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Tuberculosis Diagnostics in Ethiopia: Assessment of Laboratory Procedural Capabilities and Limitations

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This is to certify that the doctoral study by

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Walden University
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Abstract

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MPH, George Washington University, 1999

BS, Marymount University, 1984

Doctoral Study Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Tuberculosis (TB) is a curable and preventable disease; however, in 2015, 10.4 million people were diagnosed with TB, making it one of the top 10 causes of mortality. A major part of the TB disease burden is carried by low and middle-income countries. In Ethiopia, which ranks 15th among 22 countries with a high burden of TB and multidrug resistant TB (MDR-TB), important diagnostic and treatment gaps persist. This quantitative descriptive study was primarily aimed to determine levels of adherence to standardized TB laboratory procedures by calculating and reporting the number of sputum samples, and reporting valid and documented results of laboratory Ziehl Neelsen (ZN) stain tests and MDR-TB tests for each suspected TB patient at a community health center TB laboratory in Addis Ababa, Ethiopia. The social theory of unanticipated consequences for purposive or social action was the theoretical framework for this study. Study results revealed that the optimal number of 3 samples sputum specimens collected for each suspected TB patient was submitted only for 48.1% of the study population. Also, regarding the percentage of valid and documented results for the 3 samples when performing laboratory ZN stain tests, for each suspected TB patient, there were valid results only for 72.2%, 51.2%, and 47.5% of the study participants, respectively. Finally, the percentage of valid and documented results when performing the MDR-TB test for each suspected TB patient was only 13.6%. For all the data, WHO criteria for error/undocumented results were not met. The study will contribute to changing the way Ethiopian laboratory technicians and managers address local challenges involving TB assessment, resulting in a positive social change in TB diagnosis and treatment.

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Dedication

Dedicated to my late father, Retta Wondimu who always encouraged his seven daughters to pursue higher education. To my late mother, and my late husband, Alemayehu and my two daughters Adis and Adey. Thank you for your unconditional love, support and trust.

Acknowledgments

I want to thank my committee chair Dr. Vasileios Margaritis for the constant feedback and encouragement throughout the research. Dr. Margaritis appreciated my research topic. He filled me with hope and encouraged me during the challenging part of the research study. I also want to thank my committee member, Dr. Srikanta Banerjee. I cannot forget the contributions of my former committee chair, Dr. Donald Goodwin, along with my former committee member Dr. Daniel Li. Dr. Goodwin inspired me and supported my decision to pursue a research topic relevant to my home country, Ethiopia. I live my adult life here in the United States, I always hoped to contribute in some small way to my native country, and this is a good start. I want to thank Dr. Daniel Bursa, Director General, Medical Service General Directorate Federal Ministry of Health, Ethiopia, for his understanding and support to pursue the research study. I want to thank Mr. Endalekachew Abebe, manager of the TB laboratory. I also want to thank Dr. Eyesusawit Shwangezaw and Dr. Addisalem Taye for their input throughout the research process. Finally, I couldn't have done without the support and encouragement I received from my daughters Adis and Adey, even though I took too much family time away from them. Adey encouraged me to join the DrPH program and was by my side throughout my study. I am in debt to Adis and Adey, they are the love of my life, their. constant and unconditional support helped me complete this research.

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Section 1: Foundation of the Study and Literature Review

Introduction

The genus Mycobacterium originated more than 150 million years ago . The organism *Mycobacterium tuberculosis* causes tuberculosis (TB). TB is a communicable disease (World Health Organization [WHO], 2019). The disease is spread from person to person through the air; when people with lung TB cough, sneeze, or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected. People infected with TB bacteria have a 5-15% lifetime risk of falling ill with TB. However, persons with compromised immune systems, such as people living with HIV, malnutrition, or diabetes, or people who use tobacco, have a much higher risk of falling ill (WHO, 2018). Undiagnosed and thus untreated *Mycobacterium tuberculosis* infection is deadly and if undiagnosed and untreated it leaves the country's population vulnerable to spreading the bacteria to families and to community members.

TB disease is a curable and preventable disease; however, in 2015, 10.4 million people were diagnosed with TB, making it one of the top 10 causes of death, with a death toll of 1.4 million worldwide (WHO, 2017b). Even though many steps have been taken to eradicate the disease, in 2015, TB was still one of the top 10 killers globally, ranking above HIV/AIDS as a leading cause of death from infectious disease (WHO, 2016a).

A major part of the TB disease burden is carried by low and middle-income countries (LMIC), as TB is a disease of the poor. Houben et al. (2016) said that the high burden of TB disease in LMICS requires even more accelerated TB prevention programs consistent with available resources in these countries to have a direct impact on case

identification, diagnosis, and treatment with the hopeful result of saving lives. Detection of the organism is achieved through laboratory procedures that can be simple manual procedures or expensive and highly technical automated procedures.

TB disease is a debilitating disease and treatment can only be initiated after detection of the organism causing the infection. Therefore, accurate and timely diagnosis followed by access to immediate treatment will save lives and resources. This can only be achieved through social change that empowers local level laboratory professionals and managers to own the process and initiate and sustain laboratory methodologies that consider local resources.

The rise of multidrug-resistant TB (MDR-TB) and extensively-drug resistant TB (XDR-TB) infection have created more challenges for health professionals as they continue to eradicate infections. MDR-TB is TB infection that does not respond to at least isoniazid and rifampicin, the two most powerful anti-TB drugs (WHO, 2017c). XDR-TB is a form of MDR-TB with additional resistance to more anti-TB drugs that therefore responds to even fewer available medicines. It has been reported in 117 countries worldwide (WHO, 2017c).

MDR-TB and XDR-TB continue to emerge because of the mismanagement of TB treatment and person-to-person transmission of MDR-TB infections. Most people with TB are cured by strictly following a 6-month drug regimen, but inappropriate or incorrect use of antimicrobial drugs or use of ineffective formulations of drugs (such as single drugs, poor quality medicines, or unacceptable storage conditions), and premature treatment interruption can cause drug resistance, which can then be transmitted,

especially in crowded settings such as prisons and hospitals (WHO, 2018). In some countries, it is becoming increasingly difficult to treat MDR-TB. Treatment options are limited and expensive. At $1000 U.S. dollars per patient, the new treatment regimen can be completed in 9-12 months and recommended medicines are not always available, and patients experience many adverse effects from the drugs.

The WHO (2016a) reported that the equivalent of $6.6 billion U.S. dollars was available for TB prevention, diagnosis, and treatment in low- and middle-income countries in 2016. They based their determination on data reported to the WHO for 126 countries with 97% of the world's notified TB cases. This amount in 2016 was an increase from previous years, but was still about $2 billion U.S. dollars less than the estimated requirement for this group of countries. The Who (2016a) stressed the need for $2 billion U.S. dollars and more commitment from local and international agencies.

The target to end global TB is reflected in the WHO's Sustainable Development Goals (SDG). The SDGs were adopted by the United Nations (UN) in September 2015 and covers the period 2016 to 2030. The End TB Strategy has a 20-year timeframe (20162035) and was unanimously endorsed by the WHO's member states at the 2014 World Health Assembly. Targets set for the End TB Strategy included a 90% reduction in TB deaths and 80% reduction in TB incidence by 2030, as compared to 2015 (WHO, 2016a).

Ethiopia is one of the world's oldest civilizations and one of the world's poorest countries (World Bank, 2017). It is the second-most populous country in Sub-Saharan Africa with a population of 99.4 million, and a population growth rate of 2.5% in 2015.

Poverty and dense population lead to a higher rate of transmission of communicable diseases, including TB. Ethiopia ranks 15 among the 22 countries with a high burden of TB and MDR-TB. In Ethiopia, the annual HIV-negative TB mortality and HIV-positive TB mortality is estimated to be 15,000 to 38,000 deaths and 1,600 to 7,300 deaths, respectively. Globally, 22 countries are considered to have a high burden of TB and MDR-TB and Ethiopia ranks 15 among these countries. Table 1 shows estimated TB burden in Ethiopia.

