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Epidemiology, Risk Factors and Best Practices for Improving the Case Detection

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Abbreviations

AFB	Acid-fast bacilli
AIDS	Acquired immune deficiency syndrome
BMI	Body mass index
CDR	Case detection rate
CNR	Case notification rate
DOTS	Directly observed treatment short-course
DST	Drug susceptibility testing
HEWs	Health extension workers
HIV	Human immunodeficiency virus
ICPS	The International Center for Prison Studies
KAP	Knowledge, attitude, and practice
LMICs	Low/middle income countries
MDGs	Millennium development goals
MDR-TB	Multidrug-resistant tuberculosis
NCD	Non-communicable diseases
NGOs	Non-governmental organizations
NTPs	National tuberculosis control programs
TB	Tuberculosis
TSR	Treatment success rate
WHO	World Health Organization
XDR-TB	Extensively drug-resistant tuberculosis

Chapter 1
General introduction

1. General introduction

1.1 The global tuberculosis burden and challenges to control

Despite being curable and preventable, tuberculosis (TB) remains a global public health concern, particularly in Africa and Asia [1,2]. Globally, there were an estimated 10.4 million new TB cases in 2016 of which 25% were in Africa; the continent that also has the highest rates of cases and deaths relative to its population. The annual estimated TB incidence rate in Africa for the same year was 254/100,000 population, which is remarkably high compared to the global average of 140/100,000 population. An estimated 1.3 million (10%) of the 10.4 million incident TB cases were infected with Human Immunodeficiency Virus (HIV). The proportion of the co-infection is also higher in Africa where 30% of the TB cases were infected with HIV [2].

In the same year, about 490,000 of the TB patients were reported to have multidrug-resistant of (MDR-TB); defined as being resistant to isoniazid and rifampicin, with or without resistance to any other first-line drugs [2]. MDR-TB is deadlier, harder to diagnose and much more difficult to treat [3]. More alarmingly, about 10% the MDR-TB patients have been shown to harbor extensively drug-resistant TB (XDR-TB), a very serious form of TB, where the TB bacteria become resistant to the backup or second line anti-TB drugs used to treat MDR-TB cases [4].

TB also remains the ninth top cause of death worldwide and the leading cause of a single infectious agent, ranking above HIV/AIDS [2]. It caused about 1.3 million deaths (excluding HIV co-infected cases) in 2106, and is the leading cause of death in people in the most economically productive age groups, representing a substantial economic burden [5].

In response to the continuing challenges facing the control of TB and M/XDR-TB, the World Health Organization (WHO) and the Stop TB Partnership endorsed a new global TB control strategy (the End TB strategy) in 2014. Targets set in the End TB strategy include a 95% reduction in TB deaths and 90% reduction in TB incidence by 2035, compared with 2015. The strategy also set interim milestones for monitoring the progress including achieving a case detection and treatment success rate of at least 90% in 2025, including in high-risk settings [6]. Despite this aggressive approach, huge TB control challenges remain. Missed diagnoses or delayed diagnoses, and poor access to a high-quality care represent major obstacles to the control program [2,7]. Each year an estimated three 3 million individuals with active TB diseases, i.e. about one-third of all TB cases, do not receive diagnosis and treatment [7,8]. On top of this, the rise of drug resistance is creating a public health crisis [8].

Reaching the End TB targets requires an acceleration in the rate at which TB incidence is falling globally, from 2% per year in 2016 to 10% per year by 2025, and a reduction in the TB mortality rate from 16% in 2016 to 6% in 2025 [2] (Figure 1.1). In its Global TB

Reports, WHO highlighted detection of missed cases as a priority action to reach the milestones [7]. WHO's current directly observed treatment short course (DOTS) strategy, which relies primarily on passive case detection, has been proven to be an insufficient stand-alone TB control strategy [9]. Active case finding or systematic screening (usually using chest X-ray in addition to the symptom inquiry), has therefore been recommended to be used as a complement to the existing DOTS approach [10,11]. WHO recommends systematic screening of TB close contacts, those living with HIV, and suggests active screening of people in high-risk settings such as prisons [11]. While such guidelines have generally been under practice in the general populations, high-risk settings such as prisons remain overlooked [12]. Particularly, in prisons of low-income countries, resource scarcity limits the implementation of the available screening approaches and the lack of accurate and reliable data hinders the development of potentially sustainable intervention models [13].

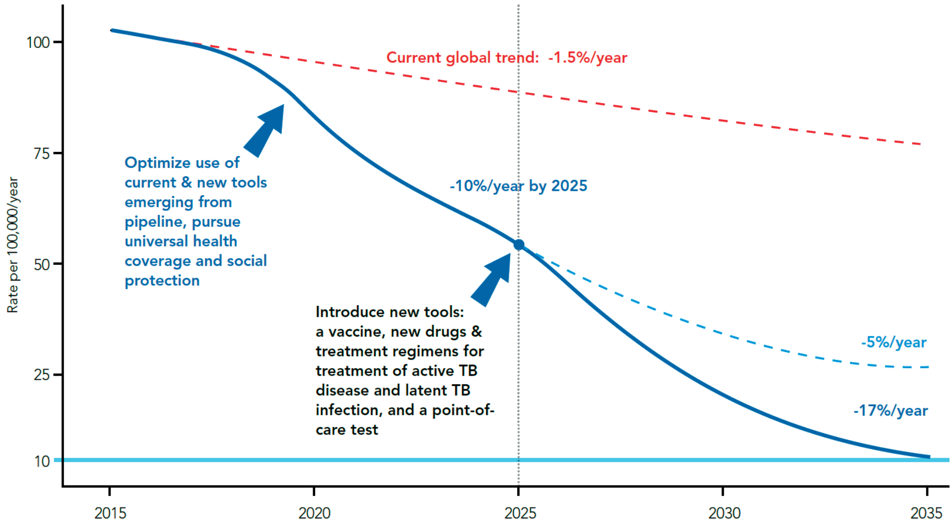

Figure 1.1: Desired decline in global TB incidence rates to reach the 2035 targets. (Available from: www.who.int/tb/End_TB_brochure.pdf)

1.2 National burden of tuberculosis and challenges to control

1.2.1 Ethiopia- country profile

Geography

Ethiopia, identified as African's oldest independent country and one of the cradles of humankind, is located in the Horn of Africa. It is bordered by Eritrea to the north and north-east, Djibouti and Somalia to the east, Sudan and South Sudan to the west, and Kenya to the south (Figure 1.2). Ethiopia is the tenth largest country in Africa covering an area of

1,104,300 square kilometers. Ethiopia's landscape is so diverse ranging from the highest peak approximately 4,550 meters above sea level (Ras Dejen/Ras Dashen in Gondar) to the lowest at about 130 meters below sea level (at Dallol in the Afar depression) [14,15].

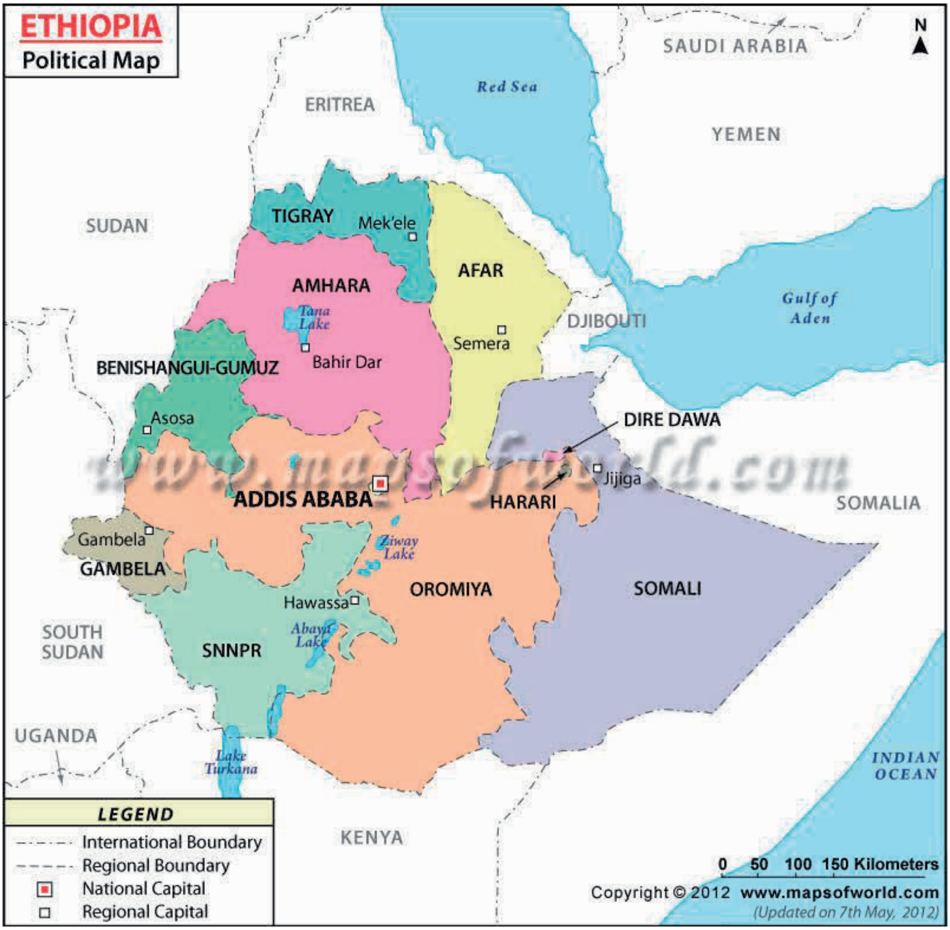

Figure 1.2: Map of Ethiopia, its regional states and city administrations. (Source: https://www.bizbilla.com/country-maps/ethiopia.html).

Demographic situations and governmental structure

Ethiopia is the second most populous country in Africa. There are more than 80 ethnic groups in the country with more than 80 different spoken languages. Amharic is the federal working language. According to a projection from 2007 census, the total population was estimated to be 104 million in 2017 with an annual population growth rate of 2.6%. Nearly half (45%) of the population is under the age of 15 years, and only 3% are above the age of 65. The male to female ratio is almost equal (50.5% male and 49.5% female). The life expectancy is 63.2 years for males and 66.9 years for females. The majority of the population (76%) lives in the highland areas where farming is the major occupation to lead life. About 8% of the population lives in lowland areas and are mostly pastoralist [14-16].

The current government of Ethiopia is a federal system. It comprises nine regional states (Tigray, Afar, Amhara, Oromia, Somali, Benishagul Gumuz, Southern Nations Nationalities and Peoples Region (SNNPR), Gambella, and Harari) and two city Administrative Councils (Addis Ababa and Dire Dawa) (Figure 1.2). The capital city is Addis Ababa. The regional states and administrative councils are further subdivided into about 817 basic decentralized administrative units called woredas. The woredas are further divided into many kebeles, the smallest local administrative units in the governance hierarchy [14,15].

Similarly, the prison system in Ethiopia is organized at federal and regional level. The regional prisons are further divided as zonal, district, and local jails. Zonal and federal level prisons are the largest prisons. In 2015, there were 6 federal prisons and 120 regional prisons. Oromia regional state had the largest number of prisons (37 prisons; 17 zonal and 20 district prison), followed by Amhara regional state (29 prisons; 11 zonal and 18 district prisons). Tigray regional state had seven zonal and three district prisons [17]. The current studies were conducted in selected prison of the Tigray and Amhara regional states (Figure 1.2). The first three studies were conducted only in the prisons of Tigray while the fourth study (the randomized controlled trial) was done in prisons of both regions.

Health system

Despite huge progress made on health sector development in Ethiopia, the health status of the population remains relatively poor. Preventable communicable (infectious) diseases remain the major health problems. Recently, there is also a growing burden of non-communicable diseases (NCD) putting Ethiopia under a double burden of the scenario. Analysis from the 2015 Global Burden of Disease showed that the mortality rates attributed to communicable, maternal, neonatal, and nutritional (CMNN) disorders and NCDs in Ethiopia were 337 and 286.9 per 100,000 populations, respectively [18,19].

Health policy in Ethiopia focuses on the promotion, prevention, and control of diseases and injuries [20]. The health system is organized by regional governments and district health offices below them; comprising four levels including a primary health care unit, district hospital, zonal hospital and specialized hospital. A primary health care unit comprises one health center and five satellite health posts, which is the lowest tier of Ethiopia's health care system. Since 2004, the government of Ethiopia launched a community-based initiative to provide essential health services to the community under a health extension program (HEP). Health extension workers (HEWs) have been trained and deployed to health posts with the aim of preventing major communicable diseases and promote health in the community. Each Kebele has its own health post with two HEWs who provide a package of at least 16 basic services to rural populations, including TB prevention and treatment follow-up [21,22]. The National Tuberculosis and Leprosy Control program, which is under Ethiopia's Federal Ministry of Health (FMOH), functions at national and regional levels with the goal of using HEWs to ensure equitable provision of TB control service.

1.2.2 Burden of tuberculosis and challenges to control

Ethiopia is one of the 30 world's high TB, TB/HIV, and MDR-TB burden countries. According to the recent WHO estimate, Ethiopia had 182,000 incident TB cases (177/100,000 populations) in 2016. More than 8% of the TB cases were HIV co-infected in the same year. Moreover, 1.7% of the new and 14% of previously treated cases were estimated to harbor MDR/rifampicin-resistant TB (RR TB) [2].

However, there has been encouraging progress on TB control in Ethiopia. Ethiopia started the DOTS strategy in 1992 and implemented a new "Stop TB strategy" in 2004; to fight the emergence of drug-restraint TB strains and the rise in TB/HIV co-infection rate [23]. By careful implementation of this global strategy, Ethiopia was able to achieve Millennium Development Goals (MDGs) of halving TB incidence, prevalence, and mortality by 2015 [8]. The country has drastically reduced the TB incidence rate from 419/100,000 population in 1995 to 177/100,000 population in 2016 [2,24]. Ethiopia is also one of the few countries in high-burden regions where the decline in the TB incidence has exceeded 4% in 2106, which is double compared to the global average of the 2% decline [2].

Despite these achievements, however, TB still causes more than 26,000 fatalities annually in Ethiopia, which is equivalent to more than 70 deaths every day [2]. In addition, as the majority of these TB cases occur among the most productive age groups, TB imposes a significant economic burden, impeding Ethiopia's progress toward middle-income status [25].

Notably, the low case detection rate (estimated as notifications of new and relapse cases divided by the estimated incidence per year) is the major obstacle for the TB control program in Ethiopia. In 2014, the case detection rate was estimated to be 62%, which is below the WHO target and Ethiopia was among the top ten countries that accounted for 74% (2.4% million) of missed TB cases [7]. This 38% case-detection gap means that an estimated 95,000 Ethiopians who develop TB each year are not diagnosed and treated, becoming a source of continual transmission to their families and communities until they die or possibly get spontaneous remission [2]. Shortage of health workers, low service coverage, low health-seeking behavior, and lack of efficient TB diagnostics are some of the factors for the low case detection rate in the country [26].

The involvement of HEWs in the TB control program in the rural communities in Ethiopia has significantly improved the WHO DOTS approach [27]. However, only 30% of the Woredas have such a service, and high-risk settings such as prisons have not been considered [28]. Further, the majority of the health facilities (both public and private) have limited capacity to diagnose TB. According to a recent report, 69% of the health facilities had at least some TB diagnostic services, but in 59% of these, the only available TB diagnostic is sputum microscopy. Only 6% and 2% of the health facilities (above health post level) have chest-X ray equipment and GeneXpert rapid TB diagnostics kits, respectively [29,30]. This implies that much more work should still be done in improving the TB service care in the country.

1.3 The global prison population and burden of tuberculosis

The global prison population

The world's prison population keeps growing over time. It has increased by almost 20% since 2000. It is estimated that more than 10 million people are detained around the world. Around half of these are in three countries: the United States, China, and Russia. However, the imprisonment rates vary considerably in different regions of the world. For example, the median prison population for southern Asian countries is 74 per 100,000 persons whereas it is 188 per 100,000 persons for western African countries [31].

Ethiopia has the second highest number of prisoners in Africa. According to the International Center for Prison Studies (ICPS), there were about 112,361 (136/100,000 persons) prisoners in 2010. Despite this, the healthcare service of prisons is weak and remains overlooked by the national health sector. It has lacked the resources and capacity needed to implement rigorous screening, diagnosis and treatment measures for TB and other communicable diseases among prisoners [31,32].

Burden of tuberculosis in prisons

Prisons worldwide are known for having high rates of communicable diseases such as TB [12]. TB disproportionately affects vulnerable populations such as prisoners. According to a review of studies from both high and low-income countries, TB incidence rates among prisoners remain much higher (from 5 to up to 50 times) than the average levels reported in the corresponding general populations [33,34]. The situation is worsened by the emergence and spread of drug-resistant TB, particularly MDR and XDR TB [35]. The high levels of TB in prisons can partly be because prisoners often come from populations that are considered high risk for developing TB (alcohol and drug users, homeless people, mentally ill individuals, and people returning to prison and undocumented immigrants from areas with a high incidence of TB) [36,37].

However, prisons themselves provide ideal conditions for TB transmission. Prisons globally share generic problems of overcrowding, poor ventilation, and inadequate healthcare facilities, which exacerbate TB spreading [38,39]. The bacterium causing TB is distributed in tiny liquid droplets that are produced when someone with active TB coughs, sneezes, spits, or speaks, enabling one person to infect many others. This makes

TB and MDR TB a particular concern in congregated settings such as prisons [34]. Numerous other factors such as poor nutrition, drug addiction, and the presence of other diseases, particularly HIV infection, also increase the risk of acquiring active TB disease and further transmission of the disease in prisons [36,40].

While prisons in high-income countries account for a substantial proportion of the TB burden, TB in prisons poses a major problem in low- and middle-income countries (LMICs), especially in Sub-Saharan Africa and in the countries of the former Soviet Union. Approximately 4-6% of TB cases reported in the United States occur among the incarcerated people [41]. In Europe, the average TB rates have been shown to be 17 times higher than in the general population – ranging from 11 times higher in Western Europe to 81 times higher in Eastern Europe [42]. Moreover, drug-resistant TB is increasingly being reported from prisons in Eastern European countries. A recent systematic review of the published studies from prisons in this region showed that the prevalence of MDR-TB was high ranging from 12.0% -71.2% and the average MDR prevalence was 16 times higher than the worldwide prevalence estimated by the WHO in 2014 [43].

In the Sub-Saharan African region, the high burden of HIV infection and poverty make the situation much worse. Recent studies from prisons in this region showed TB prevalence rates ranging from 0.89-5.8% with a high TB/HIV co-infection rate [44-46]. About 44% of prisoners with TB in a South African prison and 37% in Zambian prisons were co-infected with HIV [45,47]. Co-infection rates ranging from 4.4% to 34.6% have also been reported from Ethiopian prisons [48,49]. More alarmingly, MDR-TB as high as 9.5% has also been reported from some prisons in this region including from Ethiopian prisons [50,51]. This high rate of TB and HIV co-infection and the alarmingly increasing MDR-TB burden made TB control efforts very complicated in these resource-limited prisons and might disrupt the recent progress made in TB and HIV control [52]. It is much more difficult to diagnose TB in patients with HIV and to diagnose and treat MDR-TB [53]. This warrants the urgency to strengthen the health care system in such prisons and generate reliable data in order to implement sustainable intervention models.

1.4 Prison-community interactions

Prisons are not mere static settings. They represent dynamic communities where at-risk groups congregate in a setting that exacerbates disease and its transmission [36]. Prison health is a critical part of public health, as health problems within and outside prisons are interrelated. Particularly, this is pronounced for the transmittable diseases such as TB and HIV. TB propagates in prisons because of several reasons: prisons receive TB; prisons concentrate TB; prisons disseminate TB; prisons make TB worse, and prisons export TB [12,36].

Prisoners often come from socio-economically disadvantaged communities where the burden of TB and HIV are already high and access to medical care is limited [54]. However, entry-screening activities are not routinely performed in many countries (often in those with a high TB burden) and such newly incarcerated prisoners are often put with other prisoners all day long in overcrowded and poorly ventilated rooms, putting all the occupants at risk of TB infection [13]. The new prisoners also often create favorable conditions for drug resistance by entering with partially treated TB or by interrupting treatment upon arrival [12].

The crowded and poorly ventilated conditions of prisons facilitate the spread of TB. In addition, in resource-limited countries, the prison health services are very poor and many prisoners with active TB remain without being diagnosed [13]. As the movement of prisoners within the same prison or between prisons is common, prisoners with such undetected TB can disseminate the disease to other parts of the prison or even to different prisons [12].

TB and the resistant forms of TB can also spill out into the community through staff, visitors and inadequately treated former inmates and create a public health hazard; TB does not respect prison walls [36]. In a systematic review, the median estimated fraction of TB in the general population attributable to the exposure in prisons for TB was 8.5% in high-income countries and 6.3% in low-income countries suggesting a significant risk to the general population [33]. In addition, a recent study from Brazil indicated that ex-prisoners had 23% more cases of TB than the general population and, in the four-year period, 25% of the TB cases occurred among prisoners who represented only <1% of the population [55]. Figure 1.3 shows the prisons-community interactions with respect to TB and HIV.

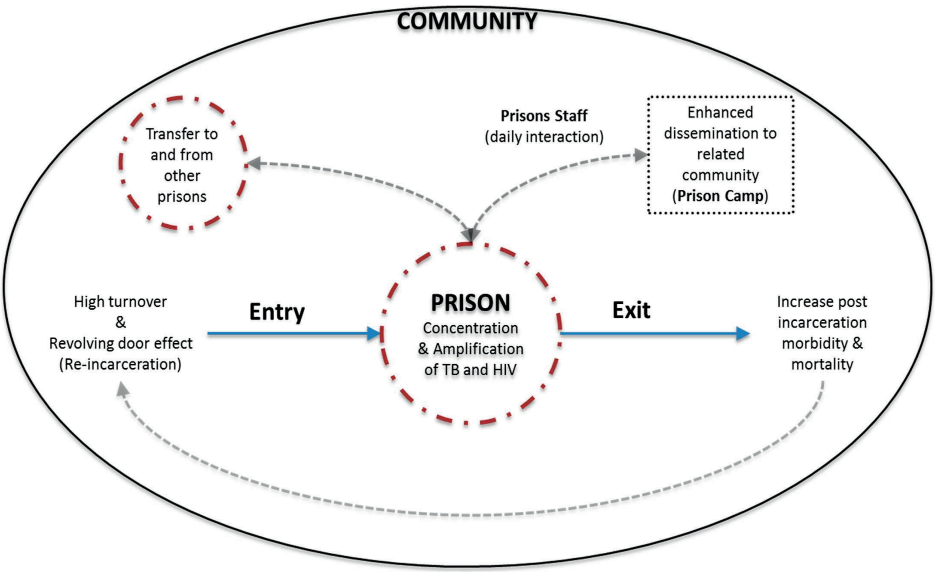

Figure 1.3. Prison-community interactions.

TB disseminates to the general community through released prisoners and prison staffs. The revolving door effect of re-incarceration further concentrates TB within prisons or jails, increasing transmission within the prisons and to the outside community. Adapted from Henostroza G et.al, Plos One, 2013.

1.5. Problem statement

In summary, prisoners are at a disproportionally high risk of developing TB and drug-resistant TB and the disease remains as one of the top killers of prisoners, especially in resource-limited countries such as in Sub-Saharan Africa [13]. The case-fatality rate among TB cases can reach 24%, but in some prisons, TB accounts for 50% of the overall prison deaths [56]. Moreover, prisons represent a reservoir for TB, pumping the disease into the civilian community, which creates serious consequences, in particular, in countries with poor TB controls programs [36] . Hence, failure to control TB in prisons has a potential to disrupt the control programs in the general population. Cognizant of this problem, WHO has published guidelines for TB control in prisons including early detection and supervised treatment of TB cases, prompt isolation of contagious inmates, swift performance of contact investigations, and appropriate use of infection control methods [57]. However, the lack of resources or organized health systems limits the implementation of such guidelines in prisons of the low-income countries including in Ethiopia [13]. On the other hand, accurate data required to develop optimized and cost-effective interventions, to tackle the ominous problem of TB in prisons of such countries are scanty and unreliable. Therefore, there is an urgent need to accurately define the burden of TB, factors driving TB in prisons and design best-fitted intervention models for such settings.

1.6 Aims, scope, and outline of this thesis

Aim

The aim of this thesis is to determine the burden and associated risk factors for undiagnosed TB among prisoners, to define the treatment success rate of prisoners with TB and risk factors for unsuccessful outcome, to assess the level of knowledge, attitudes, and practices (KAP) of prisoners about TB, and to assess the impact of trained prisoners (inmate peer educators) on TB case detection, treatment success rate, and pre-treatment symptom duration in prisons.

The specific research questions, which this thesis aims to answer, are:

1. What is the prevalence and what are the risk factors for undiagnosed TB among prisoners in the Tigray region of Ethiopia?
2. What is treatment success rate of the prisoners with TB in northern Ethiopia, and what are the associated risk factors for unsuccessful outcome?
3. How is the level of knowledge, attitudes, and practices (KAP) of prisoners about TB in northern Ethiopia?
4. Does empowering and involving inmate peer educators in the TB control improves TB case detection, shortens pre-treatment symptom duration, and increases treatment success in a resource-limited prison setting?

Scope

This thesis is focused on TB case finding and developing feasible intervention models for TB control in Ethiopian prisons. Cross-sectional design and retrospective analysis were used to generate evidence on the burden of undiagnosed TB and level of KAP of prisoners, and treatment success rate, respectively. We employed an experimental design (cluster-randomized trial) to assess the impact of trained prisoners on the TB control program in the prisons.

Outline

The findings and implications the research questions included in thesis are organized in six chapters. Chapter 2 describes the burden of undiagnosed TB and associated risk factors for such TB cases among prisoners. Prisoners from nine prisons in Tigray were actively screened for symptoms of TB and TB was diagnosed using smear microcopy and culture. In Chapter 3, we report on the treatment success rate of prisoners with TB and risk factors for unsuccessful outcome. Chaper 4 describes the level of knowledge, attitudes, and practices (KAP) of prisoners about TB in northern Ethiopia. The cluster-randomized trial, which was designed based on the gaps identified in the above-mentioned studies, is presented in Chapter 5. In this trial, we assessed the impact of trained inmate peer educators on improving TB case detection, treatment success rate, and reducing pre-treatment symptom duration in northern Ethiopian prisons. Lastly, Chapter 6, outlines the key findings and methodological considerations of the studies presented in this thesis and illustrates the possible implications for practice and further research.

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Chapter 2

Half of Pulmonary Tuberculosis Cases Were Left Undiagnosed in Prisons of the Tigray Region of Ethiopia: Implications for Tuberculosis Control

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Abstract

Introduction Prison settings have been often identified as important but neglected reservoirs for TB. This study was designed to determine the prevalence of undiagnosed pulmonary TB and assess the potential risk factors for such TB cases in prisons of the Tigray region.

Methods A cross-sectional study was conducted between August 2013 and February 2014 in nine prisons. A standardized symptom-based questionnaire was initially used to identify presumptive TB cases. From each, three consecutive sputum samples were collected for acid-fast bacilli (AFB) microscopy and culture. Blood samples were collected from consented participants for HIV testing.

