ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PHARMACY

DEPARTMENT OF PHARMACOLOGY AND CLINICAL PHARMACY

PRE AND INTRA COVID 19 ERA COMPARISON OF DETECTION AND CLINICAL OUTCOMES AMONG PATIENTS WITH TUBERCULOSIS; A FOUR-YEARS RETROSPECTIVE FOLLOW-UP STUDY IN SELECTED PUBLIC HOSPITALS IN ADDIS ABABA, ETHIOPIA, 2023.

BY: RUTH HADGU (MPHARM CANDIDATE)

A THESIS TO BE SUBMITTED TO DEPARTMENT OF PHARMACOLOGY AND CLINICAL PHARMACY, SCHOOL OF PHARMACY, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY AS A REQUIREMENT FOR THE FULFILLMENT OF MSC IN PHARMACY PRACTICE.

JUNE, 2023

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Advisor: Legese Chelkeba. (MSc, Ph.D., Associate Professor of Clinical Pharmacy)

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ABSTRACT

Background: Tuberculosis (TB) is still the biggest cause of death from an infectious disease worldwide, with over 10 million people becoming infected each year. The coronavirus disease 2019 (COVID-19) outbreak has severely disrupted health-care systems and people's overall well-being around the world. People with TB are more likely to develop severe disease or die than people with COVID-19. The coexistence of COVID-19 with pulmonary TB can create a diagnostic dilemma and additional diagnostic challenges for clinicians. Despite these difficulties, there is not enough data to determine how COVID-19 affects TB patient detection and outcomes.

Objective: To compare the detection and clinical outcomes of patients with TB pre and intra COVID-19 periods in selected public Hospitals of Addis Ababa, Ethiopia, 2023.

Methods: A retrospective observational follow-up study was undertaken among TB patients with pre- and intra-COVID-19 era comparisons. This study was carried out in five public hospitals in Addis Ababa, which were chosen using a stratified sample technique. A 1.2-structured ODK version 2022 questionnaire was employed. Finally, it was exported to SPSS version 26 for analysis. Bivariate analysis at a P-value of 0.25 and multivariable analysis at a P-value of 0.05 were applied to announce for statistical significance

Results: Patients who had known treatment outcomes in the selected hospitals were 375 during the COVID-19 period, compared with 469 TB during pre – COVID-19 period, showing a 20% decline in TB testing. Despite the decrement of susceptible (10.6%) and rifampicin resistance (RR) TB (47.7%), there was a 54.3% of multi-drug resistance (MDR) TB increment during the COVID-19 period. Overall, there was significantly lower treatment success rate of TB during COVID-19 period (75.7% vs. 81.2%, p< 0.001), with higher rate of loss to follow up (8.8% vs. 6.2%, p= <0.001) as well as death (12.8% vs. 8.7%, p= < 0.001) compared with pre-C0VID-19 period. Factors such as treatment method in the pre-COVID-19 and age category, educational level, type of tuberculosis, and HIV status during COVID-19 period were significant indicators of successful TB treatment.

Conclusion and recommendation: COVID-19 had a substantial detrimental influence on overall TB detection, RR-TB/MDR-TB, treatment success, lost-to-follow-up and mortality. To reduce the impact on TB case detection, the TB program must rapidly adjust to the new normal, strengthen patient-centered TB care, embrace digital health technology, increase awareness of generation, and guarantee that other opportunities given by the pandemic will be utilized.

Key words: Tuberculosis, covid-19, Detection, clinical outcomes, Addis Ababa, Ethiopia.

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Acronyms and abbreviations

AACA-Addis Ababa City Administration

ACF- Active Case Finding

AFB - Acid-fast bacilli

HMIS- Health Management Information systems

LMICs- Low-income and middle-Income Countries

MDR-TB -multidrug-resistant tuberculosis

ODK- Open Data Kit

RR-TB- Rifampicin resistance tuberculosis

SARS-CoV-2- Severe Acute Respiratory Syndrome Coronavirus

SPSS- Statistical Package for Social Sciences

SSA- Sub-Saharan Africa

TB- Tuberculosis

VIF- Variance Inflation Factor

WHO- World Health Organization

1. Introduction:

1.1. Background:

Tuberculosis (TB) remains one of the most serious challenges to global health (1). One-quarter of the world's population is thought to be infected with Mycobacterium tuberculosis, making it the leading infectious cause of death (2). According to the World Health Organization's (WHO) 2018 global TB report, 1.6 million people died in 2017 and 10 million got TB(3).

Despite improvements in TB the disease still poses a serious threat to public health, particularly in Africa. The Sub-Saharan region of the continent is where it is least under control (4). In 2015, there were an estimated 237 cases of TB reported in Africa per 100,000 people, more than double the global average of 133 cases per 100,000 people.(5).

In Ethiopia, TB is still a major public health problem. The country is among the 22 high TB burden countries with high number of missed and infectious TB cases in the community. The prevalence and incidence of TB in Ethiopia in 2014 were 211 and 214 per 100,000 populations respectively. TB is among the top ten causes of admission and deaths in adults in Ethiopia. Increasing trends of multidrug resistance TB is a serious public health challenge for the country (6).

Close contacts of tuberculosis (TB) patients with positive sputum acid-fast bacilli (AFB) smears are at greater risk of contracting the disease and infection (7). Unfavorable TB treatment outcomes and an increased risk of TB can both be attributed to low socioeconomic status. Low levels of education, unemployment, low income, poverty, smoking, and alcohol use have all been linked to TB in SSA (8). Early diagnosis of infectious TB cases in the community is the main objective of tuberculosis control efforts in nations with a high TB incidence (9).

After exposure to smear-positive pulmonary TB cases and prompt administration of a complete course of treatment, the development of TB in an exposed individual occurs in two stages. The majority of TB control programs in underdeveloped countries use passive case-finding, depending on suspect TB cases to present to health facilities, as active case-detection is challenging on a broad scale and involves the commitment of significant human and financial resources for a relatively poor yield of cases. Delays in diagnosis and the beginning of effective treatment raise TB-related morbidity and mortality rates as well as the possibility of community spread (10). Ethiopia shares many of the same issues as other low-income nations, including a lack of resources, low education levels, poor incomes, poverty, and a labor shortage(11).

The coronavirus disease 2019 (COVID-19) outbreak has caused severe disruptions to healthcare systems and the overall well-being of people around the world (12). Evidence now points to respiratory droplets as the primary means of transmission for both COVID-19 and TB, with the lungs serving as their primary site of entry. As a result, patients with COVID-19 and TB co-infections may fare worse (13).

Similarly, people who have structural lung disease or active TB are probably more likely to develop COVID-19. They demonstrate that those with severe COVID-19 are more likely to have latent or active TB or post-TB sequelae, and those with SARS Cov-2 should be monitored for the development of TB (14).

1.2.Statement of the problem

In Ethiopia, the top ten reasons for hospitalization and fatalities are related to tuberculosis (TB)(6). Ethiopia was included as one of the 22 countries with the highest TB burden in the WHO's 2014 global report, with estimated incidence and prevalence rates of 258 per 100,000 and 237 per 100,000, respectively (15). According to hospital statistics provided by the Ethiopian Ministry of Health (EMOH), TB is the third-most common cause of outpatient morbidity and mortality and the fourth-most common reason for hospital admission (16).

Studies carried out in many nations suggest a potential inverse relationship between COVID-19 and TB. Patients with TB are more likely than patients with COVID-19 alone to have poor outcomes from COVID-19, and patients who are co-infected with COVID-19 and TB are more likely to experience severe illness or death. When COVID-19 and pulmonary TB co-occur, health care professionals may face a diagnostic dilemma and new challenges. Similar infrastructure and knowledge are required for the diagnosis, management, and containment of both diseases because TB and COVID-19 both have respiratory symptoms (17). COVID-19 makes it stressful for TB patients to visit medical institutions for diagnosis and treatment, and the pandemic's high demand for medical personnel makes it difficult to conduct routine TB case follow-ups (12).

Ethiopia revealed its first COVID-19 case on March 13, 2020. On April 8, 2020, a state of emergency was proclaimed. At the outset, the population as a whole was in a state of fear and avoided public health services for fear of contracting COVID-19 (18). A study on the effects of the COVID-19 pandemic on TB treatment and prevention in Addis Ababa has been conducted. All of the information was gathered from the health management information systems (HMIS) of the Addis Ababa health bureau between April 2019 and March 2021 (19). Due to the absence of actual time patient-level data in the area, there is therefore insufficient understanding about the impact of COVID-19 on the diagnosis, treatment initiation, and clinical outcomes of TB treatment. Therefore, the aim of this study was to assess the detection rate and clinical outcomes of TB patients during pre- and intra-Covid-19 period in the public hospitals in Addis Ababa, Ethiopia.

Data was also directly collected from public hospitals, which were specifically chosen based on the health institutions providing TB services.

1.3.Significance of the study

Ethiopia is one of seven high-burden countries to reach the first goal of the End TB Strategy—a 20% reduction in TB incidence between 2015 and 2020—due to the government's significant efforts to combat the disease (12). A lot needs to be done to improve the preventive and standard of care for TB, and it is essential to pay close attention to both of these factors at all levels of the system.

