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ORIGINAL ARTICLE

A retrospective study to investigate the impact of immigration on tuberculosis control program by DOTS strategy in Gazan Province, Saudi Arabia

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Abstract
Background Tuberculosis (TB) is an infectious disease, which is a significant global public health concern. The use of directly observed therapy of short course (DOTS) is the strategy recommended by the World Health Organization (WHO) to cure TB. In this paper, the effectiveness of the DOTS is assessed using data collected in 2014 from the Gazan Province, Saudi Arabia (SA). The assessment is impacted by migration from high prevalence countries into SA. The association between immigration and TB is not well documented and studied in the literature. We will address this problem and identify other factors influencing the success of DOTS.
Methods Descriptive methods are used in this study. The logistic regression model is used to identify significant factors of success or non-success of the DOTS. The data has missing observations. Multiple imputations were carried out to fill in missing outcomes and completed data sets are analyzed further.
Results The results show that none of the predictors have a significant role in treatment outcome. The cure rate for the study population is 90.3% after excluding defaulters and deportees. If we include 29 defaulters and 68 deportees assuming treatment failed for these cases, the cure rate is 67%, which is far below the WHO goal of 85%. After multiple imputations, the cure rate is 91.7%.
Conclusions Increasing number of migrants into low prevalence countries may affect TB epidemiology. In view of the huge gap, 67 versus 91.7% in the cure rates, we firmly recommend that health and immigration authorities in SA work together to see that TB treatment is completed before deportation.

Keywords Epidemiology · Tuberculosis · DOTS · Immigration · Surveillance

Introduction

Tuberculosis (TB) is an infectious disease and an important public health and medical concern. Its epidemiological mode of transmission is also of concern. TB is caused by the bacteria *Mycobacterium tuberculosis* that most often affects the lungs but can also affect any organ. Pulmonary TB accounts for 70% of all cases and extra pulmonary TB accounts for 30% (Alwani et al. 2015). TB spreads from person to person through the air when people with lung TB cough, sneeze, or spit, thereby propelling the TB germs into the air. TB is preventable and curable and it is second only to HIV/AIDs as the greatest killer worldwide due to the single infectious agent (Zumla et al. 2015). TB is out of control in many parts of the world where the global burden of tuberculosis remains high due to high rates of HIV coinfection, especially in Southeast Asia, sub-Saharan Africa, and Eastern Europe (Dye et al. 1999).

In 2013, 9 million people contracted TB and 1.5 million died from the disease around the world, which translates into a global incidence of 128 per 100,000 (Zumla et al. 2015). TB occurs in every part of the world and affects all ages. Emergence of multi-drug resistant TB is also worrisome; it is estimated that about 480,000 people developed multi-drug

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resistant TB (MDR-TB) throughout the world in 2013 (WHO 2016). In low-incidence countries, migrants face high risk of exposure to TB infection due to overcrowded living and working conditions, increased vulnerability to HIV, malnutrition and substance abuse, marginalization, and social exclusion (IOM 2014). Migrants have difficulty in getting healthcare access and have poor health-care-seeking behavior due to lack of education and health illiteracy. Stigma and cultural beliefs are other factors; additionally, they are afraid of getting caught, losing their jobs, losing economic sustenance, and finally being deported. All these problems lead to a delay in TB diagnosis among migrants and thus spread the disease among the local population. TB is a social disease and migration, as a social determinant of health, increases TB-related morbidity and mortality among migrants and surrounding communities (Peiro and Benedict 2009). WHO had started a new strategy known as directly observed treatment short-course (DOTS) to stop spread of TB globally. The goal is to achieve a cure rate of at least 85% by strict implementation of DOTS in all countries' national TB control programs. Strict implementation means a good adherence to the treatment. Currently, more than 200 countries are implementing DOTS in their national TB control program including the USA. The unique features of the program are:

1. Permanent reporting system of TB notification to the Ministry of Health (MOH), and thereby to WHO, is mandatory for both physicians and laboratories. This reporting system was enacted when TB came under the direct surveillance of WHO.
2. Contact tracing which is conducted through a strict monitoring system and follow-ups are reviewed by case holding until the treatment is complete or TB is cured. The MOH policy is to treat all the tuberculosis patients for free. It is mandatory to admit all open cases of TB, i.e., smear positive, at least in the initial intensive phase of the first 2 months or until sputum conversion takes place from positive to negative.

