Effect of COVID-19 pandemic on TB notification in Addis Ababa, Ethiopia

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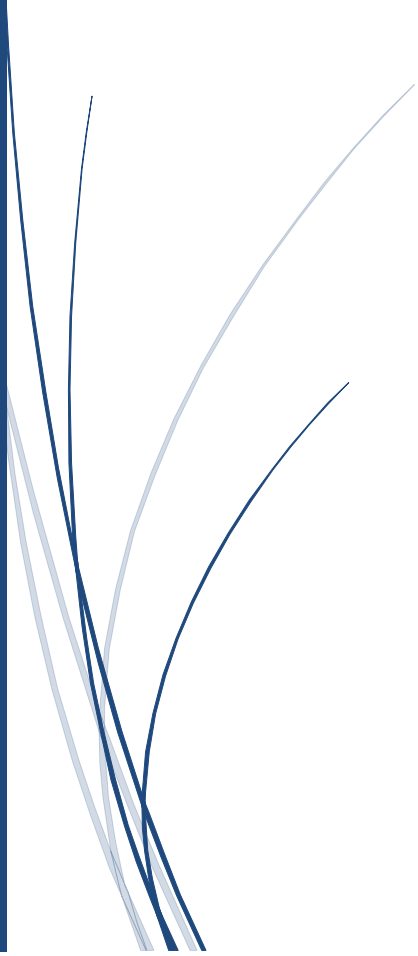

Effect of COVID-19 pandemic on TB notifications in Addis Ababa, Ethiopia

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Science in Public Health

by

Simon Genet Woldesenbet

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The thesis, **Effect of COVID-19 pandemic on TB notifications in Addis Ababa, Ethiopia**, is my own work.

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Abbreviations

AIDS acquired immunodeficiency syndrome

CNR case notification rate

CI confidence interval

DOTS Directly Observed Therapy Short-Course

GIS Geographic Information System

HIV Human Immunodeficiency Virus

LISA Local Indicators of Spatial Autocorrelation

MATCH Mapping and Analysis for Tailored Disease Control and Health System Strengthening

NTP National TB programme

OKP Orange Knowledge Program

SDG Sustainable Development Goal

TB tuberculosis

UHC universal health coverage

UN United Nations

USAID United States Agency for International Development

WHO World Health Organization

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Last but not least, I would like to express my profound gratitude to the Dutch government, the minister of foreign affairs, and the Nuffic OKP Scholarship Fund for supporting me to pursue my study at the prestigious Royal Tropical Institute (KIT).

Abstract

Introduction: Tuberculosis is the main cause of morbidity and the second leading cause of mortality in Ethiopia. Efforts to battle the TB pandemic have increasingly expanded. However, the indirect effects of the COVID-19 pandemic might disrupt TB service delivery. In this study, we assessed the effect of COVID-19COVID-19 on TB service as measured by TB notifications in Addis Ababa city.

Methodology: A retrospective observational study was done using routine TB program data, complemented with spatial and population data from other sources**.** We used the least squared regression model to estimate the change in TB notification trends due to COVID-19 restrictions. To create all maps and visualize distributions across sub-cities QGIS 3.24 was used. Additionally, a literature review was done to investigate the contributing factors that impacted TB notifications during the pandemic (2020).

Key Findings: Compared to the pre-COVID-19 era, the total number of TB notifications decreased by 20% over the COVID-19 period ($P<0.05$). The geographical distribution showed that there were significant differences in Total TB notifications across the different sub-cities ($P<0.05$). The largest decline, of 34%, was reported in the Nifasilk Lafto sub-city compared to the pre-COVID-19 period. The literature study found stigma, fear of contracting COVID-19, government regulations, and an overworked healthcare system as the factors affecting TB notification.

Conclusion: The COVID-19 pandemic showed a detrimental effect on Addis Ababa's TB notification rate. This emphasizes how crucial it is to strengthen TB services, including implementing alternative innovations, merging TB and COVID-19 services to lessen obstacles to TB diagnosis.

Key words: Tuberculosis, Case Notification Rate, TB diagnosis, COVID-19

Word count: 11,185

CHAPTER ONE

1.0 Introduction

I have been working on tuberculosis (TB) and COVID-19 in Ethiopia for the last four years with the Armauer Hansen Research Institute and implementing partners of the Ministry of Health. Finding new cases of TB has been a major issue and source of concern for research projects and other stakeholders whose work is advancing TB care and research in Ethiopia. My interest in doing this research was driven by the high prevalence of tuberculosis in Ethiopia, the ongoing COVID-19 pandemic's indirect consequences, and the necessity to use resources wisely to locate the most cases possible. I recognized the need for a new approach to program data analysis and interpretation that gives rich, in-depth information through maps, charts, and literature reviews. This inspired me to take on the difficult task of completing my thesis on the impact of COVID-19 on TB notification in the capital city of Ethiopia, which was severely afflicted by the pandemic. This thesis investigates the time trend of TB case notification and the geographical distribution of TB case notification rate among the eleven sub-cities of Addis Ababa and proposes possible explanations for the trends found.

The results of the study will be shared with the National TB Program, the Ethiopian Ministry of Health, and other significant TB stakeholders. The study's conclusions will also be used to give recommendations for TB programs. Finally, I'm hoping that this will encourage the National TB program and its implementation partners to conduct detailed research by frequently examining data sets at the subnational level using innovative methods like the MATCH framework.

This research is divided into six chapters: An overview of TB and COVID-19 is given in Chapter 1; the problem description, justification, and objectives are examined in Chapter 2; Methodology is presented in Chapter 3; The study's findings are presented in Chapter 4; Results are discussed in Chapter 5, and the study is concluded with suggestions in Chapter 6.

1.1 Background

The coronavirus disease 2019 (COVID-19) epidemic, which began in Wuhan, China, and was declared a worldwide pandemic by the World Health Organization (WHO) on March 11, 2020, has caused the loss of millions of lives and put a burden on healthcare systems all over the world. Some countries utilized population-wide lockdowns as a critical component of larger virus control methods to break the transmission of the virus(1,2). Essential health services like those for HIV infection and/or acquired immunodeficiency syndrome (AIDS), tuberculosis, malaria, routine immunization, noncommunicable diseases, nutrition, and reproductive, maternal, newborn, child, and adolescent health services have been interrupted by COVID-19 in the most countries, with ongoing and evolving interruptions as the pandemic persists (3). TB case diagnosis, treatment initiation, and treatment adherence were all substantially impeded during the epidemic (4).

Tuberculosis takes approximately 1.4 million lives worldwide each year, following only coronavirus disease (COVID-19) as the top cause of death in 2020(5). During the pre-COVID-19 period (in 2019), there were around 10.0 million new tuberculosis infections and 1.5 million tuberculosis deaths worldwide(6). Over the previous few decades, efforts to battle the TB pandemic have increasingly expanded. By the end of 2019, 78 countries were on pace to fulfill the 2020 End TB targets of reducing TB incidence and mortality by 80% and 90%, respectively, compared to 2015 rates(6). However, lockdowns, economic turmoil, healthcare worker sickness and attrition, overburdened health facilities, and fear of healthcare facilities are all effects of the COVID-19 pandemic that have disrupted health service delivery (7).As a result, there is a significant worldwide delay in meeting already settled goals(7).

Ethiopia has a population of over 115 million people, making it Africa's second most populated country. 19.5 years old is the median age, and 78.7% of people live in rural areas. With a per capita income of USD 850 in 2019, it is also one of the least resourced countries on the list (8). The country's health-care system is a three-tiered structure (primary, secondary & tertiary) (9). Tuberculosis (TB), malaria, Human Immunodeficiency Virus (HIV) infection and acquired immune deficiency syndrome (AIDS), and maternal mortality are the main health concerns in Ethiopia, (10).

In the last two and a half decades, Ethiopia has proven achievements in lowering common infectious illnesses, although diseases such as TB remain the leading causes of morbidity and mortality in the nation (11). According to the 2018 WHO Global TB report, the incidence of TB in Ethiopia is 151 per 100,000 population, which ranks the country amongst the 30 nations with a the highest TB burden globally (12). Tuberculosis is the main cause of morbidity, the third greatest cause of hospitalization, and the second leading cause of mortality in Ethiopia (13). Addis Ababa, which is the capital city of Ethiopia with a population of 3,122,000 has total of 93 health centers and 11 public hospitals. The city has a high TB burden with prevalence, incidence ,and mortality rates of 314, 246.58, and 28.20 (all per 100,000 populations) respectively(14,15). Similarly, TB is among the leading three causes of years of life lost(YLLs)and years of healthy life lost due to disability (YLDs) in the city (16).

1.1.1 COVID-19 in Ethiopia

On March 13, 2020, Ethiopia reported its first case of COVID-19 in Addis Ababa. Two days later, the WHO declared the disease to be pandemic. In the first six months, Ethiopia had tested 237464 suspects, with 5425 (2.3 percent) cases having been confirmed positive; 89 (case fatality rate (CFR) = 1.6 percent) of these cases had died, while 1688 (31.1 percent) had recovered (17). As of June 11, 2021, there were 273,678 confirmed positive cases confirmed, of whom 4231 died (case fatality rate = 1.55%) (18). The

largest number of cases and fatalities across Ethiopian regions was reported from Addis Ababa City Administration (71.6%) (19). Hospitals resources such as human resource, laboratory, outpatient and emergency services was transferred to COVID-19, reducing patients' normal access to care for other diseases such as TB (20).

1.1.2 Government Containment Measures

In order to tackle COVID-19, the government has stepped up its planning and response activities and established a national preparedness and response coordination system through an Emergency Operation Center(21). On March 16, 2020, the government-imposed restrictions on public gatherings, including those for religious ceremonies, sporting events, and concerts. It also ordered school closings and mandated remote work for high-risk government employees. The government at the time called that routine activities continue while being subject to containment measures (22). On the other hand, Addis Abeba and the nine Regional States and two City Administrations imposed travel restrictions and suspended flights. Mass transit and taxi services were forced to adhere to new working hours regulations and only operate at 50% of their capacity. Similar to other countries, Ethiopia stopped flights to 30 disease-affected nations on March 23, 2020, and to more than 80 nations on March 29, 2020. Closed land boundaries On March 23, 2020, Ethiopia deployed security personnel and shut all land crossings (23).

Political parties took part On April 5, 2020, the country's prime minister gathered with the heads of different political parties to discuss and achieve an agreement on the impact and containment of COVID-19 State of emergency issued when the number of cases increases. On April 8, 2020, the government proclaimed a five-month national state of emergency due to the country's steadily increasing caseload. (22,23). Additionally, Ethiopian government implemented thorough and rigorous contact tracing, mandatory quarantine, and treatment. In order to expand the number of quarantine centers and their capacity to more than 50,000 beds, the government deployed the dorms, medical facilities, and other structures at public institutions(21).

CHAPTER TWO

2.1 Problem Statement

The COVID-19 pandemic, and actions taken in response to it, have had far-reaching consequences on other diseases, poverty, food security, and economic growth(3). In low-income and middle-income countries, a particular concern has been the potential impact on three major health priorities, specifically, HIV, tuberculosis, and malaria, due to a disruption to health services. These three illnesses are prevalent in many low- and middle-income nations, and millions of people rely on large-scale programs to control and treat them (24). Substantial progress has been achieved in recent years in lowering the burden of TB, and ambitious objectives for attaining extremely low levels of burden by 2030 have been established as part of the Sustainable Development Goals (SDG)(25). According to the Global Tuberculosis Report 2020, the global TB incidence rate is decreasing, but not quickly enough to meet the 2020 target of a 20% decrease(26). Positively, the WHO European Region has virtually reached the 2020 target, with a 19% reduction in TB incidence rate between 2015 and 2019, while the African Region has made considerable progress, with a 16% drop between those years(26).Nonetheless, Control program interruptions might cause significant setbacks and exacerbate COVID-19's effects. The World Health Organization (WHO) has found that the COVID-19 pandemic has had a significant impact on TB control efforts (5). This has disrupted tuberculosis (TB) care and service delivery, slowing progress in the battle against the illness by many years(27). The severity of this setback can be intensified when new COVID-19 strains reach more low- and middle-income nations in 2021 (28). By late 2020, both high and middle-income nations, even those where COVID-19 had been well-controlled, had seen significant decreases in TB case notifications (29). Reduced TB notification raised concerns about delayed case discovery and treatment completion. As a result, it is expected that there will be an increase in Mycobacterium tuberculosis transmission and, as a result, greater death rates (30).