This study was done to examine the detection and clinical outcomes of patients with tuberculosis in the pre- and intra Covid-19 periods. This will aid in the documentation of how COVID-19 affects TB diagnosis and treatment outcomes, It is an important breakthrough to deal with upcoming health crises caused on by new illnesses, natural disasters, and social conflicts.

2. Literature review

Tuberculosis is an infectious illness that is a primary cause of death globally. Around the world, 1.2 million people died from tuberculosis (TB) in 2019, according to estimates. Although tuberculosis rates are slowly declining, they are not decreasing quickly enough to reach the World Health Organization's End TB Strategy goal (20).

In Ethiopia, tuberculosis is the leading cause of disease, the third-leading cause of hospital admissions, and the second-leading cause of mortality. Ethiopia was unable to get a diagnosis in a timely manner. A number of factors contribute to the issue, including a lack of tools for TB case detection, a shortage of healthcare professionals, a lack of basic infrastructure, and a lack of diagnostic tools and supplies (21).

The goal of this evaluation of the literature is to determine how COVID-19 affects the diagnosis, start of treatment, and clinical outcomes for patients with tuberculosis. To find relevant publications, we systematically searched information via electronic databases such as MEDLINE (PubMed) and Google Scholar from February 1 to May 15, 2022..To find suitable published papers, we utilized the terms "detection," "initiation," and "treatment outcomes" along with Ethiopia in free text and Medical Subject Headings (MeSH).

2.1.The Corona virus Disease 2019 (COVID-19) Pandemic and TB

There are significant disruptions to healthcare systems, especially TB programs, as a result of the current COVID-19 epidemic, which is a worldwide health emergency. TB is a long-lasting bacterial illness, whereas COVID-19 is an acute viral illness that is highly contagious. Both COVID-19 and tuberculosis (TB), which mostly affects the lungs, impact the respiratory system and share symptoms such coughing, fever, and breathing difficulties (22).

Another major source of concern is the termination of therapy for MDR-TB. Patients with MDR-TB are being asked to return to TB-specialized facilities for testing and treatment during the next month because second-line MDR-TB drugs are not generally available. Fears of infection while traveling or in the hospital have diminished excitement for these visits, restricting hospitals' capacity to deliver efficient TB services (23).

2.2. Impact of covid-19 in TB detection and treatment initiations

Both TB and COVID-19 are infectious illnesses transmitted through the air that primarily affect the lungs. Coughing, fever, and shortness of breath are common symptoms of both diseases. Testing for COVID-19 or TB should be done in accordance with the clinical characteristics, history, and local TB burden of TB patients to ensure that their diagnostic needs are not underestimated (24).

The number of national TB cases detected in China declined by 20% in February 2020 compared to February 2019 (23). Weekly counts of reported cases in India fell by 75% in the three weeks following the implementation of a strict national lockdown, compared to an average of 45875 weekly cases in the previous weeks of 2020, due to a combination of factors such as delays in entering data onto the real-time national online TB surveillance system, decreased attendance at health services, reassignment of health personnel, and a decrease in TB testing (17). In contrast, Brazil's national TB program reported no recent increased in weekly TB cases (25).

WHO analyzed the impact of the COVID-19 pandemic on TB services in the European region, twenty-nine nations reported monthly tuberculosis notifications for the first half of 2019 and 2020, which declined by 35.5% during the first three months of 2020 compared to the first three months of 2019, more than six fold the average annual decrease of 5.1% documented from 2015 to 2019. In 2020, the amount of patients engaged in rifampicin-resistant (RR) or multidrug-resistant TB (MDR) treatment dropped by 33.5%. The highest severity score for movement restrictions was seen between April and May 2020, correlating with the biggest reported drop in TB notifications (26).

According to a 2020 study conducted in the Republic of Korea, TB diagnosis was delayed during the COVID-19 pandemic. The median time to start TB treatment (25 days) in 2020 rose by 3 days compared to the previous three years (22 days) (p 0.0001). During the August outbreak the time to TB diagnosis was 4 days longer than in the previous three years. From February to March 2020, the compliance rate with the required timing for individual case investigations in Daegu and Gyeongbuk provinces was 2.2% lower than in other locations in 2020. The rate was 13% lower in public health centers than in other locations (80.3% vs. 93.3%, p = 0.0003) (27).

An Indonesian study found that the outbreak has affected all TB services, including case detection and quick testing. In 2020, there were around 41% fewer TB cases in Indonesia than in 2019. When cases were detected during the COVID-19 pandemic, programs and activities were halted due to insufficient advice on TB active case finding (ACF) operationalization, particularly ACF. If a passive case arises, it may be due to patients' movement restrictions in order to receive therapy. Furthermore, fear of getting the virus when attending a health care facility may undermine the overall goal of early detection and treatment. Several institutions have restricted their services in order to lessen the risk of transmission. The majority of TB institutions in Indonesia have received COVID-19 certification at the provincial level, resulting in considerable delays in TB diagnosis due to increased workload (28).

From January 2018 to March 2021, a retrospective analytic analysis of RR-TB diagnoses in South Africa was done. Control measures for COVID-19 and health-care system modifications were mapped to better understand how these may have impacted access to RR-TB diagnostic services throughout this time period. During the study period, 628 patients were diagnosed with RR-TB. In 2020, 195 RR-TB cases were diagnosed, with the first quarter accounting for the bulk (35%, n = 1469). In the remaining patients, 17% (n = 14 33), 23% (n = 14 44), and 25% (n = 14 49) were diagnosed in the second, third, and fourth quarters, respectively. There were significant drops in monthly diagnosis, most notably in April 2020 and Q3 of 2020, when diagnosis decreased by 25% and 21%, respectively, as compared to the same periods in 2019 (29).

A retrospective examination of TB case notification and detection at a Nigerian university teaching hospital reported a 35% and 34% decrease in the number of presumptive TB and active TB cases detected, respectively, when compared to the same period in 2019 (17).

The influence of the COVID-19 pandemic on TB care delivery and treatment results was studied in Sierra Leone. Presumptive TB cases decreased by 12.7% in the first three quarters of 2020 compared to the same time in 2019. Children and women were hit the hardest, with a 20% decline in tuberculosis testing. The greatest significant drop in presumptive cases occurred in April and May of 2020, correlating with the rapid period of the nationwide lockdowns imposed in response to COVID-19 (30).

A study conducted in Addis Ababa, Ethiopia, to assess the impact of COVID-19 on TB services during the pre-COVID-19 era and the COVID-19 era found that total TB detection, bacteriologically confirmed TB, and engagement in TB detection decreased by 11% and 11.8%, respectively, during the COVID-19 period. During the same time span, rifampicin resistance increased by 27.7%. A comparison analysis revealed a considerable decrease in these TB service markers (19).

2.3.Treatment outcomes of Tuberculosis before and after covid-19

Even in normal times, the nature of tuberculosis, with extensive treatment regimens and poor outcomes owing to drug resistance produced by medication withdrawal, are significant difficulties, but they are magnified in a pandemic scenario with numerous and severe isolation measures. This moves directly observed therapy to self-administered therapy, for which digital-health devices like electronic medication monitors and video-supported therapy has been advised to assure treatment adherence. In the face of COVID-19, tuberculosis clinical trials confront discontinuation risks and other obstacles(31).

The COVID-19 pandemic offers a unique challenge to healthcare delivery to patients with multidrug-resistant tuberculosis (MDR-TB) and threatens to disrupt worldwide control efforts (32). The difficulties in tuberculosis diagnosis, notification, care, and cure are particularly concerning in light of global antimicrobial resistance. Despite the fact that multidrug-resistant tuberculosis is expected to account for up to one-third of antimicrobial resistance deaths worldwide, only a minority of MDR tuberculosis patients have access to all-oral treatment regimens. Long, hazardous regimens involving intravenous or intramuscular injections continue to be the norm in many low- and middle-income (LMIC) nations (33).

A study done in Northern Italy during the most severe phase of the COVID-19 epidemic (March-April 2019 to March-April 2020) revealed that despite efforts to keep TB services fully operational, the TB center saw a significant drop in the number of TB diagnoses and an increase in the proportion of patients who were lost to follow-up or died (34).

Another study conducted in Kenya to assess the immediate effects of COVID-19 on TB and HIV programs found that there was a slight increase in treatment success in the COVID-19 period (2.0%), primarily due to a decrease in patients (2.2%), but other adverse program outcomes were comparable between the two periods (35).

