**Title: High Utility of Active Tuberculosis Case finding in an Ethiopian Prison**

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## Abstract

**Setting:** Hawassa Prison, Southern Region of Ethiopia.

**Objective:** Determine the burden of pulmonary tuberculosis (TB) among incarcerated persons utilizing active case finding.

**Design:** Cross sectional study. Persons incarcerated were screened for TB using a symptom screen; those with a cough of ≥2 weeks had spot and morning sputum samples collected for AFB smear microscopy and molecular diagnostic testing (Xpert MTB/RIF).

**Results:** Among 2068 prisoners, 372 (18%) had a positive cough screen. The median age of these 372 persons was 23 years, 97% were male and 63% were from urban areas. Among those with a positive symptom screen, 8 (2%) had a positive AFB sputum smear microscopy result and 31 (8%) had a positive Xpert TB/RIF. The point prevalence of pulmonary TB at the prison was 1748 per 100,000 persons. In multivariate analysis, persons with a cough >4 weeks were more likely to have TB (OR = 3.34, 95% CI 1.54-7.23).

**Conclusion:** A high prevalence of TB was detected among inmates at a large Ethiopian prison. Active case finding using a cough symptom screen in combination with the Xpert had high utility and the potential to interrupt transmission of *M. tuberculosis* in correctional facilities in high burden, low- and middle-income countries.



**Key words: Active TB case finding, prison, Xpert MTB/RIF**

## INTRODUCTION

Tuberculosis (TB) disease burden is higher in prisons compared to the general population. Prisons are often neglected reservoirs for TB disease and can be significant amplifiers of disease both in prison and the community [1,2]. Transmission of drug-resistant strains, overcrowding, poor living conditions, limited health care, inadequate TB treatment and control strategies, and high rates of HIV infection all contribute to the disproportional burden of TB in prisons [2]. The World Health Organization (WHO) estimates [3] the prevalence of TB in prisons to be 10-100 fold higher than the general population. The median estimated fraction of TB in the general population attributable to the exposure in prisons for TB is 8.5%[4].

Globally, close to three million cases of active TB each year are undiagnosed by existing health systems [5], including many in the prison system, especially in sub-Saharan Africa [6,7]. Lack of active surveillance and monitoring programs and well-equipped laboratory facilities for TB diagnosis contribute to low case finding among persons in prisons [8]. Furthermore, overcrowding of prisons in low to middle-income countries provides a favorable environment for the transmission of *Mycobacterium tuberculosis*. In high burden TB countries, those who are incarcerated often come from underprivileged communities with higher risk and rates of TB [9].

The impact of TB in prisons extends beyond prison walls into surrounding communities [10]. Failure to control TB in prisons leads to enhanced TB transmission in the community, including drug-resistant disease [11]. Thus, TB control in prisons is a major public health priority. However, there is limited understanding regarding TB epidemiology in African prisons. Previous studies carried out in African prisons reported 10 to 35 times higher TB prevalence in prisoners than in

64 the general population[12-15]. In many TB high burden settings in low and middle income
65 countries, there is no effective TB control program in place in prisons.
66
67 Ethiopia is among the high TB burden countries globally with an incidence rate of 192 per
68 100,000 populations[5]. There are six Federal and 120 regional prisons and detention centers in
69 Ethiopia [16]. Most prisoners are incarcerated in an overcrowded and poorly ventilated
70 environment. The health service in prisons is often poorly organized, lacks skilled manpower and
71 laboratory facilities for TB diagnosis [4]. Even though there is emerging prison TB prevention and
72 control efforts in Ethiopia, it has been limited to a few prisons. Previous studies in the Ethiopian
73 prisons reported point prevalence of TB ranging from 349 to 1913 per 100,000 populations[2,17-23].
74 However, there are no data on the burden of TB in Hawassa Prison one of the largest prisons in
75 the Southern Ethiopia. Therefore, we aimed to estimate the burden of TB in this prison and
76 assess the value of active TB case finding in a prison setting.
77
78 **Methods**
79 *Study design/setting*
80 A cross-sectional study design was utilized to screen prison inmates for pulmonary TB as
81 described below from June 15 through July 13, 2015and HIV serologic testing was offered from
82 January 13 through February 10, 2016 at the Hawassa Prison, a regional prison in Southern
83 Ethiopia. Hawassa Prison has a capacity of approximately 2,500 inmates and an average stay of

18 months per inmate. It has a clinic that provides general healthcare that performs sputum microscopy.

