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Distribution and Determinants of Tuberculosis, Kingdom of Saudi Arabia, 2005 – 2012

By

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By

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M.B.B.S.
Taibah University
2010

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Abstract

Distribution and Determinants of Tuberculosis,
Kingdom of Saudi Arabia, 2005 – 2012
By Fahad Almutairi

Introduction: Tuberculosis (TB) remains a public health threat in KSA with many challenges that limit its prevention and control. And the laboratory plays a key role in an effective TB program. So to understand how to meet these challenges, we calculated the TB incidence rates (IRs) in KSA from 2005 – 2011 and assessed the laboratory capabilities by determining the proportion of laboratory-confirmed TB cases.

Methods: We estimated the TB IRs and 95% confidence interval (CI) stratified by nationality, gender, and administrative regions from 2005 – 2012. We also calculated the proportion of TB cases by age category, employment status, and nationality.

Results: The overall KSA TB IRs showed statistically significant decrease from 15.80 per 100,000 population in 2005 (95%CI=15.29 - 16.31) to 13.16 in 2012 (95%CI=12.74 - 13.58). The IRs for males and females were similar from 2005 – 2008. But from 2009 – 2012, the IRs for males were greater than those of females. And the IRs of non-Saudis were approximately twice those of Saudis during the study period. Mecca region had a consistently greater IR over the study period compared with other regions (25.13 per 100,000 [95%CI=24.7 – 25.56]). Riyadh region had the second highest IR (17.9 cases per 100,000 population [95%CI=17.53 – 18.27] followed by Jazan (17.1 cases per 100,000 population [95%CI=16.31 – 17.89]. Non-Saudis from these countries had the greatest proportion of TB cases: Indonesia (15.4%); Yemen (12.9%); India (9.7%); and Pakistan (8.4%). Individuals < 15 years of age made up 14.2% of the TB cases, those aged 21-30 made up 27.7% of the cases, and those ≥ 65 composed 7.4% of the cases. By employment status, we observed employed non-Saudis with the greatest proportion of TB (32%), followed by unemployed Saudis (22.38%). The proportion of laboratory-confirmed cases of reported TB was 57% from 2005 – 2012. Medina and the Eastern Region had the greatest proportion of laboratory-confirmed cases of reported TB (64%) followed by Mecca (60%).

Discussion: There were a decrease in the overall TB IRs over the study period. The IRs were greater among non-Saudis compared to Saudis. Medina and Eastern Region had the greatest proportion of laboratory-confirmed cases of reported TB. We note that for effective prevention and control, TB screening should be implemented for all non-Saudi workers at ports of entry. Plus, laboratory-screening capacity for all reported cases of TB should be evaluated throughout the country and strengthened.

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Chapter One

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* [1]. It primarily affects the lungs, but can occur in many other places such as the bones and intestines [1]. Those with pulmonary TB are the main transmission sources for spread [1]. TB is an airborne infection that can be detected by a laboratory test called sputum smear. Once individuals become sputum smear positive for TB, there is a 5-10% chance that they will develop the clinical manifestations of TB within their lifetime, with the greatest risk occurring 5 years immediately following their initial infection [1]. TB co-infections greatly increase the risk of developing symptomatic TB [1]. Untreated sputum smear positive cases usually die within 5-8 years, or sooner if they develop symptoms [1]. Children < 5 years of age who are infected with TB are at great risk for developing meningitis or a severe form of infection called military TB due to the immaturity of their immune systems [1]. Risks factors for developing TB symptoms include comorbidities like HIV and diabetes mellitus, as well as malnutrition, immunosuppression, excess alcohol consumption, smoking, or being elderly [1].

TB is a global public health threat, with an estimated 9 million new cases per year and 2 million deaths [1]. To treat a patient with TB, multiple, relatively expensive antibiotics should be administered for many months. This is unfortunate, since TB is a disease that is linked to poverty [2]. In 1993, a new strategy called DOTS (directly-observed therapy, short-course) was developed to fight TB at the global level [1]. This is the current strategy for TB control [1]. Since the introduction of DOTS, mortality rates from TB have dropped 45% [2].

However, TB is very difficult to combat due increasing resistance to antibiotic treatment [1]. In 2013, 9 million new TB cases were identified with 1.5 million deaths [3]. TB is considered the second most common cause of death after HIV among all infectious diseases [4]. One of the

Millennium Development Goals is, by this year, to cut TB prevalence to half of its 1990 number and reduce its incidence. WHO has recently released a strategy for the post-2015 era whose aim is to end the global TB epidemic by 2035 [2].

The Kingdom of Saudi Arabia (KSA) is a fast developing country that has experienced tremendous changes over the previous decades. By improving its standard of living, KSA has succeeded in minimizing infectious disease-related mortalities. With rapid development, it has become a major destination for many immigrants from developing countries, who currently make up about one-third of the Saudi population [5]. This has caused major shifts in the status of many infectious diseases, including TB. Additionally, 2-3 million pilgrims travel to KSA yearly to perform Hajj, most of them from developing countries. This presents many challenges to KSA in controlling infectious diseases like TB.

According to the Central Department of Statistics, KSA has a population of around 30 million; ⅓ composed of non-Saudi immigrants. The incidence rate for TB has ranged from 11-16 per 100,000 population per year since 2000 [6,2]. From 1991 – 2010, 64,345 cases of TB were diagnosed in KSA [7]. Pulmonary TB, the infectious type, accounts for 73% of these cases [7]. Due to factors such as the high number of immigrants and pilgrims, TB is not fully controlled in KSA. The mortality rate among TB patients reached a peak in 2003, when it was 7.2% among Saudis and 6.2% among non-Saudis [8]. Since then, the incidence and mortality rates have decreased, but the threat persists.

TB continues to be a public health threat in KSA with many challenges that limit its prevention, control, and elimination. And the laboratory plays an important role in the diagnosis and confirmation. No previous study has tried to assess the scope of the laboratory testing program, for TB in KSA. And no prior study has determined the trends and shifts of TB in KSA.

This study analyzed the laboratory results for reported cases of TB to determine which were confirmed based on WHO guidelines [9].

Previous studies about TB in KSA focused only on gender, region, age group, and Saudi or non-Saudi nationality. In this study, we studied the trends of TB in KSA from 2005 – 2011 in more detail, identifying associations such as the relationship of TB to occupational status and the range of the TB laboratory-testing program overall and by region. This study provides information that can help in the development of more cost effective screening programs that target the groups most vulnerable to acquiring TB in KSA. In addition, this study aimed to identify social determinants associated with TB in KSA.

Chapter Two

Literature Review

Global TB Burden

In 1993, the World Health Organization (WHO) declared TB a global emergency [4]. It remains a major health problem. In 2012, 8 million new cases were identified and 1.3 million deaths were reported worldwide [2]. It is estimated that 3 million people are undiagnosed or unreported and untreated [2]. Among global infectious disease threats, TB is the second most common cause of death after HIV [4]. TB treatment is costly, and the disease is usually more prevalent among people of low socioeconomic status [2].

The presence of multidrug resistant (MDR) strains of TB makes the disease very difficult to prevent, treat, and control [2]. The worldwide incidence rate (IR) for TB peaked in 2004, reaching 142 cases per 100,000 population [4]. Most of the new cases in 2012 were reported in Asia (58%) and Africa (27%) [2]. One of the Millennium Development Goals is to cut the prevalence of TB to half of what it was in 1990 and reduce its incidence by 2015 [2]. Since the IR has been decreasing since 2006, this part of the goal has been achieved [2]. WHO has recently released a strategy for the post-2015 era that aims to end the TB epidemic worldwide by 2035 [2].

Worldwide TB prevalence and mortality rates were declining before the incidence rates began to decline in 1990 [2]. This decline could be attributed to a strategy called DOTS (directly observed treatment, short course) [2]. This strategy focuses on getting a bacteriologic diagnosis and administering a short course of chemotherapy treatment under direct observation [2]. About 320,000 cases of the 1.3 million fatal cases observed in 2012 were HIV co-infected [2]. Mortality rates from TB have dropped 45% since 1990 [2].

TB in KSA

KSA has experienced tremendous development over the past 50 years. This has resulted in major improvements to the health of the population; however, infectious diseases like TB have proven to be unexpectedly challenging. With the vast development of KSA and its transportation infrastructure, there has been a large influx of both pilgrims and non-Saudi workers. Every year, 2-3 million pilgrims visit the city of Mecca for the Hajj and gather in a small area, which can set the stage for TB transmission. In addition, ⅓ of the Kingdom's population is composed of non-Saudis [5]. Most of the pilgrims and non-Saudi workers come from countries that have a higher burden of infectious diseases, including TB.