Results Out of 809 presumptive TB cases with culture result, 4.0% (95% CI: 2.65-5.35) were confirmed to have undiagnosed TB. The overall estimated point prevalence of undiagnosed TB was found to be 505/100,000 prisoners (95% CI: 360-640). Together with the 27 patients who were already on treatment, the overall estimated point prevalence of TB would be 793/100,000 prisoners (95% CI: 610-970), about four times higher than in the general population. The ratio of active to passive case detection was 1.18:1. The prevalence of HIV was 4.4% (36/809) among presumptive TB cases and 6.3% (2/32) among undiagnosed TB cases. In a multivariate logistic regression analysis, chewing Khat (adjusted OR = 2.81; 95% CI: 1.02-7.75) and having had a close contact with a TB patient (adjusted OR = 2.18; 95% CI: 1.05-4.51) were found to be predictors of undiagnosed TB among presumptive TB cases.

Conclusions This study revealed that at least half of symptomatic pulmonary TB cases in Northern Ethiopian prisons remain undiagnosed and hence untreated. The prevalence of undiagnosed TB in the study prisons was more than two folds higher than in the general population of Tigray. This may indicate the need for more investment and commitment to improving TB case detection in the study prisons.

Introduction

Finding and successfully treating all tuberculosis (TB) patients is the cornerstone of the Global Strategy to Stop TB [1]. However, a World Health Organization(WHO) report from 2013 indicated that a key obstacle to achieving this goal has been that many people with TB are currently being 'missed' by health systems [2]. It is anticipated that the majority of these cases could be among the poorest people of the world [2]. Exploring undiagnosed TB was therefore greatly emphasized by WHO and mentioned as a priority area of research [2].

Prisoners are at a disproportionately high risk of TB and HIV infection [3]. Many people in prisons could have undiagnosed TB, especially in the Sub-Saharan African prisons, where the prison cells are extremely overcrowded, health services are very poor, and HIV infection and malnutrition are very prevalent [4,5]. Previous studies in the Sub-Saharan African prisons reported TB prevalence rates ranging from 3.5%-5.8% [6-10] with a high TB/HIV co-infection rate. About 44% of prisoners with TB in a South African prison [9] and 37% in Zambian prisons [10] were co-infected with HIV.

In Ethiopia, prisoners are incarcerated in an overcrowded and poorly ventilated environment [11]. The prison health services are poorly organized, lacking skilled manpower and laboratory facilities for TB diagnosis [11]. There is no protocol for screening prisoners on admission, during incarceration or on discharge. TB diagnosis relies merely on a referral of prisoners to health facilities outside prisons which usually imposes a serious inconvenience to patients [11]. As a consequence, a number of prisoners with TB in Ethiopian prisons could remain undiagnosed which is a serious risk not only for other prisoners but, through visitors and the prison personnel, also has implications for the general population [12]. Estimating the magnitude of undiagnosed TB and identifying factors contributing for acquiring TB can help assessing the level TB control program in a given setting and is crucial in designing strategies that will improve the TB control programs. Despite this, only limited work has been done on TB or TB/HIV in Ethiopian prisons. Previous studies from Gondar [13] and Eastern Ethiopian prisons [14] reported a seven and nine-fold higher proportion of TB than in the general population, respectively. However, these studies were limited in scope in that the former was focused only on smear-positive cases while the latter didn't include HIV investigation. Besides, in Ethiopia, the socioeconomic, lifestyle and environmental conditions differ across regions [15] and could affect the distribution of TB diseases. The burden of TB in prison of the Tigray region is not yet defined. Therefore, this study aimed at determining the prevalence of undiagnosed pulmonary TB (henceforth called undiagnosed TB) and assessing the potential risk factors for such TB cases in nine prisons of the Tigray region.

Methods and Materials

Study setting

This study was conducted in prisons of the Tigray Regional State, northern Ethiopia. Ethiopia is one of the countries with a high TB/HIV burden in the Sub-Saharan Africa [2]. Ethiopia had an officially registered prison population of 112,361 (136/100,000 persons) in 2010 [16], which is higher than the imprisonment rates observed in some Sub-Saharan African countries such as in Kenya (121/100,000 persons), and Malawi (76/100,000 persons). But, this is lower than the imprisonment rates in South Africa (294/100,000 persons), and Rwanda (492/100,000 persons) [16]. There were a total of nine prisons in the Tigray region located in the cities: Adigrat, Adwa, Alamata, Axum, Humera, Maychew, Mekelle, Shire and Wukro. All the nine prisons were included in the study. The study was focused only in prisons of the Tigray region of Ethiopia merely due to funding limitations.

Study design and population

This was a cross-sectional study conducted in nine prisons of the Tigray Regional State between August 2013 and February 2014. Prisoners were our study populations; prison guards were not included due to resource limitations. Inclusion criteria for initial screening were: providing written informed consent, being an age of ≥ 18 years and not being treated for TB at the time of the screening. Participants providing written consent for HIV testing and having had clinical symptoms of pulmonary TB (cough of ≥ 2 weeks and sputum production with at least one of the other symptoms such as night sweating for at least 2 weeks, fever for at least two weeks, chest pain for at least 2 weeks and /or unintentional weight loss) provided sputum samples for subsequent bacteriological testing.

Sampling procedures and specimen collection

At the time of the study, there were about 9326 prisoners held in nine prisons of which 27 were already on anti-TB treatment. All prisoners who were not taking anti-TB treatment (n = 9299) were initially screened for a cough of any duration by prison nurses through a cell to cell visit in each prison. Then, senior nurses, recruited from TB clinics of nearby hospitals, performed further screening using a symptom-based questionnaire adapted from the international guideline of TB screening protocol in prisons [17]. A presumptive TB case was defined as a participant with symptoms of TB including having a cough of ≥ 2 weeks and able to produce sputum with at least one of the other symptoms such as night sweating for at least 2 weeks, fever for at least two weeks, chest pain for at least 2 weeks and /or unintentional weight loss. Prisoners with a cough of < 2 weeks, and those with ≥ 2 weeks but unable to produce sputum were not considered as presumptive TB cases and hence were excluded. Accordingly, about 1231 presumptive TB cases were identified. However, the number of presumptive TB cases included for subsequent bacteriological testing was 844 (68%). A proportional stratified sampling technique was employed to assign the required number of samples from each prison according to their total number of prisoners. The number of participants included ranged from 49 in Adawa to 231 in Mekelle prison and they were enrolled following a simple random sampling technique. The remaining 387 presumptive TB cases were not included for bacteriological testing due to financial constraints to undertake culture. However, the final estimation was calculated by considering these untested presumptive TB cases by extrapolation in which the extrapolation was done by assuming a same prevalence of TB among 387 untested presumptive TB cases as the tested ones.

Data were collected on the socio-demographic characteristics and health status of prisoners including age, sex, educational status, cigarette smoking and Khat chewing habit, duration of imprisonment, time of symptom development, and history of sharing a cell with previously diagnosed TB patients (close contact history) using a structured questionnaire. A close contact was defined in this study as a person with prolonged frequent contact exposure (at least a total of 8 hours of direct exposure during the period of infectiousness preceding the diagnosis of the index case) [18]. Information on the referral system was also collected by interviewing presumptive TB cases that had a history of reporting TB-like complaints to the prison staff for a referral. A checklist was used to collected data on the conditions of prisons. To minimize recall bias for some questions such as time of symptom development, we used a carefully constructed questionnaire with specific details and the participants were given enough time before answering the questions. The body weight and height was also measured. Body mass index (BMI) was calculated for each participant and their nutritional status was categorized according to the WHO standards [19]. Then, three consecutive early morning sputum samples were collected from each participant and samples were stored at -20 °C for a maximum of 2-3 weeks until transported in an ice box to the Armauer Hansen Research Institute (AHRI) in Addis Ababa for culturing. We collected three early morning sputum samples instead of the routine spot-morning-spot algorithm in order to maximize the detection of undiagnosed TB cases because of that early morning sample has been shown to have a high incremental yield than spot samples [20].

Laboratory methods and diagnostic criteria

Direct microscopic examination of the sputum samples for AFB and culturing was performed at AHRI using solid media. Prior to culturing, sputum samples were decontaminated by the Petroff's method following the standard operational procedures. In brief, an equal volume of sputum sample was mixed with an equal volume of 4% NaOH (Sodium hydroxide) and concentrated at 3000 rpm for 15 minutes. The sediment was neutralized with 2N HCL (Hydrochoric acid), in the presence of phosphate buffer, using phenol red as an indicator to make the inoculums for culture. Then, 3 Lowenstein-Jensen slants, two containing 0.75% glycerol and one containing 0.6% pyruvate were inoculated per each sputum sample. Culture tubes were incubated at 37°C and growth was checked weekly for up to 8 weeks. A bacteriologically confirmed TB case was defined as a presumptive TB case with two smear-positive sputum samples by the direct microscopy and/or positive culture for *M.tuberculosis*. Undiagnosed TB was defined in this study as a bacteriologically confirmed TB in a person not being treated at enrollment. Confirmed TB patients were referred to a nearby health facility and were treated as per the national guidelines.

Prior to HIV testing, all consenting prisoners were offered a pre-test HIV counselling by the screening nurses. Testing was conducted using the rapid HIV test kits according to the current National algorithm recommended by the Federal Ministry of Health of Ethiopia. Samples were tested first with HIV (1+2) Antibody Colloidal Gold (KHB). Positive samples were confirmed with Stat-Pak while discordant results were resolved by HIV-1/2 Unigold Recombinant assay. Post-test HIV counseling was also done and the result was given only for those wanting to know their HIV status with linkage to health facilities for appropriate care.

Data analysis

Data were entered using Epi Data entry version 3.1 software and analyzed using SPSS version 21. Our outcome variable of interest was comparing prisoners with undiagnosed TB with those without TB in the subset of presumptive TB cases. The analysis of risk factors was limited to the undiagnosed TB cases; all the 27 TB patients that were already on treatment were not included. Bivariate and multivariate logistic regression analysis was performed to examine the association of independent variables with acquiring undiagnosed TB. Covariates with p-values of ≤ 0.25 in a bivariate analysis and collinearity matrix index of ≤ 0.7 were considered for inclusion in the multivariate model. However, due to the small number of outcomes ($n = 32$), only those variables strongly related with bacteriologically confirmed TB ($P < 0.1$) in the bivariate analysis were included in the final model. P values of ≤ 0.05 were considered as statistically significant.

Ethical issues

The study was approved by ethical review committees of the College of Health Sciences, Mekelle University, and AHRI/ALERT (Armauer Hansen Research Institute/All African Leprosy) ethics review committees. All participants were enrolled after they provided us a written informed consent including for HIV testing. Presumptive TB cases that were not included in the study due to financial constraints were referred for regular health care to nearby hospitals. For all illiterate participants, data collectors informed each respondent and confirmed the willingness of the participants by signing on the informed consent sheet. The consent procedure for these illiterate participants was also approved by both ethics review committees. A brief education was provided for those prisoners that refused to know their HIV status so as to improve their awareness.

Results

Conditions of prisons

During our study, we observed that TB control was inadequate in the study prisons. All the nine prisons had a clinic, but only two clinics (of Mekelle and Adigart prisons) have a building with more than one room. All clinics were staffed by nurses, but there were no physicians. None of the clinics had services for sputum smear microscopy and there was no protocol for entry, periodic or exist screening of prisoners for TB. TB diagnosis was performed following the passive case finding strategy which relied on a referral of prisoners to health facilities outside prisons. However, we also observed the lack of an adequate referral system, meaning that prisoners were only referred after repeated complaints of TB symptoms, or when they developed severe signs and symptoms. Materially, the inmates were poorly housed; inmates slept on mats or on a very poor quality mattress on the floor. The number of prisoners per room varied for each prison, ranging from 18-172 with an average of 64. Rooms were generally overcrowded and had poor ventilation systems. Most rooms had a narrow sized window while some others had no windows at all.

Prevalence of undiagnosed pulmonary TB and HIV infection

Fig. 1 summarizes the study recruitment flow and undiagnosed TB outcomes. Of the 844 presumptive TB cases enrolled, complete data with interpretable culture results were available for 809 (96%) cases in which 4.0% ([32/809]; 95% CI: 2.65-5.35) were confirmed to have undiagnosed TB. Assuming that the prevalence among the 387 untested prisoners with a cough was also 4%, the estimated point prevalence of undiagnosed TB in the total prison population would be 32+15/9299 = 0.505 % or 505/100,000 prisoners (95% CI: 360-640). Together with the 27 patients who were already on treatment, the estimated point prevalence of TB would be 32 +15 +27/9326 = 0.793% or 793/100,000 prisoners (95% CI: 610-970), about four times higher than in the general population. The ratio of newly detected TB cases through active case finding to those detected following passive case detection (to those already on treatment) was about 1.18:1 (32/27) indicating that for every TB case that is found, at least one case is undetected. Of the 32 undiagnosed TB cases, the majority (84.4% [27/32]) were smear-negative /culture positive cases while 5 cases were smear-positive /culture positive. There were no smear-positive /culture negative cases. Twenty-seven were newly infected cases and 5 of the undiagnosed TB cases reported a previous TB treatment. All cases were male prisoners; all 21 female prisoners enrolled were culture negative. The majority (75% [24/32]) of undiagnosed TB cases responded that they had a history of reporting their TB-like symptoms to the prison health personnel for one or more time. The prevalence of HIV was 4.4% (36/809) among presumptive TB cases and 6.3% (2/32) among undiagnosed TB cases. Both of these HIV positive cases with undiagnosed TB were smear-negative.

Characteristics of presumptive TB cases and relation to undiagnosed pulmonary TB

Of 809 participants, the majority (788 [97%]) were men. The mean age of the presumptive TB cases was 33 years (range 18-82 years). The average duration of imprisonment at the time of the screening was 2 and half years (range 1 month-21 years), the majority (63%) of undiagnosed TB cases were imprisoned for more than a year. More than three-forth (82%) of the presumptive TB cases developed a cough after entering the prison and the majority (516 [64%]) had a cough for 4 weeks or longer. The median BMI among the presumptive TB cases was 19.9 kg/m^2 (range 13.7-31.8) and 203 (25%) of them were malnourished (BMI < 18.5 kg/m^2). About 76 (9.4%) of the presumptive TB cases had chewed Khat and 171 (21.2%) smoked cigarettes.

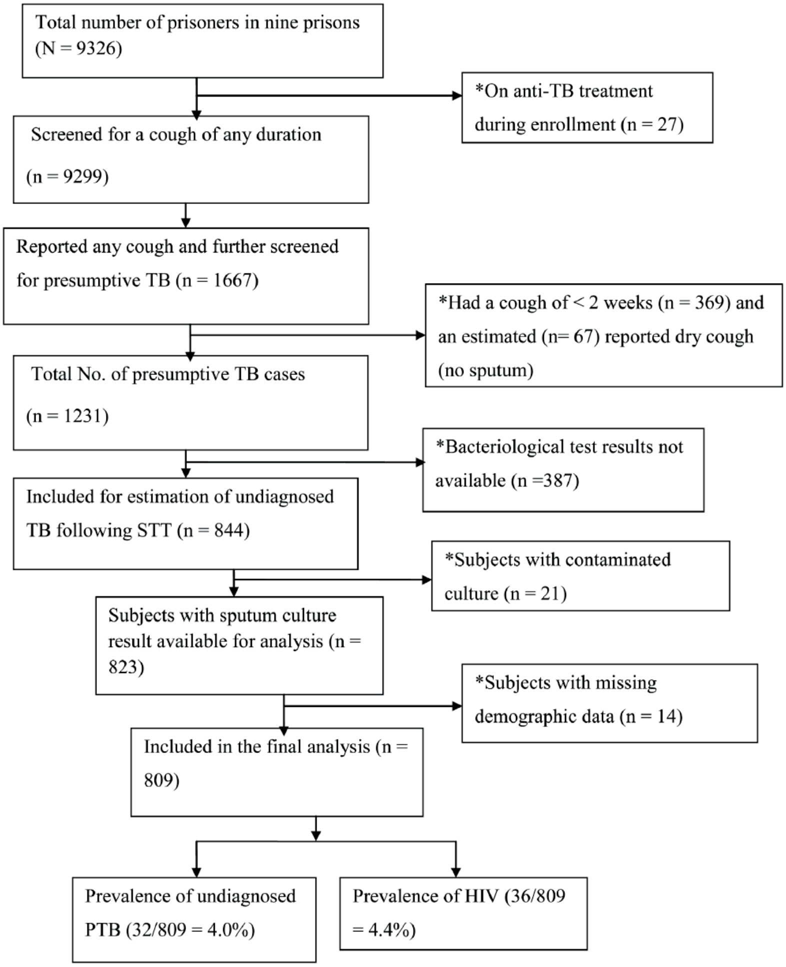

Fig. 1. Flow chart of study inclusion, exclusion and diseases (PTB and HIV) outcomes.

* = Excluded; SST = Stratified sampling technique; PTB = Pulmonary TB; HIV = human immunodeficiency virus

The prevalence of undiagnosed TB in the study population (presumptive TB cases) did not significantly differ across the nine prisons included in this study (Table 1).

Table 1: The distribution of undiagnosed TB among presumptive TB cases by prison sites in northern Ethiopia as analyzed by the binary logistic regression (n = 809).

Prison site	Presumptive TB cases included in the analysis, n (%) (N = 809)	Confirmed undiagnosed TB cases, n (%) (N = 32)	OR (95% CI)	P-value
Axum	59 (7.3)	1 (1.7)	Ref.	
Mychew	66 (8.2)	0 (0)	0.00	0.98
Adwa	44 (5.4)	1 (2.3)	1.3 (0.08-22.18)	0.83
Adigrat	97 (11.9)	3 (3.1)	1.9 (0.18-18.22)	0.59
Shire	131 (16.2)	6 (4.6)	2.9 (0.33-23.65)	0.35
Humera	68 (8.4)	3 (4.4)	2.7 (0.27-26.45)	0.40
Alamata	58 (7.2)	2 (3.4)	2.1 (0.18-23.49)	0.56
Mekelle	231 (28.6)	13 (5.6)	3.5 (0.44-26.99)	0.24
Wukro	55 (6.8)	3 (5.5)	3.3 (0.34-33.17)	0.30

CI = Confidence interval; OR = Odds ratio; Ref. = Reference

The relationships of demographic and clinical risk factors with undiagnosed TB among the presumptive TB cases are presented in Tables 2 and 3, respectively. There was a significant association between chewing Khat and acquiring undiagnosed TB; the risk of acquiring undiagnosed TB among chewers being about 3 times higher than non-chewers (OR = 3.47; 95% CI: (1.51-8.03); p = 0.004). Having a history of close contact with TB patients was also associated with undiagnosed TB (OR = 2.32; 95% CI: 1.13-4.76; p = 0.02). On the other hand, the potential socio-demographic risk factors including cigarette smoking, history of sharing a cell with TB patients, age variation and duration of incarceration were not significantly associated with undiagnosed TB. Similarly, there was no association between undiagnosed TB and the potential clinical risk factors such as duration of a cough, a previous history of reporting TB-like complaints to the prison staff, BMI, and HIV infection status.

Table 2: Bivariate analysis of the socio-demographic and prison related factors for undiagnosed TB outcome among presumptive TB cases in northern Ethiopian prisons (n = 809).

Variable	Presumptive TB cases included in the analysis, n (%)	Confirmed undiagnosed TB cases, n (%)	Presumptive TB cases without undiagnosed TB, n (%)	OR (95% CI)	P-value
Age (years)					
18-44	655 (81.0)	28 (4.3)	627 (95.7)	1.68 (0.58-4.85)	0.34
≥45	154 (19.0)	4 (2.6)	150 (97.4)	Ref.	
Educational status					
No formal education	209 (25.8)	5 (2.4)	204 (97.6)	Ref.	
Have formal education	600 (74.2)	27 (4.5)	573 (95.5)	1.92 (0.73-5.05)	0.18
Cigarette smoking (current)					
No	638 (78.8)	21 (3.3)	617 (96.7)	Ref.	
Yes	171 (21.2)	11 (6.4)	160 (93.6)	2.02 (0.95-4.28)	0.06
Chewing Khat* (current)					
No	733 (90.7)	24 (3.4)	709 (96.6)	Ref.	
Yes	76 (9.)	8 (9.3)	68 (90.7)	3.47 (1.51-8.03)	0.004
Sharing a cell with a TB patient					
No	620 (76.6)	23 (3.7)	597 (96.3)	Ref.	
Yes	189 (23.4)	9 (4.8)	180 (95.2)	1.29 (0.59-2.86)	0.52
TB contact history					
No	600 (74.2)	18 (3.0)	582 (97.0)	Ref.	
Yes	209 (25.8)	14 (6.7)	195 (93.3)	2.32 (1.13-4.76)	0.02
Duration of incarceration					
<12 months	324 (40.0)	12 (3.7)	312 (96.3)	Ref.	
≥12 months	485 (60.0)	20 (4.1)	465 (95.9)	1.12 (0.54-.232)	0.76
No of prisoners per cell					
≤50	261 (32.2)	8 (3.0)	253 (97.0)	Ref.	
>50	548 (67.7)	24 (4.4)	524 (95.6)	1.45 (0.64-3.26)	0.37

TB = tuberculosis; OR = Odds ratio; CI = Confidence interval; * = Catha edulis; Ref. = Reference

Table 3: The association of clinical characteristics of presumptive TB cases with undiagnosed TB outcome in northern Ethiopian prisons by bivariate analysis in the binary logistic regression (n = 809).

Variable	Presumptive TB cases included in the analysis, n (%) N = 809	Confirmed undiagnosed TB cases, n %) N = 32	Presumptive TB cases without undiagnosed TB, n (%) N = 777	OR (95% CI)	P-value
Chest pain					
No	182 (22.5)	4 (2.2)	178 (97.8)	Ref.	
Yes	627 (77.5)	28 (4.5)	599 (95.5)	2.08 (0.72-0.61)	0.17
Night sweating					
No	166 (20.5)	4 (2.4)	162 (97.6)	Ref.	
Yes	643 (79.5)	28 (4.4)	615 (95.6)	1.85 (0.64-5.33)	0.26
Duration of cough					
<4 weeks	293 (36.2)	10 (3.4)	283 (96.6)	Ref.	
≥4 weeks	516 (63.8)	22 (4.3)	494 (95.7)	1.26 (0.58-2.69)	0.55
Time of occurrence of cough					
Before imprisonment	146 (18.1)	7 (4.8)	139 (95.2)	1.29 (0.55-3.03)	0.57
After imprisonment	663 (81.9)	25 (3.8)	638 (97.2)	Ref.	
Previous TB-like symptom report *					
No	282 (34.9)	8 (25.0)	274 (97.2)	Ref.	
Yes	527 (65.1)	24 (75.0)	503 (95.4)	1.63 (0.72-3.69)	0.24
BMI					
<18.5	203 (25.0)	12 (6.0)	191 (94.0)	1.84 (0.88-3.84)	0.11
≥18.5	606 (75.0)	20 (3.3)	586 (96.7)	Ref.	
HIV infection					
No	773 (95.6)	30 (3.9)	743 (96.1)	Ref.	
Yes	36 (4.5)	2 (5.5)	34 (94.5)	1.46 (0.33-6.34)	0.62
Previous history of TB treatment					
No	681 (84.2)	27 (3.9)	654 (96.1)	Ref.	
Yes	128 (18.8)	5 (3.9)	123 (96.1)	1.06 (0.56-3.15)	0.92

*** =** Previous reporting of TB-like symptoms to the prison personnel for one or more time; TB = Tuberculosis; BMI = Body mass index; OR = Odds ratio; CI = Confidence interval; Ref. = Reference

After fitting into the multivariable logistic regression model, chewing Khat (adjusted OR = 2.81; 95% CI: 1.02-7.75; p = 0.04) and having had close contact with a TB patient (adjusted OR =2.18; 95% CI: 1.05-4.51; p = 0.03) remained independently associated with undiagnosed TB (Table 4).

Table 4: Multivariate logistic regression model showing risk factors associated with undiagnosed TB among the presumptive TB cases Northern Ethiopian prisons (n = 809).

Variable	Presumptive TB cases included in the analysis, n (%)	Confirmed undiagnosed TB cases, n %)	Presumptive TB cases without undiagnosed TB, n (%)	AOR (95% CI)	P-value
Cigarette smoking					
No	638 (78.8)	21 (3.3)	617 (96.7)	Ref.	
Yes	171 (21.2)	11 (6.4)	160 (93.6)	1.25 (0.51-3.12)	0.62
Chewing Khat*					
No	733 (90.7)	24 (3.4)	709 (96.6)	Ref.	
Yes	76 (9.3)	8 (9.3)	68 (90.7)	2.81 (1.02-7.75)	0.04
TB contact history					
No	600 (74.2)	18 (3.0)	582 (97.0)	Ref.	
Yes	209 (25.8)	14 (6.7)	195 (93.3)	2.18 (1.05-4.51)	0.03

TB = Tuberculosis; AOR = Adjusted odds ratio; CI= Confidence interval; * = Catha edulis; Ref. = Reference

Discussion

This study revealed that at least half of symptomatic pulmonary TB cases in Northern Ethiopian prisons remain undiagnosed and hence untreated, which is an important public health concern. Out of 809 presumptive TB cases with culture result, 4.0% (95% CI: 2.65-5.35) were confirmed to have a bacteriologically positive undiagnosed TB. The overall estimated point prevalence of undiagnosed TB was found to be 505/100,000 prisoners (95% CI: 360-640). This figure is more than two folds higher than the estimated prevalence of undiagnosed TB in the general population of Tigray (216/100,000 population) [21].

Previous surveys from the Sub-Saharan African prisons reported TB prevalence rates ranging from 3.5%-5.8% [6-8] (1.9% from Eastern Ethiopian prisons) [14]. Although it might be difficult to directly compare our figure with these findings because of differences in study design (some were longitudinal) [9], sampling strategies, and screening methodologies (some used X-ray and symptom-based screening) [9,10], our figure is much lower than these reports. One of the reasons for this difference could be due to the differences in the burden of TB in the general populations as these countries had a higher prevalence of TB than Ethiopia [2,22]. Our finding (0.5%) is also much lower than that observed in a prison of Gondar in the northwest Ethiopia (1.5%) [13], especially if we consider that the latter was limited only to smear-positive cases. This discrepancy could partly be attributed to the methodological difference between the two studies in which the criteria to consider as presumptive TB case was cough of ≥ one week in the Gondar study whereas, in our study the criteria was cough of ≥ 2 weeks with at least other symptoms such night seating for at least 2 weeks and may affect the sensitivity of the screening. Moreover, the Gondar study included both pulmonary and extra-pulmonary TB cases while our study was limited only to pulmonary TB cases.

According to the WHO 2014 report, Ethiopia has already achieved the Millennium Development Goals (MDGs) of halving TB incidence, prevalence, and mortality by 2015 indicating a progress on TB control [22]. Together with the rising rates of MDR-TB [23], however, the presence of undiagnosed TB in Ethiopian prisons could disrupt this progress as TB could spread to the community through visitors, prison staff and discharged prisoners. The national TB control program should, therefore, emphasize Ethiopian prisons.

In this study, the majority (84% [27/32]) of undiagnosed TB cases were smear-negative. This figure is unexpectedly high, but we trust our findings as we assured the quality of the smear microscopy in that up-to-date operational procedures were used and two skilled laboratory technologists examined each slide preparation independently. Moreover, our finding is in keeping with studies that show a higher proportion of TB cases detected through active case finding are smear-negative cases when compared with those identified in the passive case finding strategy [9,24,25] imposing a diagnostic challenge to health care workers. Smear-negative cases are also responsible for a substantial proportion of TB transmission (13% to 41%) [26,27].