2.4.Conceptual frame work

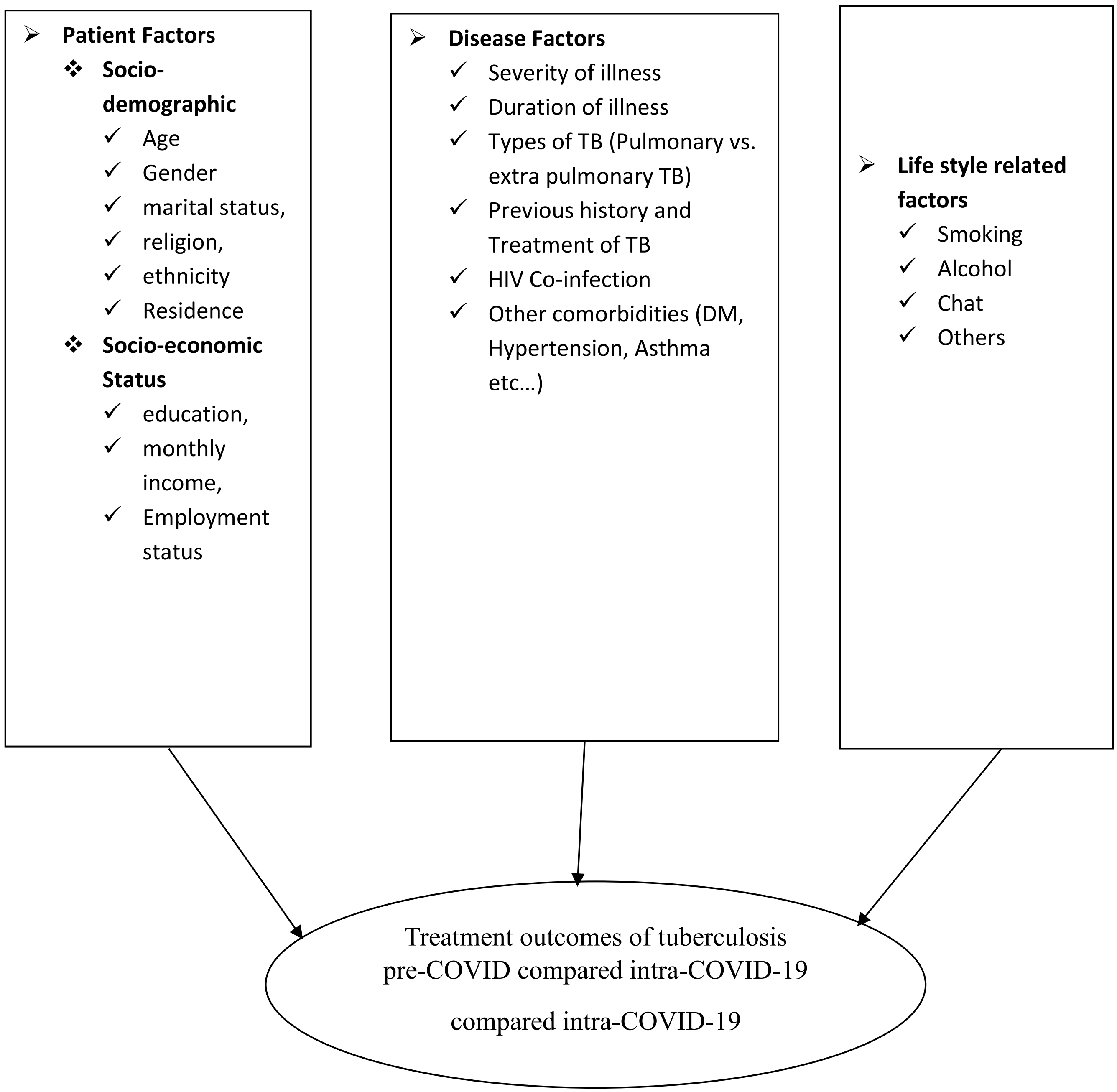

Figure 1: Conceptual frame work for treatment and clinical outcomes of tuberculosis

3. Objectives:

3.1 General objective:

- To compare the detection and clinical outcomes of patients in TB during pre and intra COVID- 19 periods in selected public Hospitals of Addis Ababa, Ethiopia, from March 13, 2018 to March 12, 2022.

3.2 Specific objectives:

- To assess the detection of TB cases during pre and intra COVID- 19 periods in selected public Hospitals of Addis Ababa, Ethiopia from March 13, 2018 to March 12, 2022.
- To compare the rate of MDR-TB or R resistant TB during pre and intraCOVID-19in selected public Hospitals of Addis Ababa, Ethiopia from March 13, 2018 to March 12, 2022.
- To compare the treatment outcomes of TB during pre and intra COVID- 19 in selected public Hospitals of Addis Ababa, Ethiopia from March 13, 2018 to March 12, 2022.
- To determine predictors of poor outcomes among patients with TB during pre and intra COVID-19 from March 13, 2018 to March 12, 2022.

4. Methodology

4.1.Study settings

Addis Ababa is Ethiopia's capital and largest city, with a population of 5,228.000 million in 2022 (37). There are eleven public hospitals in Addis Ababa that provide tuberculosis treatment; six are from the Addis Ababa city administration, and five are from the federal government. This study was carried out in five public hospitals in Addis Ababa, Ethiopia, which were chosen using a stratified sample technique based on their supply of tuberculosis care. These included the Addis Ababa city administration's Zewditu Memorial Hospital, Yekatit Hospital, and Ras Desta Hospital, as well as the federal government's Alert Hospital and St. Peter Hospital. Tikur-Anbessa Specialized Hospital was excluded from the study due to a lack of follow-up; patients were directed to a nearby health facility.

4.2.Study period:

This study was conducted from August, 2022 to September, 2022.

4.3.Study design:

Retrospective observational follow up study was conducted among TB patients with pre and during COVID- 19period'scomparisonsPopulation:

4.4.Population:

4.4.1. Source population:

All presumed TB patients medical record who visited the TB centers at the five public Hospitals of Addis Ababa, Ethiopia from March, 2018 to March, 2022.

4.4.2. Study population:

All patients' medical record with clinically or bacteriologically confirmed TB in the five public Hospitals of Addis Ababa, Ethiopia from March, 2018 to March, 2022 and fulfilling the inclusion criteria.

4.5.Eligibility criteria

4.5.1. Inclusion criteria

For Pre Covid-19 era

- All patients medical record with clinically or bacteriologically confirmed TB in the selected five public hospitals based on the health facilities providing tuberculosis services from March 13, 2018 to March 12, 2020

For intra Covid-19 era

- All TB patients medical records with clinically or bacteriologically confirmed TB in the selected five public Hospital is based on the health facilities providing tuberculosis services from March 13, 2020 to March 12, 2022

4.5.2. Exclusion Criteria:

- All patients with incomplete medical records during both periods.
- Patients who were diagnosis with TB, but had no follow-up in the selected hospitals for both time periods (March 13, 2018 to March 12, 2022)
- Tikur Anbessa specialty hospital was excluded from this study because no patients' treatment outcomes were recorded.

4.6.Sample size determination and sampling technique:

4.6.1. Sample Size Determination:

Recent study has been powered to find a 4.1 % difference in relative risk of mortality between pre-COVID and intra-COVID eras among patients with TB For us to have 90% power to detect a 5% difference in mortality between the pre-COVID and intra-COVID groups, with alpha = 0.05, we required 816 patients (440 and 375 in each group) (19).

4.6.2. Sampling technique and procedure:

The public hospitals in Addis Ababa, which provided TB treatment services, were first categorized into two groups based on the Addis Ababa city administrative hospitals and federal government hospital by stratified sampling technique. Then, six public hospitals, which were selected by a simple random sampling technique using allocation proportional to size, were included in this study based on the health facilities providing TB services. Tikur Anbessa Specialized Hospital was excluded from the study because of no follow up; they were referred to nearby health facilities after detection. The study population allocated for each public hospital was based on the number of TB patients who visits TB centers from all presumed patient medical record. The period for the pre COVID-19era was between March 13, 2018 to March 12, 2020 the data was collected from the patient's medical record with clinically or bacteriologically confirmed TB.The data during COVID-19erawas collected fromMarch 13,2020 to March 12, 2022(36).