KSA has a national infectious disease registry. The country is divided into 13 regions, and each reports infectious diseases and other reportable health conditions to the Ministry of Health (MoH) [5]. TB is among the infectious diseases requiring mandatory reporting [5]. All TB cases in the 13 regions are reported monthly to the MoH [7]. The earliest available data describing TB trends in KSA goes back to 1991 [7].

The MoH established a national TB control program (NTB) in 1972 [10]. This program oversees and improves public health surveillance for TB and finds and treats active TB patients [4,7]. The NTB decided to implement DOTS in 1999 [10]. The administration of the TB vaccine, Bacillus Calmette–Guérin (BCG), is mandatory for all children at birth and is a required condition for entry into school. Vaccine coverage for all children is 97% [7]. If someone in KSA is diagnosed with TB, he or she is eligible for treatment in any public hospital at no cost including citizens and non-citizens [7].

From 1991 to 2010, 64,345 cases of TB were diagnosed in KSA [7]. In 2011, 3,872 cases were added to the total [5]. Pulmonary TB accounted for 73% of these cases [7]. Men constituted 62% of TB cases [7]. Just over half of all cases (52%) were Saudi nationals, while the other 48% were non-Saudis [7]. Almost 70% of the reported cases occurred in Mecca and the central regions, where ½ of the Saudi population lives [7].

TB trends have remained constant in the 20-year period from 1991 – 2010 [7]. It started with 15 per 100,000 population in 1991 and the highest IR in KSA during this period was 17.2 per 100,000 population, reported in 1999 [7]. This is a moderate IR compared to other developing countries [6]. It has decreased since then, dipping as low as 11.8/100,000 from 2005 – 2009 [6]. The highest IRs among the regions were reported from Mecca and Jazan regions, with rates of up to 29.5 per 100,000 population [7]. The IR rose significantly in Mecca region over this 20-year period ($p < 01$) compared to other regions [7].

Non-Saudis had an IR that was 2-3 times higher than Saudis in all regions over this same period [7]. In the 10-year period from 2000 – 2010, the IR for non-Saudis showed a downward trend [7]. This might be explained by a treatment strategy that was started by the NTB in 2000 [7]. In 2000, the NTB implemented DOTS in KSA, a treatment strategy that depended on direct observed treatment of TB cases in short courses [7]. This strategy was successful in decreasing the IR among non-Saudis but not among Saudis [7]. The TB IR among Saudis increased between 1995 – 2010 ($p < 0.01$) [5].

The IR was greater among Saudi males compared to females [4]. The lower IR in Saudi females can be explained by their low participation in public events in KSA [4]. It also can be attributed to non-reporting due to fear of stigma [4].

By age, TB IR was greatest among those > 45 years of age [7]. Over a 20-year period (1991 – 2010), the incidence among children < 15 years of age was constant (1.8 - 2.8 per 100,000 population) [7]. TB in children reflects active transmission from adults [7]. Those aged 15 – 24 showed an increase in the IR from 15.7 per 100,00 in 2000 to 20.9 per 100,000 in 2009

($p \leq 0.05$) [4]. The IR among those ≥ 65 years of age decreased from 65.2 per 100,000 in 2000 to 43.9 per 100,000 in 2009 ($p \leq 0.05$) [3].

Non-Saudis in KSA

Non-Saudis have a 2-3 times higher IR of TB than Saudis [4, 7]. In general, migration is a complex phenomenon that can affect the epidemiology of any disease locally and globally [2]. In this case, we can attribute the high IR of TB among non-Saudi immigrants to multiple factors. First, many of them come from countries that have a high IR of TB such as Pakistan, India, Bangladesh, Yemen, and Indonesia [7]. India and Indonesia are among the top five countries with the highest number of TB cases worldwide [11]. In addition, many foreign workers live together in crowded places [7]. TB is an airborne infection and its transmission is more likely in crowded places. Also, many non-Saudi immigrants work in stressful jobs and have poor nutritional status [7]. This can lead to immune system suppression and the activation of a latent TB infection, if present [2]. Some foreign workers are not in the country legally, and many of these will not seek medical care because of their fear of deportation by their employers.

Only health workers and domestic laborers are screened for TB upon entry [7]. In a 10-year period (2000 – 2010), the incidence rates for non-Saudis showed a downward trend [7]. This might be explained by the DOTS strategy implemented in 2010 [7]. This also might be attributed to the fact that, since 2000, non-Saudis have been allowed to receive healthcare for free in the government facilities and have been able to access both private and government healthcare facilities without the fear of deportation [4].

Mecca Region

Mecca region shows a 2-3 times higher IR of TB compared to other regions [7]. Each year there is an influx of 2-3 million pilgrims visiting Mecca for the Hajj season. Pilgrims will gather in crowded confined spaces; these spaces favor the transmission of airborne infections. In 1994, a study conducted in two major hospitals in Mecca city demonstrated that 20% of all pneumonia admissions were due to TB, which was the most common cause of pneumonia among pilgrims [12]. Furthermore, travelers coming back from Hajj have demonstrated higher rates of TB skin test conversion compared to travelers coming from other endemic areas [13]. Tuberculin skin reaction among non-vaccinated subjects was higher in urban communities (20%) compared to rural areas (10%) [12].

Pilgrims have free access to government healthcare facilities, so TB cases among them are reported from the Mecca region [4]. This is one reason for the higher IR of TB in this region. In addition, 40% of all non-Saudis live in Mecca [7]. Also, as mentioned, a large portion of the pilgrims and non-Saudi immigrants come from countries that have high burden of TB [7].

TB in Health Workers

Health workers are at increased risk of TB infection compared to the general public since they are in frequent contact with TB patients [14]. In addition, many health workers in KSA are recruited from countries that have a high TB prevalence [14]. To address this, health workers are screened for TB upon entering the country [7]. Health facilities themselves can act as foci, facilitating the spread of TB to vulnerable patients who then carry it into their communities [14]. A study conducted in a tertiary hospital in Riyadh over a 3-year period (2008 – 2010) found that 24.5% of the hospital's health workers who came into contact with active TB patients had a convert tuberculin skin test [14]. Furthermore, the compliance rate among all health workers in this hospital who were prescribed isoniazid for prophylaxis (with a recommended course of 9 months) was only 17.4% [14]. It was noted that Saudi health workers were four times more likely to complete the prophylactic treatment than non-Saudis [14].

TB Mortality in KSA

According to WHO data protocols, anyone with TB who dies while receiving anti-TB treatment is considered a TB fatality [8]. A study released in 2010 analyzing data from 2001 – 2010 showed the mortality trends for TB in KSA [8]. The TB mortality rate peaked in 2003, reaching 7.2% among Saudis and 6.2% among non-Saudis [8]. The rate's decline from 2004 to 2010 can be attributed to the built up of the government's policy of offering free treatment to all TB patients regardless of nationality in government health facilities, started in 2000.

In the above study, the case fatality rates were greatest among the oldest age group (>65), reaching 20.8% among Saudis and 25.2% among non-Saudis [8]. Mortality rates were lowest among those < 15 years old, who accounted for 1.2% of deaths among Saudis and 3.1% among non-Saudis [8]. The high case fatality rate in the oldest age group can be attributed to increases in the prevalence of other diseases (e.g., cancer, liver disease, renal disease, cardiovascular disease) among this population [8].

Regarding gender, the case fatality rates were greater among Saudi males (7.3%) as compared to Saudi females (5.3%) (OR=1.4; 95% CI=1.24-1.58) [8]. This is probably due to confounding factors other than gender. Relapsed TB patients were significantly more susceptible to death than new patients among both Saudis and non-Saudis [8]. This could be due to drug resistance or non-compliance with medications. Those who were HIV seropositive were significantly more susceptible to death than those who were HIV seronegative among both Saudis (95% CI=2.7-10.06) and non-Saudis (95% CI=6.98-21.22) [8].

Association Between TB and HIV

TB has a strong relation to HIV. According to one study, active TB is 50 times more likely to affect those with HIV than those without [15]. Another study found that the IR of TB among people with HIV in KSA was 30 times greater than that among the general public [16]. TB is the primary cause of death in HIV patients [15]. WHO estimates that TB is responsible for 13% of deaths among people with HIV [15]. TB can occur early in the course of an HIV infection despite a high CD4 T-lymphocyte count [15]. HIV can render individuals more susceptible to extra-pulmonary TB, which often progresses unnoticed [15]. In a study conducted in King Faisal Specialist Hospital in Riyadh in 2009, 7.4% of TB patients also had HIV [15].