This study identified two important risk factors for undiagnosed TB; chewing Khat and having had close contact with a TB patient. However, we should mention that risk factors for undiagnosed TB could also be risk factors for acquiring TB in general (whether bacteriologically confirmed or not) as we compared newly diagnosed bacteriologically confirmed TB with non-TB and not undiagnosed with those already diagnosed. Though having had close contact with a TB patient was associated with undiagnosed TB, sharing a cell with a TB patient was not. This is due to the fact that TB contact history in our study included not only those having had contact while in prison, but also those having had contact history before they entered the prison. In this study, three-fourths of TB cases that chewed Khat developed a cough while in prison. In a previous study in Eastern Ethiopian prisons, chewing Khat was not associated with TB [14]. However, a human rights analysis report indicated that chewing Khat significantly contributed to the rise of TB cases in Somalia [28]. One of the explanations for the association could be that people are more exposed to disease transmission due to the fact that they chew Khat in groups in poorly ventilated rooms for many hours. Given that chewing Khat is becoming a common practice in Ethiopia, it could become a significant risk for TB transmission, particularly in overcrowded settings such as prisons and refugee camps. Hence, providing health education focusing on this problem is important to reduce TB transmission.

The HIV prevalence among undiagnosed TB cases in this study (6.3%) is much lower than a previous report from the prison of Gondar (34.6%) [13] and other studies in the Sub-Saharan African such as 44% in a South African prison and 37% in Zambian prisons [10]. The difference with other Sub-Saharan African prisons could be explained by variations in the burden of HIV in the general populations in that South Africa and Zambia had

8-10 times higher HIV prevalence than Ethiopia [29,30]. The discrepancy with the prison of Gondar might partly be due to differences in the number study sites and sample size in that we included nine prisons while this study was conducted in one prison facility in the city of Gondar which could be in a high burden area. The association between TB and HIV infection is a well-documented phenomenon in the general population [31]. Some studies have also shown this association in the prison population. A study from Cameron prison showed an association between prevalent TB (including that on treatment) but not with undiagnosed TB while studies from Gondar [13] and South African prisons demonstrated an association between undiagnosed TB and HIV infection [9]. In our study, HIV infection was not associated with the presence of undiagnosed TB. The relatively short duration of our study (7 months) might have limited the ability to show an association with HIV infection. Compared to the general population, HIV infection may be a less important risk factor for acquiring TB where the risk among HIV-negative prisoners is also high.

Although the association between time of occurrence of a cough and undiagnosed TB was not statistically significant, the majority (78% [25/32]) of undiagnosed TB cases developed a cough after entering the prison. About 69% (22/32) had coughed for ≥ 4 weeks; some prisoners even have been coughing for more than 2 years. This extended lag time could be due to the weak referral system in the study prisons. We found out that prisoners in our study sites were referred only after repeated complaints of TB symptoms, or when they developed severe signs and symptoms. This would contribute to the ongoing spread of TB within the prison and to the community. However, there was no statistically significant association between duration of imprisonment and undiagnosed TB due to the fact that a substantial proportion of patients in our study (37.5% [12/32]) acquired TB in a shorter period after imprisonment (during the first 11 months of their imprisonment). The overcrowded and poorly ventilated cells, lengthy imprisonment (62.5% of undiagnosed TB cases were imprisoned for a year or more), the increased susceptibility of prisoners (due to poor nutrition and poor sanitation) and the very poor health care system exacerbate the problem in the study prisons. Hence, if we want to see our TB control efforts succeeded, much more attention should be given to introducing and strengthening TB diagnostic services in Ethiopian prisons. To a minimum, the study prisons will need to introduce sputum microscopy service, undertake entry screening, at least, using TB symptom questionnaire, promote a symptom-based screening of prisoners, strengthen the referral system for all prisoners with TB symptoms and ensure segregation and treatment of TB patients.

However, studies have shown that a considerable proportion of TB patients without symptoms were diagnosed with pulmonary TB indicating the insufficiency of symptom-based screening to capture undiagnosed TB cases [32,33]. For effective TB control in prisons, international guidelines recommend X-ray screening in addition to standardized symptom screening for all prisoners entering a high TB risk prisons [17]. A systematic review also indicated that the application of X-ray and symptom questionnaire screening yields better detection of TB cases and suggests the need to incorporate this algorithm in prisons of low/middle-income countries (LMIC) [34]. However, the feasibility and cost-effectiveness of X-ray screening (with or without symptoms) is still questionable in resource-limited prisons settings. Given the high sensitivity of X-ray screening as compared to symptom-based screening alone [35], the government and/ or non-governmental organizations (NGOs) will need to invest in helping evaluate the feasibility and cost-effectiveness of this algorithm and introduce it as a complementary screening tool in addition to the symptom-based inquiry.

New point-of-care TB tests could also benefit Ethiopian prisons. In this regard, the GeneXpert MTB/RIF has proven to be feasible, accurate and effective, giving a sensitivity 97% and specificity 99.2% in an analysis conducted in the general population of five distinct LMIC sites [36]. However, the feasibility and cost-effectiveness of this technology as a routine point-of-care diagnostic test in prisons of resource-limited settings (low-income countries) is not well established and needs a full investigation.

Strengths and Limitations

One may argue that taking a random sample from the 9299 prisoners (the total number of prisoners minus those already on TB treatment), would be a better strategy to quantify the prevalence of undiagnosed TB. However, we would be missing those presumptive TB cases that should immediately be detected and treated. We tried to undertake a mass screening strategy considering the importance of not missing cases, and the high prevalence of TB in this population. But, as we found more presumptive TB cases than expected, we faced financial constraints and hence culture was done for about 68% presumptive TB cases. The remaining presumptive TB cases were also not left as they were; they were immediately referred to nearby health facilities for diagnosis and immediate treatment. The fact that we had extrapolated positive culture results for the presumptive TB cases that weren't able to obtain cultures was a limitation of this study. However, as we used a representative sample, we trust that our final estimate is reliable. Moreover, we didn't include chest X-ray examination; instead, we relied on symptomatic screening and hence some prisoners that were unable to produce sputum and those non-symptomatic TB cases which could have been detected by chest X-ray might have been missed. The relatively short study duration and the fact that the duration of a cough had to be at least 2 weeks were also limitations of our study.

Conclusions

This study revealed that more than half of symptomatic pulmonary TB cases in northern Ethiopian prisons remain undiagnosed and hence untreated with a more than two-fold higher prevalence of undiagnosed TB than in the general population of Tigray. Chewing Khat and TB contact history were found to be predictors of undiagnosed TB among presumptive TB cases. The squalid prison conditions such as overcrowding, poor ventilation system and absence of segregation could contribute to the ongoing and enhanced transmission of TB within the prison and to the community. This implies that there is an urgent need for more investment and commitment to improving TB case detection in the study prisons.

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Chapter 3

Tuberculosis Treatment Outcome and Predictors in northern Ethiopian Prisons: a five-year retrospective analysis

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Abstract

Background The prison situations are notorious for causing interruptions of tuberculosis (TB) treatment and occurrence of unfavorable outcomes. In Ethiopian prisons, though TB treatment programs exist, treatment outcome results and factors contributing to unsuccessful outcome are not well documented. In this study, we assessed the treatment outcome of TB cases and identified risk factors for unsuccessful outcome in northern Ethiopian prisons.

Methods A retrospective record review was conducted for all prisoners diagnosed with TB between September 2011 and August 2015. Outcome variables were defined following WHO guidelines.

Results Out of the 496 patients, 11.5% were cured, 68% completed treatment, 2.5% were lost to follow-up, 1.6% were with a treatment failure, 1.4% died, and 15% were transferred out. All transferred out or released prisoners were not appropriately linked to health facilities and might have lost to treatment follow-up. The overall treatment success rate (TSR) of the five years was 94% among the patients who were not transferred out. The odds of unsuccessful outcome were 4.68 times greater among re-treatment cases compared to the newly treated cases. The year of treatment was also associated with variations in TSR; those treated during the earlier year were more likely to have unsuccessful outcome. Sputum non-conversion at the second-month check-up was strongly associated with unsuccessful outcome among the smear-positive cases.

Conclusions The mean TSR of the prisoners in the study prisons was quite satisfactory when gauged against the target level set by the End TB Strategy. However, the lack of appropriate linkage and tracking systems for those prisoners transferred or released before their treatment completion would have a negative implication for the national TB control program as such patients might interrupt their treatment and develop drug-resistant TB. Being in a re-treatment regimen and sputum non-conversion at the second-month check-up were significantly associated with unsuccessful treatment outcome among the all forms of and smear-positive TB cases, respectively.

Background

Globally, the burden of tuberculosis (TB) is higher in vulnerable populations such as prisoners and is reported to be up to 100 times higher than in the general population [1]. In Sub-Saharan African prisons, TB remains as one of the fastest growing epidemics [2,3]. The high prevalence of human immunodeficiency virus (HIV) infection and the lack of well-organized TB diagnostic and treatment systems [2,4] contribute to the disproportionate burden of TB in the Sub-Saharan African prisons.

Inadequate TB treatment will lead to the emergence of drug-resistant strains [5]. The prison situations are notorious for causing interruptions of TB treatment and occurrence of unfavorable outcomes [6]. In some prisons, up to 24% of the TB cases have been shown to harbor multidrug-resistant TB (MDR-TB) which makes TB control efforts very complicated [7]. In Russian and Brazilian prisons, 12% [8] and 8% [9] of the TB cases have been reported to default their treatment, respectively. In a Ugandan prison, 43% of the prisoners with TB had defaulted their treatment [10]. The TB treatment category, HIV co-infection, smoking, alcoholism, and a lack of family support have been indicated as factors affecting TB treatment success in prisons [8,9,11].

In Ethiopian prisons, TB treatment programs exist and are integrated within the national TB control program where the prison health staff provides treatment based on the national guidelines [12]. However, treatment outcome results and the potential factors for unsuccessful outcome are not well documented. According to a report in 2013 from the prison of North Gondar, the treatment success rate (TSR) of the prisoners ranged from 42%-80% within the ten years period [13]. However, this study was not comprehensive in that it did not assess the potential factors that might be affecting the treatment success. Evaluating the treatment outcome results and identifying the risk factors for the unsuccessful outcome will help to identify the gaps between the national TB treatment policy and practice in prisons and initiate evidence-based interventions. This study was designed to assess the treatment outcome of TB cases and identify risk factors for unsuccessful outcome in Northern Ethiopian prisons.

Methods

Study setting and diagnostic criteria

This study was carried out in prisons of the Tigray Regional State, northern Ethiopia. Out of the nine prisons in Tigray, four prisons, located in the cities Alamata, Humera, Mekelle and Shire, were randomly selected and included in the study. Information regarding the TB diagnostic and treatment services in these settings have been described elsewhere [14]. In general, conditions of the four prisons were comparable where the prisons had only poorly equipped clinics staffed with diploma holding nurses. There were also no sputum microscopy, GeneXpert or drug susceptibility testing (DST) services in the clinics of the prisons and the TB diagnosis relied merely on a referral of prisoners to health facilities outside prisons [14]. The diagnosis was carried out at the referral sites using the direct smear microscopy and/or chest X-ray, and pathological investigation following the national guidelines [15]. Accordingly, a presumptive TB case with at least two initial sputum smear examinations positive for AFB (acid-fast bacilli) by direct smear microscopy or one sputum examination positive for AFB and having radiographic abnormalities consistent with active pulmonary TB is considered as a smear-positive TB (PTB+) case. A patient having symptoms suggestive of TB with at least 3 initial smear examinations negative for AFB on the direct microscopy and with radiological abnormalities consistent with pulmonary TB is defined as a smear-negative pulmonary TB (PTB-) case. On the other hand, if a patient has TB involving organs other than lungs as proven by histopathological evidence from a biopsy or based on strong clinical evidence consistent with active extra-pulmonary TB (EPTB) he/she is categorized as having EPTB.

Prisoners diagnosed with TB were linked to the directly observed treatment short-course (DOTS) clinic of the nearby health facilities where they were registered and started the treatment according to the national guidelines [15]. Afterwards, the prison health personnel collected drugs weekly from such facilities and continued the treatment within prisons. The treatment is given based the patients' treatment category. Newly diagnosed TB cases are provided with the six months treatment regimen where they take a combination of four drugs (rifampicin, isoniazid, pyrazinamide, and ethambutol) during the first two months of the intensive phase and continue with the two of the drugs (rifampicin and isoniazid) for the remaining four months. On the other hand, the previously treated cases are treated for eight months. This regimen consists of eight weeks treatment with streptomycin, rifampicin, isoniazid, pyrazinamide, and ethambutol followed by four weeks treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol during the intensive phase, followed by five months with rifampicin, isoniazid, and ethambutol. Bacteriological follow-up examinations (sputum smear check-ups) are done at the end of the second, fifth, and sixth month of therapy for all new sputum-positive patients and at the end of the intensive phase of treatment (the third month), and at the end of the fifth and eighth months of treatment for the previously treated sputum smear-positive patients. The treatment follow-up data was regularly reported back to the health facilities for registration as the study prisons lacked standardized logbooks to register.

Study design and data collection

This was a retrospective analysis in which the profile and treatment outcomes of all prisoners diagnosed with TB between September 2010 and August 2015 was retrieved from the TB treatment follow-up clinics of the four selected prisons. Patients' information such as age, sex, the type of TB case, the treatment category, the date of treatment initiation and completion, weight at the time of treatment initiation, HIV status, and other related data were recorded using a standardized recording format by the prison nurses.

Outcome definition

The referral sites and/or the DOTS centers use the standard national TB case definitions and treatment outcomes adopted by WHO [16]. The categories of outcome include: cured (a TB patient who was smear- or culture-positive at the beginning of the treatment but who became smear- or culture negative in the last month of treatment and on at least one previous occasion), treatment completed (finished the treatment with resolution of symptoms but without smear or culture result), treatment failure (remained or became smear-positive at the end of 5 months or later), lost to follow-up (missed treatment for at least eight consecutive weeks), transferred out (transferred to another site during the treatment), died (patients who died from any cause during the course of treatment). We further grouped the outcomes into successful treatment (sum of cured and treatment completed) and unsuccessful treatment which is the sum of treatment failure, loss to follow-up, and death as per the WHO standard definition [17].

Data analysis

Data were entered using Epi Data entry version 3.1 software and analyzed using SPSS version 21. We compared prisoners with unsuccessful treatment outcome with those having successful outcome. Even though it was already one of the elements of the unsuccessful outcome, death was specifically considered as an additional outcome variable because we were interested to see its relationship with body weight at treatment initiation. Bivariate and multivariate logistic regression analyses were performed to examine the association of independent variables with our outcome variables. Covariates with p-values of ≤ 0.25 and collinearity matrix index of ≤ 0.7 in the bivariate analysis were considered for inclusion in the multivariate model. A p-value of ≤ 0.05 was considered to define a statistical significance.

Ethics approval and consent to participate

The study was approved by ethical review committee of the College of Health Sciences, of Mekelle University. Moreover, the confidentiality of the patients' information was safeguarded. Requirement of informed consent was waived by the ethical review committee due to the retrospective design of the study.

Results

Socio-demographic and clinical characteristics

The baseline characteristics of TB patients (n = 496) are shown in Table 1. The majority (97%) was male, and the mean age was 30 years (range 15-18 years). Extra-pulmonary TB patients accounted for 43% of the TB cases; 30% of total cases had PTB-. Out of the 123 (25%) PTB+ cases, repeated smear was done for 119 (97%) at the end of the 2nd month of treatment and nine were still smear-positive. Eleven percent of the TB cases were HIV-infected; the co-infection rate being slightly higher among EPTB cases (13%). However, the difference was not statistically significant.

Table 1: Socio-demographic and clinical characteristics of the 496 patients with tuberculosis in northern Ethiopian prisons, 2011-2015.

Characteristic	n (%)
Sex	
Male	480 (97)
Female	16 (3)
Age, years	
15-24	201 (40)
25-34	173 (35)
≥ 35	122 (25)
Weight at treatment initiation (Kg)	
< 50	221 (45)
≥ 50	275 (55)
Form of TB	
PTB+	123 (25)
PTB-	150 (30)
EPTB	211 (43)
EPTB & PTB	12 (2)
Treatment category	
New case	481 (97)
Retreatment case	15 (3)
HIV status	
Negative	424 (85)
Positive	54 (11)
Unknown	18 (4)
Antiretroviral treatment (ART)[a]	
On ART at time/within in 3 months of TB treatment	46 (85)
Not on ART	3 (6)
Unknown	5 (9)

Characteristic	n (%)
Use of co-trimoxazole prophylaxis[a]	
On co-trimoxazole at time/within 3 months of TB treatment	40 (74)
Not on co-trimoxazole	14 (26)
Site	
Alamata	73 (14)
Humera	163 (33)
Mekelle	183 (37)
Shire	77 (16)

[a]The denominator is HIV co-infected patients (n = 54); HIV: human immunodeficiency virus, TB: tuberculosis, PTB+: smear-positive pulmonary tuberculosis, PTB-: smear-negative pulmonary tuberculosis, EPTP: extra-pulmonary tuberculosis

Trend of the TB types

The five-year trend of all the TB types is shown in Figure 1. The number of PTB- cases showed variation across years steadily increasing in the recent year; more than half of the TB cases (51.8%) were PTB- between the September 2014 and August 2015. On the other hand, the number of EPTB cases roughly decreased over the five years.

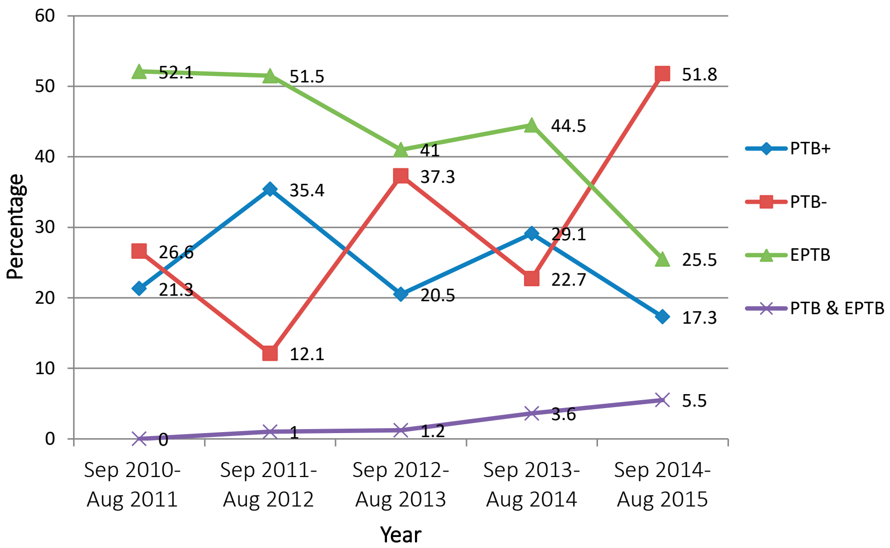

Figure 1 Trends of all forms of registered TB cases (n = 496) in the DOTs center of four northern Ethiopian prisons, 2010-2015. Aug: August, Sep: September; PTB+: smear-positive pulmonary tuberculosis; PTB-: smear-negative pulmonary tuberculosis; EPTP: extra-pulmonary tuberculosis

Treatment outcome and trends

The mean treatment success rate (TSR) of the five years was 94% (395/422) among the patients who were not transferred out. As shown in figure 2, the TSR steadily increased from 87% during September 2010-August 2011 to 97% in September 2013-August 2014. Overall, 57 (11.5%) were cured, 338 (68%) had completed treatment, 12 (2.5%) were lost to treatment follow-up, 8 (1.6%) were with treatment failure, 7 (1.4%) died, and 74 (15%) were transferred out with outcome unknown. All the prisoners transferred to other prisons or released during the course of their TB treatment were not appropriately linked to health facilities.

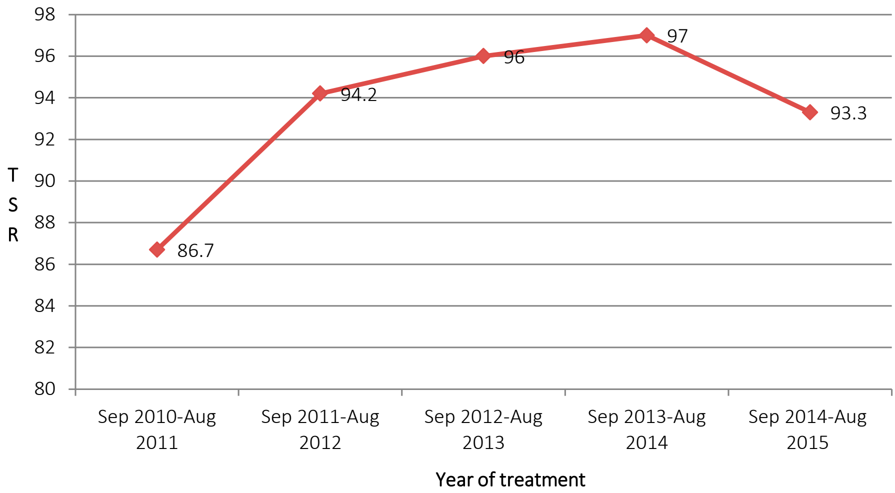

Figure 2 Trends of treatment success rate for all forms of the TB cases (n = 496) from four northern Ethiopian prisons, 2010 to 2015. Aug: August; Sep: September; TSR: Treatment Success Rate; TB: Tuberculosis.

Treatment success rate and associated factors

The treatment success rate and associated predictors are shown in Table 2. After excluding the transferred out prisoners and dichotomizing the outcome variable, further analysis was done for the 422 cases. In the multivariable analysis, the odds of having unsuccessful outcome was significantly higher among the retreatment cases compared to the newly treated ones (AOR = 4.68; 95% CI = 1.02-21.4). Prisoners that were treated during September 2010-August 2011 were also more likely to have unsuccessful outcome, compared to those treated during September 2011-August 2012 (AOR = 0.28; 95% CI = 0.08-0.92), September 2012-August 2013 (AOR = 0.24; 95% CI = 0.06-0.98), and September 2013 -August 2014 (AOR = 0.17; 95% CI = 0.05-0.67). Sputum non-conversion at the second-month check-up was strongly associated with unsuccessful outcome among the smear-positive cases. There was no association between unsuccessful outcome and HIV status, the weight at treatment initiation, the study site, and the form of the TB case. When we perform the analysis considering death as an outcome variable, the odds of dying among patients with a weight at initiation of < 50 Kg was 8.4 times higher (OR = 8.39; 95% CI = 1.01- 70.34) compared to the other group.

Table 2: Factors related to unsuccessful treatment outcome among northern Ethiopian prisoners with tuberculosis in the bivariate and multivariate logistic regression analysis (n = 422). AOR: adjusted odds ratio; COR: crude odds ratio; CI: confidence interval; Ref = reference.

Characteristic	Treatment outcome		COR (95 % CI)	P- value	AOR (95 % CI)	P- value
	Unsuccessful n (%)	Successful n (%)				
Sex						
Female	2 (14.3)	12 (85.7)	2.56 (0.54-12.04)	0.26	-	
Male	25 (6.2)	383 (93.8)	Ref			
Age, years						
15-24	8 (4.6)	164 (95.4)	0.62 (0.23-1.71)	0.36	-	
25-34	11 (7.9)	129 (92.1)	0.86 (0.86-1.09)			
≥ 35	8 (7.3)	102 (92.7)	Ref			
Weight at initiation (Kg)						
< 50	15 (8.4)	164 (91.6)	1.76 (0.83-3.86)		1.72 (0.75-3.98)	0.2
≥ 50	12 (4.9)	231 (95.1)	Ref			
Form of TB[a]						
PTB+	8 (7.6)	97 (92.3)	1.22 (0.48-3.14)	0.48	-	
PTB -	8 (6.1)	124 (93.9)	0.96 (0.37-2.45)	0.38		
EPTP	11 (6.3)	163 (93.7)	Ref			
Non-conversion at the 2nd month[b]						
Yes	2 (12.5)	4 (87.5)	9.1 (1.33-62.16)	0.02	-	
No	5 (5.2)	91 (94.8)				
Type of TB case						
Retreatment case	3 (25.0)	9 (75.0)	5.36 (1.36-21.11)	0.01	4.68 (1.02-21.4)	0.04
New case	24 (5.8)	386 (94.2)	Ref			
HIV status[c]						
Positive	4 (8.5)	43 (91.5)	1.36 (0.45-4.14)	0.58	-	
Negative	23 (6.4)	338 (93.6)	Ref			
Year						
Sep 2010-Aug 2011	10 (13.3)	65 (86.7)	Ref			
Sep 2011-Aug 2012	5 (5.8)	81 (93.2)	0.41 (0.13-1.23)	0.11	0.28 (0.08-0.92)	0.04
Sep 2012-Aug 2013	3 (4.2)	69 (95.8)	0.28 (0.07-1.07)	0.06	0.24 (0.06-0.98)	0.047
Sep 2013-Aug 2014	3 (3.0)	97 (97.0)	0.21(0.05-0.76)	0.018	0.17 (0.05-0.67)	0.01
Sep 2014-Aug 2015	6 (6.7)	83 (93.3)	0.48 (0.16-1.36)	0.16	0.45 (0.14-1.43)	0.18
Site						
Mekelle	12 (8.6)	127 (91.4)	Ref			
Alamata	1 (1.4)	72 (98.6)	0.15 (0.02-1.15)	0.07	0.14 (0.02-1.18)	0.07
Shire	5 (6.8)	68 (93.2)	0.78 (0.26-2.30)	0.65	0.53 (0.16-169)	0.28
Humera	9 (6.6)	128 (93.4)	0.74 (0.3-1.83)	0.52	0.64 (0.23-1.72)	0.38

[a]Patients with both PTB & EPTB were not included; [b]Analysis limited to the smear-positive cases; [c]Analysis limited to patients with known HIV status; HIV: human immunodeficiency virus; Kg: kilogram; PTB+: smear-positive pulmonary tuberculosis; PTB- : smear-negative pulmonary tuberculosis; EPTB: extra-pulmonary tuberculosis

Discussion

In this study, the overall treatment success was found to be 94% for the prisoners that complete their treatment while in prison. However, all the prisoners transferred to other prisons or released during their treatment were not appropriately linked to health facilities and might have lost to treatment follow-up. TB treatment category, the year of treatment, and sputum non-conversion at the second-month check-up (for smear-positive cases) were statistically associated with unsuccessful treatment outcome.

The observed treatment success rate (94%) is slightly higher than the findings from similar studies in the general population of Tigray (89.2%) [18], northeast Ethiopia (90.1%) [19] and is in the range of the target level set by End TB Strategy (a TSR of ≥ 90%) [20]. It also remains remarkably higher than reports from Southern (85.2%) [21], Western (70.8%) [22] and northwest (85.6%) [23] Ethiopia. More specifically, the loss to follow-up (2.5%) and death rates (1.4%) in our study are lower than the loss to follow-up and death rates recorded in the previous studies [18,21,22] which ranged from 3.2%-35.5% and 3.3%-58.8%, respectively. In all the above-mentioned studies, the TSR was calculated in a similar way with our study where the transferred out patients were not considered. The discrepancy with findings could partly be attributed to differences in settings that might account for the variation in the DOTs performance. In prisons, it easier to administer DOTs and monitor the progress as the patients are accessible to the prison health personnel [24]. In addition, we observed that the prison health personnel provided the TB drugs under strict supervision not only during the first two months but also during the four months of the continuation phase, which might result in an increased likelihood of better treatment outcome in prisons.

