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Sami Mushabab Alqahtani Date

Impact of Mobile Teams on Tuberculosis Treatment Outcomes, Ministry of Health, Riyadh Region, Kingdom of Saudi Arabia, 2013 – 2015

By

Sami Mushabab Alqahtani

MPH

Hubert Department of Global Health

_____

Scott JN McNabb, PhD, MS

Committee Chair

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By

Sami Mushabab Alqahtani MD, King Khalid University (2011)

Thesis Committee Chair: Scott JN McNabb, PhD, MS

An abstract of

a thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

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ABSTRACT

OBJECTIVE: Evaluate the impact of the Tuberculosis (TB) Mobile Teams on treatment outcomes in Riyadh region by comparing patients who received treatment under mobile teams and those who did not, from 2013 to 2015. These findings will provide information to the National TB Control Program (NTCP) on whether or not expansion of mobile teams to cover the whole country will help TB prevention and control towards its elimination.

METHODS: This is a retrospective, descriptive study using NTCP data from 2013—2015 from Riyadh, Saudi Arabia. Descriptive analyses were used to summarize characteristics of TB case-patients served by mobile teams and those not. The chi-square test measured the significant differences between mobile served case=patients and those not. Exposure was whether or not the TB case-patient was under the care of the mobile team; the outcome of interest was whether or not treatment was successful, defined as "treatment completed" and "cured".

RESULTS: The ratio of treatment success among mobile team case-patients was 1.28 greater than among those not served by mobile teams. Chi-square test showed a statistical significant finding (Probability Ratio= 1.28;95% CI= 1.21,1.35, P-value= <0.01). Mobile teams increased the treatment success rate to 92%, compared to 71.77% among those not served by mobile teams. TB mobile teams reduced the mortality rate to 1.18% among case-patients, compared to 9.31% among those not served by mobile teams. Failure of treatment rates reached 17.19% those not served by mobile teams but only 0.86% among mobile team case-patients. Lost to follow-up rates reduced to 1.93% in mobile team patients, in comparison to 9.61% among non-mobile teams patients.

CONCLUSION: This study provides important information on the efficacy of using mobile teams to improve TB outcomes in Riyadh region, Saudi Arabia to achieve greater program outcomes. Data showed that community mobilization of mobile teams is an effective strategy to enhance TB treatment, reduced mortality and lost-to-follow-up and improve TB treatment outcomes. We recommend implementing a full-scale rollout of TB mobile team system all over the KSA, along with ongoing monitoring and evaluation of the mobile team's effectiveness by the NTCP.

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Chapter 1: Introduction

"If the number of victims which a disease claims is the measure of its significance, then all diseases, particularly the most dreaded infectious diseases, such as bubonic plague, Asiatic cholera, et cetera, must rank far behind tuberculosis." (Robert Koch, 1882).

Despite improvement in diagnosis, treatment, and prevention of tuberculosis (TB), it remains a significant public health concern globally and is considered a re-emerging infectious disease. The 2016 Global TB report showed that almost one-third of the world's population was infected with TB, with around 10.4 million new cases per year. There were 480,000 new cases of multi-drug resistant TB (MDRTB) and an additional 100,000 new cases of rifampicin-resistant TB (RRTB). Over 1.4 million deaths resulted from TB and an additional 400,000 TB–related deaths among people living with Human Immunodeficiency Virus (HIV). Unfortunately, from 2014 to 2015, the drop in TB incidence was only 1.5% globally [1].

One of the targets of the Sustainable Development Goals (SDGs) for 2030, implemented by the United Nations in 2015, is to end the global TB epidemic. The World Health Assembly, in 2014, approved the WHO End TB Strategy (2014), which demands by 2030, a 90% reduction in TB deaths, an 80% reduction in the TB incidence rate (as compared with 2015) and that no TB-effected household faces catastrophic costs [1]. To meet the first milestones of the End TB Strategy, huge efforts are needed to fast-track the decline in incidence to a 4%–5% annual decline by 2020 [1].

Such efforts are needed in the Kingdom of Saudi Arabia (KSA), which is the third largest country in terms of land area in the Middle East, representing the vast majority of Arabian Peninsula [2], and is a low-to-middle TB burden country according 2015 reports by the World Health Organization (WHO), with an incidence rate of 12 per 100,000 [3]. According to the KSA

Ministry of Health (MoH) statistics, overall TB incidence showed an uprising trend from 1992 onwards, with a peak in 1999 (12.2 cases per 100,000 population), which then started to drop only slightly[4]. Currently, the total number of new cases of pulmonary TB in 2015 was 2,505, with an incidence rate of 7.95 cases per 100,000 population. The total cases of non-pulmonary TB reached 841, with an incidence rate of 2.67 per 100,000 population [5].

The KSA MoH implemented a National TB Control Program (NTCP) which has worked for > 30 years in response to the plan to eliminate TB [6]. Based on the WHO End TB Strategy, the NTCP has developed ambitious targets: to raise the cure rate of smear positive TB to more than 85%, to detect more than 70% of TB cases, and decrease the incidence rate of pulmonary smear positive TB among in the nation to 1 per 100,000 population. NTCP also adopted the Directly Observed Therapy short course (DOTs) program in 1999, which is the standard WHO TB treatment strategy.

Due to the efforts of NTCP in 2015, TB treatment coverage was 87%. However, the treatment success rate of new and relapsed cases was 62.0%, which still remains below the international target set by the WHO (85%) [1]. Non-adherence and drug interruption are major barriers towards TB control in Saudi Arabia [7]. Researches shows that the most important aspect in TB treatment success is patient adherence with the prescribed drugs. It is unsure whether the patient takes the prescribed medicines even if the patient visits clinics regularly. As a result of non-compliance and drug interaction, drug resistance and relapse occurs [8]. With that being said, improved control efforts and widespread implementation of DOTs by NTCP has not led to the expected fall in TB trends [9].