TB Surveillance, Diagnosis, and Treatment in KSA

TB surveillance is conducted by general practitioners in the primary health centers and hospital outpatient clinics [4]. For suspected cases, diagnosis is confirmed using mycobacterial culture, sputum smear microscopy, radiography, histopathology, and molecular techniques that are only available in some laboratories [4]. The presence of a positive culture or smear defines a TB case, according to WHO guidelines [9].

A study of the treatment outcomes of 147 Saudi TB patients in a governmental tertiary hospital in Jeddah from 1993 – 1999 showed a 69.4% success rate for treatment [10]. Poor compliance was the main reason treatment failure, although other factors, such as drug resistance, might have contributed as well [12].

Drug-resistant TB in KSA

Multi drug-resistant TB (MDR-TB) poses a growing threat to the treatment of TB in KSA and worldwide. MDR-TB is resistant to isoniazid and rifampicin (and potentially other drugs as well) [6]. These two drugs are the principle first line treatment for TB [6]. Drug resistance might have emerged due to improper treatment or non-compliance to treatment [6]. Around 250,000 patients were identified as having MDR-TB in 2009, a decrease from 2008, when 440,000 were identified [6].

TB resistance to isoniazid in Saudi regions ranged from 4.4% to 40%, and it is greatest in Jazan [6]. TB resistance to rifampicin ranged from 2.9% to 20.4%; it was highest in Jazan [6]. A study conducted in 2012 in the Najran region found that 38.2% of TB patients had resistance to at least one anti-TB agent [6]. Isoniazid resistance was greatest (which also had the highest sensitivity against TB), followed by rifampicin [6]. The higher rates of drug resistance in Najran and Jazan regions can be explained by their proximity to Yemen, which has the highest TB IR of all the Arab countries [6]. In general, there were no statistically significant findings in drug resistance rates between Saudis and non-Saudis [11]. A study conducted in Riyadh region in 2002 showed that patients' treatment outcomes were not affected by their having single-drug resistant TB [11].

A study conducted in a tertiary hospital in Jeddah from 1992 – 1999 showed that MDR-TB could have a prevalence of 20.7% in Jeddah region [12]. Another study concerning anti-TB drug resistance among patients in KSA from 2009 – 2010 was published in 2013 [16]. This study found that 5.4% (95% CI=4.7- 6.2) had mono resistance to isoniazid while 8.1% (95% CI= 7.2-9.1) had mono resistance to rifampicin [16]. However, treatment outcomes were not affected by mono-drug resistance, especially when both first-line drugs were administered together.

In the same study, MDR-TB was found among 1.8% (95% CI=1.4 - 2.4) of new patients and 15.9% (95% CI=15.4 - 16.5) of relapsed and previously treated TB patients [16]. The high percentage of MDR-TB in previously affected patients could have been due to non-compliance or improper treatment. Being a non-Saudi, living in the Mecca region, and having pulmonary TB were the strongest independent predictors for acquiring MDR-TB [16]. Compared to the findings of other studies conducted at the global level by WHO, the rates for drug resistant TB are among the lowest for newly diagnosed cases [16]. This study also found that anti-TB drug resistance is highest in the western region and lowest in the eastern region [16]. These findings contradict those from another study released in 2011 that indicated that the two southern regions of Najran and Jazan had the highest anti-TB drug resistance [6].

Chapter Three: Manuscript

Abstract

Introduction: Tuberculosis (TB) remains a public health threat in KSA with many challenges that limit its prevention and control. And the laboratory plays a key role in an effective TB program. So to understand how to meet these challenges, we calculated the TB incidence rates (IRs) in KSA from 2005 – 2011 and assessed the laboratory capabilities by determining the proportion of laboratory-confirmed TB cases.

Methods: We estimated the TB IRs and 95% confidence interval (CI) stratified by nationality, gender, and administrative regions from 2005 – 2012. We also calculated the proportion of TB cases by age category, employment status, and nationality.

Results: The overall KSA TB IRs showed statistically significant decrease from 15.80 per 100,000 population in 2005 (95%CI=15.29 - 16.31) to 13.16 in 2012 (95%CI=12.74 - 13.58). The IRs for males and females were similar from 2005 – 2008. But from 2009 – 2012, the IRs for males were greater than those of females. And the IRs of non-Saudis were approximately twice those of Saudis during the study period. Mecca region had a consistently greater IR over the study period compared with other regions (25.13 per 100,000 [95%CI=24.7 – 25.56]). Riyadh region had the second highest IR (17.9 cases per 100,000 population [95%CI=17.53 – 18.27] followed by Jazan (17.1 cases per 100,000 population [95%CI=16.31 – 17.89]. Non-Saudis from these countries had the greatest proportion of TB cases: Indonesia (15.4%); Yemen (12.9%); India (9.7%); and Pakistan (8.4%). Individuals < 15 years of age made up 14.2% of the TB cases, those aged 21-30 made up 27.7% of the cases, and those ≥ 65 composed 7.4% of the cases. By employment status, we observed employed non-Saudis with the greatest proportion of TB (32%), followed by unemployed Saudis (22.38%). The proportion of laboratory-confirmed cases of reported TB was 57% from 2005 – 2012. Medina and the Eastern Region had the greatest proportion of laboratory-confirmed cases of reported TB (64%) followed by Mecca (60%).

Discussion: There were a decrease in the overall TB IRs over the study period. The IRs were greater among non-Saudis compared to Saudis. Medina and Eastern Region had the greatest proportion of laboratory-confirmed cases of reported TB. We note that for effective prevention and control, TB screening should be implemented for all non-Saudi workers at ports of entry. Plus, laboratory-screening capacity for all reported cases of TB should be evaluated throughout the country and strengthened.

Introduction

TB is a major public health threat. With an estimated 9 million new cases per year and 2 million attributable deaths [1], TB is the 2nd most single common cause of death after HIV out of all other infectious diseases [4]. The reduction of TB is a Millennium Development Goal, but it remains a major public health problem. The WHO has recently released a strategy for the post 2015 era whose aim is to end the global TB epidemic by 2035 [2].

The Kingdom of Saudi Arabia (KSA) is a fast developing country that has experienced tremendous changes over the previous decades. By improving its standard of living, KSA has succeeded in minimizing infectious disease-related mortalities. With the rapid development, it has become a major destination for many immigrants from developing countries who currently make up about ⅓ of the Saudi population [5]. This has caused major shifts in the status of many infectious diseases including TB. In addition, 2-3 million pilgrims will travel to KSA yearly to perform Hajj, mostly from developing countries. This presents many challenges to KSA in controlling infectious diseases like TB. According to the Central Department of Statistics, KSA has a population of around 30 million. One-third of this population is composed of non-Saudi immigrants. The IR for TB has ranged from 11-16/100,000 per year since 2000 [6,2]. From 1991 – 2010, 64,345 cases of TB were diagnosed in KSA [7]. Pulmonary TB, the infectious type, accounts for 73% of these cases [7]. Due to factors such as the high number of immigrants and pilgrims, TB is not fully controlled in KSA. The mortality rate among TB patients reached a peak in 2003, when it was 7.2% among Saudis and 6.2% among non-Saudis [8]. Since then, the incidence and mortality rates have decreased, but the problem persists.

TB remains a public health problem in KSA with many challenges that limit its control and elimination. Furthermore, no previous study has tried to assess the sensitivity of the TB screening program in KSA. In addition, previous studies on the trends of TB have focused only on gender, region, age group, and Saudi or non-Saudi nationality. This study aims to investigate the trends of the IR of TB in KSA over an 8-year period (2005 – 2012) stratified by gender, nationality, and the 13 administrative regions. In addition, this study aims to identify the distribution of TB cases among age groups, occupation, and immigrant nationalities.

In this study we analyzed the reported laboratory results for reported TB cases to determine which TB cases were confirmed based on WHO guidelines to achieve confirmation [9]. This helped us identify the capacity of the TB laboratory testing program overall and by region. The results of this study demonstrated the need to do a formal evaluation of the TB program in KSA.

Methods

TB is an infectious disease requiring mandatory reporting [5]. Surveillance for TB cases is population-based and conducted in both primary health centers and hospitals [4]. All suspected TB cases were reported monthly to the MoH from all the regions [7] (c.f., Appendix 1). For suspected cases in the health centers, diagnosis was confirmed using mycobacterial culture, sputum smear microscopy, radiography, histopathology, and molecular techniques that are only available in some laboratories [4].

TB case data were obtained from the Saudi MoH as de-identified, individual-level data collected from 2005 – 2012. KSA has a national disease registry in which all reportable health conditions including infectious diseases are reported to the MoH [5]. Our data provided results from the culture, smear, and radiography of each reported case.

We estimated the IR and 95% confidence interval (CI) of TB for the population in KSA from 2005 – 2012 in order to investigate the trend of the IR over the study period. We also estimated the IRs stratified by nationality, gender, and administrative regions. IRs were estimated using the number of cases per year over the total population per 100,000 individuals.