Table 1

TB Disease Burden in Ethiopia 2014

	Number (thousands)	Rate per 100,000 population
Mortality (excludes HIV+TB)	32 (22-43)	33 (23-44)
Mortality (HIV+TB only)	5.5 (4-4-6.8)	5.7 (4.6-7)
Prevalence (includes HIV+TB)	190 (160-240)	200 (161-243)
Incidence (includes HIV+TB)	200 (160-240)	207(168-250)
Incidence (HIV+TB only)	19 (15-23)	19 (15-24)
Case detection, all forms (%)	60 (49-73)	

The Federal Ministry of Health (FMOH, 2015) reported that important diagnostic and treatment gaps persist and listed the irregular supply of laboratory reagents as one of the top challenges. From 2014 to 2015, the TB case detection rate (number of cases notified divided by the number of cases estimated for that year) in Ethiopia was

67.3%, which was below the 83.0% target set by the WHO for the same year. Reves and Angelo (2016) noted that a major impediment to achieving the End TB Strategy in Ethiopia is the low TB case detection rate, which was 60% in 2015. Reves and Angelo said that 25% of the estimated 2,200 MDR-TB patients were identified. Therefore, it is important to increase the detection rate of TB and MDR-TB in Ethiopia.

Reviewing laboratory procedures may provide a better understanding of the challenges public health officials face when seeking to improve TB and MDR-TB detection rates in Ethiopia. To aid in this endeavor, this doctoral study assessed daily TB laboratory procedures at Community Health Center TB Laboratory in Addis Ababa from August 1, 2015 to December 31, 2016.

In this section, the problem statement, purpose, research questions, theoretical framework, literature review regarding concepts under study, assumptions, definitions, and scope and delimitations will be discussed.

Problem Statement

There is a problem regarding delay and accurate diagnosis and treatment for TB patients. Houben et al. (2016) said that the high burden of TB disease in LMICs requires even more accelerated TB diagnosis tools and prevention programs. Ethiopia is one of the high burden countries (HBCs), and it will be the focus of my proposed research. Improving the low TB case detection rate is a challenge that Ethiopia faces, as the country is moving to achieve End TB Strategy objectives by 2035. The WHO (2016a) reported that the rate of decline in TB incidence was as low as 1.5% from 2014 to 2015,

which is a much lower annual rate compared to the 4.5% yearly rate of decline needed by 2020 to meet the 2030 TB objective.

Another area of concern when considering how to enhance TB prevention is a delay in diagnosis. Although, there are regional variations for the delay in TB diagnosis and treatment, Bogale, et al. (2017) stated in Northwestern Ethiopia, it generally ranges from 40–97 days. Many factors cause a delay in diagnosis and treatment, but it is mainly related to health care seeking behavior, health system delivery, and timely diagnosis and treatment (Bogale et al. 2017).

There are various procedures to diagnose TB. A direct sputum smear examination using Ziehl Neelsen (ZN) staining is the most commonly-used procedure in many low-income counties, including Ethiopia. The method is low-priced, but its low sensitivity is a problem (Kivihya-Ndugga, van Cleeff, Juma, & Kimwomi, 2004). Depending on the number of specimens examined, ZN detects 30- 60% of culture-positive TB suspects. Moreover, a collection of sputum samples on three consecutive days is required, which is burdensome for patients and makes compliance difficult. Therefore, this might delay diagnosis and treatment. Polymerase chain reaction (PCR) techniques have higher sensitivity and specificity than conventional smear examination with ZN stain. However, the presence of a reliable support system that includes training and timely technical backing is highly recommended to make the PCR testing worthwhile. Among culture-positive patients, a single direct MTB/RIF test identified 551 of 561 patients with smear-positive tuberculosis (98.2%) and 124 of 171 with smear-negative tuberculosis (72.5%). Testing three samples increased the sensitivity to 90.2% (Sujata, 2014). It is important to

investigate that diagnostic tools are accurate, adhere to WHO standards, and are supported by available resources in the local area to have a direct impact on case prevention and saving lives.

Purpose of the Study

This quantitative descriptive study primarily aimed to determine levels of adherence to standardized TB laboratory procedures by calculating and reporting the number of sputum samples from each suspected TB patient, and the valid/documented results of laboratory ZN stain test and MDR-TB test for each suspected TB patient at a Community Health Center TB laboratory in Addis Ababa, Ethiopia. Second, I compared these data to similar data reported by the WHO and other countries to ascertain how Ethiopia stands regarding these standardized procedures.

There are significant inequalities that exist among and between countries in terms of their ability to access TB diagnostic and treatment. Of the estimated 9.6 million people who fell ill with TB globally in 2014, 6 million (62.5%) were reported to national authorities (WHO, 2015). Worldwide, 37.5% of TB cases went undiagnosed or were not reported to local governments/health authorities, posing a high risk of transmission to communities. TB diagnosis and treatment is an essential part of any country's health delivery system, and there are multiple factors contributing to delays in diagnosis and low case detection rates. The proposed research explored laboratory procedural capabilities and limitations in a community health center TB laboratory in Addis Ababa, a major urban city in Ethiopia.

From 2015 to 2016, the laboratory at a community health center TB laboratory in Addis Ababa used the ZN acid-fast bacilli (AFB) stain procedure to determine the presence and absence of tuberculosis bacteria in sputum samples. Also, the community health center used a Gene- Xpert PCR instrument to determine the presence and absence of MTB and to determine if the organism is resistant to rifampin. The device is endorsed for use in resource-limited settings. Rifampin is one of the first-line antibiotics used to treat TB infection; therefore, determining if TB organisms are resistant to rifampin enables clinicians to adjust medication and help TB infection control programs stop the spread of rifampin-resistant TB in the community.

The ZN AFB stain procedure requires three sputum samples from patients suspected to have TB infection. There are several steps that the laboratory is required to follow to produce reliable laboratory results. The procedural steps that the Community Health Center TB laboratory in Addis Ababa use and the WHO laboratory manual will be described in detail. Daily activities of the laboratory will be obtained from secondary data. Data will include the number of sputum samples collected, number of ZN stain performed, the number of ZN stain results documented, results of Gene Xpert PCR tests documented, and number of laboratory test results errors, invalid results, and no result documentation. The study analyzed any undocumented laboratory results, error codes, and invalid laboratory results as a measure of the level of the laboratory's procedural capabilities and limitations.

Research Questions

RQ1: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the number of sputum samples for detection of *mycobacterium tuberculosis* for suspected TB patients?

RQ2: Between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of valid/documented results when performing the laboratory ZN stain test for suspected TB patients?

RQ3: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of valid/documented results when performing laboratory MDR-TB tests for suspected TB patients?

Theoretical Foundation of the Study

Global health issues involve unique social dynamics that set them apart from all other social phenomena. Kleinman (2010) stated that global health is often viewed as a collection of health problems rather than a science discipline. However, the social theory of unanticipated consequences for purposive (or social) action can help understand challenges Ethiopia is facing in fighting TB. Sociologist Robert Merton first introduced the theory in 1936. Merton (1936) said one acts rationally by selecting means based on the available evidence, and yet the health goal may not be attained. Unorganized action refers to acts of individuals, and the formally organized action refers to like-minded individuals who form an association to achieve a common purpose. Unanticipated consequences may follow both types of action. Merton was interested in consequence of community/sate organized action, not organized efforts of individuals (De Zwart, 2015).

Limited knowledge can be the sole barrier to correctly anticipating a future outcome. Solinas-Saunders and Stacer (2015) said that some health interventions result in unintended consequences that are unpredictable while some are seen and prevented. One example is the unintended consequence of China's one-child per family population control policy, which gave birth to a sexual revolution in China (Kleinman, 2010).

Merton's theory of unintended consequences of social action is useful to investigate how decision-makers decide what is beneficial for a local area. But Solinas-Saunders and Stacer (2015) noted that many factors are intertwined and choices are formed within a social context constrained by time and space. One's action rationality is a function of their interpretation of reality in the context of a social system (Merton, 1936). Rationality is not synonymous with objectivity. Rationality is subjective since it is determined by human actions within the boundaries of an existing social structure (Solinas-Saunders & Stacer, 2015). Based on Merton's theory of unintended consequence of purposive action, the demand for social engagement is pressing, as is the need for immediate results.

