Burden of tuberculosis and challenges related to screening and diagnosis in Ethiopia

Hussen Mohammeda,c,⁎, Lemessa Oljirab, Kedir Teji Robah, Esther Ngadayad, Tigest Ajemec, Tewodros Hailef, Achenef Kidanej, Tsegahun Manyazewalc, Abebaw Fekaduc,e, Getnet Yimerd,g

a Department of Public Health, College of Medicine and Health Sciences, Dire Dawa University, Dire Dawa, Ethiopia
b School of Public Health, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia
c Centre for Innovative Drug Development and Therapeutic Trials for Africa, College of Health Sciences, Addis Ababa University, P.O. Box 1362, Dire Dawa, Ethiopia
d Muhimbili Research Centre, National Institute for Medical Research, Dares Saalem, Tanzania
e Global Health and Infection Department, Brighton and Sussex Medical School, Brighton, United Kingdom
f Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia
g Ohio State Global One Health initiative, Office of International Affairs, The Ohio State University, Addis Ababa, Ethiopia
h School of Nursing and Midwifery, College of Health and Medical Sciences, Haramaya University, Harar, Ethiopia

ARTICLE INFO

Keywords:
Tuberculosis
Screening
Diagnosis
Xpert mtb/rif assay
Maternal and child health
Ethiopia

ABSTRACT

Introduction: One-third of tuberculosis (TB) cases in Ethiopia are missing from care for reasons that are not well studied. The aim of this study was to assess TB burden and identify challenges related to TB screening and diagnosis in Ethiopia.

Methods: A facility-based cross-sectional study was conducted in seven health facilities selected from two regions and 2 city administrations of Ethiopia using stratified random sampling procedures. The data of 1,059,065 patients were included from outpatient department, HIV clinic, diabetic, and maternal-child health clinics. Data were collected from October to December 2018 using a retrospective review of three years’ facility data (2015 to 2017) supplemented by a semi-structured interview with purposively selected health care workers and heads of the health facilities.

Results: A total of 1,059,065 patients visited the health facilities in three years, of these, 978,480 (92.4%) were outpatients. Of the total, 20,284 (2%) were presumptive TB cases (with 14 days or more cough), 12.2% (2483/20,284) of which had TB. For the type of TB, 604 (24.3%) were smear-positive pulmonary TB (PTB), 789 (31.8%) were smear-negative PTB, 719 (29%) were extra-pulmonary TB, and data were missing for the rest. TB screening was integrated into HIV clinic, outpatient department, diabetic clinic but not with the maternal and child clinics. High patient load, weak TB laboratory specimen referral system, and shortage of TB diagnostic tools including Xpert MTB/RIF assay and chest X-ray, were the major challenges in the screening and diagnosis of TB.

Conclusion: The burden of TB was high in the study setting, and frequent interruption of laboratory reagents and supplies hampered TB screening and diagnostic services. Realizing the END-TB strategy in such resource-limited settings requires sustainable TB diagnostic capacity and improved case detection mechanisms, with national TB programs strongly integrated into the general health care system.

1. Introduction

Tuberculosis (TB) is the leading cause of mortality and morbidity among infectious diseases around the globe. According to the 2018 global TB report of the World Health Organization (WHO) [1], 10 million people developed TB and 1.6 million died in 2017, where 300,000 deaths were among HIV-positive patients. There were fewer than 10 new cases per 100,000 populations in most high-income countries [1], which clearly indicate TB as the disease of the poor. For instance, in Africa, where only 13% of the world population are...
represented, an estimated 24% of existing TB cases worldwide occur in the region [2], and access to essential TB diagnostics, care and treatment services are very limited [3,4]. Similarly, Ethiopia is among countries highly affected by TB epidemics and one of the least developed in the world. According to the 2018 global TB report, there were 117,705 TB cases reported in the country, 28,600 died (3600 TB/HIV co-infected) and of the annual $93 million needed for TB care and control, the country’s domestic contribution was only 11% [1].

Concerted efforts during the past two decades were performed under the directly observed treatment, short course (DOTS) strategy and later the Stop TB strategy have made remarkable progress worldwide in controlling TB and providing better care and treatment. The overall TB control effort requires a rigorous screening, diagnosis, and treatment of patients [5]. However, there were large gaps between the estimated number of new TB cases and the number of TB reported to national TB programs as the 2018 WHO report indicated: of 10 million estimated new cases worldwide, only 6.4 million (64%) cases were reported. Due to a mix up of missed or delayed diagnosis, and problems with access to quality of care, the risk of premature mortality, sufferings, and catastrophic financial consequences are substantial [6].