This study investigates the impact of immigration on the TB control program in Gazan, SA, which is geographically close to Yemen. Yemen is among the 22 high prevalence TB countries. Many Yemenis enter SA, both legally and illegally to seek employment and medical treatment, since primary care is free for all people in SA. However, all the legal immigrants are screened for TB and other infectious diseases at the time of entry, but there is no control over migrants who enter illegally. We need to learn the epidemiology of TB in immigrant population vis-à-vis the citizens.

Gazan-Saudi Arabia profile The Kingdom of Saudi Arabia is in the Arab peninsula. It has a total population of 28.7 million, of which 20 million are Saudi nationals. Saudi Arabia is a rich oil-producing country with 25% of the world's oil reserves. The two biggest cities, Mecca and Medina, receive approximately 4–5 million pilgrims year-round from all over the world. (The Royal Embassy of Saudi Arabia, Washington DC 2012). Most of the travelers to Mecca and Medina are adults from high prevalent TB countries having health issues. Due to overcrowding during the main season of Hajj, transmission of airborne infections including TB occurs (Memish et al. 2014). The most common cause of pneumonia in hospitalized pilgrims during Hajj is pulmonary TB with overcrowding being one source of its spreading (Wilder-Smith et al. 2005). In the last two decades, many developmental activities, like expansion of residential areas and mosques, require foreign labor, especially in the construction sector, which adds to the problem of TB importation; a substantial labor force in Gazan is from Yemen both legal and illegal.

Gazan is a southern province in Saudi Arabia and it stretches some 300 km along the southern Red Sea coast, just north of Yemen. The ex-King of SA, Abdallah declared Gazan as an economic city where many developmental projects are slated. It covers an area of 11,671 km^2 and has a population of 1,365,110 as of the 2010 census.

Saudi Arabia is an active donor and partner of WHO and is committed to stop TB. Primary, secondary and tertiary healthcare services are free of cost to all the Saudi nationals. Also, primary care and emergency services are provided free to all non Saudi nationals and for visitors such as pilgrims.

What is DOTS?

History and background of DOTS

DOTS refers to the Direct Observation Treatment Short course of tuberculosis, the erradification of which suffers from two major constraints—irregular treatment, and insufficient treatment using other than the standard first line of drugs, which are sensitive to TB bacteria. People with tuberculosis require treatment for at least 6–8 months with multiple drugs to attain a complete cure and avoid drug resistance. It is difficult for many patients to stick to the standard treatment regimen and complete their prescribed course of medications. This irregularity of and non-adherence to treatment results in prolonged infectiousness, relapse of TB, development of drug resistance, or even death. When resistance to TB drugs occurs, it is difficult to treat the disease and very expensive with a second line of drugs. The price may be as high as a thousand times the cost of initially treating the drug sensitive infection (WHO 2012). Hence, the WHO developed a new strategy known as DOTS regimen, which is patient centered, community based, and cost effective. DOTS is simple to implement, improves patient's compliance, and prevents transmission of the disease and MDR-TB (Jamison et al. 2006). Prior to implementation

of DOTS, the cure rate was between 31 and 37% and TB was out of control in many parts of the world (Alwani et al. 2015) where treatment regimens were not consistent from physician to physician and from center to center (Maher et al. 1997).

A study was conducted in Ethiopia to assess the knowledge of private practitioners (PPs) with regard to TB control, their practice of TB diagnosis, treatment, and monitoring. A total of 120 PPs responded to a self-administered questionnaire. At least two to five TB cases were diagnosed in their clinics per week. The results, according to 81.5% of the PPs, indicated that the correct anti-tuberculosis treatment regimen recommended by the National Tuberculosis Program (NTP) was being used by only 9.7% of the doctors, while 63% listed 68 different regimens, whereby 41% of the PPs monitored treatment using chest X-ray (CXR) alone, while 21.0% used CXR in combination with another diagnostic tool. To summarize the study, 80% of the PPs did not maintain a TB register, and case holding was nonexistent; however, there is a huge lack of information on anti-TB drugs, which shows that irrational use of the few available anti-TB drugs may lead to the emergence and spread of drug resistant-TB (Sagbakken et al. 2008). Several other studies show that private providers are likely to prescribe antibiotics irrationally, do not monitor the effects of treatment, maintain clinical records and case holding, or do not notify the public health system about the cases of the disease theay are treating. These are all contributory factors to a surge in MDR-TB (Udwadia and Pinto 2007).