Two population databases were used. The first was the Saudi Central Department of Statistics (CDS), whose data were used to estimate the IR for the total population and by nationality and gender. Since the population data stratified by region were not available in the CDS database, we used another database from the MoH to obtain the region level data. Nationality was classified as Saudi and non-Saudi, and regions were grouped into the 13 administrative regions.

We also calculated the proportion of TB cases by nationality, age category, and employment status. Age was divided in categorical variables of 5-year duration. Employment status was grouped into four categories: employed, unemployed, student, or prisoner. Since prisoners live in crowded conditions and are more susceptible to TB transmission, they were categorized separately. Students were categorized separately because schools are usually crowded and can act as foci to spread infection to the community.

We also calculated the proportion of laboratory-confirmed cases from the reported TB cases for each region based on the WHO diagnostic criteria of confirming cases by either positive culture or smear [9]. All calculations and analysis were done using Excel 2013.

Ethical Considerations

This study was determined to be IRB-exempt because all analyses were performed on secondary data de-identified prior to analysis. Prior to data collection, all portions of the study were reviewed by Emory's IRB and determined to meet the criteria for exemption.

Results

The overall TB IR in KSA decreased from 2005 – 2012. The risk difference between 2005 (OR=15.8; 95%CI=15.29 – 16.31) and 2012 (OR=13.16; 95%CI=12.74 – 13.58) was statistically significant according to the confidence intervals (Table 1).

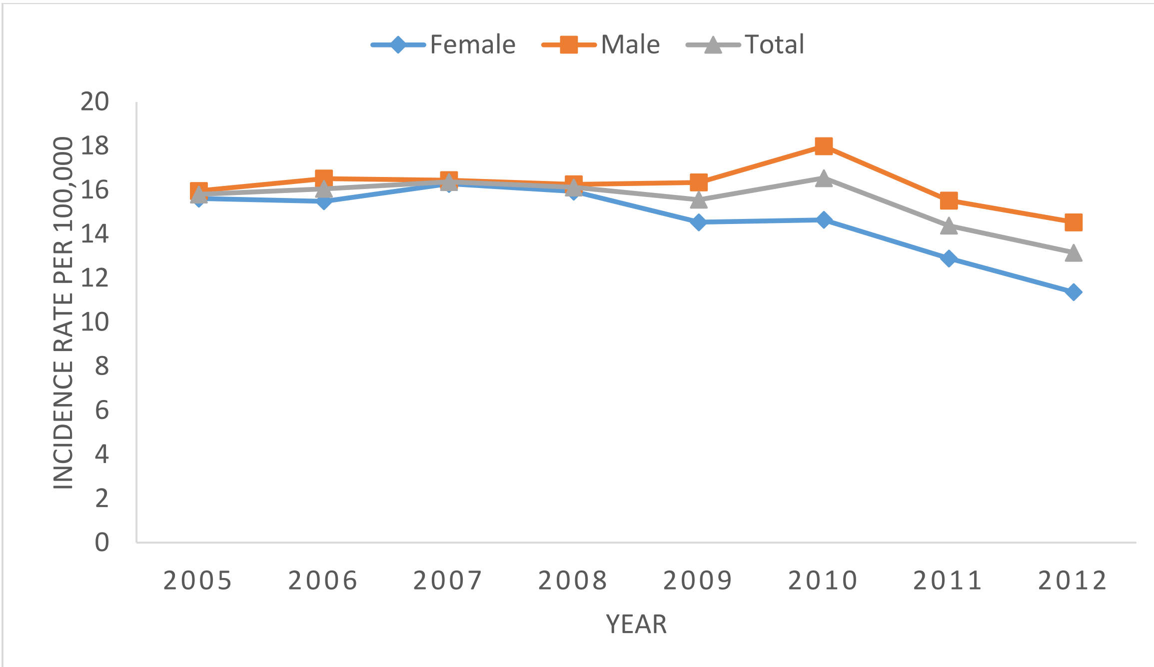
Table 1. Reported Cases of Tuberculosis and Incidence Rates, by Year, Kingdom of Saudi Arabia, 2005 – 2012

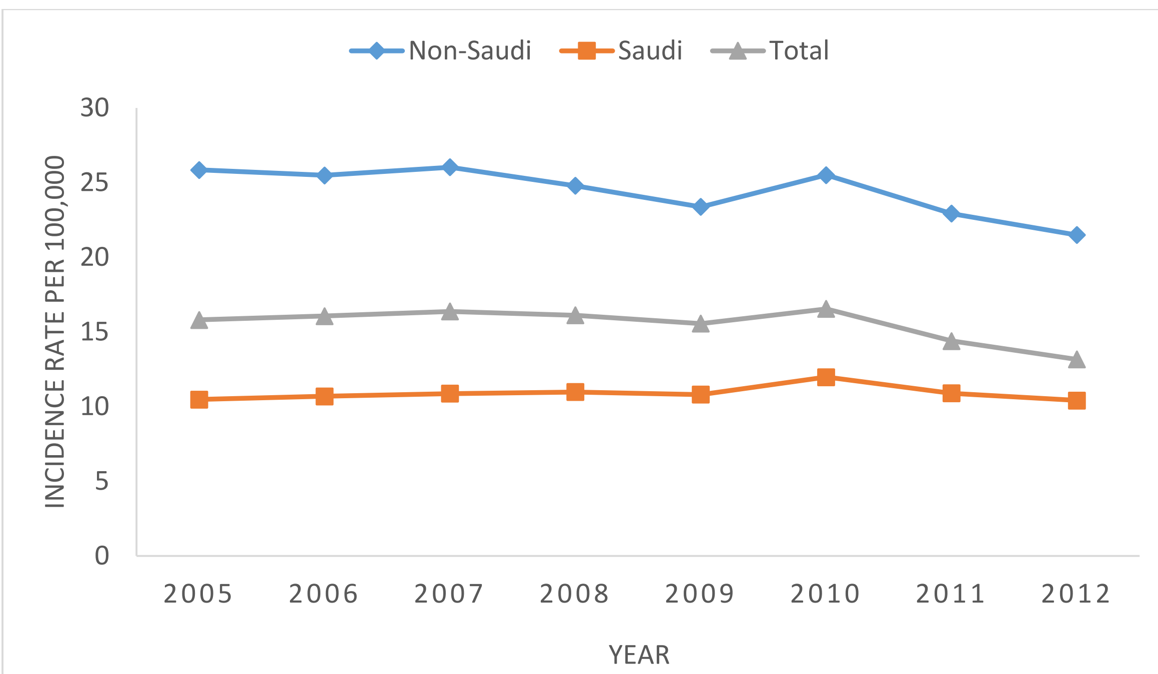
Year	#	IR°	95% CI•
2005	3,687	15.80	15.29 - 16.31
2006	3,875	16.06	15.55 - 16.57
2007	4,084	16.37	15.87 - 16.87
2008	4,156	16.12	15.63 - 16.61
2009	4,149	15.56	15.09 - 16.03
2010	4,558	16.54	16.06 - 17.02
2011	4,083	14.39	13.95 - 14.83
2012	3,843	13.16	12.74 - 13.58
Total	**32,435**		

°IR = Incidence rate per 100,000 population
•CI = Confidence Interval

The TB IRs of both males and females were similar from 2005 – 2008 (Figure 1); after that, from 2009 – 2012, the IRs of males were higher than those of females. The IRs of non-Saudis were about twice those of Saudis during the study period (Figure 1), although the IRs for both groups remained stable.

Figure 1. Incidence Rates of Reported Cases of Tuberculosis, by Gender and Nationality, Kingdom of Saudi Arabia, 2005 – 2012





By region, we observed that Mecca had a consistently greater IR over the study period compared with other regions (25.13 per 100,000 [95%CI=24.7 - 25.56]) (Figure 2). Riyadh was the region with the second highest IR (17.9 per 100,000 [95%CI=17.53 - 18.27]) followed by Jazan (17.1 per 100,000 [95%CI=16.31- 17.89]). Hail had the lowest TB IR over the study period (6.1 per 100,000 [95%CI=5.4-8.6]).

