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## Distribution and determinants of tuberculosis in the Kingdom of Saudi Arabia from 2005 to 2012

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## ABSTRACT

Tuberculosis (TB) remains a public health threat in the Kingdom of Saudi Arabia (KSA) with many challenges that limit its prevention and control. To understand how to meet these challenges, this study calculated the TB incidence rates (IRs) in KSA from 2005 to 2012, which were stratified by nationality, sex, and administrative regions. Furthermore, laboratory capabilities were assessed by determining the proportion of laboratory-confirmed TB cases. The overall TB IRs decreased from 15.80/100,000 population in 2005 [95% confidence interval (CI) = 15.29–16.31] to 13.16/100,000 population in 2012 (95% CI = 12.74–13.58). The IRs were greater for males than for females from 2009 to 2012. The IRs of non-Saudis were approximately two times those of Saudis during the study period. Mecca had greater IR during the study period compared with other regions [25.13/100,000 (95% CI = 24.7–25.56)]. Among non-Saudis, those from Indonesia and Yemen had the greatest proportion of TB cases. (15.4% and 12.9%, respectively). Individuals <15 years of age comprised 14.2% of the TB cases. Employed non-Saudis had 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 to 2012. For effective prevention and control, TB screening should be implemented for non-Saudi workers at ports of entry and laboratory-screening capacity for TB should be evaluated.

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## 1. Introduction

Tuberculosis (TB) is a major public health threat with an estimated 9 million new cases per year and 2 million attributable deaths [1]. In 2014, TB ranked alongside human immunodeficiency virus (HIV) as the single most common cause of death among all other infectious diseases, with the number of deaths from TB surpassing that from HIV in the following years [2]. Reduction of TB infection rates is a Millennium Development Goal, but the infection remains a major public health problem. The World Health Organization (WHO) has recently released a strategy for the post-2015 era, which aims to end the global TB epidemic by 2035 [3].

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

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minimizing infectious disease-related mortalities. With it rapid development, the country has become a major destination for many immigrants from developing countries who currently make up about one-third of the Saudi population [4]. In addition, 2–3 million pilgrims travel to KSA yearly to perform Hajj, mostly from developing countries. These factors have caused major shifts in the status of many infectious diseases and presented many challenges to KSA in controlling infectious diseases, including 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 incidence rate (IR) for TB has ranged from 11/100,000/year to 16/100,000/year since 2000 [5]. From 1991 to 2010, 64,345 cases of TB were diagnosed in KSA [6]. Pulmonary TB, the infectious type, accounts for 73% of these cases [6]. Because of 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 reported to be 7.2% among Saudis and 6.2% among non-Saudis [7]. Since then, the incidence and mortality rates have decreased, but the problem persists.

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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 sex, region, age group, and nationality (Saudi or non-Saudi). This study aims to investigate the trends of the IR of TB in KSA over an 8-year period (2005–2012) stratified by sex, 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, the reported laboratory results of TB tests were analyzed to determine which TB cases were confirmed based on WHO guidelines [8]. This helped us identify the capacity of the TB laboratory testing programs overall and by region. The results of this study demonstrated the need to perform a formal evaluation of the TB program in KSA.

## 2. Methods

TB is an infectious disease requiring mandatory reporting [4]. Surveillance for TB cases is population based and conducted in both primary health centers and hospitals [9]. All suspected TB cases were reported monthly to the Ministry of Health (MoH) from all KSA regions [6]. For suspected cases in health centers, the diagnosis can be confirmed using methods such as mycobacterial culture, sputum smear microscopy, radiography, histopathology, and molecular techniques [9]. However, the reported data contain only results from the laboratory tests of smear and culture, possibly because these options are more commonly available in all laboratories than other laboratory tests.

TB case data were obtained from the Saudi MoH as deidentified, individual-level data collected from 2005 to 2012. KSA has a national disease registry in which all reportable health conditions, including infectious diseases, are reported to the MoH [4]. This study's data provided results from the culture, smear, and radiography analysis of each reported case.

This study estimated the IR and 95% confidence interval (CI) of TB for the population in KSA from 2005 to 2012 to investigate the trend of the IR over the study period. The IRs were estimated and stratified by nationality, sex, 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, whose data were used to estimate the IR for the total population and by nationality and sex. Because the population data stratified by region were not available in the Central Department of Statistics database, another database from the MoH was used to obtain the region-level data. Nationality was classified as Saudi or non-Saudi, and regions were grouped into the 13 administrative regions.