In response, NTCP added mobile teams in Riyadh and Jizan aiming to decrease the default rates and improve patient outcomes through community outreach. This addition is

expected to lower the incidence. Therefore, based on such results, the expansion of mobile teams to cover the whole country is currently under consideration by NTCP [10, 11].

In Riyadh city, which is the location this study focused on, there are currently 20 mobile teams distributed according to population density. Every mobile team is fully equipped and consists of a physician, nurse, heath inspector, and driver. The mobile teams' main objective is to ensure adherence to all aspects of the DOTs therapy strategy when treating TB patients in a holistic care approach. Every TB patient is eligible to receive service by mobile teams except for those patients who require hospitalization [11].

The aim of this study is to evaluate the impact of the TB Mobile Teams on TB treatment outcomes in Riyadh region by comparing patients who received treatment from mobile teams and those who did not, from 2013 to 2015. The findings of this study will help NTCP determine whether to expand mobile teams to cover the whole country to help in TB control and move forward toward elimination.

Chapter 2: Literature Review

Tuberculosis (TB)

TB is an airborne disease caused by the bacterium *Mycobacterium tuberculosis*. *M. tuberculosis* spreads via airborne particles called droplet nuclei which are expelled when a person with infectious TB coughs, sneezes, shouts, or sings. Transmission occurs when droplet nuclei are inhaled and reach the alveoli of the lungs via the nasal passage, respiratory tract, and bronchi. TB is not transmitted by sharing environmental objects (i.e., phones, dishes, utensils, food). A common site of infection are the lungs (pulmonary TB); however, infection can occur in different sites of the body (extra-pulmonary TB) such as the lymphatic system, pleura, central nervous system, genitourinary systems, bones, and joints. The risk of acquiring infection depends on duration and closeness of contact, infectiousness of source, volume of air space, and ventilation.

TB disease can be deadly. However, not everyone infected with TB bacteria becomes sick. Thus, two TB-related situations exist: latent TB infection (LTBI) (90% of cases) and TB disease (10% of cases). Persons with TB disease are usually infectious and can spread bacteria to others while persons with LTBI are not [12].

After the primary infection, host defenses (cell-mediated immunity) develop 3-8 weeks after infection and contain the infection in 90% of infected individuals with latent TB infection. In latent infection cases, TB bacilli are dormant, but present and remain viable for many years with no illness or symptoms and infected persons are not infectious to others. Positive tuberculin skin test (PPD) or Interferon Gamma Release Assay (IGRA) confirm latent TB diagnosis [12].

In contrast, active TB disease occurs in 10% of infected persons. In these cases, infection progresses to primary TB disease within weeks of infection. This commonly happens in young,

elderly, and immune-suppressed persons. Diagnostic features include lower or middle-lobe disease, and less caseation necrosis and cavitation of lung lobes. Also, reactivation of the disease can happen, which means active TB disease develops after latent TB infection. To differentiate reactivation disease from primary TB disease, reactivation is commonly diagnosed in the lung apex and causes necrosis and cavitary lesions in lung lobes [12].

TB Symptoms

Symptoms of TB include fever, chills, night sweats, appetite loss, weight loss, and easy fatigability. For pulmonary TB, productive cough (cough with sputum), chest pain, and hemoptysis (blood in sputum) are the main symptoms. Symptoms of other sites of TB (extra-pulmonary) are based on the local site of infection (e.g. swollen lymph nodes observed with lymphatic TB) [12].

TB Infection Risk Factors

Risk factors of developing primary TB disease after infection include:

- HIV / AIDS
- Recent infection (within past 2 years, especially in infants and young children)
- Substance abuse (especially drug injection)
- Silicosis
- Chest radiograph suggestive of prior TB
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy
- Diabetes mellitus
- Cancer of the head or neck
- Hematologic diseases

- End-stage renal disease
- Intestinal bypass or gastrectomy
- Low body weight (≥ 10% below ideal)[12].

TB Treatment

Active TB disease is treated with a regimen of multiple medications for at least six months. Four, first-line drugs are considered the standard treatment: Isoniazid, Rifampin, Pyrazinamide, and Ethambutol. Duration of treatment depends on drugs used, isolate's vulnerability, and patient response to the prescribed drugs. Major goals of TB treatment according to the U.S. Centers for Disease Control and Prevention include:

- Cure patient, minimize risk of death/disability, prevent transmission to others
- Provide safest, most effective therapy in the shortest amount of time
- Prescribe multiple drugs to which the organisms are susceptible
- Never treat with a single drug or add single drug to failing regimen
- Ensure adherence and completion of therapy [12].

Treatment completion is defined as ingesting the prescribed number of doses within the specified time. After treatment, follow-up is not necessary for patients with a satisfactory response. However, patients with drug-resistant TB must have individualized follow-up evaluation. Drug-resistant TB can develop as a result of primary or secondary resistance. Initial infection with resistant organisms results in primary resistance. Secondary or (acquired) resistance is acquired during therapy due to patients being treated with an insufficient regimen, patients not taking drugs as prescribed, or other special conditions, such as drug malabsorption or drug-drug interactions. Multidrug-resistant TB (MDR TB) poses a high risk for treatment failure, relapse, additional acquired resistance, and/or death [12].