According to Merton (1936), available knowledge is another way in which decision-makers' conclusions are restrained. When trying to decide what type of treatment, diagnostic procedures, or medical equipment is appropriate, decision-makers need information about local resources, culture, practices, needs, and wants of the local area. Solinas-Saunders and Stacer (2015) said acquiring sufficient knowledge takes energy and time, that actors including local health professionals and international agencies may not have. There is a need for immediate results or imperious immediacy of

interest. Consequently, decision-makers are limited in their ability to anticipate consequences of purposive actions correctly. They lack knowledge or the ability to translate knowledge into empirical data with the need to obtain immediate results limits the ability to predict results with certainty (Merton, 1936). Therefore, the proposed study assessed day-to-day laboratory activities to understand challenges and limitations that were not apparent at the time of decision making. The issue of Ethiopia's limited infrastructure, insufficient technical training, and limited troubleshooting abilities of laboratorians need to be considered in full before making any decisions. It is also crucial to investigate infrastructure capabilities, training, and technical support. These activities should be determined, sustained, and managed by the country's local health department managers with total backing from decision-makers and international agencies.

Nature of the Study

The study encompassed descriptive quantitative analysis of secondary data from August 1, 2015 to December 31, 2016 obtained from a community health laboratory in Addis Ababa, Ethiopia. The variables under study are number of specimens collected, TB microscopic test results, and MDR-TB test results using the Gene Xpert instrument, as indicated in laboratory records.

The WHO (2013) indicated that three consecutive sputum microscopies can identify 95- 98% smear-positive samples. The WHO (2013) said to collect the first specimen, early morning at home. The second sample should be collected when the patient presents to the laboratory on visit #1 and bring the third specimen the following day (visit #2). Alternatively, microscopic examination of two consecutive sputum

specimens collected on the same day may be performed. The minimum expectation the WHO set for HBCs is 90%. Analysis of laboratory functions will determine what the laboratory currently is doing and should be doing based upon WHO recommendations. The study involved data obtained from a community h/ealth center using descriptive statistics to understand gaps and successes of the laboratory procedural steps. Data analysis included data from the collection of three sputum specimens, results of sputum smear microscopic tests, and results of Gene Xpert PCR tests during August 1, 2015 to December 31, 2016. Secondary data for this study did not include patients' treatment information. Therefore, the study did not examine associations between laboratory patient results and treatment success or failure.

Literature Search and Strategy

The literature review is central to the research study. A literature review provides the foundation for research by including those articles that highlight the importance of the research questions. After formulating research questions, researchers move to understand what studies have been done and conclusions have been reached involving the research questions. During the literature review, reviewers seek to synthesize published research findings that relate to the research questions. It is also essential that reviewers evaluate literature for applicability, thoroughness, and significance as they apply to research questions. A necessary part of the literature review includes health information data, and population surveys conducted by local or international organizations.

I used CINAHL, MEDLINE, and Thoreau to access many full-text and peer-reviewed articles. I also used the websites of the WHO, Centers for Disease Control and

Prevention (CDC), National Institute of Allergy and Infectious Diseases (NIAID), Tuberculosis Research Advisory Committee (TRAC), and the FMOH. I reviewed annual reports and articles related to MTB infections, diagnosis, and treatment. Search terms used were: *Mycobacterium tuberculosis*, *high burden countries*, *MTB diagnosis*, *TB in Ethiopia*, *TB laboratory in Addis Ababa*, *TB laboratory*, *GeneXpert instrument*, *MDR-TB and TB case detection rate*, *TB microscopic*, *laboratory procedures*, and *TB in Sub-Sharan Africa*.

Literature and journals reviewed include articles published between 2009 and 2017. The journal articles I reviewed addressed burdens of TB and TB diagnosis in Ethiopia extensively. Other topics of interest were poverty, access to healthcare, laboratory management, TB laboratory procedures in Ethiopia, and laboratory management systems in other LMICs.

Literature Review

Addis, Birhan, Derseh, Sahle, and Gizaw. (2013) said that a considerable contributor to the root cause of dissatisfaction for Ethiopian healthcare professionals is poor quality of laboratory support. Haile, Mesfin, McNerney, and Gezehegn. (2014) said a major challenge for Ethiopian laboratories is to get continued commitments from managers and administrators to maintain laboratory excellence. Shortage of reagents and other consumable materials, including quality control materials, and lack of adequate resources for training laboratory personnel is a countrywide problem in Ethiopia.

Countries with limited resources do not need to adapt to recent technologies beyond their reach. Many highly technologically-advanced methodologies require initial

training, the ability to troubleshoot and correct instrument error messages, daily quality control and preventative maintenance of instruments, and ongoing competency verification. Sinishaw, Gebregorgis, and Shiferaw (2015) researched 82 health centers in the Amahara region in Ethiopia, and found that 40.2% of the health centers were understocked in terms of at least one reagent that is required to diagnose TB infection. Moreover, 93% of the 82 health centers did not fulfill the standard for effective distribution of laboratory supplies (Sinishaw et al., 2015). Reagents, supplies, and technical assistance are out of reach for some laboratories, which causes delays of test results or can produce incorrect results. Such delay defeats the purpose of engaging in the use of advanced technology. Ridderhof, Deun, Kam, Narayan, and Azize (2007) said that TB laboratories could either serve as a vehicle for progress or can inhibit further progress in TB control.

About half of the medical equipment in developing countries are poorly maintained; therefore, they are often out of order (Fonjungoa et al. 2012). Manalebh, Demissie, Mekonnen, and Abera (2015) conducted a cross-sectional study to evaluate sputum smear microscopy in 37 public-private mix (PPM) laboratories in the Western Region, Ethiopia. Manalebh et al. (2015) employed onsite evaluation and blind rechecking, and 67.6% of PPM-DOTS laboratories were found to be below standard recommended physical space. The quality of AFB staining reagents were also found to be substandard in private DOTS laboratories. These led to poor quality of sputum smear microscopy, and internal quality control was not regularly practiced. Sinishaw et al. (2015) found 7% of laboratories in Ethiopia's Amhara region use poor quality specimens.

Smear thickness and evenness were not acceptable in 66.2% and 62.7% of laboratories, respectively. The study also confirmed an inefficient supply distribution system which left many health centers with no or low stocks of TB reagents and supplies. Reagents and supplies are also central to quality assurance processes. Decentralized quality assurance processes improve TB microscopic test results. Melese et al. (2016) said external quality assurance (EQA) processes were expanded from four regional laboratories to 82 EQA centers, which included 956 health facilities (HFs). The EQA process involved rechecking AFB smears for false negatives (FN) and false positives (FP). The EQA process led by the Ethiopian Public Health Institute (EPHI) and funded and supported by the CDC was the gold standard. Training and mentoring laboratory professionals and instituting internal quality assurance (IQA) occurred during the period between 2012 and 2014 and the FP rate declined from 0.6% to 0.2%, and the FN fell from 7.6% to 1.6%. Melese et al. (2016) said that direct sputum microscopy for AFB using light microscopy is a test predominantly used to detect bacteria worldwide. The test is cost-effective, easy to train people to perform, and does not require a sophisticated instrument. But sputum microscopy for AFB heavily relies on external and internal QA, continuous quality improvement programs, and a reliable source of reagents.

Fonjungoa et al. (2012) said that laboratories should follow standard operating procedures with functioning equipment to obtain reliable and reproducible results that maintain turnaround time. Birhanaselassie (2015) said that laboratory service facilities and health facilities in Ethiopia have been reported to be very weak and limited. Birhanaselassie (2015) also identified many areas of concern, including lack of close

follow-up and supervision by hospital managers and governmental health agencies. These gaps are directly linked to ineffective laboratory processes. Clinical laboratories are an essential part of the healthcare system. Failed laboratory management systems can lead to unreliable diagnostic methodologies and inappropriate treatment, which can lead to increased morbidity and mortality (Birhanaselassie, 2015). Often, LMIC laboratories receive highly sophisticated laboratory instruments such as the Gene Xpert instrument at a reduced price. However, they usually have limited power to negotiate for low-cost consumables and employee training, so potential improvements in laboratory capabilities are often not realized.

The two most commonly-used microscopic procedures to recover TB organisms from a sputum sample are conventional ZN microscopy and fluorescence microscopy. Fluorescence microscopy is more sensitive (10%) and takes less time (WHO, 2011). However, it requires expensive mercury vapor light sources with regular maintenance and a dark room, which makes it inaccessible in most resource-limited countries. The WHO (2011) said LED microscopy was developed mainly to give resource-limited countries access to the benefits of fluorescence microscopy. LED microscopes are available in Ethiopia; they are less expensive, require less power, and can run on batteries.