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

This study also calculated the proportion of laboratoryconfirmed cases of the reported TB cases for each region based on the WHO diagnostic criteria of confirming cases by either positive culture or smear [8]. All calculations and analysis were done using Excel 2013 (Microsoft, Redmond, WA, USA).

#### 2.1. Ethical considerations

This study was determined to be Institutional Review Board exempt because all analyses were performed on secondary data deidentified prior to analysis. Prior to data collection, all portions of the study were reviewed by Emory University's Institutional Review Board and determined to meet the criteria for exemption.

## 3. Results

The total number of TB cases included in this study that have been diagnosed between 2005 and 2012 was 32,435. The overall TB IR in KSA decreased from 2005 to 2012. The rate difference between 2005 (IR = 15.8; 95% CI = 15.29–16.31) and 2012 (IR = 13.16; 95% CI = 12.74–13.58) was statistically significant according to the CIs (Table 1).

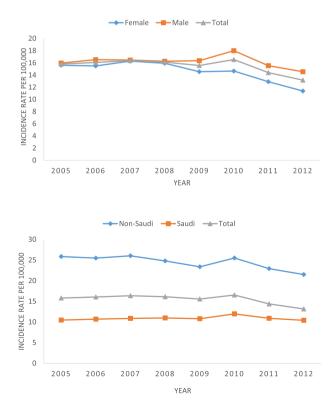
The TB IRs of both males and females were similar from 2005 to 2008 (Fig. 1); however, from 2009 to 2012, the IRs of males were

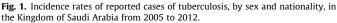
Table 1

Reported cases of tuberculosis and incidence rates, by year, in the Kingdom of Saudi Arabia, from 2005 to 2012.

Year	Ν	IR <sup>a</sup>	95% Confidence interval
2005	3687	15.80	15.29-16.31
2006	3875	16.06	15.55-16.57
2007	4084	16.37	15.87-16.87
2008	4156	16.12	15.63-16.61
2009	4149	15.56	15.09-16.03
2010	4558	16.54	16.06-17.02
2011	4083	14.39	13.95-14.83
2012	3843	13.16	12.74-13.58
Total	32,435		

<sup>a</sup> IR = incidence rate per 100,000 population.





higher than those of females. The IRs of non-Saudis were about two times those of Saudis during the study period (Fig. 1), although the IRs for both groups remained stable.

By region, this study observed that Mecca had a consistently greater IR over the study period compared with other regions [25.13/100,000 (95% CI = 24.7-25.56); Fig. 2]. Riyadh was the

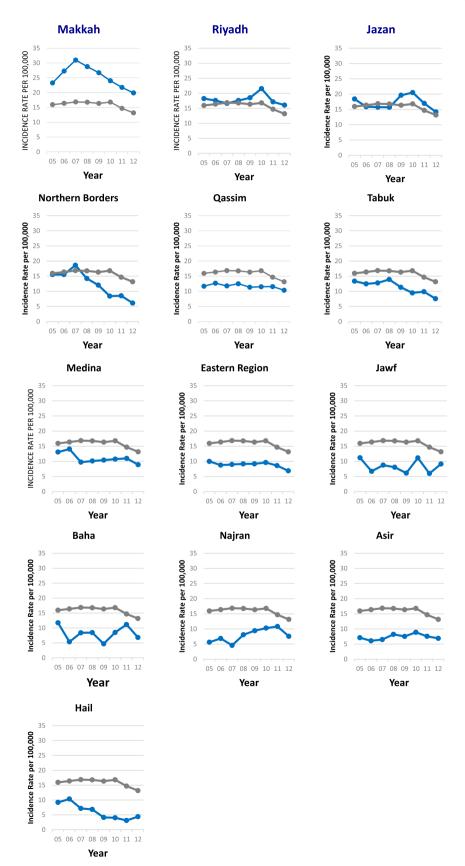


Fig. 2. Incidence rates of reported cases of tuberculosis, by region, in the Kingdom of Saudi Arabia from 2005 to 2012.

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region with the second highest IR [17.9/100,000 (95% CI = 17.53-18.27)] followed by Jazan [17.1/100,000 (95% CI = 16.31-17.89)]. Hail had the lowest TB IR during the study period [6.1/100,000 (95% CI = 5.4-8.6)].