Directly Observed Therapy - Short Course (DOTs):

WHO DOTs has become the universal standard treatment in developed and developing countries. Given that patient nonadherence results in inadequate treatment which can lead to treatment failure, relapse, ongoing transmission, and drug resistance, DOTs is a preferred management strategy for all patients where health-care workers watch a patient swallow each dose. Nearly all regimens can be intermittent if given as DOTs. Also, DOTs reduces the total number of doses and the duration of treatment [12]. In other words, DOTs is considered to be the optimal and effective approach for controlling and treating TB because of the following:

- Short duration of treatment helps patients to adhere to treatment
- Rapid conversion of sputum from positive to negative decreases the chances of infection transmission
- The high cure rate compared with low cost
- Decreases complications of tuberculosis
- Decreases the chance of emergence of drug resistant tuberculosis
- Decreases the mortality rate [13]

After many years of dealing with different TB treatment method, DOTs strategy has emerged as the best solution to many problems especially non-adherence, and has been proven effective in several parts of the world. DOTs strategy reduced the treatment failure rate from 17.6% to 6.2% in a large Chinese study [14]. Furthermore, primary and acquired TB drug resistance have been found to reduce as a result of DOTs strategy implementation, from 13% and 14% to 6.7% and 2.1%, respectively, according to Weis et al [15]. Moreover, in the long run, DOTs strategy is considered to be more cost-effective in comparison with other TB treatment and control methods [16].

Global Burden of TB

Tuberculosis (TB) is one of the leading causes of mortality and morbidity worldwide. According to the WHO's Global Tuberculosis Report, 1/3 of the world's population is infected with TB. Regarding TB incidence, there were an estimated 10.4 million new TB cases worldwide in 2015, 65% of them (5.9 million) were among men, 34% (3.5 million) among women and 10% (1.0 million) among children. Globally, there was only a 1.5% rate of decline in TB incidence noticed from 2014 to 2015. [1].

TB mortality accounted for around 1.4 million TB deaths in 2015 and an additional 0.4 million TB-associated deaths among people living with HIV. TB remained one of the top 10 causes of death worldwide in 2015, even though the number of TB deaths fell by 22% between 2000 and 2015 [1].

Globally, while significant diagnostic and treatment gaps persist, 49 million deaths were prevented by TB treatment between 2000 and 2015. Regarding MDRTB, there were an estimated 480,000 new cases of MDRTB, and an additional 100,000 people with rifampicin-resistant TB (RR-TB) who were also newly qualified for MDRTB treatment in 2015 [1].

TB in the Middle East

The Middle East is the region that ranges from Turkey in the North, to the Arabian Peninsula in the South, from the Eastern Mediterranean region (EMRO), to the western side of the Indian subcontinent. Approximately 5% of the world's population (around 400 million people) live in EMRO according to the WHO. Egypt (90 million), Iran (78 million), Turkey (78 million), Iraq (35 million) and Saudi Arabia (31 million) are EMRO's highest populated countries [3]. TB has been a recognizable disease in the Middle East since ancient times [17]. However, recently, a TB crisis is underway given that since the beginning of 2011, the health

systems in EMRO have been affected by the dramatic political changes in the Middle East, with major events occurring in Egypt, Syria, and some of the Gulf states and Yemen [18]. Due to economic and religious conflicts in the region, there are currently major migration patterns occurring within EMRO which are resulting in a constant external source of TB transmission [17].

58,252 TB cases were recorded in EMRO in 2014, and seven countries (Iran, Iraq, Turkey, Egypt, Syria, Saudi Arabia, and Yemen) reported the majority (96%) of the cases. Turkey was the biggest contributor of TB burden in this region (22% of cases). Two countries (Iraq and Yemen) reported a burden of more than 50 per 100,000 population, whereas five countries reported a TB burden of less than 25 per 100,000 population [19].

Kingdom of Saudi Arabia (KSA)

KSA is located in the southwestern side of Asia and constitutes the bulk of the Arabian Peninsula. Geographically, KSA is the fifth-largest country in Asia with a land area of approximately 2,150,000 km^2. KSA is bordered by Jordan and Iraq to the north, Kuwait, Bahrain, Qatar, and the UAE to the east, Oman and Yemen to the south, and the Red Sea to the west. The population of the country has increased by 45.8% in the past 25 years, reaching 32,612,641 in 2015, comprised of 20,427,357 KSA nationals and 12,185,284 non-Saudi nationals [20]. Life expectancy in KSA was 74.3 years in 2015, which exceeds the regional average by 6 years, and exceeds the global average by 4 years. The percentage of the population under 15 years of age is 29.12%, which is almost similar to that of the Eastern Mediterranean region (34%), and higher than the percentage reported globally (27%). The crude birth rate (per 1,000 persons) is 21, lower than both the regional (31.4) and global (24.3) rates. The crude death rate (per 1,000 population) is 3.9, lower than the regional rate (6.3) and is almost half the global

rate (7.9). The infant mortality rate (per 1,000 live births) is 7.4, 83% less than the regional rate (44) and 80% less than the global rate (37) [5].

TB in KSA

KSA has experienced vast economic expansion which has resulted in improvement of social and health services. This has led to an influx of large numbers of foreign workers (currently there are 12,185,284 non-Saudi nationals [20]), which is a potential population health risk for KSA, given that international travel, immigration and movement of populations can facilitate the spread of TB [21]. In fact, 56% of reported TB cases have been found among non-Saudis, in comparison to 44% for Saudi-nationals [5]. A 2 to 3 times higher TB incidence rate has been noticed in the immigrant nationals compared to KSA nationals (this is similar to the results of other developed countries [16]). More than 10 million immigrants living in KSA come from TB endemic areas [4], such as Bangladesh, India, Indonesia, Pakistan, and Yemen [21]. In fact, the majority of foreigners come from high TB burden countries.

Furthermore, they usually live in crowded housing conditions with poor nutrition. These conditions make them prone to reactivation of latent TB infection. Additionally, more than two million pilgrims visit the country for the Hajj annually[4]. TB control in KSA was affected as a result of this high foreign influx [21]. However, despite these effects, it should be noted that MoH annual statistical data indicated a declining trend of incidence among non-Saudis and a stable trend among KSA nationals [22].