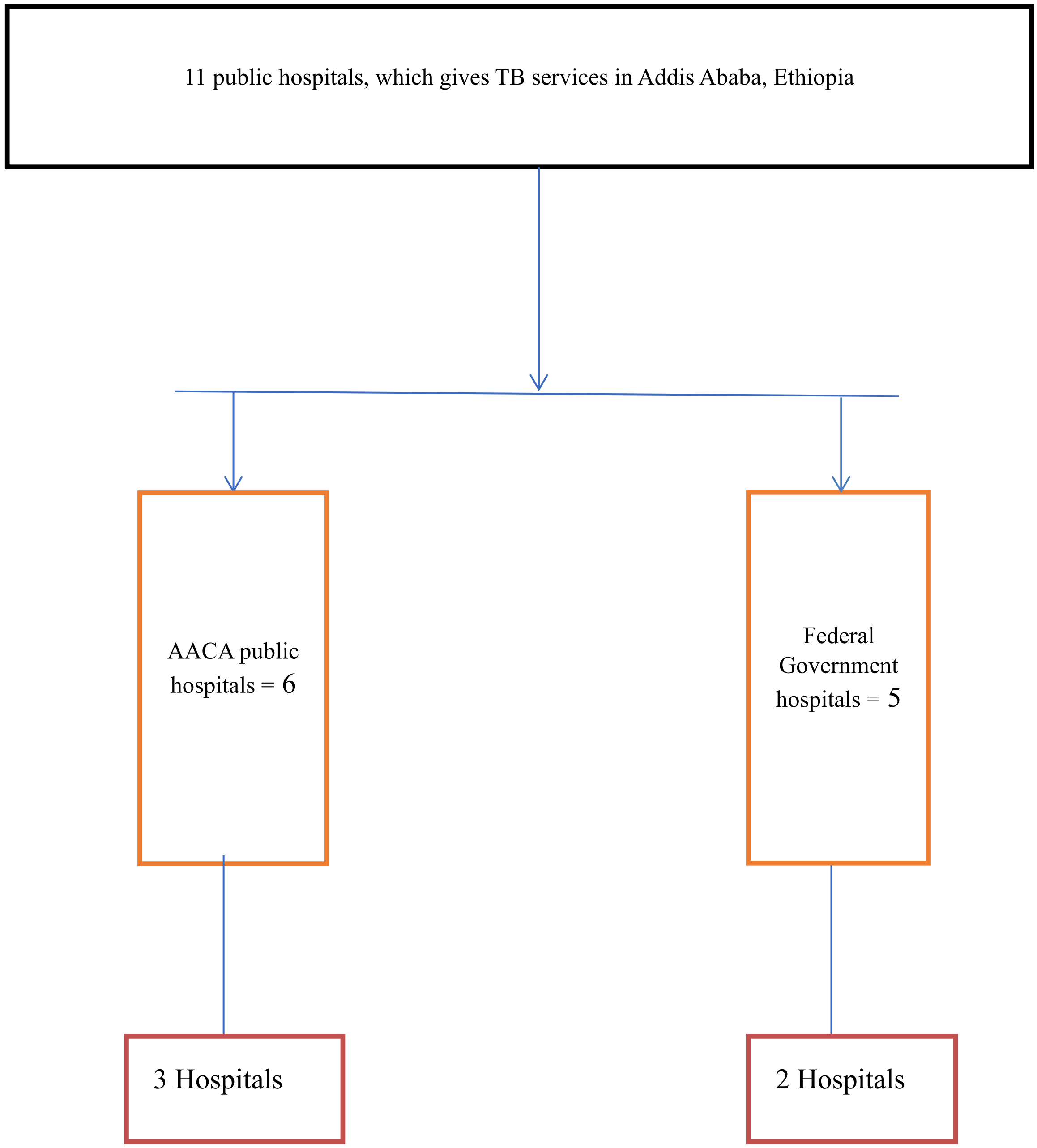

Figure 2: sampling technique and procedure

4.7. Instruments and Data collection:

4.7.1. Data collection procedure

Six pharmacists were trained for two days before collecting data. The study population was assigned to each public hospital based on the number of TB patients who visited TB facilities from all supposed patient medical records throughout the data collection period.

4.7.2. Data collection tool:

Data was collected using a systematic approach adopted from research on the COVID-19's influence on tuberculosis detection, treatment start, and clinical outcomes. The data abstraction format (questioners) was created in English to aid in the extraction of information on case detection and patient clinical outcomes. The tool includes socio-demographic information (such as gender, age, education status, and place of residence), anatomical site of TB (pulmonary vs. extra-pulmonary), drug resistance type (rifampin resistance (RR) vs. MDR), previous treatment (new vs. previously treated), diagnosis method (bacteriologically vs. clinically), HIV status (HIV-infected vs. not infected), comorbidities (hypertension, diabetes mellitus, asthma, etc.), and WHO treatment outcomes. (Cured, completed, lost to follow up, transferred/not evaluated, failed treatment, died). The ODK version 2022.1.2 software was used to collect the data, along with the Kobo Toolbox humanitarian response server to store the collected data.

4.8.Data quality assurance:

A pre-test was performed on the study population to confirm that the data abstraction format was compatible with the needs of the study. Any errors discovered during the pre-testing phase were fixed and incorporated into the final version of the data abstraction format. The lead investigator provided two days of training to the data collectors prior to data collection to ensure data quality. During data collection, the supervisor and data collectors evaluated and checked the obtained data for completeness and consistency, and they were immediately notified if the survey forms were incomplete or incorrectly filled out. For improved quality control, the supervisor chose a hospital at random each day and revisited the hours to ensure they were appropriately gathered. ODK version 2022.1.2 software was used to collect the data along with the Kobo Toolbox server to store the collected data.

4.9.Study variables

4.9.1. Dependent variable/ Outcome variable

- Rate of TB detection during pre- and intra-COVID-19
- Treatment outcomes of TB Patients during pre- and intra-COVID-19

4.9.2. Independent variable:

- Socioeconomic factors (like education, monthly income, employment status)
- Demographic factors (Age, Sex)
- Life style related factors (smoking status, alcohol drinking status. Chat and others)
- Disease related factors (comorbidities, type of comorbidity, laboratory-confirmed TB, clinically confirmed TB, Presumptive TB, Pulmonary vs. extra-pulmonary TB)
- Patient type (Newly diagnosed, Relapsed)
- Treatment modality (Directly Observed Therapy, Monthly dispensing for self-administration)

4.10. Statistical analysis:

The data was collected using ODK version 2022.1.2 software, which was then stored on the Kobo Toolbox server before being exported to SPSS version 26 for final analysis. Before exporting the data, it was examined for completeness and frequency to rule out any missing values. The data was then coded and revalued in SPSS, and frequency distributions were run, as well as additional cleansing, missing values and errors confirmed. Descriptive statistics were used to describe the sample, and numerical data was presented as the mean, standard deviation, proportion, or percent. Using binary logistic regression, the link or statistical association between TB treatment success and chosen independent covariates was explored.

Pearson's chi-square or Fisher's exact tests were used to investigate associations between categorical variables. To investigate predictors of treatment success, a binary logistic regression model was used. The bivariate analysis includes known or potential factors influencing TB treatment results. Age, gender, type of TB (pulmonary versus extra pulmonary), patient type (newly diagnosed versus relapse), mode of TB diagnosis (laboratory confirmed versus clinically diagnosed), treatment technique (DOT versus self-administered therapy by monthly dispensing), and HIV status were among those considered. After filtering for multi-co-linearity, factors in the bivariate analysis with p values less than 0.25 were included in the multivariable analysis. An adjusted odds ratio (AOR) with 95% confidence intervals (CI) was used to summarize the findings. Statistical significance was defined as $p<0.05$ in all analyses. Tables, figure and texts were taken to report the findings.

4.11. Operational definition:

TB case detection: Tuberculosis, both clinically and bacteriologically confirmed(30).

A laboratory-confirmed TB case: was a patient with Mycobacterium tuberculosis complicated illness verified by culture.

Multidrug-resistance (MDR)-TB: Resistance to at least isoniazid and rifampicin, two most important first-line drugs(37).

WHO treatment Outcomes (38)

- **Cured:** Treatment has been finished, and culture on samples taken at the end of treatment and on at least one previous occasion has turned negative.
- **Completed:** Although the treatment was completed, the case did not meet the criteria for cure or treatment failure.
- **Failed:** Five months or later into treatment, the culture or sputum smear remains positive or becomes positive again.
- **Died:** Death occurred before the patient was cured or therapy was completed, regardless of the cause.
- **Defaulted:** The therapy was interrupted for two months or longer due to a non-care provider decision; or the patient was lost to follow up for two months or more prior to the conclusion of treatment, except if transferred.
- **Transferred:** The patient was referred to another clinical unit for treatment, and there is no information on the patient's outcome.

➢ **Treatment success** (30)

- **Good treatment outcome:** Tuberculosis patients who was cured or completed their treatment.

- **Poor treatment outcome:** Tuberculosis patients who failed treatment, defaulted treatment, were transferred to other health facilities, or died before being cured or completing their treatment.

4.12. Ethical consideration:

The departmental research and ethical review committee of the department of pharmacology and clinical pharmacy of Addis Ababa University, as well as the public health research and emergency management directorate of the Addis Ababa health bureau, provided ethical approval. In order to conduct the research, an official letter of authorization was filed with the selected five public hospitals in Addis Ababa based on the health institutions providing tuberculosis care. Throughout the study period, information was recorded secretly and confidentiality was assured. The obtained data was kept strictly confidential, and no one but the members of the research team had access to it. All paper and computer records from the study were held in a safe location under lock and key, and any report did not include their name or contact information.

4.13. Dissemination of the result:

The outcomes of this study will be shared with the five Addis Ababa public hospitals and Addis Ababa University's collage of health sciences, department of pharmacology, and clinical pharmacy. Efforts will be made to publish this paper and to present in different national and international conferences.

