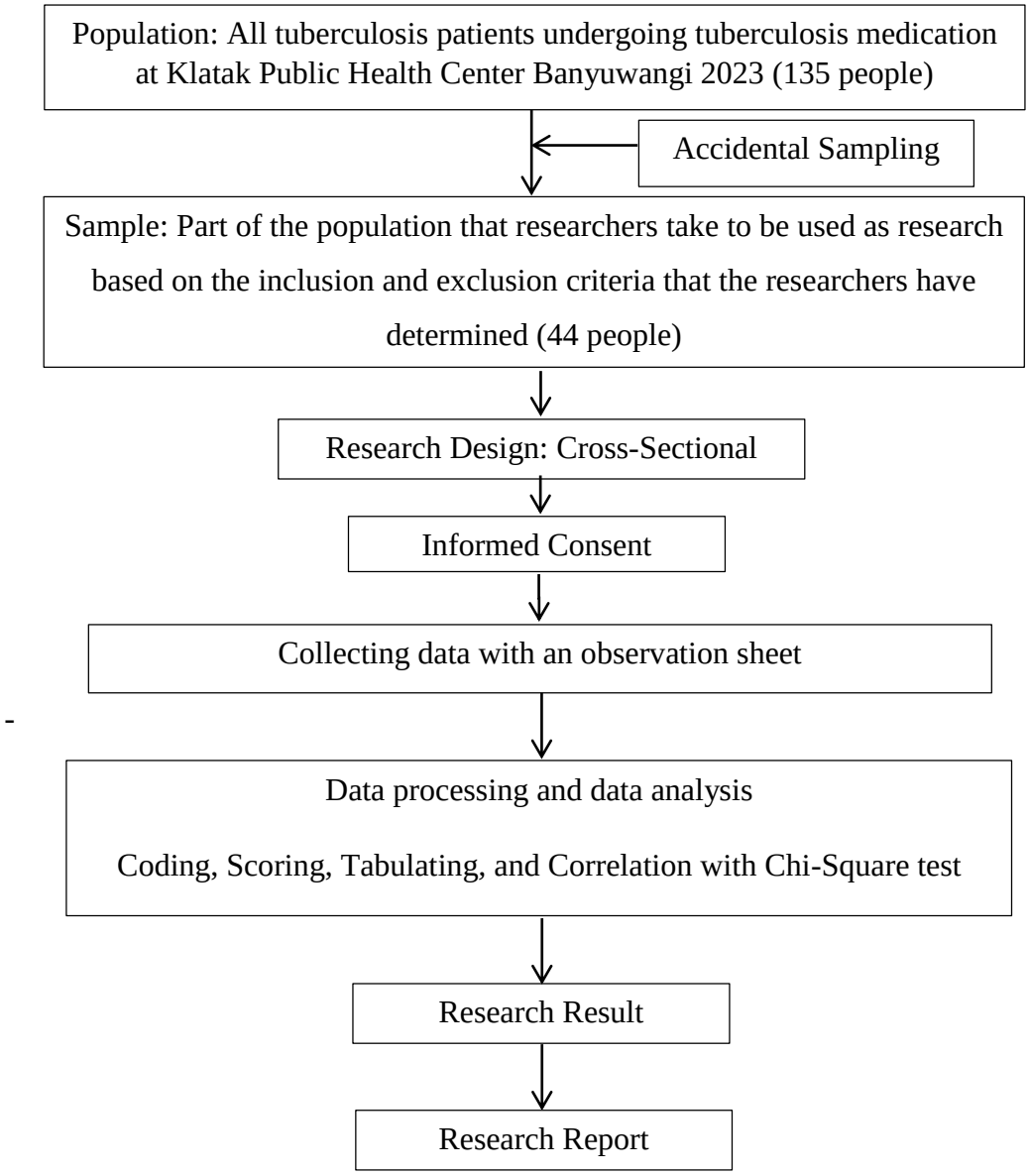

Figure 4.1 Framework of The Correlation Between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

4.3 Population, Samples, and Sampling Technique

4.3.1 Population

The population in the study are subjects (humans; clients) who meet predetermined criteria (Nursalam, 2020). The population in this study were all tuberculosis patients undergoing tuberculosis medication at the Klatak Public Health Center, is 135 people.

4.3.2 Samples

The sample consists of an affordable part of the population that can be used as research subjects through sampling (Nursalam, 2020). The samples in this study were part of tuberculosis patients undergoing tuberculosis medication at Klatak Public Health Center Banyuwangi 2023, with 44 patients.