As part of SDGs to end the global TB epidemic by 2030, the Strategic and Technical Advisory Group for Tuberculosis (STAG-TB) provides technical guidance to the WHO. The STAG-TB provides objective, ongoing technical, and strategic advice to the WHO related to TB care and control. The WHO (2016d) supported the inclusion of patients and affected communities to enable their voice to inform policymaking and

program planning at every level. The literature review indicates shortages of laboratory consumables and lack of close follow-up and supervision from managers and governmental health agencies leads to incomplete and delayed laboratory results. The proposed study will reiterate the importance of engaging local laboratory professionals and managers and empowering them to own laboratory support processes. Highly advanced technology might not always be fitting. The study can encourage and educate Ethiopian laboratorians and managers to consider local resources before adapting TB laboratory methods. Building confidence in laboratory managers to be decision-makers in their local area will lead to positive social change.

Haile et al. (2014) said that the level of commitment among laboratory managers in Ethiopia varies and affects the continuity of good laboratory practice. Haile et al. (2014) said that there is a country-wide problem regarding purchasing of reagents, laboratory consumables, and quality control materials.

Addis et al. (2013) said that 86.7% of physicians and nurses in Ethiopia have encountered lost laboratory reports. Loss of laboratory results were not directly associated with the healthcare provider's level of dissatisfaction. However, it represents a possible compromise in providing timely treatment to patients.

Mala, Moser, Dinant, and Spigt (2014) conducted a study in Tigray, Ethiopia to understand why TB service providers in Ethiopia do not follow treatment guidelines. Thirty-nine TB care providers participated in a focus group discussion. Healthcare providers developed negative expectations about the results of sputum smear microscopy tests. There are three main reasons for noncompliance of TB treatment guidelines. The

first is Ethiopia's limited ability to correctly diagnose TB and give the right treatment. Second is the lack of clarity of local guides with recommendations when to retest those patients whose initial tests are negative. Third is the lack of complete diagnosis and treatment documentation. Also, there are five factors that influence noncompliance among TB care providers: insufficient diagnostic modalities, ambiguity in guidelines and recommendations, poor patient care documentation, state of healthcare services, and healthcare providers in government-run or private hospitals showing little interest in following national guidelines.

Fiseha and Demissie (2015) emphasized the importance of decentralized TB treatment centers in Ethiopia. Patients are not able to comply with direct observation treatment (DOT) because treatment centers congregate in the city, away from the rural community. Moreover, enhanced severity of the disease when co-infection with HIV reduces adherence. The study also gives insights about factors that influence TB treatment adherence. One is the patient's belief about the curability of TB disease. Second is support from family, friends, the community, and health professionals, all of whom can help the patient to seek treatment and adhere to the medication regimen.

Temesgen and Demissie (2014) conducted a study in the Amhara region in northwestern Ethiopia to assess the knowledge and practice of M. tuberculosis infection control (TBIC). The study involved 313 healthcare providers in four hospitals. In the study, TBIC knowledge and practice were used as dependent variables. Independent variables establishing TBIC knowledge and practice were sociodemographic characteristics, years of service, level of education, professional categories, job location,

and training regarding TBIC. Knowledge about TBIC was a strong predictor of good TBIC practice. Only 18% of participants were trained on TBIC. Years of service or level of education was not associated with TBIC knowledge. Even though there was a high prevalence of TB with a high probability of TB nosocomial transmission, most health facilities in Ethiopia do not have TBIC practices. Therefore, patients and providers are at risk of exposure to TB, especially at high caseload facilities.

Fiseha and Demissie (2015) found that healthcare workers (HCWs) shared their concern about contracting TB/MDR-TB due to the absence of standard TB IC measures. Given the high cost of infection control processes, most low-income countries cannot afford to implement them.

Kivihya-Ndugga et al. (2004) discussed Nairobi, Kenya, where sputum specimens from 1, 396 TB suspected patients were analyzed for the presence of TB using the PCR assay. The result showed a sensitivity and specificity at 93% and 84%, respectively. The concern is the cost-effectiveness and operational effectiveness for low-income countries with high-burden of TB.

Scherer et al. (2004) said when using culture as a gold standard, a sensitivity ranges from 77% to more than 95%. However, for smear-negative specimens, PCR sensitivity has been reported to be below 90%. Scherer et al. (2004) also examined sensitivity for HIV positive versus HIV negative patients, showing lower sensitivity for HIV positive patients.

Definitions

Definitions of terms used in the study are as follows:

Acid-fast bacilli (AFB): is a type of bacteria that causes tuberculosis and certain other infections (WHO, 2010).

Colour test: A simplified and more timely TB culture method when compared with traditional culture methods. It was designed to assist with more timely confirmation of TB infections, particularly in low resource settings. The colour test combines the thin-layer agar technique with a simple colour-coded quadrant format, selective medium to reduce contamination and colorimetric indication of bacterial growth to simplify interpretation. DST patterns for isoniazid (INH), rifampicin (RMP), and ciprofloxacin (CFX) were determined using the Colour Test for 201 archived *Mycobacterium tuberculosis* isolates.

Extensively-Drug Resistant Tuberculosis (XDR-TB): A form of multidrug-resistant TB with additional resistance to more anti-TB drugs that therefore responds to even fewer available medicines. It has been reported in 117 countries worldwide (WHO, 2017c).*Xpert MTB/RIF Assay:* A qualitative, nested real-time PCR in vitro diagnostic test for the detection of TB complex DNA in raw sputum. In specimens where MTB-complex is detected, the Xpert MTB/RIF assay also detects rifampin-resistance associated with mutations of the rpoB gene (WHO, 2017c).

Latent TB Infection: TB bacteria can live in the body without making a person sick. In most people who breathe in TB bacteria and become infected, the body can fight the bacteria to stop them from growing. Latent TB infections can activate to become TB (CDC, 2017).

Multi-Drug Resistant Tuberculosis (MDR-TB): The bacteria that cause TB can develop resistance to the antimicrobial drugs used to cure the disease. MDR-TB is TB that does not respond to at least isoniazid and rifampicin, the two most powerful anti-TB drugs (WHO, 2017c).

TB-LAMP: A manual assay that requires less than one hour to perform and can be read with the naked eye under ultra violet light. The WHO (2016c) recommended that the TB-LAMP can be used as a replacement for microscopy for the diagnosis of pulmonary TB in adults with signs and symptoms of TB.

Xpert MTB/RIF: An automated, cartridge-based nucleic amplification assay for the simultaneous detection of TB and rifampicin resistance directly from sputum which takes less than 2 hours (WHO, 2017a).

Ziehl-Neelsen (ZN) Stain: A smear prepared directly from sputum specimens and it is the most widely available test for diagnosis of TB in resource-limited settings. ZN microscopy is highly specific, but its sensitivity is variable (20-80%) and is significantly reduced in patients with extrapulmonary TB or HIV (WHO, 2010).

Assumptions

According to the WHO (2017b), there is a global caution practiced when using country health information system (HIS), including vital registration because of concerns with information/data quality and completeness. The WHO emphasized the need to strengthen each country's HIS, in-order to provide a more solid empirical basis for monitoring the national health situation and trends. The first and primary assumption of this study is that all data provided for use in this study were accurate and reliable.

The second assumption of this proposed study is that undocumented information on the health center log reflects incomplete laboratory work. It is not clear if the patient refused to submit sputum specimen or employees did not give adequate specimen collection instruction to the patient. It may be the patient could not produce sputum specimen. It is not clear if there was no designated area for the patient to collect the specimen. The WHO (2017c) affirmed that the global health estimates represent the best estimate by the WHO based on the evidence available to it.

Scope and Delimitations

The study was based on secondary data obtained from a community health center in Addis Ababa, one of the largest cities in Ethiopia. Addis Ababa is an urban city with adequate roads, transportation system, and has an accessible healthcare system. Therefore, the city is not representative of most towns in Ethiopia.

One limitation of the study involves obtaining reliable data. Most data received from local areas are estimates. Therefore, many international agencies, including the WHO confirmed that available data are at best an estimate. Therefore, another limitation is an incomplete result documentation process. The secondary data from the community health center TB laboratory in Addis Ababa may reflect gaps in the specimen collection and documentation of laboratory results.