When compared with prison specific studies, the overall TSR in this study (94%) is higher than the findings from the prison in Gondar which ranged from 42-80% across the ten years [13]. The time difference could not exclusively be the reason for this discrepancy because the TSRs in this study were still smaller than the TSR in our study during the years that overlapped with our study period. Other factors such as differences in the healthcare delivery service between the prisons of the two regions and the commitment of the prison health personnel in delivering the DOTS service might be possible reasons. Higher rates of loss to follow-up were reported elsewhere in prisons in Uganda (43.0%) [10], and Brazil (13.0%) [9]. Similarly, the 1.4% death rate observed in this study is lower than those recorded in Ugandan (5.0%) [10], South African (1.8%) [11] and Brazilian (2.0%) prisons [9]. One possible explanation for this variation could be the difference in the burden of HIV co-infection, which has been shown to be associated with unsuccessful treatment outcome[19,25]. For example, 54% of the study participants in the South African prison [11] were co-infected with HIV [11] whereas only 11% of the TB cases had HIV co-infection in our study.

Our study demonstrates that the DOTS program is effectively functioning for prisoners that complete their TB treatment while in the study prisons. However, the absence of appropriate linkage for those prisoners transferred to other prisons or released during their treatment raises a public health concern. It is more likely for such patients to end up with a loss to follow-up or treatment failure if not death. Those patients who survived would be at high risk to develop of drug-resistant TB [10]. This also implies that the community would be at risk of being infected with a resistant strain from these patients. For the national TB program to be successful, governmental and non-governmental organizations (NGOs) should take the initiative in establishing improved linkage between the prison and public health facilities. For example, a mobile-based communication system involving the prison health personnel, the health professionals at a public health facility, and the released prisoners could be a good approach in tracking released prisoners and reducing loss to treatment follow-up [26].

In this study, as it could be expected, previously treated cases were more likely to have unsuccessful treatment outcome compared to new cases which is consistent with several previous reports [11,18]. One of the reasons could be the high level of treatment failure and hence possible development of drug-resistant strains in retreatment cases [27]. In addition, patient-related behavior might also have contributed to the unsuccessful outcome; a study indicated patients that were already lost to follow-up previously could be reluctant and tend to interrupt their treatment again [28]. Due attention should be given to such patients to make sure that they are taking the full course of treatment and immediate referral should be done for MDR screening if they already had a treatment failure. Year of treatment was also associated with variations in treatment outcome; in general, those treated during the earlier year (September 2010-Augst 2011) were more likely to have unsuccessful outcome compared to the latest years, indicating improvements in the DOTS performance over years. This could be due to the increasing efforts of the national TB control program in introducing and implementing the TB/HIV collaborative activities in healthcare settings and prisons in recent years [29].

Unlike several previous reports [11,19,25], in this study, HIV co-infection was not associated with unsuccessful outcome. The difference in the sample size and burden of the co-infection rate might be possible reasons for this. In addition, the prison health personnel reported that they routinely supervise the TB treatment progress of prisoners including those co-infected with HIV which might have contributed to the improved outcome in both groups. Though it was not associated with unsuccessful outcome, body weight at initiation of anti-TB treatment (< 50 Kgs) was found to be a significant predictor of death of the patients, which is in agreement with previous reports [30,31]. The relationship between TB and malnutrition is bidirectional. Severe TB disease renders patients to be malnourished and malnourished individuals are at a high risk to develop severe TB diseases and end up with unfavorable treatment outcomes [32]. Hence, the death of patients might be attributed to the severity of the TB disease itself or due to the malnutrition and associated consequences. Closer nutritional monitoring and earlier initiation of nutrition support are important to rescue severely malnourished TB patients [32]. In smear-positive cases, sputum non-conversion at the second-month check-up was a predictor of unsuccessful outcome. This might be partly related to the drug resistance development. In 2015, the incidence of multidrug-resistant /rifampicin-resistant (MDR/RR-TB) in Ethiopia was estimated to be 2.7% among the new and 14% among retreatment TB cases [20]. In the Tigray region of Ethiopia, 55% of the presumptive MDR cases have been shown to harbor MDR strains [33]. We suggest that such prisoners should be immediately referred for DST.

Furthermore, an overview of the TB profile data showed that the majority of the patients in our study were EPTB and PTB- cases, which is consistent with the previous reports from the general population in Ethiopia [34,35]. The exact causes for the high proportion of EPTB in Ethiopia remain unknown, however, the high potential for a wrong diagnosis (due to the poor diagnostic facility), and poor immunologic and nutritional status have been shown to be associated with high rates of EPTB and PTB- cases [36,37]. This might suggest the need to incorporate a more accurate diagnostic test, such as the GeneXpert MTB/RIF assay, in Ethiopian prisons.

This study has some limitations mainly inherited from the retrospective design. As we relied on historical records, we were not able to add some important variables such as alcoholism, smoking, substance abuse, nutritional status, and lack of family support, which are known to be related to the variations in the TB treatment outcome[38]. Tracking the prisoners transferred between prisons was also not possible, as the information was not clearly indicated in the treatment recording protocol.

Conclusions

The mean treatment success rate of the prisoners in the study prisons was quite satisfactory when gauged against the target level set by the End TB Strategy. However, the lack of appropriate linkage and tracking systems for those prisoners transferred or released before their treatment completion would have a negative implication for the national TB control program as such patients might interrupt their treatment and develop drug-resistant TB. Being in a re-treatment regimen and sputum non-conversion at the second-month check-up were significantly associated with unsuccessful outcome among all forms of and smear-positive TB cases, respectively. The concerned authorities should take an urgent action to help establish improved linkages between the prison and public health facilities to prevent possible loss to follow-up of released prisoners and due attention should be given to the previously treated cases.

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Chapter 4
Tuberculosis knowledge, attitudes, and practices among northern Ethiopian prisoners: implications for TB control efforts

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Abstract

Introduction Although awareness is an important component in tuberculosis (TB) control, we do not know how much Ethiopian prisoners know about TB. This study assessed the level of knowledge, attitudes, and practices (KAP) of prisoners about TB in eight northern Ethiopian prisons.

Methods Data were collected cross-sectionally from 615 prisoners using a standardized questionnaire between March and May 2016. The outcome variables were defined considering the basic elements about TB.

Results Out of 615 prisoners, only 37.7% mentioned bacteria as a cause of TB while 21.7% related TB to exposure to cold wind. Eighty-eight per cent correctly mentioned the aerial route of TB transmission and 27.3% had perceived stigma towards TB. The majority (63.7%) was not aware of the possibility of getting multi-drug-resistant strains when they would not adhere to treatment. Overall, only 24% knew the basic elements about TB, 41% had favorable attitudes, and 55% had a good practice. Prisoners who were urban residents were generally more knowledgeable than rural residents (adjusted OR = 2.16; 95% CI = 1.15-4.06). Illiterates were found to be less knowledgeable (adjusted OR = 0.17; 95% CI = 0.06-0.46), less likely to have a favorable attitude (adjusted OR = 0.31; 95% CI = 0.15-0.64), and less good practice (adjusted OR = 0.35; 95% CI = 0.18-0.69). Significant differences were also observed between the different study prisons.

Conclusions Knowledge of prisoners regarding the cause of TB and consequences of non-adherence to TB treatment was low. Knowledge on the transmission, symptoms, and prevention was fairly high. Health education interventions, focused on the cause and the translation of the knowledge to appropriate practices, are needed in all the study prisons. Special attention should be given to less educated prisoners, and to prisons with a high number of prisoners and those in remote areas.

Introduction

Even though the incidence of tuberculosis (TB) has decreased worldwide, it remains a global health challenge. An estimated 10.4 million people developed TB in the year 2015 of which one-quarter was from Africa [1]. The disease is more prevalent in congregate settings such as prisons [2]. Especially, it is much worse in Sub-Saharan prisons due to the added problems of human immunodeficiency virus (HIV) and poverty [3]. In Ethiopian prisons, a four to nine-fold higher prevalence of TB has been reported compared to the general population [4,5].

The global focus of TB control programs is on early diagnosis and treatment of cases in high TB and HIV-endemic areas [1]. However, the low TB case detection rate and the emergence of multi-drug-resistant strains have been a challenge [1,6]. Raising communities' awareness contributes for early diagnosis of TB which is one of the pillars of the End TB Strategy [1]. Studies documented a positive association between TB knowledge and care seeking and treatment adherence [7-9]. However, the level of knowledge should be known, also in relation to previous reports, before informed decisions can be made when designing and implementing appropriate educational interventions. In this regard, studies conducted in the general populations of Sub-Saharan countries documented misconceptions ranging from 66.3% to 99.7% of the population on the etiology (cause) of TB, 27.6% to 90.1% on the symptoms, 0.1% to 48.6% on the transmission and 33.4% to 92.9% on prevention methods [10-16]. Stigma towards TB patients has been reported in up to 58.3% of the respondents [10,14]. Literacy status, socio-cultural differences, gender, and spatial variations have been reported to be factors affecting TB knowledge, attitude and practices (KAP) [11,13,16].

Baseline data regarding prisoners' knowledge of TB and related factors are limited. Studies conducted in prisons of Brazil [17] and Texas [18] reported gaps on some specific TB KAP variables. In a Brazilian prison, only 5.0% and 3.6% of the prisoners could mention the TB symptoms and prevention methods, respectively, and in a USA prison 43.0% of the prisoners had a perceived stigma towards TB. To our knowledge, in Sub-Saharan prisons, only one study assessing prisoners knowledge was conducted six years ago in Eastern Ethiopian prisons [19]. This study reported a moderate level of knowledge about TB and revealed some misconceptions about its causes, control and prevention. This study was, however, limited in scope in that it did not address the attitude, and was only conducted among presumptive TB cases.

Moreover, in culturally diversified countries like Ethiopia, TB knowledge-level has been reported to show significant spatial variations [16]. In addition, through the Internet and intensive educational campaigns, healthcare information can reach many people quickly and increase the level of knowledge among people [20]. In a previous study among Ethiopian prisons we observed quite some TB cases with long-lasting symptoms without being diagnosed [4], so we expect that KAP among Ethiopian prisoners is still very low. This study aimed at assessing the level of knowledge, attitude, and practices of prisoners about TB and related factors.

Methods

Study setting

This study was conducted in eight northern Ethiopian prisons located in the regions Tigray (Mekelle, Abi Adi, Alamata, Humera, and Wukro) and Amhara (Dessie, Debre Tabor, and Finote Selam) between March and May 2016. In 2015, Ethiopia ranked 10th among the 22 high TB burden countries with an estimated TB incidence of 192 per 100,000 people [1]. The country had a registered prison population of 112,361 (136/100,000 persons) in 2010 [21], which is higher than the imprisonment rates observed in some Sub-Saharan African countries such as in Kenya (121/100,000 persons), and Malawi (76/100,000 persons) [21].

Study design and sampling technique

This was a cross-sectional study, which was also part of a baseline measurement for an educational interventional study aimed to increase TB screening and case detection rate in northern Ethiopian prisons. Larger prison centers located in the main cities of Amhara and Tigray regions were considered as eligible while small jails were excluded (n =22). Larger prisons were defined as institutions that incarcerate people for longer periods of time, such as many years, while small jails were institutions that confine people for shorter periods of time. A multistage cluster sampling technique was employed to randomly select the study prisons and the prisoners. Only prisoners who would stay imprisoned for a year or longer from the date of the selection were included, since this baseline measurement was part of an intervention study. Prisoners younger than 18 years of age and those mentally ill were excluded.

Sample size determination

The sample size was determined using a single proportion formula, $n_1 = z^2p\ (1\text{-}p)/d^2$, where n_1 was the initial sample size, considering a confidence level of 95%, an estimated overall proportion of good knowledge about TB of 52% [12], and a precision of 5%. After using a finite population correction, ($n_2 = n_1/(1+ (n_1/N))$), where N was the total number of the prisoners in the study sites (N = 8,874), multiplying by 1.5 to account for the clustering effect, and adding a 15% non-response rate, we obtained a final sample size of

634. This figure was then proportionally allocated to each prison as per the total numbers of prisoners.

Questionnaire and interviewing

We used a semi-structured standardized KAP questionnaire to collect data. The questionnaire was designed in English following the WHO guidelines [22] and was translated into the local languages, Amharic and Tigrigna. The questionnaire consisted of 38 questions, divided into two parts. Part one addressed the socio-demographic characteristics and prison history. The second part addressed aspects related to TB knowledge, attitude, and practices. Briefly, questions regarding the etiology, transmission, prevention, and treatment of TB, beliefs, and feelings about TB and TB patients were included. The interviewing was done by trained data collectors (prison nurses, or trained inmates). For sites with a shortage of prison health professionals, prisoners who were relatively educated (some with a diploma in clinical nursing) were recruited and trained for two days on how to undertake the interview. The interviewing process was closely monitored by the investigators in which the first one-fourth of the interviews were monitored by listening and observing the interviewing process. The investigators also stayed close around the interviewing area to assist the interviewers on call for any ambiguity for the rest of the interviews.

Statistical analysis

Data were entered in EpiData version 3.1 software and the analysis was performed using SPSS version 20.0. Descriptive statistics was used to report frequencies and proportions. Bivariate and multivariate logistic regression analysis was performed to examine the association of independent variables with our outcome variables. Our outcome variables of interest were knowledge about TB, attitude towards TB, and practice. We checked whether there was a clustering effect at the prison level for the outcome variables following the mixed procedure for a possible consideration of the multilevel logistic model. We found, however, that there was no statistically significant variability in the intercepts of the outcome variables across the prison sites; the p values for the intercept estimates of knowledge, attitude, and practice were 0.14, 0.25, and 0.13, respectively.

Knowledge was assessed considering the following crucial elements: able to recognize germ/bacteria as a cause of TB, able to recognize the airborne route of transmission, able to recognize a cough of 2 weeks and longer as a symptom, able to realize covering mouth and nose when coughing/sneezing as a prevention measure, and able to know the free TB treatment availability. Prisoners that mentioned all these five items were categorized as having a 'good' knowledge and those who missed one or more of these items were categorized as having 'poor' knowledge. Attitude was assessed using three questions:

able to mention that TB is a very serious disease, showing a favorable reaction if suspected having TB related symptoms (i.e. seeking health care instead of being ashamed of or hopeless), and showing a compassion and desire to help people with TB. Prisoners that mentioned these three items were categorized as having a 'favorable' attitude and the others were categorized as having 'unfavorable' attitude. Similarly, practice was assessed using two questions: preference of modern health care for treatment and the intention to visit the facility as soon as realizing having a TB related symptom. Prisoners who mentioned these two items were categorized as having a 'good' practice and the rest were categorized as having a 'poor' practice. All the potential predictor variables were tested against the dichotomized knowledge, attitude, and practice. Multi-collinearity among the independent variables was assessed considering the variance inflation factor of greater than 10 (for our data, the maximum was 3.86). Covariates with p-values of ≤ 0.25 in the bivariate analysis were considered for inclusion in the multivariate model. Accordingly, the multivariate models for the level of knowledge, attitude, and practice consisted of five, four, and six variables, respectively. Educational status and prison site were included in the three models. In addition, age group and occupation were added to the final models of the knowledge and practice level whereas residence was included in the knowledge and attitude model. Duration of imprisonment was added to the attitude model and knowledge and attitude level to the practice model. Comparisons between subgroups with the outcomes were expressed as odds ratios (OR) with a 95% confidence interval (CI). A p-value of ≤ 0.05 was considered to declare a statistically significant association.

Ethical consideration

The study protocol was approved by the ethical review committee of the College of Health Sciences, Mekelle University. All participants were asked for a written informed consent, and those consented were enrolled. For all illiterate participants, data collectors informed each of them and confirmed the willingness of the participants to sign the informed consent sheet. The consent procedure for these illiterate participants was also approved by the ethics review committee.

Results

Socio-demographic characteristics

Of the total number of invited participants (n = 634), five (1%) refused to participate in the study. Fourteen questionnaires with missing demographic characteristics were excluded, so the final analysis was performed with 615 participants. The number of participants included ranged from 22 in Abi Adi to 173 in Mekelle prison. Of the 615 participants, the majority 597 (97%) was male. The median age was 28 years with an interquartile range (IQR) of 12 years. The median duration of imprisonment was 13 months (IQR = 29 months). Almost half (46%) of the participants was farmer and 13% was illiterate. Thirty-seven participants (6%) reported a history of having TB disease.

Knowledge about tuberculosis

The prisoners' knowledge about TB is shown in Table 1. In this study, only 37.7% of the participants recognized germ/ bacteria as a cause of TB. Twenty-two percent mentioned that it is mainly caused by exposure to cold. The majority (88.0%) correctly mentioned that TB is transmitted through coughing droplets and 65.7% mentioned covering the mouth when coughing/sneezing as a measure to prevent TB. However, 11.9% and 15.0% of the participants mentioned inappropriate methods including keeping windows closed when they are with chronically coughing people and/or TB patients in a room and avoiding shaking hands, respectively. The majority (88.3%) described that TB is curable with modern drugs, but about one-third (35.5%) did not know the free TB treatment availability.

Table 1: Knowledge of northern Ethiopian prisoners about tuberculosis stratified by the status of the previous history of TB disease, 2016 (N = 615).

Variable	Had history of TB, n (%)	Had no TB ever, n (%)	Total, n (%)	p-value**
	n = 37	n = 578	N = 615	
Cause of TB				0.65
Bacteria*	17 (45.9)	215 (37.2)	232 (37.7)	
Cold wind	5 (13.5)	128 (22.1)	133 (21.7)	
Smoking	3 (8.2)	43 (7.4)	46 (7.5)	
Spoiled soil (soil with a bad odor)	5 (13.5)	61 (10.6)	66 (10.7)	
Poor hygiene	2 (5.4)	53 (9.2)	55 (8.9)	
Don't know	5 (13.5)	60 (10.4)	65 (10.6)	
Others¶	0 (0)	18 (3.1)	18 (2.9)	
Mode of transmission				0.45
Through coughing droplets*	36 (97.3)	506 (87.6)	542 (88.0)	
Through shaking hands	0 (0)	28 (4.8)	28 (4.6)	
Though sharing dish	0 (0)	22 (3.8)	17 (2.8)	
Don't know	1 (2.7)	22 (3.8)	28 (4.6)	
Signs and symptoms+				
Cough for 2 weeks or above*	28 (75.7)	458 (79.2)	486 (79.1)	0.67
Hemoptysis	20 (54.1)	278 (48.1)	298 (48.5)	0.51
Weight loss	16 (43.2)	272 (47.1)	288 (46.8)	0.73
Ongoing fatigue	11 (29.1)	190 (32.9)	201 (32.7)	0.85
Persistent fever	12 (42.4)	157 (27.2)	169 (27.5)	0.57
Don't know	1 (2.7)	35 (6.1)	36 (5.9)	0.72
Others¶¶	40 (108.1)	347 (60.1)	387 (62.9)	1.00
Prevention methods+				
Cover mouth when coughing/sneezing*	23 (62.2)	381 (65.9)	404 (65.7)	0.72
Washing hands	11 (29.7)	188 (32.5)	199 (32.4)	0.86
Avoiding handshakes	6 (16.2)	86 (14.9)	92 (15.0)	0.81
Isolating TB patients	12 (32.4)	214 (37.1)	226 (36.7)	0.73
Closing windows	4 (10.8)	69 (11.9)	73 (11.9)	1.00
Avoid sharing dishes	10 (27.0)	163 (28.2)	173 (28.1)	1.00
Vaccination	10 (27.0)	169 (29.2)	179 (29.1)	0.85
Good nutrition	14 (37.8)	130 (22.5)	144 (23.4)	0.04
Don’t know	0 (0)	27 (4.7)	27 (4.4)	0.39
Is TB curable				0.16
Yes	36 (97.3)	507 (87.7)	543 (88.3)	
No	1 (2.7)	71 (12.3)	72 (11.7)	
Know free TB treatment availability				0.59
Yes*	26 (70.1)	371 (64.2)	397 (64.5)	
No	11 (29.9)	207 (35.8)	218 (35.5)	

Variable	Had history of TB, n (%)	Had no TB ever, n (%)	Total, n (%)	p-value**
	n = 37	n = 578	N = 615	
Risk of defaulting from treatment+				
Death	28 (75.7)	458 (79.2)	486 (79.1)	0.54
Relapse	12 (32.4)	256 (44.3)	268 (43.6)	0.17
No cure	13 (35.1)	232 (40.1)	245 (39.8)	0.61
Drug resistance	17 (45.9)	206 (35.6)	223 (36.3)	0.22
Don't know	2 (5.4)	8 (1.4)	10 (1.6)	1.00
Vulnerability for TB				0.43
Prisoners	26 (70.3)	440 (76.2)	466 (75.8)	
General community	11 (29.7)	138 (23.8)	149 (24.2)	

*: the five crucial elements; ¶: curse/demon, malnutrition; +: multiple responses possible; ¶¶: chest pain, skin rash, nausea, severe headache; **: p-value from the chi-square test

TB knowledge and associated factors

Table 2 shows the relationships between TB knowledge, using the five crucial points, and potential predictor variables. Of 615 participants, 149 (24%; 95% CI = 21%-28%) had a good level of knowledge about TB. Government employees had a significantly higher level of knowledge compared to farmers (AOR 2.92; 95% CI = 1.21-7.03). Prisoners that were urban dwellers were more knowledgeable than rural prisoners (AOR = 2.16; 95% CI = 1.15-4.06). There was also an association between the level of education and TB knowledge. Another interesting finding was that there appeared to be a significant variation in the level of TB knowledge across the study prisons: compared to prisoners of Mekelle, prisoners of Debre Tabor (AOR = 2.71; 95% CI = 1.36-5.42), and Finote Selam (AOR = 4.16; 95% CI = 2.05-8.43) were more knowledgeable, whereas those imprisoned in Wukro (AOR = 0.12; 95% CI = 0.03-0.57), and Humera (AOR = 0.21; 95% CI = 0.06-0.74) were less knowledgeable.

Table 2: Factors related to the level of knowledge about tuberculosis among northern Ethiopian prisoners in the bivariate and multivariate logistic regression analysis (N = 615).

Variable	Knowledge level			
	Good, n (%)	Poor, n (%)	COR (95% CI)	AOR (95% CI)
All participants (N = 615)	149 (24)	466 (76)		
Age, years				
18-45	136 (25)	406 (75)	1.55 (0.82-2.91)	1.08 (0.51-2.26)
≥ 46	13 (18)	60 (82)	Ref	
Educational status				
Illiterate	7 (9)	72 (91)	0.13 (0.06-0.29)	0.17 (0.06-0.46)
Read and write only	10 (14)	62 (86)	0.22 (0.1-0.43)	0.21 (0.08-0.52)
Primary	42 (16)	215 (84)	0.25 (0.16-0.39)	0.27 (0.15-0.48)
Secondary or above	90 (44)	117 (56)	Ref	
Occupation before imprisonment				
Government employee	45 (60)	30 (40)	8.11 (4.62-14.3)	2.92 (1.21-7.03)
Student	22 (24)	69 (76)	1.73 (0.97-3.07)	0.77 (0.33-1.76)
Unemployed	5 (3)	12 (97)	2.25 (0.76-6.72)	0.53 (0.13-2.09)
Private worker	33 (22)	117 (78)	1.53 (0.92-2.52)	0.59 (0.26-1.33)
Farmer	44 (16)	238 (84)	Ref	
Residence				
Urban	95 (34)	185 (66)	2.67 (1.82-3.92)	2.16 (1.15-4.06)
Rural	54 (16)	281 (84)	Ref	
History of TB				
Yes	7 (19)	30 (91)	0.72 (0.31-1.67)	-
No	142 (25)	436 (75)	Ref	
Length of imprisonment				
>12 months	74 (19)	323 (81)	0.92 (0.64-1.33)	-
≤12 months	75 (34)	143 (66)	Ref	
Prison site				
Wukro	2 (5)	40 (95)	0.15 (0.04-0.65)	0.12 (0.03-0.57)
Abi-Adi	4 (18)	18 (92)	0.67 (0.22-2.09)	1.23 (0.37-4.47)
Humera	3 (5)	57 (95)	0.16 (0.05-0.53)	0.21 (0.06-0.74)
Alamata	11 (23)	37 (77)	0.89 (0.42-1.92)	1.58 (0.66-3.79)
Dessie	28 (27)	75 (73)	1.13 (0.65-1.96)	1.12 (0.58-2.14)
Debre Tabor	27 (34)	53 (66)	1.54 (0.86-2.74)	2.71 (1.36-5.42)
Finote Selam	31 (36)	56 (64)	1.67 (0.96-2.92)	4.16 (2.05-8.43)
Mekelle	43 (25)	130 (75)	Ref	

AOR: adjusted odds ratio; COR: crude odds ratio; CI: confidence interval; TB: tuberculosis; ref: reference

Attitudes and practices about tuberculosis

The majority of the participants (84.2%) believed that TB is a very serious disease. Sixty-nine percent mentioned that they would not feel feared or ashamed when they would have TB symptoms, but would simply visit a health care facility. A considerable proportion (27.3%) had stigmatizing thoughts towards TB patients (i.e. they mentioned that they fear such people and would stay away from them or would not show any feeling instead of showing compassion and a desire to help). The majority (82.6%) preferred to visit modern health care (Table 3).

Table 3: Attitudes and practices of northern Ethiopian prisoners about tuberculosis stratified by the status of the previous history of TB disease, 2016 (N = 615).

Variable	Had history of TB, n (%)	Had no TB ever, n (%)	Total, n (%)	p-value**
	n = 37	n = 578	N = 615	
Thought on seriousness of TB diseases				0.23
Very serious*	30 (81.1)	488 (84.4)	518 (84.2)	
Somewhat serious	4 (10.8)	71 (12.3)	75 (12.2)	
Not serious	3 (8.1)	19 (3.3)	22 (5.6)	
Reaction if had TB symptoms				0.29
Fear	6 (16.2)	115 (19.9)	121 (19.7)	
Shame	2 (5.4)	23 (4.0)	25 (4.1)	
Sadness/hopelessness	4 (18.8)	40 (6.9)	44 (7.2)	
Visit health facility*	25 (67.6)	400 (69.2)	425 (69.0)	
Feelings about people with TB diseases				0.69
I feel compassion and a desire to help*	30 (81.1)	417 (72.1)	447 (72.7)	
I feel compassion, but stay away from such people	4 (10.8)	111 (19.2)	115 (18.7)	
I fear them because they may infect me	2 (5.4)	35 (6.1)	37 (6.0)	
I have no particular feeling	1 (2.7)	15 (2.6)	16 (2.6)	
Choice for TB treatment				0.027
Modern health care¶	29 (78.4)	479 (82.9)	508 (82.6)	
Traditional healers	5 (13.5)	23 (4.0)	28 (4.5)	
Holy water	1(2.7)	39 (6.7)	40 (6.6)	
Don't know	2 (5.4)	37 (6.4)	39 (6.3)	
Time point to visit health facility				0.73
When treatment of my own does not work	0 (0)	16 (2.8)	16 (2.6)	
As soon as realizing the symptoms might be related to TB¶	24 (64.9)	376 (65.1)	400 (65.0)	
After 3-4 weeks of having symptoms	12 (32.4)	165 (28.5)	177 (28.8)	
I would not go to a doctor	1 (2.7)	21 (3.6)	22 (3.6)	

TB: Tuberculosis; *: the three crucial elements for attitude; ¶: the two crucial elements for practice;**: p-value from the chi-square test

Overall attitude and associated factors

The attitude of prisoners towards TB and the relationship with the potential predictor variables is summarized in Table 4. Less than a half (41%; 95% CI = 37-45) of the prisoners had a favorable attitude towards TB. Respondents that were able to mention that TB is a very serious disease, those showing a favorable reaction if suspected having TB related symptoms and a desire to help people with TB were considered as having a favorable attitude. Significant variations in the level of attitude were observed by the educational level and study sites. By occupation, students (AOR = 1.88; 95% CI = 1.1-3.5) were found to have a higher level of favorable attitude compared to farmers.