5. Results

5.1.Socio - demographic and clinical characteristics of TB patients

In the five hospitals, a total of 38,848 patients were tested for TB cases over the relevant study periods, with 20,821 (53.6%) and 18,025 (46.4%) occurring during the pre-COVID-19 and during COVID-19periods, respectively. A total of 7070 TB cases were detected. Only 844 of these patients completed their follow-up at the chosen set of hospitals. A total of 254 patients were treated at Zewditu Memorial Hospital, 204 at St. Peter Hospital, 196 at Alert Hospital, 90 at Yekatit Hospital, and 100 at RasDesta Hospital, respectively, which yielded 5 TB cases per 100 person – years or 50 TB cases per 1000 person – years.

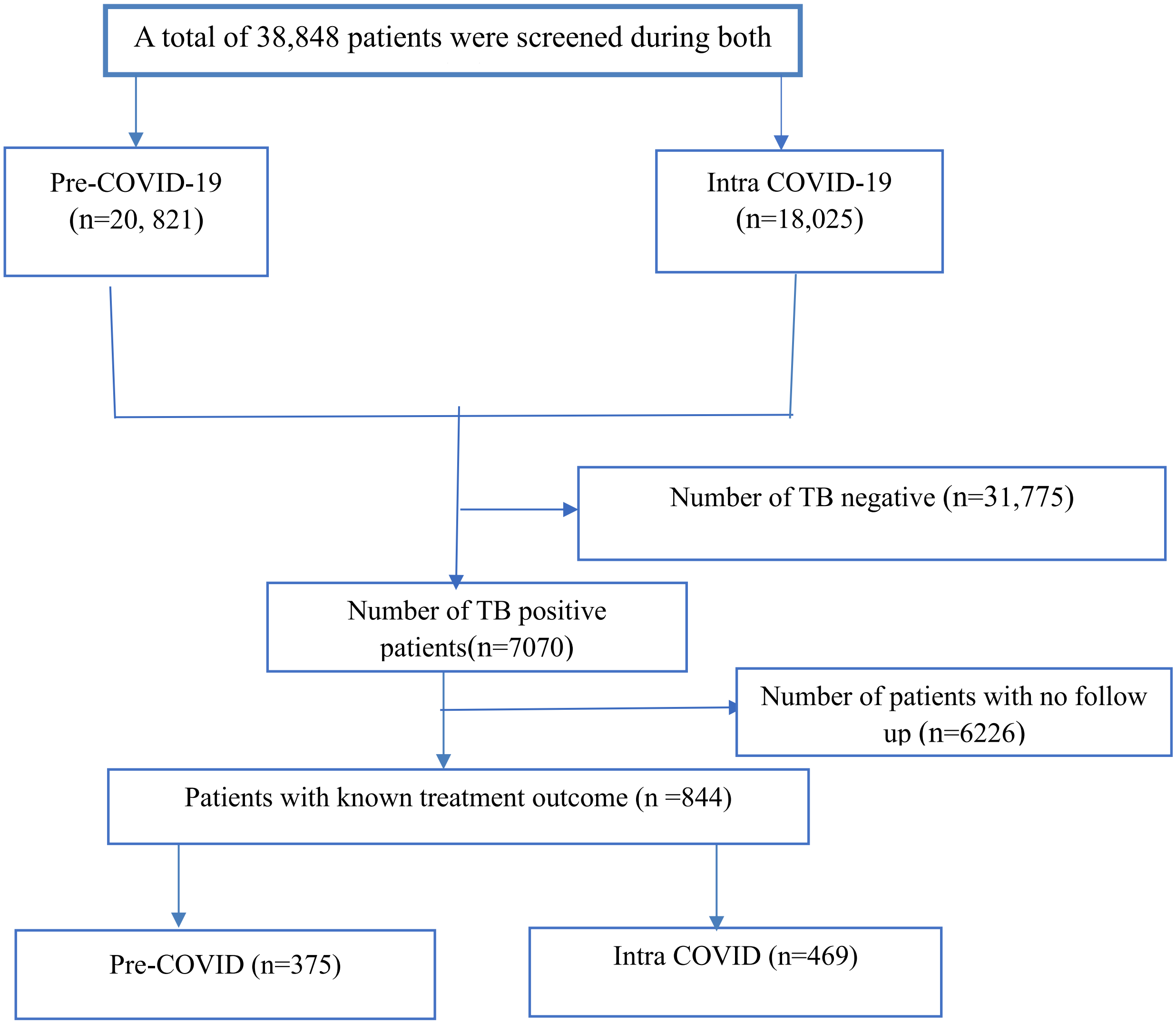

Figure 3: The schematic representation of total TB screening and detection during pre-COVID-19 and Intra-COVID-19 periods.

The mean age of the patients was 34.5 (±15.7), and almost half, 408 (48.3%) of them were females. Among these; about two third 673 (79.7%) of them were urban residents, 365 (43.2%) of them had secondary school (9-12) educational background, and half 422 (50%) of the patients were employed.

A total of 197 (23.3%) patients were substance users. The majority of 497 (58.9%) them were newly diagnosed TB patients, and 590 (69.9%) had pulmonary TB, as well as around two-thirds (616) of them being laboratory-confirmed TB cases. The majority of the patients (483, 57.2%) were infected with susceptible to TB, followed by rifampicin-resistant TB (294, 34.8%), and MDR TB (67, 7.9%). Almost half (425, 50.4%) of them had no contact history with MDR TB, and only 146 (17.3%) of the patients were identified by culture for drug resistance status. Two hundred seventy-one (32.1%) of the patients were HIV positive, with most of them 247 (91%) on ART. The majority of the patients (664, 78.7%) had no co-morbidity, followed by severe acute malnutrition (165, 19.5%), diabetes mellitus 11 (1.3%), and hypertension (0.5%), respectively. About two-third of patients (69.9%) were taking their TB treatment through directly observed therapy. Only 163 (19.3%) of the patients interrupted their TB treatment **(Table 2)**. The majority of the patients 370 (43.8%) were cured from TB, followed by treatment completed 291 (34.5%), died 89 (10.5%), lost to follow-up 62 (7.3%), failed treatment 31 (3.7%), and transferred out 1 (0.1%) **(Figure 4).**

Table 1**: Socio - demographic and clinical characteristics of TB patients** at **public hospitals of Addis Ababa, Ethiopia, 2023 (n = 844).**

Characteristics	**Frequency (N)**	**Percent (%)**
Age category (in years)		
≤ 15	62	7.3
> 15	782	92.7
Sex		
Male	436	51.7
Female	408	48.3
Residence		
Urban	673	79.7
Rural	171	20.3
Educational level		
No formal education	74	8.8
Primary school	58	6.9
Secondary school	365	43.2
College/ University	347	41.1
Occupation		
Employed	422	50
Unemployed	422	50
Substance use		
Yes	197	23.3
No	647	76.7
Patient type		
Newly diagnosed	497	58.9
Relapsed	347	41.1
Type of TB		
Pulmonary	590	69.9
Extra pulmonary	254	30.1
Mode of diagnosis		
Laboratory confirmed	616	73
Clinical diagnosis	228	27
TB status		
Susceptible	483	57.2
Rifampicin resistance	294	34.8
MDR	67	7.9
Contact history of patients with MDR- TB		
Yes	137	16.2
No	425	50.4
Unknown	282	33.4
Drug resistance identification method		
GeneXpertMTB/RIF	698	82.7
Culture	146	17.3
HIV status		
Positive	271	32.1
Negative	546	64.7
Unknown	27	3.2
ART status		
Not on ART	590	69.9
On ART	247	29.3
HIV status known but, not on ART	7	0.8
Comorbidity		
No comorbidity	664	78.7
DM	11	1.3
Hypertension	4	0.5
Sever acute malnutrition	165	19.5
Other medication the patientsweretaking		

Yes	14	1.7
No	830	98.3
Treatment method		
Directly observed therapy	590	69.9
Monthly dispensing	254	30.1
Treatment interruption		
Never interrupted	681	80.7
Interrupted	163	19.3

TB: Tuberculosis, MDR: Multidrug resistance, HIV: Human Immunodeficiency Virus, ART: Antiretroviral therapy, DM: Diabetes mellitus, WHO: World Health Organization**.**