*Study population*

All prisoners without known TB were eligible to participate; informed consent was required for enrollment. Enrollment was performed by nurses from the prison clinic and prison's health committee (prison inmates selected by prison authorities to facilitate health work between the inmates and the prison clinic). They provided study information to the prisoners by visiting their cells, asked those interested in participating to come to the prison clinic to receive further details about the study. All study participants had a cough screen performed and those with a positive screen (cough $\geq$ 2 weeks) provided informed consent and were interviewed including for the presence of other symptoms and asked to submit two sputum samples (1 spot and 1 morning). Five persons were already on anti-TB treatment and were excluded except for estimating point prevalence. We defined pulmonary tuberculosis (PTB) as prison inmates whose sputum sample were positive by Gene Xpert MTB/RIF assay.

HIV screening was carried out after providing pre-counseling education by a trained prison nurse. Additionally, HIV testing was offered and performed for participants diagnosed with active TB cases after obtaining consent.

*Study variables*

A structured questionnaire was used to collect patient demographics, history of prior TB treatment, incarceration history, tobacco and chat use based on self-report of prison inmates.

*Laboratory*

For each participant with a positive cough screen, spot and morning sputum samples were collected in the prison health clinic. AFB smear microscopy was done using regular light microscopy using Ziehl-Neelsen (ZN) technique [24]. The remaining portions of the samples were transported daily to the regional public health laboratory that is about 500 meters far using ice. The two sputum samples were pooled into a single container and stored in -20 freezer until transport to Armauer Hansen Research Institute (AHRI) in Addis Ababa.

External quality control was done for all the slides by an independently experienced laboratory technician at AHRI who was blinded to AFB microscopy and Xpert MTB/RIF results.

The HIV screening was performed based on the national testing algorithm. In brief, blood samples from finger prick 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.

*Data management*

All data were double entered into an online REDCap database [25] and analyzed using STATA v.1. In univariate analysis, differences in categorical variables were tested using the Chi-square test, and for continuous variables a two-sample t-test was used. A multivariable logistic regression

model was used to evaluate the independent association of potential risk factors with TB diagnosis. Model building and selection was based on the purposeful selection of covariates strategy as previously described, based on epidemiological findings in the univariate analysis and biological plausibility[26]. A p-value of <0.05 was considered significant.

*Ethical consideration*

The study was approved by Addis Ababa University, AHRI Institutional Review Boards and the Ethiopian National Ethics Review committees. Study permission was also obtained from the Ethiopian Regional Health Bureau and prison administration. Patients with active TB started treatment in the prison clinic. Newly diagnosed HIV positive participants were linked to a nearby health institution providing HIV care.

## Results

Among 2155 inmates, 2068 (98%) consented to participate and had a cough screen performed. From this group, 372 (18%) inmates reported a cough ≥ 2 weeks (Figure 1). Among those with a positive cough screen, the median age was 23 years (inter quartile range ([IQR] 20-28 years), 362 (97%) were male and 10 (3%) were female. The majority of prisoners (n=329, 88%) had no prior history of imprisonment and most were from an urban area (n=235, 63%) (Table 1). There were 293 (73%) patients who reported having a fever, 315 (85%) night sweats and 241 (65%) weight loss. The median number of prisoners per cell was 162 ([IQR] 14 – 360) and the median duration of imprisonment at the time of screening was 10 months ([IQR] 0.5-2 years).