Figure 2. Incidence Rates of Reported Cases of Tuberculosis, by Region, Kingdom of Saudi Arabia, 2005 – 2012

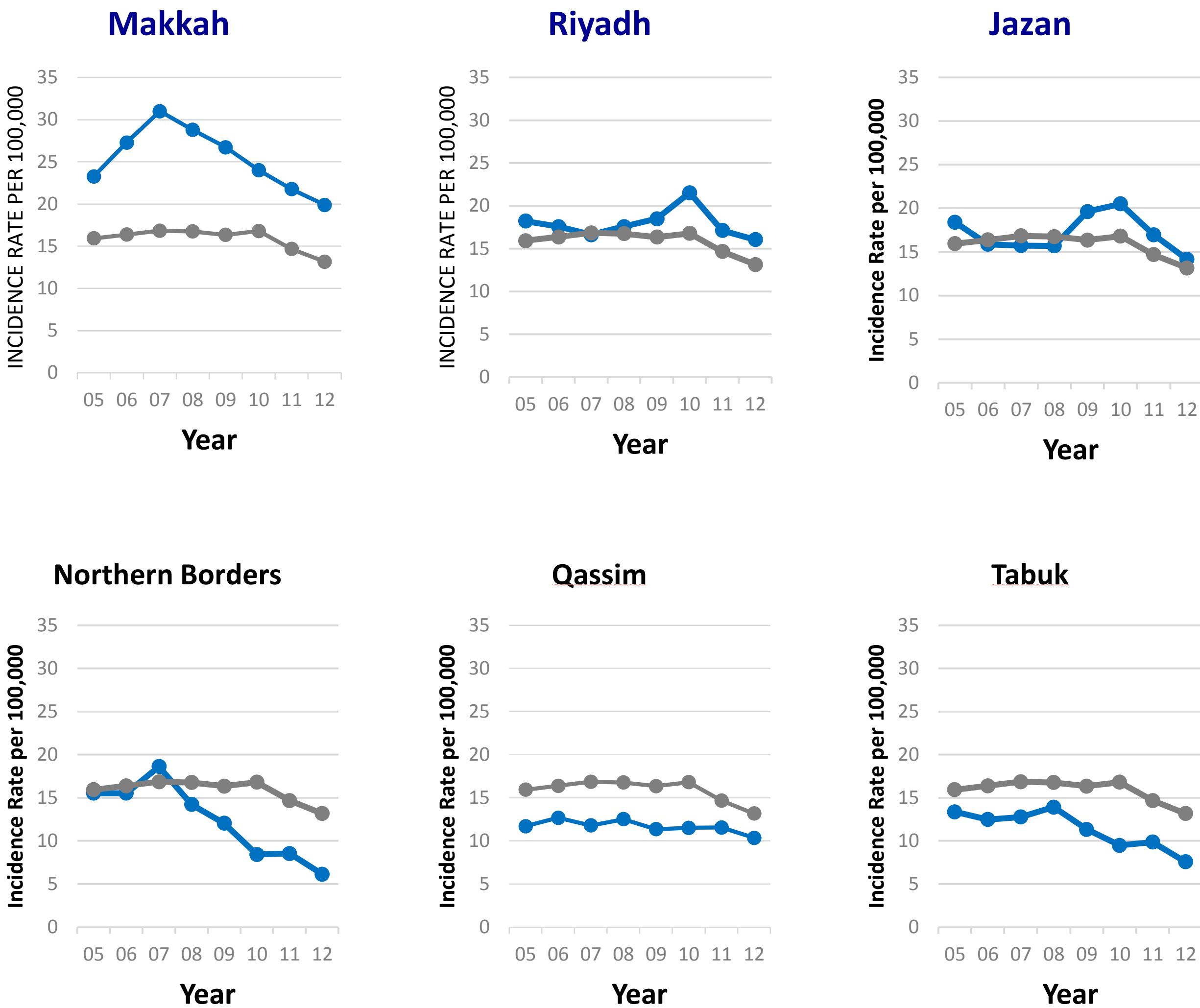
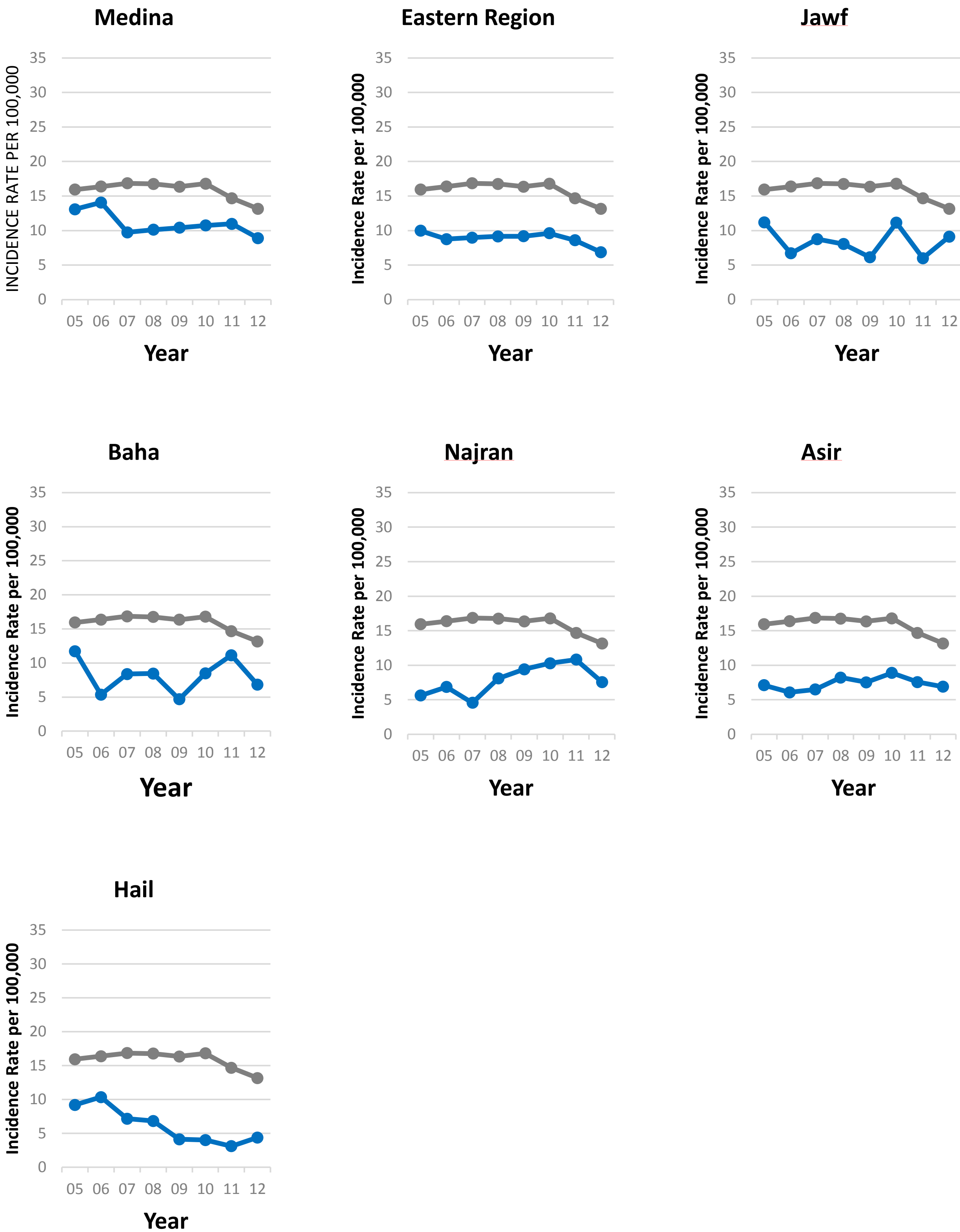


Figure 2. Continue



Investigating the proportion of TB cases by nationality, non-Saudis from these countries had the highest proportion of TB cases: Indonesia (15.73%); Yemen (12.91%); India (9.71%); and Pakistan (8.36%) (Figure 3). By age category, we observed that individuals < 15 years of age made up 14.21% of the TB cases, those aged 21-30 made up 27.73% of the cases, and those age 65 and over composed 7.41% of the cases (Figure 4). By employment status, we observed that the employed non-Saudis had the highest proportion of TB (56.42%), followed by unemployed Saudis (39.46%) (Figure 5). Students had 15.33% of all TB cases, while 11.22% of all cases were prisoners.