There was no single guideline for using a standard regimen. Usually patients feel better after 3–4 weeks of treatment with anti-TB drugs, which may make them stop the treatment abruptly. Actually, complete eradication of TB bacteria takes at least 6 months using a multi-drug regimen. There were no TB registers and case holding for follow-up by the physicians, thus, the chance of registering the same patient at multiple places was enhanced and was occurring. Duplication of registration misleads the incidence rate and hence increases the prevalence rate (Raviglion and Pio 2002). The flow chart in Fig. 1 outlines the DOTS strategy.

Summary of why DOTS needs to be followed:

- We cannot predict who will and will not take medications as directed. People from all social classes, educational background, age, gender, and ethnicity can have problems taking the medications correctly as prescribed by the doctors.
- Studies show that 86–90% of patients receiving DOTS, complete therapy, compared to 61% for those on self-administered therapy.
- DOTS helps patients finish TB therapy as quickly as possible without unnecessary gaps.
- DOTS helps prevent TB from spreading to others.
- DOTS decreases the risk of drug resistance which results from erratic or incomplete treatment.
- DOTS decreases the chances of treatment failure and relapse (WHO 2009).

Disease classification and definitions for terms used in the DOTS

Latent tuberculosis infection (LTBI): a person has tuberculosis infection without any signs and symptoms of disease. TB bacteria remains in the body as dormant inactive state without expressing tuberculosis disease.
Smear positive patient: a patient with at least two sputum specimens positive for acid fast bacilli (AFB) by microscopy or a patient with one sputum specimen positive for AFB and radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB.
Smear negative patient: a patient with radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB, whereby the sputum exam was negative at least three times, and the physician has decided to treat the patient with anti-TB drugs.
Pulmonary TB: a patient with at least two sputum specimens positive for AFB by microscopy or a patient with one sputum specimen positive for AFB and radiographic abnormalities determined by a medical officer to be consistent with active pulmonary TB.
Extra pulmonary TB: a patient with one mycobacterial culture positive specimen from an extra pulmonary site or a patient with histological or clinical evidence consistent with active tuberculosis.
New case: a patient who has been diagnosed with TB for the first time in his life, and historically was never considered having active TB in the past.
Cured: a patient who has received a full course of anti-TB drugs and his smear becomes negative after 2 months of the initial phase and remains negative at the fourth- and sixth-month intervals is considered cured.
Failure: a patient received the full course of anti-TB drugs and his smear remains positive after 2 months of initial phase and remains positive at the end of the fourth and sixth months.
Relapse: a patient who had been diagnosed and received complete course of treatment and has been considered cured from TB, but now is smear positive.
Defaulter: a patient on treatment who did not show up for more than 3 days.
Multiple drug resistance TB (MDR-TB): a patient is resistant to the first line of drugs (at least to two drugs Rifampicin and Isoniazid).
Extensive drug resistance TB (XDR-TB): extensively drug-resistant TB is a rare type of MDR-TB, that is