*Pulmonary tuberculosis and HIV infection*

Among those with a positive cough screen, 8 (2%) had a positive AFB sputum microscopy and 31 (8%) of 372 had a positive Xpert TB/RIF test results and thus had active pulmonary TB disease per our study definition. The results of the AFB sputum microscopy were concurred with the quality control readings at AHRI. All positive smear microscopy samples had a positive Xpert TB/RIF test. By considering the 5 PTB cases which were already on anti-TB treatment during the study period, the overall point prevalence of PTB at the prison was 1789 per 100,000 persons. Among the 31 confirmed TB cases, 3 had a prior history of TB treatment. The median time in prison for TB cases was 8 months and the majority (n=19, 61.3%) had been imprisoned for ≤ 1 year; 28 (90%) were living with > 100 inmates per cell. One TB case with a prior history of TB treatment had rifampicin resistance detected by the Xpert and was confirmed as MDR TB by culture and drug susceptibility testing with resistance to isoniazid, rifampicin, streptomycin and ethambutol.

For HIV screening, among2186 inmates incarcerated during the testing period, 2040 (93%) agreed to testing and nine (0.4%) were HIV seropositive. HIV testing was performed on 16 of the 31 inmates with pulmonary TB and none were positive.

*Predictors of PTB*

Duration of cough predicted TB in univariate analysis. In multivariate analysis, the presence of a cough > 4 weeks was independently associated with an increased risk of having PTB (OR = 3.34, 95% CI 1.54-7.23) (Table 2).

## Discussion

Utilizing an active TB case finding strategy combining symptom screening and molecular diagnostic testing, we detected 31 previously undiagnosed cases of active pulmonary TB in a large Ethiopian prison. Along with the five known cases of TB, we found a TB prevalence of 1789 per 100,000 in the prison population. This prevalence is over 16 times higher than the prevalence found in the general Ethiopian population [27]. Our results highlight the utility of active TB case finding utilizing a cough screen and Xpert RIF/MTB testing among high risk populations including persons incarcerated in prisons in a high TB burden country.

The prevalence of TB at the Hawassa Prison was high despite a low HIV seroprevalence (0.4%) among those incarcerated. None of those persons found to have PTB in our study were HIV seropositive. The HIV prevalence among prison inmates in our study is lower than previous reports from the prisons in other areas of Ethiopia including Gondar (7.6%) [18], Tigray (4.4%) [21], and in 13 prisons in the country (4.4%) [20]. The lower prevalence of HIV infection in our study might reflect lower HIV prevalence in the southern region compared to other parts of Ethiopia [28].Stigma in general is one of the major factors in hindering people from seeking health care services in the country, however, in the prison setting the acceptance rate for the HIV screening was high (93% agreed to HIV testing).

Delays in diagnosis and incomplete treatment of TB are major challenges in most prison settings in resource-limited countries. These could be related to the limited availability of healthcare

193 services in the prisons and lack of TB diagnostics in many prison settings [8,11]. In many high
194 burden, low and middle-income countries, TB control activities in prisons are not well integrated
195 into national TB control programs [8], including in Ethiopia [16]. In prison settings, the use of
196 diagnostic tools with high sensitivity and specificity is recommended [29]. Our study highlights the
197 utility of active TB case finding that utilizes a rapid molecular diagnostic test. Prior to our study,
198 there was no ongoing surveillance for TB in the prison, and the only available diagnostic tool in
199 the prison, AFB smear microscopy, was insensitive in our study and did not detect 75% of TB
200 cases that were identified by Xpert MTB/RIF. Our study provides important data to support the
201 an active TB case finding strategy that uses a cough symptom screen plus Xpert MTB/RIF in
202 prison settings in order to increase the case detection, identify drug-resistant TB, and improve
203 TB control activities by allowing separation of those with active PTB from other inmates.
204
205 The prevalence of TB in the Ethiopian prisons has been reported to range from 349 to 1913 per
206 100,000 prison populations [2,17-23]. The observed PTB point prevalence in our study (1789 per
207 100,000) was higher than reported from most previous Ethiopian studies [17-23] but within this
208 range. The difference in the prevalence of TB in Ethiopian prisons could be due to the
209 methodological differences employed in the studies for screening and diagnosis of cases,
210 differing prevalence of HIV co-infection among those incarcerated in different regions and
211 differences in the burden of the disease in the study areas. Studies conducted in the sub-Saharan
212 African prisons also reported high prevalence of PTB ranging from 5.1% to 47.7% positivity
213 [13,30,31]. The high prevalence of TB in prison settings can impact TB transmission in communities
214 as well as prisons settings can amplify TB transmission and after release from prison, former
215 inmates can transmit TB to contacts in the community [4,10].