In Ethiopia, the TB case detection was 68%, which was below the WHO's target [7], and is even lower among women and children. TB case notification was 117,705, despite 172,000 estimated cases. Over two-thirds of TB cases in the country were pulmonary TB (PTB) cases, while the burden of extra pulmonary TB (EPTB) was 31%, twice the global proportion [1].

Even if the national TB program (NTP) guideline identified who should be screened and investigated for TB, practically, fewer patients were screened and scrutinized [7]. Ethiopia has been using the passive case finding, which misses the less advantaged patients in the community [8]. DOTS geographic coverage is 90%, whereas the health facility coverage is 75% [9] and despite the existence of TB guideline [10]. In the country, 89% of public hospitals provide smear microscopy and about 80% of them have provided chest X-ray [10]; however, only 8% of TB patients initiated TB care in those facilities [11]. At the primary care level, lack of adequate TB care services made the TB patient-pathways to care long and complex [12].

There is a growing concern on how to increase TB case detection in Ethiopia [7]. For this reason, the country endorsed the WHO TB control strategy the “End TB Strategy” in 2015, putting systemic screening of contacts and risk groups as critical components [13,14]. We, therefore, described here the TB burden and challenges related to TB screening and diagnosis in Ethiopia.

2. Methods and materials

2.1. Study setting and design

The study was conducted in two of the 9 regional states and 2 city administrations of Ethiopia: Oromia National Regional State, and the Harari National Regional State, Addis Ababa City Administration, and Dire Dawa City Administration. In Addis Ababa City Administration, the capital of Ethiopia, there were 899 public and private health facilities, of which 195 (22%) were providing TB care and treatment services. In Dire Dawa City Administration, there were 71 public and private health facilities, of which 21 (42%) were providing TB care and treatment services, and for Harari National Regional State, there were 44 health facilities and 16 (36.4%) of these had TB care and treatment services. Oromia National Regional State covers one-third of the country’s population, where we selected East Hararghe zone, one of the 20 zones of the region, for this study. In the zone, there were 662 public and private health facilities, of which 59 (9%) were providing TB care and treatment services (Table 1). This cross-sectional study was conducted from October to December 2018 using a retrospective review of three years’ facility data (2015 to 2017) supplemented by a semi-structured interview with purposively selected health care workers and heads of the health facilities.

2.2. Sampling procedures

The selection of health facilities followed stratified random sampling. The study included two National Regional States and two City Administrations. Two regions (Oromia and Harari National Regional States) were randomly selected from nine (9) regional states of Ethiopia. East Hararghe zone was selected randomly from Oromia National Regional State. We included two City Administrations (Dire Dawa and Addis Ababa). A total of seven health facilities, 4 urban and 3 rural, were selected. These were: Zewditu Memorial Hospital and Kazanchis Health Center from Addis Ababa; Sabian General Hospital and Melka Jebdu Health Center from Dire Dawa; Haramaya General Hospital and Chelenko Primary Hospital from East Hararghe zone of Oromia National Regional State; and Hiwot Fana Specialized University Hospital from the Harari National Regional State. Fig. 1 summarizes the site selection process.

The study included the data of 1,059,065 patients from outpatient department, HIV clinic, diabetic, and maternal-child health. The study was supplemented by semi-structured interviews. With purposive sampling, facilities’ heads and other health care workers were selected. Based on this, a head of each health facility (n = 7), and a focal health care provider at each facility’s DOTS clinic, ART clinic, outpatient department or diabetic clinic, and maternal child health (n = 28) were included to provide information.

2.3. Data collection and analysis

Data sources were primarily the electronic health management information system (eHMS): a national facility-based health data aggregation system that enables all health care services organizations and providers to register and capture data according to the national guideline [17]. At all health facilities, data were entered into computers through eHMS by trained data clerks. We also reviewed TB registers, laboratory registers (primarily acid-fast bacilli and Xpert MTB/RIF assay registration books), outpatient department (OPD) registers, antenatal care register, delivery register, postnatal care register, family planning register, prevention of mothers to child transmission of HIV (PMTCT) register, anti-retroviral therapy register, diabetes mellitus register, and central triage register. Data were abstracted from computer-based and/or paper-based sources or archives using a checklist.

To supplement the secondary data, semi-structured interviews were held, using interviewer-administered open-ended questions, with the selected health facilities’ heads and health care workers at respective units of selected health facilities to assess the challenges related to TB screening and diagnosis. Trained experts conducted the interviews. Only new visitors of OPDs attendees, for patients with follow up such as diabetes, PMTCT, and ART, a patient counted once. Data were managed through checking the presence of required data, completeness of checklists, and identifying sources to get missed data. Based on this, when data were missed from the electronic records, the data were collected from paper-based records. Trained data collators visited the health facilities up to three times and contacted different health care workers who have been working at health facilities’ units during the three years. Finally, data were entered and cleaned using Microsoft Excel 2010. Descriptive data analysis was performed by Microsoft Excel 2010. The data collected through semi-structured interviews were analyzed by considering the key-words related to screening and diagnoses of TB and explained narratively. We used the National TB control guidelines of Ethiopia for the screening, diagnosis, and treatment of TB cases, for case definition and treatment outcomes [7].