According to preliminary estimates by the United States Agency for International Development (USAID), the pandemic may have resulted in over 1 million fewer cases being reported in 24 high TB burden countries alone in 2020, with a relative reduction of 7% in Africa, a 15% reduction in Central Asia and Europe, and a 27% reduction in Asia compared to 2019(31).In 2020, there were 10 million incident tuberculosis cases globally, with Africa accounting for around 25% of all TB cases (26). According to a World Health Organization (WHO) report, TB case notifications in High Burden Countries (HBC) decreased by 18% between 2019 and 2020 (from 7.1 to 5.8 million cases) (5). During the early months of the pandemic, TB notifications in HBCs declined drastically. TB service infrastructure and resources were shifted to the pandemic response. Due to limited access (clinic closures, health worker shortages, or to avoid crowds), fear of catching COVID-19, or stigma associated with TB and COVID-19, many vulnerable persons with untreated tuberculosis have difficulties accessing tuberculosis care (32,33). According to the global survey, 50 percent of patients with tuberculosis in Kenya reported difficulty receiving TB care due to limited public transportation (cost and availability of transport)(32).Similarly , 62 percent of persons with tuberculosis in India reported they didn't want to visit their regular facility because they were afraid of catching COVID-19(28). This delay in seeking treatment has resulted in an increasing number of persons being ignored, resulting in an increase in community-based tuberculosis transmission, more severe forms of the disease, and TB mortality (34).

In a study of 567 TB health professionals from 64 low- and middle-income countries, 233 (41%) reported tuberculosis patients had found it significantly more difficult or impossible to get care at facilities since the epidemic began. Similarly, 162 (29 percent) of respondents felt providing TB diagnostic tests was difficult or almost impossible(7). Besides, National Tuberculosis Program (NTP) employees are involved in COVID-19-related activities, which are disturbing TB initiatives, according to a Stop TB Partnership study

of 20 high-burden TB countries(32). COVID-19 patients are being treated in TB isolation units, and TB/infectious disease experts are being shifted to COVID-19 treatment. SARS-CoV-2 has been detected in TB laboratories, which is ruining TB testing. The supply and transportation of tuberculosis drugs has been hampered (35). These factors, on the other hand, contribute to prolonged diagnostic delays, poor treatment results, and drug-resistant (DR) TB, all of which contribute to the current and future spread of TB (36).

Ethiopia's government is now implementing the global End TB Campaign, with the goal of eradicating tuberculosis by 2035. this has been done by intensive TB screening, early diagnosis, proper treatment, and universal drug sensitivity testing (DST) (37). The country was one of 78 throughout the world that were on track to fulfill the 2020 target for reducing TB incidence(26). The current COVID-19 scenario in Ethiopia, on the other hand, has hampered implementation and impeded progress toward achieving TB plan milestones and objectives (10). COVID-19 was first detected in Ethiopia on March 13, 2020, infecting 227 255 people out of 2 437 495 samples examined (positive 9.32 percent), leading in 3146 fatalities (as of 11 April 2021). The number of cases is rapidly rising, with nearly three-quarters of those happening in and around Addis Ababa (38). Due to this pandemic the Ethiopian government was posed movement restrictions. Interregional mobility restrictions, schools closed and elections postponed, state of emergency announced, mandatory facemask, and 14-day quarantine for people arriving from outside Ethiopia(39). Aside from the Ethiopian government's limitations, the population was fearful of contracting COVID-19 and hence avoided coming to health institutions (40).

With the challenge created by COVID-19 to the world's health systems, particularly in resource limited nations such as Ethiopia, hindered access to basic health care services and indirectly caused morbidity and mortality from reasons other than the pandemic itself(41).According to the WHO assessment on COVID-19 and the national TB programs of 100 countries including Ethiopia, there has been a decline in outpatient visits, national TB staffs have been involved in the COVID-19 pandemic, and outpatient facilities have been moved to Covid-centers (42). For example, from the end of March 2020 where the first COVID case was identified in Ethiopia, there have been significant reductions in TB case detection(22). According to the data from the Dire Dawa Health Bureau, there were 110 TB cases in the period 1 April to 30 June 2020, which was about three times lower than cases detected in the previous reporting periods(18). There will be an increase in TB mortality as a result of this TB diagnostic and care interruption. COVID-19's enormous health-care-system disruption is also impeding progress toward health-care goals like the End TB Strategy 2030 (43,44). Restricted access to medical care has increased the number of late, disseminated TB presentations, which are linked to poor treatment results and mortality, much like the 2014–15 Ebola virus disease epidemics. In fact, during the next five years, the COVID-19 pandemic is expected to result in a 20 percent rise in TB mortality worldwide(45). Policymakers, experts, and government officials must put in more effort to enhance testing capacity and bring about behavioral changes in the public to alleviate the already existing issues. To develop strategies for action, empirical data on the effect of COVID-19 on TB notification are crucially needed.

2.2 Justification of the study

A lot of studies have been conducted on the impact of COVID-19 on essential health services. These studies discovered that movement restrictions or lockdown, transportation challenges, and anxiety as a result of coronavirus infection might all be factors affecting health-care utilization .Although several studies have focused on the impact of COVID-19 on essential healthcare services(46), none of them showed the geographical ,temporal ,and spatial trend of TB notifications in the context of COVID-19 in Addis Ababa city, which is the focus of this research . To build targeted interventions and present the evidence for informed decision-making on TB, it will be crucial to do this. The National TB Program staff and other organizations might be guided on how to allocate resources for case-finding efforts by a geographical study of the spread of the disease combined with the time trend. Similarly, the data can provide useful insight to

NTP surveillance systems into where and why TB cases are missed.

The WHO states that a widely available indicator that can be used to determine the impact of disruptions brought on by the COVID-19 pandemic on essential TB services at the country level is the national number of notified cases of TB. This study used TB notification as a measure because of this (47). This indicator reflects both supply-side (e.g., capacity to continue providing services) and demand-side impacts on access to diagnosis and treatment (e.g. Concerns about the risks of visiting medical facilities during a pandemic, willingness and capacity to seek care in the context of lockdowns and related limitations on travel, and stigma connected to parallels in symptoms related to TB and COVID-19) (48).As a result, we will examine the influence of the COVID-19 pandemic on TB notification using secondary data provided from the Ministry of Health's DHIS2 data source for Addis Ababa. These are critical for understanding COVID-19's impact on tuberculosis and for designing measures to improve TB services based on it. Addis Ababa was selected as study area because besides TB burden this city contributes 71.6% of reported COVID-19 cases(18). the findings of this study will be utilized to assist policymakers and stakeholders in properly managing the indirect impacts of COVID-19 on tuberculosis to meet the ENDTB plan by 2030.

2.3 Research Questions

1. What was the state of TB notification in Addis Abeba's sub-cities before (2019) and during (2020) the COVID-19 pandemic?

2.To what extent does TB notification vary between sub-cities before and during the pandemic?

3. What were the major factors influencing TB notification in Addis Abeba during the pandemic?

2.4 Research Objectives

General objectives: To analyze the effects of COVID-19 pandemic on TB care as measured by TB notification in the selected health facilities in Addis Ababa, Ethiopia, to provide findings for policy makers, National and international actors supporting TB control endeavors.

2.4.1 Specific Objectives:

- To determine the temporal trend of TB notification (new and relapse TB cases) rate before and during COVID-19 pandemic
- To visualize the geographical distribution of the total TB notification (new and relapse TB cases) before and during COVID-19
- To identify factors affecting the trend of TB patients' visits to the health facility during the pandemic
- To provide empirical results on the status of tuberculosis notification for policymakers and players involved in the fight against tuberculosis

CHAPTER THREE

3.0 Methodology

3.1 Study design

A retrospective observational study was done using routine TB program data, complemented with spatial and population data from other sources**.** The study used data from the district health information system 2 (DHIS2) to conduct a retrospective interrupted time series analysis to determine the impact of COVID-19 on TB notification before and during the pandemic.

3.2 Study Area

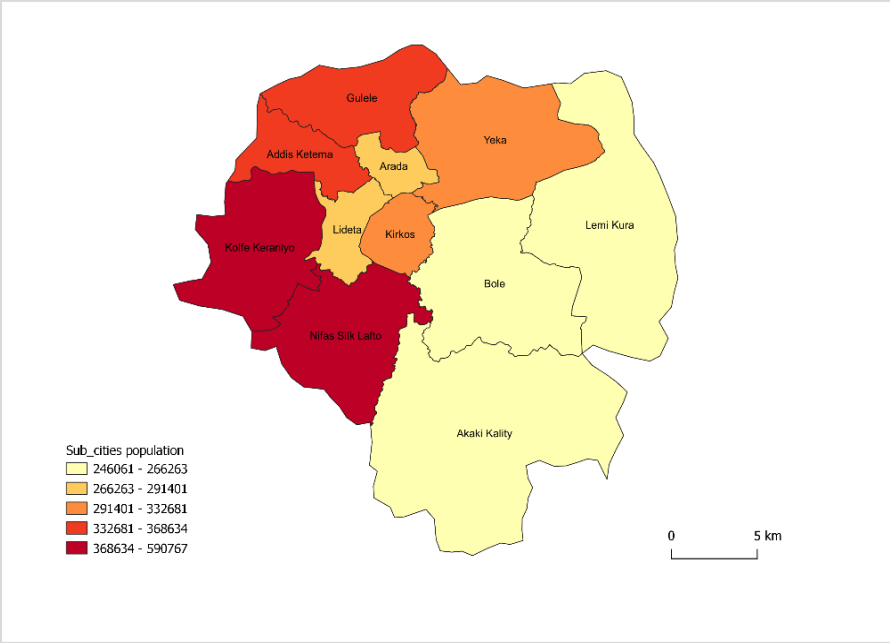

Figure 1: The population distribution among sub-cities in Addis Ababa (49)

The study area of the research was All the eleven sub-cities of Addis Ababa city. Addis Abeba, the capital of Ethiopia and the African Union, is frequently referred to as the "African Capital" because of its historical, diplomatic, and political significance for the continent. With an altitude of 7,726 feet (2,355 meters) above sea level on the foothills of the Entoto Mountains, it is the third-highest capital city in the world. It is located in the geographic center of the nation. According to the most recent forecast (2020), the city has a population of 4794000 residents (50). In the city, there are eleven boroughs (sub-cities). The most populous of the sub-cities is Kolfe Keranio, with 590767 residents, followed by Nifasilk Lafto, with 435752 residents (51).

There are seven public hospitals and one hundred public health centers in the city, which are divided into three categories: health centers, regular hospitals, and specialist hospitals(52). All health facilities at all levels of healthcare offer TB care with the support of several national specialized TB activities, such as the recently launched End TB program. Every health facility, using a nationally standardized and coordinated reporting form, reports TB cases to the city's administrative health bureau once a quarter(52).

3.3 Study Period, Data Source and Variables

The research was based on data provided between March 2019 and December 2020. There was a Pre Covid phase before March 2020, a Lock down period during the Covid era from April to July 2020, and a COVID-19 period from March 2020 to December 2020. Aggregate patient numbers with new clinically diagnosed, bacteriologically confirmed, new and relapse Pulmonary TB patients, stratified by 11 sub-cities (4^{th} level administrative unit in Ethiopia), were among the data variables. Data sources for the analysis were used nationally aggregated, routinely captured tuberculosis programme data supplied by the Ministry of Health's (MOH) district health information system 2 (DHIS-2). This central repository receives data from every health facility. Every health institution uses a nationally defined and organized reporting form to submit TB case reports to the city's administrative health bureau every quarter.

After reviewing the data, a monitoring and assessment team clarified and corrected any irregular or incomplete data before final national-level data aggregation. We also used data from the Ministry of Health's (MOH) District Health Information System 2 (DHIS-2) data on the quarterly number of COVID-19 cases reported in the study area to assess the COVID-19 infections throughout the same period. Without the use of any patient identification, this study conducted a population-level analysis. The data from DHIS2 was extracted and divided into two periods: the COVID-19 era (from March 2020 to December 2020) and the pre-COVID-19 era (From March 2019 to March 2020). The data was obtained using national HMIS indicators for tuberculosis services, which are reported on a quarterly basis. The overall TB notification (new and relapse) data then retrieved based on variables namely sub-city, study year and quarter.

3.4 Inclusion and Exclusion Criteria

The study looked at TB data for 2019 and 2020, as well as COVID-19 data from March 2020 to December 2020. The paper includes evidence published only in English-language on tuberculosis and COVID-19. Studies that are not connected to COVID-19 and tuberculosis (TB), as well as those published prior to 2010, will be excluded.

3.5 Data Analysis

After data were obtained, Excel and SPSS V.24 were used to manage, describe, and analyze the data. To calculate the proportion of each indicator, we conducted descriptive data analysis. For quarterly TB notifications during 2019 & 2020, we used an interrupted time series analysis (53) to determine the change in quarterly TB notifications during COVID-19 time (2020), compared with quarterly notifications during 2019 & 2020. We used least squared regression model including an interaction term between quarter and restriction measures to estimate the change in trend due to COVID-19 restrictions. Sub-city was added as an additional covariate to account for variation in TB notification between reporting units(54).