Investigating the proportion of TB cases by nationality, non-Saudis from the following countries had the highest proportion of TB cases (Fig. 3): Indonesia (15.73%), Yemen (12.91%), India (9.71%), and Pakistan (8.36%). By age category, individuals <15 years of age constituted 14.21% of the TB cases, those aged

21–30 constituted 27.73% of the cases, and those aged  $\geq$ 65 constituted 7.41% of the cases (Fig. 4). By employment status, the employed non-Saudis had the highest proportion of TB (56.42%), followed by unemployed Saudis (39.46%) (Fig. 5). Students comprised 15.33% of all TB cases, whereas prisoners comprised 11.22% of all cases.

Of the 32,435 suspected TB cases in this study, 18,429 were laboratory confirmed by either culture or smear using the WHO guidelines, with the culture test suggested to be more conclusive

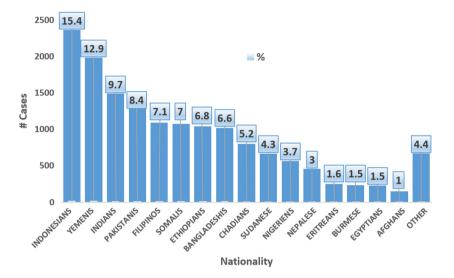


Fig. 3. Number and proportion of reported cases of tuberculosis, by nationality, in the Kingdom of Saudi Arabia from 2005 to 2012.

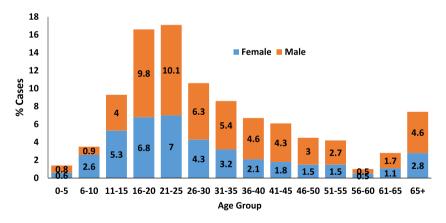


Fig. 4. Proportion of reported cases of tuberculosis, by age group and sex, in the Kingdom of Saudi Arabia from 2005 to 2012.

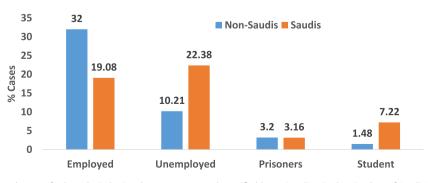


Fig. 5. Proportion of reported cases of tuberculosis, by Employment status and stratified by nationality, in the Kingdom of Saudi Arabia from 2005 to 2012.

than a smear test [8] (Table 2). Of the remaining suspected cases, 8474 tested negative for TB via culture or smear, whereas 5505 cases were not tested for TB using culture or smear (Table 3).

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 to 2012. The region with the greatest proportion

#### Table 2

Culture and smear test results for reported cases of tuberculosis, in the Kingdom of Saudi Arabia, from 2005 to 2012.

Culture	Smear test	Ν	Diagnosis tests final 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	8195	Negative
	Not done	5505	Not done

#### Table 3

Laboratory outcomes of reported cases of tuberculosis, in the Kingdom of Saudi Arabia, from 2005 to 2012.

Final outcome of diagnostic tests	Ν	(%)
Positive	18,429	57
Negative	8474	26
Not done	5505	17
Total	32,435	100

of laboratory-confirmed cases 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).

## 4. 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 with females over the last 4 years of the study period (2009–2012). Non-Saudis had about two times the TB IR of Saudis. The TB IR was highest in Mecca compared with other regions, followed by Riyadh and Jazan. When stratified by age group, TB was found in 1.4% of those aged <5, 12.81% in those aged 6–15, and 7.41% of those aged >65. Regarding TB laboratory testing, there was a 15% difference between the regions with the greatest and lowest laboratory-testing proportion. The findings from this study regarding TB IR trend are agreeable with the findings from previous studies that overlap with the study period [4,6,9].

This decrease in TB IR from 2005 to 2012 can potentially be attributed to the positive impact of directly observed treatment (DOTS), which was implemented in 2000 by the National TB Program [6]. It could also be attributed to the policy change that has enabled non-Saudis to seek diagnosis and treatment for TB without the fear of deportation, which encourages them to seek medical services; however, this does not eliminate the possibility to be dismissed by their employer for having TB, which might prevent some to seek diagnosis and treatment [9]. In addition, the higher IR in males compared with females could be explained by the fact that

#### Table 4

Number and proportion of laboratory-confirmed cases of reported tuberculosis, by region, in the Kingdom of Saudi Arabia, from 2005 to 2012.