Table 4: Factors related to the level of attitude about tuberculosis among northern Ethiopian prisoners in the bivariate and multivariate logistic regression analysis (N = 615).

Variable	Level of attitude		COR (95% CI)	AOR (95% CI)
	Favorable, n (%)	Unfavorable, n (%)		
All participants (N = 615)	250 (41)	365 (59)		
Age, years				
18-45	220 (41)	322 (59)	0.98 (0.59-1.61)	-
≥46	30 (4)	43 (96)	Ref	
Educational status				
Illiterate	19 (24)	60 (76)	0.25 (0.14-0.45)	0.31 (0.15-0.64)
Read and write only	20 (3)	52 (97)	0.31 (0.17-0.55)	0.34 (0.16-0.68)
Primary	96 (37)	161 (63)	0.48 (0.33-0.69)	0.46 (0.29-0.72)
Secondary or above	115 (56)	92 (44)	Ref	
Occupation before imprisonment				
Government employee	33 (44)	42 (56)	1.88 (1.12-3.18)	0.92 (0.44-1.94)
Student	50 (55)	41 (45)	2.92 (1.79-4.75)	1.88 (1.1-3.5)
Unemployed	8 (47)	9 (53)	2.13 (0.79-5.74)	1.38 (0.44-4.41)
Private worker	76 (51)	74 (49)	2.46 (1.63-3.71)	1.41 (0.76-2.62)
Farmer	83 (29)	199 (71)	Ref	
Residence				
Urban	138 (49)	142 (51)	1.94 (1.39-2.68)	0.93 (0.56-1.53)
Rural	112 (33)	223 (67)	Ref	
History of TB				
Yes	14 (38)	23 (62)	0.88 (0.44-1.75)	-
No	236 (41)	342 (59)	Ref	
Length of imprisonment				
>12 months	161 (41)	236 (59)	1.12 (0.81-1.55)	-
≤12 months	89 (40)	129 (60)	Ref	

	Level of attitude			
Variable	Favorable, n (%)	Unfavorable, n (%)	COR (95% CI)	AOR (95% CI)
Prison site				
Wukro	9 (21)	33 (79)	0.3 (0.14-0.67)	0.29 (0.13-0.68)
Abi Adi	14 (64)	8 (36)	1.94 (0.78-4.87)	2.44 (0.93-6.39)
Humera	30 (50)	30 (50)	1.11 (0.61-1.99)	1.42 (0.74-2.71)
Alamata	2 (4)	46 (96)	0.05 (0.01-0.21)	0.06 (0.01-0.24)
Dessie	57 (53)	46 (47)	1.38 (0.84-2.24)	1.42 (0.75-2.71)
Debre tabor	24 (30)	56 (70)	0.48 (0.27-0.83)	0.56 (0.31-1.03)
Finote selam	32 (37)	55 (63)	0.65 (0.38-1.09)	0.94 (0.53-1.68)
Mekelle	82 (47)	91 (53)	Ref	

AOR: adjusted odds ratio; COR: crude odds ratio; CI: confidence interval; TB: tuberculosis; ref: reference

Overall practice and associated factors

More than half of the prisoners, 55% (95% CI = 51.1-58.9), had a good practice related to TB. There was a significant variation in practice by the level of education and study sites. Having a good TB knowledge (COR = 1.49; 95% CI = 1.03-2.18) and a favorable attitude (COR = 1.41; 95% CI = 1.02-1.95) were also associated with having a good practice but was only in the bivariate analysis (Table 5).

Table 5: Factors associated with the level of practice towards tuberculosis among northern Ethiopian prisoners in the bivariate and multivariate logistic regression analysis (N = 615).

	Level of practice			
Variable	Good, n (%)	Poor, n (%)	COR (95% CI)	AOR (95% CI)
All participants(N = 615)	338 (55)	277 (45)		
Age, years				
18-45	293 (54)	249 (46)	0.73 (0.44-1.01)	0.74 (0.42-1.29)
≥46	45 (62)	28 (38)	Ref	
Educational status				
Illiterate	31 (39)	48 (61)	0.41 (0.24-0.69)	0.35 (0.18-0.69)
Read and write only	40 (56)	32 (44)	0.79 (0.46-1.36)	0.55 (0.27-1.11)
Primary	140 (55)	117 (45)	0.75 (0.52-1.09)	0.7 (0.44-1.11)
Secondary or above	127 (61)	80 (39)	Ref	
Occupation before imprisonment				
Government employee	48 (64)	27 (26)	1.52 (0.89-2.57)	0.94 (0.48-1.85)
Student	48 (53)	43 (47)	0.96 (0.59-1.53)	0.65 (0.36-1.15)
Unemployed	8 (47)	9 (53)	0.76 (0.29-2.21)	0.51 (0.18-1.45)
Private worker	82 (55)	68 (45)	1.03 (0.69-1.54)	0.82 (0.49-1.38)
Farmer	152 (54)	130 (46)	Ref	
Residence				
Urban	159 (57)	121 (43)	1.15 (0.83-1.58)	-
Rural	179 (53)	156 (47)	Ref	
History of TB				
Yes	21 (57)	16 (43)	1.08 (0.55-2.11)	-
No	317 (55)	261 (45)	Ref	
Length of imprisonment				
>12 months	203 (51)	194 (49)	1.05 (0.76-1.44)	-
≤12 months	135 (62)	83 (38)	Ref	
Prison site				
Wukro	22 (52)	20 (48)	0.8 (0.41-1.58)	0.95 (0.47-1.94)
Abi-Adi	13 (59)	9 (41)	1.05 (0.43-2.59)	1.18 (0.46-3.1)
Humera	20 (25)	40 (75)	0.37 (0.19-0.68)	0.38 (0.2-0.72)
Alamata	15 (32)	33 (68)	0.33 (0.17-0.66)	0.39 (0.19-0.82)
Dessie	53 (51)	50 (49)	0.77 (0.47-1.26)	0.77 (0.46-1.23)
Debre Tabor	58 (72)	22 (28)	1.93 (1.08-3.42)	2.18 (1.19-4.0)
Finote Selam	57 (66)	30 (34)	1.39 (0.81-2.36)	1.44 (0.8-2.58)
Mekelle	100 (58)	73 (42)	Ref	
Knowledge				
Good	93 (62)	56 (38)	1.49 (1.03-2.18)	1.05 (0.67-1.63)
Poor	245 (53)	221 (47)	Ref	
Attitude				
Favorable	150 (60)	100 (40)	1.41 (1.02-1.95)	1.32 (0.92-1.92)
Unfavorable	188 (52)	177 (48)	Ref	

AOR: adjusted odds ratio; COR: crude odds ratio; CI: confidence interval; TB: tuberculosis; ref: reference

Discussion

This study revealed gaps in knowledge, attitudes and practices among northern Ethiopian prisoners with regard to TB. Only about four out of ten prisoners were able to recognize germ/bacteria as a cause of TB. The large majority related TB to exposure to cold wind, spoiled soil (a soil with a bad odor), poor hygiene, and smoking. The majority (63.7%) was not aware of the possibility of getting multi-drug-resistant strains due to treatment non-adherence. Overall, only 24% knew the basic elements about TB, 41% had favorable attitudes, and a bit more than a half (55%) had a good practice towards TB. TB knowledge, level of attitude and practice were all significantly related to the level of education, and study sites.

When compared to a previous report from Eastern Ethiopian prisons, the proportion of prisoners that mentioned the correct cause of TB is remarkably high in our study (37.7% vs. 1.6%) [19]. Knowledge on the transmission (88.0% vs. 74.1%) and free treatment availability (64.5% vs. 50.3%) is also higher in the current study. This discrepancy could be due to the time difference; knowledge level could vary over time owing to the routine health education activities and improved public media access [23]. The prison health personnel reported that they sometimes provide health education to prisoners about health issues in general. The spatial difference, and associated socio-cultural differences, between the two Ethiopian studies might also partly explain the discrepancy [16]. Similarly, the knowledge about the cause of TB (37.7%), a cough of 2 weeks or more as a TB symptom (79.1%), the airborne route of transmission (88.0%), and covering mouth/nose when coughing as a method of prevention (65.7%) was also higher when compared with reports from the general population in different parts of Ethiopia [10-14,24]. One explanation of this variation could be the fact that prisons are ideal settings for health interventions [25]; in prisons, it is easy to provide health education since a lot of people can be reached at one time compared to the scattered remote areas of the general population.

Very specific comparison with prisons of other Sub-Saharan countries was not possible due to the lack of similar published data. However, studies conducted in Brazilian [17] and USA (Texas) [18] prisons reported a much lower knowledge level. In addition to the time difference, the difference in the prevalence of TB might explain the discrepancy, especially for the prison in the USA [26]. In those areas, prisoners might not give much attention to TB while it is a common issue in high burden areas.

In general, from the above comparisons, we see that northern Ethiopian prisoners had a fairly high level of knowledge about the symptoms, transmission, and prevention of TB. This might suggest good health seeking behavior among our prisoners since several studies showed an association between knowledge of TB and early treatment seeking [7,9]. However, this seems not entirely true in daily practice since in our previous TB survey, half of the TB cases were left undiagnosed for long periods; some were even coughing for more than two years [4]. Other factors such as a poor referral system might also contribute significantly to severe treatment delay [4]. Therefore, we suggest that educational interventions in the study prisons should not only focus on delivering the message, but should also ensure that the knowledge gained can lead to appropriate treatment through regular monitoring and evaluation and clearly defined treatment protocols. We also observed a relatively high level of knowledge on the cause of TB; but, this can be called not good enough as the majority (62%) remained having several misconceptions. The 'exposure to cold wind' was the most frequently mentioned misconception. This is not surprising as this misconception is common in Ethiopia as shown by previous studies from the general population [11-13], and eastern Ethiopian prisons six years ago [19]. This misconception could still be an important catalyst for the spread of TB, especially in the severely overcrowded Ethiopian prisons [4,27]. It is completely contra-effective if people would tend to keep their windows closed to protect them from the "cold wind", while ventilation is important in preventing TB. Our observation substantiates this report in that 12% mentioned keeping windows closed as a preventive measure when they are with chronically coughing people and/or TB patients in a room. This issue should be stressed when delivering health education in Ethiopian prisons.

In the current study, about one-fourth had perceived stigma towards TB patients which is slightly higher than the study from Brazil (21.6%) [17], but lower than those observed in the USA (43.0%) [18], Amhara region (58.3%) [10], and southwest Ethiopia (51.2%) [14]. The relatively favorable outcome on this variable in our study could be the result of routine health education that has been delivered to the prisoners. In our study prisons, the prison health professionals reported that they provide routine health education to prisoners on infectious diseases including TB. Stigmization has been shown to have a direct impact on health care seeking and infection prevention [7]. In order to avoid the social isolation, TB patients may deliberately conceal their status, infecting many more people. This would particularly have severe consequences in prison settings. While the relatively low level of stigmatization in our study is encouraging, further efforts are still needed to ensure more acceptable and useful attitudes towards TB.

With regard to the practice, although the majority (82.6%) had preference to the modern health care, it is worthy to note that a substantial proportion preferred traditional healers (herbs) and holy water sites as a first priority for treatment. This is in line with the previous studies from eastern Ethiopian prisons [19] and reports from the general population in Tigray [12], Amhara [10], and Afar [11] regions. Such misconceptions should be targeted as they contribute to treatment delay and spreading of the disease [7,8]. However, TB control in Sub-Saharan prisons remains neglected by policy makers [28]. Studies suggest the need to shift from considering TB in prisons as a problem of the prison population to considering it as a problem to the larger civilian community [29,30]. We suggest that, for the national TB program to be successful, the concerned bodies such as the federal ministry of health, regional health bureaus, and non-governmental organizations (NGOs) should give priority attention to Ethiopian prisons and use this scientific evidence to help design and provide appropriate health education in the settings. The prison health personnel should be given a sensitization training tailored at the identified misconceptions and continuous support is needed to ensure the quality and the sustainability of the health education.

We also identified some factors that were associated with prisoner's KAP of TB. The level of education was one of the independent predictors for KAP which is consistent with previous reports in Ethiopia [12,13] and elsewhere [31,32]. This relationship could be taken as an opportunity to consider peer mentorship; relatively educated prisoners could be trained and provide routine health education to their fellow inmates, especially in resource-limited prisons of the Sub-Saharan Africa. By occupation, prisoners who were government employs were more likely to have a higher awareness about TB. This is an expected relation as these groups are highly educated compared to farmers. There was also knowledge variability by residence; urban dwellers being more knowledgeable. This is in agreement with previous findings [12]. Differences in literacy status, and access to health service and media might justify the relation.

There was also a significant variation of the TB KAP across the study sites. Compared to prisoners of Mekelle, prisoners of Debre Tabor and Finote Selam were more knowledgeable, whereas those imprisoned in Wukro and Humera were less knowledgeable. This local variation is consistent with the previous reports from Eastern Ethiopian prisons [19] and Ghana [16]. From our observations, the number of health personnel (prison nurses) and the availability of a media center in the study prisons were roughly comparable. Mekelle prison had a slightly better medical clinic and more adequate drug stocks. The differences in the commitment of the prison health personnel in delivering health information might otherwise justify the discrepancy. Humera prison is in a remote area with a relatively harsh weather condition which might influence health personnel's routine activities. These findings might indicate the need to consider geographical differences when designing and implementing educational interventions on TB so as to make the maximum impact.

Some limitations of the study should be mentioned. The fact that we used different interviewers for different prisons might have influenced the consistency of the interview. Our study also shares limitations of other studies that use KAP questionnaires. The truthfulness of the respondents' answers remains difficult, especially for the attitude and belief items [17]. Considering these issues, the data collectors were well trained and informed not to give leading questions and strict supervision was done throughout the interview process.

Conclusions

This study revealed that knowledge of prisoners about the cause of TB and consequences of non-adherence to TB treatment was low. Knowledge on the transmission, symptoms, and prevention was fairly high. However, the overall knowledge on the basic elements of

TB remains low and appeared to significantly vary by study site, and socio-demographic characteristics of prisoners. Health education interventions, focused on the cause and the importance of early diagnosis and treatment are needed in all the study prisons, but special attention should be given to less educated prisoners, and prisons with a high number of inmates and those in remote areas.

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Chapter 5

Trained inmate peer educators improve tuberculosis case detection in a resource-limited prison setting in Ethiopia: a cluster-randomized trial

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Abstract

Background: To improve tuberculosis (TB) case detection, interventions that are feasible with available resources are needed. In this study, we investigated whether involving trained prison inmates in a TB control program improves TB case detection, shortens pre-treatment symptom duration, and increases treatment success in a resource-limited prison setting in Ethiopia.

Methods: Sixteen prisons (with a total population of 18,032) were matched into pairs based on geographical proximity and size. Randomization was done within matched pairs in which eight prisons were assigned to the intervention and the remaining to the control group. From each intervention prison, a few prison inmates were selected and trained for three days about TB. The trained prison inmates then provided health education to all other prison inmates about TB every two weeks for one year and undertook routine symptom-based TB screening. In the control prisons, cases were detected using the existing passive case finding approach. The primary outcome was the case detection rate at the end of the year, measured at cluster (prison) level. The trial was registered at ClinicalTrials.gov, number NCT02744521.

Findings: During the one-year study period, 75 new TB cases were detected in the intervention prisons, while 25 new cases were detected in the control prisons. Consequently, the mean case detection rate was significantly higher in the intervention prisons compared to the control prisons (mean difference 52.9, 95% CI 17.5-88.3, $p = 0.010$). The pre-treatment symptom duration in the intervention prisons was shortened by 8.6 days on average, but this difference was not statistically significant. In addition, the chance of having good knowledge about TB (adjusted OR = 2.54; 95% CI = 1.93-3.94) and good practice (adjusted OR = 1.84: 95% CI = 1.17-2.96) was significantly higher in the intervention prisons. We did not find a significant difference in the treatment success rate, but it was high for both groups (98.4% for the intervention vs. 97.5% for the control prisons, $p = 0.791$).

Interpretation: Involving trained inmate peer educators in the TB control program in Ethiopian prisons significantly improved the TB case detection rate.

Introduction

With an estimated yearly 10.4 million new cases worldwide and 1.4 million deaths, tuberculosis (TB) still takes a huge death toll, especially for the poorest people [1]. Major obstacles in the global fight against TB are a failure to detect the disease early and 'missed' TB cases. Each year more than three million active TB cases are missed by health systems (either remain undiagnosed or diagnosed but not reported) [1]. As a consequence, undiagnosed cases remain a source of onward transmission of the disease. Many undetected cases occur in overlooked, but high-risk settings such as prisons [2]. Particularly, the Sub-Saharan African prisons are known to be affected by undetected TB. Studies from some of the countries in the region indicated that 0.5% to 7.6% of the prison inmates have undiagnosed, but active TB, constituting a large source of TB transmission not only for other prison inmates but also to the general population [3-5]. In Ethiopian prisons, a systematic review of the published studies reported about a four-fold higher prevalence (888 per 100,000 prison population) of TB than the national average [6]. The emergence of multidrug-resistant (MDR) TB adds to the problem, as was shown in a study in Zambian and Ethiopian prisons, where up to 9.52% of the TB cases were MDR and TB was the highest cause of mortality in some of these prisons [7,8].

The focus on the directly observed treatment short course (DOTS) approach, without active case finding, proves to be insufficient to end the TB epidemic [9]. Use of systematic screening through an entry and exit screening and frequent mass screening using a combination of screening and diagnostic tools (usually sputum smear microscopy and chest-X-ray) seems needed and has been shown to improve TB case finding in prisons [10]. However, resource scarcity and a shortage of health personnel limit its applicability in prisons of poor countries [11]. We, therefore, need alternative methods to improve access to such diagnostic services and increase case finding in prisons. Community-based active case-finding interventions that include improved access to health care, have shown an increase in TB case detection and treatment success rate in different high burden regions [12,13]. In prisons, a pre-post interventional study from India suggested an increase in TB case finding through the use of regular educational mobilization by the prison authorities and prison health staff [14]. However, the approach demands trained manpower and should be proved using an experimental design before scale-up and adaptation.

The use of peer education, thus training prison inmates themselves on health related issues, could be a very cost-effective alternative, and it has already been shown to improve HIV screening and prevention in prisons [15,16]. However, to our knowledge, peer education as a model to fight TB in prisons is not practiced on a wide scale and there are no published trials investigating the potential impact of such a program. We performed a cluster randomized controlled trial to assess whether empowering and involving prison inmates in TB control, improves TB case detection in a resource-limited prison setting.

Methods

Study design and participants

We conducted a cluster randomized controlled trial over a one-year period, from April 2016 to April 2017, in two large regions in Ethiopian, where we randomized prisons to an intervention group or a control group. Prisons in the regions Amhara and Tigray were assessed for eligibility (n = 39). Larger prisons (n = 22) were considered to be eligible while small prisons (n = 17) were excluded. Larger prisons were defined as institutions that incarcerate people for longer periods of time, such as many years, while small jails were institutions that confine people for shorter durations. The 22 prisons were then matched into pairs based on geographical proximity and size of the prisons (11 matched pairs, five of which were in Tigray and the remaining in Amhara). We included all five matched prison pairs from Tigray for the randomization, considering their proximity and hence feasibility. We randomly selected three matched pairs from Amhara, considering distance and thus the logistical and financial impact (Fig. 2). Finally, we considered the following prisons for the randomization; Mekelle vs. Shire, Adawa vs. Abi Addi, Humera vs. Adigrat, Maichew vs. Alamata, Wukro vs. Axum, Dessie vs. Woldia, Fenote Selam vs. Debre Markos, and Debre Tabor vs. Bahir Dar.

The Ethical Review Committee of Mekelle University approved the study protocol and all participants who received screening, and/or were involved in the knowledge, attitude, and practice (KAP) survey provided written informed consent. The trial was registered at ClinicalTrials.gov, number NCT02744521.

Randomization and blinding

The study prisons were randomly allocated 1:1 to the intervention or control group. One of the investigators (MS) who did not have knowledge of the characteristics of the prisons randomized the prisons to the intervention or control condition using a random generator. The physicians and laboratory professionals involved in the TB diagnosis and the assessors of the outcomes and intervention check were blinded. However, it was not possible to mask the supervisors and trained prisoners.

Procedures

After a brief discussion with the prison staff on the objectives and procedures of the intervention, we recruited inmate peer educators for each prison in consultation with the prison staff. The following criteria were used for selection: previous experience in coordinating health issues (priority was given to those involved in TB/HIV control activities), being relatively educated (10th grade or more, priority was given to health professionals), displaying good behavior (as witnessed by the prison health personnel), and length of stay in the prison (at least the subsequent 12 months). We selected three to six prison inmates in each prison. The recruited prison inmates received a three-day training course about the cause, transmission, symptoms, diagnosis, prevention, and treatment of TB and consequences of nonadherence to TB treatment (training material attached as an appendix). We also briefly trained them about symptom-based TB screening, identification of presumptive TB cases, and supporting TB patients to improve adherence to the TB treatment. In addition, we provided them with brochures and posters illustrating the cause, transmission, symptoms, and treatment of TB.

After the training, but before trained prison inmates (peer educators) started their activities, they were assessed for their capability to perform the desired activity (screening and education). We assessed whether they were capable of identifying presumptive TB cases by providing them simulated presumptive TB and non-presumptive TB cases and verifying their conclusions using a checklist. Peer educators that passed the assessment criteria then organized inmates into groups and provided education about TB, its prevention, control, and its relation with HIV every two weeks for one year. Peer educators were assigned to specific blocks and/or rooms in the prisons with monthly rotations. Each time, they did a campaign and gathered the prison inmates either in an open field in the prisons' compound or in a hall (for those with a good setup). The peer educators then delivered education about TB to the large group using audio devices. For those who could not gather for security reasons, the peer educators provided the education by organizing them in small groups in the rooms. In the meantime, they actively searched symptomatic prison inmates and undertook routine symptom-based TB screening using a standardized TB screening protocol. They also screened new entrants upon arrival in the prisons.

Prison inmates who had a cough for two or more weeks (any duration if HIV positive) with or without other symptoms (according to the national guideline) were considered as presumptive TB cases and were linked to the prison health personnel for a referral to the hospitals. Briefly, each time, the peer educators took the screened prison inmates with presumptive TB to the responsible prison health personnel and insisted for an immediate referral. The prison health personnel then organized the screened prison inmates in small groups and referred them to the nearby hospitals (once or twice in a week depending on the number of cases). Vehicles from the prisons were used to transport the screened prison inmates and the prisons' guards accompanied each visit as part of their daily roles. At the hospitals, the referred prison inmates should follow the routine patient management procedures to get a diagnosis. All hospitals follow the national TB diagnosis and treatment algorithm (Fig. 1) [17], even though the diagnosis still relied on direct smear microscopy and chest-X-ray. The criteria for smear-negative diagnoses were based on physicians' judgment using the evidence from the X-ray and empiric treatment.

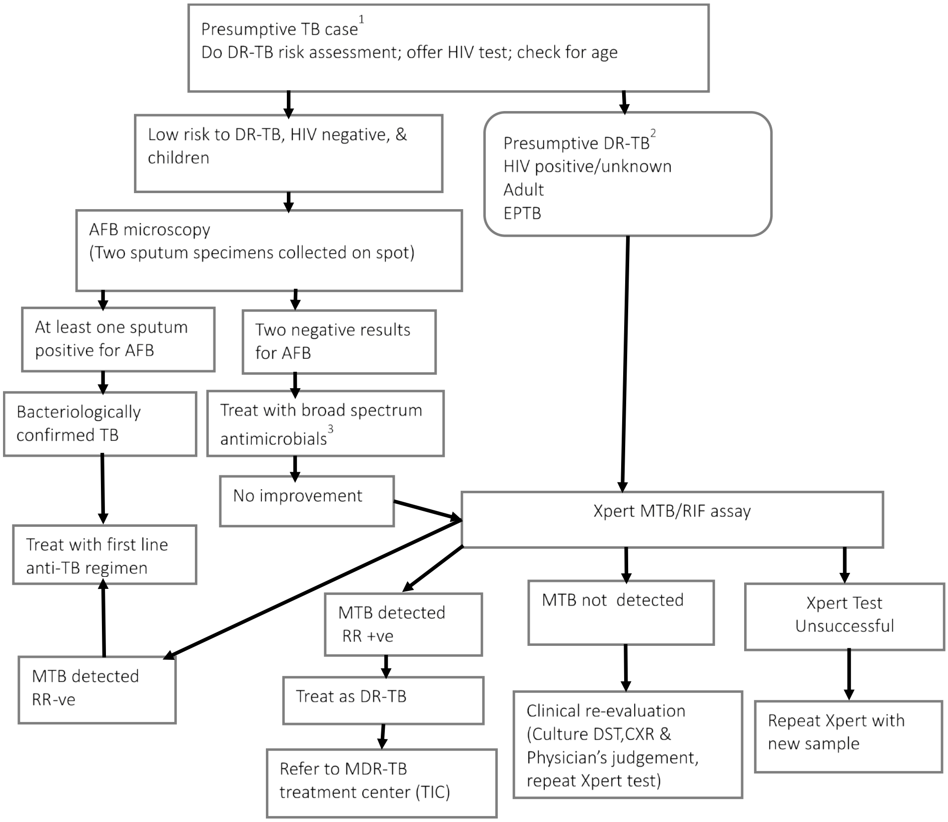

Fig.1: The National TB Diagnostic Algorithm

TB: Tuberculosis, DR-TB: Drug-resistant tuberculosis, HIV: Human Immuno-deficiency Virus, AFB: Acid fast bacilli; ETPB: Extra-pulmonary tuberculosis: MTB: *Mycobacterium tuberculosis*; RIF: Rifampicin; RR-TB: rifampicin resistant tuberculosis; CXR: Chest X-ray: MDR-TB: Multidrug-resistant tuberculosis

[1]Presumptive TB is defined as having signs and symptoms consistent with TB; mainly a cough of two or more weeks (cough of any duration if HIV positive)

[2]Presumptive DR-TB is defined as having a previous history of anti-TB treatment or a contact history with a known/ presumed patient with a DR-TB.