Summary and Conclusion

Clinical laboratories are an integral part of a healthcare system. Laboratories play a significant role in the diagnosis of a disease. The need to standardize laboratory procedures across continents is vital. Health care-seeking behavior of the patient can

delay diagnosis and treatment. However, once the patient arrives at the laboratory, patients must receive full service. A failure to give full laboratory service is a lost opportunity to diagnose and treat a patient.

The proposed study can provide an evaluation of the day-to-day activities of a community health TB laboratory revealing the success and the challenges faced even with the availability of high-technology instruments, like the Gene Xpert MDR-RIF-R PCR assay.

It is considered vital to building on what a laboratory can achieve using current procedures before moving into the use of instruments that require technical assistance. Assessing, understanding, and revising existing procedures will require direct participation from the local laboratory management group with the support of international health agencies. The study will also recommend ways to improve the current processes. The suggested procedures will build on what Ethiopia already achieved and suggest optimal laboratory excellence to detect TB infections.

Section 2: Research Design and Data Collection

Introduction

This study involves the evaluation of the collection and analysis of specimens once the patient arrives in laboratory to complete and release TB test results for laboratory technicians. The study examined and reported proper documentation of each step during the laboratory process. The design choice advances the importance of attention to details at each step of the laboratory process.

There are many laboratory processes and procedures to diagnose TB. TB may be present in sputum, gastric lavage fluids, cerebrospinal fluid, urine, and a variety of tissues. One procedure that is widely used is the AFB microscopic test. The purpose of AFB microscopy is to detect AFB through microscopic examination of clinical specimens. The light microscopy of ZN staining is prepared directly from sputum specimens. The method is a widely used test for diagnosis of TB in resource-limited settings.

The laboratory test starts with collecting sputum samples, followed by staining and microscopic analysis to determine the absence or presence of AFB organisms. The Xpert MTB/RIF PCR assay was recommended by the WHO in 2015 to be used as an initial diagnosis for all people suspected to have pulmonary TB. To understand the challenges faced by a health center in Addis Ababa, Ethiopia this study examined TB laboratory procedures at one of the TB laboratories in the area.

The variables under study are the number of specimens collected, TB microscopic test results, and TB and MDR-TB test results using the Gene Xpert instrument, as

indicated in laboratory records. Data records are identified numerically as 1 through 160 participants.

Research Design and Rationale

The goal of the study was to investigate the potential challenges of TB laboratories. The study applied the descriptive quantitative research design to assess incomplete laboratory steps and test results based on a sample size of 160 laboratory records from between August 2015 and December 2016. Laboratory records involved numerical identifiers to itemize variables. The study analyzed secondary data obtained from a community health center TB laboratory in Addis Ababa to perform descriptive statistics for the collection of sputum specimen from TB-suspected patients, tresults ZN microscopic tests, and the Gene Xpert instrument to detect MDR- TB. Since this study used secondary data and there were no inferential research questions, the descriptive quantitative design was most appropriate.

Methodology

The study objective was to determine adherence to standardized TB laboratory procedures, using SPSS descriptive analysis and frequencies, which includes frequency analysis for variables, number of specimens collected from TB-suspected patients, sputum smear TB microscopy test results, and MDR-TB testing results using the Gene Xpert instrument as indicated in laboratory records. Data records were identified numerically.

The dataset was identified using numerical numbers with a sample size of approximately 160 suspected TB patients from August 2015 to December 2016. Due to

the fact that all data were included in the statistical analysis and there were no inferential statistics, effect size and statistical power cannot be calculated.

Descriptive statistics and frequency table options allow the analysis of each coded step to calculate frequency and a corresponding graph to visually represent how the laboratory adhered to TB processing and resulting procedures set by the WHO. Descriptive statistics include the number of processes that were resulted, not documented, flagged as errors, or showed invalid results (error, invalid, undocumented, specimen not collected) as part of the study. More specifically, the percentage of valid/documented results when performing the ZN stain test and MDR-TB test for each suspected TB patient was evaluated to see if they met WHO criteria; 5-15% error/undocumented results are acceptable (WHO, 2015a). For failed laboratory steps, the study will make a recommendation for improvement.

The research questions for this study are:

RQ1: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the number of sputum samples for detection of *mycobacterium tuberculosis* for suspected TB patients?

RQ2: Between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of valid/documented results when performing the laboratory ZN stain test for suspected TB patients?

RQ3: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of

valid/documented results when performing laboratory MDR-TB tests for suspected TB patients?

Data Analysis

Variables and codes under study are displayed in Table 2. More specifically, Table 2 includes information regarding the number of specimens collected, TB microscopic test results, and TB and MDR-TB test results using the Gene Xpert instrument, as indicated in laboratory records. All variables are categorical; therefore, descriptive statistics include frequency percentages for each code per variable. Additionally, for ZN and MDR-TB tests, a ratio of valid results was reported (number of valid documented cases/all cases). All analyses were conducted using SPSS v. 24.

The laboratory is required to collect three sputum samples from each TB-suspected patient. The laboratory is also required to perform ZN staining for each sputum and record microscopic results for each sputum sample. In addition, the laboratory is also required to perform MDR-TB test using the Gene Xpert PCR instrument for each MDR-TB suspected patients. Collecting three sputum samples and performing ZN stains for each sputum sample and microscopic reading to obtain and document three ZN stain results for each TB patient is required. In addition, Gene Xpert PCR test results are required for all MDR-TB suspected patients.

The study assessed the percentage of failed test. For example, if no test result is documented, if invalid test result documented, and error test result is documented. The study also assessed if, corrective action process is in place to correct failure of laboratory

test. The study was limited to assessing the performance of the laboratory only. The study does not assess or confirm patient diagnosis or treatment.

Table 2

Study Variables and Codes

Variables	Codes
Number of sputum specimen collected from each TB infection suspected patient	0- None 1- 1 2- 2 3- 3 4- Not documented
ZN stain sputum microscopic test result	1- Negative 2- 1-9 + 3- 10-99 ++ 4- >= 100 +++ 5- Not Documented
MTB/RIF Assay results using the Xpert PCR instrument	0- TB Detected 1- TB Not Detected 2- TB Detected RIF Detected 3- TB Detected RIF Not Detected 4- Instrument Error/invalid 5- Not documented

Threats to Validity

A secondary analysis examines data that were primarily collected for some purpose other than the research studies. Secondary data will expedite and strengthen this proposed research study. Secondary data will support the doctoral research as the data will help develop, answer, and elaborate upon the research question. Result of a research study is vital to the degree that it can be interpreted accurately and confidently. Accurate and confident interpretation of a result is at the center of validity discussion. In this study,

I analyzed the frequencies of events to establish a high occurrence of disagreeable laboratory events that might affect patient health outcomes. The study result was valid since it reflects the rate of laboratory results obtained and the frequency of undocumented result and failed results. The study does not calculate associations between variables, and thus no internal validity threats exist. Additionally, I do not generalize the results of the study to other populations, since they are useful to evaluate TB data collection and analysis procedures only in Ethiopia. The only threat to this study can be potential issues with the secondary data, such as missing cases or incomplete data and I worked with the health center to address these issues as much as I could.

Ethical Procedures

Research should always be conducted ethically. It is important to get the required permission when a research study involves human subjects and accessing patient health information. This study was conducted using a secondary data set without any direct interaction with patients, and no patient identifiers are used. The laboratory record used numerical identifiers to itemize variables. I received approval by Addis Ababa University Research Review Board (AAURRB) to receive and analyze the data. Additionally, Walden IRB also approved this study (#12-17-19-0466211). All data will be stored in password-secured files in my computer for at least 5 years per Walden policy.

Summary

Clinical laboratories are an integral part of a healthcare system. Laboratories play a significant role in the diagnosis of a disease. The need to standardize laboratory procedures across continents is vital. Health care-seeking behavior of the patient can

delay diagnosis and treatment. However, once the patient arrives at the laboratory, patients must receive full service. A failure to give full laboratory service is a lost opportunity to diagnose and treat a patient. The study objective is to determine adherence to standardized TB laboratory procedure using SPSS which includes frequency analysis for variables, number of specimens collected from each TB suspected patient, sputum smear TB microscopy test results, and MDR-TB testing results using the Gene Xpert instrument as indicated in laboratory records.