The semi-structured interviews had questions related to the functionality and use of Xpert MTB/RIF Machine. The questions were designed to understand if the facilities have a functional Xpert MTB/RIF.
Machine, how they get preventive and curative maintenance services, from where the facility supplies are coming from, and if there were challenges to the use of Xpert MTB/RIF technology. Similarly, there were questions related to chest X-ray, understanding if the facilities have a functional chest X-ray machine, its type and capacity, and if there were challenges in the management and use of such technologies. The interviews also enabled to capture information on TB patient flow process at OPDs, challenges in the process, and how the facilities handle data.

TB screening and diagnosis related were also included to understand if TB screening and case detection activities are practiced at different departments, including OPD, MCH (ANC, FP, PMTCT, PNC, Labor ward), ART, and diabetic clinics. We also captured detailed information on costs associated with TB patients, from registration to treatment.

2.4. Ethical consideration

The Institutional Review Board (IRB) of the College of Health Sciences, Addis Ababa University approved the study. Letters of permission were obtained from respective health facilities. Informed verbal consent was obtained from each head and health care workers to ensure that they have participated in the study voluntarily.

3. Results

3.1. Health facilities’ descriptions

All the seven health facilities had different units/services, including outpatient departments, ante-natal care, delivery services, postnatal care, anti-retroviral therapy, diabetes mellitus, and family planning among others. Four of the facilities were located in urban area. The daily patients flow and the number of health care workers vary based on the type and location of health facilities. All five hospitals had smear microscopy, Xpert MTB/RIF assay, and chest X-ray services. Two health facilities had only smear microscopy (Table 2).

In seven health facilities, there were no special OPDs for patients reporting cough. Like other patients, they follow the standard; they visit central triage first as Ethiopia has implemented a centralized card room. To contact health care workers at OPDs, a patient registered on a piece of follow-up card and medical card. After visiting the center triage room, they passed through a long process within the compound of facilities. Tuberculosis patients’ pathways in particular health facilities showed (Fig. 2).

3.2. TB burden and treatment outcomes

A total of 1059,065 patients visited the health facilities in three
years. Of these, 978,480 (92.4%) visited the outpatient department, 34,477 (3.3%) visited the anti-retroviral therapy clinic, 27,656 (2.6%) visited the prevention of mother to child transmission of HIV clinic, and 18,452 (1.7%) visited the diabetes clinic (Table 3). Of all patients who had visited health facilities, 20,284 (2%) presumptive TB cases (with 14 days of cough) were identified. Overall, the prevalence of TB cases among presumptive TB cases was 12.2% (2483/20,284). Of 2483 patients enrolled into care, 2314 (93.2%) were screened for HIV; 311 (13.4%) were found HIV seropositive. Of enrolled, bacteriologically confirmed were 604 (24.3%), 789 (31.8%) were clinically diagnosed but were smear-negative TB, and 719 (29%) were diagnosed as extra-pulmonary TB. Overall, the treatment success rate was 1973 (79.4%), in which 455 (18.3%) were cured, and 1518 (61.1%) completed the treatment. Unsuccessful treatment rate was 139 (5.6%), in which 9

Table 2

| Name of health facilities                        | Available health units/services                                      | laboratory and X-ray capacity for TB | Setting          | Catchment population | Patients follow-up / month | No. of Health workers |
|-------------------------------------------------|---------------------------------------------------------------------|-------------------------------------|------------------|----------------------|---------------------------|-----------------------|
| Sabian General Hospital                         | Medical, Surgical, Pediatric, Obstetrics wards, DOTS, ART, DM, Immunizations | X-ray                               | Urban            | 70,711               | 9000                      | 72                    |
| Melka Jebdu Health Center                       | OPDs, ANC, delivery, PNC, DOTS, ART, DM, FP, Immunization          | Xpert MTB/RIF Smear Microscopy      | Rural            | 32,533               | 2430                      | 38                    |
| Hiwot Fana Specialized University Hospital      | Medical, Surgical, Pediatric, Obstetrics and Gynecology wards, DOTS, ART, DM, Immunizations | X-ray                               | Urban            | 5.8 million          | 15,000                    | 378                   |
| Haramay General Hospital                        | Medical, Surgical, Pediatric, Obstetrics wards, DOTS, ART, DM, Immunizations | X-ray                               | Rural            | 1,143,909            | 10,500                    | 177                   |
| Zewditu Memorial Hospital                      | Medical, Surgical, Paediatric, Obstetrics and Gynecology wards, DOTS, ART, DM, Immunizations | X-ray                               | Urban            | 5 million            | 32,628                    | 535                   |
| Kazanchis Health Center                         | OPDs, ANC, delivery, PNC, DOTS, ART, DM, FP, Immunization          | Xpert MTB/RIF Smear Microscopy      | Urban            | 74,849               | 8750                      | 48                    |
| Chelenko Primary Hospital                       | Medical, Surgical, Pediatric, Obstetrics wards, DOTS, ART, DM, Immunizations | X-ray                               | Rural            | 675,000              | 14,940                    | 82                    |