[3]Broad spectrum antimicrobials (excluding fluoroquinolone and anti-TB drugs) is to be given for 10-14 days

After the investigation, the referred prison inmates received medicines as needed (anti-TB drugs, broad-spectrum antimicrobials or other drugs depending on the type of disease diagnosed) and returned to the prisons. The entire procedure (from referral to diagnosis and treatment) took 2-3 working days on average. Subsequently, the prison health personnel collected the TB drugs weekly from the hospitals or nearby health facilities and the patients continued the treatment within the prisons according to the national guidelines [17]. The peer educators undertook a follow-up, provided education on treatment adherence, and encouraged the patients to adhere to the prescribed TB treatment. Bacteriological follow up examinations were done at the hospitals according to the national guidelines and the peer educators facilitated the referral for checkups as well. The peer educators also followed up those prisons inmates receiving an empirical antibiotic treatment, and rescreened and facilitated a re-referral if they did not improve within two weeks.

To incentivize the peer educators, we paid them 150 Ethiopian birr (about US$ 5.5) per month. There were also other motivations for the peer educators such as the desire to support others, the promise to receive a certificate of recognition, and increased opportunities for parole (as promised by the concerned bodies). Supervisors (prison health professionals) assigned to the intervention prisons regularly followed the intervention progress and kept an eye on the daily activities of the peer-educators.

The control sites followed the existing passive case finding system (self-referral to nearby hospitals, which use the same guidelines as in the hospitals for intervention prisons). However, we provided them a standardized up-to-date referral protocol, which was also used in the intervention sites.

Supervisors in the control sites, who were also informed about the aim of the study and the intervention, regularly followed the ongoing routine activities, with equal frequency as in the intervention sites. To control possible contaminations, the principal investigator (KA) supervised all activities closely through regular visits and phone calls in both groups.

Data on the socio-demographic and clinical characteristics, such as age, sex, and the pre-treatment symptom duration, were collected from the TB confirmed cases in both groups. Baseline data were recorded from the DOTS centers of each prison.

Outcomes

The main aim of the intervention was to detect more new cases of TB in the follow-up year. The primary outcome measure was the case detection rate (CDR) which is calculated as the number of TB cases detected divided by the estimated number of incident TB cases per year. The estimated number of TB cases (denominator) was determined by considering the WHO estimate of year 2016 for Ethiopia and attributing a fourfold TB burden to prisons (as illustrated in our prevalence survey) [1,3] and the numerator was estimated from the unpublished review of a two years DOTS record in some study prisons. Secondary outcome measures included treatment success rate (TSR) and pre-treatment symptom duration. TSR was defined as the sum of cure (smear or culture negative in the last month of treatment and on at least one previous occasion) plus treatment completion (finished the treatment with resolution of symptoms but without smear or culture result). The pre-treatment symptom duration (time from symptom onset to treatment initiation) was measured by the duration of coughing in days.

An additional outcome measure was the level of Knowledge Attitude and Practice (KAP) of the prisoners. A sample of prison inmates was randomly selected (with proportional allocation to the total number of prison inmates in each prison) and data were collected using a standardized pre-tested semi-structured questionnaire. KAP was assessed at the end of the study period in both the intervention and control prisons. The KAP outcome variables were defined considering certain selected questions (basic elements) about TB (Table 5).

Statistical analysis

We calculated the sample size accounting for the between-cluster variation, the anticipated effect size, and cluster size using a formula suggested by RJ Hayes and S Bennett [18], $C = 2+ (Z\alpha/2 + Z\beta)^2 [X_0 * Av (1/n0j) + X_1 * Av (1/n1j) + K^2 (X_02 + X_12)]/ (X_0-X_1)^2$, for pair-matched cluster randomized trials of unequal cluster size. In this formula, $Z\alpha/2$ and $Z\beta$ are the standard normal values corresponding to a level of significance α of 0.05 ($Z0.975 = 1.96$) and a power of 80% ($Z_0.80 = 0.84$); X_0 is the estimated average annual pulmonary TB CDR in the control sites (= 40%); X_1 is the average annual pulmonary TB CDR expected in the intervention sites (assuming a 50% increase, it would be 60%); K is the coefficient of variation (= 0.25); Av (1/n0j) is the mean of the reciprocals of the cluster sizes (person-years) in the control group (= 0.001); and Av (1/n1j) is the mean of the reciprocals of the cluster sizes (person-years) in the intervention group (= 0.0014). Substituting these values in the formula, the computation provides 8.6 pairs and we included eight pairs in the study considering feasibility. In addition, the sample size for the KAP study was determined using a formula, $n = (Z\alpha/2 + ZB)^2 [X_0 *(1-X_0) + X_1 (1-X_1)]/ (X_0-X_1)^2$, considering individual level randomization [18]. Similarly, $Z\alpha/2$ and $Z\beta$ are the standard normal values corresponding to a level of significance α of 0.05 ($Z0.975 = 1.96$) and a power of 80% ($Z_0.80 = 0.84$); and X_0 (22%) and X_1 (33%) are the estimated baseline mean good knowledge level and expected mean good knowledge level after the intervention (also considering a 50% increase), respectively. Substituting these values and multiplying by 1.5 to account for the clustering effect, the final sample size was fixed to be 631 for each group.

Data were entered in EpiData version 3.1 software and analyzed using IBM SPSS Statistics for Windows (version 20.0. Armonk, NY). Numerical data were presented by means (SD), where frequencies and percentages were used for categorical data. Differences in demographic and clinical characteristics of the presumptive TB and active TB cases between the intervention and control prisons were assessed using chi-square test for categorical variables and independent-samples t-test for numerical variables.

Analysis for the CDR (primary outcome) and TSR (secondary outcome) was performed at the prison level using the paired-samples t-test, where Wilcoxon signed-rank test was used as sensitivity analysis. Analysis for the pre-treatment symptom duration was done considering patients as a unit of analysis. A linear mixed model analysis was used, taking into account the clustering of patients in prisons (random intercept on prison level), to assess the significance of the mean difference in pre-treatment symptom duration between the two groups. To verify the robustness of the model's output, we also performed a sensitivity analysis by applying the same model after logarithmic transformation of the pre-treatment symptom duration. In addition, we used the generalized estimating equations (GEE) model to assess differences in the case notification rate (expressed as all cases detected and notified per 100,000 population), and KAP levels between the intervention and control groups. Group effects were expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). The pre-treatment symptom duration was adjusted for cluster size and region, while the case notification rate (CNR) was adjusted for the baseline CNR in addition to cluster size and region. The overall KAP levels were adjusted for cluster size, region, and educational level. Multicollinearity among the independent variables was assessed, where variance inflation factor greater than ten indicates a multicollinearity problem. Two-sided p-values ≤ 0.05 were considered statistically significant.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Participants flow and recruitment

Fig.2 shows the flow of prisons and study population. During the one year study period, we examined 1124 presumptive TB cases (899 in the intervention and 225 in the control prisons) from 16 prisons (N = 18,032). Of these, 75 TB cases were detected in the intervention prisons and 25 TB cases were detected in the control prisons (Fig. 2). Forty-six (61%) and eight (32%) of the cases were smear-negative in the intervention and control prisons, respectively. Three cases (two in the intervention and one in the control prisons) were positive by the Xpert test but all were susceptible to rifampicin.

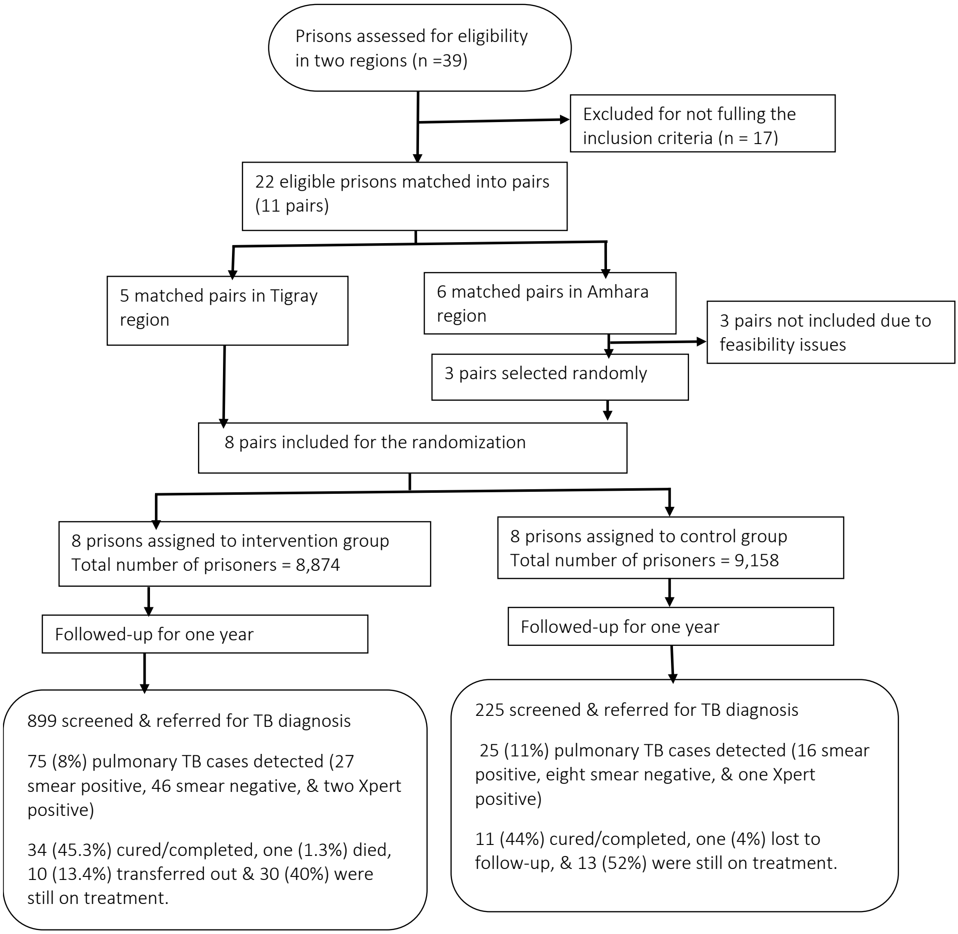

Fig. 2: Trial flowchart

Baseline data

Table 1 shows the baseline characteristics of the prisons and study population for the two groups. While the mean cluster size of the two groups was comparable, the baseline case notification rate was slightly higher in the intervention compared with the control prisons. The average floor space per prisoner was larger in the intervention sites compared to the control prisons.

Table 1: Baseline characteristics of the prisons and study population.

Variable	Study site	
	Intervention	Control
Number of prisons	8	8
Number of prisoners	8,874	9,158
Male, n (%)	8,651 (97)	8,944 (98)
Female, n (%)	223 (3)	214 (2)
Mean cluster size (SD)	1,109 (694)	1,144 (547)
Average floor space per prisoner (m^2)	1.3	0.7
Baseline CNR (per 10^5 person years)	574	481

CNR = case notification rate; m = meter; SD = standard deviation

Patients' profile

The proportion of presumptive TB cases examined for TB was four times higher in the intervention prisons compared to the control group. The demographic and clinical characteristics of the presumptive TB and TB cases were approximately similarly distributed between the two groups. Although the proportions of females screened ($p < 0.001$) and with TB ($p = 0.014$) were significantly higher in the control prisons, the numbers were still very small for both groups. The mean age of the presumptive TB cases was also higher in the control group ($p = 0.003$) (Table 2).

Table 2: Demographic and clinical characteristics of the presumptive TB and TB cases between the intervention and control prisons.

Variable	Study site		P value
	Intervention n= 8,874	Control n = 9,158	
Presumptive TB cases, n (%)	899 (10)	225 (2)	
Mean age (SD)	32 (13)	35 (14)	0.003#
Sex			< 0.001*
Male, n (%)	889 (99)	213 (95)	
Female, n (%)	10 (1)	12 (4)	
TB patients (n =100)	75	25	
Mean age (SD)	30 (12)	34 (13)	0.120#
Sex			0.014*
Male, n (%)	74 (99)	23 (92)	
Female, n (%)	1 (1)	2 (8)	
Number of HIV positive, n/total tested (%)	4/60 (6.7)	4 /19 (21.1)	0.090*
Number with unknown HIV status, n/total (%)	15/75 (20)	6 /25 (24)	0.050*

HIV = Human immunodeficiency virus; SD = Standard deviation; *** =** chi-square test; # = independent samples t-test

Outcomes and estimation

The mean CDR was significantly higher in the intervention prisons compared with the control prisons (79.8% vs. 26.9%, p = 0.010). In addition, the pre-treatment symptom duration was shortened by 8.6 days on average in the intervention prisons though this was not statistically significant (p = 0.404) (Table 3). This difference remained not significant after a log-transformation of pre-treatment symptom duration (p = 0.589). There was no significant difference in treatment success, but it was high for both groups (98.4% for the intervention vs. 97.5% for the control prisons, p = 0.791).

Table 3: Case detection rate, treatment success rate, and pre-treatment symptom duration of pulmonary TB patients (n = 100) in Ethiopian prisons after 12 months follow-up.

Variables	Study site		Treatment effect (95% CI)	P value
	Intervention Mean (SD)	Control Mean (SD)		
Case Detection Rate	79.8 (48.3)	26.9 (13.7)	52.9 (17.5-88.3)	0.010*
Treatment Success Rate	98.4 (4.6)	97.5 (7.1)	0.88 (-6.6-8.4)	0.791
Pre-treatment symptom duration in days	35 (23)	40 (35)	-8.6⁺ (-30.8-13.6)	0.404**

* remains significant in the Wilcoxon signed-rank test (p = 0.018)
⁺adjusted treatment effect using the linear mixed model
** intraclass correlation coefficient (ICC) = 0.257. ICC is not applicable for the rest.
SD: Standard deviation; CI: Confidence interval

We have also determined the Case Notification Rate (CNR). The overall CNR was 0.8% (800/100,000 prisoners) in the intervention and 0.3% (300/100,000 prisoners) in the control prisons. Further, as presented in Table 4, prisoners in the intervention group had a 1.633 times higher odds of being diagnosed with TB compared with those in the control prisons (adjusted OR = 1.633; 95% CI = 1.630-1.636). The CNR was significantly increased in prisons of Tigray than the prisons in the Amhara region (adjusted OR = 0.959: 95% CI = 0.957-0.961). The odds of finding the cases increased with an increase in baseline CNR (adjusted OR = 1.239; 95% CI = 1.238-1.240) while it decreased with an increase in cluster size (adjusted OR = 0.976; 95% CI = 0.976-0.977).

Table 4: The adjusted impact of educational and screening interventions on TB case finding in Ethiopian prisons.

Variables	AOR (95% CI)	P value
Study group		
Intervention	1.633 (1.630-1.636)	< 0.001
Control	ref.	
Region		
Tigray	0.959 (0.957-0.961)	<0.001
Amhara	ref.	
Baseline CNR (every 50 increase)	1.239 (1.238-1.240)	<0.001
Cluster size (every 500 increase)	0.976 (0.976-0.977)	<0.001

AOR = Adjusted odds ratio; CI = Confidence interval; CNR = Case notification rate; ref. = Reference

Trends of TB case finding

Fig. 3 shows the trends of finding cases over the intervention period. The trends were consistently higher in the intervention prisons compared to the control prisons.

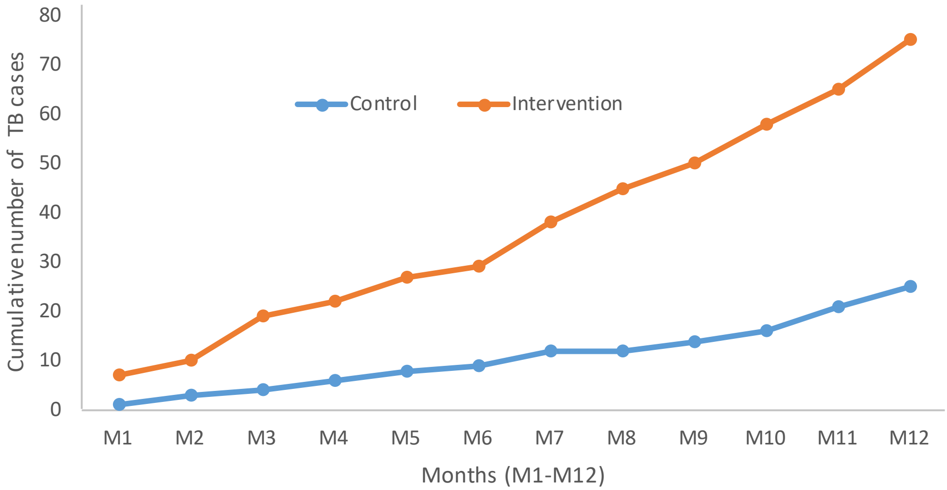

Fig.3: Trends of TB case detection in Ethiopian prisons over a one year intervention period, 2016/17.

Knowledge, attitude, and practice

There were significant differences on several KAP elements among randomly selected prisoners in both groups. The proportion of prisoners who recognized the real cause of TB, knew the free treatment availability, and mentioned visiting a health care facility for TB symptoms at their earliest time possible, was significantly higher in the intervention prisons compared to the control prisons. In general, there were significant improvements in the overall knowledge ($p < 0.001$), and practice ($p = 0.003$) levels in the intervention compared to control prisons (Table 5). The differences remained significant after adjustment for educational level, region, and cluster size in a GEE model (adjusted OR = 2.54; 95% CI = 1.93-3.94 for good knowledge level and adjusted OR = 1.84: 95% CI = 1.17-2.96 for good level of practice). However, there was no significant difference in favorable attitude between of the two groups (adjusted OR = 0.80: 95% CI = 0.52-1.25).

Table 5: Knowledge, attitude, and practice relating TB among prisoners in intervention and control prisons in Ethiopia.

Variables	Study site		P value**
	Intervention (N = 601) n (%)	Control (N = 617) n (%)	
Knowledge			
Germs/bacteria cause TB*	368 (61)	216 (35)	<0.001
TB transmits through coughing droplets*	571 (95)	555 (90)	0.227
Coughing for 2 or more weeks might be a TB symptom*	549 (91)	519 (84)	0.359
Covering mouth when coughing/ sneezing prevents TB*	525 (87)	527 (85)	0.951
Know the free TB treatment availability*	511 (85)	408 (66)	0.001
Attitude			
Perceive TB as a very serious disease¶	477 (79)	531 (86)	0.095
Visit health facility for TB symptoms¶	403 (67)	388 (63)	0.594
Feel compassion and a desire to help TB patients¶	417 (69)	389 (58)	0.324
Practice			
Prefer to visit modern health care+	581 (96)	588 (95)	0.838
Visit health care as soon as realizing TB related symptoms+	420 (70)	342 (55)	0.005
Overall KAP			
Prisoners with good knowledge	275 (46)	155 (23)	< 0.001
Prisoners with favorable attitude	225 (37)	227 (34)	0.887
Prisoners with good practice	410 (68)	330 (49)	0.003

* = Prisoners that mentioned all these five items were categorized as having a 'good' knowledge and those who missed one or more of these items were categorized as having 'poor' knowledge; ¶ = Prisoners that mentioned these three items were categorized as having a 'favorable' attitude and the others were categorized as having 'unfavorable' attitude; + = Prisoners who mentioned these two items were categorized as having a 'good' practice and the rest were categorized as having a 'poor' practice; ** = p-value from the chi-square test; TB = Tuberculosis; KAP = Knowledge, attitude and practice.

Discussion

To our knowledge, this study is one of the few randomized controlled trials conducted in prisons to investigate the impact of trained inmate peer educators on improving important health outcomes among prison inmates. We have shown that involving trained prison inmates in TB awareness and symptom-based screening significantly improved the TB case detection rate. In addition, it was possible to shorten the pre-treatment symptom duration by 8.6 days on average, though this difference was not statistically significant. We did not find a significant difference in the treatment success rate, but it was high for both groups.

Previously, only a few studies have been conducted in prisons on this topic. A pre-post interventional study from Indian prisons showed an increase in TB case finding through regular educational mobilization of the prison inmates by the prison authorities and prison health staff [14]. Moreover, a qualitative report from Zambian prisons reported that trained inmate peer educators successfully facilitated the TB screening and treatment adherence support for their fellow prison inmates [4]. Even though the former study involved professionals (and not peer educators) and the latter was only qualitative, both studies suggested that enhanced case finding with improved access to diagnostic services in prisons has value in improving TB case detection, which is consistent with our findings.

The findings of the current study have important clinical and public health policy implications, particularly in prisons of poor countries where the TB burden is high and the internationally recommended TB diagnostic and treatment algorithms have generally not been implemented [10,19]. Our study shows that the TB case detection in resource-limited prisons could significantly be improved by involving the prison inmates themselves in the TB control program with very little monetary support to the trained prison inmates and voluntarily supervision by the prison health personnel. Surprisingly, these achievements were attained solely by employing active symptom-based entry and ongoing screening and creating improved access to the routinely available diagnostic tools. This might imply that, in such resource-poor, high-risk settings, TB programmers and NTPs should not only focus on adapting and introducing the better screening and diagnostic tools (such as the Xpert MTB/RIF rapid), but also may need to give a priority in using such potentially feasible and sustainable public health interventions.

In a subgroup analysis on smear status, the proportion of smear-negative cases detected was higher in the intervention prisons (61%) compared to the controls (32%). This could be due to the fact that the active screening was done not only for patients with prominent TB symptoms but also for those with mild symptoms (at least coughing for 2 or more weeks) who tend to be smear-negative [20,21]. On the other hand, such patients might not have been diagnosed in the control sites as a priority for referral is given for those with severe symptoms who tend to be smear-positive [20]. However, it is worthy to mention that our reliance on the routinely available diagnostics (microscopy and X-ray), without considering culture (the gold standard diagnostic) [22], and the possible variability in the performance of clinicians across the hospitals could have affected our results.

The ultimate goal of improved TB case finding interventions should be reducing TB burden through early detection and disrupting the chain of transmission [23]. With the continuous health education campaigns, subsequent preventive actions (such as opening the windows) and active screening, we anticipated that the majority of undiagnosed TB cases in the intervention prisons would be detected in the beginning of the intervention unless new cases were constantly being introduced through the entry of new prisoners. However, in the trend analysis, the number of TB cases detected remained high throughout the intervention period and may suggest a sustained transmission of the disease. This might be due to the relatively short intervention period. The impact of improved case finding on TB burden is likely to be seen only after several years of delay [24], hence a trial could be considered over a period long enough to measure such impact. A study from a Bangladeshi prison, for example, showed an incredible drop in reported TB cases over five years after the implementation of intensified case finding interventions [25]. The effect of infection prevention measures would be minimal in prisons of poor countries where the prison cells are overcrowded and poorly ventilated, and segregation of symptomatic prison inmates is not practical due to lack of rooms for such purpose [26].

Further analysis shows that prisons in Tigray had a better performance in finding cases than prisons in the Amhara region. This variation could partly be attributed to differences in the capacity and cooperation level of referral sites (hospitals). The hospitals in Tigray received and investigated all referred prison inmates with presumptive TB, while one of the hospitals in the Amhara region (Dessie referral hospital) raised concerns about resource availability and limited the number of presumptive TB cases to be diagnosed (giving priorities for those with prominent symptoms), which might have influenced the performance of trained prisoners. The odds of case finding increased with increasing the baseline CNR. This relation is expected, as prisons with high baseline TB prevalence would tend to have a high burden of undiagnosed TB. Yet, interestingly, this might imply that those prisons with a high burden of TB could be the ones that would be greatly benefited from such interventions.

Furthermore, the proportion of prison inmates with a good knowledge and good practice was significantly higher in the intervention prisons. Previously, an intervention study that involved health professionals has shown improvements in the awareness and practices of TB in the general population in Ethiopia [27]. However, as our study involved the prison inmates themselves, it would have particular implications for addressing TB KAP gaps in prisons of resource-poor countries where there is a shortage of health professionals.

One of the drawbacks of cluster-randomized trials is that the baseline characteristics tend to distribute in an unbalanced manner among the groups if the clusters are few [28]. In our study, the randomization was done following matching of prisons into pairs, which avoids such a problem to a certain extent. In addition, as the mean cluster size was high and the intervention effect large, the study had an acceptable level of statistical power. A possible limitation of this intervention is that we did not consider the dynamic nature of the prison population for estimation of the end outcomes. We considered the number of prison inmates at baseline of the study as a denominator for the estimation of the outcomes. However, data collected on the number of prison inmates from the study prisons each month during the intervention period showed that the average number of prison inmates was not significantly different throughout the years suggesting that our estimation was still reliable. Another limitation could be a possible recall bias for some questions such as time of symptom development. We used a carefully constructed questionnaire with specific details and the participants were given enough time to think calmly and thoroughly before answering the questions to minimize such bias. Additionally, for a long-term implementation of peer interventions in prisons the “peer retention” issue could be a challenge; due to a subsequent release and transfer of the trained peers, frequent recruitment and training might be needed.

This intervention model could be scaled-up in other Ethiopian prisons and could possibly be adapted in other prisons in resource-limited countries with a high TB burden. Several setting-specific issues should be taken into account when considering implementation in other settings. In our study prisons, the prison inmates were socialized (staying in friendly groups and moving freely in the compound) and the prison health personnel and guards supported all activities pertaining to the intervention. With the scarcity of prison health professionals, high burden of undiagnosed TB, and the potentially similar conditions as in Ethiopian prisons [26], we believe that our intervention model would be applicable to fight TB in the prisons of other Sub-Saharan African countries. Our intervention model could also be applied to other health issues in prison populations. Evidence from systematic reviews of the published studies from prisons suggested that peer education interventions were effective in reducing risky sexual behavior, significantly reducing the risk of HIV transmission, and were acceptable to prison inmates [15, 16].

In conclusion, involving trained inmate peer educators in the TB control program in Ethiopian prisons significantly improved the TB case detection rate. This intervention model has a high potential for widespread implementation across Ethiopian prisons and could be considered for adaptation by prisons in other resource-limited regions with a high burden of TB.

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Chapter 6

General Discussion

Introduction

In this chapter, we discuss the main findings, conclusions and recommendations of the studies presented in this thesis. Furthermore, the strengths and limitations of the studies are summarized and suggestions for further research are highlighted.

Key findings include a high prevalence of undiagnosed TB among prisoners, a lack of a linkage and tracking system for prisoners transferred or released before treatment completion, a poor knowledge level of prisoners about TB, and a highly effective intervention for TB case finding in resource-limited prisons.

Undiagnosed tuberculosis among prisoners

Our active case finding survey revealed that the prevalence of undiagnosed TB was high among northern Ethiopian prisoners with more than a half (55%) of the symptomatic TB cases left undiagnosed for a long time (up to 2 years). This represents a hidden epidemic, which poses a serious health risk for prisoners and the general population. In Ethiopia, the prison health care services are very weak and no systematic screening has been done either at the time of entry, follow-up or exit from prisons [1,2]. In addition, as there are no adequate segregation systems, such symptomatic and potentially diseased prisoners stay together with other prisoners in the overcrowded and poorly ventilated rooms, becoming a source of onward transmission to their fellow prisoners, and potentially to the general population through visitors, prison staff and discharged prisoners [2-4].

Similarly, a high prevalence of undiagnosed TB (ranging from 3.5% to 7.7%) has been reported from other prisons in LMICs, including prisons from Georgia, Bangladesh, Zambia, and South Arica [5-8]. This possibly refers to the limited access to timely TB services in prisons and indicates the inadequate performance of the internationally recommended passive case-finding strategies in these settings.