Section 3: Presentation of the Results and Findings

Introduction

The study used a quantitative descriptive design to determine levels of adherence in a community health center TB laboratory in Addis Ababa, Ethiopia to standardize TB laboratory procedures. The study involved sputum samples from each suspected TB patient, and the valid/documented results of laboratory ZN stain test and MDR-TB test for each suspected TB patient at the center under study.

RQ1: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the number of sputum samples for detection of *mycobacterium tuberculosis* for suspected TB patients?

RQ2: Between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of valid/documented results when performing the laboratory ZN stain test for suspected TB patients?

RQ3: During the period between August 1, 2015 and December 31, 2016 at a community health center TB laboratory in Addis Ababa, what was the percentage of valid/documented results when performing laboratory MDR-TB tests for suspected TB patients?

Data Collection of Secondary Data Set

The study used secondary data collected by the TB laboratory from August 1, 2015 to December 31, 2016. Patients who come to this laboratory are suspected of having TB infections, and they are referred by primary care physicians to submit sputum samples for laboratory examination. Typically, urban cities in Ethiopia have access to

transportation; therefore, patients in Addis Ababa have the option of using a city train or taxi. The TB laboratory is a government-run laboratory, and patients are charged a reduced fee for laboratory services compared to private laboratories.

Results

The variables under study are the number of specimens collected, TB microscopic test results, and TB and MDR-TB test results using the Gene Xpert instrument, as indicated in laboratory records. Data records were identified numerically as 1 through 162.

Descriptive statistics data analysis was performed using SPSS version 25. All variables are categorical and reported as frequencies (%).

In Table 3, 1.2% of the sample was RMP detected and 2.5% was RMP resistant indeterminate. It is indicated that in 86.4% of the sample, tests were not performed, and of 13.6% test that was performed, 2.5% were recorded as errors.

Table 3

Frequency Table for MTB-RIF Assay Xpert Instrument

	Frequency	Percent	Valid Percent
TB not detected	12	7.4	7.4
TB detected RMP resistant detected	2	1.2	1.2
TB detected RMP resistant not detected	4	2.5	2.5
Error	4	2.5	2.5
Not performed	140	86.4	86.4
Total	162	100.0	100.0

For 4.4% and 21.5% of participants' two sputum samples and one sputum sample were submitted, respectively. The optimal number of three samples was submitted only for the

48.1% of the study population and 25.9% of patients for whom no sputum samples were provided.

Table 4

Sputum Samples Collected Per Patient

		Frequency	Percent	Valid Percent
	0	41	25.3	25.9
	1	34	21.0	21.5
	2	7	4.3	4.4
	3	76	46.9	48.1
	Total	158	97.5	100.0
Missing	System	4	2.5	
Total		162	100.0	

In addition, Tables 5, 6 ,and 7 show that for samples 1, 2, and 3there were results only for 72.2%, 51.2%, and 47.5% of study participants, respectively, and for the rest no evaluation was peformed.

Table 5

Frequency Table: Sample 1

	Frequency	Percent	Valid Percent
no +	106	65.4	65.4
+	1	.6	.6
++	6	3.7	3.7
+++	4	2.5	2.5
Not performed	45	27.8	27.8
Total	162	100.0	100.0

Table 6

Frequency Table: Sample 2

	Frequency	Percent	Valid Percent
no +	75	46.3	46.3
+	2	1.2	1.2
+++	6	3.7	3.7
Not performed	79	48.8	48.8
Total	162	100.0	100.0

Table 7

Frequency Table: Sample 3

	Frequency	Percent	Valid Percent
no +	69	42.6	42.6
++	4	2.5	2.5
+++	4	2.5	2.5
Not performed	85	52.5	52.5
Total	162	100.0	100.0

Summary

For RQ1, where the number of sputum specimens collected was evaluated for each suspected TB patient, an optimal number of three samples was submitted only for 48.1% of the study population and no sputum were provided for 25.9% of patients.

For RQ2, where the percentage of valid/documented results for samples 1, 2, and, 3 when performing the laboratory ZN stain test for each suspected TB patient was evaluated there were results only for 72.2%, 51.2%, and 47.5% of study participants, respectively, and for the rest no evaluation was peformed.

For RQ3, where the percentage of valid/documented results when performing the MDR-TB test for each suspected TB patient was evaluated, it was indicated that in 86.4% of the sample, the test was not not performed and among 13.6% of that population, 2.5% was recorded as having errors. For all research questions, WHO criteria for 5-15% error/undocumented results were not met.

Section 4: Application to Professional Practice and Implications for Social Change

Introduction and Key Findings

The principal purpose of this study was to determine level of adherence to standardized TB laboratory procedures by calculating and reporting the number of sputum samples from each suspected TB patient, as well as valid and documented results of ZN stain tests and MDR-TB tests for each suspected TB patient at a community health center TB laboratory in Addis Ababa, Ethiopia. In this section, I will provide the key results for each research question and how these results compare to WHO criteria.

For RQ1, where the number of sputum specimens collected was evaluated for each suspected TB patient, the optimal number of three samples was submitted only for 48.1% of the study population, and no sputum was provided for 25.9% of the patients. For RQ2, where the percentage of valid and documented results for samples 1, 2, and, 3 when performing the laboratory ZN stain tests for each suspected TB patient was assessed, there were results only for 72.2%, 51.2%, and 47.5% of study participants, respectively, and for the rest no evaluation was performed. Therefore, the WHO criteria of 5-15% error/undocumented results were not met. In exploring RQ3, for which the percentage of valid and documented results when performing the MTB-RIF-TB test for each suspected TB patient was evaluated, 86.4% of the sample MTB-RIF-TB test was not performed; this is significantly high compared to WHO criteria of 5-15% for error and undocumented results.

Second, I will compare these data to similar data reported by the WHO and other countries to ascertain how Ethiopia stands regarding standardized procedures and

discussed potential deviations from these standards. In this section, I will discuss the results of the study compared to the WHO and Sub-Saharan African countries with similar demographics. Second, I will discuss these results based on the theoretical framework I suggested in Section 1. In this section, I will also discuss interpretations of the study results in relation to the theoretical framework. I will also discuss and compare TB laboratory studies and results from other Sub-Saharan countries.

Interpretation of the Results

Onyebujoh et al. (2017) said that Africa is home to 26% of estimated incidences of all TB cases (2.7 million) and TB death rates in Africa are three times greater than the global average. Summer et al. (2019) said it is sometimes assumed that the only constraint is the health sector budget; however, even if funding is available, it may take time to allocate necessary staffing and infrastructure to deliver TB services. Improving equitable access to TB diagnosis and treatment remains the most pressing need for Africa, where laboratory services play a pivotal role (Onyebujoh et al., 2017).

Since 2011, investments in molecular TB diagnostics have multiplied, as reflected by the deployment of an increasing number of Cepheid GeneXpert systems across Africa. However, these efforts were not being translated into an increased diagnosis of TB cases or increased laboratory confirmations of cases that were notified (Onyebujoh et al., 2017).

Onyebujoh et al. (2017) said that the numbers of laboratories providing TB diagnostic services using smear microscopy and GeneXpert have gradually increased. However, the overall number of new laboratory-confirmed tuberculosis cases has not

increased. As a more sensitive and accurate molecular diagnostic tool, the potential of GeneXpert technology to improve the diagnosis of tuberculosis/HIV cases has yet to be fully realized since it was introduced in 2011.

Summer et al. (2019) said in South Africa, mathematical models are increasingly being used to compare strategies for TB control without detailed information regarding implementation. Decision-makers need information about local resources, infrastructure, culture, practices, needs, and wants of the local area.

For RQ1, three samples were submitted only for 48.1% of the study population, and for 25.9% of the patients, no sputum samples were provided. In some cultures, people may need a covered area or a room to collect sputum samples, and in many resource-limited countries, restrooms are not always available. Testing three samples can increase the sensitivity of TB diagnosis to 90.2% (Sujata, 2014).