Categorical variables were reported as frequencies (percentages). Per sub-city, the percentage change in TB notifications before and after the COVID-19 limitation was calculated as follows: (((Number of new and relapse TB cases in 2020 − Number of new and relapse TB cases in 2019))* 100% / New and relapsed tuberculosis cases in 2019(1). A positive percentage change indicated a net increase in TB cased being notified as compared to the reference value of 2019, whereas a negative percentage change indicated a net decrease from 2019. Between periods, the study was compared each of the selected indicators on a quarterly and yearly basis (COVID-19 era and pre-COVID-19 era). To determine the rate ratios comparing registrations per study period in the COVID-19 era with the pre-COVID-19 era, will be adjusted for year,

independent samples t-test was carried and also significance of the differences in TB notification among Addis Abeba's sub-cities was demonstrated using multivariable regression with interaction terms, quarter, sub-cities, and measure. The statistical test will make use of The 95 % confidence interval (CI) and level of significance (5%)(54,55). In order to create all maps and visualize and compare the population, aggregate case notification counts, and case notification rate, across sub-cities QGIS 3.24 (Open Source Geospatial Foundation) was used (56). In addition, GeoDa-LISA for spatial cluster analysis was used to illustrate the spatial patterns(57).

Finally, A review of recent literature regarding effects of COVID-19 on TB notifications was used to explore the factors contributing to the change in TB notification during COVID-19 period and to contextualize the secondary data analysis.
the keywords "COVID-19", "Tuberculosis(TB)", "prevalence", "magnitude", “Impact” , "TB notification", “poverty”, “stigma” ,"TB case report", “TB diagnosis”, "developing country", "Ethiopia" to identify references from search engines (PUBMED, VU library, Google scholar), and existing evidences on TB and COVID-19 .all the key words are combined with TB,COVID-19 and Ethiopia, as described in the annex. Only the English language was used.

3.5.1 Conceptual Framework

To visualize the contributing factors, the study also used the Mapping and Analysis for Tailored disease Control and Health system strengthening (MATCH) approach which is a Patient pathway conceptual framework. Through exposure to screening, diagnosis, and therapy, this analytical model looked at how and why people become lost along the care pathway. It is predicated on the knowledge that a fraction of patients cannot access the subsequent level of care because of certain obstacles (58). Which enables the visualization of differences in health inequalities as reported by health programs. It will also help to analyze the performance of health-care systems in detecting and diagnosing TB , as well as give crucial information for future planning (58). Furthermore, By increasing the capacity of TB programs in the planning of timely and locally tailored interventions aimed at identifying and treating people with TB, this framework aims to provide a way to study TB and other data to identify areas for targeted case-finding or TB program strengthening)(59). It supports the collection of disaggregated geographical, temporal, and demographic data, as well as sub-national TB data, for more targeted planning and monitoring of TB initiatives(59).

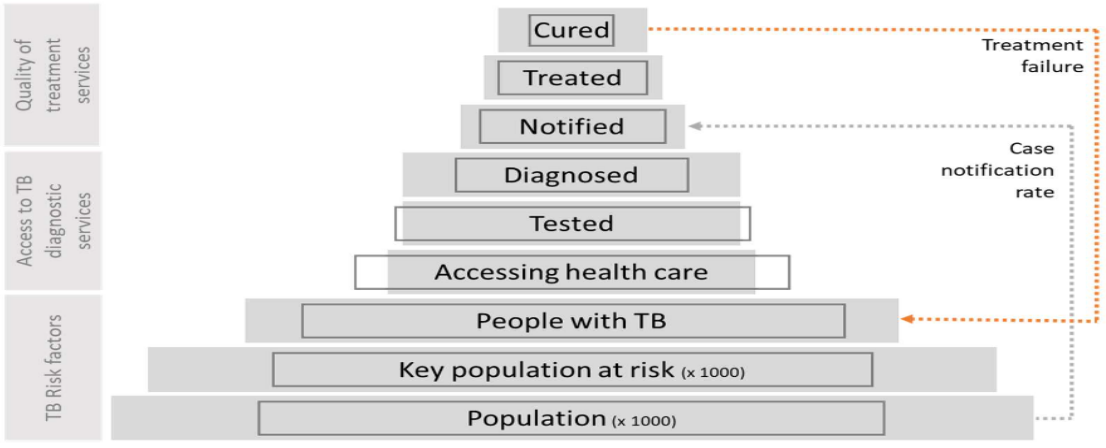

Figure 2: The Patient Pathway Framework(59: p.3)

3.6 Operational Definitions

Table 1: Operational Definition of terms

Indicators	Definition
Presumptive TB Cases	include those who have a chest X-ray abnormality indicative of TB, a progressive cough that lasts for two weeks or more (or longer for HIV-positive people), a fever, night sweats, weight loss, or any combination of these symptoms(61).
A bacteriologically confirmed TB case	is a patient from whom at least one biological specimen is positive for mycobacterium TB either by smear microscopy, Xpert MTB/RIF, or culture(61).
A clinically diagnosed TB case	is a patient who is identified with active TB by an experienced physician despite not meeting the criteria for a bacteriological proven case and is chosen to get a complete course of TB therapy(61).
New TB	patients that have never been treated for TB or have taken anti-TB drugs for less than one month(61).
Relapse	patients who were declared cured or treatment completed at the end of their most recent treatment course and is now diagnosed with a recurrent episode of TB(61).
TB case notification rate	the number of new and relapsed cases of tuberculosis reported to the national health authority over a given time period per 100,000 people(61).

3.7 Limitation of Study Design

The data used in this research is a retrospective survey, which means that none of the relationships cannot be interpreted as causal. This kind of observational cross-sectional design have low inferential strength. Furthermore, the missing data limited the explorative power of the study.

3.8 Ethical considerations

The KIT Research Ethics Committee (REC) was asked for waiver to perform the study. Individual participants are not involved in the study, nor is there any dangerous procedure for which informed consent is necessary. The study's data was also obtained with the Ministry of Health's permission. To ensure anonymity, the data for the study is aggregated and totally anonymized, with no personal identifiers that can be linked back to individuals.

CHAPTER FOUR

4.0 Study findings/results

4.1 Temporal trend of TB notification (New and relapse TB cases) before and during COVID-19 pandemic

For this study, data from the DHIS2 were examined for 24 months (12 months during the pre-COVID-19 (2019) and COVID-19 era (2020)). The research found a total of 7640 recorded TB cases reported by the eleven Addis Ababa sub-cities over these times. Following the identification of COVID-19 in Addis Ababa, Ethiopia, and the implementation of transmission control measures, the overall number of TB notifications decreased by 838 cases (20%), from 4239 pre-covid cases to 3401 cases during COVID-19 period. Total TB notification trends amongst sub-cities are depicted in Figure 3 along with the total number of new TB cases reported in each sub-city during the pre-COVID-19 and COVID-19 periods. Throughout COVID-19, there were between 14 and 29 percent fewer reported new cases of TB in sub-cities (table 2). Contrarily, only the Arada sub-city showed an increase in TB notifications during the Covid 19 era, with a 21 percent increase over the same quarter in 2019. However, the number of TB cases recorded during the COVID-19 period decreased by a greater percentage (29%) in the Addis Ketema sub-city (Figure 3).

Table 2: Total TB notification and percentage of change among sub-cities in Addi Ababa

Sub-regions	Total TB notifications		
	Pre-COVID-19 era %(N=4239)	COVID-19 era %(N=3401)	Percentage Change
Addis Ketema Sub-City	16(683)	14(484)	-29%
Akaki Kality Sub-City	10(423)	9(322)	-24%
Arada Sub-City	8(321)	11(390)	21%
Bole Sub-City	6(248)	5(181)	-27%
Gulele Sub-City	7(308)	7(234)	-24%
Kirkos Sub-City	8(346)	8(272)	-21%
Kolfe Sub-city	11(451)	10(339)	-25%
Lemi Kura Sub-City	10(429)	9(321)	-25%
Lideta Sub-City	5(230)	6(189)	-18%
Nifas Silk Lafto Sub-City	10(428)	11(366)	-14%
Yeka Sub-City	9(372)	9(303)	-19%

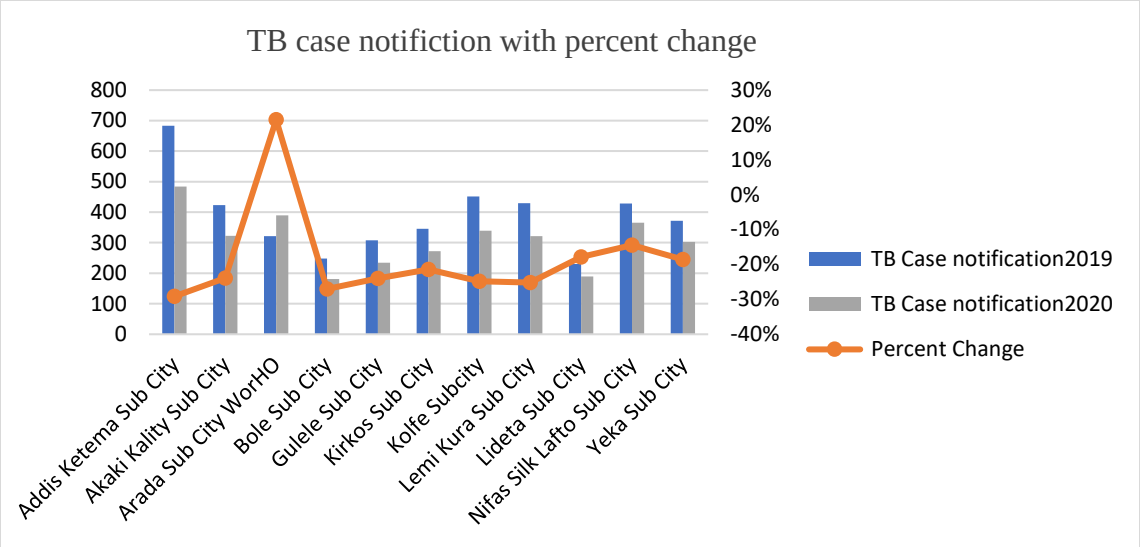

Figure 3: Total TB notification and percentage of change among sub-cities in Addi Ababa

The following graph (figure 4) depicts the trend of TB case notifications during the years before and during COVID-19. The results demonstrated that the TB notification pattern changed throughout both time periods. However, the quarterly number of TB cases drastically declined throughout the COVID-19 era, with the largest drop between quarters year on year is that of Q3 2019 to Q3 2020., when it fell by 41% from 1249 cases (pre COVID-19) to 733 cases (during COVID-19). Similarly, the overall TB cases notified before the restriction measures showed some decline starting from quarter one, but after the containment of COVID-19 restriction measures (April 2020) the decline becomes sharp and significant compared to the respective quarter in the previous year (figure 5).

Overall, there is a statistically significant difference (P<0.001) on TB CN before and after the implementation of restriction measures. Among sub-cities, Bole showed a significant reduction (P<0.007) in TB notification after the COVID-19 restriction measure. The results showed that for every unit increase in restriction measures across sub-cities every quarter, the number of TB cases reported in Bole sub-city decreased by 30 (Table 3).