The inclusion and exclusion criteria of this study were as follows:

1) Inclusion Criteria

Inclusion criteria are the general characteristics of research subjects from a target population that can be reached and will be studied. Scientific considerations should be guided when determining inclusion criteria (Nursalam, 2020). In this study, the inclusion criteria are:

a. Patients undergoing tuberculosis medication > 1 month
b. Patients who agreed to be respondent

2) Exclusion Criteria

Exclusion criteria are excluding/removing subjects who meet the inclusion criteria from research for various reasons (Nursalam, 2020). In this study, the exclusion criteria are:

a. New patients diagnosed with tuberculosis at the time the researchers conducted the study
b. The patient has never taken medication for tuberculosis
c. The patient has difficulty communicating or has a mental disorder
d. Patients diagnosed with diabetes mellitus before tuberculosis
e. Patients have other complications of the disease

4.3.3 Sampling Technique

The sampling technique is a sampling technique by selecting a sample from among the population according to what the researcher wants (objectives/problems in research) so that the sample can represent the characteristics of the population that have been known before (Nursalam, 2020). The sampling technique used in this study was accidental sampling. Accidental sampling is a form of non-probability sampling that involves taking a population sample that is close at hand rather than carefully determined and obtained (Showkat & Parveen, 2017). The researcher used an accidental sampling because the sample determination was based on chance. Anyone who happens to meet the researcher within the specified time limit can be used as a sample if it is deemed that the person they meet matches the predetermined inclusion criteria.

4.4 Identification of Variable

Variables are behavior or traits that give different values to things such as objects, people, etc. (Soeparto, Putra, & Haryanto, 2000) in Nursalam's 2020 book.

4.4.1 Independent Variable

Independent variables are variables that influence or their value determines other variables (Nursalam, 2020). The Independent Variable in this study is Tuberculosis Medication.

4.4.2 Dependent Variable

A dependent Variable is a variable whose value is determined by other variables (Nursalam, 2020). The dependent variable in this study is Blood Glucose Level.

4.5 Operational Definition

An operational definition is to describe or explain all the variables and terms that will be used in research operationally to make it easier for the reader or presenter to interpret the meaning of the research (Nursalam, 2020).

Table 4.1 Operational Definition of The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

No	Variable	Operational Definition	Indicator	Measuring Instrument	Scale	Score
1.	Independent: Tuberculosis Medication	Tuberculosis medication is a medication that must be consumed by tuberculosis sufferers regularly and on time	The frequency of taking medication, the type of drug, drug dosage, and duration of medication will be concluded with the stage of tuberculosis medication	Observation Sheet	Nominal	1. Intensive Stage 2HRZE : Isoniazid 75 mg, Rifampicin 150 mg, Pyrazinamide 400 mg, and Ethambutol 275 mg. Consumed every day. Duration: 1-2 months 2. Advanced Stage 4HR3 : Isoniazid 150 mg, Rifampicin 150 mg. Consumed 3 times a week. Duration: 2-6 months, additional 3 months if after 6 months of medication still found tuberculosis bacteria.
2.	Dependent: Blood Glucose Level	The range of glucose concentration values in the body	The results of blood glucose levels with a glucometer	Observation Sheet	Nominal	1. Normal 60 – 139 mg/dl 2. High ≥ 140 mg/dl

4.6 Data Collection and Data Analysis

Data collection is approaching the subject and collecting the characteristics needed in a study (Nursalam, 2020).

4.6.1 Research Instrument

Research instruments are tools used to collect data in research. The research instrument followed the measurement objectives and the theory used as a basis (Purwanto, 2018). The instrument used in this research was the observation sheet for tuberculosis medication and blood glucose level

4.6.2 Research Location and Time

This research was conducted in Klatak Public Health Center from 22nd August 2023 to 12th August 2023.

4.6.3 Data Collection

Data collection is a process of approaching the subject and collecting the characteristics of the subject needed in a study (Nursalam, 2020). Data collection techniques in this study include:

1) Researchers apply to conduct initial data at the Banyuwangi Institute of Health Sciences Center for Development and Community Service
2) Researcher submits a letter of initial data application to the Banyuwangi Health Office
3) The researcher submitted a letter of recommendation for initial data requests from the Banyuwangi Health Office and the LPPM STIKES to the Klatak Health Center.

4) The researcher coordinated with the head of the Klatak Banyuwangi Health Center.
5) Researchers provide informed consent sheets to respondents
6) Researcher conducted interviews to fill out the observation sheet and checked blood glucose levels
7) Researchers recapitulate research results and process results.

4.6.4 Data Analysis

Data analysis is crucial to achieving the primary research objective: answering research questions revealing phenomena. The raw data cannot describe the desired information to answer the research problem (Nursalam, 2020).