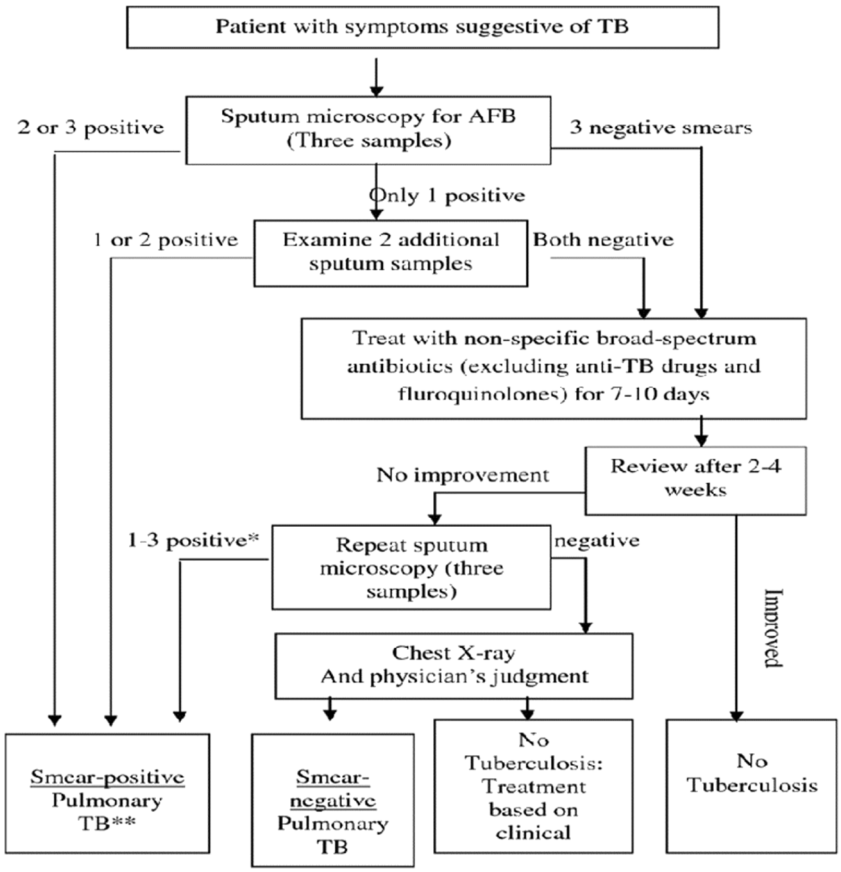

Fig. 1 Diagnosis and treatment flow chart. Source: WHO website

resistant to Isoniazid and Rifampin, plus any Fluoroquinolone and at least one of three injectable second-line drugs i.e., Amikacin, Kanamycin, or Capreomycin (Zumla et al., 2012).

Risk factors for developing tuberculosis (CDC 2016):

1. Immune system dysfunction: diseases and medications that disrupt the immune system include HIV/AIDS, diabetes, certain cancers, end-stage renal disease, cancer drugs and medications that prevent transplant rejection
2. Travel to endemic areas: 22 countries have been declared as having high prevalence TB by WHO
3. Poverty, low socio-economic communities
4. Substance abuse and work location
5. Alcohol and tobacco smoking
6. Healthcare workers have regular contact with people who are sick and, therefore, have a higher risk for contracting tuberculosis
7. Nursing homes and old age residential health facilities
8. Refugee camps
9. Prisons and detention centers
10. Crowded housing

Using an extensive source of data, it is found that TB is one of the most common causes of morbidity and the most common cause of death in HIV-positive adults living in less-developed countries (Corbett et al. 2003). The risk of active tuberculosis is substantially elevated in people who drink more than 40 ml of alcohol per day, and/or have an alcohol abuse disorder. This may be due to both increased risk of infection related to specific social mixing patterns associated with alcohol use as well as influence of alcohol on the immune system itself and of alcohol-related conditions (Lönnroth et al. 2008). It is observed that there is consistent evidence that tobacco smoking is associated with an increased risk of TB (Lin et al. 2007).

Diabetes and TB coexistence

Diabetes is known to decrease the strength of a healthy immune system, as TB is prone to infect weaker immune systems. Several studies have suggested that diabetes mellitus (DM) increases the risk of active tuberculosis. The mounting prevalence of DM in TB endemic areas may critically affect TB control. DM is associated with an increased risk of TB regardless of study design and population. People with

DM may be important targets for interventions such as active case finding and treatment of latent TB and efforts to diagnose, detect, and treat DM may have a beneficial impact on TB control. Considering these associations, and how DM and TB are known to occur together more often across the world, it often poses challenges in managing both (Jeon and Murray 2008).

Goals

1. Assess how effective the DOTS program is in the Gazan Province using data on Saudi nationals and immigrants.
2. Determine factors affecting the cure rate of TB using a method based approach.
3. Predict the outcome of the DOTS program for illegal immigrants if they had not been deported.
4. Use the study for policy prescriptions.

Aims

1. Assess the cure rate of TB among patients who are Saudi Citizens and that of legal immigrants.
2. Examine the impact of immigration status (Saudi or non-Saudi) on the success of DOTS.
3. Examine the impact of Bacillus Calmette-Guerin (BCG) vaccination on the success of DOTS.
4. Examine the role of DM management on the success of DOTS.

Materials and methods

Study design

The data is a retrospective review of all registered cases of tuberculosis in 1 year (2014) that were treated in Gazan. Data obtained from the Department of Primary Care, Regional Directorate of Health Gazan SA.

Methods

As a first step, we used simple descriptive statistics to assess how effective the DOTS program, using complete data shown in Tables 1, 2 and 3. In Table 1, the composition of various populations in Gazan DOTS program is presented by gender. In Table 2, a detailed distribution of adherence of the DOTS program is laid out. In Table 3, diabetes and the BCG vaccination status is presented among the participants of the program. In Fig. 2, composition of participants in the DOTS program over the years 2006–2014 is given, while in Fig. 3, age distribution of the participants is detailed.