Figure 3. Number and Proportion of Reported Cases of Tuberculosis, by Nationality, Kingdom of Saudi Arabia, 2005 – 2012

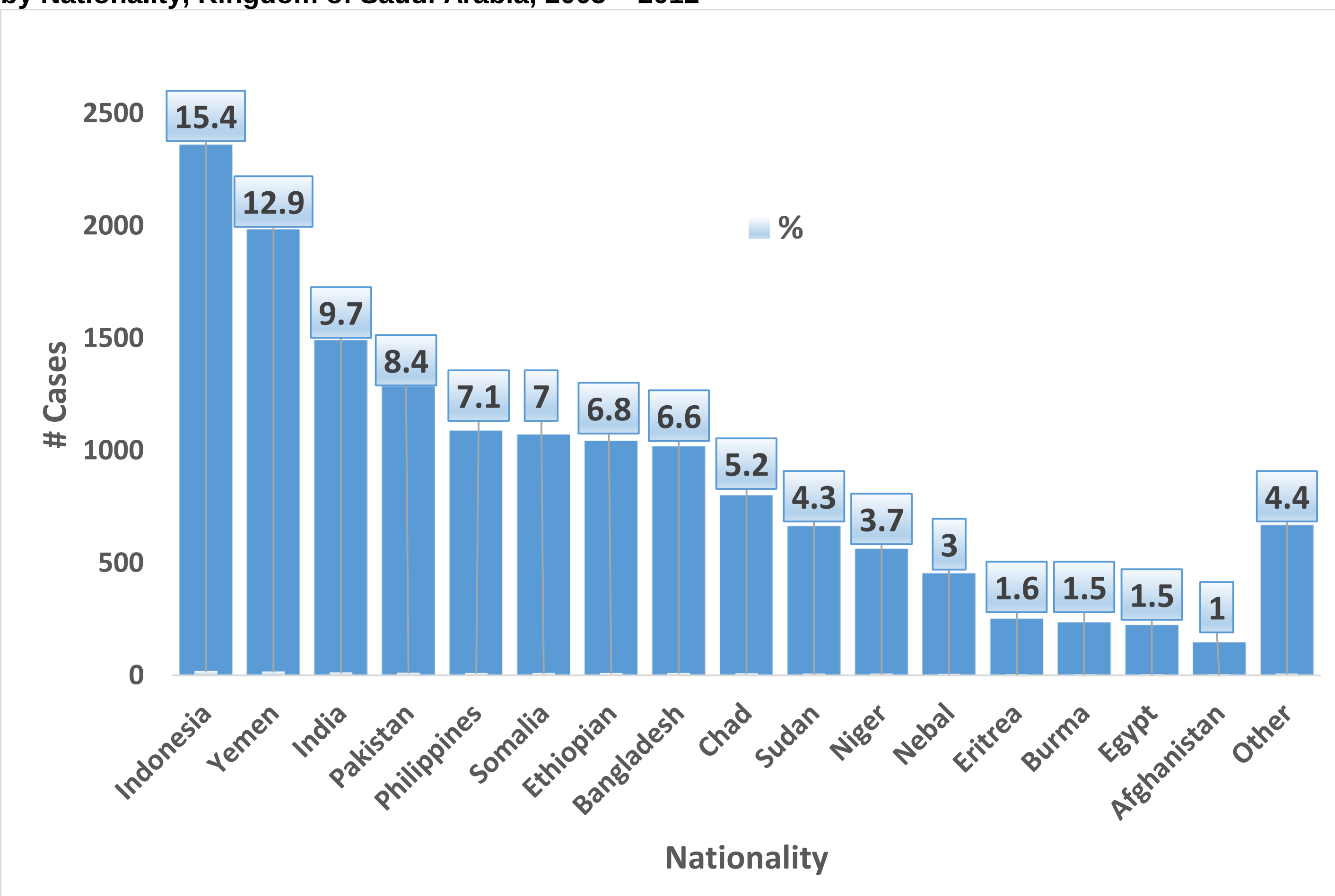


Figure 4. Proportion of Reported Cases of Tuberculosis, By Age Group and Gender, Kingdom of Saudi Arabia, 2005 – 2012

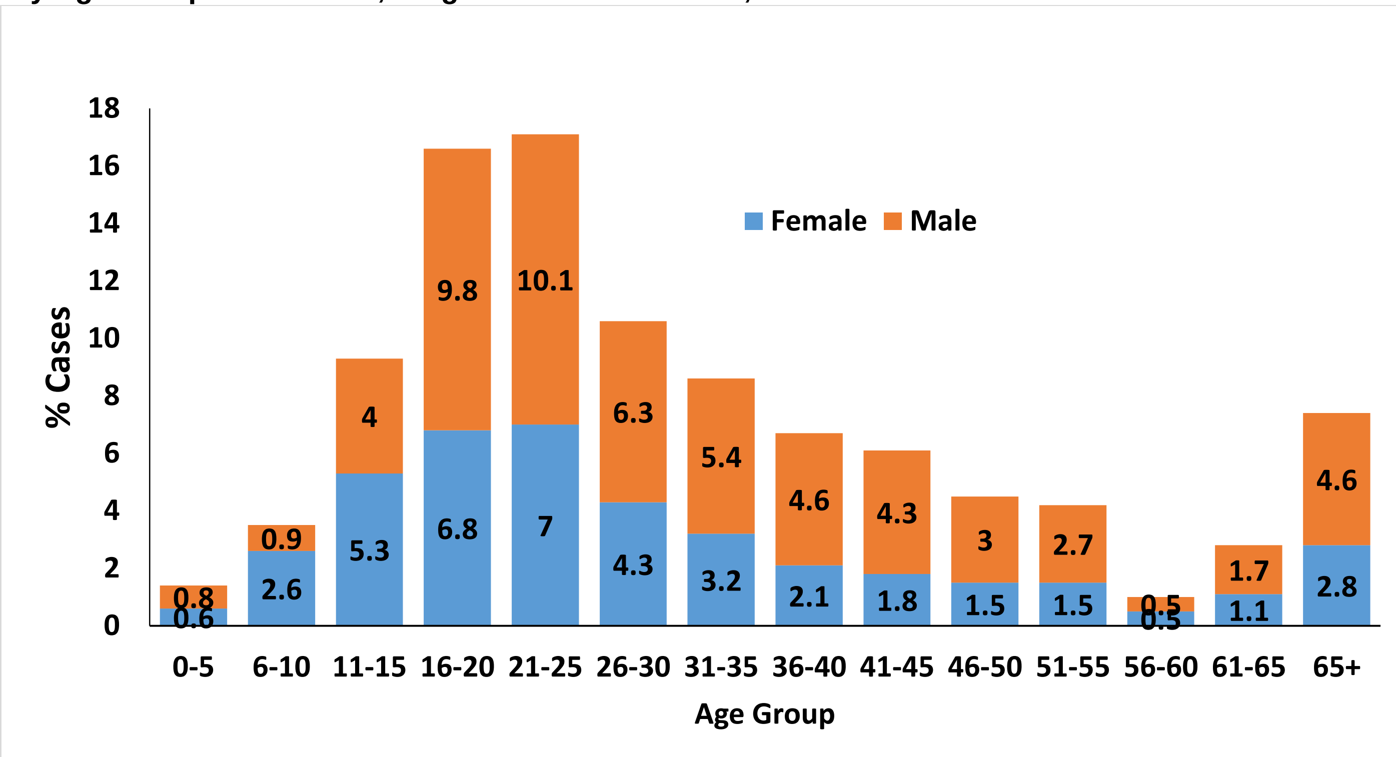
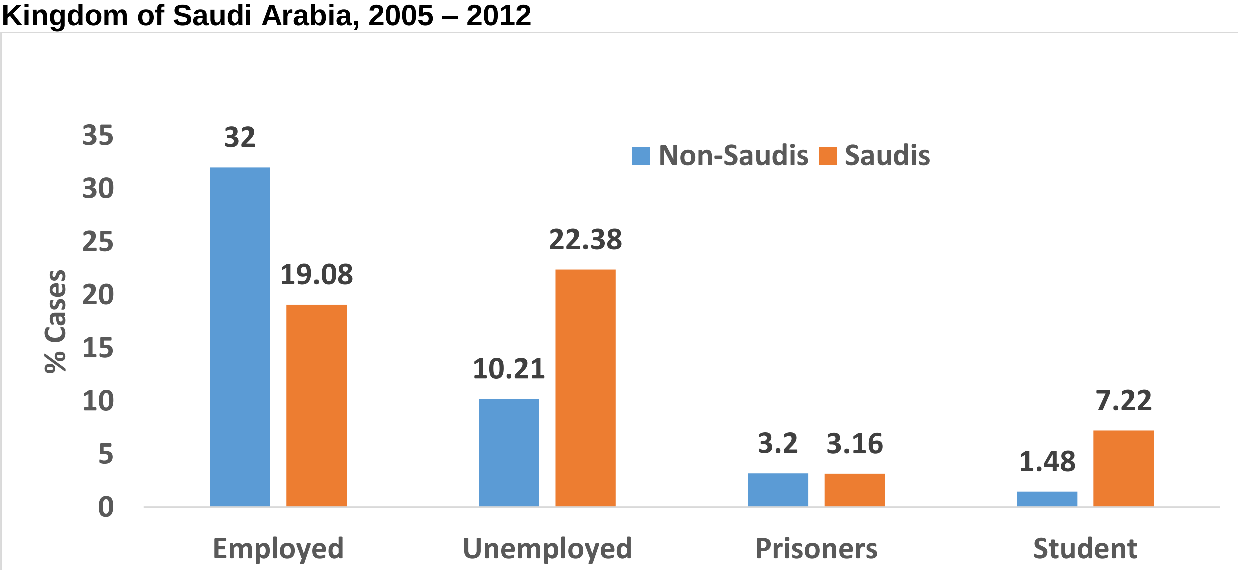


Figure 5. Proportion of Reported Cases of Tuberculosis, by Employment or Status and Stratified by Nationality, Kingdom of Saudi Arabia, 2005 – 2012



Of the 32,345 suspected TB cases in this study, 18,413 were laboratory-confirmed by either culture or smear using the WHO guidelines [9] (Table 2). Of the remaining suspected cases, 8,493 tested negative for TB via culture or smear, while 5,529 cases were not tested for TB using culture or smear (Table 3).