OPDs: outpatient departments; ANC: ante-natal care; PNC: postnatal care; DOTS: directly observed treatment, short course; ART: anti-retroviral therapy; DM: diabetes mellitus; FP: family planning.

OPDs: outpatient departments; ART: anti-retroviral therapy; RCH: reproductive and child health; FP: family planning; ANC: antenatal care; PNC: postnatal care; PMTCT: prevention of mother to child transmission; DOTS: directly observed treatment, short course.

Patients with cough of 2 weeks or more (any duration for HIV positive)

Homes/Institutions

Contact screening for children ≤ 5 years

Card Room

Central Triage

Health facilities

OPDs

DOTS clinics

Diabetes

ART

RCH

• FP
• ANC
• PMTCT
• PNC

Delivery

Laboratories

• Sputum smear microscopy or
• Xpert MTB/RIF assay and/or
• Chest X-ray (for screening and/or diagnostic support)

OPDs: outpatient departments; ART: anti-retroviral therapy; RCH: reproductive and child health; FP: family planning; ANC: antenatal care; PNC: postnatal care; PMTCT: prevention of mother to child transmission; DOTS: directly observed treatment, short course.

Fig. 2. Tuberculosis patients’ pathways in government health facilities in Ethiopia, 2019.

OPDs: outpatient departments; ART: anti-retroviral therapy; RCH: reproductive and child health; FP: family planning; ANC: antenatal care; PNC: postnatal care; PMTCT: prevention of mother to child transmission; DOTS: directly observed treatment, short course.
| Table 3 | Patients flow, TB notifications, and treatment outcomes at study health facilities for three years (2015–2017), Ethiopia, 2019. |
|---------|------------------------------------------------------------------------------------------------------|
| Patients follow at selected units in last three years |  |
| TB notification | Bacteriological confirmed | Clinical diagnosed | EPTB | HIV | HIV screened | HIV + | Total enrolled | Cured | Completed | Failed | Died | LTFU |
| Years | OPDs | ART | DM | PMTCT | Presumptive TB |  |  |  |  |  |  |  |  |  |  |
| Sabian General Hospital |  |
| 2015 | 58,585 | 743 | 194 | 1110 | ND | 21 | 45 | 47 | 108 | 36 | 113 | 24 | 90 | 1 | 5 | 2 |
| 2016 | 55,419 | 787 | 794 | 1528 | 490 | 41 | 66 | 95 | 199 | 47 | 202 | 24 | 115 | 0 | 4 | 9 |
| 2017 | 62,029 | 854 | 1531 | 1779 | 1116 | 57 | 85 | 85 | 210 | 23 | 210 | 31 | 203 | 1 | 6 | 6 |
| Melka Jebdu Health Center |  |
| 2015 | 17,364 | 88 | 6 | 528 | ND | 4 | 47 | 14 | 65 | 2 | 65 | 5 | 54 | 0 | 4 | 2 |
| 2016 | 15,056 | 91 | 7 | 800 | 115 | 14 | 45 | 29 | 84 | 2 | 88 | 3 | 61 | 0 | 0 | 9 |
| 2017 | 18,636 | 95 | 10 | 1116 | 186 | 30 | 35 | 19 | 84 | 7 | 84 | 10 | 81 | 0 | 1 | 0 |
| Hiwot Fina Specialized University Hospital |  |
| 2015 | 38,812 | 1860 | 196 | 532 | 2045 | 44 | 63 | 48 | 132 | 8 | 157 | 41 | 115 | 0 | 1 | 0 |
| 2016 | 42,420 | 2120 | 205 | 956 | 2380 | 49 | 42 | 53 | 144 | 16 | 155 | 42 | 113 | 0 | 0 | 0 |
| 2017 | 59,520 | 2190 | 445 | 1124 | 3064 | 60 | 36 | 44 | 144 | 17 | 146 | 50 | 96 | 0 | 0 | 0 |
| Haramaya General Hospital |  |
| 2015 | 36,073 | 241 | 523 | 2742 | 680 | 8 | 37 | 17 | 52 | 8 | 67 | 20 | 32 | 0 | 6 | 4 |
| 2016 | 38,629 | 258 | 572 | 2223 | 754 | 59 | 36 | 39 | 132 | 7 | 135 | 21 | 67 | 0 | 8 | 2 |