National TB Control Program (NTCP)

The KSA Ministry of Health (MOH) implemented NTCP which worked for over 30 years dealing with both KSA nationals and the influx of foreign workers and their impact on TB incidence [4]. NTCP is progressing towards achieving its targets, which are to:

A. Raise the cure rate of PTB smear positive TB to more than 85%
B. Detect more than 70% of the estimated TB cases
C. Decrease the incidence rate of pulmonary smear positive TB among nation to 1 per 100 000 population [23]

NTCP is actively engaged in programmatic management of MDRTB, although it is not a major problem in the country. Furthermore, the program aims to control and eliminate tuberculosis in the country to the degree that it poses no danger on health, economic, or social aspects of the community. In order for this to be done, NTCP aims to ensure that all components of the tuberculosis elimination objectives are adhered to, especially the following:

1) identification of high risk groups
2) management of latent TB infection
3) continuous updates of legislation regarding the management of TB and MDRTB among both nationals and non-nationals
4) enhanced access to new diagnostics
5) expanded collaboration with all related stakeholders [23]

Additionally, in order to lower the incidence of TB, NTCP has mandated that all children are vaccinated with Bacillus Calmette-Guérin (BCG) at birth. Also, it has been mandated that TB treatment is accessible freely to all patients in government hospitals [4].

As discussed earlier, in KSA, TB incidence showed an uprising trend since 1992 with a peak in 1999 (12.2 cases per 100,000 population), then it started to drop slightly. The section below will examine the current trends of TB in KSA.

Table 1: Reported Cases and Incidence Rates of Tuberculosis, KSA, 2011 – 2015[5]

2011		**2012**		**2013**		**2014**		**2015**	
Reported cases	*Incidence rate*	*Reported cases*	*Incidence rate*	*Reported cases*	*Incidence rate*	*Reported cases*	*Incidence rate*	*Reported cases*	*Incidence rate*
2641	(9.31)	2577	(8.83)	2447	(8.16)	2509	(7.59)	2505	(7.95)

Table 1 shows a decrease in the TB incidence rate since 2011, with the exception of 2015, as it showed a minimal increase. The total number of new cases of pulmonary TB in 2015 was 2,505, with an overall incidence rate of 7.95 cases per 100,000 population. The total cases of non-pulmonary TB reached 841 with an overall incidence rate of 2.67 per 100,000 population. The TB-related mortality rate is estimated at 2.1 per 100,000 population [5].

In the epidemiologic analysis of pulmonary TB, Saudis represented 44% of reported TB cases in comparison to 56% for non-Saudis. 68% of cases were reported among males in comparison to 32% among females. The highest percentage of pulmonary TB cases were discovered among the age group of 15 to <45 years (71%), followed by the age group > 45 years (24%). The highest incidence rate was reported from Jeddah province (16.4 per 100,000 persons)[5].

Regarding non-pulmonary TB, Saudis represented 49% of the reported cases in comparison to 51% for the non-Saudis. 33% of cases were female, in comparison to 67% for males. The highest percentage of cases were reported among the age group 15 – <45 years (67%), followed by the age group ≥45 years (27%). Similar to pulmonary TB, the highest incidence rate was reported from Jeddah Province (5.21 per 100,000 persons) [5].

To execute their objectives, NTCP started to implement DOTs in all regions of KSA. In 2015, TB treatment coverage was 87%. However, unfortunately, even with this level of treatment coverage, improved control efforts and the implementation of DOTs, the expected fall in TB trends has not occurred [9]. For example, the treatment success rate of new and relapsed cases registered was 62.0% [3], which still remains below the international target set by the WHO (85%)[1].; multi-drug resistant TB (MDRTB) was estimated at 2.6% among new total smear positive cases and 20% among previously treated cases [3]. In response to these statistics, NTCP has added mobile teams in Riyadh and Jizan cities. This addition is expected to lower the incidence of the disease. Therefore, based on such results, the expansion of mobile teams to cover the whole country is currently under consideration [10, 11].

TB Mobile Teams

The KSA MoH's NTCP decided after continuous monitoring and evaluation to develop new strategies to achieve target goals. For example, mobile teams have been created to monitor TB patients and implement the WHO's DOTs strategy. The use of these mobile teams has resulted in the:

1. Reduction of hospital admission loads of newly diagnosed TB patients as well as patients visiting hospitals for follow-up
2. Close monitoring and evaluation of TB patients
3. Decrease in the number of patients lost to follow-up
4. Improvement of TB surveillance due to improved reporting trends
5. Improvement of healthcare service quality to TB patients
6. Increased access for TB patients and their contacts to health education, which has resulted in increased adherence to treatment completion

7. Countering of stigma towards the disease [11]

The mobile team strategy has been implemented in only two cities in KSA: Riyadh and Jizan. Riyadh city is the capital city with the highest population density (6.195 million) [24]. Currently there are 20 mobile teams in Riyadh city distributed according to population density. Every mobile team is fully equipped and consists of a physician, nurse, heath inspector, and driver. Based on the monitoring and evaluation of the mobile team reports in Riyadh and Jizan, expansion to cover the whole country is being considered. Mobile teams' duties include:

1. Implementing DOTs strategy by visiting patients at home 3 times per week, delivering medication, observing patients while taking the medication, and ensuring patients follow treatment plan
2. Taking sputum samples from the patient and sending them to the central laboratory and then sending the results back to the treating physician
3. Testing patients' contacts with the tuberculin test and referring positively-tested contacts to the hospital for required investigations before starting protective therapy. Also, re-doing the test for negatively-tested contacts after 2 months to confirm negative status
4. Accessing the Health Electronic Surveillance Network (HESN) and updating the information of patients and their contacts, including results for every visit
5. Developing monthly reports about patients, contacts, results, visits and activities for the NTCP
6. Providing community health promotion and education in the catchment area [11]

Every TB patient is eligible to receive service by mobile teams except for patients who require hospital admission [11].