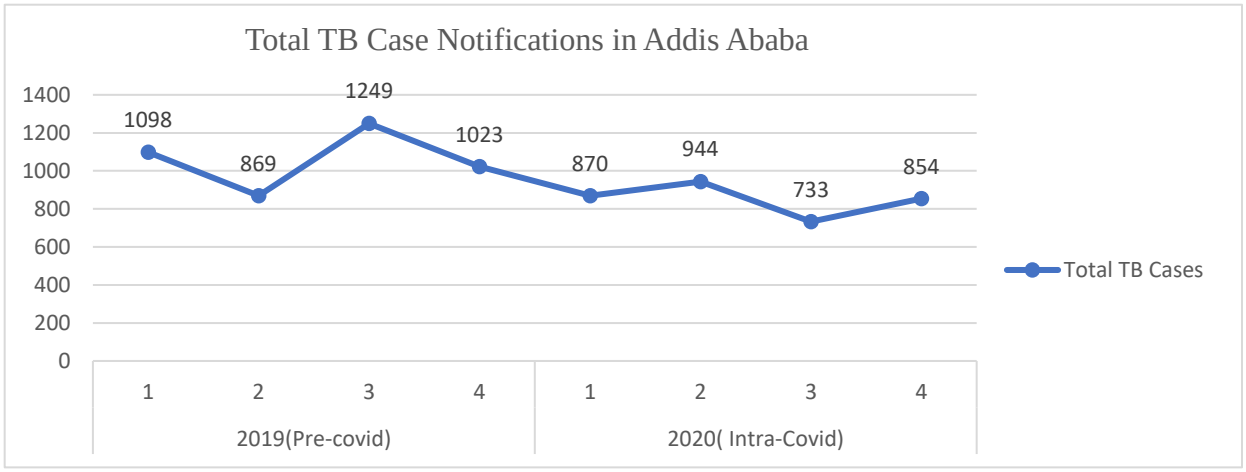

Figure 4: Total TB notification per quarter in Addis Ababa

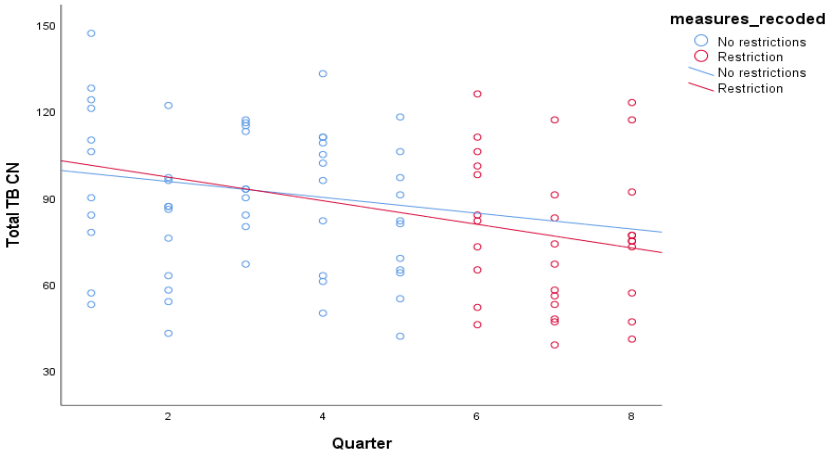

Figure 5: Shows the Total TB notification per quarter among sub-cities in Addis Ababa before and after restriction measures. The eleven sub-cities of the pre-Covid era (when there were no restrictions) are represented by the blue circles, whereas the covid era is represented by the red circles (with restriction). Before and after the restriction, the blue and red lines, respectively, depict the trend of the TB CN per quarter.

Parameter Estimates

Table 3: Least squared regression with interaction terms; quarter, sub-cities, and measure

Dependent Variable: Total TB CN				
Parameter	**B**	**P-value**	**95% Confidence Interval**	
			Lower Bound	Upper Bound
Intercept	110.602	0.000	86.748	134.457
Q1(Jan -March)	-5.106	0.479	-19.398	9.186
Q2(Apr-Jun)	-2.909	0.663	-16.141	10.323
Q3(Jul-Sep)	4.773	0.475	-8.459	18.005
Q4(Oct-Dec)	0[a]	.	.	.
Restriction Measures	-18.485	0.001	-29.289	-7.681
Addis Ketema Sub-City	61.500	0.000	39.557	83.443
Akaki Kality Sub-City	8.750	0.429	-13.193	30.693
Arada Sub-City	4.500	0.684	-17.443	26.443
Bole Sub-City	-30.750	0.007	-52.693	-8.807
Gulele Sub-City	-16.625	0.135	-38.568	5.318
Kirkos Sub-City	-7.125	0.520	-29.068	14.818
Kolfe Sub-city	14.375	0.196	-7.568	36.318

Lemi Kura Sub-City	9.375	0.397	-12.568	31.318
Lideta Sub-City	-32.000	0.005	-53.943	-10.057
Nifas Silk Lafto Sub-City	14.875	0.181	-7.068	36.818
Yeka Sub-City	0[a]	.	.	.

To illustrate the degree of change in reported TB cases between the two study periods, an independent sample t-test was conducted. The results showed that there is a statistically significant difference between the two periods (before and during COVID-19) in terms of the total number of reported TB cases, with a P value of <0.004 (Table 4).

Group Statistics

Table 4: Independent T-test comparing the total TB CN before & during the pandemic period

Year	**N**	**Mean**	**SE**	**T-test of difference of means**		
				t	P-value	95% CI
2019	44	36.41	3.07	NA	NA	NA
2020	44	26.36	3.07	2.95	0.004	3.2-16.8

TB Diagnosis/Bacteriologically Confirmed TB case notifications

The below graph (figure 6) illustrated the change in the number of patients diagnosed with Bacteriological confirmation. The output showed there is a decline in the number of Bacteriologically confirmed TB case notifications from 2115 during the pre-covid period to 1842 during the COVID-19 era, which is a 13% decline. However, the independent t-test result showed that the change is non-significant with a p-value of 0.445 (table which is greater than p=0.05 (Table 5).

COVID-19 Cases

Figure 7 demonstrates that COVID-19 cases in Addis Abeba city began to rise in the third quarter of 2020, rising from 550 cases in quarter two to 18449 in three and continuing to rise in quarter four.

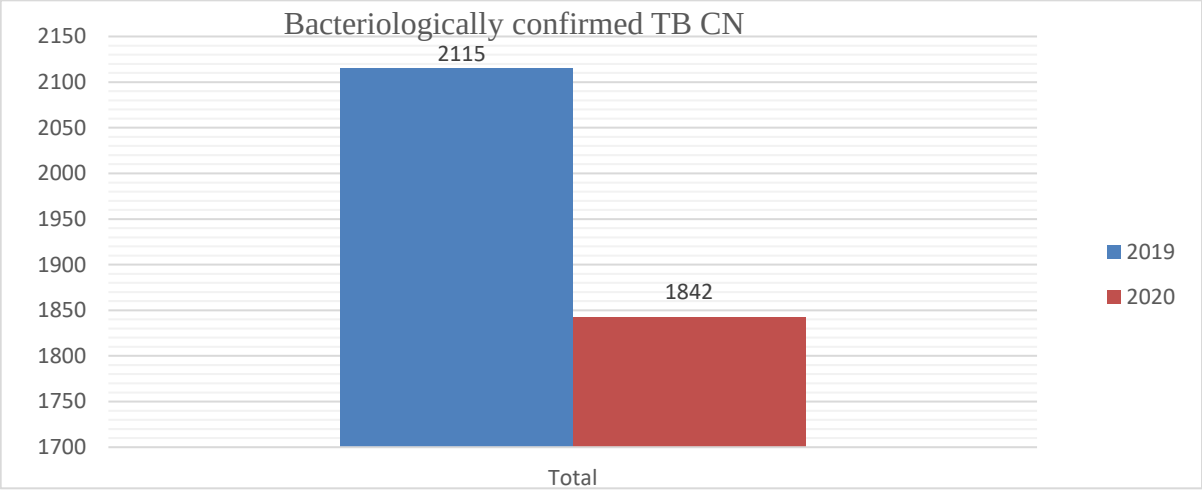

Figure 6: Bacteriologically confirmed TB notification before & during the pandemic

Table 5: Independent T-test comparing the Bacteriologically confirmed TB CN before & during the pandemic period in Addis Ababa

Year	N	Mean	SE	T-test of difference of means		
				t	P	95% CI
2019	44	24.41	2.783	NA	NA	NA
2020	44	22.27	2.783	7.68	0.445	-3.396-7.669

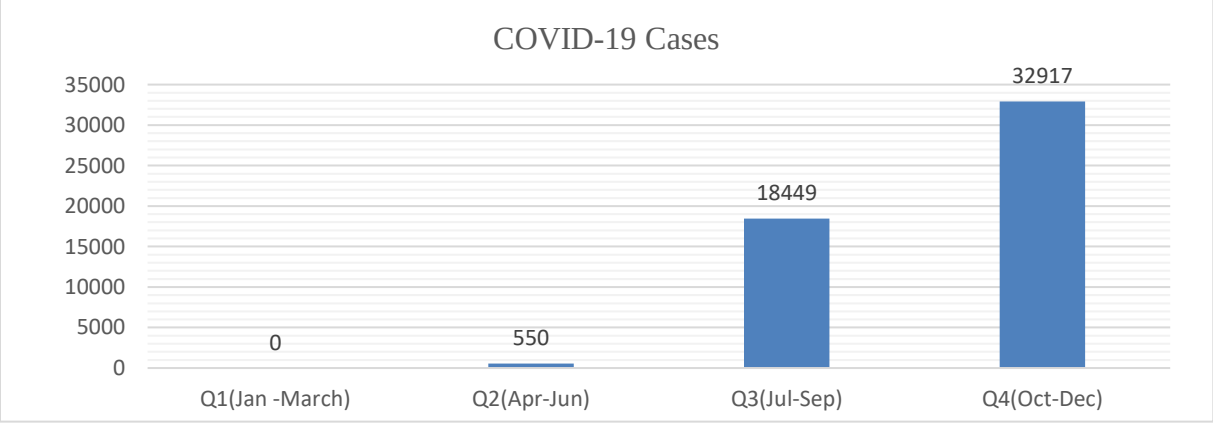

Figure 7: the number of COVID-19 cases reported in 2020 in Addis Ababa

4.2 The geographical distribution of the total TB notification (New and relapse TB cases) before and during COVID-19

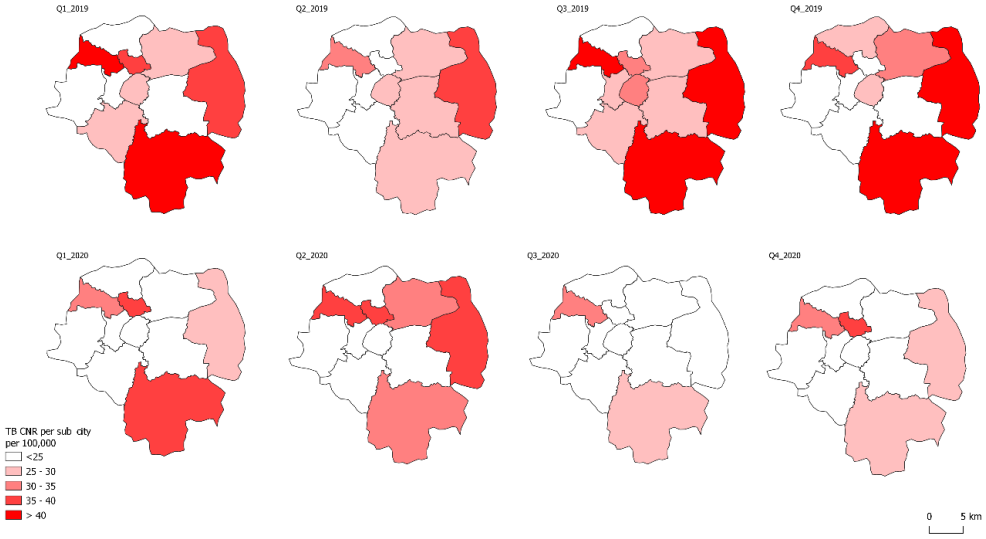

Figure 8: The geographical illustration of TB notification rate (TB CNR) Before and during COVID-19 time per quarter sub-cities in Addi Ababa

The map in figure 8 above shows the geographical differences in the quarterly TB notification rates for each sub-city between the pre-COVID-19 and COVID-19 eras. Kolfe Keranyo Sub-city was the only one whose rate of TB notifications varied just little throughout all time periods. At the start of the pandemic (Quarter 1), Nifasilk Lafto Sub-city had the biggest drop (34 percent), followed by Yeka Sub-City, which has decreased by 29 percent. The second quarter, when the government started implementing restrictions, Bole sub-city showed a 27 percent decrease in the TB notification rate. In the third quarter, the pandemic had a greater impact on all the sub-cities, which caused the largest decline in TB notifications. Bole, Gulele, Lideta, Lemi Kura, and Addis Ketema Sub-cities all showed a significant fall in this quarter, with decreases of 56 percent, 43 percent, 42 percent, and 41 percent, respectively. The Arada sub-city had an increase of 83 percent in TB CNR in the following quarter (Quarter 4), despite the fact that other sub-cities witnessed a decline. The influence of COVID-19 on TB care as determined by TB notification in one sub-city was expected also have an impact on nearby sub-cities throughout the area. Spatial analysis showed that for instance, Nifasilk Lafto, Bole, and Lemikura sub-cities similarly saw a fall in TB notification when the Akaki Kality sub-city did.

4.3 Literature review results on factors affecting the trend of TB patient's pathway of care during the pandemic

According to global reports, Access to and delivery of TB health services, including TB diagnosis, treatment, and prevention, have been significantly hampered by COVID-19 in many contexts with high TB

burdens due to inadequate capacity and equipment, restrictions on transportation (affecting health care professionals, patients, goods, and stock), and resource reallocation(31). Individual TB patients have difficulty getting TB services due to concerns about SARS-CoV-2 infection, stigma, movement limitations, shortened hours for health facility openings, or diminished financial means to cover care or transportation (31). According to a study that looked at the real-time, patient-level effects of COVID-19 on the clinical care and treatment of TB patients in Addis Abeba, 18.9% of the participants missed appointments for their follow-ups during the COVID-19 outbreak due to factors like fear of contracting COVID-19, transportation issues, a partial lockdown, a lack of money for travel to a medical facility, an inability to obtain face masks, and pressure placed on providers(62).