| 2017 | 27,933 | 261 | 602 | 2064 | 1508 | 39 | 55 | 31 | 123 | 1 | 125 | 26 | 51 | 0 | 4 | 3 |
| Zewditu Memorial Hospital |  |
| 2015 | 89,540 | 7011 | 2994 | 1464 | ND | 4 | 19 | 39 | 121 | 28 | 62 | 7 | 54 | 2 | 4 | 7 |
| 2016 | 115,054 | 7022 | 4745 | 1528 | 1518 | 8 | 10 | 34 | 117 | 25 | 55 | 4 | 49 | 0 | 3 | 6 |
| 2017 | 114,949 | 7239 | 3512 | 1479 | 2930 | 11 | 9 | 35 | 110 | 33 | 66 | 6 | 40 | 0 | 2 | 2 |
| Kazanchis Health center |  |
| 2015 | 53,616 | 1115 | 176 | 867 | 186 | 11 | 19 | 25 | 87 | 21 | 186 | 44 | 90 | 0 | 2 | 3 |
| 2016 | 34,368 | 1186 | 280 | 792 | 90 | 4 | 13 | 13 | 92 | 13 | 101 | 22 | 41 | 1 | 6 | 1 |
| 2017 | 52,752 | 1247 | 202 | 588 | 90 | 8 | 0 | 6 | 79 | 11 | 115 | 28 | 56 | 1 | 1 | 0 |
| Chelenko Primary Hospital |  |
| 2015 | 15,025 | 22 | 440 | 896 | 1023 | 68 | 46 | 17 | 71 | 3 | 127 | 6 | 37 | 2 | 1 | 2 |
| 2016 | 14,436 | 23 | 490 | 1588 | 1143 | 30 | 52 | 16 | 93 | 1 | 148 | 28 | 42 | 1 | 2 | 7 |
| 2017 | 18,264 | 24 | 528 | 1952 | 966 | 35 | 29 | 13 | 67 | 2 | 76 | 13 | 31 | 0 | 2 | 3 |
| Total | 978,480 | 34,477 | 18,452 | 27,656 | 20,284 | 604 | 789 | 719 | 2314 | 311 | 2483 | 455 | 1518 | 9 | 62 | 68 |
| Percentage (%) | 92.4 | 3.3 | 1.7 | 2.6 | 2 | 24.3 | 31.8 | 29 | 93.2 | 13.4 | 12.2 | 18.3 | 61.1 | 0.4 | 2.5 | 2.7 |

OPDs: outpatient departments; ART: anti-retroviral therapy; DM: diabetes mellitus; PMTCT: prevention of mother to child transmission; EPTB: extra pulmonary tuberculosis; HIV: human immunodeficiency virus; LTF: lost to follow up; ND: no data.
(0.3%) treatment failed, 62 (2.5%) died, and 68 (2.7%) were lost to follow up (Fig. 3). TB treatment outcomes of 371 (14.9%) TB cases were not documented. Tuberculosis case detection was not integrated into maternal health in formal ways, such as ante-natal care, delivery and postnatal care.

3.3. Presumptive TB cases and TB diseases

In three years of the study, at study facilities the number of presumptive TB cases were increased from 3934 (19.4%) in 2015, 6490 (32.0%) in 2016 to 9860 (48.6%) in 2017. Similarly, bacteriological confirmed pulmonary TB cases were increased from 121 (20%) in 2015 to 273 (45%) in 2017 (Fig. 4).

3.4. Challenges related to TB screening and diagnosis

3.4.1. Screening of TB

In all hospitals and health centers there were no health services insurance schemes. Patients paid out of their pockets except for the payment services exempted such as anti-TB drugs and supplementary drugs (i.e. vitamin B6). However, if TB patients were admitted as inpatients, they were expected to pay for services like non-TB patients. At hospitals, TB symptoms screenings were conducted at OPDs, diabetes mellitus clinic, ART, and only at PMTCT from the maternal care units. None was done at maternal health care units. The main screening symptom is cough of two weeks or more except for known HIV positive that screened for cough of any duration but the interviewee indicated as the screening of TB was less implemented at the facility when compared with as per the national TB guideline. The TB symptoms screening recording format was found at health facilities units, such as OPDs, DM clinic, ART, and only at PMTCT from maternal care units; however,
there were no organized reports for how many patients screened for TB.