Chapter 3: Manuscript

Introduction

Despite improvement in diagnosis, treatment, and prevention of tuberculosis (TB), it remains a significant public health concern globally and is considered a re-emerging infectious disease. The 2016 Global TB report showed that almost one-third of the world's population was infected with TB, with around 10.4 million new cases. There were 480,000 new cases of multi-drug resistant TB (MDRTB) and an additional 100,000 new cases with rifampicin-resistant TB (RRTB). 1.4 million deaths resulted from TB and an additional 400,000 TB–related deaths among people living with Human Immunodeficiency Virus (HIV). Unfortunately, from 2014 to 2015, the drop in TB incidence was only 1.5% globally [1].

One of the targets of the Sustainable Development Goals (SDGs) for 2030, implemented by the United Nations in 2015, is to end the global TB epidemic. The World Health Assembly, in 2014, approved the WHO End TB Strategy (2014), which demands by 2030, a 90% reduction in TB deaths, an 80% reduction in the TB incidence rate (as compared with 2015) and that no TB-effected household faces catastrophic costs [1]. To meet the first milestones of the End TB Strategy, huge efforts are needed to fast-track the decline in incidence to a 4–5% annual decline by 2020 [1].

Such efforts are needed in the Kingdom of Saudi Arabia (KSA), which is the third largest country in terms of land area in the Middle East, representing the vast majority of Arabian Peninsula [2], and is a low-to-middle TB burden country according 2015 reports by the World Health Organization (WHO), with an incidence rate of 12 per 100,000 [3]. According to the KSA Ministry of Health (MoH) statistics, Overall TB incidence showed an uprising trend from 1992 onwards, with a peak in 1999 (12.2 cases per 100,000 population), which then started to drop

only slightly[4]. Currently, the total number of new cases of pulmonary TB in 2015 was 2,505, with an incidence rate of 7.95 cases per 100,000 population. The total cases of non-pulmonary TB reached 841, with an incidence rate of 2.67 per 100,000 population [5].

The KSA MoH implemented a National TB Control Program (NTCP) [11] which worked for over 30 years in response to the world plan to eliminate TB [6]. Based on the WHO End TB Strategy, the NTCP has developed ambitious targets: to raise the cure rate of smear positive TB to more than 85%, to detect more than 70% of the estimated TB cases, and to decrease the incidence rate of pulmonary smear positive TB among in the nation to 1 per 100,000 population. Also, NTCP has adopted the Directly Observed Therapy short course (DOTs) program in 1999, which is the standard WHO TB treatment strategy.

Due to the efforts of NTCP in 2015, TB treatment coverage was 87%. However, the treatment success rate of new and relapsed cases was 62%, which still remains below the international target set by the WHO (85%)[1]. Non-adherence and drug interruption are major barriers towards TB control in KSA [7]. Research shows that the most important aspect in TB treatment success is patient adherence with the prescribed drugs. It is unsure whether the patient takes the prescribed medicines even if the patient visits clinics regularly. As a result of non-compliance and drug interaction, drug resistance and relapse occurs [8]. However, improved control efforts and widespread implementation of DOTs by NTCP has not led to the expected fall in TB trends [9]. In response to this, NTCP has added mobile teams in Riyadh and Jizan cities aiming to decrease the default rates and improve patient outcomes through community outreach. This addition is expected to lower the incidence of the disease. Therefore, based on such results, the expansion of mobile teams to cover the whole country is currently under consideration by NTCP [10, 11].

In Riyadh city, which is the location this study focused on, there are currently 20 mobile teams distributed according to population density. Every mobile team is fully equipped and consists of a physician, nurse, heath inspector, and driver. The mobile teams' main objective is to ensure adherence to all aspects of the DOTs therapy strategy when treating TB patients in a holistic care approach. Every TB patient is eligible to receive service by mobile teams except for those patients who require hospitalization [11].

The aim of this study is to evaluate the impact of the TB Mobile Teams on TB treatment outcomes in Riyadh region by comparing between case-patients who received treatment under mobile teams and those who did not, from 2013 to 2015. The findings will help NTCP in the decision on whether to expand mobile teams to cover the whole country to help in TB control and move forward towards the elimination of the disease.

Methods

Data source

TB is one of many notifiable diseases in KSA. According to the MoH Department of Infectious Diseases, healthcare facilities should report new TB cases monthly to NTCP[25]. These reports include demographical, clinical, epidemiologic data. NTCP then publishes the data after deep analysis via the Annual Statistical Health report [5].

Study design

This is a retrospective study using the NTCP data from 2013 to 2015. Mobile TB teams have been implemented in two cities only (Riyadh and Jizan)[11]. Riyadh city is the capital with the highest population density (6.195 million)[24] and therefore this study used NTCP data from Riyadh to compare TB case-patients served by mobile teams and those not.

Study variables

There are 10 variables included in the study.

1. Year (three sub-variables: 2013, 2014, 2015)
2. Team (two sub-variables: mobile, non-mobile)
3. Age (continuous variable)
4. Sex (two sub-variables: male, female)
5. Nationality (two sub-variables: Saudi, non-Saudi)
6. Patient type (two sub-variables: new, relapse)
7. TB site of infection (three sub-variables: pulmonary, extra-pulmonary, both)
8. Acid Fast Bacilli (AFB) test result (three sub-variables: positive, negative, not done)
9. Human Immunodeficiency Virus (HIV) test result (three sub-variables: positive,

negative, not done)

10. Treatment outcome (six sub-variables: complete treatment, cured, failed, died, not evaluated yet, lost to follow up)

Ethics

This study was based on secondary data without any personal identifiers; it did not meet the category of human subject research and was reviewed by Emory University Institutional Review Board (IRB).