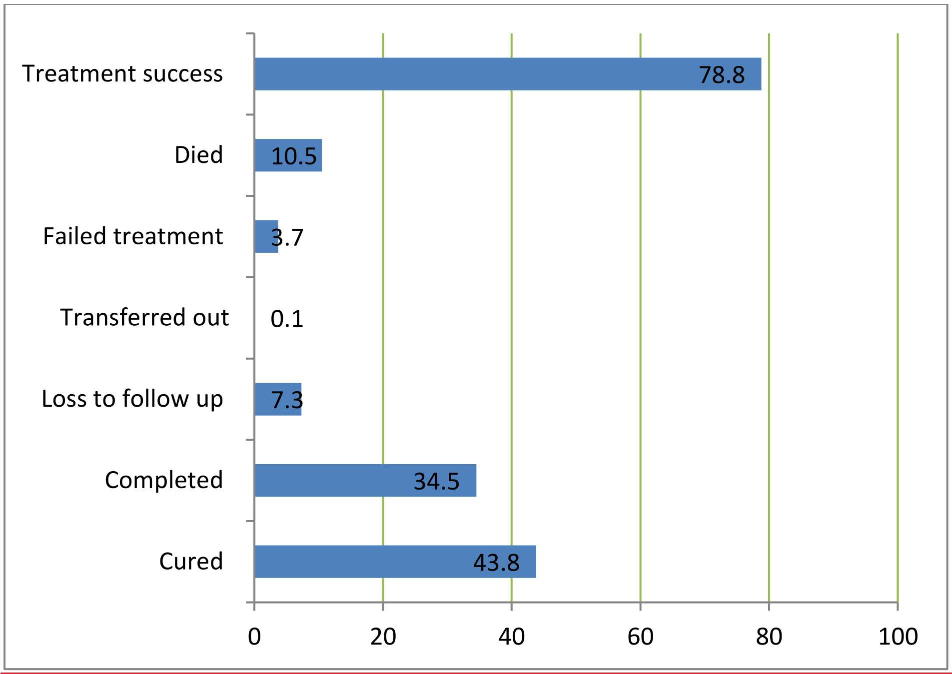

Figure 4: WHO treatment outcome of Tuberculosis

5.2. Comparison of presumptive and laboratory – confirmed TB cases during pre- and intra- COVID – 19 periods.

For this study, four years of total data were analyzed, including two years prior to COVID-19 and two years following it. A total of 7070 registered TB cases were discovered during this period. During the pre-COVID-19 and during post COVID-19 periods, respectively, 3740 (52.9%) and 3330 (47.1%) of these cases were recorded.

However, among the chosen hospitals, the number of patients who had follow-up and had known treatment results was 375 during the COVID-19 era compared to 469 TB tests during the pre-COVID-19 period, indicating a 20% decrease in TB testing. This resulted in a 36.8% and an 18.6% drop in TB testing among children and adults, respectively. During the intra COVID-19 period, there was also a decrease in newly diagnosed cases by 11.7%, relapsed cases by 30.7%, pulmonary cases by 25.4%, and extra-pulmonary cases by 6% of TB. The gender distribution for TB testing did not, however, alter significantly between the pre- and intra COVID-19 periods (P-value = 0.59).

There was a 27.5% of decline in laboratory confirmed TB testing during the intra – COVID-19 period as compared with pre – COVID-19 period. Despite the decrement of susceptible by 10.6% and RR TB by 47.7%, there was a 54.3% of MDR TB increment during the intra – COVID-19 period compared with the pre – COVID-19 era. There was also a significance difference in the human immunodeficiency virus (HIV) status regarding TB testing (P- value < 0.001) between the two time periods (**Table 2)**.

Table 2:**Comparison of TB cases during pre- and intra- COVID – 19 periods at public hospitals of Addis Ababa, Ethiopia, 2023 (n = 844).**

Characteristics	Pre-COVID-19	Intra- COVID-19	Change in Pre- and Intra COVID-19 totals	P- Value
Gender				
Male	247	189	-23.5%	0.59
Female	222	186	-16%	
Age category				
Children (≤ 15 years)	38	24	-36.8%	**< 0.001**
Adults(> 15 years)	431	351	- 18.6%	
Residence				
Urban	379	294	- 22.4%	**0.025**
Rural	90	81	-10%	
Educational level				
No formal education	39	35	- 10.25%	0.005
Primary school	28	30	+ 7%	< 0.001
Secondary school	198	167	-15.7%	0.077
College/ University	204	143	-30%	
Occupational status				
Employed	224	198	- 11.6%	0.110
Unemployed	245	177	-27.8%	
Substance use				
Yes	107	90	- 15.9%	**<0.001**
No	362	285	-21%	
Patient type				
Newly diagnosed	264	233	-11.7%	**< 0.001**
Relapsed	205	142	-30.7%	
Type of TB				
Pulmonary TB	338	252	-25.4%	**< 0.001**
Extra pulmonary TB	131	123	-6%	
Mode of diagnosis				
Laboratory confirmed TB	357	259	-27.5%	**0.019**
Clinical diagnosis	112	116	+ 3.6%	
TB status				
Susceptible	255	228	-10.6%	**< 0.001**
Rifampicin resistance	193	101	-47.7%	0.805
MDR TB	21	46	+54.3%	
Contact history of patients with MDR TB				
Yes	77	60	- 22%	0.094
No	233	192	-17.6%	0.95
Unknown	159	123	-22.6%	
Drug resistance identification method				
GeneXpertMTB/RIF	406	292	-28.07%	0.269
Culture	63	83	+ 31.7%	
HIV status				
Positive	169	102	-39.6%	**<0.001**
Negative	293	253	-13.6%	< 0.001
Unknown	7	20	+65%	
ART status				
Not on ART	308	282	- 8.4%	**<0.001**
On ART	157	90	-42.7%	
HIV status known but, not on ART	4	3	-25%	
Comorbidity				

No comorbidity	356	308	- 13.48%	**0.007**
Diabetic Mellitus	9	2	-77.7%	0.29
Hypertension	4	0	-100%	0.27
Sever acute malnutrition	100	65	-35%	
Treatment method				
DOT	265	247	-6.8%	0.371
Monthly dispensing	204	128	-37.25%	
Treatment interruption				
Never interrupted	387	294	-24%	< **0.001**
Interrupted	82	81	-1.2%	

TB – Tuberculosis, MDR – Multidrug resistance, HIV – Human Immunodeficiency Virus, ART – Anti retroviral therapy, DOT – Directly Observed Therapy, WHO – World Health

5.3.Comparison of Tuberculosis treatment outcome during the pre – and intra – COVID-19 periods

There was very strong significant difference between treatment outcome of TB (Chi square = 809.253, df = 5, Phi and Cramer's V = 0.979, p – value, <0.001) between pre – and intra – COVID-19 periods. Overall, there was significantly lower treatment success rate of TB during intra – COVID-19 period (75.7% versus 81.2%, p – value, <0.001), with higher rate of loss to follow up (8.8% versus 6.2%, p – value = <0.001) and higher rate of death (12.8% versus 8.7%, p – value = < 0.001) as compared to pre – COVID-19 period respectively. However, there was lower rate of cure TB patients (37.9% versus 48.6%, p – value, < 0.001) as well as lower rates of completed TB treatment (change in pre and intra COVID -19 totals – 7.3%, p – value, < 0.001) during the intra COVID – 19 period as compared with pre COVID – 19 period **(Table 3**).

Table 3**: comparison of characteristics and treatment outcome of patients during pre-COVID-19 and intra – COVID-19 periods at public hospitals of Addis Ababa, Ethiopia, 2023 (n = 844).**

Characteristics	Pre – COVID-19 N (%)	Intra – COVID-19 N (%)	P – value
WHO treatment outcomes			
Cured	228 (48.6)	142 (37.9)	**< 0.001**
Completed	151 (32.2)	140 (37.3)	**< 0.001**
Loss to follow up	29 (6.2)	33 (8.8)	**< 0.001**
Transferred/not evaluated	-	1 (0.3)	
Failed treatment	20 (4.3)	11(2.9)	**< 0.001**
Died	41(8.7)	48 (12.8)	**< 0.001**
Treatment success			
Yes	381 (81.2)	284 (75.7)	**< 0.001**
No	88 (18.8)	91 (24.3)	**< 0.001**

5.4. Factors associated with Tuberculosis treatment success during the pre – and post– COVID-19 periods

Educational level, substance use, patient type, type of TB, mode of diagnosis, TB status, and treatment method were candidates for multivariable analysis at a p-value less than 0.25 during the pre-COVID-19 period after being filtered for multi-co-linearity by the variance inflation factor (VIF), which had a mean of 2.005 and all the selected variables had a VIF of less than 5.

However, only the treatment modality was a significant predictor of TB treatment success in the pre-COVID-19 period, with a p-value of 0.05 in a multivariable analysis. Patients who received their anti-tuberculosis medication while being closely monitored (by DOT) were less likely to experience poor treatment outcomes than those who received their medication by monthly dispensation (AOR = 0.577; 95% CI: 0.337–0.987) **(Table 4)**.