Our study looked at data, literature, and model analyses from domestic and overseas sources to depict the determinants that prevent TB patients Pathway of care during the COVID-19 period. Nevertheless, Due to the lack of data on treatment outcomes at the time of this analysis, only the parts of the pyramid related to case notification (i.e., from population to notified) as illustrated in the Patient Pathway framework (Figure 4) were analyzed by this literature review.

4.3.1 TB Risk Factors

4.3.1.1Population at risk /Patient related factors:

Poverty

According to the World Bank report, as a result of COVID-19, between 40 and 60 million people would live in severe poverty in 2020, increasing the rate of extreme poverty worldwide by 0.3 to 0.7 percentage points, reaching about 9 percent(52). Since poverty is a well-known risk factor for contracting the disease, this will have a long-term effect on the burden of TB(52). In many LMICs, including Ethiopia, tuberculosis is a disease of poverty that primarily affects the most vulnerable members of society who also have the least access to basic medical treatment(25). This has a significant role in determining health outcomes, particularly for those who have TB. In an ideal situation, consultations, lab tests, and treatment for TB would all be provided for free in the public sector in Ethiopia (61). Similar to this, certain private medical institutions that fall within the public-private mix model offer free TB testing and treatment. However, regardless of the kind of health issue, there is a common cost that must be paid by every patient registering at a medical facility(61). According to research conducted in Addis Abeba, patients suffered significant costs during the pre-treatment stage accounting 53.6% of total costs, highlighting the financial hardship TB patients bear while picking the correct service to confirm the diagnosis. The whole cost might be catastrophic, worsening the link between poverty and TB(63).

Numerous socioeconomic and behavioral characteristics that potentially facilitate the spread of the coronavirus in Ethiopia are also known to facilitate the spread of M. tuberculosis(36). Moreover, the economic problems brought on by the COVID-19 epidemic put additional strain on the communities, causing missing hospital visits(7). Evidence revealed that patients' visits to the TB screening and diagnostic clinics in Addis Abeba were impacted by the COVID-19 containment measures that were in place. According to these research, patients' decreasing incomes and extra expenditures for safety devices like face masks and hand sanitizers were significant causes of missed medical appointments (64).

All things considered, COVID-19 will have a disproportionately negative impact on the poorest and most disadvantaged individuals in Africa, who already have the highest rates of both infectious and non-communicable illnesses and the least access to basic healthcare. Many undiagnosed and active TB patients will be among them; as a result, they are extremely likely to experience poorer TB-related outcomes(36).

Fear of acquiring COVID-19

According to studies, In the City of Addis Ababa Healthcare-seeking behavior of patients has been altered by the public's awareness of disturbing medical information and the issuance of stay-at-home orders (65). A research on the effects of COVID-19 on patients' health seeking behavior in Addis Abeba revealed that patients' fears of contracting the virus at the hospital were the primary reason for missing appointments, accounting for 70% of missed appointments from March to June 2020(66). Similar to this, a key informant interview done at Addis Abeba's primary healthcare facilities noted that the low patient flow was mostly caused by people' fears of contracting the COVID-19 virus (67). Additionally, a survey carried out in tertiary healthcare institutions in Addis Abeba revealed that the odds of a patient being lost to follow-up were 19 times higher in those who reported having a fear of COVID-19 than in those who did not (66).

Stigma/discrimination

Evidences showed that ,Patients with chronic cough may be hesitant to seek care because of the "new" stigma and fear about COVID-19 (36).Furthermore, some patients have encountered stigma, particularly after recovering from the COVID-19 infection and being accused of visiting high-risk environments (68). The stigma and misinformation around TB have substantially risen in Addis Abeba as a result of the symptoms of COVID-19 and TB being similar (68). This scenario has also happened in other countries with a high TB burden. According to the findings of a global community-based survey,56% of people with TB from Kenya reported feelings of shame because of the overlapping symptoms with COVID- 19(69). In the same survey, 62 percent of Indians with TB said they avoided going to their regular facility for fear of catching COVID-19 (69). Similarly , People were concerned that if they sought services for TB, healthcare professionals or community members would mistakenly believe they had COVID-19, according to a research conducted in 64 low- and middle-income countries(7).

Due to the poverty, fear of acquiring COVID-19 and stigma, the trend of patient visits to get essential health services including TB care declined in Ethiopia(4). For instance, The average number of patients visiting medical, surgical, pediatric, and psychiatry average outpatient visits decreased by more than half compared to the same period the previous year, according to national studies conducted in Ethiopia(70). The average number of patients accessing emergency departments declined by 47% throughout the COVID season, and outpatient visits decreased by 57 percent from pre-covid to post-covid (70). A similar research in Ethiopia found that between March and June 2020, outpatient visits in the regions most affected by the COVID-19 epidemic, mainly Addis Ababa, decreased by 24 percent in comparison to the same times prior to the pandemic(46).

4.3.2 Access to TB diagnostic services

4.3.2.1 Government restriction measures:

A temporary law of the Ethiopian government to combat COVID-19 resulted in the prohibition of mass gatherings, the closure of schools and universities, restrictions on public transportation, the suspension of sporting and religious events, and the imposition of quarantine and isolation (52).

According to research conducted in Ethiopia, one of the main challenges for TB patients was the disruption of transportation, particularly during the lockdown period from April to July 2020, which hindered their access to healthcare facilities and resulted in their missing follow-up visits. The COVID-19 lockdowns had a tremendous influence on transporting people to medical facilities (62). Even though there are few statistics

on the accessibility of TB care during the pandemic in Addis Ababa, Ethiopia, the worldwide survey discovered a marked decrease in the number of patients visiting healthcare institutions. According to the research on sub-Saharan Africa, 50 percent of TB patients in Kenya reported difficulty getting to medical care because of limited access to public transportation (cost and availability of transport) (69).

On the other hand ,Reduced access to health care has reportedly been a result of COVID-19 preventative efforts that government called for the use of facemasks and social isolation (22). There were, however, few facemasks available in Addis Ababa during the early stages of the COVID-19 pandemic. Through massive donations, commercial manufacturing, and local production, this was quickly reversed. Evidences, however, reveals that despite being aware of the preventive benefits of masks, TB patients could not afford to purchase a facemask (62). Additionally, these preventative procedures put a financial strain on the patients. According to a survey conducted at Addis Abeba's sub-city health clinics, purchasing facemasks (50.5%), soaps for handwashing (50.6%), and disinfectants (50%) were the most expensive COVID-19 preventive measures that put a financial strain on patients (62). This finding is supported by research conducted in Malawi, which found that although face masks were made mandatory at health facilities during the pandemic, patients did not want to wear them because they were expensive and felt like they were "suffocating" them, according to TB officials. Patients who attempted to enter facilities without a mask were turned away (i.e., not examined by a healthcare professional) and frequently did not return (71).

4.3.2.2 Health system factors:

In sub-Saharan Africa, COVID-19 has had a profound impact on every aspect of the healthcare system. Accessing and using essential healthcare services has become more challenging due to inadequate resources in healthcare facilities, overcrowding in hospitals, a shortage of health care providers (HCPs), a lack of guidelines on the continuation of non-COVID-19 services, and discouragement among HCPs due to a lack of materials (72). According to reports in Africa, over 50% of HCPs reported partial or complete interruptions in TB care services, immunization, vitamin A supplementation, nutrition preventive services, HIV treatment services, and surgeries. Interruptions were higher in Nigeria, Burkina Faso, and Ethiopia (72). According to a WHO report from 2021, 66% of nations, including Ethiopia, continue to cite issues with the health staff as the main causes of interruptions in key health services, such as TB. The availability of essential medications, diagnostics, and the personal protective equipment (PPE) required for safe and effective healthcare delivery is still affected by supply chain disruptions in close to one-third of nations(73).

According to worldwide reports, TB treatment and diagnostic services were impacted by the overburdening of health care systems caused by COVID-19 patients in several ways: (1) diverting resources (both human and financial) away from ordinary services to handle the epidemic; (2) focusing on pandemic management and response with inadequate supervision and responsibility of TB programs among health care and political leadership, the media, and the public; (3) Health care workers feeling stressed and anxious, which are important risk factors for mistakes and poor treatment; (4) Health care workers being forced into quarantine, being sick, or passing away, which prevents them from being accessible for normal services (52). According to national reports, Health institutions in Addis Ababa that have been offering TB care and treatment services have been designated as COVID-19 isolation and treatment centers, according to research on the containment of COVID-19 in Ethiopia and its implications for tuberculosis care(10). COVID-19 has received more human and material resources for TB, which has had an impact on case identification and treatment. Health care providers are afraid for their families and themselves since they are giving services without the necessary personal protective equipment (PPE)(10).

Furthermore, studies conducted in Addis Abeba found that because of increased patient loads, inadequate infrastructure, and other factors, the workforce was at risk of catching the virus. It was claimed that it was challenging to deliver health services due to a lack of space (which is in conformity with physical distance restrictions). As a result of the heightened risk and personnel workload, several services have been

rescheduled: The COVID-19 outbreak presented the most challenging challenges for medical professionals.(74). On the other side, the government policy providing leave permission for those over 65 or with comorbid conditions contributed to the increased workload. As a result, this has increased the burden and aggravated the medical staff (74). A report from one of the biggest specialized hospital in Addis Ababa (Tikur Anbesa Specialized Hospital) showed that the overcrowding and the limited availability of personal protective equipment justifiably increase the fear of acquiring COVID 19 in this setting, which could decline follow-up visits(75).

CHAPTER FIVE

5.0 Discussion

5.1 Temporal trend of TB notification (New and relapse TB cases) before and during COVID-19 pandemic

This study on the COVID-19 pandemic's effects on TB notifications in Addis Ababa, Ethiopia adds to the growing evidence that the COVID-19 pandemic hinders efforts to combat TB. It has revealed a significant reduction in TB case notifications concurrent with the emergence of the COVID-19 epidemic. Our findings agree with preliminary studies on COVID-19 impacts on TB diagnosis and treatment from other contexts (72,73). Following the confirmation of COVID-19 cases and the adoption of mitigation measures intended to stop further COVID-19 transmission, the overall TB detection rate in our research throughout the COVID-19 period (March 2020–December 2020) was demonstrated to be significantly lower by 19.5%. This result highlights the significance of rigorous and ongoing surveillance of significant public health issues during the COVID-19 pandemic and subsequent pandemics.

The impact of the pandemic on the tuberculosis notification rate in this study is slightly lower than what was reported from facilities in Nigeria 34%, South Africa 33%, and 43% in Uganda 43%, 24% in South Korea (76,77). Similarly, the research outputs from different high TB burden countries also illustrated a higher decline compared to our study(73). However, our study result aligns with a recent report from WHO showing an overall 21% shortfall in TB case notifications in 84 countries in 2020 compared with 2019 (78). In contrast, our analysis revealed a greater drop in TB notification than the earlier study in Addis Ababa, which revealed an 11% decline(76). In our analysis, Third quarter TB notification in general in Addis Ababa city decreased by the most (-41%) during the pandemic compared to the respective quarter during pre-covid ere; this result may be explained by the start of the government's pandemic response as a result of an increase in the number of COVID-19 cases (figure 8). This finding is consistent with a Global Fund analysis from 502 health institutions in Asia and Africa, which found that TB referrals fell by 59 percent in the second and third quarters of 2020 compared to the same time in 2019(28). Similarly , The result corresponds to another study's finding from Addis Abeba which shows that the overall decline in patient flows declined by 69% (79). The significance of these results is that it points out the feasibility of coordinated public health measures in response to the pandemic and its impact on essential services like TB diagnosis and screening. This impact posed risk to public health programs by hindering their efforts to eradicate tuberculosis. Similarly, the pandemic has serious outcomes for the affected individuals by exposing them to missed or delayed diagnoses. As a result, drug-resistant TB, and a low cure rate for TB due to delayed diagnosis are probable negative outcomes.

5.2 The geographical distribution of the total TB notification (New and relapse TB cases) before and during COVID-19

Regarding geographical distribution, the TB notification rate in the various sub-cities varied substantially. The variation across sub-cities may be influenced by factors including sociodemographic characteristics, the economy, and illiteracy. However, our study did not analyze the factors underlying such variability due to a lack of data and evidence about determinants among sub-cities. From sub-cities, Nifasilk Lafto recorded the biggest drop, which had 34% decline, and in Yeka Sub-city, which accounts for more than 29% decline of tuberculosis notifications during overall (2020) COVID-19 period compared to pre-covid (2019).

Surprisingly, however, the TB notification rate in the Arada sub-city increased during the epidemic. This finding is supported by studies conducted in Zambia, which also revealed an increase in bacteriologically confirmed TB cases throughout the COVID-19 period compared to the previous year(33). Well-equipped laboratories, staff, and facilities, as well as the parallel TB services that encouraged those TB patients to travel to health facilities for examination, are a few of the likely factors listed to complement this result (33). The Zambia National Tuberculosis and Leprosy Programme also developed a strategy to start systematic symptoms-based screening of all people visiting the health facility for active tuberculosis diseases, regardless of the reason for presentation, by increasing the number of tuberculosis diagnostic facilities offering facility-based active case-finding and initiating household contact tracing by training community-based health care workers(33).