Statistical analyses

Descriptive analyses were used to summarize characteristics of TB case-patients served by mobile teams and those not. Chi-square tests measured the significant differences between mobile and non-mobile groups. Exposure was whether or not the TB case-patient was served by the mobile team; the outcome was whether or not treatment was successful. According to the United Nations [26] developmental goals, "treatment success rates are calculated from the data as the proportion of new smear-positive TB cases registered under DOTS in a given year that successfully completed treatment, whether with ("cured") or without ("treatment completed") bacteriologic evidence of success" [26]. SAS™ (SAS Institute Inc., Cary, NC, USA) was the platform used to perform all analyses. All P-values were two-tailed. P-value <0.05 was considered significant. Rates were compared using probability of success ratios and 95% confidence interval.

Results

From 2013 to 2015, there were 1,600 TB patients in Riyadh region registered in the NTCP database with treatment outcomes recorded (Table 1). 58.38% (934) of patients were served by mobile teams, while 41.63% (666) were not. Overall, patients ranged from 7 months old to 101 years old, with a mean age of 36.4 years. Male case-patients accounted for 71.56% (1145) and females 28.44% (455). Also, 40.69% (651) were Saudi case-patients, while the majority, 59.31% (949), were non-Saudi. Only 4.19% (67) were relapsed TB case-patients (received treatment previously and confirmed cured but had redeveloped smear-positive pulmonary TB) [27], while 95.81% (1533) were new TB patients. Pulmonary TB was the most prominent TB site, with 69.56% (1113), extra-pulmonary with 27.94% (447), and the combination of pulmonary and extra-pulmonary with 2.50% (40). Additionally, 58.63% (938) had AFB sputum smear positive results at the start of the treatment, 29.88% (478) had negative result, and the smear was not done for 11.50% (184) patients. The majority of case-patients were HIV negative, 66.13% (1058), only 1.25% (20) were tested positive and 32.44% (519) were not tested.

We found 684 (40.5%) of all patients were cured based on at least three negative consecutive sputum smear tests. However, 690 (43.13%) patients were classified as having completed the treatment, so, overall treatment success rate (completed + cured patients) was 83.63% (1,338). Treatment failure was 1.19% (19) which includes TB patients who, "while on treatment, remained smear-positive; or once more became smear-positive at the fifth month or later during the course of treatment, or those who were initially smear-negative before starting treatment and became smear-positive after the second month of treatment" [27]. Furthermore, 73

(4.56%) patients died, 82 (5.13%) patients were lost to follow-up, and 88 (5.50%) patients have not yet been evaluated by healthcare professionals.

A descriptive analysis of variables by mobile vs. non-mobile teams showed that both mobile and non-mobile teams had almost the same distribution of patient gender (Table 1). Mean age for mobile team served case-patients was 34 years, while 40 years for non-mobile team served case-patients. 71.31% of mobile team served case-patients were non-Saudi, in contrast, the majority of non-mobile team served case-patients were Saudi (57.51%). New pulmonary TB was the main TB site among patients of both arms. The AFB sputum smear test was not done in 23.12% of non-mobile team served case-patients, which is high compared to mobile team served case-patients, as only 2.75% did not undergo the test. Moreover, 52.85% of non-mobile team served case-patients did not have HIV test results, while, only 3.21% of mobile team served case-patients did not undergo the test.

Table 1: Characteristics of TB Case-patients between Mobile Team Served versus Non-mobile Team Served Case-Patients, Riyadh Region, Kingdom of Saudi Arabia, 2013 – 2015

TB Case-patient Profile		All Case-patients (n=1600)		Mobile-team Served (n=934)		Non-mobile Team Served (n=666)	
		n	(%)	n	(%)	N	(%)
Gender	*Male*	1145	(71.56)	674	(72.16)	471	(70.72)
	Female	455	(28.44)	260	(27.84)	195	(29.28)
Age	*Mean*	36.4		33.9		39.9	
	Median	31		30		34	
	Mode	25		25		28	
	Range	0.7-101		3-83		0.7-101	
Nationality	*Saudi*	651	(40.69)	268	(28.69)	383	(57.51)
	Non-Saudi	949	(59.31)	666	(71.31)	283	(42.49)
Case-patient type	*New*	1533	(95.81)	897	(96.04)	636	(95.5)
	Relapse	67	(4.91)	37	(3.96)	30	(4.5)
TB site	*Pulmonary*	1113	(69.56)	673	(72.06)	440	(66.07)
	Extra-pulmonary	447	(27.94)	237	(25.37)	210	(31.53)
	Both	40	(2.50)	24	(2.57)	16	(2.40)
AFB[a] result	*Positive*	938	(58.63)	609	(65.20)	329	(49.4)
	Negative	478	(29.88)	295	(31.58)	183	(27.48)
	Not done	184	(11.50)	30	(3.21)	154	(23.12)
HIV[b] status	*Positive*	20	(1.25)	9	(0.96)	11	(1.65)
	Negative	1058	(66.13)	755	(80.84)	303	(45.50)
	Not done	519	(32.44)	167	(17.88)	352	(52.85)
Treatment outcome	*Success[c]*	1338	(83.62)	860	(92.08)	478	(71.77)
	Completed	690	(43.13)	359	(38.44)	331	(49.7)
	Cured	648	(40.5)	501	(53.64)	147	(22.07)
	Died	73	(4.56)	11	(1.18)	62	(9.31)
	Failed	19	(1.19)	8	(0.86)	11	(17.19)
	Lost to follow up	82	(5.13)	18	(1.93)	64	(9.61)
	Not Evaluated yet	88	(5.50)	37	(3.96)	51	(7.66)