Table 4**: Factors associated with Tuberculosis treatment success during the pre – COVID-19 periods at public hospitals of Addis Ababa, Ethiopia, 2023 (n = 469).**

Characteristics	**Treatment success**		**Bivariate analysis**		**Multivariable analysis**	
	Yes	**No**	**COR(95% CI)**	**P-value**	**AOR(95% CI)**	**P-value**
Educational level						
No formal education	32	7	0.987(0.405,2.409)	0.978	1.725(0.651,4.573	0.273
Primary school	19	9	2.138(0.896,5.100)	0.087	2.391(0.928,6.162)	0.071
Secondary school	163	35	0.969(0.582,1.614)	0.904	1.020(0.591,1.761)	0.943
College/ University	167	37	1	1	1	
Substance use						
Yes	78	29	1.909(1.147,3.178)	0.013	1.737(0.990,3.046)	0.054
No	303	59	1	1	1	
Patient type						
Newly diagnosed	236	28	0.287(0.175,0.470)	0.000	0.687(0.194,2.428)	0.560
Relapsed	145	60	1	1	1	
Type of TB						
Pulmonary	264	74	2.343(1.271,4.317)	0.006	1.725(0.793,3.754)	0.169
Extra pulmonary	117	14	1	1	1	
Mode of diagnosis						
Laboratory confirmed	282	75	2.025(1.077,3.810)	0.029	0.906(0.397,2.067)	0.815
Clinical diagnosis	99	13	1	1	1	
TB status						
Susceptible	229	26	0.284(0.101,0.795)	0.017	0.395(0.087,1.797)	0.230
Rifampicin resistance	137	56	1.022(0.377,2.768)	0.966	0.961(0.336,2.752)	0.942
MDR	15	6	1	1	1	
Treatment method						
DOT	285	58	0.651(0.396,1.071)	0.091	0.577(0.337,0.987)	**0.045***
Monthly dispensing	96	30	1	1	1	

DOT: direct observable therapy, TB: tuberculosis, MDR: multidrug resistance TB

In a multivariable analysis, factors such as age category, educational level, type of TB, and HIV status were significant predictors for the TB treatment success at a P-value of <0.05. Those TB patients aged below 55 years old had a lower likelihood of having poor treatment success than these 55 years old and above (AOR = 0.311; 95% CI: 0.140 – 0.693).

On the opposite hand, pulmonary TB patients had two times higher probability of having poor treatment success than extra pulmonary TB patients (AOR = 2.040; 95% CI: 1.017 – 4.098). HIV status was also one of the most important predictors of TB treatment success; those HIV positive TB patients had 12 times higher odds of poor treatment success than the unknown HIV status TB patients (AOR = 12.13; 95% CI: 2.632 – 55.96). With regard to educational level, TB patients who were with no any formal education had 3.5 times likelihood of having poor treatment success than those with college or university educational background (AOR = 3.456; 95% CI: 1.227 – 9.735) **(Table 5)**.

Table 5**: Factors associated with Tuberculosis treatment success during the post–COVID-19 periods at public hospitals of Addis Ababa, Ethiopia, 2023 (n = 375).**

Characteristics	**Treatment success**		**Bivariate analysis**		**Multivariable analysis**	
	Yes	**No**	**COR(95% CI)**	**P-value**	**AOR(95% CI)**	**P-value**
Age category						
< 55 years	259	70	0.322(0.170,0.609)	0.000	0.311(0.140,0.693)	**0.004***
>= 55 years	25	21	1	1	1	
Educational level						
No formal education	20	15	2.948(1.346,6.456)	0.007	3.456(1.227,9.735)	**0.019***
Primary school	22	8	1.429(0.578,3.537)	0.440	2.168(0.752,6.249)	0.152
Secondary school	128	39	1.198(0.696,2.061)	0.515	1.413(0.761,2.621)	0.273
College/ University	114	29	1	1	1	
Substance use						
Yes	61	29	1.710(1.012,2.888)	0.045	1.230(0.633,2.391)	0.541
No	223	62	1	1	1	
Patient type						
Newly diagnosed	187	46	0.530(0.329,0.856)	0.009	0.427(0.076,2.419)	0.336
Relapsed	97	45	1	1	1	
Type of TB						
Pulmonary	181	71	2.020(1.163,3.508)	0.013	2.040(1.017,4.098)	**0.045***
Extra pulmonary	103	20	1	1	1	
Mode of diagnosis						
Laboratory confirmed	191	68	1.440(0.844,2.455)	0.181	0.897(0.452,1.781)	0.757
Clinical diagnosis	93	23	1	1	1	
COVID-19 vaccination status						
Fully vaccinated	55	28	1.886(1.073,3.314)	0.027	1.399(0.714,2.741)	0.328
Partially vaccinated	65	19	1.083(0.588,1.993)	0.798	1.013(0.496,2.069)	0.972
Not vaccinated	163	44	1	1	1	
TB status						
Susceptible	182	46	0.578(0.285,1.171)	0.128	0.989(0.149,6.579)	0.991
Rifampicin resistance	70	31	1.012(0.475,2.158)	0.975	1.187(0.491,2.873)	0.703
MDR	32	14	1	1	1	
HIV status						
Positive	54	48	5.037(1.390,18.25)	0.014	12.13(2.632,55.96)	**0.001***
Negative	213	40	1.064(0.298,3.801)	0.924	1.751(0.414,7.416)	0.447
Unknown	17	3	1	1	1	
Treatment method						
DOT	175	72	2.360(1.349,4.129)	0.003	1.158(0.574,2.337)	0.682
Monthly dispensing	109	19	1	1	1	

6. Discussion

This study evaluated the detection rate and clinical outcomes of tuberculosis patients in selected public hospitals in Addis Ababa, Ethiopia, between March 13, 2018 and March 12, 2022. There was a significant decrease in overall TB case detection throughout the COVID-19 periods (March 13, 2020 to March 12, 2022), but an increase in MDR TB, a decrease in DOT therapy, and a decrease in TB treatment success.

When compared to the pre-COVID-19 periods in this study, there was an overall 20% decrease in the identification of TB patients who had follow-up and had known treatment results during the COVID-19 periods. The impact on children was the greatest, with a 36.8% decline in TB testing. This is consistent with an 11% decline in the Addis Ababa, Ethiopia, retrospective study and with earlier research by the WHO, China, Indonesia, Uganda, Nigeria, and South Africa in 29 European countries, which decreased by 35.5%, 20%, 41%, 43%, 34%, and 33%, respectively, during the COVID-19 periods. In the three weeks after India's stringent national lockdown was put into effect, there was also a 75% decrease in weekly counts of recorded TB cases. However, there have been no significant improvements in the number of weekly TB cases in Brazil's national TB program (17,19,23,25,28,38–41).

This disparity could be attributable to fear of the disease or the interventions taken to combat the epidemic. Since the COVID-19 illness, most countries, including Ethiopia, have focused all of their attention, political will, and limited personnel and financial resources from an already overcrowded and underfunded health system on controlling the pandemic. This could be related to the COVID-19 pandemic lockdown. The fall in TB notification rates, however, does not always represent a decrease in incidence but rather reflects under diagnosis. Due to missed diagnoses, there has been a significant decrease in TB case identification, leading to a buildup of undiscovered TB, resulting in continuing TB transmission and greater rates of latent TB infection. However, in the study done in Brazil, there might not have been a noticeable change in that short study period.

In this study, there was also a 27.5% decrease in laboratory-confirmed TB testing during the intra covid-19 periods compared to the pre covid-19 periods. In contrast, research conducted in Sierra Leone found a 37% increase in laboratory-confirmed TB testing over the COVID-19 period. During the COVID-19 period, there was also an increase in laboratory-confirmed tuberculosis testing in Malawi and Zimbabwe (43, 44). This decrease could be attributed to the financial resources from an already overcrowded and underfunded health system on controlling the pandemic. Despite a decrease in susceptible and rifampicin-resistant TB (10.6% vs. 47.7%), there was a 54.3% increase in MDR TB over the intra covid-19 periods in this study. This is similar to the findings of a study undertaken in Addis Ababa, Ethiopia, to assess the influence of the COVID-19 pandemic on tuberculosis prevention.

There was significantly higher self-administration of treatment through monthly dispensing during intra – COVID-19 period (p – value = 0.002) as compared with pre – COVID-19 period (34.1% vs. 26.9%) in this study. This is consistent with a study done in Sierra Leone and in Addis Ababa (19,30). This might be due to COVID-19 lockdown, economic burden, movement restriction or the disease stigma.

In this investigation, the treatment success rate for tuberculosis was significantly lower during the intra COVID-19 period (75.7% versus 81.2%, p value = 0.000) compared to the pre COVID-19 periods. Similarly, in Addis Ababa research, the success rate of TB therapy fell from 82.4% before covid-19 to 77.6% during the COVID-19 pandemic. This is also consistent with research conducted in Korea, which found that from 89.4% before covid-19 to 84.5% after COVID-19, reduced TB treatment success increased the likelihood of poor treatment outcomes and the development of drug resistance (DR-TB, exacerbating the country's existing DR-TB problem.

However, in a study conducted in Sierra Leone, treatment success rates were significantly higher during the intra-COVID-19 period as compared to the pre-COVID-19 period, and there was a minor increase in treatment success during the COVID-19 period (2.0%) in a study conducted in Kenya (19,27,30,35). This could be related to a drop in the number of patients who have not been evaluated.

In this study, there were lower rates of cured patients and completed therapy but greater rates of loss to follow-up and mortality during the COVID-19 periods compared to the pre-COVID-19 years. Similarly, during the COVID-19 pandemic, there were significantly higher rates of TB-related deaths and losses to follow-up in a study conducted in Sierra Leone in 2021 and in research conducted in Northern Italy during the peak of the COVID-19 outbreak, the proportion of patients who were lost to follow-up or died increased (31,35).