Emerging data suggest that, in order to end the TB epidemic, dependence on the passive case-finding approach should be abandoned, especially in prisons of high-TB burden regions [6,9]. Despite being resource demanding, active case finding strategies have contributed significant gains over the WHO endorsed DOTS approach in reducing the TB burden [10]. A systematic review of published studies on screening practices in prisons showed that prisons implementing routine TB screening had significantly lower TB burden than prisons without routine screening policies [11].

In order to tackle the problem of undiagnosed TB in prisons, case finding should systematically be performed at different levels. Most importantly, as prisoners often come from poor communities with a high TB burden, entry-screening programs are needed to detect the undiagnosed active TB cases early and reduce the harmful consequences of such cases in the overcrowded settings [12]. In addition, entry screening captures cases that discontinued treatment due to incarceration, reducing the emergence of drug-resistance in prisons [9]. A report from Mongolian correctional facilities, for example, indicated that there was a remarkable drop (60%) in active TB notification after establishing systematic screening programs upon entry into jails and prisons for 10 years [13].

Mass screening, often conducted in the context of cross-sectional prevalence surveys, has also been useful in finding undiagnosed TB cases, but is not recommended as a sole means of finding active TB cases in a prison. This approach should be complemented with other strategies (entry screening, contact investigation and ongoing passive case finding) to ensure that prisoners with TB who entered a prison or cases that occurred between the periodic surveys are detected effectively [9]. For example, use of a combination of systematic screening and X-ray screening upon entry for two years has reduced the TB prevalence by 53% in a Brazilian prison [14]. In addition, periodic mass screening may not be sustainable in resource-limited countries [9]. Entry and referral screening, with a periodic screening at release, has been effective for case finding and suggested for such countries, instead of the resource-intensive mass screening [5].

The lack of sensitive screening and diagnostic tools remain a huge challenge for the TB control program in prisons, especially in resource-limited countries [15]. According to a systematic review, use of X-ray screening and symptom screening has a better accuracy for TB detection in prisons, and the algorithm has been recommended to be adapted in the prisons of high-TB risk countries [11]. Despite this, most of the prisons in such countries (75%) have relied on symptom-based screening, largely due to resource limitation [11]. Symptom screening is less sensitive and may underestimate the actual prevalence of active TB in a prison [16]. Reliance on the WHO symptom-based algorithm would have led to a missed diagnosis in 79.1% and 61.8% of the TB cases in Brazilian and Bangladeshi prisons, respectively [6,17]. Similarly, 33% of the prisoners with culture-positive TB in Zambian prisons did not report any of the symptoms and thus would have been missed [5]. Such findings caution against the use the symptom algorithms and strongly highlight the need for the development of more sensitive screening and diagnostic algorithms for prisons of resource-limited countries. However, given the importance of early TB diagnosis in these overcrowded and endemic settings, local governments of LMICs should invest more at least to incorporate the best available screening tool (radiography-based screening) in addition to symptom inquiry in prisons [17].

Bacteriological-based active case-finding surveys (use of both microscopy and culture) have better yield for detecting TB, especially for HIV infected prisoners, where symptoms are usually minor, or radiological findings are absent [11,18]. However, as culture is resource-intensive and time-consuming, it would not be feasible to be used as a routine diagnostic test in resource-limited prisons and high burden regions. Rapid and accurate point-of-care tools are thus required to overcome the challenges of undiagnosed TB in prisons. Such novel tests need also be able to detect drug resistance rapidly and monitor treatment progress, to detect insufficient treatment sooner. However, the

WHO endorsed molecular test, GeneXpert (MTB/RIF), has also been shown to have a remarkable diagnostic performance, where the test simultaneously detects rifampicin resistance (key component of the first-line treatment regimen) and provides results in significantly less time [19]. Pragmatic data show that MTB/RIF is feasible, accurate and effective, giving a sensitivity of 97% and specificity of 99% for TB detection in the general population of LMICs in Africa [20]. MTB/RIF is also expected to have excellent performance in prison settings in LMICs [21,22], but empiric data on its effectiveness, cost-effectiveness and feasibility (implementation strategy) in such settings are scarce.

Another important issue related to undiagnosed TB in prisons is HIV infection. HIV infection is a major risk factor for the development of active TB in those who acquire new *M. tuberculosis* infection or have latent TB [23]. Thus, health services for prisoners must be aligned synergistically for both diseases, especially in prisons of Sub-Saharan Africa where the HIV prevalence is very high [24]. Provision of isoniazid preventive therapy (IPT) for HIV patients may effectively interrupt the progression of infection to active TB disease and minimize the transmission of *M. tuberculosis*. However, concerns remain whether IPT should be started in settings with short imprisonment stays or when isoniazid resistance is a big concern [21,25]. Novel tests that can predict the progression of latent TB to active TB (and identify the high-risk groups) would be important to guide preventive therapy and address such challenges.

In general, in order to keep the good progress on TB control and possibly achieve the 2035 End TB targets, Ethiopia should give due emphasis to addressing undiagnosed TB in its prisons. The National TB control program (NTP) and related stakeholders should work in establishing systems that strengthen active screening and improve access to diagnosis. As a first step, NTP should introduce the routinely available diagnostic tools (at least sputum microscopy) in the prison clinics. Equally important are introducing entry screening programs (at least, using TB symptom questionnaire), strengthening the referral system for all prisoners and guards with TB symptoms, strengthening TB/HIV collaborative activities, and ensuring segregation and treatment of the detected cases [9]. Even though it could be challenging to implement such activities routinely with the available resource in the increasing Ethiopian prison population, our new intervention model included in this thesis presents good options to overcome the challenges. However, in order to end the epidemic, the Ethiopian government will need to invest much more in transforming the prison health care system, improving prison conditions, particularly reducing overcrowding, and adapting and introducing the globally recommended approaches in the prisons.

Tuberculosis treatment outcome and loss to treatment follow up

Findings from analysis of five-year retrospective treatment outcome data in four northern Ethiopian prisons showed that the overall treatment success rate for prisoners who initiate and complete their treatment while in the same prison was high (94%), which suggests that the DOTS program is effectively functioning in our study prisons.

However, prisoners released or transferred to other prisons during the course of their TB treatment were not linked to health facilities. A major concern is that such patients are often more likely to interrupt their treatment and develop drug-resistant TB strains [26]. As prisoners are often poor and unemployed [27], released prisoners may not be able to afford to pay transportation to go and receive treatment at a healthcare facility or may give priority to searching a job. In addition, released or transferred prisoners may not have enough knowledge about the harmful consequences non-adherence to TB treatment and might be reluctant to continue their treatment [28]. Such patients, therefore, impose a serious health risk to other prisoners and the community. Released prisoners may import the potentially drug susceptible and curable former TB strain in a form of drug-resistant strain back to the previous prison through re-incarceration, propagating the vicious cycle of the transmission [18].

This issue brings serious challenges to the TB control efforts in Ethiopia and urges the need to implement appropriate interventions. NTP and the prison authorities should take immediate initiatives in establishing strategies that tackle this problem. Such a strategy could be establishing and strengthening communication systems between the transferring and receiving prisons or between the releasing prisons and public health facilities. For example, mobile-based tracking systems have been shown to improve TB/HIV treatment adherence in general populations [29,30] and could be good options to track prisoners released or transferred before treatment completion. In addition, limiting the transfer of prisoners on anti-TB treatment (especially during the intensive phase), except when the transfer is compulsory for security or other health conditions, would help to reduce loss to follow-up [31].

Tuberculosis knowledge, attitudes, and practices (KAP) among prisoners

The results of our KAP survey from eight northern Ethiopian prisons showed that a substantial proportion of prisoners (41%) had favorable attitudes about TB, and more than a half (55%) had a good practice towards TB. However, only 24% of them knew the real cause of TB. The majority related it mainly either to exposure to cold wind, spoiled soil (a soil with a bad odor), poor hygiene, or smoking, which is similar to misconceptions reported in previous studies from Eastern Ethiopian prisons and communities in different parts of Ethiopia [32-34].

Such misconceptions should be targeted, as they contribute to treatment delay and spreading of the disease [35-37]. Particularly, the misconception of cold wind, locally known as nefas/b'ird, can affect care-seeking behavior and fuel the spread of TB in the overcrowded Ethiopian prisons. It is more likely that prisoners with such misconception would keep their windows closed to protect them from the "cold wind" creating ideal conditions for TB spread [28]. This scenario is popular among people who often use public transports in Ethiopia where most passengers will complain if anyone tries to open a window. Smoking could also lead to delayed diagnosis and treatment, as smokers may perceive their prolonged cough as a cause of smoking instead of TB. This has implications for Ethiopian prisons where 21% of the prisoners with a cough symptom have been shown to be smokers [38].

Another interesting finding was that the majority (63.7%) of the prisoners were not aware of the possibility of getting MDR strains due to treatment non-adherence. This poses a great concern to NTP, also as mentioned above, due to that those prisoners released or transferred to other prisons before treatment completion are not linked to health facilities.

In general, our findings signify the need to implement health education interventions in the prison settings across the country. An educational intervention model that involved trained health professionals has previously been shown to successfully transform such misconceptions, thus significantly improving TB diagnosis and treatment compliance in the general population in Ethiopia [39]. However, adapting this intervention approach to Ethiopian prisons may be difficult due to the shortage of health professionals. Thus, much more efforts are urgently needed to design the most appropriate and sustainable educational intervention models to these settings.

Training prisoners for tuberculosis case finding: opportunities and challenges

The findings from the randomized controlled trial show that, despite some programmatic challenges, empowering and involving prisoners in TB awareness campaigns and symptom-based screening was highly effective in increasing TB case detection rates, and reducing misconceptions about TB, in resource-limited prison settings. Previously, a systematic review suggested that peer education interventions were highly accepted by prisoners and effective at reducing risky behaviors among prisoners [40]. Moreover, a qualitative study from Zambian prisons indicated that trained inmate peer educators had a significant contribution in assisting the TB/HIV screening and treatment services [5]. Recently, the USAID advocates peer-education programs for inmates and staff as a potential strategy to reduce TB/HIV burden in Tanzanian prisons [41]. However, to our knowledge, the current study is the first to empirically assess the impact of such interventions on TB control in prisons.

The findings of this study have wider clinical and public health policy implications, especially in prisons of Sub-Saharan African countries. It is clearly defined that, at a minimum, all convicted inmates in the high TB burden countries should be given symptom-based screening upon entry and that the referral system should be strengthened for those residing in prisons [9]. However, such assessments are not usually done in most prisons in the Sub-Saharan region, because of human resource and other constraints [15]. Increasing the health service coverage through training of health workers to fill this gap seems a remote possibility. The current intervention model demonstrates the best option to address the chronic shortage of human resource in such settings, and enhances TB screening and case detection through improved access to the available diagnostic facility.

The success of peer-based health interventions in prisons, as also clearly observed in our study, is largely dependent on organizational support, and the social context within prisons (prisoner relationships and prison life) [42]. The prison authorities and health staff need to recognize and support peer educators. In addition, there should be a positive and respectful peer-to-peer interaction to effectively deliver peer-based interventions in prisons. In our study prisons, prisoners were well socialized (staying in friendly groups and moving freely in the compound) and the prison health personnel and security forces supported all activities pertaining to the intervention. Within this context, opportunities exist to scale up the current intervention model to all prisons in Ethiopia. As the healthcare delivery, imprisonment systems, and socialization levels across Ethiopian prisons are similar [43], we believe that this intervention model can easily be scaled-up to other Ethiopian prisons with a minimal funding support and commitment from the government. Such approaches are not completely new to Ethiopian prisons; there is a trend of selecting certain prisoners (so-called “Yettena Abbat” or “father of health”) and grant them a responsibility to handle health-related issues of their fellow prisoners. Those prisoners are in charge of facilitating the examination of prisoners with complaints of any disease by the prison health professionals. The current intervention model can, therefore, be launched within the same framework.

The intervention model can also be adapted in prisons of other Sub-Saharan African countries where undiagnosed TB is high and trained health professionals are scarce [15]. Similar to our study prisons, inmates in such prisons live crowded together, which creates an opportunity to deliver awareness campaigns and undertake screening activities [15,44]. Moreover, similar intervention models can be applied to other health issues in prison populations in Ethiopia (such as for mental disorders), as well as in high-income countries, as also highlighted in observational studies [42].

However, during our project implementation, we encountered several programmatic and clinical challenges and these should be considered when scaling-up or adapting the intervention model. First, even though the number of presumptive TB cases identified through the active screening was high, one of the referral facilities complained about resource constraints and resisted to undertake a diagnosis at its maximum capacity. Loss of inmate follow-up was also a challenge for prisoners released or transferred before treatment completion, as our study prisons had not established systems for tracking such patients. Moreover, while prison health professionals in our study have incredibly supported the intervention, a qualitative study from Zambian prisons highlighted that they encountered resistance from some prison personnel to undertake the supervision voluntarily [5]. The recognition and mitigation of such resistances will, therefore, be critical to the sustainability of such interventions. Another possible challenge for such interventions is that peer educators may sometimes lack technical knowledge and confidence to correct client misconceptions and concerns [45]. Adequate training and assessment should, therefore, be given to peer educators before they start delivering the service.

Lessons learned from the perspective of a researcher

We successfully explored the feasibility of working in prisons of resource limited regions. From a distance, it seems very difficult and complicated to work in such settings, but we received excellent cooperation from the prison authorities, prison health personnel, and prisoners together with us managed to conduct a large randomized trial covering 16 prisons in two big regions of Ethiopia. Rather paradoxically, the captive nature of the prisons also created a conducive environment for us to easily conduct health education, screening, and treatment follow-up interventions.

The trial was carried out with a small budget (student scholarship funding from Nuffic) illustrating the possibility of conducting even complicated intervention research in resource-constrained environments. People from different sectors were generally cooperative and human labor was relatively cheap for the intervention, follow-up, and supervision services. Thus, our experiences are a good example for other researchers in resource-limited regions.

Strengths and limitations

The major strength of our study is its comprehensiveness: we investigated the broad spectrum of TB (from defining the extent of the problem to designing and implementing a feasible intervention strategy) in a neglected and high-risk setting. Nevertheless, several limitations must be considered. First, due to feasibility issues, the number of clusters included in the randomized trial was relatively small. However, the number of people in each cluster (cluster size) was large and the sample size was estimated considering a power of 80%, which is sufficient. The randomization was done after matching prisons into pairs, so to avoid a possible deranged distribution of baseline characteristics among the study groups. We therefore believe that this limitation did not systematically affect our findings. Then, we did not consider extrapulmonary TB cases for the active case screenings, and the drug-resistance pattern of our TB isolates was not determined due to diagnostic and logistic obstacles.

Conclusions

Based on our findings, we come to the following conclusions and forward recommendations for the concerned bodies, including for TB service providers, program managers, and policymakers.

1. The high prevalence of undiagnosed TB in Ethiopian prisons represents a serious health risk for prisoners and the general population and threatens recent progress made on TB control in Ethiopia.
2. The absence of entry, follow-up, and exit screening in Ethiopian prisons means that these settings are freely serving as importers, amplifiers, and exporters of TB and drug-resistant TB.
3. The lack of appropriate linkage and tracking systems for prisoners transferred or released before treatment completion threatens national TB control efforts, with the risk of TB and drug-resistant TB spread in the general population.
4. Prevailing misconceptions on the cause of TB and consequences of non-adherence to TB treatment among prisoners, contribute to treatment delay and potentially fuel the spread of TB and drug-resistant TB in overcrowded Ethiopian prisons. Moreover, it creates opportunities for the emergence and spreading of drug-resistant TB strains in the general population, where prisoners released before treatment completion join without linkage to public health facilities.
5. Empowering and involving prisoners in TB awareness creation campaigns and symptom-based screening was highly effective in improving TB case finding (detecting of the undiagnosed TB) and reducing misconceptions of TB in resource-limited prisons.
6. Despite programmatic challenges, opportunities exist to scaling-up the current intervention model to all prisons in Ethiopia and adapt it to similar settings elsewhere, especially in Sub-Saharan Africa.
7. In order to end the TB epidemic, more efforts must be put into transforming the health care system and the overcrowded conditions of the prisons, and adapting the globally recommended screening and diagnostic approaches (notably the radiography-based screening and Xpert assay) in the prisons. If we want to see our TB control efforts succeeded in Ethiopia, the government should pay much more attention for prisons and should invest in introducing and strengthening such diagnostic services in the prisons and will need to consider using simple public health intervention like ours.
8. Conducting randomized trials is possible in resource-limited regions even with a limited budget, and conducting research in prisons of developing countries is perhaps easier than perceived.

Future study plans

While the current intervention incurred minimal costs, due to the fact that the peer educators and supervisors were generally volunteers, further cost-effectiveness assessment may be needed before large-scale and sustainable implementations are initiated. Importantly, the long-term costs of training and supervising inmate peer educators should be investigated and established. In addition, further empirical assessments are needed to establish effective approaches for tracking released prisoners during their course of TB treatment and prevent the possible loss to follow-up, and emergence of drug-resistant TB in the community.

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Summary

The studies presented in this thesis defined the burden of TB and factors driving TB in Ethiopian prisons and explored a potentially feasible intervention model for TB control in resource-limited prison settings.

Chapter 1 regards the results of relevant literature upon which we structured our research questions. It describes the existing challenges facing the global TB control program and justifies the rationale for the planned investigations.

Despite the huge progress on its control, TB remains a global public health concern. With an estimated 10.4 million incident cases worldwide and 1.4 million deaths each year, TB still takes a huge death toll, particularly in Africa. Ethiopia remains one of the 30 world's high TB/MDR-TB burden countries where more than 26,000 TB fatalities occur every year. The majority of the TB cases and fatalities occur among the most productive age groups, imposing a significant economic burden and impeding the country's progress toward middle-income status.

Missed or delayed diagnoses and poor access to the high-quality care represent major obstacles to the global TB control program. Each year an estimated three million individuals with active TB do not receive a diagnosis and remain a source of onward transmission of the disease, particularly in low- and middle-income countries. Overlooking high-risk populations such as prisoners from control programs is a major factor for these failures. This is particularly important for prisons in Sub-Saharan Africa, including Ethiopian prisons, where HIV infection and poverty are prevalent, and the internationally recommended TB control guidelines (early case detection and treatment, prompt isolation of contagious inmates, etc.) are not under practice. The lack of resources and organized health systems in prisons of these countries limits the implementation such guidelines. On the other hand, accurate data required to develop optimized and potentially feasible interventions, to tackle the ominous problem of TB in prisons of such countries, are scanty and unreliable.

Considering these gaps, we centered this thesis on the following four principal objectives. First, we investigated the prevalence and factors associated with undiagnosed TB among prisoners. Second, we determined the treatment success rate (TSR) of prisoners with TB and assessed the risk factors for unsuccessful outcome. Third, we assessed the knowledge, attitudes, and practices (KAP) of prisoners about TB. Fourth, based on the findings of these studies, we designed and executed an intervention to tackle the problem of poor knowledge and a high burden of undiagnosed TB in prisons.

The study investigating the prevalence of undiagnosed TB is presented in Chapter 2. In total, 9299 prisoners were screened for TB symptoms using a standardized symptom-based questionnaire in nine prisons of Tigray. Sputum samples were collected from 844 symptomatic patients and direct microscopy and culture were done for TB diagnosis. HIV testing was conducted using rapid test kits. Moreover, data on sociodemographic and general health status of the participants were collected using a structured questionnaire.

Our findings show that the prevalence of undiagnosed TB was high among prisoners in Tigray. Out of 809 presumptive TB cases with culture result, 4.0% were confirmed to have undiagnosed TB. The overall estimated point prevalence of undiagnosed TB was 505/100,000 prisoners. In addition, 4.4% (36/809) the presumptive TB cases, and 6.3% (2/32) undiagnosed TB cases were infected with HIV. Chewing Khat (OR = 2.81), and having had a close contact with a TB patient (OR = 2.18) were found to be predictors of undiagnosed TB among presumptive TB cases.

The prevalence found in this study is more than two folds higher than the estimated prevalence of undiagnosed TB in the general population of Tigray (216/100,000 population). This is a serious problem because undiagnosed patients would become a source of continual transmission to their fellow prisoners, and potentially to the general population through visitors, prison staff and discharged prisoners. In conclusion, much effort is needed to improve TB case detection in the study prisons.

Chapter 3 presents the results of a retrospective analysis on the treatment outcome of TB cases and risk factors for unsuccessful outcome in northern Ethiopian prisons. In this study, the profile and treatment outcomes of all prisoners diagnosed with TB between September 2010 and August 2015 was retrieved from the TB treatment follow-up clinics of the four selected prisons. Patients' information such as age, sex, the type of TB case, the treatment category, the date of treatment initiation and completion, weight at the time of treatment initiation, HIV status, and other related data were recorded using a standardized recording format.

Our analysis has shown a high rate of treatment success (94%) for the prisoners that initiate and complete treatment while in the same prison. Briefly, out of the 496 patients, 11.5% was cured, 68% completed treatment, 2.5% was lost to follow-up, 1.6% was with a treatment failure, 1.4% died, and 15% was transferred out. Surprisingly, none transferred out or released prisoners were appropriately linked to health facilities. The odds of unsuccessful outcome was 4.68 times greater among re-treatment cases compared to the newly treated cases. The year of treatment was also associated with variations in TSR; those treated during the earlier year were more likely to have an unsuccessful outcome. Sputum non-conversion at the second-month check-up was strongly associated with unsuccessful outcome among the smear-positive cases.

While the high rate of treatment success in the study prisons is encouraging, the lack of linkage and tracking systems for those prisoners transferred or released before their treatment completion will have a negative implication for the national TB control program as such patients might interrupt their treatment and develop drug-resistant TB. The national TB control program (NTP) and the prison authorities should, therefore, take immediate initiatives in establishing strategies that tackle this problem.

In chapter 4, we described the findings of the KAP survey. Data on the socio-demographic characteristics, prison history, and KAP measures were collected from 615 northern Ethiopian prisoners using a semi-structured standardized questionnaire. The outcome variables were defined considering selected items (so-called basic elements) about TB. Accordingly, levels of KAP were dichotomized and categorized as 'good' knowledge vs. 'poor' knowledge, `favorable' attitude vs. `unfavorable' attitude, and 'good' practice vs. `poor' practice.

Our findings suggest gaps in knowledge, attitudes, and practices with regard to TB among the participating prisoners. Only about four out of ten prisoners were able to recognize germ/bacteria as a cause of TB. The majority related it mainly either to exposure to cold wind, spoiled soil (a soil with a bad odor), poor hygiene, or smoking. In addition, 63.7% was not aware of the possibility of getting MDR strains due to treatment non-adherence. Overall, only 24% knew the basic elements about TB, 41% had favorable attitudes, and a bit more than a half (55%) had a good practice towards TB. Prisoners who were urban residents were generally more knowledgeable than rural residents (OR = 2.16). Illiterates were found to be less knowledgeable (OR = 0.17), less likely to have a favorable attitude (OR = 0.31), and a less good practice (OR = 0.35). Significant differences were also observed between the different study prisons.

The identified misconceptions should be targeted, as they would contribute to treatment delay and spreading of the disease. Particularly, the misconception of cold wind, locally known as 'nefas/bird', could affect care-seeking behavior and fuel the spread of TB in the overcrowded Ethiopian prisons. This urges the need to design and implement appropriate and sustainable educational intervention models in the prison settings across the country.

Based on the results of the above-mentioned studies, we conducted a cluster-randomized trial to assess the impact of trained inmate peer educators on improving TB case detection, treatment success rate, and reducing pre-treatment symptom duration in northern Ethiopian prisons. This study is described in chapter 5. Sixteen prisons in the two regions of Ethiopia (with a total population of 18,032) were first matched into pairs. Randomization was then done within matched pairs in which eight prisons from each pair were assigned to the intervention and the remaining ones to the control group. From each intervention prison, prisoners were selected and trained for three days about TB. The trained prisoners (inmate peer educators) then provided health education about TB every two weeks on a regular basis for one year and undertook routine symptom-based TB screening for a referral. The primary outcome measure was the case detection rate at the end of the one year intervention period. In the control prisons, cases were detected within the existing passive case finding approach.

During the one-year study period, 75 and 25 pulmonary TB cases were detected in the intervention and control groups, respectively. The mean case detection rate was higher in the intervention prisons than in the control prisons (79.8% vs. 26.9%). It was also possible to shorten the pre-treatment symptom duration by 8.6 days on average, though this difference was not statistically significant. In addition, the overall TB knowledge (OR = 2.54) and practice (OR = 1.84) levels were significantly improved in the intervention prisons. We did not find a significant difference in the treatment success rate but it was high for both groups.

The findings of this trial demonstrate that empowering and involving prisoners in TB control is highly effective in increasing TB case detection rate and reducing misconceptions about TB in the study prisons. This intervention could be scaled-up in other Ethiopian prisons and adapted in other prisons in resource-limited countries with a high TB burden. However, several setting specific issues should be taken into account when considering implementation in other settings. A prison system that faces a high level of violence and distrust among prisoners, would probably not be good for implementing an intervention like ours. Moreover, as peer educators may not always be volunteers, the long-term cost of training and supervising the inmate peer educators should be investigated for large-scale and sustainable implementations.

In the final chapter of this thesis, chapter 6, we present the key findings, methodological considerations, strength and limitations, and conclusions of the studies presented in this thesis. In general, the prevalence of undiagnosed TB was high in the study prisons and misconceptions about the cause of TB and consequences of non-adherence to TB treatment were prevailing among the prisoners. There was also a lack of linkage and tracking systems for prisoners transferred or released before treatment completion. These findings pose serious public health implications and threaten national TB control efforts, with the risk of TB and drug-resistant TB spread in prisons and the general population. We explored that empowering and involving prisoners in TB control program improves TB case finding (detecting of the undiagnosed TB) and reduce misconceptions. The NTP should put more efforts in scaling-up of such intervention model to all prisons in Ethiopia and in transforming the health care system in the prisons.