Table 1 Data summary: gender versus residence status

Nationality	Gender distribution		Total
	Men	Women	
Saudi	104 (62%)	65 (38%)	169 (47%)
Non-Saudi (immigrants)	162 (84%)	31 (16%)	193 (53%)
Subtotal	266 (73%)	96 (27%)	362
Legal immigrants (residence permit)	27 (57%)	20 (43%)	47
Non-legal immigrants	135 (92%)	11 (8%)	146
Total	162	31	193

In the second step, we have fitted a logistic regression model with outcomes (two levels: cured and non-cured) as response variables and have assessed its goodness-of-fit as well as the significance of the predictors, while in the third step, the model omits all missing data. There are 29 defaulters and 68 deportees for whom information on outcome, obviously, is not available. In the extreme case, we have treated these cases as having non-cured outcome and refitted the logistic regression model. The cure rate is calculated afresh. Fourthly, regarding multiple imputations, the model reportedly built in step 3 as unsatisfactory. We do not know what will be the outcome for all defaulters and deportees. We use a multiple imputation technique to fill in missing values in all variables. We use R package "MICE" to carry out multiple imputations (Van Buuren and Groothuis-Oudshoorn 2000). The acronym MICE stands for multiple imputation by chained equations. The core idea in the MICE program is that it builds an appropriate regression model that regresses the variable of interest on the rest of the variables using all non-missing data. This procedure is used to fill in the missing values of all variables including the outcome (Van Buuren and Groothuis-Oudshoorn 2000). In our analysis, we obtained five completed data sets and we analyzed each completed data set. Next, we examined the significance of each predictor in the model, focussing especially on "BCG vaccination" and "diabetes". Lastly, we assessed how effective the DOTS program actually is.

Results

Data summary

A summary of salient features of the Gazan TB data is provided in Tables 1, 2, and 3. The total number of TB patients in Gazan province along with their residence status is provided in Fig. 2. The trend is upward and the surge

Table 2 Adherence of the DOTS program

	Those who stayed in the DOTS program		Those who did not stay in the DOTS program		
	Cured	Failure	Deported	Defaulters	Total
Outcome	243 (67%)	22 (33%)	68	29	362

in TB cases reported is visible from 2008 to 2010 (Fig. 2). It is during this period that surveillance activity has increased in relation to active case findings. The principle author of this report oversaw the DOTS program in Gazan via the good teamwork of health care personnel during 2008–2010. In the general population, the incidence rate has been increasing over a span of 8 years culminating in 2014. In the year 2014, the number of cases among the non-Saudis, especially undocumented immigrants, is higher than the Saudis (Fig. 2). The age distribution of the patients is summarized in Fig. 3 in the form of a non-parametric density curve, which captures the shape of the distribution.

The age of the patients ranges from 0.17 to 86 years, whereby there are four children under the age of 5, the median age is 28 years and 75% of patients are below 34 years of age. (Fig. 3).

Logistic regression:

We have fitted a logistic regression model to the original data with the binary outcome variable (cured/not cured). The predictors are: age; sex; nationality; BCG; symptoms; smear; and diabetes. These predictors are described only if they are not already self-explanatory.

Age

Sex (male = 1; female = 2).
Nationality (Saudi = 1; non-Saudi = 0).
BCG (yes = 1, no= 0).
Symptoms (The number of months the patient had symptoms before the treatment started).
Smear (Pos., Neg.).
Diabetes (yes = 1, no = 0).

Table 3 Diabetes and BCG vaccination status

Diabetes	Diabetes, yes 48 (13%)	Diabetes, no 314 (87%)
BCG vaccination	BCG received 172 (48%)	BCG not received 190 (52%)

The output is presented in the Appendix. The salient features are:

1. The model is given by:

$$Ln\ \frac{Pr(cure)}{Pr(non\text{–}cure)} = -2.56 + 0.02^{*}\text{age.} - 0.91^{*}\ \text{S} + 0.91^{*}\ nationality + 0.13^{*}\text{BCG}\ 0.02^{*}\ symptoms - 0.14^{*}\ smear\ \text{POS} - 1.73^{*}\ diabetes$$

2. 97 observations were removed because of missing observations before the model is fitted. These missing observations come from deportees (68) and defaulters (29).
3. The model fit is good with the residual deviance 140.07 on 257 degrees of freedom.
4. None of the predictors are significant at 5% level. Nationality is borderline significant at 10% level. The *p*-value for diabetes is just over 10%.
5. Even though none of the predictors are significant, they are collectively significant with residual deviance 140.07 on 257 degrees of freedom with *p*-value 1.00 for goodness of fit.
6. The cure rate when 97 observations were removed by the model–fitting exercise was 90.3%.
7. In the extreme case, we can deem that the treatment (DOTS) failed for the deportees and defaulters. In such a case, the cure rate is 67% which is below the threshold value of 85% set by WHO.