Dzodanu et al. (2019) said that in many developing countries, the diagnosis of TB is mostly based on the ZN staining technique. The ZN method, however, is reported to be low and variable, ranging from 20 to 80%, often depending on the diligence with which specimens are collected, smears are made, and stained smears are examined. The WHO guideline is to collect three specimens per patient. Parsons et al. (2011) said examination of only two smears in place of three could ease the workload of laboratories, decrease time for diagnosis and initiation of treatment, and decrease the number of patients dropping out of the diagnostic pathway by one third, particularly in countries with a high microscopy workload. In addition, patients will spend less time at the diagnostic facility. However, reduction of the number of specimens examined for the

screening of TB patients from three to two specimens should be recommended only in settings with a well-established laboratory network and fully-functional EQA program for smear microscopy, including onsite evaluation and followup training for problem laboratories. Also, reducing the number of sputum specimens collected may leave a significant number of cases undetected, especially if it becomes the only means of diagnosis.

RQ2 involves the percentage of valid and documented results when performing laboratory ZN stain tests for each suspected TB patient. My study revealed that the results for samples 1, 2, and, 3 when performing the laboratory ZN stain test for each suspected TB patient, were only 72.2%, 51.2%, and 47.5% of study participants, respectively, and for the rest no evaluation was performed. This negative result highlights the importance of a reliable support system that includes training. Haile et al. (2014) said that there is a country-wide problem regarding the purchasing of reagents, laboratory consumables, and quality control materials. Merton's theory of unintended consequences of social action is useful to investigate how decision-makers decide what is beneficial for a local area. Solinas-Saunders and Stacer (2015) said that many factors are intertwined, and the choices are formed within a social context constrained by time and space. One's action rationality is a function of their interpretation of reality in the context of a social system (Merton, 1936). In 22 high burden countries (of which Ethiopia is one) with 80% of tuberculosis cases worldwide, a systematic review of 37 eligible studies of serial sputum specimen results indicated that almost 85.8% of TB cases were detected with the first sputum specimen. With the second sputum specimen, the average incremental yield

was 11.9%, while the incremental yield of the third specimen, when the first two specimens were negative, was 3.1%.

RQ3 regarding the Gene-Xpert instrument test indicated that in 86.4% of the sample, the test was not performed, and of 13.6 % test that was completed, 2.5% was recorded as an error. The Xpert MTB/RIF PCR assay was recommended by the WHO in 2015 to be used as an initial diagnosis for all people suspected to have pulmonary TB). Xpert MTB/RIF is an automated, cartridge-based nucleic amplification assay for the simultaneous detection of TB and rifampicin resistance directly from sputum in less than two hours (WHO, 2017a). However, the presence of a reliable support system that includes training, infrastructure, and timely technical backing is highly recommended to make the PCR testing worthwhile. Summer et al. (2019) discussed the critical impact and cost-effectiveness of TB case detection, where sometimes it is assumed that the only constraint is the health sector budget. However, even if funding is available, it may take time to allocate the necessary staffing and the infrastructure to deliver TB services. Rice (2017) stated that the detection of (MTBC and RIF resistance has been well documented in low-resource settings with high TB-incidence. However, few studies have assessed its accuracy in low TB incidence settings with high resources. A retrospective study evaluated the performance of Xpert MTB/RIF using clinical sputum specimens routinely collected from suspect pulmonary TB patients in San Diego County, California. Xpert MTB/RIF results were compared to acid-fast bacilli (AFB) smear microscopy, mycobacterial culture, and phenotypic drug susceptibility testing (DST) (Rice 2017). In this study, the Xpert MTB/RIF assay was performed following CDC recommendations

for PCR testing to be performed on at least one respiratory specimen, from each patient with signs and symptoms of pulmonary TB. In general, the Xpert MTB/RIF assay was used to test the first AFB smear-positive specimen collected from each patient, as well as AFB smear-negative specimens per clinician request in patients with a high suspicion of pulmonary TB. Of 751 sputum specimens, 134 (17.8%) were MTBC culture-positive and 2 (1.5%) were multidrug-resistant (MDR) (Rice 2017).

Xpert MTB/RIF detected 35 of 47 smear-negative culture-positive specimens and excluded 124 of 137 smear-positive culture-negative specimens. Xpert MTB/RIF also correctly excluded 99.2% (121/122) of nontuberculous mycobacteria (NTM) specimens. It also eliminated all 33 NTM false-positives by smear microscopy. Xpert MTB/RIF sensitivity and specificity for the detection of RIF resistance were 100% (2/2) and 98.3% (116/118), respectively (Rice, 2017). The success of such scenario underscores the availability of an in-built infrastructure in developed countries, that might be taken for granted while implementing high-tech instruments in developing countries. More often the lack of funding for such project might sufficiently been addressed however, it might not only be a lack of funding, Summer et al. (2019) discuss the critical impact and cost-effectiveness of TB case detection, where sometimes it is assumed that the only constraint is the health sector budget. However, even if funding is available, it may take time to allocate the necessary staffing and the infrastructure to deliver TB services.

The study by Ardizzoni et al. (2015) describes the performance of Xpert and critical lessons learned during two years of implementation under routine conditions in 33

projects located in 18 countries supported by Médecins Sans Frontières across varied geographic, epidemiological and clinical settings. Routine laboratory data were collected, using laboratory registers. Qualitative data such as logistics, human resources, and methodology approval were collected using a questionnaire. First, Xpert was used as the initial test, with microscopy in parallel, for all possible TB cases. Second Xpert was used for patients at risk of MDR-TB, or with HIV associated TB, or presumptive pediatric TB; and the third Xpert was used if test is the initial test for high-risk patients as an add-on test to microscopy. The average MTB detection rate was 18.5%, 22.3%, and 11.6% for the above three different tests, respectively.

The results microscopic tests in parallel with Xpert as an add-on test to microscopy test increased laboratory TB confirmation by 49.7%. The major drawback of the test was the high rate of inconclusive results, which correlated with factors such as defective modules, cartridge version (G3 vs. G4), and staff experience. Operational and logistical hurdles included infrastructure renovation, basic computer training, regular instrument troubleshooting, and maintenance, all of which required substantial and continuous support (Ardizzoni et al. 2015).

Considering the results from these studies, we are confident the challenges faced in low-resource settings with high TB-incidence, needs attention to address the lack of comprehensive technical assistance, including the formulation of policies, infrastructure issues and plans to address operational issues.

Study Results and Theoretical Framework

It is essential to investigate that diagnostic tools are accurate and supported by available resources in the local area to have a direct impact on case prevention and saving a life. Merton (1936) explains this situation that decision-makers act rationally by selecting a means based on the available evidence, and yet the goal may not be attained. Merton (1936) further explains that the most obvious limitation to correct anticipation of consequences of an action is the existing state of experience. Therefore, limited knowledge can be the sole barrier to correctly anticipating a future outcome. Solinas-Saunders and Stacer (2015) said that some health interventions carry unintended consequences that are unpredictable while some are seen and prevented. For example, if we apply Merton's theory of compassion for those marginalized (poverty-stricken TB patients), it often motivates purposive social action. Based on Merton's theory of unintended consequence of purposive action, the demand for social engagement is pressing, as is the need for immediate results.

According to Merton's theory, available knowledge is another way in which decision-makers' conclusions are restrained. When trying to decide what type of treatment, diagnostic procedure, or medical equipment is appropriate, decision-makers need information about local resources, culture, practices, needs, and wants of the local area. They lack knowledge, or their ability to translate knowledge into empirical data with the need to obtain immediate results limits the ability to predict the outcome with certainty (Merton, 1936).

The issue of the country's limited infrastructure, insufficient technical training, and limited troubleshooting abilities of laboratorians need to be considered in full before making any decisions. It is also crucial to investigate the availability of infrastructure capabilities, training, and technical support. These activities should be determined, sustained, and be managed by the country's local health department managers with the total backing by decision-makers and international agencies.

Xpert MTB/RIF Studies in Sub-Saharan Africa

In 2010, the WHO endorsed the use of Xpert MTB/RIF, a rapid diagnostic assay that can identify *Mycobacterium tuberculosis* and resistance to rifampicin. WHO recommendation included the use of Xpert MTB/RIF as a primary diagnostic test for adults with suspected drug-resistant TB, for children and adults with suspected TB in settings with high HIV prevalence, and the detection of extra-pulmonary TB. Resources permitting, Xpert may also be used as an initial diagnostic test for all patients with suspected TB or as a follow-on test to microscopy for adults with smear-negative results (WHO, 2011a).