Table 2. Culture and Smear Test Results for Reported Cases of Tuberculosis, Kingdom of Saudi Arabia, 2005 – 2012

Culture	Smear Test	#	Outcome
Positive	Positive	874	Positive
	Negative	627	Positive
	Not Done	82	Positive
Negative	Positive	93	Positive
	Negative	253	Negative
	Not Done	26	Negative
Not Done	Positive	16,753	Positive
	Negative	8,195	Negative
	Not Done	5,505	Not Done

Table 3. Laboratory Outcomes of Reported Cases of Tuberculosis, Kingdom of Saudi Arabia, 2005 – 2012

Outcome	#	(%)
Positive	18,429	57
Negative	8,474	26
Not done	5,505	17
Total	**32,435**	**100**

Based on confirmed TB cases by either positive culture or smear, the overall proportion of laboratory testing for TB in KSA was 56.77% from 2005 – 2012. The region with the greatest proportion of laboratory testing was Medina (64.18%), followed by the Eastern Region (63.71%) and Mecca (59.78%). The regions with the lowest proportion of laboratory testing were Hail and Northern Borders (39.93% each) (Table 4).

Table 4. Number and Proportion of Laboratory-confirmed Cases of Reported Tuberculosis, by Region, Kingdom of Saudi Arabia, 2005 – 2012

	Asir			Baha			Eastern Region			Hail			Jawf		
Year	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**
2005	129	72	56	62	32	52	333	206	62	53	16	30	44	36	82
2006	113	80	71	29	15	52	299	171	57	61	22	36	27	12	44
2007	116	65	56	33	18	55	320	194	61	40	12	30	34	19	56
2008	150	80	53	34	17	50	334	198	59	39	15	38	32	18	56
2009	140	89	64	19	14	74	341	219	64	24	15	63	25	16	64
2010	170	87	51	35	20	57	395	233	59	24	12	50	49	23	47
2011	148	83	56	47	31	66	362	259	72	19	5	26	27	11	41
2012	141	85	60	30	14	47	303	232	77	28	18	64	43	25	58
Total	**1,107**	**641**	**58**	**289**	**161**	**56**	**2,687**	**1,712**	**64**	**288**	**115**	**40**	**281**	**160**	**57**

	Jazan			Medina			Mecca			Najran			Northern Borders		
Year	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**
2005	221	115	52	200	137	69	1407	697	50	24	9	38	43	14	33
2006	195	116	59	220	130	59	1688	975	58	30	14	47	44	14	32
2007	203	123	61	159	85	53	1894	1058	56	21	6	29	55	17	31
2008	207	124	60	169	111	66	1799	1123	62	38	16	42	43	17	40
2009	268	168	63	179	124	69	1696	1067	63	46	29	63	37	14	38
2010	280	180	64	191	134	70	1660	1078	65	52	26	50	27	12	44
2011	237	140	59	200	121	61	1544	932	60	56	23	41	28	18	64
2012	207	105	51	170	113	66	1486	946	64	41	21	51	21	13	62
Total	**1,818**	**1,071**	**59**	**1,488**	**955**	**64**	**13,174**	**7,876**	**60**	**308**	**144**	**47**	**298**	**119**	**40**

	Qassim			Riyadh			Tabuk		
Year	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**	**#**	**•LCC**	**(%)**
2005	127	60	47	956	498	52	88	41	47
2006	141	61	43	944	508	54	84	34	40
2007	128	45	35	985	541	55	96	42	44
2008	139	66	47	1065	564	53	107	40	37
2009	129	68	53	1155	608	53	90	35	39
2010	140	59	42	1460	722	49	75	32	43
2011	144	77	53	1191	580	49	80	45	56
2012	135	68	50	1174	634	54	64	31	48
Total	**1,083**	**504**	**47**	**8,930**	**4655**	**52**	**684**	**300**	**44**

•LCC = Laboratory-confirmed cases

Discussion

The overall IR of TB in KSA showed a statistically significant decrease from 2005 to 2012. The TB IR was generally higher among males compared to females over the last 4 years of the study period (2009 – 2012). Non-Saudis had about twice the TB IR of Saudis. The TB IR was highest in Mecca region compared to other regions, followed by Riyadh and Jazan. TB was found in 1.4% of age group <5, while the age group 6 –15 year olds made up 12.81% of the cases, and the age group >65 made up 7.41%. Regarding TB laboratory testing, there was a 15% difference between the regions with greatest and lowest laboratory-testing proportion.

This decrease in TB IR from 2005 to 2012 could be attributed to the build effect of the introduction of DOTS by the National TB Program in 2000 [7]. It could also be attributed to the policy change that enabled non-Saudis to seek diagnosis and treatment for TB without the fear of deportation, which would have encouraged them to seek medical services [4]. The higher IR in males compared to females could be explained by the fact that males in KSA are more engaged in public events than females [4]. Many of these events occur in crowded places conducive to airborne transmission.

The high TB IR in non-Saudis compared to Saudis could be attributed to multiple factors. First, most of the immigrants in KSA come from countries with a high TB IRs such as Pakistan, India, Bangladesh, Yemen, and Indonesia [7]. Second, many immigrants live in crowded conditions conducive to TB transmission, have poor diets, and engage in physically stressful manual labor, rendering them more susceptible to the disease. Furthermore, although the government stopped deporting non-Saudis diagnosed with TB, many are still afraid to seek medical services because they fear being dismissed by their employers.

The high TB IR in Mecca region could be explained by the presence of a high proportion of immigrants and by the 2.5 million pilgrims that visit the holy city each year. Many of the pilgrims and immigrants come from countries with a high IR of TB. The high IR in Riyadh could be attributed to a higher frequency of reporting due to the presence of large number of tertiary hospitals that treat patient from all over the kingdom. In addition, it is a major destination for work for non-Saudis. The high IR in Jazan region could be attributed to its proximity to Yemen, which has a high overall TB IR.

The presence of TB cases among children < 5 years of age indicates ongoing active transmission. This is also indicated by the fact that those in the 6 –15 year old category made up 12.81% of the cases; the immune system is thought to be more resistant to TB during this age range than during any other [1]. The high proportion of TB cases in the ≥ 65 age group could reflect a high prevalence of latent TB among younger persons, whose TB may have been activated after their immune systems weakened.

The difference between regions in TB laboratory testing could be attributed to the presence of a larger number of tertiary hospitals in the regions with high proportion of laboratory-testing; these facilities are better equipped to perform laboratory investigations than other health centers.

A limitation encountered was the lack of population statistics stratified by age, employment status, and non-Saudi nationality. This prevented further calculations and analysis of the IRs. Also, there was a lack of population statistics for Mecca city alone that prevented further analysis. A key strength of this study is that it used case-based instead of aggregated data. This type of data provided results for the culture, smear, and radiography for each patient and made it possible to filter out confirmed cases based on the smear and culture laboratory results in accordance with WHO guidelines [9].

For effective TB control in KSA, the DOTS approach should be supported and continued. In addition, special attention needs to be paid to the high IR among non-Saudis. A screening program needs to be implemented to test all non-Saudi workers for TB at their ports of entry. Furthermore, once TB patients are diagnosed inside KSA, their contacts should be screened, including family members, roommates, and co-workers.

Special attention needs to be given to the Mecca region for better control of TB. Pilgrims should be screened for TB before they are granted a Hajj visa. In addition, health authorities should encourage the use of facemasks by pilgrims and workers around the holy areas during the Hajj season. All residents of Mecca should be encouraged to get the anti-TB vaccine. Further studies need to be done to identify the precise impact of Hajj on Mecca region's TB IR. All residents of Jazan should be also encouraged to get the anti-TB vaccine due to Yemen's proximity to Yemen.

