Susceptibility Pattern and Epidemiology of *Mycobacterium tuberculosis* in a Saudi Arabian Hospital*  
A 15-Year Study From 1989 to 2003

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**Objectives:** The objective of this study was to examine the prevalence and trends of drug resistance of *Mycobacterium tuberculosis* at the Saudi Aramco Medical Services Organization.

**Methods:** We retrospectively identified *M tuberculosis* isolates from January 1989 to December 2003. Antimicrobial susceptibility and clinical data were collected and analyzed.

**Results:** From 1989 to 2003, 276 nonrepetitive culture-positive cases were identified. There were 236 Saudis (84.6%), and the remainder were non-Saudis (15.4%). *M tuberculosis* isolates were obtained from pulmonary specimens (49%) and extrapulmonary sites (51%). The resistance rates of *M tuberculosis* to tested first-line agents were as follows: isoniazid, 12.5%; ethambutol, 7.5%; streptomycin; 6.9%; and rifampin, 1.1%. The resistance rate to isoniazid and streptomycin was 1.8%, the rate to isoniazid and rifampin was 0.7%, and the rate to isoniazid and ethambutol was 2.5%. The resistance rate to isoniazid, ethambutol, and streptomycin was 0.7%

**Conclusion:** *M tuberculosis* resistance to isoniazid showed a decreased rate over the study period from 20 to 5.7%. The rate of multidrug-resistant *M tuberculosis* remained low.

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**Key words:** incidence; resistance; Saudi Arabia; tuberculosis

**Abbreviation:** MDR-TB = multidrug-resistant *Mycobacterium tuberculosis*

*Mycobacterium tuberculosis* is a major cause of morbidity and mortality throughout the world. The number of cases of tuberculosis showed an initial decline in the United States from 84,304 in 1953 to 22,201 in 1985.1 The number of reported cases of tuberculosis in the United States increased in 1992 by 18%.1 The reversal of the downward trend was due to multiple factors, including the AIDS epidemic and the emergence of drug resistance. Drug resistance of *M tuberculosis* also shows marked geographic variation from one country to the other and ranges from 0 to 18%.2 In Saudi Arabia, the pattern of resistance of *M tuberculosis* also shows marked regional variation.3 There is only one published study about the prevalence of drug resistance of tuberculosis in the Eastern Province of Saudi Arabia. Thus, we undertook this study to evaluate the prevalence and trends of resistance of *M tuberculosis* in the Saudi Aramco Medical Services Organization in the Eastern Province of Saudi Arabia.

**Materials and Methods**

All pulmonary and extrapulmonary tuberculosis patients with positive culture results from January 1989 to December 2003 were included in the study. The medical records were reviewed for the age, sex, nationality, and the site of the culture. Cultures were performed at the mycobacteriology laboratory of the Saudi Aramco Medical Services Organization using the conventional Lewes-Johnson media.5 *M tuberculosis* was isolated by standard procedures.5 *M tuberculosis* complex was identified by conventional biochemical tests. Antimycobacterial sensitivity testing was done by the disk method as described by Wayne and Krasnow.6 Although this is a retrospective study, quality control was usually performed during susceptibility testing using the reference strain.

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Concentrations of the drugs used were as follows: isoniazid, 1 μg/mL and 5 μg/mL; rifampin, 5 μg/mL; streptomycin, 10 μg/mL; and ethambutol, 25 μg/mL. The tested isolate was considered resistant if the proportion of the tested isolate was >1% of the control population. Drug-resistant tuberculosis was calculated for single first-line agents. Multidrug-resistant *M. tuberculosis* (MDR-TB) was defined as resistance to two or more first-line drugs.

Statistical analysis was performed using statistical software (SPSS version 10.0; SPSS; Chicago, IL). Trends in incidence rates over the 15-year period from 1989 to 2003 were examined for all culture-positive cases. A linear trend analysis was used, and a proportion test was adopted to examine the significant difference between proportions.

### Results

From 1989 to 2003, a total of 279 distinct positive culture findings for *M. tuberculosis* were identified. The annual incidence rates per 100,000 populations are shown in Figure 1. The incidence in 1989 was 5.2/100,000, decreased to 3.5/100,000 in 1993, increased to 11.1/100,000 in 1998, and reached 7.6/100,000 in 2003. An increasing trend in incidence rates of culture-positive tuberculosis was observed during the study period. This was statistically significant ($\chi^2 = 19.647$; $p = 0.0001$).

Of the total patients, there were 236 Saudis (84.6%), and the remaining 43 patients (15.4%) were non-Saudis. Of the non-Saudis, 19 were Philippine, 10 were Indian, 1 was Sir Lankan, 3 were Indonesians, 5 were European, 3 were Pakistani, 1 was Lebanese, and 1 was Canadian. Of the total patients, 133 were male (47.7%) and 146 were female (52.3%). The age range was 0.125 to 89 years (mean age ± SD, 49 ± 20 years). The isolates were obtained from pulmonary specimens ($n = 140, 49%$) and extrapulmonary sites ($n = 135, 51%$). The source of four isolates could not be identified. The majority of the extrapulmonary isolates were obtained from lymph nodes (95 of 135 isolates, 70%). The other extrapulmonary sites include bone and joints ($n = 16, 11.8%$), peritoneum/ascetic fluid ($n = 10, 7.4%$), urine ($n = 7, 5%$), gastric aspirates ($n = 4, 3%$), and skin ulcers ($n = 3, 2%$).