4. Discussion

In this study, we found that the number of presumptive TB cases were 20,284 and the number of TB cases diagnosed bacteriological or clinical were 2483 in three years (2015–2017). Passive screening for TB cases performed at outpatient departments, antiretroviral therapy clinics, diabetes mellitus clinics, and at prevention of mother to child transmission of HIV units; it did not at maternal health services units (i.e. family planning, ANC, Delivery, and PNC). The acknowledged challenges facing the TB control program performance related to TB screening and diagnosis included insufficient resources both financial and human resources, interrupted supply of reagents, equipment and supplies at the laboratories, and delay of referred samples return back to the facility.

One in ten presumptive TB cases (12.2%) were diagnosed with TB and this is comparable with a study from Addis Ababa (10%) [18]. Presumptive TB cases increased by the years of this study from 19.4% in 2015 to 48.6% in 2017. Bacteriologically-confirmed TB cases also increased by the years of study from 20% in 2015 to 45% in 2017 (Fig. 4). This could be due to Xpert MTB/RIF assay introduced by the NTP. This is corroborated with a study from central Ethiopia that showed that Xpert MTB/RIF assay increased TB detection rate by 47.4% compared with smear microscopy [19].

In Ethiopia, TB case finding follows a passive TB case finding approach as facilities’ heads and other health care workers indicated. It has started since DOTS’ strategy was endorsed in 1994 as a preferred strategy with the recommendation of “case detection by sputum smear microscopy among symptomatic patients’ self-reporting to health facilities” [9].

The result of this study indicated that the screening of TB was not integrated into maternal health care units, except in the PMTCT. In Ethiopia, screening for TB case finding activities has been done mainly for patients visiting at the OPDs, targeted screening for clinical risk groups namely, HIV or diabetic patients, and increased exposure to TB (e.g. prisons) [7]. TB case finding has been given less emphasis in other departments, such as RCH clinics where the majority of females attend. However, a study in Ethiopia revealed that, from infectious diseases, TB is ranked as the number one killer among females [20]. Another study
Table 5
TB diagnostic service availability and challenges at study sites in Ethiopia, 2019.

| Health facilities          | Hospital          | Melka Jebdu Health Center | Hiwot Fina Specialized University Hospital | Haramaya General Hospital | Zewditu Memorial Hospital | Kazanchis Health Center | Chelenko Primary Hospital |
|----------------------------|-------------------|---------------------------|------------------------------------------|--------------------------|---------------------------|-------------------------|--------------------------|
| **TB laboratories**        |                   |                           |                                          |                          |                           |                         |                          |
| 1 Microscopy               |                   |                           |                                          |                          |                           |                         |                          |
| - Present or absent        |                   |                           |                                          |                          |                           |                         |                          |
| 2 Chest X-ray              |                   |                           |                                          |                          |                           |                         |                          |
| Have a functional CXR     |                   |                           |                                          |                          |                           |                         |                          |
| Types of CXR              |                   |                           |                                          |                          |                           |                         |                          |
| - Digital X-ray            | Yes               | No                        | Yes                                      | Yes                      | Yes                       | Yes                     | Yes                      |
| - Normal X-ray             | No                | Yes                       | No                                       | No                       | No                        | No                      | No                       |
| Challenges related to CXR |                   |                           |                                          |                          |                           |                         |                          |
| - Shortage of radiologists| NA                | NA                        | NA                                       | NA                       | NA                        | NA                      | NA                       |
| Health insurance          |                   |                           |                                          |                          |                           |                         |                          |
| - No                       | No                | No                        | No                                       | No                       | No                        | No                      | No                       |
| How much is the chest X-ray service? | 40 Birr (1.4US$) | 30 Birr (1US$) | 35 Birr (1.2US$) | 15 Birr (0.5 US $) | NA | 50 Birr (1.5US$) | |
| Has a functional Xpert MTB/RIF assay | Yes | No | Yes | Yes | No | Yes | Yes | |
| Who maintain or services or calibrate? | Government | NA | Government | Government | Government | NA | Government | Government |
| Xpert MTB/RIF assay linked with the central lab (TB lab)? | TB lab | NA | TB lab | Central lab | TB lab | NA | Central lab | |
| Xpert MTB/RIF assay Cartridges supply by whom? | Government | NA | Government | Government | Government | NA | Government | Government |
| Shortage of cartridge supply | NA | NA | NA | NA | NA | NA | NA | |
| Shortage of power supply related to Xpert MTB/RIF assay | NA | NA | NA | NA | NA | NA | NA | |
| Xpert MTB/RIF assay Shortage of trained personnel | Mentioned at all health facilities | |

NA: not applicable for those facilities that had no diagnostic equipment at study time, next question(s) skipped; CXR: chest X-ray.
from Tanzania also showed that the prevalence of smear-positive TB among women with a cough attending RCHI was 3.8% [21]. The current practice of TB case finding in Ethiopia not only reduces national TB program (NTP) efforts of putting more infectious TB cases into care but also has a detrimental effect on women’s lives and their children [22]. To simplify patient flow and to reduce waiting times, to integrate TB screening and diagnostic into ante-natal care services would influence the TB program to obtain more TB cases [23]. Thus, in Ethiopia, the screening and diagnosis of TB among this group need to get due emphasis.