1) Coding

Coding is giving code to the data to convert qualitative data into quantitative. Data coding is needed, especially in data processing, manually or using a computer program (Adiputra et al., 2021). Coding for variable tuberculosis medication in this study:

1: Intensive Stage

2: Advanced Stage

Coding for variable blood glucose levels in this study:

1 : Normal

2 : High

2) Scoring

Scoring is the process of giving a score to each variable. The next step is to sum and categorize data that has been coded according to the provisions (Harahap, 2021). Scoring for variable tuberculosis medication in this study:

1 : Intensive Stage

2HRZE : Isoniazid 75 mg, Rifampicin 150 mg, Pyrazinamide 400 mg, and Ethambutol 275 mg.

Consumed every day.

Duration: 1-2 months

2 : Advanced Stage

4HR3 : Isoniazid 150 mg, Rifampicin 150 mg.

Consumed 3 times a week

Duration: 2-6 months

Scoring for variable blood glucose levels in this study:

1 : Normal 60 – 139 mg/dl

2 : High ≥ 140 mg/dl

3) Tabulating

Tabulating is entering data into already available tables for raw data and for data used to calculate specific data precisely (Adiputra et al., 2021).

4) Statistical Analysis

a. Univariate Analysis

The univariate analysis describes the characteristics of each variable in the study (Notoatmodjo, 2022). Standard deviation, range, percentage, and frequency were used to describe demographic data (age, gender, education level, job, tribe, religion, income, and duration of tuberculosis medication). All analyses used SPSS 21 for Windows.

b. Bivariate Analysis

Bivariate analysis is used to determine the interaction of dependent and independent variables in the form of correlation (Sujarweni, 2015). The statistical test by the researcher used the Chi-Square test using SPSS 21 for Windows. If the value obtained in the statistical test shows a p-value < 0.05, then there is a significant correlation between tuberculosis medication and blood glucose levels in patients with tuberculosis. In other words, Ho is rejected, whereas if $p \geq 0.05$ means Ho is accepted or there is no significant correlation between tuberculosis medication and blood glucose level in patients with tuberculosis.

Table 4.2 Statistical Analysis of The Correlation between Tuberculosis Medication and Blood Glucose Level in Patients with Tuberculosis at Klatak Public Health Center Banyuwangi 2023.

No.	Aims	Variable	Measurement Scale	Statistic Approach
1.	Identification of demographic data variables	1. Age 2. Gender 3. Marital status 3. Education 4. Job 5. Tribe 6. Religion 7. Income level 8. Duration of tuberculosis medication 9. Medication history 10. Disease history	Ratio Nominal Nominal Ordinal Ordinal Nominal Nominal Ordinal Ordinal Ordinal Ordinal	Statistical Descriptive
2.	The Correlation between Tuberculosis Medication and Blood Glucose Level	1. Tuberculosis Medication (Observation Sheet) 2. Blood Glucose Level (Observation Sheet)	Nominal Nominal	Chi-Square

4.7 Research Ethics

Ethical issues in research using human subjects are still a developing central issue (Nursalam, 2020). This research received ethical approval on 14th August 2023 from the Health Research Ethics Committee of Banyuwangi

Institute of Health Sciences with the number of ethics 160/KEPK-STIKESBWI/VIII/2023. In this study, participants will be protected confidentially. Before the research process was carried out, participants were first explained the benefits and objectives of the research. After agreeing, the participant was given an informed consent sheet to sign the consent letter to become a participant. Ethical issues that need to be considered are as follows:

4.7.1 Justice

Subjects must be treated somewhat before, during, and after participating in the research without discrimination if they are unwilling or excluded (Nursalam, 2020).

4.7.2 Informed Consent

Subjects must obtain complete information about the purpose of the research to be carried out and have the right to participate freely or refuse to become respondents. The informed consent must also state that the data obtained will only be used for knowledge development (Nursalam, 2020).

4.7.3 Anonymity

The researcher removes all information about the respondent's identity when presenting the research results and displaying data, such as the respondent's name and other characteristics. By applying anonymity, confidentiality in the research will be ensured (Heryana, 2020).

4.7.4 Confidentiality

Researchers ensure that data is presented anonymously to maintain participant privacy and that data related to participants, such as addresses and others, are stored safely (Heryana, 2020).

4.7.5 Non-Maleficence

Non-maleficence is the obligation not to harm the patient. The simply stated principle supports several moral rules: do not kill, do not cause pain or suffering, do not cripple, do not cause offense, and do not take other people's goods of life (Varkey, 2020).

4.8 Research Limitations

1) Observation Sheet

   Observation sheets for tuberculosis medication currently no longer use 4 categories but only have 1 category with 2 different stages. So, there are a few changes to the observation sheet.

2) Coding & Scoring

   Previously, there were changes to the tuberculosis medication observation sheet, so coding scoring was adjusted to the updated observation sheet.

3) Sampling Techniques

   Sampling determination in this study differed from the proposal that had been made, where the sampling technique used was accidental sampling, so the number of samples used was three-quarters of the original plan, which was 44 respondents.