Contrary to our research, several studies demonstrating COVID-19's unanticipated effects on TB care have been conducted at the national level. It is therefore challenging to compare the results of our study with information from these other studies. Research conducted in Zimbabwe, however, revealed an overall decline of 40.6 percent in the number of persons presenting with presumptive pulmonary TB at the city level in Harare city as compared to the pre-COVID-19 period (80). These geographic findings of our study emphasize the value of rigorous and ongoing monitoring of hotspot and cold spot regions, as well as public health issues, during the COVID-19 and future pandemics, which helps to allocate resources and target interventions. Furthermore, the substantial heterogeneity identified at the sub-city level in Addis Abeba highlights the significance of doing an in-depth assessment at the community or sub-national level.

5.3 Factors affecting the trend of TB patient's pathway of care during the pandemic

The findings of this study indicated that TB patients' inability to access TB diagnostic services, or at least their delay in doing so, was the primary reason for the decrease in TB notifications during the COVID-19 pandemic. A study on the impact of the COVID-19 pandemic and meeting tuberculosis targets also noted that the main effects of COVID-19 were on TB diagnosis and enrollment as opposed to TB incidence (27). The quantitative results of our study supported this hypothesis, which demonstrates a 13% reduction in TB cases that were bacteriologically confirmed during the pandemic compared to the pre-covid period. Similarly, research done in Addis Abeba, which found that overall, there were 11.8 % fewer TB cases with bacteriological confirmation during the COVID-19 era. The variation in those studies conducted in Addis Ababa might be due to the sample size difference. Similar to that, The detection rate of all kinds of TB decreased by a range of 4 percent to 18 percent over the COVID-19 era's quarters (April 2020 to March 2021) (76). Another study in Sierra Leone also showed that there was a 35% decline in laboratory confirmed cases after the implementation of the COVID-19 containment measures(1). The reallocation of healthcare personnel for the pandemic response and the rearrangement of diagnostic facilities and health centers for COVID-19 diagnosis and isolation are two potential explanations for this decline in TB diagnoses. This explanation is consistent with research from high-TB burden nations in Africa. For instance, it was recently reported in Nigeria that 300 GeneXpert machines will be used to scale up diagnosis of COVID-19 (36). Similar findings in India indicated that diagnosing COVID-19 was prioritized above TB, delaying diagnosis(81).

The stigma associated with TB is one of the initial explanations for this study's finding of poor TB diagnosis and notification. In Addis Ababa, the stigma associated to TB has long been a problem. Research on stigma among TB patients in the city complemented this(82). According to this study, the fear of infection is the source of the TB stigma (82). The present COVID-19 outbreak, however, further makes this stigma worse. This is supported with information from our review of the literature, which revealed that utilization of healthcare services was quite difficult in the early period of the COVID-19 epidemic. Despite experiencing symptoms that were similar to those of both diseases, some persons may not have sought testing due to the stigma already associated with TB and the stigma imposed by COVID-19. Similarly, according to

qualitative research conducted in Malawi, fewer people are seeking TB diagnosis because of the stigma attached to COVID-19, which has symptoms that are similar to TB symptoms(6). Stigmatization may be lessened with the use of health education(82). Therefore, there is a critical need for an innovative health education platform that links the two diseases.

Another explanation for the low accesses and demand to diagnostic services could be the mitigation efforts by the government. This notion is supported by research conducted in South Africa that claims that patients' limited mobility was a major factor in the drop in diagnostic tests(83). The interventions posed by Ethiopian government to "flatten the curve" in COVID-19 responses, will be disproportionately more challenging to implement for the poorest, who frequently live in overcrowded conditions, have no or limited access to drinking water, and make inadequate incomes from daily wages. Our literature review results depicted that most of TB patients belonged to lower socioeconomic classes and were already having trouble paying their bills and buying food (reference). As a result, their existing worries about their quality of life would have been made worse by the addition of the fear of isolation or quarantine (36). Previous studies also depicted that reducing the impact of the high cost associated with the illness is of serious concern for TB control because of the negative relationship between TB and poverty (63). Since poverty is anticipated to contribute to both increased TB transmission and lower TB detection due to restricted financial access to TB care, it is important to assess the dual relationship between poverty and TB reporting in Ethiopia, highlighting its significance for decision support.

Similarly, another primary obstacle for the TB patients was the interruption of transportation, especially during the partial lockdown period, which limited their access to healthcare facilities and caused them to miss follow-up appointments. The findings that COVID-19 lockdowns significantly impacted patients' access to transportation to healthcare centers was in line with earlier research done in Ethiopia(22) and other parts of Africa(6). Furthermore, among those patients who requested to seek medical advice, the diagnosis of TB was delayed, as most non-emergency services were suspended during the pandemic due to the scarcity of health experts and overburdened health facilities. The findings of this study's literature analysis are consistent with earlier researches in Ethiopia that suggest that the COVID-19 epidemic has drastically impacted routine TB diagnosis, care, and treatment. (22,62). This pandemic's indirect impact might be considerably reduced by keeping important program aspects such as TB diagnosis and recovery activities with the goal of preserving TB initiative progress. As a result, despite efforts that encourage social distancing, patients must have access to care and diagnosis for essential services for the major public health problems like TB.

Another factor that our study identified for the low TB notifications during the pandemic was the absence of proper information regarding the pandemic. Particularly among communities in Ethiopia where the frequency of HIV infection, TB, anemia, and malnutrition is substantially greater, very little is known about the pathobiological processes of the COVID-19 induced by the new SARS-CoV-2 (36). Our literature review revealed that patients' healthcare-seeking behavior in Addis Abeba was influenced by the public's awareness of distressing medical information as well as the problem of stay-at-home orders. As a result, fewer individuals sought diagnoses, which will have a lot of detrimental impacts. However, because there were no data on clinical outcomes of TB patients notified during the study period (March 2019 to December 2020), our study did not examine the impacts. Results from neighboring countries in Africa, on the other hand, give some evidence and complement this hypothesis, estimating that over the next five years, TB fatalities might rise by 4-16%, while TB incidence could increase by 3-9%(30). For instance, at the beginning of the pandemic, modeling analysis predicted that a three-month suspension of TB services due to COVID-19 lockdown followed by a ten-month return to normal would result in an additional 25,000 TB cases and 12,500 TB deaths in Kenya over the course of five years, primarily due to accumulation of undetected TB during lockdown (30). TB mortality was also anticipated to rise by 20% in high-burden, low- and middle-income countries, with delays in new TB patients being diagnosed and treated promptly (25).

5.4 Relevance of the Framework

The study was directed through the analysis and interpretation of the results by the conceptual framework of Mapping and Analysis for Tailored disease Control and Health system strengthening (MATCH) (84). It helped the analysis to explore factors contributing to the variation in TB notification before and during the pandemic. The framework was friendly to apply and helped in the synthesis of important information in ways that decision- and policymakers can quickly comprehend. However, owing to a lack of data on lost to follow-ups, treatment outcome and death, I was unable to fully describe some of the concepts (cured, treated). When I return to my Country, I plan to regularly analyze TB statistics using this framework.

5.5 Strength & Limitation of the study

This study has its strength and limitations. As a strength, it compared the indirect impact of the COVID19 pandemic on TB care services as measured by TB notification by taking data from DHIS2 multicenter reports before and during the COVID-19 pandemic. The use of data over a 2-year period, which permits both studies of patterns in healthcare usage before and after the onset of COVID-19 and year-on-year comparisons, and analysis of data provided from numerous healthcare institutions located throughout sub-cities in the capital are key strengths. Additionally, the study employed a variety of techniques, including temporal, geographical, and literature reviews, to assist triangulation of findings.

The following are a few of this study's limitations. First, the study's retrospective design relied on the accuracy of the health facilities' records throughout the sub-cities, which might have been impacted by the COVID-19 lockdowns. Furthermore, due to time constraints and data collection challenges, the qualitative technique (key informant interviews) and proxy indicators such as distance from facility and poverty level were not employed. As a result, the primary cause of the decline in TB notifications across sub-cities has not been revealed with this study. However, this study used a literature review to examine some of the factors. On the other hand, the study was limited to health facilities located across sub-cities in Addis Ababa, and therefore may not be representative of Ethiopia as a whole. Second, because aggregate data were used, the individual cascade of care for TB case identification and testing could not be properly understood. Lack of programmatic data also made it impossible to compare COVID-19 at the sub-city level to declining health care utilization or scarce resources (lower testing rates).

Furthermore, the likelihood of direct interactions between COVID-19 and TB was not examined in the current investigation. However, using aggregated data collected quarterly, trends in TB notification could be described. The study did not use qualitative approaches to investigate probable causes of the low TB notification; instead, it focused simply on the TB cascade's trajectory by using literature review.

CHAPTER SIX

6.0 Conclusion

This research aimed to address the research questions of what the temporal and geographic trends of TB notification were before and during the COVID-19 pandemic period based on quantitative, spatial, and literature review analysis. In addition, it aimed to investigate the reasons that contributed to the decline in TB notification during the pandemic throughout the Addis Ababa sub-cities. Despite the limited data provided for this study, it can be concluded that the TB notification in Addis Ababa city was negatively impacted by the COVID-19 epidemic. The two-year report from Addis Ababa's eleven sub-cities District Health Information System (DHIS2) data showed that notification of TB cases fluctuated even before the pandemic's onset. The present COVID-19 pandemic's effects on health and the economy, as well as the public health measures implemented to curb the virus's spread, however, causes the decrease to worsen. this decline in TB case reports may potentially be a sign of more widespread interruption of several basic healthcare services.

The effects of the pandemic on TB notifications across sub-cities in Addis Ababa varied substantially, according to this study, from having no immediate effect in certain sub-cities to having an instant negative impact of more than 25% in others during COVID-19 period. This heterogeneity may have a variety of contributors. Due to a lack of data, the study was unable to identify the causes of heterogeneity. However, the study examined several factors that contributed to a general drop in TB notification throughout Addis Ababa city. Our findings imply that the TB control efforts in Addis Ababa city were substantially impacted by the succession of measures, state of emergency declaration, and government instructions made to prevent the spread of COVID-19 as well as the public reaction to them. Furthermore, the stigma associated with TB and COVID-19, and the overburdened health care system as a result of the epidemic were likely the main contributing reasons. To resolve these issues, it is possible to undertake a properly planned public health response that included active case-finding strategies for TB, and it was associated with a restoration of tuberculosis case notifications to pre-pandemic levels. Similarly, by educating the public (via various media) that vital health services are still accessible and open to everyone in need of them, the ministry of health and the municipal administration health bureau might have an influence.

To maintain the achievements and improvements made in the battle against tuberculosis over the preceding 10 years, the TB program must immediately change to the new normal in order to address the difficulties posed by the pandemic. This will aid in the continuation of efforts to achieve the End TB program's objectives. To do so, the national TB program must strengthen patient-centered approach to TB care, embrace digital health technology, raise awareness, strengthen community-based active TB case finding, and sustain TB screening services.

Furthermore, to address some of the questions this study's hypothesis highlights, more investigation would be needed. A more thorough study using both a qualitative and quantitative methodology might provide insights into the effects.

6.1 Recommendation

In this study, the most important issues that contributed to the low TB case notification during the current COVID-19 pandemic were government restriction measures, an overburdened health system, stigma, and misinformation about the pandemic. Reflecting on these challenges, this study put out the following recommendations to help improve the city's TB care service in terms of case notification rate (CNR).

First, Expanding the simultaneous COVID-19 and TB testing is urgently needed. Expanding the existing diagnostic services for TB patients will be crucial to improving case findings. The Ethiopian Ministry of Health, the National Tuberculosis Program Office, Hospitals, and Diagnostic Facilities are the relevant stakeholders needed to make this happen. The expansion of the existing laboratory infrastructures, training of current employees, recruiting of new qualified personnel, and the creation of national guidelines for concurrent testing of both illnesses are all part of strengthening these services. The availability of staff benefit plans and personal protection equipment is also necessary to motivate and keep the current staff members.

Secondly, promoting the human rights of people who are most vulnerable by speaking out against stigma and discrimination can help the public health response, which is impeded by stigma and fear surrounding infectious diseases like TB and COVID-19. The relevant stakeholders involved include Government, Media, communities, and the Ministry of health. This may be done by organizing media campaigns, creating engagement activities, and generating and disseminating awareness-raising materials via mainstream and social media.