In this study, factors like age category, educational level, type of tuberculosis (pulmonary vs. extra-pulmonary), HIV status during intra COVID-19 periods, and treatment method (DOT vs. monthly dispensing) in the pre COVID-19 period were significant predictors of TB treatment success at a P-value of 0.05. Patients who received their anti-tuberculosis treatment while being closely monitored (by DOT) were less likely to experience poor treatment outcomes than those who received their medication by monthly dispensation. Furthermore, compared to individuals 55 years of age and older, TB patients under the age of 55 were less likely to experience poor treatment outcomes.

Patients with pulmonary tuberculosis, on the other hand, had a twofold higher risk of poor treatment outcomes than patients with extra-pulmonary tuberculosis. HIV status was also one of the most important indicators of tuberculosis treatment effectiveness; HIV-positive TB patients had a 12 times greater chance of poor treatment success than TB patients with unknown HIV status. In terms of educational level, TB patients with non-formal education had 3.5 times the odds of poor treatment success than those with a college or university education. In other studies conducted in Sierra Leone, Nigeria, and other meta-analyses, characteristics such as youngful age, freshly diagnosed vs. recurring TB, pulmonary TB, and HIV-negative status were predictors of treatment outcomes before COVID-19 and after COVID-19 periods (30,42–44).

This is supported by the fact that taking their anti-tuberculosis treatment under direct observation (by DOT), having a higher level of education, and being young could contribute to the good treatment success of the tuberculosis patients. Whereas having comorbidities like HIV/AIDS has a negative influence on the treatment success of tuberculosis.

7. Strengths and Limitations of the Study

7.1. Strength of the study

- This study was multi-centered raises the representativeness of the results.
- The data for this study were gathered using ODK version 2022.1.2 software, and they were stored on a Kobo Toolbox humanitarian response server to reduce mistake.

7.2. Limitation of the study

- The data was restricted to public hospitals, preventing generalization to all Addis Ababa health institutions.
- The study's retrospective design depended on clinic records being accurate, which may have suffered during the COVID-19 lockdowns.
- Only cases that had been notified were included in the retrospective study's analysis. It is likely that some TB patients passed away before receiving a diagnosis and that some instances were unreported, making it impossible to include them.

8. Conclusion and Recommendation

8.1.Conclusion

Covid-19 significantly reduced total TB detection, RR-TB/MDR-TB, DOT therapy, and TB treatment success. In this study, there was a significant decline in the detection of TB patients with known treatment outcomes during the covid-19 era compared to pre COVID-19times. Children were the most affected, with a 36.8% decrease in tuberculosis testing. Despite a decrease in susceptible and rifampicin-resistant TB, there was a significant increase in MDR TB over the covid-19 period. There was also much more self-administration of therapy via monthly dispensing during the post-covid-19 era than before covid-19.

Overall, the success rate of tuberculosis therapy was much worse during the intra-COVID-19 period, with greater rates of death and loss to follow-up than during the pre-covid-19 period, respectively. However, compared to precovid-19 eras, there were fewer patients who were cured of TB and finished their treatment during the COVID-19 eras.

In this study, features included age group, educational level, type of tuberculosis (pulmonary vs. extra-pulmonary), HIV status during intra COVID-19 periods, and treatment mode (DOT vs. monthly dispensing) in the pre COVID-19 period were significant predictors of TB treatment success. Patients under the age of 55 who received their anti-TB medicine from the DOT were less likely to experience unsatisfactory treatment outcomes. On the other hand, individuals with pulmonary TB, along with those who were HIV positive and had TB, were more likely to have poor treatment outcomes.

8.2.Recommendations

- The country will be able to continue the advancements made during the previous decade to combat TB and the control programs and to meet the objectives of the End TB program by strengthening current programs and adopting new ones.
- The FMOH and non-governmental organizations should improve the patient-centered approach to TB care by using digital health technology, promoting public awareness, boosting community-based active TB case detection, and integrating the COVID-19 and TB screening program.
- Especially in high-risk populations, hospital managers and healthcare professionals should use the COVID-19 service to address the community and screen for TB, such as during vaccination.
- In order to prevent diagnosis delays, awareness efforts should be launched that are directed at the whole health sector and address the potential clinical picture overlap between COVID-19 and TB.
- Researchers should do more studies using a different methodology, such as a prospective qualitative approach or hybrid methodology.
- To overcome the difficulties, make sure that other possibilities that the pandemic brings are fully taken advantage of to lessen their influence on TB case discovery.

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Annexes

Annexes- 1: information sheet

Name of the investigator: Ruth Hadgu (MSc Candidate)

Thesis Title: Pre and during covid 19 era comparison of detection and clinical outcomes among patients in tuberculosis; retrospective follow up study in selected public hospitals in Addis Ababa, Ethiopia, 2023.

Thesis Objective: To compare the detection and clinical outcomes of patients in Tuberculosis pre and during Covid-19 eras in selected Government Hospitals of Addis Ababa, Ethiopia, 2023.

Study Techniques: To achieve the planned objective of the study which includes; socio demographic, clinical factors, WHO treatment outcomes and treatment success.The data was collected from patients' medical records on four-year study.

Confidentiality: The collected information was kept confidential and used only for research purpose. No one except the investigator of the research had access to the information collected. The name and/or other personal information of patients was not notified in any report. All paper and computer record of the study was kept in a secured place under lock when not in use.

Person to contact: If the data collectors, supervisors, or other public hospitals administrative staffs had any question regarding the study they wasfree to contact me in person or by the following addresses.

Cell phone: 0912446177

Email: ruthhadgu44@gmail.com

Annex- 2: Public Hospitals Consent

This is a study to be carried out at the selected public hospitals of Addis Ababa. The main purpose of this study is to compare the detection and initiation of treatment and clinical outcomes of patients in Tuberculosis pre and during Covid-19 eras in selected Government Hospitals of Addis Ababa, Ethiopia. The result of this will be used to provide information about the impact of covid-19 on the detection, treatment initiation and clinical outcomes of tuberculosis. Which will help to document the impact of covid- 19 on the detection, initiation and the clinical and treatment outcomes of Tuberculosis.

Any patient's personal information such as the name, any private details will be kept confidential throughout study period and the generated information will be disclosed in full. The public hospitals have full right to accept or refuse study whenever it needs. Whenever there is need of more information/ explanation on proposed study the principal investigator could be contacted in person or through phone number: **+251912446177 (Ruth Hadgu main investigator).** Finally, if you agreed whether the study will be conducted at your institution, please confirm it by putting your sign.

The participant public hospitals   Principal investigator:

Annex- 3: A check list for data collection tool

Data was collected using a structured questionnaire which is adapted from a similar studies conducted in Sierra Leone on impact of COVID-19 on Tuberculosis Case Detection and Treatment Outcomes (30). And study conducted in Ethiopia on impact of COVID-19 pandemic on TB prevention and care in Addis Ababa, Ethiopia (19). Then, was adjusted according to the study's objectives and study design to collect data to compare the detection and clinical outcomes of patients in Tuberculosis pre and during Covid-19 in selected public Hospitals of Addis Ababa, Ethiopia, 2023.

Instruction:

- ❖ Do not write names
- ❖ Write or tick appropriately in the space provided

1. **Socio-demographic factors**

NO	Questions and filter	Coding category	Skip to
1.01	Age	…………………………… …yrs.	
1.02	Gender	1, Male 2, Female	
1.03	Residence	1, Urban 2, Rural	
1.04	Religion	1, Orthodox 2, Muslim 3, Catholic 4, Protestant 5, Other (specify……)	
1.05	Educational level	1, No formal education 2, Primary school 3, Secondary school 4, College/university	
1.06	Occupation	1, employed 2, Unemployed	
1.07	Substance use	1, Alcoholic drink 2, Smoking 3, Chat 4, Others	

2. Clinical characteristics of the patients

NO	Questions and filter	Codding category	Skip to
2.01	Patient type	1, Newly diagnosed 2, Relapsed	
2.02	Type of Tuberculosis	1, Pulmonary 2, Extrapulmonary	
2.03	Mode of diagnosis	1, Laboratory confirmed 2, Clinical diagnosis	
2.04	TB status	1, Susceptible 2, Rifampin resistance (RR) 3, MDR	
2.05	Contact history of patient with MDR-TB	1, Yes 2, No 3, Unknown	
2.06	Drug resistance identification method	1, GeneXpert MTB/RIF 2, Culture 3, Clinical	
2.07	HIV status	1, Positive 2, Negative 3, Unknown	
2.08	ART status	1, Not applicable 2, On ART 3, HIV status known but, ART status unknown	
2.09	Comorbidity	1, No comorbidity 2, Diabetic Mellitus 3, Hypertension 4, Immune compromise 5, Others (specify) ………	
2.10	Other medication the patient is taking	1, Yes (name of the medications……………………….) 2, No other medication	
2.11	Treatment method	1, Directly Observed Therapy 2, Monthly Dispensing for Self-administration	

2.12	Treatment interruption	1, Never interrupted 2, Interrupted	
2.13	WHO treatment Outcomes	1, Cured 2, Completed 3, Lost to follow up 4, Transferred/not evaluated 5, Failed treatment 6, Died	
2.14	Treatment success	1, Yes 2, No	