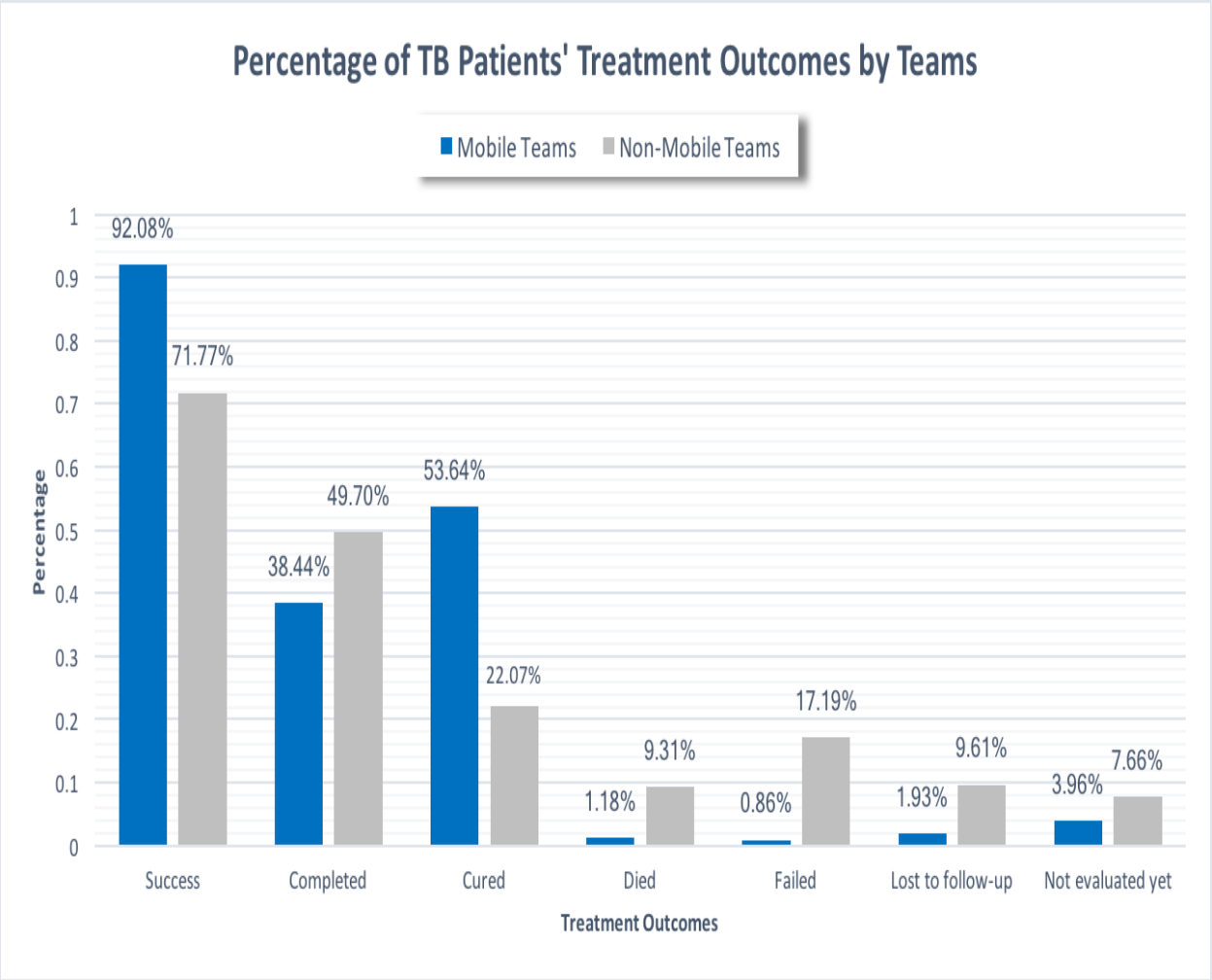
[a] *Acid Fact Bacilli sputum smear test.*

[b] *Human Immunodeficiency Virus.*

[c] *Treatment Success= Completed + Cured.*

The percentage of treatment outcomes by mobile-team served and non showed that, in comparison to non-mobile team served case-patients, mobile team served case-patients increased the rate of treatment success to 92.08% (Figure 1). Moreover, the teams helped reduce mortality, treatment failure, and lost to follow-up rates by 1.18%, 0.68%, and 1.93% respectively.

Figure 1: TB Case-patient Treatment Outcomes between Mobile-served versus Non-mobile Served, Riyadh region, Kingdom of Saudi Arabia, 2013 – 2015



The ratio of treatment success among mobile team patients was 1.28 higher than those among non-mobile teams (Table 2). Chi-square showed statistical significance (ratio=1.28;95% CI=1.21,1.35, p-value=<0.01). Possible confounders were considered (e.g., nationality, patient type, TB site, AFB results, HIV status) (Table 3). A statistically significant impact was observed in most levels after stratification by precise confidence intervals and p-values = <0.01.

Table 2: Probability ratio of Treatment Success between Mobile-team Served Tuberculosis Case-patients compared to Non-mobile Team Served Case-patients, Riyadh region, Kingdom of Saudi Arabia, 2013 – 2015

	Mobile Teams Vs. Non-mobile Teams		
	Ratio	95% CI	P-value
Treatment Success	1.28	(1.21 , 1.35)	<0.001

Table 3: Probability ratio of treatment success among mobile team patients compared to non-mobile team patients, stratified by possible confounders.