In 2014, 4.8 million Gene Xpert cartridges were acquired in the public sector in 116 countries of the 145 countries eligible for concessional pricing, and Ethiopia was one of these countries (Umubyeyi et al. 2016). Its availability at lower-level health facilities like Community health TB laboratory is an added benefit to improving access to testing. However, Umubyeyi et al. (2016), states that studies and models have presented potential uses and impacts of the test. Still, few results have been published on the implementation program of Xpert instruments at a large scale.

Umubyeyi et al. (2016) state that the implementation of Xpert was conducted in five Sub-Saharan African countries. It was done in collaboration with the US Agency for International Development, the African Society of Laboratory Medicine, the WHO and the Global Fund to Fight AIDS, Tuberculosis, and Malaria in five Sub-Saharan African countries, which are, the Republic of Congo, Eritrea, Ethiopia, Ghana, and Kenya.

The study results from two countries illustrate the direct impact of these interventions: in Kenya, 8221 Xpert tests were conducted in 2015, of which 1830 (22.3%) were positive for *M. tuberculosis*, and 81 (4.4%) were rifampin resistant. In Ethiopia, evaluation after the first year of implementation (July 2013–December 2014) showed a 22% increase in the number of drug-resistant TB cases detected, while total TB cases detected rose from 58 802 to 63 168 (7.5%). The contribution of Xpert to TB case detection was 2% (source: Ethiopia National TB Program, 2015). Regarding the impact of Xpert on patient care, the study state that there are no significant or systematic improvements linking diagnosed patients to treatment. Generally, empirical treatment remained the rule, even with the availability of additional information about drug resistance, for example, with Xpert MTB/RIF testing. Overall, the utilization of the Xpert machines was at 15% of full capacity, representing a missed opportunity to diagnose potential TB and drug-resistant TB cases due to poor referral and transport systems.

Umubyeyi et al. (2016) state to achieve the maximum impact from innovative diagnostics systems, like Xpert, countries should improve the quality of health care, commit the resources needed, and implement a strategic plan for laboratory services and involve laboratory experts to guide implementation. The research study at the

Community Health Center TB Laboratory showed a need for attention to details that can come from a commitment and involvement of the local laboratory experts with knowledge and experience.

Social Change

Due to limited access to a well-developed health insurance system, about 80 % of private health expenditure in Ethiopia is via Out of Pocket Payments (OOPs,) and private insurance institutions cover only 1.5 % of private healthcare expenditure. Providing healthcare to individuals working informally or who live in rural areas is a significant challenge in developing countries (Badacho et al., 2016).

Considering the challenges faced by government health facilities and by the patient in developing countries, the proposed study at the Community Health Center TB laboratory will evaluate TB laboratory procedures and share its findings. The laboratories must provide detailed and complete laboratory test results once the patient managed to travel to the Community Health Center and paid out-of-pocket charges. The situation might erode patient's confidence and affect their compliance of submitting required samples for laboratory tests. Undiagnosed infection creates a cycle of disease leaving the country's population vulnerable by spreading the infection to family and community members.

TB laboratory processes need to be structured, systematized, and entirely led by local laboratory managers and Directors, supported by government officials and international agencies, to have a sustained impact. Empowering local professionals and

laboratory managers to be engaged and make sound decisions based on local resources is a positive social change.

Limitation of the Study

Global health estimates represent the best estimate by WHO based on the evidence available to it. Clinical laboratories are part and parcel of the healthcare services; in that respect, the proposed study results will be shared with the FDRE MOH. The study result can be extrapolated to represent other urban cities in Ethiopia to give insights to TB laboratory professionals and managers. However, this study population is not representative of all regions in Ethiopia, especially the rural areas.

Recommendations

It is vital to evaluate what a laboratory can achieve using the current procedures before starting to use an instrument that requires high technical assistance. Assessing, understanding, and revising existing procedures will require direct participation from the local laboratory management group with the support of international health agencies.

The study recommends a direct and step by step participation of local laboratory professionals and laboratory managers to decide which laboratory instrument or procedure will work best to enable them to complete and obtain a valid result for each laboratory test. The study also recommends that local laboratory professionals and laboratory managers should plan a test validation process using a previously confirmed positive and negative patient samples or a positive and a negative quality control sample to validate the testing process and the new instrument. Once validation is successful, the local laboratory professionals and laboratory managers should develop an

implementation plan. Making sure that infrastructures, including electricity, water, consumables, training of all laboratory technicians, including all trouble-shooting training, are completed before starting the TB testing. It is a widespread problem that instruments remain inoperative for an extended period waiting for a technical assistant from medical device companies that are not always nearby (Umubyeyi et al., 2016).

For failed laboratory steps, the study recommends clear documentation of why a laboratory process failed. The research also suggests that the laboratory should document what steps were taken to correct any failure of the laboratory process. Clinical laboratories play a significant role in identifying and treatment of a specific disease. However, throughout this research study, it is cited that the infrastructure, level of support for surveillance, research, and training in health care fields in Ethiopia is minimal. However, based on this study's results, it is suggested that the laboratory professionals who are managing the TB laboratory or those who are overseeing the laboratory procedures need to be fully engaged to make sure that TB laboratory tests are performed and obtain a valid test result. WHO allows 5-15% error or invalid results. The study recommends that the ZN microscopic test with no results, error/invalid test result and less than three sputum samples should have:

- Documentation to explain why the test failed
- Documentation for corrective action. One example of a corrective action could be repeating the test and releasing the test result the same day.
- Documentation of reason for less than three sputum samples collection and a corrective action.

I also recommend future studies to analyze the reason for the failure of a process (error, invalid, undocumented, not collected) as part of the study.

Implications for Professional Practice and Social Change

The study captures the day to day activities of a community health TB laboratory revealing the success, and the challenges faced when implementing the use of high-tech instruments like the Gene Xpert MDR RIF-R PCR Assay. It is vital to evaluate resources in terms of infrastructure, technical, and material resources before implementing a highly specialized process that requires immediate attention and support. Assessing, understanding, and evaluating existing laboratory procedures is only a start. The study result will be disseminated including to FDREMOH.

The answer to Ethiopia's TB disease complexity should come from Ethiopians leadership of scientific research. This can only happen with full engagement of laboratorians and researchers in understanding the local laboratory concerns and other related problems, no matter how small and redressing it from their point of view, ensuring the sustainability of resources needed. Zumla et al. (2015) ascertained that the more African scientists and researchers take on the leadership role, it has become imperative that other funding agencies consider aligning their research and capacity building investments in Africa to have a cooperative and growing effect. It is only through the empowerment of the next generation of African scientific leaders who will conduct the highest level of research that Africa will be able to generate local solutions to local health issues.

Umubyeyi et al. (2016) stated that Implementation of Xpert MTB/RIF, new technology, requires better country preparedness. Training, policies, and plans to address operational issues, comprehensive technical assistance, significant laboratory infrastructure improvement, and finally, the development of a TB laboratory strategic plan from the local government official and laboratory managers. It should include a proposal to the roll-out of Xpert Gene Xpert MDR RIF-R PCR Assay and coordinate support from donors and partners.

Umubyeyi et al. (2016) continue to discuss that countries with low resources have suffered from a lack of comprehensive technical assistance, including the formulation of policies and plans to address operational issues.

In Ethiopia, to fulfil these requirements, countries must coordinate the support of donors and partners and propose a budget and plan that covers technical assistance needs, the development of a TB laboratory strategic plan, including the roll-out of Xpert and the coordination of support from donors and partners.

I will analyze and share the outcome of the study to recommend an adjustment to the current processes and procedures to build on what is already achieved to move forward and empower local decision-makers to work towards sustained laboratory excellence based on available resources. Therefore, the potential impact of this study will reflect a positive social change at the individual, organizational, and government levels.

Conclusion

The study will contribute to changing the way Ethiopian laboratory technicians and managers are empowered to enable them to address the local challenges without too

much reliance on outside prompting, which will constitute a positive social change. TB laboratory processes that are structured, systematized, and entirely led by local laboratory managers and directors, supported by government officials and international agencies, will have a sustained impact. Empowering local professionals and laboratory managers to be engaged and make sound decisions based on local resources is a positive social change.

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