Thirdly, promoting a people-centered approach can help to mitigate the accessibility challenges created by the pandemic. The NTP, the Ministry of Health, community health workers, NGOs, and TB stakeholders like the KNCV Tuberculosis Foundation are among the relevant stakeholders involved. Through mobile health platforms, facility-based contact tracing and surveillance might be transferred to a home-based system to increase accessibility and reduce disruptions. Additionally, the function of community health workers should be taken into consideration to maintain TB surveillance and monitoring.

Finally, to increase active case detection, the NTP, ministry of health, research institutions, and implementing partners (KNCV Tuberculosis Fund and Global Fund) must support innovative and realistic research. Staff members working on the national and regional TB programs should be encouraged to analyze routine program data using QGIS and other free tools to learn more about existing data sets. Such evidence from the research output might guide policy and decision-makers in their processes for allocating resources, planning, and designing policies. Additionally, by identifying relevant causes and taking appropriate action, the ongoing study will assist in the response to catastrophes like the present COVID-19 pandemic.

References

1. Lakoh S, Jiba DF, Baldeh M, Adekanmbi O, Barrie U, Seisay AL, et al. Impact of covid-19 on tuberculosis case detection and treatment outcomes in sierra leone. Trop Med Infect Dis. 2021;6(3).

2. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed [Internet]. 2020 [cited 2022 Apr 24];91(1):157–60. Available from: https://pubmed.ncbi.nlm.nih.gov/32191675/

3. Gurley N, Ebeling E, Bennett A, Kashondo JK, Ogawa A, Couteau C, et al. National policy responses to maintain essential health services during the COVID-19 pandemic. 2022;(December 2021):168–70.

4. Kaba M. Maintaining essential services during the COVID-19 pandemic. Ethiop J Heal Dev [Internet]. 2020;34(3):127–34. Available from: https://www.ejhd.org/index.php/ejhd/article/view/3194

5. WHO. Global Tuberculosis Report. 2021.

6. Soko RN, Burke RM, Feasey HRA, Sibande W, Nliwasa M, Henrion MYR, et al. Effects of Coronavirus Disease Pandemic on Tuberculosis Notifications, Malawi. Emerg Infect Dis [Internet]. 2021 Jul 1 [cited 2021 Dec 26];27(7):1831–9. Available from: https://pubmed.ncbi.nlm.nih.gov/34152962/

7. Khan MS, Rego S, Rajal JB, Bond V, Fatima RK, Isani AK, et al. Mitigating the impact of COVID-19 on tuberculosis and HIV services: A cross-sectional survey of 669 health professionals in 64 low and middle-income countries. PLoS One. 2021 Feb 1;16(2 February 2021).

8. Ethiopia GNI Per Capita 1983-2022 | MacroTrends [Internet]. [cited 2022 Mar 7]. Available from: https://www.macrotrends.net/countries/ETH/ethiopia/gni-per-capita

9. Argaw MD, Desta BF, Bele TA, Ayne AD. Improved performance of district health systems through implementing health center clinical and administrative standards in the Amhara region of Ethiopia. BMC Health Serv Res. 2019;19(1):1–13.

10. Mohammed H, Oljira L, Roba KT, Yimer G, Fekadu A, Manyazewal T. Containment of COVID-19 in Ethiopia and implications for tuberculosis care and research. [cited 2021 Nov 26]; Available from: https://doi.org/10.1186/s40249-020-00753-9

11. Chilot D, Woldeamanuel Y, Manyazewal T. Real-Time Impact of COVID-19 on Clinical Care and Treatment of Patients with Tuberculosis: A Multicenter Cross-Sectional Study in Addis Ababa, Ethiopia. Ann Glob Heal [Internet]. 2021 Nov 15 [cited 2022 Jan 19];87(1). Available from: https://pubmed.ncbi.nlm.nih.gov/34824990/

12. Tuberculosis [Internet]. [cited 2021 Nov 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/tuberculosis

13. Woldemichael B, Darega J, Dida N, Tesfaye T. Treatment outcomes of tuberculosis patients and associated factors in Bale Zone, Southeast Ethiopia: a retrospective study. J Int Med Res. 2021;49(2).

14. FMOH. Guidelines on Programmatic Management of Drug Resistant Tuberculosis in Ethiopia,

Addis Ababa [Internet]. 2013 [cited 2022 Jan 26]. p. 8. Available from: https://www.bing.com/search?q=FMOH%2C+Guidelines+on+Programmatic+Management+of+Drug+Resistant+Tuberculosis+in+Ethiopia%2C+Addis+Ababa%2C+2013.+%5B8%5D&cvid=027527a138dc4b9d8735c7646239812b&aqs=edge..69i57j69i59i450l8.5252965j0j4&pglt=43&FORM=ANNAB1&PC=LCT

15. Management ND. Addis Ababa Health Atlas , 2021. 2021;

16. IMHE. GBD Compare | IHME Viz Hub [Internet]. Global Burden of Disease. 2015 [cited 2022 Jan 4]. p. 1. Available from: https://vizhub.healthdata.org/gbd-compare/

17. Scanner C. Ethiopia |Realtime coronavirus statistics [Internet]. 2021 [cited 2022 Jul 12]. Available from: https://corona-scanner.com/country/ethiopia

18. Mohammed H, Oljira L, Roba KT, Yimer G, Fekadu A, Manyazewal T. Containment of COVID-19 in Ethiopia and implications for tuberculosis care and research. Infect Dis Poverty. 2020 Sep 16;9(1).

19. EPHI and MoH. Public Health Emergency Operation Center (PHEOC), Ethiopia COVID-19 Pandemic Preparedness and Response in Ethiopia. EPHI Wkly Bull [Internet]. 2021;39:1–21. Available from: https://www.ephi.gov.et/images/novel_coronavirus/EPHI_-PHEOC_COVID-19_Weekly-bulletin_1_English_05042020.pdf

20. Harries AD, Martinez L, Chakaya JM. Monitoring the COVID-19 pandemic in sub-Saharan Africa: Focusing on health facility admissions and deaths. Int J Tuberc Lung Dis. 2020;24(5):550–2.

21. Zikargae MH. Covid-19 in ethiopia: Assessment of how the ethiopian government has executed administrative actions and managed risk communications and community engagement. Risk Manag Healthc Policy. 2020;13:2803–10.

22. Mohammed H, Oljira L, Roba KT, Yimer G, Fekadu A, Manyazewal T. Containment of COVID-19 in Ethiopia and implications for tuberculosis care and research [Internet]. Vol. 9, Infectious Diseases of Poverty. Infect Dis Poverty; 2020 [cited 2021 Nov 26]. Available from: https://pubmed.ncbi.nlm.nih.gov/32938497/

23. Ethiopian Public Health Institute. Public Health Emergency Operation Center (PHEOC), Ethiopia COVID-19 Pandemic Preparedness and Response in Ethiopia. EPHI [Internet]. 2020;37(November):1–17. Available from: https://www.ephi.gov.et/images/novel_coronavirus/EPHI_-PHEOC_COVID-19_Weekly-bulletin_1_English_05042020.pdf

24. Walker PGT, Whittaker C, Watson OJ, Baguelin M, Winskill P, Hamlet A, et al. The impact of COVID-19 and strategies for mitigation and suppression. Science (80-). 2020;369(6502):413–22.

25. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. Lancet Glob Heal [Internet]. 2020;8(9):e1132–41. Available from: http://dx.doi.org/10.1016/S2214-109X(20)30288-6

26. WHO. Global Tuberculosis Reports. The Lancet. 2020.

27. Sahu S, Ditiu L, Sachdeva KS, Zumla A. Recovering from the Impact of the Covid-19 Pandemic

and Accelerating to Achieving the United Nations General Assembly Tuberculosis Targets. Int J Infect Dis [Internet]. 2021;113(2021):S100–3. Available from: https://doi.org/10.1016/j.ijid.2021.02.078

28. Zimmer AJ, Klinton JS, Oga-Omenka C, Heitkamp P, Nawina Nyirenda C, Furin J, et al. Tuberculosis in times of COVID-19. J Epidemiol Community Health. 2021;jech-2021-217529.

29. Lai CC, Yu WL. The COVID-19 pandemic and tuberculosis in Taiwan. J Infect. 2020 Aug 1;81(2):e159–61.

30. Cilloni L, Fu H, Vesga JF, Dowdy D, Pretorius C, Ahmedov S, et al. The potential impact of the COVID-19 pandemic on the tuberculosis epidemic a modelling analysis. EClinicalMedicine [Internet]. 2020 Nov 1 [cited 2022 Apr 5];28:100603. Available from: https://jhu.pure.elsevier.com/en/publications/the-potential-impact-of-the-covid-19-pandemic-on-the-tuberculosis

31. McQuaid CF, Vassall A, Cohen T, Fiekert K, White RG. The impact of COVID-19 on TB: a review of the data. Int J Tuberc Lung Dis [Internet]. 2021 Jun 1 [cited 2022 Jan 22];25(6):436. Available from: /pmc/articles/PMC8171247/

32. Stop TB Partnership. The Impact of COVID-19 on the TB Epidemic: A Community Perspective. 2020 [cited 2022 Mar 2];1–65. Available from: https://express.adobe.com/page/xJ7pygvhrIAqW/

33. Lungu PS, Kerkhoff AD, Muyoyeta M, Kasapo CC, Nyangu S, Kagujje M, et al. Interrupted time-series analysis of active case-finding for tuberculosis during the COVID-19 pandemic, Zambia. Bull World Health Organ [Internet]. 2022 Mar 3 [cited 2022 Jun 6];100(3):205. Available from: /pmc/articles/PMC8886254/

34. Malik AA, Safdar N, Chandir S, Khan U, Khowaja S, Riaz N, et al. Tuberculosis control and care in the era of COVID-19 [Internet]. Vol. 35, Health Policy and Planning. Oxford Academic; 2020 [cited 2022 Mar 2]. p. 1130–2. Available from: https://academic.oup.com/heapol/article/35/8/1130/5896487

35. Stop TB Partnership. The TB Response Is Heavily Impacted by the COVID- 19 Pandemic. 2020 [cited 2022 Mar 3]; Available from: https://www.stoptb.org/

36. Togun T, Kampmann B, Stoker NG, Lipman M. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. Ann Clin Microbiol Antimicrob [Internet]. 2020 May 23 [cited 2022 Mar 4];19(1):1–6. Available from: https://ann-clinmicrob.biomedcentral.com/articles/10.1186/s12941-020-00363-1

37. Haileamlak A. Ethiopia is on Track of Achieving the WHO End Tuberculosis Milestone. Ethiop J Health Sci [Internet]. 2021 Jan 1 [cited 2022 Mar 4];31(1):1. Available from: /pmc/articles/PMC8188112/

38. Alene KA, Gelaw YA, Fetene DM, Koye DiN, Melaku YA, Gesesew H, et al. COVID-19 in Ethiopia: a geospatial analysis of vulnerability to infection, case severity and death. BMJ Open [Internet]. 2021 Feb 1 [cited 2022 Mar 4];11(2):e044606. Available from: https://bmjopen.bmj.com/content/11/2/e044606

39. Louisa Brain B, Adow H, Musse Jama J, Manji F, Owiso M, Adugna Tufa F, et al. COVID-19 and mobility, conflict and development in the Horn of Africa REF briefing paper. 2020;(June). Available from: www.gdi.manchester.ac.uk

40. Manyazewal T, Woldeamanuel Y, Holland DP, Fekadu A, Blumberg HM, Marconi VC. Electronic pillbox-enabled self-administered therapy versus standard directly observed therapy for tuberculosis medication adherence and treatment outcomes in Ethiopia (SELFTB): Protocol for a multicenter randomized controlled trial. Trials. 2020 May 5;21(1).

41. Dandena F, Teklewold B, Anteneh D. Impact of COVID-19 and mitigation plans on essential health services: institutional experience of a hospital in Ethiopia. BMC Health Serv Res. 2021 Dec 1;21(1).