### Resistance to Single Antituberculosis Medication

The resistance rate of *M. tuberculosis* to any single drug was 28% ($n = 78$) [Table 1]. The resistance rates of *M. tuberculosis* to the tested first-line agents were as follows: isoniazid (1 μg/mL), 12.5%; ethambutol, 7.5%; streptomycin, 6.9%; and rifampin, 1.1%. There was no statistical difference in the rate of resistance between Saudi and non-Saudi patients. In addition, there was no difference in the rate of resistance between pulmonary and extrapulmonary isolates.

### MDR-TB

MDR-TB was defined as resistance to two or more first-line agents. The rates of MDR-TB are shown in Table 2. The resistance rate to isoniazid and streptomycin was 1.8% (5 of 279 isolates), to isoniazid and rifampin was 0.7% ($n = 2$), and the rate to isoniazid and ethambutol was 2.5% ($n = 7$). The resistance rate to isoniazid, ethambutol, and streptomycin was 0.7% ($n = 2$; Table 2).

### Discussion

Tuberculosis continues to be a major concern for health-care workers throughout the world. The numbers of tuberculosis cases have declined steadily in western and central Europe, North and South America, and the Middle East, and have increased in countries of the former Soviet Union and in sub-Saharan Africa. In the United States, there were a total of 14,871 tuberculosis cases (5.1/100,000 population) during 2003, representing a 1.9% decline in
the rate from 2002.8 Tuberculosis rates have increased in certain states in the United States.8

The incidence of smear-positive tuberculosis in Saudi Arabia was estimated to be 20 per 100,000 population.9 The incidence rates of culture-positive tuberculosis in our study per 100,000 populations were 5.2 in 1989, 3.5 in 1993, 11.1 in 1998, and 7.6 in 2003. Thus, the incidence of tuberculosis in the current study showed an increasing linear trend over the study period from 1989 to 2003 (χ² = 19.647, p = 0.0001).

The prevalence of drug resistance of tuberculosis varies from one part of the world to another. In the United States, drug-resistant tuberculosis was detected in 14.2% in 199110 and 10% in 1997.11 In the United States, isoniazid resistant was the most prevalent and accounted for 8%.11 Isoniazid resistance has ranged from 0% in New Caledonia to 7.9% in Mozambique,11 and was 10% in India.12

In Saudi Arabia, the resistance rates to isoniazid vary from one part of the country to another. In Riyadh, the resistance rates ranged from 4.2 to 7.2%.13,14 Similar rates of resistance of approximately 6% were reported in Dammam4 and Taif.15 A higher rate of resistance (10.3 to 28.7%) was found in Jeddah.16–18 The highest rate of resistance (41%) was reported from Gizan and was attributed to the proximity of Gizan to the Republic of Yemen.19 In the current study, isoniazid (1 μg/mL) resistance was 12.5% and the resistance to isoniazid (5 μg/mL) was 2.9%.

The second most common resistance pattern in our study was ethambutol (7.5%). Ethambutol resistance in Saudi Arabia has also been variable and was 0% in Dammam,4 approximately 2.4% in Riyadh,14,20 1.3 to 6.9% in Jeddah, and 4% in Taif15 and Gizan.19 A high rate of ethambutol resistance was observed in Uganda (2.4%) and Thailand (3%).11 In a study12 from India, the rate of ethambutol resistance was 6.6%.

In our study, the rate of resistance of M tuberculosis to streptomycin was 6.9%. Similarly, in a study from Riyadh, streptomycin resistance was 8.8%21 and 15.9% in Taif,15 and 22.7% in Jeddah.18 The resistance rates of M tuberculosis to streptomycin were 14.5% in Sierra Lion11 and 6.6% in India.12

The resistance rate to rifampin was low (1.1%) in our study. Similarly, low resistance rates to rifampin had been reported in Dammam.4 However, higher rates of rifampin resistance were reported from Riyadh (9%),13,20 Jeddah (5.1 to 23.4%),16,17 Taif (15.3%),15 and Gizan.19 In other parts of the world, the prevalence of rifampin resistance was 0% in New Zealand and New Caledonia, 1.7% in the United States, and 1.8% in Mozambique.11

The rate of MDR-TB in our study was low. The highest rate of resistance was to both isoniazid and ethambutol (2.5%). The rate of MDR-TB in Saudi Arabia is variable, depending on the date of the study and region of the country. In Riyadh, MDR-TB ranged between 3.7% in 1979 to 1982 and 11.8% in 1986 to 1988.13 A very high rate of MDR-TB was reported from the south of the country in Gizan, where the resistance rate reached 44%.19 In the area near Dhahran where this study took place, the MDR-TB rate in Dammam was 10.5%.4 The prevalence of MDR-TB among new cases of tuberculosis was 14% in Estonia, 10.8% in Henan Province in China, 9% in Latvia, 9% in Ivanovo Province in Russia, 5% in Iran, and 4.5% in Zhejiang Province in China.11

The variability in the resistance rates of tuberculosis in Saudi Arabia is dependent on the time and location of the study as well as on the contribution of non-Saudi patients to each study.3 In our study, we found no difference in the resistance rates of Saudi and non-Saudi patients. Many studies13,14,16–18 from Saudi Arabia did not address whether the site of isolation of M tuberculosis has any impact on the resistance pattern. We found no difference in the resistance rates between pulmonary and extrapulmonary isolates.

In conclusion, in this study we examined the pattern and incidence of resistance of tuberculosis to first-line agents over time. The resistance rate to isoniazid showed a significant decline over the study period, whereas the resistance rate of rifampin remained low and stable. Further studies and continued surveillance of the resistance pattern of M tuberculosis is needed to further delineate the risk factors and to formulate the plans for the future management of tuberculosis.

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