TB control program activities that related to screening and diagnosis assessed and used. A strong recommendation was made for presumptive TB cases to be performed. About 14.9% of TB cases treatment outcomes were not achieved by paper-based or electronically, still many other activities have indicated by the participants we interviewed. For this, the reasons they mentioned were high patient flow when compared with few health care workers working at health facilities particularly for hospitals, which affected screening of target groups. For the diagnosis of TB, many challenges identified: lack of diagnostic materials such as Xpert MTB/RIF assay at some facilities particularly at health centers, and interruption of supply of reagents (e.g. cartridges). The challenges in screening identified in this study are in line with a study done in North Ethiopia [24]. And also the diagnostic challenges indicated in a study from South-West Ethiopia showed that over one-third of TB smear microscopy was not requested; and among patients sent to the laboratory, almost 10% had missed results in laboratory registers [25]. These all might have contributed to less TB detection rate in Ethiopia that calls for innovative case finding approaches [8]. To improve TB screening needs a supply and demand side. To refine the supply side depends on technologies and screening algorithms, while addressing the knowledge gap enhances demand-side among clients as a study from Philippines revealed [26].

Moreover, lack of chest X-ray was a challenge identified by interviewees. For this reason, the facilities enforced to refer their patients to other referral linked government facilities. Subsequently, TB patients were incurred high out of pocket costs (e.g. 200 Birr or 7 US$), if they visited private health institutions. In Ethiopia, patients have to pay for the cost of registration or the issue of medical cards. In diagnosis process, if patients fulfilled the screening criteria (i.e. coughing for 2 or more weeks except for HIV positive with any duration), the patients had not paid for AFB, but paid for chest X-ray given that it was ordered by physician or health care workers. If TB patients are admitted in the inpatient wards, they are expected to pay for the services except for AFB, anti-TB drugs and vitamin B6. Beside, screening and diagnosis of eligible patients have not been performed as per the guideline of NTP as indicated by the interviewees. This is in line with studies done elsewhere in Ethiopia [24,27-28]. Thus, the NTP is expected to monitor and evaluate the policy on the guideline compliance in order to achieve the high caliber End TB goal.

We observed that the patients’ pathway to be screened and diagnosed for TB was a long process in any given health facility (Fig. 2); that is why a scholar has argued that quality of health care is beyond the coverage [29]. A similar finding was reported in a study done in five countries (11). The long pathway process leads to substantial total delay and a lack of timely treatment and care of TB patients [30]. Those facilities with no Xpert MTB/RIF assay sent the samples to the facilities that had Xpert MTB/RIF assay by already established referral system according to NTP. In this case, sometimes the samples were delayed as indicated by the participants we interviewed.

Though good progress has been made in documenting the activities either by paper-based or electronically, still many other activities have to be performed. About 14.9% of TB cases treatment outcomes were not recorded. In addition to this, presumptive TB cases were not properly recorded; other options were explored and obtained them from laboratory registries (AFB and/or Xpert MTB/RIF assay). Therefore, we strongly recommend the registration log book for presumptive TB cases should be prepared and used.

The drivers of strengths in our study, among others, found in that its large sample size for three years, its large area coverage and supplemented key informant interviews that enabled us to identify the burden of TB at study setting and explored the challenges for TB screening and diagnosis in Ethiopia. Despite it having these drivers of strengths, some factors with potential to pose limit our study worth mention. In our study, we observed data incompleteness that is common in retrospective data review [31] and in Ethiopia, on average report completeness in a study of eHMIS was 78.6% [32]. As a result; presumptive TB cases could be underestimated and underreported for the study population.

5. Conclusion

The burden of TB was high in the study setting, and frequent interrupation of laboratory reagents and supplies hampered TB screening and diagnostic services. Realizing the END-TB strategy in such resource-limited settings requires sustainable TB diagnostic capacity and improved case detection mechanisms, with TB programs strongly integrated into the general health care system. The national TB program also recommended as prepare and use a separate presumptive TB cases register log at health facilities.