Prisons can also be an important source of spread of drug-resistant TB [30] and high levels of MDR TB and XDR TB have been reported in prisons globally [8]. In a study conducted in Zambia [14], resistance to at least one anti-TB drug was observed in 40 (23.8%) of cases and 16 (9.5%) were MDR-TB. Our study identified one case of rifampicin resistance TB using Xpert MTB/RIF test. This case was confirmed to be MDR TB by culture and drug susceptibility testing. A recent study [32]also reported a 9.5% of MDR TB cases in Ethiopian prison settings. These findings highlighted the emergence of MDR TB in the prison settings and further emphasize the need for strengthening TB control activities in prison settings in Ethiopia.

Our study was cross sectional in nature and thus not designed to determine the site of infection with *M. tuberculosis* (prison vs. community) among those found to have active TB disease. The number of persons per cell was high and the median length of incarceration among those with TB was 10 months; 61% of those found to have TB by Xpert were incarcerated for ≤ 1 year. A study from a prison in Gondar, Ethiopia [18] reported that an incarceration range of 2-6 months was associated with TB positivity. Further studies are needed to further evaluate site of transmission and the impact of screening persons at the time of incarceration as an additional TB control measure.

**Limitations of the study**

This study is subject to some limitations. These include having HIV testing offered about 6 months after TB screening rather than concurrently. Given the turnover in prisons, not all of those screened for TB were present when HIV testing was offered (and vice-versa). We relied on Xpert as the definitive diagnosis for TB rather than the gold standard of culture. Since the

sensitivity of culture is higher than Xpert among those that are smear negative, our findings may have underestimated the prevalence of PTB. However, since culture is not widely available in many high TB burden, resource-limited countries including Ethiopia, use of Xpert is more feasible in many settings. Among the three TB cases that had a prior history of TB treatment, a culture was performed in only one of these cases (which is the MDR case in which the Xpert MTB/RIF identified rifampin resistance). Our approach of screening only symptomatic cases could underestimate the prevalence rate as asymptomatic or subclinical cases could be missed.

## Conclusion

We found that active TB case finding which combined the use of a cough screen plus a commercially available molecular diagnostic test (Xpert) had high utility in detecting incarcerated persons with active PTB disease at a large prison in Ethiopia. Despite a low HIV seroprevalence among those incarcerated, the overall prevalence of PTB exceeded 1.7% of the prison population in Hawassa, Ethiopia. A cough >4 weeks was the only risk factor for TB identified among those with a positive symptom screen. Active TB case finding using a symptom screen in combination with Xpert has the potential to interrupt transmission of *M. tuberculosis* in correctional facilities in high burden, low and middle-income countries.

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**Authors' contributions**

YM: contributed to the conception and design of the study, acquisition of data and interpretation, and drafting and revising of the manuscript; YW, MA, DG: contributed to the design of the study and supervision and revision of the manuscript; TH: contributed to data management and analysis, GH: contributed to data acquisition; GA: Contributed to external quality control of smear microscopy; RK, HMB: contributed to data analysis and interpretation and writing the manuscript; AA: contributed to the design of the study and supervision, interpretation of data and writing the manuscript. All authors approved the final version of the manuscript.