Multiple imputations

The fitted model could be used to predict the outcome for the deportees and defaulters but it will not work if there are missing values in the predictors and there are missing values. In order to counteract the disadvantage wrought by the logistic regression model, we used the multiple imputations procedure by MICE (multiple imputations by chained equations), which fills out missing values that occur anywhere in the data. We created five completed data sets and the logistic regression model is fitted to each one of them. Imputed complete data set logistic regression output is presented in Appendix. The main conclusion we draw is summarized in the following— for each imputed data set, we calculated the cure rate as (number of cured/number of total) ×100. The cure rates are 1 = 90.88%, 2 = 90.88%, 3 = 92.26%, 4 = 91.99%, and 5 = 90.33%, with average = 90.27%.

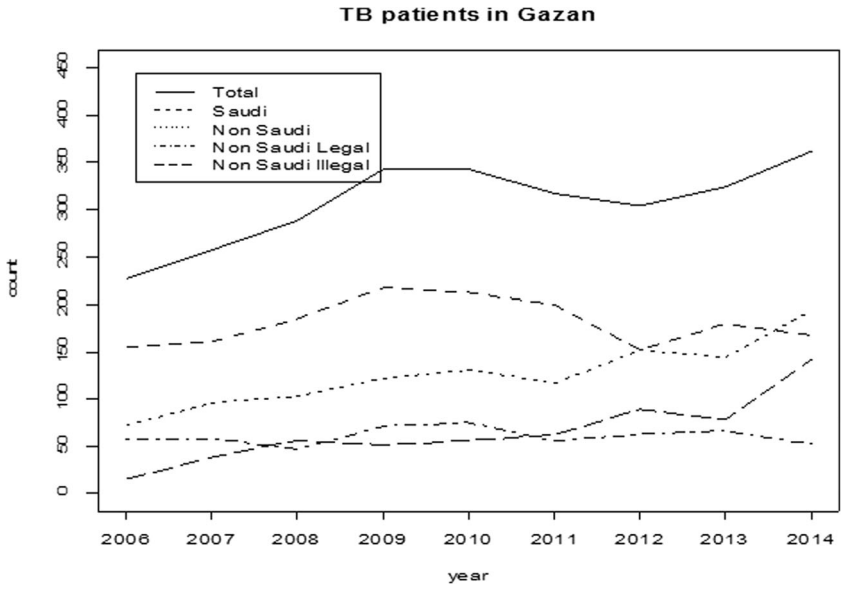

Fig. 2 Total number of TB patients along with their residence status for the years 2006 to 2014

Comments

None of the predictors are significant in every one of the completed data sets, confirming the results of the original logistic regression analysis, in which missing observations were removed.

Conclusions (summary of the results including multiple imputations):

1. Demographically, age, sex, and nationality did not play any significant role.
2. BCG vaccination did not have any impact on the treatment outcome. The disease outcome in BCG vaccinated and non-vaccinated groups was 91.96 and 89.19%, respectively. A chi-squared test was performed to examine the relationship between the BCG vaccination and disease outcome. There was no significant relationship between these variables $\{x^2(\ 1362) = 0.41, p = 0.52\}$.
3. In our study, diabetes mellitus did not have any significant impact on treatment outcome. We reckon that the DOTS regimen, when patients are directly observed for a period until the completion of the TB treatment, also facilitated the diabetics to keep their diabetes under control by strict monitoring of blood sugar and diet (OR = 0.23; 95% CI (0.3–1.74); $p = 0.12$; RR = 0.88).
4. There was no significant impact on the outcome regardless of their duration of symptoms at the time of diagnosis of TB (OR = 0.34;95% CI (0.1–1.11); $p = 0.34$; RR = 0.87).