Variable		Mobile-team Served versus Non-mobile Team Served Tuberculosis Case-patients		
		Ratio	95% CI	P-value
Nationality	*Saudi*	1.27	(1.18 , 1.36)	<0.001
	Non-Saudi	1.29	(1.19 , 1.39)	<0.001
Patient type	*New*	1.29	(1.22 , 1.36)	<0.001
	Relapse	1.08	(0.86 , 1.34)	0.6995
TB site	*Pulmonary*	1.36	(1.27 , 1.46)	<0.001
	Extra-pulmonary	1.17	(1.08 , 1.25)	<0.001
	Both	1.03	(0.67 , 1.56)	>0.999
AFB result	*Positive*	1.35	(1.25 , 1.46)	<0.001
	Negative	1.29	(1.17 , 1.42)	<0.001
	Not done	1.12	(0.96 , 1.28)	0.2160
HIV status	*Positive*	1.43	(0.74 , 2.71)	0.5449
	Negative	1.25	(1.16 , 1.34)	<0.001
	Not done	1.24	(1.13 , 1.36)	<0.001

Discussion

It is clear from the findings of this study that mobile team service of TB case-patients had a positive and significant impact on TB treatment outcomes and increased treatment success to 92%. In fact, the mortality rate among mobile team served case-patients was only 1.18%, in comparison to 9.31% among non-mobile team served case-patients during 2013 – 2015. This potentially was because TB case-patients under mobile team service were 1.28 times more likely to experience treatment success than those not. In fact, the failure of treatment was only 0.86% among mobile team served case-patients, compared to a significantly higher rate of 17.19% among non-mobile team served case-patients. This success in treatment of the mobile TB teams can be explained by their goal which is to guarantee the implementation of one of DOTs recommendations: to ensure that case-patients take the prescribed drugs under direct supervision of a healthcare professional. With the use of mobile teams, healthcare workers directly follow-up on drug adherence. The use of mobile teams resulted in a lowering of the lost-to-follow-up rate, which was reduced to 1.93%, compared to 9.61% among non-mobile team served case-patients.

Treatment success rates where high amongst mobile team served case-patients; and the completion of therapy rates among mobile team served case-patients was lower than non-mobile teams: 38.44% and 49.70%, respectively. This is either because the case-patients could not produce sputum to confirm being cured, or they had a negative smear results from the beginning of the course. However, the cure and treatment success rates were higher among mobile team served case-patients; 53.64% and 92.08%, respectively. This is in comparison to non-mobile team served case-patients whose rates were 22.07% and 71.77%, respectively. To prevent future TB drug resistance and relapse, higher cure and treatment success rates should be obtained rather than completion rates.

This statistically significant impact of mobile teams was noticed in both Saudis and non-Saudi case-patients, new TB case-patients, case-patients with different sites of TB infection (pulmonary, extra-pulmonary), case-patients with different AFB smear test results (positive and negative), case-patients with negative HIV status and those who did not do the HIV test. Results showed that relapsed case-patients, case-patients with infection in both (pulmonary + extra-pulmonary) TB sites, case-patients who did not have AFB sputum smear test results, and case-patients with a positive HIV test results experienced positive impact; results did not reach statistical significance.

Although mobile teams did a great job in diagnosing TB by AFB sputum smear, we noticed that 31.58% of case-patients tested negative. This finding could be explained by the WHO definition of a smear-negative TB case-patient which is a case-patient with "symptoms suggestive of TB, with at least two sputum specimens which were negative for AFB by microscopy, and with chest radiographic abnormalities consistent with active pulmonary TB" [27]. Also, 3.21% of case-patients who did not undergo the AFB test used other diagnostic tests such as Xpert^{TM}, which initiates TB treatment.

The strength of this study is that it is the first to measure the impact of TB mobile teams in KSA. Also, it includes the most updated data, obtained from the NTCP surveillance data; therefore, it is a useful tool for policy makers in the MoH Department of Public Health to decide whether or not to expand the use of TB mobile teams to include more cities in the near future.

One of the limitations of this study was that mobile teams were implemented by NTCP in only two Saudi Arabian cities: Riyadh and Jizan. Furthermore, this study was limited to data on Riyadh as data on Jizan was unavailable to the researchers at the time of this study. This study could be stronger if Jizan city data were included in analysis to determine whether or not the

positive impact of mobile teams was affected by geographical area of implementation. Another limitation was that data did not show the geographical distribution of the case-patients in Riyadh city nor their socioeconomic status, which may play a role in treatment success. Also, around 519 TB case-patients included in this study did not undergo an HIV test, which also may have impacted the results. Finally, the data did not show any information about TB drug resistance. MDRTB is an emerging public health threat and it would be useful to gather data regarding the effectiveness of mobile teams (following the DOTs strategy) in reducing drug resistance.

Chapter 4: Conclusion and Recommendations

TB control in KSA currently faces many challenges, including the large influx of foreign workers, illegal immigrants and religious visitors who come from high TB burdened countries. Furthermore, the global emergence of MDRTB and the TB/HIV syndemic make TB control difficult. This study showed that mobile TB teams can have a positive impact on TB control. We recommend NTCP ensures mobile teams cover the entire KSA, and that staff are fully equipped and trained periodically, especially in TB program management and case-load distribution and that continuous evaluation and monitoring occur.

Incentives should be provided to mobile team staff to ensure a sustainable and attractive work environment. Along with the use of mobile teams that adhere to DOTs, other TB control strategies should be used as well, such as providing education, holistic case management, a combination of TB pills, incentives and enablers. A combination of DOTs and these strategies can reduce acquired drug resistance, treatment failure, and relapse [12].

In conclusion, with the synergy of the TB, MDR TB, and HIV epidemics, the need to increase treatment success rates and to decrease failure and relapse rates is essential [28]. This study provides important data on the efficacy of using mobile teams to improve TB outcomes in Riyadh region, KSA. Results prove that community mobilization of these teams is an effective strategy to mitigate TB treatment failure, mortality, lost to follow-up rates and improve TB treatment outcomes. Further study about TB mobile teams in Jizan will be useful to compare between results. These results prove the need to implement a full-scale TB mobile team system all over the KSA, especially in high TB endemic regions such as Makkah [4], along with ongoing monitoring and evaluation of the mobile teams by the NTCP.

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