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363 Figure 1. Study Diagram

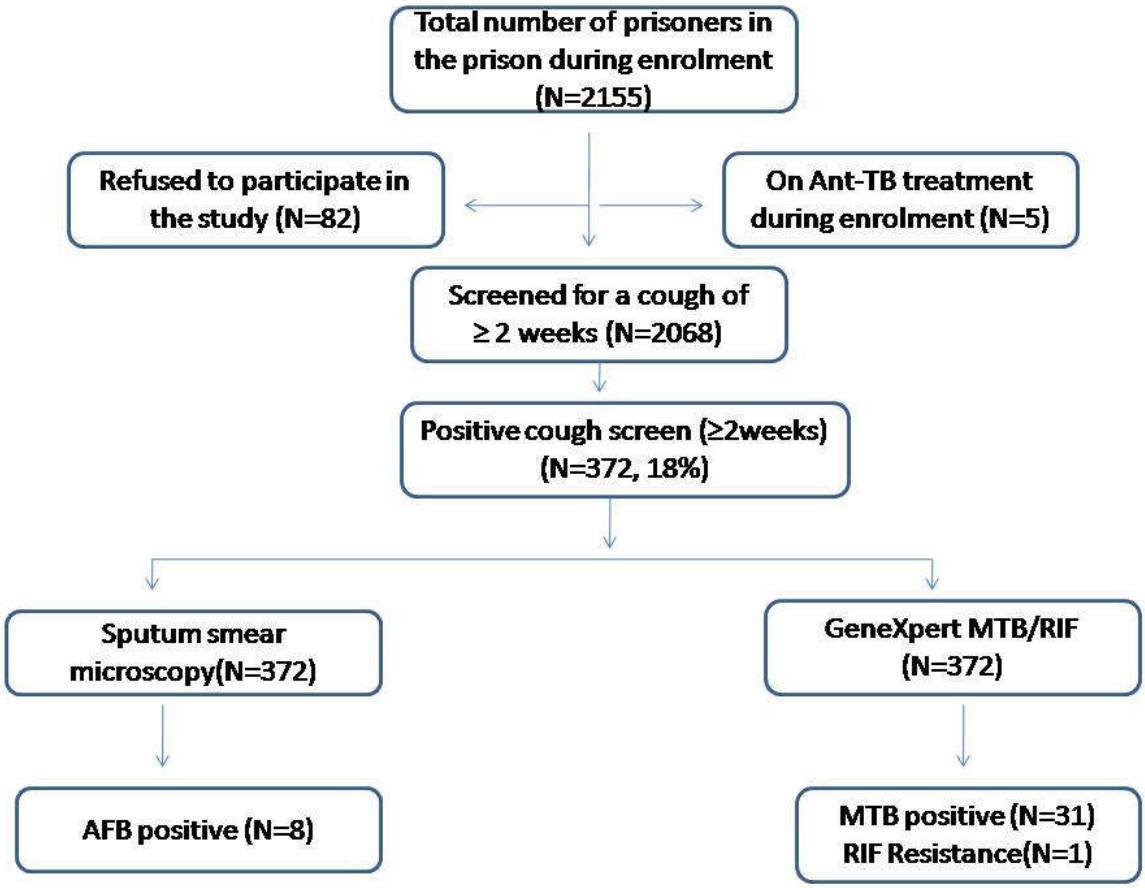


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Table 1. Predictors of having pulmonary TB among persons with a positive cough screen