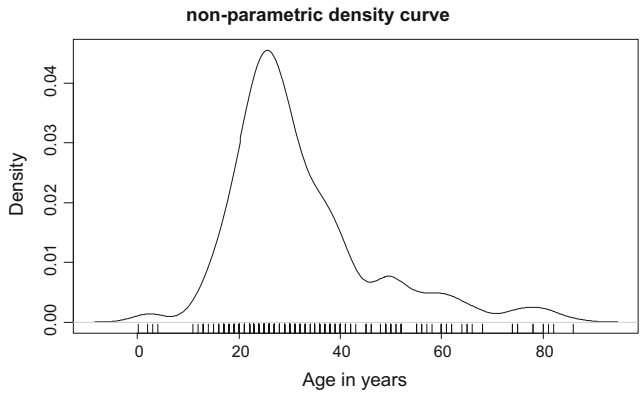

Fig. 3 Age distribution of patients

Discussion:

Incidence The total number of TB cases are increasing in the general population. The increase is due to an increase in the number of undocumented immigrants. There is no change in the incidence of TB among documented immigrants. In the year 2014, the number of cases among non-Saudis, especially undocumented immigrants, was higher than the Saudi nationals (Fig 2).

Cure rate In the extreme case of treating defaulters and deportees as though the DOTS program had failed for them, the cure rate was 67%. Multiple imputations methods, using information on the predictors, predict what could have been the

outcome of the DOTS program had they stayed on. The cure rate was 91.5%.

Advice One active case untreated can give a TB infection to at least 10 people (Murray and Salomon 1998).

We want the authorities in Immigration, Ministry of Health, and the team of DOTS in the regional sectors to understand the barriers to health care access by immigrants. Immigrants may fail to seek treatment because of the risk of deportation. Such behavior increases the spread of TB among the local population. It is important to emphasize treatment completion among the immigrants and assure them that they will not be deported while under treatment.

BCG as preventive

None of the predictors including BCG is significant individually in the logistic regression model before and after imputations; however, collectively the predictors are predictive. The efficacy of BCG Vaccine can be determined from this study. As part of the policy of the MOH, it is mandatory to give BCG to all the newborns in SA. We examined its impact on the DOTS program. In the literature, BCG efficacy is known to be from 0 to 70% (Ponnighaus et al. 1992). In this study, we discovered no significant difference in the outcome between the BCG vaccinated group and the unvaccinated group.

Diabetes associated with TB

Multiple studies of tuberculosis treatment have indicated that patients with diabetes mellitus may experience poor outcomes (Baker et al. 2011). We examined the impact of diabetics associated with TB infection on the overall outcome of the DOTS program. In this study, we discovered no significant difference in the treatment outcomes between TB patients with or without diabetes. Further research is warranted to more efficiently study the implementation of the DOTS among the coexistence of TB and Diabetes group to prevent and stop TB.

Significance/relevance to public health

Since TB is a curable and preventable disease, if risk factors are identified properly and dealt with appropriately, the spread of tuberculosis can be stopped or at least good control can be achieved. The message for the public health workers is to optimize the DOTS program implementation and to reach out to the underprivileged population who are always at risk. Even though the USA has an effective control strategy of tuberculosis by implementing DOTS, it still faces immigration as one of the challenges that need to be identified to achieve effective results. Immigrants reported high levels of stress due to fear of deportation, which affected the access to health care service; thereby affecting their emotional well-being, which is a public health concern (Esposito et al. 2015). For their social and emotional well-being, removing the barrier to health care access and educating them about their rights is the top priority regarding vulnerable populations anywhere globally.

Limitations

Our study sample is a convenient sample, since most of the patients self-reported to the health care facilities. Except for a few cases of contact who were traced by the DOTS health teamworkers, patients seeking medical advice visited clinics on their own or were brought in by their family members or the patients' employers.. This study is limited because of the likelihood that many TB patients go unreported due to fear of deportation, stigma, and other factors.

Compliance with ethical standards

Ethical approval This article does not contain any studies with human participants or animals performed. Institutional Review board approval has been obtained, Study ID 2015–5636.

Conflict of interest All authors declared that there is no conflict of interest.