ማጠቃለያ (Summary in Amharic)

<u>**ማብራሪያ**</u>፤ በዚህ የማጠቃለያ ፅሑፍ የተጠቀሱት አመተ ምህረቶች በሙሉ በአውሮፓውያን አቆጣጠር ናቸው፡፡

ይህ ጥናታዊ ፅሑፍ (thesis) በዋናነት በሰሜናዊ ኢትዮጵያ ማረሚያ ቤቶች ያለውን የቲቢ ስርጭትና ለቲቢ መስፋፋት የሚያባብሱ ምክነያቶችን በመግለፅ ለችግሩ መቀረፍ ቀላልና በታዳጊ አገሮች ሊተገበር የሚችል የቲቢ ቁጥጥር ትግበራ (intervention) ውጤትን ያካተተ ነው፡፡

ጥናታዊ ፅሑፉ ስድስት ምዕራፎችን ይዟል፡፡ **ምዕራፍ አንድ፡-** መግቢያ ሲሆን ከዚህ በፊት በተካሄዱ ጥናቶችና መረጃዎች ላይ በመመረኮዝ በዓለም እና አገር አቀፍ ደረጃ ያሉ የቲቢ ቁጥጥር ተግዳሮቶችን ያብራራል፡፡ እንዲሁም በቲቢ ቁጥጥር ዙሪያ ያሉ ክፍተቶችን በመጠቆም በዚህ ጥናታዊ ፅሑፍ የተካተቱ ንዑስ ጥናቶችን አስፈላጊነት ይገልፃል፡፡

በዚሁ ምዕራፍ በሰፊው እንደተገለጠው ምንም እንኳን ቲቢን ለመግታት በሚደረጉ ዓለም አቀፍ ስራዎች ብዙ ለውጦች የተመዘገቡ ቢሆንም አሁንም ግን ቲቢ በዓለም አቀፍ ደረጃ ካሉ ዋና ዋና የጤና ተግዳሮቶች አንዱ ነው፡፡ በየዓመቱ ወደ 10.4 ምልዮን ሰዎች በበሽታው ሲያዙ 1.4 ምልዮን ያህሉ ለሞት ይዳረጋሉ፡፡ በታዳጊ አገሮች በተለይም በአፍሪካ በሽታው በስፋት ተንሰራፍቶ ይገኛል፡፡ ኢትዮጵያ ከፍተኛ ቲቢና መደኃኒት የተላመደ ቲቢ ካለባቸዉ 30 አገሮች መካከል አንዷ ስትሆን በየዓመቱ ወደ 26,000 ሰዎች በዚሁ በሽታ ምክንያት ለህልፈተ ህይወት ይዳረጋሉ፡፡ በሽታው በተለይም አምራቹን የማህበረሰብ ክፍል በከፍተኛ ሁኔታ ስለሚያጠቃ ኢትዮጵያ መካከለኛ ገቢ ካለቸው አገሮች ተርታ ለመሰለፍ በምታደርገው ጉዞ ላይ አሉታዊ ተፅኖ ያሳድራል፡፡

አስፈላጊውን የቲቢ ምርመራ ሳያገኙ ተትው የሚቀሩ የቲቢ በሽተኞች (missed TB cases) ወይም ከብዙ መዘግየት በኋላ ምርመራ የሚያገኙ የቲቢ በሽተኞች መበራከትና ጥራት ያለው በቂ የጤና ተቋም አለመኖር ለዓለም አቀፍ የጤና ቁጥጥር ፕሮግራም ዋናዎቹ እንቅፋቶች ናቸው፡፡ በየዓመቱ ወደ 3 ምልዮን በሽታው ያለባቸው ሰዎች የቲቢ ምረመራ ሳያግኙ እንዲሁ ተትተው የሚቀሩ ሲሆን ይህም ለበሽታው መስፋፋት ከፍተኛ አስተዋፅኦ ያደርጋል፡፡ እንደማረሚያ ቤቶች ያሉ ለቲቢ በሽታ ከፍተኛ ተጋላጭ የሆኑ ቦታዎችን ትኩረት አለመስጠት ለዚህ ችግር ዋናው ምክነያት ነው፡፡ በተለይም ከሰሐራ በታች ባሉ የአፍሪቃ አገሮች ኢትዮጵያን ጨምሮ ኤ ች አይ ቪ (HIV) እና ድህነት የተንሰራፋባቸው በመሆኑና የዓለም አቀፍ የቲቢ ቁጥጥር መሰረታዊ መርሆች (ማለትም ቲቢን በቶሎ በመርመር ማከም፣ በሽታው የተገኘባቸውን ሰዎች ለብቻ ለይቶ ማቆየት ወዘተ) በበቂ ሁኔታ የማይተገበሩ በመሆኑ በነዚህ አገሮች ማረሚያ ቤቶች ችግሩ ከፍተኛ ነዉ፡፡ በሌላ በኩል በበሽታው ዙሪያ በማረሚያ ቤቶቹ በቂ ምርምር ባለመሰራቱና የመረጃ እጥረት በመኖሩ በቀላሉ ሊተገበሩ የሚችሉ የቲቢ ቁጥጥር ዘዴዎችን ለመነደፍና ለመተግበር አስቸጋሪ ያደርገዋል።

ከላይ የተጠቀሱትን ክፍተቶች በመመርኮዝ ይህ ጥናታዊ ፅሑፍ በሚከተሉት አራት ዓበይት አላማዎች ላይ ያተኩራል፡፡ በመጀመሪያ በማረሚያ ቤቶች ያለውን የቲቢ ስርጭት መጠን እና ቲቢን የሚያባብሱ ምክነያቶችን ይገልፃል፡፡ በሁለተኛ ደረጃ በቲቢ በሽታ ተይዘው የነበሩ ታራሚዎችን የቲቢ መድኃኒት

አወሳሰድና ከበሽታው የመዳን ሁኔታ (TSR) እና ላልተሳካ የቲቢ ህክምና ውጤት የሚዳርጉ ምክነያቶችን ያትታል፡፡ ሦሥተኛ ታረሚዎች ስለቲቢ ያላቸውን የግንዛቤ፣ አመላካከትና ትግበራ (KAP) ሁናቴ ይገመግማል፡፡ በአራተኛ ደረጃ ከላይ በተገለፁት ሦሥት ጥናቶች የተገኙትን መረጃዎች በማጤን የታዩ ክፍተቶችን በዘላቂነት ለመቅረፍ ችግር ፈች እና በቀላሉ ሊተገበር የሚችል የህብረተሰብ ጤና አጠባበቅ (public health) ጣልቃገብነት ትግበራ (interventions) ውጤትን ይገልፃል፡፡

የቲቢ ስርጭትን መጠን የሚገልፀዉ ጥናት **በምዕራፍ 2** በሰፊው ተብራርቷል፡፡ በዚህ ጥናት በዘጠኝ የትግይ ማረሚያ ቤቶች የሚገኙ ታራሚዎች የቲቢ መመርመሪያ መስፈርቶችን ያካተተ ቃለመጠይቅ በመጠቀም ለቲቢ ምልክቶች ተመርምረዋል፡፡ ከነዚህም 844 ታራሚዎች የአክታ ናሙና የሰጡ ሲሆን በአጉሊ መሳሪያ (microscope) እና የቲቢ ማሳደጊያ ምግብ (culture) በመጠቀም የቲቢ ምርመራ ተደርጎላቸዋል፡፡

የምርመራ ውጤቱ እንደሚያሳየው ሳይመረመር የተተወ ቲቢ (undiagnosed TB) በትግራይ ማረሚያ ቤቶች ከፍተኛ ነው፡፡ ከ809 የካልቸር ምርመራ ከተደረገላቸው ታራሚዎች መካከል 4% ሳይመረመር የተተወ ቲቢ ያለባቸው ናቸው፡፡ በአጠቃላይ በዚያች ውስን ጊዜ የነበረው የቲቢ ስርጭት መጠን ሲገመት ከ100,000 ታራሚዎች ውስጥ 505 ቱ (505/100,000) የቲቢ በሽታ ያለባቸው ናቸው፡፡ በተጨማሪም 4.4% (36/809) የቲቢ ምልክት ያለባቸውና 6.3% (2/32) ቲቢ የተገኘባቸው ታራሚዎች በ ኤች አይ ቪ የተጠቁ ናቸው፡፡ ይህ ጥናት ጫት መቃም (OR = 2.81) እና ከቲቢ በሽተኞች ጋር መቀራረብ (OR = 2.18) በቲቢ በሽታ ለመያዝ እንደሚያጋልጡ ያሳያል፡፡

በዚህ ጥናት የተገኘው የቲቢ ስርጭት መጠን (505/100,000) ከማህበረሰቡ የቲቢ ስርጭት መጠን (216/100,000) ጋር ሲወዳደር ከሁለት እጥፍ በላይ ከፍ ያለ ነው፡፡ እነደነዚህ ያሉ የቲቢ በሽተኞች በሽታውን ወደ ሌሎች ታራሚዎች እንዲሁም ወደ ማህበረሰቡ የማሰራጨት ከፍተኛ እድል ስላላቸው በትግራይ ማረሚያ ቤቶች ውስጥ ያለውን የቲቢ ቁጥጥርና ምርመራ ሂደት ለማሻሻል ያላሰለሰ ጥረት ሊደረግ ይገባል፡፡

ምዕራፍ 3፡ በትግራይ ማረሚያ ቤቶች ያለውን የአምስት ዓመታት የቲቢ ህክምና ሂደት እና ላልተሳካ የቲቢ ህክምና ውጤት የሚያጋልጡ ምክነያቶችን ያብራራል፡፡ በዚህ ጥናት ከመስከረም 2010 እስከ መስከረም 2015 በአራት የትግራይ ማረሚያ ቤቶች የጤና ተቋማት የቲቢ ህክምና የወሰዱ ታራሚዎች የጤና መረጃ እና የህክምናቸው ውጤት ተሰብስቧል፡፡ ከተሰበሰቡ መረጃዎች መካከል እድሜ፣ ፆታ፣ የቲቢ ዓይነት፣ የወሰዱት የቲቢ ህክምና ምድብ፣ ህክምና የጀመሩበትና የጨረሱበት ቀን፣ ህክምና ሲጀምሩ የነበራቸው ክብደት፣ የ ኤች አይ ቪ ምርመራ ውጤቶችና የመሳሰሉት ይገኙበታል፡፡

ውጤቱ እንደሚያሳው አብዛኞቹ ታራሚዎች (94%) የቲቢ ህክምናቸውን በአግባቡ የጨረሱና የዳኑ ናቸው፡፡ በዝርዝር ሲገለፅ ከ 496 የቲቢ በሽተኞች መካከል 11.5% ሙሉ በሙሉ ድነዋል፤ 68% ህክምናቸውን ጨርሰዋል፤ 15% በህክምና ላይ እያሉ ወደ ሌላ ተቋም ተዛውረዋል፡፡ ነገር ግን የቲቢ ህክምና በመውሰድ ላይ እያሉ የተፈቱ ታራሚዎችም ሆነ ወደ ሌላ ማረሚያ ቤት የተዛወሩ ታራሚዎች ለሚመለከተው የጤና ተቋም በአግባቡ አልተላለፉም፡፡

ይህ ጥናት እንደሚያሳየው ከዚህ በፊት የቲቢ በሽታ ያለባቸው ታራሚዎች ላልተሳካ ህክምና የመዳረግ እድላቸው ከአዲስ በሽተኞች ጋር ሲነጣጠር በ 4.68 እጥፍ ከፍ ያለ ነው፡፡ በተጨማሪም በህክምና የመዳን እድል በዓመታት የሚለያይ ሲሆን በመጀመሪያዎቹ ዓመታት የታከሙ ታራሚዎች ላልተሳካ ህክምና የመደረግ እድላቸው ከፍ ያለ ነው፡፡ ህክምና ከወሰዱ ሁለት ወራት በኋላ የአክታ ናሙናቸው የቲቢ ባክቴሪያ የሳየ የቲቢ በሽተኞችም እንደዚሁ ላልተሳካ ህክምና የመዳረግ እድላቸው ከፍ ያለ እንደሆነ ጥናቱ ያሳያል፡፡

በአጠቃላይ ይህ ጥናት በማሪሚያ ቤቶች ውስጥ እያሉ የቲቢ ህክምና የሚወስዱ ታራሚዎች የመዳን እድል ከፍተኛና ከዓለም አቀፍ የቲቢ ቁጥጥር እቅድ አኃዝ ጋር ሲወዳደርም ከበቂ በላይ እንደሆነ ያሳያል፡ ነገር ግን የቲቢ ህክምና በመውሰድ ላይ እያሉ የተፈቱ ታራሚዎችም ሆነ ወደ ሌላ ማረሚያ ቤት የተዛወሩ ታራሚዎች ለሚመለከተው የጤና ተቋም በአግባቡ አለመተላለፋቸው ለዓለም አቀፍም ሆነ አገር አቀፍ የቲቢ ቁጥጥር ፕሮግራም እንቅፋት ይፈጥራል፡፡
እንደነዚህ አይነት በሽተኞች በአብዛኛው ህክምናቸውን ስለሚያቋርጡ መድኃኒትን በተላመደ ቲቢ የመያዝና ወደ ማህበረሰቡ የማሰራጨት እድላቸው ከፍተኛ ነው፡፡ ስለሆነም አገር ዓቀፍ የቲቢ ቁጥጥር ፕሮግራም ይህንን ችግር ትኩረት ሰጥቶ ሊሰራበት ይገባል፡፡

የቲቢ ግንዛቤ፣ አመለካከትና ትግበራ (KAP) ውጤቶች **በምዕራፍ** 4 ቀርበዋል፡፡ በዚህ ጥናት ደረጃቸውን የጠበቁ ጥያቄዎችን በመጠቀም ስለማህበራዊና ኢኮኖሚያዊ ሁኔታዎች፣ ስለማረሚያ ቤቶች ሁኔታና የቲቢ ግንዛቤ፣ አመለካከትና ትግበራን በተመለከተ ከ615 ታረሚዎች መረጃዎች ተሰብስበዋል፡፡
የቲቢ ግንዛቤ፣ አመለካከትና ትግበራ ስለ ቲቢ የተመረጡ ጥያቄዎችን (መሰረታዊ ጥያቄዎችን) በመጠቀም የተገለፁ ሲሆን በዚህም መሰረት እዉቀት "መልካም እና ደካማ እውቀት"፣ አመለካከት "መልካም አመለካከትና መልካም ያልሆነ አመለካከት"፣ ትግበራ "ጥሩ ትግበራ እና ጥሩ ያልሆነ ትግበራ" በመባል ተከፍለዋል፡፡
ይህ ጥናት ተሳታፊዎች የቲቢ ግንዛቤ፣ አመለካከትና ትግበራ ክፍተቶች እንደሉባቸው ይጠቁማል፡፡ ከአስር ታራሚዎች አራት ብቻ የቲቢ መንስኤ ጀርም (ባክቴሪያ) እንደሆነ መለየት የቻሉ ሲሆን አብዛኞቹ ታራሚዎች መንስኤውን ከተለያዩ የተሳሳቱ ነገሮች ማለትም ከቀዝቃዛ ነፋስ፣ ከመጥፎ የአፈር ሽታ፣ ከንፅህና ጉድለት እና ሲጋራ ማጨስ ጋር አያይዘውታል፡፡ በተጨማሪም 63.7% ያህሉ የቲቢን መድኃኒት በማቋረጥ ሊመጣ ስለሚችለው ችግርና መድኃኒቱን በተላመደ ቲቢ የመያዝ እድል ግንዛቤ እንደሌላቸው ያሳያል፡፡ በአጠቃላይ 24% መሰረታዊ ጥሩ የቲቢ እውቀት፣ 42% መልካም አመለካከት ፣ 55% ጥሩ ልምድና የእቀት ትግበራ እንዳላቸው ጥናቱ ያመለክታል፡፡ ከገጠር ከመጡ ታራሚዎች ይልቅ የከተማ ታራሚዎች የተሻለ እዉቀት አላቸው (OR = 2.16)፡፡ ማንበብና መጻፍ የማይችሉ ታራሚዎች ዝቅተኛ እዉቀት (OR = 0.17)፣ መልካም ያልሆነ አመለካከት (OR = 0.31) እና ጥሩ ያልሆነ የትገበራ ልምድ (OR = 0.35) እንዳለቸው ጥናቱ ይጠቁማል፡፡ በተጨማሪም የግንዛቤ፣ አመለካከትና ትግበራ ሁኔታ ከማረሚያ ቤት ማረሚያ ቤት እንደሚለያይ ጥናቱ ያሳያል፡፡
በዚህ ጥናት የተለዩ ክፍተቶች አስፈለጊው ትኩረት ሊሰጣቸውና ሊሰራባቸው ይገባል፡፡ በተለይም ቲቢ በቀዝቃዛ ነፋስ ይመጣል የሚለው የተሳሳተ ግንዛቤ ታራሚዎች በጊዜው ወደ ጤና ተቋም እንዳይሄዱ ከማድረጉም በላይ በተጨናነቁ የኢትዮጵያ ማረሚያ ቤቶች ለቲቢ ስርጭት ከፍተኛ አስተዋፅኦ ይኖረዋል ፡፡ ስለዚህ ተገቢ የሆነ የቲቢ ትምህርት በኢትዮጵያ ማረሚያ ቤቶች በፍጥነት መጀመርና በዘላቂነት መተግበር አለበት፡፡
ከላይ በተጠቀሱ ገላጭ ጥናቶቻችን የታዩትን ክፍተቶች ግምት ውስጥ በማስገባት በዘፈቀደ ከተመረጡ የሰሜናዊ ኢትዮጵያ ማረሚያ ቤቶች የተወሰኑ ታራሚዎችን በመመልመልና ስለቲቢ በማስልጠን በቲቢ በሽታ ግኝት እና ህክምና ውጤት መሻሻል እንዲሁም የቲቢ በሽታ ተጠርጣሪዎች ለቲቢ ቅድመ-ህክምና የሚወስድባቸውን ጊዜ በማሳጠር ላይ ያላቸውን አስተዋፅኦ የሚገምግም የትግበራ (intervention) ጥናት አካሂደናል፡፡ ይህ ጥናት **በምዕራፍ** 5 በሰፊው ተገልጿል፡፡
ለዚህም በሁለት የኢትዮጵያ ክልሎች የሚገኙ 16 ማረሚያ ቤቶች (ጠቅላላ የታራሚዎች ብዛት = 18,032) በጥንድ በጥንድ ከተመደቡ በኋላ እያንዳዱ ጥንድ በዘፈቀ (randomly) ወደ ሁለት ቡድን ተከፍለዋል፡፡ አንደኛው ቡድን የጣልቃ ገብነት ትግበራው (intervention) የሚካሄድበት ሲሆን ሌላኛው ደግሞ ቀድሞ የነበረውን የቲቢ ምርመራ ሂደት የሚከተልና ለማነጣጠሪያ የምንጠቀምበት ነው።

በመቀጠልም ከእያዳንዱ የጣልቃ ገብነት ትግበራ ከሚካሄድባቸው ማረሚያ ቤቶች (ከስምንቱ ማረሚያ ቤቶች) የተወሰኑ ታራሚዎችን በመምረጥ የሦሥት ቀን ሥልጠና የተሰጠ ሲሆን እነዚህ ታራሚዎች በየሁለት ሳምንቱ በተካታታይ ለአንድ ዓመት ለሁሉም ታራሚዎች የቲቢ ትምህርትና ምርመራ ሰጥተዋል ። ዋናው የጥናቱ ግብ ተትተው የቆዩ ታራሚዎችን በማስመርመር የቲቢን በሽታ ግኝትና ህክምና ማሻሻል ነው።

የትግበራው ውጤት እንደሚያሳየው ትግበራው በተካሄደባቸው ማረሚያ ቤቶች በአንድ ዓመት ውስጥ 75 የቲቢ በሽተኞች ሲገኙ ትግባራው ባልተከሄደባቸው ማረሚያ ቤቶች የተገኙት ግን 25 ብቻ ናቸው። ስለሆነም ትግበራው በተካሄደባቸው ማረሚያ ቤቶች የተገኘው አማከኝ የቲቢ ስርጭት መጠን ትግበራው ካልተካሄደባቸው ጋር ሲነጣጠር በጣም ከፍ ያለ ነው (79.8 ለ 26.9)። ቲቢ ያለባቸው ታራሚዎች የቲቢ ምርመራና ህክምና ለማግኘት የሚውሰደባቸው ጊዜ ትግበራው በተደረገባቸው ማረሚያ ቤቶች በአመካኝ በ8.6 የቀነሰ ሲሆን ነገር ግን ልዩነቱ በስታቲስቲክስ የተደገፈ አይደለም። በተጨማሪም ትግበራው በተካሄደባቸው ማረሚያ ቤቶች የታራሚዎች የቲቢ እውቀት (OR = 2.54) እና ትክክለኛ የቲቢ ቁጥጥር መርሆችን የመተግበር ስራ (OR = 1.84) ከፍ ያለና ልዩነቱም በስታቲስቲክስ የተደገፈ እንደሆነ ጥናቱ ያሳያል። የቲቢ ህክምና ውጤትን በተመለከተ ግን ልዩነት የሌለ ሲሆን ነገረ ግን በሁለቱም ቡድን ጥሩ እንደበረ ጥናቱ ያመለክታል።

በአጠቃላይ የዚህ ጣልቃ ገብነት ትግበራ ዉጤት ታራሚዎችን ስለቲቢ በማሰልጠን በቲቢ ቁጥጥር ስራ ውስጥ ማሳተፍ በማረሚያ ቤቶች ያለውን የቲቢ በሽታ ምርመራ፣ ታራሚዎች ስለቲቢ የሚኖራቸውን እውቀት እና የትግበራ ልምድ ለማሻሻል በጣም ውጤታማ እንደሆነ ያሳያል። ይህ አሰራር ጥናቱ ባልተደረገባቸው ሌሎች የኢትዮጵያ ማረሚያ ቤቶች በቀላሉ መተግበር የሚችል ከመሆኑም ባሻገር እንደ ኢትዮጵያ ባሉ ሌሎች ድሃ አግሮችም እንደአስፈላጊነቱ ተሻሽሎ ሊተገበር ይችላል። ነገር ግን ትግበራው በየአገራቱ ማረሚያ ቤቶች ያሉትን ዝርዝር ጉዳዮች ግምት ውስጥ ማስገባት አለበት። ለምሳሌ ግጭት የበዛበትና በታራሚዎች መካከል መከባበር የሌለበት ማረሚያ ቤት ለትግበራው ላይመች ይችላል። በተጨማሪም የሚሰልጥኑት ታራሚዎችም ሆኑ የማረሚያ ቤት የጤና ባለሙያዎች ሁልጊዜ ስራውን በፈቃደኘነት ሊያከናውኑት ስለማይችሉ ለዘላቂ ትግበራ የክፍያ ጉዳይ ታሳቢ መደረግ አለበት።

በዚህ ጥናታዊ ፅሑፍ (thesis)የተካተቱ ጥናቶች ዓበይት ግኝቶች፣ የምርምሮቹ ጥንካሬ እና ድክመቶች እንዲሁም የማጠቃለያ ሃሳቦች በመጫረሻው ምዕራፍ (**ምዕራፍ** 6) ተብራርተዋል። ሳይመረመር የተተወ ቲቢ (undiagnosed TB) እና ቲቢን እና የቲቢ ህክምናን በተመለከተ ያሉ የተሳሳቱ ግንዛቤዎች በማረሚያ ቤቶቹ ከፍተኛ እንደሆኑ ጥናቶቹ ያመለክታሉ። በተጨማሪም በቲቢ ህክምና ላይ እያሉ የተፈቱም ሆነ ወደ ሌላ ማረሚያ ቤት የተዛወሩ ታራሚዎች ለሚመለከታቸው የጤና ተቋማት በአግባቡ እንዳልተላለፉ ጥናቶቹ ይጠቁማሉ። ይህ ጉዳይ ለማህበረሰብ ጤና ከፍተኛ ጠንቅ ሲሆን በአገር አቀፍ የቲቢ ቁጥጥር ፕሮግራም አሉታዊ ተፅዕኖ ያሳድራል። እነዚህ ታራሚዎች ከወጡ ወይም ከተዛወሩ በኋላ ህክምናቸውን ሊያቋርጡ ስለሚችሉ መድኃኒትን ለተላመደ ቲቢ የመጋለጥ እድላቸው ከፍተኛ ስለሆነ ችግሩን የተወሳሰበ ያደርገዋል። በአጠቃላይ በማረሚያ ቤቶች ያለውን ከፍተኛ የቲቢ በሽታ ችግር ለመቅረፍ በጣልቃ ገብነት የትግበራ ስራችን የተገመገመው ዘዴ ቀላልና በጣም ውጤታማ በመሆኑ አገር አቀፍ የቲቢ ቁጥጥር ፕሮግራም ትኩረት ሰጥቶ ሊሰራበትና በሁሉም የአገራችን ማረሚያ ቤቶች ሊተገብረው ይገባል።

Valorization:
practical implications of findings

In this section, we present the possible programmatic and policy implications of the key findings on TB control in prisons of resource-limited regions. The targeted audiences for this thesis can be researchers, TB service providers, program managers, policymakers, prisoners, and even the community.

A major challenge to the global TB control program is reducing the failure to detect and treat active TB cases early, particularly in resource-limited countries. Even though the lack of sensitive screening and diagnostic tools remain a major contributing factor to this failure, poor awareness and limited accessibility to the routinely available TB diagnostic services also contribute largely, especially among poor people and prisoners. This is particularly alarming in prisons of Sub-Saharan African countries where a shortage of trained healthcare workers and a poor infrastructure limit the use of the international recommended TB control strategies, while the lack of accurate data hinders the design and implementation of optimized and cost-effective interventions. The studies presented in this thesis provide crucial evidence that fills such gaps in Ethiopian prisons and potentially in other prisons of Sub-Saharan Africa.

The three observational studies described in chapters 2-4 show that there was a high prevalence of undiagnosed TB, and even those diagnosed were not effectively treated where patients who were released or transferred before treatment completion were not appropriately linked to health facilities. Furthermore, more than two-thirds (76%) of the prisoners had misconceptions about TB, particularly on the real cause of TB and possible consequences of non-adherence to TB treatment, which can have a potential implication in fuelling the spread of TB. These findings have significant implications for the TB control programs.

Primarily, they may serve as a catalyst to draw the attention from researchers, TB service providers, program managers, and policymakers to neglected prison settings. This has, for example, been demonstrated by some of the stakeholders in our study area (regional health bureaus) where they started discussions with non-governmental organizations once we had a workshop and communicated the findings. Given these identified gaps, TB programmers need to help design and implement simple, feasible and sustainable intervention models. The randomized trial presented in this thesis could be the best option for addressing issues of poor screening practices and access to care, but filling the gap of the lack of appropriate linkage and tracking of the patients released or transferred before treatment completion remains an important research question.

The results of our randomized controlled trial show that empowering and involving prisoners in TB awareness campaigns and symptom-based screening is highly effective in increasing TB case detection rate and reducing misconceptions about TB in Ethiopian prisons. Basically, TB awareness, access to care, and early case detection in prisons can successfully be improved by training and involving adequate numbers of prison healthcare workers in the TB control program. However, this is unattainable in a short period for resource-limited countries like Ethiopia. Our innovative intervention (which involves prisoners instead of health professionals) is, therefore, the best option to address the chronic shortage of human resource in prisons of poor countries and control TB effectively. The intervention may ultimately be adapted in the prisons of other Sub-Saharan African countries where undiagnosed TB is highly prevalent and trained health professionals are scarce.

Our findings also have relevant socio-economic implications. Although cost-effectiveness was not thoroughly investigated, our intervention incurred minimal costs and will minimize wastage of resource if adapted. Our study findings advocate early case detection and treatment of TB, which improves the quality of life of patients, and reduce TB-related costs as well as the negative social consequences in the prisons, family, and the wider community.

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Kelemework Adane

Biography

Kelemework Adane Asamre was born on December 25, 1986, in Baso Liben, a rural Woreda in East Gojjam, from his father Adane Asmare and his mother Alemitu Teferra. He attended his primary education at Yelamgej primary school and his secondary school studies in Menkorer secondary school and Dibza preparatory school in Debre Markos. Kelemework obtained his BSc degree in Medical Laboratory Technology in 2008 from Haramaya University and a Master degree in Tropical & Infectious Disease in 2011 from Addis Ababa University. His Master's thesis was focused on the molecular epidemiology of *M.tuberculosis* in rural communities in Ethiopia where he performed the lab work at Armauer Hansen Research Institute, a prestigious research institute in Addis Ababa. Kelemework joined Mekelle University in 2008 as a graduate assistant and was promoted to a lecturer in 2011. Since then, he has been teaching Microbiology and Immunology for medical and health science students. Kelemework has also been active in research and community service and has published several articles in international peer-reviewed journals. In 2014, Kelemework got a scholarship from Nuffic and joined Maastricht University for a Ph.D. study.

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