6. Availability of data and materials

Data will be available upon request from the correspondence author

CRediT authorship contribution statement

Hussen Mohammed: Conceptualization, Project administration, Data curation, Formal analysis, Writing - original draft, Writing - review & editing. Lemessa Oljira: Supervision, Data curation, Writing - review & editing. Kedir Teji Roba: Supervision, Data curation, Writing - review & editing. Esther Ngadaya: Supervision, Data curation, Writing - review & editing. Tewodros Haile: Data curation, Writing - review & editing. Achene Kidane: Data curation, Writing - review & editing. Tsegahun Manyazewal: Data curation, Writing - review & editing. Abebaw Tekie: Supervision, Data curation, Writing - review & editing. Getnet Yimer: Supervision, Data curation, Writing - review & editing, Funding acquisition, Project administration.

Declaration of Competing Interest

Authors declared that there are no conflicts of interest.

Ethical statement

The Institutional Review Board (IRB) of the College of Health Sciences, Addis Ababa University approved the study. Letters of permission were obtained from respective health facilities. Informed verbal consent was obtained from each head and health care workers to ensure that they have participated in the study voluntarily.

Acknowledgments

The authors are thankful to the Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa), Addis Ababa University for providing technical support and managing the grant. The authors also thankful Haramaya University for assisting implementation of the project, and acknowledge all the study facilities for giving us permission to collect the data.

Funding

This study was part of EXIT-TB project which is part of the European
& Developing Countries Clinical Trials Partnership 2 (EDCTP2) program supported by the European Union (grant number CSA2016S-1608). The funder had no role in the conception, data collection, analysis and write up of this study.

References

[1] World Health Organization. Global tuberculosis report. Geneva, Switzerland. 2018.
[2] World Health Organization Regional Office for Africa. WHO African region communicable diseases cluster annual report, Geneva, Switzerland. 2016.
[3] Sullivan BJ, Esmaili BE, Cunningham CK. Barriers to initiating tuberculosis treatment in sub-Saharan Africa: a systematic review focused on children and youth. Glob Health Action 2017;10(1):1290317.
[4] Nkengasong et al., laboratory medicine in low-income and middle-income countries: progress and challenges. Lancet 2018;391:1873-5.
[5] World health organization. Systematic screening for active tuberculosis: an operational guide. 2015.
[6] Lonnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, et al. (2010). New WHO report gives hope to millions of people living with tuberculosis. Lancet 2010;375:1814–29.
[7] Federal Ministry of Health. National guidelines for TB, DR-TB and leprosy in Ethiopia. 2017. Addis Ababa, Ethiopia.
[8] Yassin MA, Datiko DG, Tulloch O, Markos P, Aschalew M, Shargie EB, et al. (2016). Innovative community-based approaches doubled tuberculosis case notification and improve treatment outcome in Southern Ethiopia. PLoS ONE 2013;8:e63174.
[9] Federal Ministry of Health. Tuberculosis, leprosy and TB/HIV prevention and control program manual. 4th ed. 2008. Addis Ababa, Ethiopia.
[10] Federal Ministry of Health. Services availability and readiness assessment (SARA). Addis Ababa, Ethiopia: Ethiopian Public Health Institute; 2016.
[11] Hanon C, Osberg M, Brown J, Durham G, Chin D. Barriers to initiating tuberculosis treatment in sub-Saharan Africa: a systematic review focused on children and youth. Glob Health Action 2017;10(1):1290317.
[12] Vassar M, Holzmann M. The retrospective chart review: important methodological considerations. J Educ Eval Health Prof 2013;10:12–4.
[13] Lee S, Lau L, Lim K, Ferma J, Dodd Cole D. The presence of cough and tuberculosis: a systematic review of the diagnostic yield of cough. BMC Health Services Research 2005;9(1):1183–203.
[14] Turnbull ER, Kancheya NG, Jennifer HB, Topp SM, Henostroza G, Reid SE. A model of tuberculosis screening for pregnant women in resource limited settings using Xpert MTB/RIF. J Pregnancy 2012. https://doi.org/10.1155/565049.
[15] Gebregeziabber SB, Yimer SA, Bjune GA. Qualitative assessment of challenges in tuberculosis control in West Gojjam Zone, Northwest Ethiopia: health workers’ and tuberculosis control program coordinators’ perspectives. Tuberc Res Treat 2016. https://doi.org/10.1155/2036234.
[16] Lee S, Lau L, Lim K, Ferma J, Dodd Cole D. The presence of cough and tuberculosis: active case finding outcomes in the Philippines. Tuberc Res Treat 2019.
[17] Federal Ministry of Health. National TB- leprosy and TB/HIV control program annual performance review meeting October 1-4, for the period from July 2017 to June 2018 (a year). 2018. Addis Ababa, Ethiopia.unpublished document.
[18] Federal Democratic Republic of Ethiopia Central Statistical Agency. Population projection of Ethiopia for all regions at Wereda level from 2014-2017. 2017. Addis Ababa, Ethiopia.