Appendix

Acronyms and abbreviations

DOTS	Direct observation treatment of tuberculosis short course
Symptoms	Duration of symptoms (cough, fever and weight loss) before the start of DOTS
Smear	Sputum test may be positive or negative depends on presence of TB bacillus
Diabetes	TB patients who have or do not have diabetes
Outcome	Results after completion of DOTS
BCG	Bacilli Calmette Guerin, which vaccinate against tuberculosis
OR	Odds ratio
RR	Relative risk
CI	Confidence interval

Logistic regression output

```
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.55549    1.00404  -2.545   0.0109 *
Age           0.01859    0.01518   1.225   0.2207
Sex          -0.90952    0.59406  -1.531   0.1258
Nationality   0.90615    0.53777   1.685   0.0920
BCG           0.13162    0.54081   0.243   0.8077
Symptoms      0.01797    0.01598   1.125   0.2606
SmearPOS     -0.13980    0.47073  -0.297   0.7665
Diabetes     -1.72518    1.05133  -1.641   0.1008
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
    Null deviance: 151.62  on 264  degrees of freedom
Residual deviance: 140.07  on 257  degrees of freedom
  (97 observations deleted due to missingness)
AIC: 156.07
Number of Fisher Scoring iterations: 6
```

Logistic regression output for five completed data sets by multiple imputations

```
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.01356    0.88430  -2.277   0.0228 *
Age           0.01164    0.01425   0.817   0.4139
Sex          -1.02757    0.57417  -1.790   0.0735.
Nationality2  0.85936    0.44512   1.931   0.0535.
BCG          -0.33828    0.48475  -0.698   0.4853
Symptoms      0.01153    0.01544   0.747   0.4552
Smear2        0.22079    0.40580   0.544   0.5864
Diabetes     -1.75996    1.04409  -1.686   0.0919 .
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
    Null deviance: 202.02  on 361  degrees of freedom
Residual deviance: 188.07  on 354  degrees of freedom
AIC: 204.07
Number of Fisher Scoring iterations: 6
Imputed data set #2
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.31053    0.89534  -2.581  0.00986 **
Age           0.01490    0.01429   1.042  0.29723
Sex          -1.06233    0.57442  -1.849  0.06440 .
Nationality2  0.74237    0.43473   1.708  0.08770 .
BCG           0.22065    0.47108   0.468  0.63950
Symptoms      0.01866    0.01475   1.265  0.20576
Smear2        0.13226    0.40430   0.327  0.74357
Diabetes     -1.75748    1.04283  -1.685  0.09193 .
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
Null deviance: 202.02  on 361  degrees of freedom
Residual deviance: 189.11  on 354  degrees of freedom
AIC: 205.11
Number of Fisher Scoring iterations: 6
Imputed data set #3
Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.516493   0.869194  -2.895  0.00379 **
```

```
Age           0.014527   0.013893   1.046  0.29573
Sex          -0.956744   0.527323  -1.814  0.06963 .
Nationality2  0.979662   0.428643   2.285  0.02228 *
BCG           0.436873   0.465922   0.938  0.34842
Symptoms      0.017522   0.015108   1.160  0.24616
Smear2        0.009343   0.394012   0.024  0.98108
Diabetes     -1.894054   1.040686  -1.820  0.06876 .
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
    Null deviance: 211.64  on 361  degrees of freedom
Residual deviance: 195.82  on 354  degrees of freedom
AIC: 211.82
Number of Fisher Scoring iterations: 6
Imputed data set #4
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.67809    0.80621  -3.322 0.000894 ***
Age           0.02213    0.01325   1.670 0.094968 .
Sex          -0.56868    0.49688  -1.145 0.252410
Nationality2  0.57587    0.42231   1.364 0.172688
BCG           0.04137    0.44728   0.092 0.926307
Symptoms      0.02240    0.01407   1.592 0.111422
Smear2       -0.33379    0.39253  -0.850 0.395135
Diabetes     -1.88716    1.04559  -1.805 0.071093 .
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
    Null deviance: 216.34  on 361  degrees of freedom
Residual deviance: 202.62  on 354  degrees of freedom
AIC: 218.62
Number of Fisher Scoring iterations: 6
Imputed data set #5
Coefficients:
              Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.381465   0.889665  -2.677  0.00743 **
Age           0.017819   0.014288   1.247  0.21234
```

```
Sex          -0.967865   0.577472  -1.676  0.09373 .
Nationality2  0.686006   0.445556   1.540  0.12364
BCG           0.003118   0.479503   0.007  0.99481
Symptoms      0.020054   0.014587   1.375  0.16919
Smear2       -0.002432   0.411485  -0.006  0.99528
Diabetes     -1.713043   1.045691  -1.638  0.10138
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
(Dispersion parameter for binomial family taken to be 1)
    Null deviance: 197.10  on 361  degrees of freedom
Residual deviance: 184.58  on 354  degrees of freedom
AIC: 200.58
Number of Fisher Scoring iterations: 6
```

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