42. Kasaeva T. Joining forces to end TB and COVID-19 [Internet]. World Health Organization. 2020 [cited 2022 Jan 26]. p. 1–11. Available from: https://www.who.int/news/item/12-05-2020-joining-forces-to-end-tb-and-covid-19

43. Sounderajah V, Ashrafian H, Aggarwal R, Fauw J, Denniston AK, Greaves F, et al. The fight to end tuberculosis must not be forgotten in the COVID-19 outbreak. nature.com [Internet]. [cited 2022 Jan 19]; Available from: https://www.nature.com/articles/s41591-020-0917-1

44. Malik AA, Safdar N, Chandir S, Khan U, Khowaja S, Riaz N, et al. Tuberculosis control and care in the era of COVID-19. Health Policy Plan [Internet]. 2020 Oct 1 [cited 2022 Mar 2];35(8):1130–2. Available from: https://academic.oup.com/heapol/article/35/8/1130/5896487

45. Wingfield T, Karmadwala F, MacPherson P, Millington KA, Walker NF, Cuevas LE, et al. Challenges and opportunities to end tuberculosis in the COVID-19 era. Lancet Respir Med [Internet]. 2021 Jun 1 [cited 2022 Jul 18];9(6):556–8. Available from: http://www.thelancet.com/article/S2213260021001612/fulltext

46. Shuka Z, Mebratie A, Alemu G, Rieger M, Bedi AS. Use of healthcare services during the COVID-19 pandemic in urban Ethiopia: evidence from retrospective health facility survey data. BMJ Open [Internet]. 2022 Feb 23 [cited 2022 Apr 5];12(2):e056745. Available from: https://pubmed.ncbi.nlm.nih.gov/35197352/

47. Global Health Expenditure Database [Internet]. [cited 2022 Jun 2]. Available from: https://apps.who.int/nha/database/country_profile/Index/en

48. WHO WHO. COVID-19 and TB [Internet]. 2021 [cited 2022 Jul 5]. Available from: https://www.who.int/publications/digital/global-tuberculosis-report-2021/covid-19

49. WorldPop. WorldPop: Population Counts [Internet]. 2018 [cited 2022 Aug 8]. Available from: https://hub.worldpop.org/geodata/summary?id=49635

50. Addis Ababa, Ethiopia Metro area population 1950-2021. [Internet]. [cited 2022 Mar 5]. Available from: https://www.bing.com/search?q=4+Addis+Ababa%2C+Ethiopia+Metro+area+population+1950-2021.+Available%3A+htts%3A%2F%2Fwww.macrotrends.net%2Fcities%2F20921%2Faddis-ababa%2Fpopulation&cvid=bb887b4517fa4bf49777ab2650201628&aqs=edge..69i57.782j0j1&pglt=43&FORM=A

51. Home | Addis Ababa City Government | Government of Ethiopia [Internet]. [cited 2022 Jul 3]. Available from: https://cityaddisababa.gov.et/en/sub_administration

52. Alene KA, Wangdi K, Clements ACA. Impact of the COVID-19 Pandemic on Tuberculosis Control: An Overview. Trop Med Infect Dis [Internet]. 2020 Sep 1 [cited 2022 Jun 19];5(3):123. Available from: /pmc/articles/PMC7558533/

53. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: A tutorial. Int J Epidemiol. 2017 Feb 1;46(1):348–55.

54. Multivariate Regression | Brilliant Math & Science Wiki [Internet]. 2021 [cited 2022 Jul 13]. Available from: https://brilliant.org/wiki/multivariate-regression/

55. Laerd Statistics. Independent T-Test - An introduction to when to use this test and what are the variables required | Laerd Statistics [Internet]. Laerd Statistics. 2016 [cited 2022 Jul 13]. Available from: https://statistics.laerd.com/statistical-guides/independent-t-test-statistical-guide.php

56. Welcome to the QGIS project! [Internet]. [cited 2022 Jul 12]. Available from: https://www.qgis.org/en/site/

57. Introduction A, Analysis D. GeoDa on Github [Internet]. 2016 [cited 2022 Jul 12]. p. 1–6. Available from: https://geodacenter.github.io/

58. Jones RL, Burk-Rafel J. The Match. Acad Med. 2017;92(6):731.

59. Blok MB& L. Match : M Apping and a Nalysis for T Ailored Disease C Ontrol and H Ealth. 2017;(October):1–40.

60. Rood E, Khan AH, Modak PK, Mergenthaler C, Van Gurp M, Blok L, et al. A Spatial Analysis Framework to Monitor and Accelerate Progress towards SDG 3 to End TB in Bangladesh. ISPRS Int J Geo-Information 2019, Vol 8, Page 14 [Internet]. 2018 Dec 29 [cited 2022 May 10];8(1):14. Available from: https://www.mdpi.com/2220-9964/8/1/14/htm

61. MOH. GUIDELINES FOR MANAGEMENT OF TB, DR-TB AND LEPROSY IN ETHIOPIA. 2017;

62. Chilot D, Woldeamanuel Y, Manyazewal T. Real-Time Impact of COVID-19 on Clinical Care and Treatment of Patients with Tuberculosis: A Multicenter Cross-Sectional Study in Addis Ababa, Ethiopia. Ann Glob Heal [Internet]. 2021 Nov 15 [cited 2021 Nov 26];87(1):1–13. Available from: http://www.annalsofglobalhealth.org/articles/10.5334/aogh.3481/

63. Shimeles E, Tilahun M, Hailu T, Enquselassie F, Aseffa A, Mekonnen A, et al. Time Interval for Diagnosis of Tuberculosis and Related Expenditure in Selected Health Centers in Addis Ababa, Ethiopia. Adv Public Heal. 2019 Dec 3;2019:1–11.

64. Chilot D, Woldeamanuel Y, Manyazewal T. COVID-19 Burden on HIV Patients Attending Antiretroviral Therapy in Addis Ababa, Ethiopia: A Multicenter Cross-Sectional Study. Front Med. 2022;9(March):1–10.

65. Abebe W, Worku A, Moges T, Tekle N, Amogne W, Haile T, et al. Trends of follow-up clinic visits and admissions three-months before and during COVID-19 pandemic at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia: an interrupted time series analysis. BMC Health Serv Res. 2021 Dec 1;21(1).

66. Aklilu TM, Abebe W, Worku A, Tadele H, Haile T, Shimelis D, et al. The Impact of COVID-19 on Care Seeking Behavior of Patients at Tertiary Care Follow-up Clinics: A Cross-Sectional Telephone Survey. Addis Ababa, Ethiopia. medRxiv [Internet]. 2020;28:2020.11.25.20236224. Available from: https://www.medrxiv.org/content/10.1101/2020.11.25.20236224v1%0Ahttps://www.medrxiv.org/content/10.1101/2020.11.25.20236224v1.abstract

67. Shimels T. The Trend of Health Service Utilization and Challenges Faced During the COVID-19 Pandemic at Primary Units in Addis Ababa: A Mixed-Methods Study. Heal Serv Res Manag Epidemiol. 2021;8:1–8.

68. Shimels T. The Trend of Health Service Utilization and Challenges Faced During the COVID-19 Pandemic at Primary Units in Addis Ababa: A Mixed-Methods Study. Heal Serv Res Manag Epidemiol [Internet]. 2021 [cited 2022 Jun 19];8:23333928211031120. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34291123

69. Action global health advocacy partnership, global coalition of TB activists, global TB caucus, et al. The impact of COVID- 19 on the TB epidemic: a community perspective, 2020. [Internet]. 2020 [cited 2022 Jul 3]. Available from: https://www.bing.com/search?q=Action+global+health+advocacy+partnership%2C+global+coalition+of+TB+activists%2C+global+TB+caucus%2C+et+al.+The+impact+of+COVID-+19+on+the+TB+epidemic%3A+a+community+perspective%2C+2020.+Available%3A+https%3A%2F%2Fspark.adobe

70. Dandena F, Teklewold B, Anteneh D. Impact of COVID-19 and mitigation plans on essential health services: institutional experience of a hospital in Ethiopia. BMC Health Serv Res [Internet]. 2021 Dec 1 [cited 2022 Jun 19];21(1). Available from: https://pubmed.ncbi.nlm.nih.gov/34654411/

71. Soko RN, Burke RM, Feasey HRA, Sibande W, Nliwasa M, Henrion MYR, et al. Effects of coronavirus disease pandemic on tuberculosis notifications, malawi. Emerg Infect Dis. 2021;27(7):1831–9.

72. RESEARCH PBA, NETWORK IS& E, ARISE. Health Care Utilization and Service Disruption due to COVID-19. ARISE, Africa Res Sci Educ Netw. 2021;

73. WHO. COVID-19 continues to disrupt essential health services in 90% of countries [Internet]. Https://Www.Who.Int/News/Item/23-04-2021-Covid-19-Continues-To-Disrupt-Essential-Health-Services-in-90-of-Countries. 2021 [cited 2022 Jun 27]. p. 0–4. Available from: https://www.who.int/news/item/23-04-2021-covid-19-continues-to-disrupt-essential-health-services-in-90-of-countries

74. Shimels T. Has the COVID-19 Pandemic Impacted Healthcare Service Uptake at Hospitals in Addis Ababa? Ethiop J Health Sci [Internet]. 2021 Jul 1 [cited 2022 Jun 19];31(4):689–98. Available from: https://pubmed.ncbi.nlm.nih.gov/34703167/

75. Shimels T. Has the COVID-19 Pandemic Impacted Healthcare Service Uptake at Hospitals in Addis Ababa? Ethiop J Health Sci [Internet]. 2021 Jul 1 [cited 2022 Jun 24];31(4):689. Available from: /pmc/articles/PMC8512930/

76. Arega B, Negesso A, Taye B, Weldeyohhans G, Bewket B, Negussie T, et al. Impact of COVID-19 pandemic on TB prevention and care in Addis Ababa, Ethiopia: A retrospective database study. BMJ Open. 2022;12(2):1–6.

77. Kwak N, Hwang SS, Yima AJ. Effect of COVID-19 on Tuberculosis Notification, South Korea. Emerg Infect Dis. 2020;26(10):2506–8.

78. World Health Organization (WHO). WHO analysis of data from 84 countries shows that the Covid-19 pandemic has had a severe impact on essential TB services [Internet]. [cited 2022 Jul 5]. Available from: https://www.medrxiv.org/content/10.1101/2020.04.28.20079582v1

79. Beyene NW, Sitotaw AL, Tegegn B, Bobosha K. The impact of COVID-19 on the tuberculosis control activities in Addis Ababa. Pan Afr Med J [Internet]. 2021 Mar 8 [cited 2021 Nov 26];38(243):243–243. Available from: https://europepmc.org/articles/PMC8164422

80. Thekkur P, Takarinda KC, Timire C, Sandy C, Apollo T, Kumar AMV, et al. Operational research to assess the real-time impact of covid-19 on tb and hiv services: The experience and response from health facilities in harare, Zimbabwe. Trop Med Infect Dis. 2021;6(2).

81. Prasad R, Singh A, Gupta N. Tuberculosis and COVID-19 in India: Challenges and opportunities. Lung India [Internet]. 2020 Jul 1 [cited 2022 Jul 23];37(4):292. Available from: /pmc/articles/PMC7507925/

82. Tadesse S. Stigma against tuberculosis patients in Addis Ababa, Ethiopia. PLoS One. 2016;11(4):1–11.

83. Ismail N, Moultrie H. Impact of COVID-19 intervention on TB testing in South Africa. Natl Inst Commun Dis South África [Internet]. 2020;(May):1–7. Available from: https://www.nicd.ac.za/wp-content/uploads/2020/05/Impact-of-Covid-19-interventions-on-TB-testing-in-South-Africa-10-May-2020.pdf

84. Rood E, Khan AH, Modak PK, Mergenthaler C, Van Gurp M, Blok L, et al. A spatial analysis framework to monitor and accelerate progress towards SDG 3 to end TB in Bangladesh. ISPRS Int J Geo-Information. 2019;8(1):1–11.

Appendices

ANNEX I: Keywords combination with Boolean operators in literature search process

Tuberculosis		COVID-19		Addis Ababa
		Pandemic		Ethiopia
OR				Developing Countries
TB		Impact		Africa
	AND	Prevalence	AND	Sub-Saharan Africa
		Diagnosis		Global
		Notification		
		Lockdown		
		Stigma		
		Restriction		
		Burden		
		Magnitude		
		Mortality		

ANNEX II: KIT Waiver

KIT Royal Tropical Institute

RESEARCH ETHICS COMMITTEE

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To: Simon Genet
By E-mail: s.woldesenbet@student.kit.nl

Amsterdam, 12-05-2022

Subject Decision Research Ethics Committee S-186

Dear Simon Genet

The Research Ethics Committee (REC) of Royal Tropical Institute has reviewed your application for a waiver for a "The effect of Covid-19 on TB notification" (S-186) study that was originally submitted on 9-5-2022

Your proposal has been exempted from full ethical review based on the following considerations:

a. the data will be anonymized and stored in a safe place, only accessible for a selection of the research team;
b. the data has been approved by the data owner (organization who collected the data)
c. informed consent has not been given but it would not be feasible or practicable to ask informed consent to the participants to whom the data belong (anymore);
d. the research has important social, educational or scientific value
e. the research poses no more than minimal risks to participants and does not give rise to the disclosure of the participant's identity

The Committee grants this waiver provided that you inform the GDPR project officer about your research project for GDPR monitoring purposes.

The Committee requests you to inform the Committee if substantive changes to the protocol are made, important changes to the research team take place or researchers are added to the research team. Moreover, the Committee requests you to send the final report of the research containing a summary of the study's findings and conclusions to the Committee, for research managing and training purposes of the REC. Failure to submit the report to the REC, or implement GDPR measurements may have consequences for your next research proposal.

Wishing you success with the research,

Sandra Alba
Co-chair of the KIT REC

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