Year	Asir			Baha			Eastern R	Eastern Region				Jawf			
	N	LCC	%	N	LCC	%	N	LCC	%	N	LCC	%	N	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	5
2008	150	80	53	34	17	50	334	198	59	39	15	38	32	18	5
2009	140	89	64	19	14	74	341	219	64	24	15	63	25	16	6
2010	170	87	51	35	20	57	395	233	59	24	12	50	49	23	4
2011	148	83	56	47	31	66	362	259	72	19	5	26	27	11	4
2012	141	85	60	30	14	47	303	232	77	28	18	64	43	25	5
Total	1107	641	58	289	161	56	2687	1712	64	288	115	40	281	160	5
Year	Jazan			Medina Mecca		Najran			1			Northern Borders			
	N	LCC	%	N	LCC	%	N	LCC	%	N	LCC	%	N	LCC	%
2005	221	115	52	200	137	69	1407	697	50	24	9	38	43	14	3
2006	195	116	59	220	130	59	1688	975	58	30	14	47	44	14	3
2007	203	123	61	159	85	53	1894	1058	56	21	6	29	55	17	3
2008	207	124	60	169	111	66	1799	1123	62	38	16	42	43	17	4
2009	268	168	63	179	124	69	1696	1067	63	46	29	63	37	14	3
2010	280	180	64	191	134	70	1660	1078	65	52	26	50	27	12	4
2011	237	140	59	200	121	61	1544	932	60	56	23	41	28	18	e
2012	207	105	51	170	113	66	1486	946	64	41	21	51	21	13	e
Total	1818	1071	59	1488	955	64	13,174	7876	60	308	144	47	298	119	4
Year	Qassim				Riyadh			Tabuk							
	N LCC		:	%	N		LCC		%	N		LCC		%	
2005	1	27	60		47	956		498		52	88		41		4
2006	1	41	61		43	944		508		54	84		34		4
2007	1	28	45		35	985		541		55	96		42		4
2008	1	39	66		47	1065		564		53	107		40		3
2009	1	29	68		53	1155		608		53	90		35		3
2010	1	40	59		42	1460		722		49	75		32		4
2011	1	44	77		53	1191		580		49	80		45		1
2012	1	35	68		50		1174			54			31		
Total	1	083	504	L	47	8930		4655			52 684		300	1	4

LCC = laboratory-confirmed cases.

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males in KSA are more engaged in public events than females [9]. Many of these events occur in crowded places conducive to airborne transmission.

The high TB IR in non-Saudis compared with Saudis could be attributed to multiple factors. First, most of the immigrants in KSA come from countries with high TB IRs such as Pakistan, India, Bangladesh, Yemen, and Indonesia [6]. 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 [6]. 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 employer(s) [6].

The high TB IR in Mecca could be explained by the presence of a high proportion of immigrants and by the 2.5 million pilgrims who 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 a large number of tertiary hospitals that treat patients from all over KSA. In addition, it is a major employment destination for non-Saudis. The high IR in Jazan could be attributed to its proximity to Yemen, which has a high overall TB IR.

The presence of TB cases among children aged <5 indicates ongoing active transmission. This was also indicated by the fact that those in the 6–15-year-old category comprised 12.81% of the cases; the immune system is thought to be more resistant to TB during this age range than any other age [1]. The high proportion of TB cases in the  $\geq$ 65-year age group could reflect a high prevalence of latent TB among young 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 certain regions that engage in a 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 calculation and analysis of the IRs. In addition, there was a lack of population statistics for Mecca city that prevented further analysis. Another limitation of this study is that most of the suspected cases of TB were laboratory confirmed using the smear test, which is less conclusive than a culture [8]. This resulted in having approximately 43% of TB cases with no laboratory confirmation, which does not eliminate the possibility of overdiagnosing the cases based on clinical symptoms and radiological investigations alone. A key strength of this study is that it used case-based data instead of aggregated data. This type of data provided the culture, smear, and radiography results for each patient and made it possible to filter out confirmed cases based on the smear and culture laboratory results in accordance with the WHO guidelines [8].

Continued support for the DOTS approach can have a positive impact on TB control in KSA. 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 vulnerable residents of Mecca should be encouraged to get the anti-TB vaccine. Further studies need to be performed to identify the precise impact of Hajj on Mecca region's TB IR. All vulnerable residents of Jazan should be also encouraged to receive the anti-TB vaccine due to its 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 regarding the ability of laboratories to detect and diagnose TB cases, and training should be provided if necessary. Furthermore, TB testing should be performed by a central laboratory located in each region that receives specimens from health centers that are not equipped to conduct the testing themselves.

### **Conflicts of interest**

All authors have no conflicts of interest to declare.

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