| Characteristic | Total (n=372 (%) | No TB (n=341) | TB (n=31) | Univariate analysis | |
|---|---|---|---|---|---|
| | | | | OR (95% CI) | *P*-Value[a] |
| Sex (Male) | 362 (97) | 331 (97) | 31 (100) | | |
| Age (year), mean | 26 | 26 | 24 | | 0.08[b] |
| Illiterate | 322 (87) | 294 (86) | 28 (90) | 1.49 (0.43-5.10) | 0.52 |
| Unemployed | 346 (93) | 319 (94) | 27 (87) | 0.46 (0.14-1.44) | 0.18 |
| Not married | 209 (56) | 192 (56) | 17 (55) | 1.06 (0.50-2.22) | 0.87 |
| Duration of cough in weeks | | | | | |
| 2- 4 | 93(25) | 78 (23) | 15 (48) | | |
| >4 | 279 (75) | 263 (77) | 16 (52) | 3.16 (1.49-6.68) | 0.003 |
| Fever | 273 (73) | 247 (72) | 26 (84) | 1.97 (0.73-5.30) | 0.17 |
| Night sweats | 315 (85) | 289(85) | 26 (84) | 0.93 (0.35-2.64) | 0.89 |
| Loss of appetite | 235 (63) | 213 (62) | 22 (71) | 1.46 (0.65-3.28) | 0.35 |
| Weight loss | 241 (65) | 219 (64) | 22 (71) | 1.36 (0.60-3.05) | 0.45 |
| Chest pain | 338 (91) | 308 (90) | 30 (97) | 3.21 (0.42-24.3) | 0.13 |
| Shortness of breath | 252 (68) | 228 (67) | 24 (77) | 1.69 (0.71-4.06) | 0.23 |
| Previous imprisonment | 43 (12) | 42 (12) | 1(3) | 0.23 (0.03-1.78) | 0.16 |
| Previous TB treatment | 34 (9) | 31 (9) | 3 (10) | 1.07 (0.30-3.72) | 0.91 |
| Tobacco use (smoking cigarettes) at time of incarceration | 110 (30) | 104(31) | 6 (19) | 0.54 (0.21-1.37) | 0.19 |
| Chewing chat | 171 (46) | 159 (47) | 12 (38) | 0.72 (0.34-1.53) | 0.39 |
| Incarceration period in years | | | | | |
| ≤ 1 | 180 (48) | 161 (47) | 19 (61) | | |
| 1-3 | 113 (30) | 106 (31) | 7 (23) | 0.55 (0.22-1.37) | 0.20 |
| >3 | 79 (21) | 74 (22) | 5 (16) | 0.54 (0.19-1.49) | 0.28 |
| Contact with known TB patient in the prison | 90 (24) | 83 (24) | 7 (23) | 0.90 (0.37-218) | 0.82 |
| Presence of coughing people in the cell | 191(51) | 175 (51) | 16 (52) | 1.01 (0.48-2.11) | 0.97 |
| No. of prisoners per cell | | | | | |
| ≤100 | 35 (9) | 32 (9) | 3 (10) | | |
| >100 | 337 (91) | 309 (91) | 28 (90) | 0.96 (0.27-3.35) | 0.95 |

CI- confidence interval; OR-odd ratio; TB-tuberculosis

a- *p*-value for Chi-square test unless otherwise stated; b-*p*-value for two-sample t-test

Table 2. Multivariate analysis of predictors of pulmonary tuberculosis among prison inmates with a positive cough screen

| Characteristics | Multivariate analysis | |
|---|---|---|
| | OR (95% CI) | *P*- Value |
| Duration of cough in weeks | | |
| 2-4 | 1.00 | |
| ≥4 | 3.34 (1.54-7.23) | 0.002 |
| Previous imprisonment | 0.32 (0.04-2.50) | 0.28 |
| Tobacco use | 0.63 (0.24-1.64) | 0.35 |
| Incarceration period in years | | |
| ≤ 1 | 1.00 | |
| 1-3 | 0.48 (0.19-1.23) | 0.13 |
| >3 | 0.52 (0.18-1.51) | 0.23 |

OR, odds ratio; CI, confidence interval