To improve the laboratory-confirmation of TB screening programs throughout KSA, access to culture or smear testing should be available to all health centers. In addition, assessments should be conducted of the ability of laboratories to detect and diagnose TB cases, and training should be provided if necessary. TB testing could also be performed by a central laboratory located in each region that received specimens from health centers not equipped to conduct the testing themselves.

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Chapter Four

Conclusion

The overall TB IR in KSA showed a statistically significant decrease from 2005 to 2012. This decrease could be attributed to the build effect of introducing DOTS (directly observed treatment, short course) by the National TB Program in 2000 [7]. It is also be attributed to the policy change that enabled non-Saudis to seek diagnosis and treatment for TB without the fear of deportation, which would have encouraged them to seek medical services [4]. Further research studies could be done to detect the precise decrease in IR attributable to DOTS. The IR before 2000 ranged from 13.6 to 17.2 per 100,000 population [7].

TB incidence was higher among non-Saudis (who make up 1/3 of the Saudi population) compared to Saudis. Most non-Saudis come from countries with high TB IRs and live in conditions that render them more susceptible [7].

Among the regions, the TB IR was highest in Mecca, followed by Riyadh and Jazan. The high incidence in this region can be attributed to the Hajj ritual. Each year, about 2.5 million people visit the holy mosque in Mecca. The densely crowded areas can be prime transmission points of airborne infections like TB, and the strenuous conditions sometimes associated with undertaking Hajj can render the individuals susceptible to diseases. The high IR in Riyadh could be attributed to the higher frequency of reporting due to the presence of a large number of tertiary hospitals that treat patients from all over the Kingdom. In addition, it is a major destination for non-Saudi workers. The high IR in Jazan region could be attributed to its proximity to Yemen. Further studies need to be done in Jazan to identify the definitive cause.

According to the confidence intervals in the last 3 years of our study period (2010 – 2012), the TB IR was higher in males than females, and this was statistically significant. This could be attributed to the fact that males in KSA are more often in attendance at public events than females, but further studies are needed to find the definite causes of this difference.

Most TB cases in this study were 25-35 years of age, and the highest proportion of cases occurred among employed non-Saudis, followed by unemployed Saudis.

Based on the diagnostic criteria of case confirmation by either positive culture of smear, the proportion laboratory-confirmed cases out of all reported TB cases in the screening program was 56.77%.

A limitation encountered was the lack of population statistics stratified by age, employment status, and non-Saudi nationality. This prevented further calculations and analysis of the incidence rates. Also, there was a lack of population statistics for Mecca city that prevented further analysis.

A key strength of this study is that it used case-based instead of aggregated data. These data provided results for the culture, smear, and radiography for each patient. This made it possible to filter out the confirmed cases based on the smear and culture laboratory results in accordance with WHO guidelines [9].

For effective TB control in KSA, the DOTS approach should be supported and continued. In addition, special attention needs to be paid to the high IR among non-Saudis. A screening program needs to be implemented to test all non-Saudi workers for TB at their ports of entry. Furthermore, once TB patients are diagnosed inside KSA, their contacts should be screened, including family members, roommates, and co-workers.

Special attention needs to be given to the Mecca region for better control of TB. Pilgrims should be screened for TB before they are granted a Hajj visa. In addition, health authorities should encourage the use of facemasks by pilgrims and workers around the holy areas during the Hajj season. All residents of Mecca should be encouraged to get the anti-TB vaccine. Further studies need to be done to identify the precise impact of Hajj on Mecca region's TB IR. All residents of Jazan should be also encouraged to get the anti-TB vaccine due to Jazan's proximity to Yemen.

To improve the laboratory-confirmation of TB screening programs throughout KSA, access to culture or smear testing should be available to all health centers. In addition, assessments should be made of laboratories' abilities to detect and diagnose TB cases and training should be provided if necessary. TB testing could also be performed by a central laboratory located in each region that would receive specimens from health centers not equipped to do the testing themselves.

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Appendix 1:

Kingdom of Saudi Arabia
Ministry of Health
Assistant Deputy for Preventive Medicine
National Tuberculosis Control Program
District___________________________ Form 13

إستمارة تبليغ وتقرير طبي عن حالة درن (Notification & Medical report of TB case)

الجزء الأول: البيانات الشخصية (First Part: Personal Data):

إسم المريض (Patient name):..	العمر (Age):	الجنس (sex):
الجنسية (Nationality):	المهنة (Occupation):	
رقم الحفيظة للسعوديين (I.D. No. for Saudis):	تاريخ الإصدار (Issue Date): / /	مكان الإصدار (Issue place:
رقم الإقامة لغير السعوديين (Iqama NO. for Non-Saudis):	تاريخ الإصدار (Issue Date): / /	مكان الإصدار (Issue place:
رقم جواز السفر (Passport No.):	تاريخ الإصدار (Issue Date): / /	مكان الإصدار (Issue place:
إسم الكفيل (Sponsor's name):..	رقم الهاتف (phone No.):	
رقم الحفيظة (I.D. No. for Saudis):	تاريخ الإصدار (Issue Date): / /	مكان الإصدار (Issue place:
عنوان الكفيل (Sponsor's address):..		
عنوان عمل الكفيل (Work address of the sponsor):.. رقم الهاتف(phone No.) :		
عنوان سكن المريض (Patient's address):...		
عنوان عمل المريض (Work address):..	رقم الهاتف (phone number):	
الجهة المحولة للمريض:..		

الجزء الثاني (Second Part):

أ- الفحص السريرى (Signs & symptoms):

تاريخ بداية الأعراض (date of onset): / /

1- كحة (Cough): ☐

☐

ب - التاريخ المرضي السابق (Past Medical

1- البول السكري (Diabetes M.): ☐

2- أمراض رئوية (Lung diseases): ☐

3- فشل كلوي مزمن (chronic renal failure): ☐

المدة بالأسبوع (Period in weeks):	
2- بلغم (Sputum):	
3- نفث دموي (Heamoptysis):	
4- حرارة (Fever):	
5- تعرق ليلي (Night sweating):	
6- ألم بالصدر (Chest pain):	
7- نقص الوزن (loss of weight):	
8- فقدان الشهية (Loss of appetite):	
9- أعراض وعلامات أخري & other signs)	

4- نقص المناعة المكتسب (AIDS):	
5- مثبطات المناعة (Immunosuppressive therapy):	
فترة العلاج بالسنوات Treatment period in)	
6- سرطان (Cancer):	
نوعه (Type):	
7- سابقة التطعيم بالـ بي سي جي history of BCG)	
التاريخ بالسنوات period in years):	
الندبة (Scare):	
8- علاج سابق للدرن Previous history of TB)	
مدة العلاج بالشهور (Period in months):	
البلد المعالج (treating country):	
نتيجة المعالجة السابقة treatment outcome of previous treatment):	

ج – الفحوصات والتحاليل (Investigations):

إختبار التيوبركلين (Tuberculin test): ☐ ملم   مزرعة بصاق (Sputum culture): ☐

فحص البصاق (Sputum smear): ☐   عينة باثولوجي (Pathology): ☐

رقم العينة ☐ التاريخ / /   مكانها (pathology site):..

أشعة الصدر(X- Ray) : ☐   سرعة الترسيب للدم (ESR): ☐   ALT ☐ AST ☐

نتيجة فحص الـ HIV :	ARV therapy:	Cotrimoxazole:
Date of test: \ \	Start Date: \ \	Start Date: \ \

بذل سوائل (Fluid aspiration):

بلوري (Pleural) ☐   تيموري ☐   نخاعي (CSF) ☐   بريتوني (Peritoneal) ☐

د- التصنيف حسب مكان الإصابة (Classification according to site):   رئوي (Pulmonary) ☐   خارج الرئة (EP) ☐

هـ- تصنيف المريض (patient classification):

جديد (New) ☐   منتكس (Relapse) ☐   عاود بعد انقطاع (TAD) ☐   محول (Transferred) ☐   أخرى Others ☐

و- النظام العلاجي (Treatment category):

CAT1	☐	CAT2	☐	CAT3	☐	CAT4	☐

1- أدخل المستشفى بتاريخ (Date of Hospitalization):..بتاريخ / /

2- بدأ العلاج بمركز صحي (Starting treatment in a PHC):..بتاريخ / /

3- حول للعلاج إلى (Transferred to):..بتاريخ / /

4- أعطي موعد مع الأخصائي الاجتماعي بتاريخ.. بتاريخ / /

إسم الطبيب المعالج **التوقيع** **التاريخ**

√ = Yes × = No POS = Positive NEG = Negative ND = Not done

قراءة اختبار التيوبركلين تكتب بالمليمتر