

Mycobacterium tuberculosis Saudi Arabia

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ABSTRACT

Objective: To present the available data on the prevalence of all isolates of *Mycobacterium tuberculosis* from the Kingdom of Saudi Arabia. **Methods:** In a meta-analysis, 12 studies published between 1979 and 2001 were included. Medline-indexed and non-indexed journals were searched. **Results:** Twelve studies met the criteria. A total of 6,316 isolates between 1979 and 2001 were included. Resistance to at least one agent was 18.4%. The first-line agent was found in 10.9%, while polyresistance was noted in 7.6%. Multidrug-resistance (MDR-TB) was observed in 1.1% of isolates. **Conclusion:** *Mycobacterium tuberculosis* is still a major cause of morbidity and mortality in Saudi Arabia. The prevalence of MDR-TB is increasing. The overall resistance rate to at least one agent was 18.4%. The first-line agent was found in 10.9%, while polyresistance was noted in 7.6%. Multidrug-resistance (MDR-TB) was observed in 1.1% of isolates.

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The impact of tuberculosis (TB) has grasped the international attention after an increasing number of cases in developed countries. Control measures implemented had several weaknesses in their targeted achievements. In Saudi Arabia, the resurgence of TB in many areas was also associated with increasing resistance to anti-TB drugs. Multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB) is associated with higher rates of failure and death than in drug-susceptible TB and is more difficult and expensive to treat. A survey report on anti-TB drug resistance was conducted by the WHO.

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presented to hospitals for diagnosis. Twelve reports represent an important portion of these containing susceptibility results covering the time period 1979 and 2000 years. In this report, we look at the primary of the reports for the susceptibility testing of *M. tuberculosis* in Saudi Arabia. Although constitutes a large number of the isolates in the region, only 4 country and the whole of the Eastern Mediterranean Region. not included in the table as an

Methods. This meta-analysis was not answering 2 questions: 1) Why was rifampin resistance rates for the various first-line agents in Saudi Arabia and reported from KSA? 2) How have the resistance rates over the last 2 decades? We have reviewed in Medline all reports containing data on *M. tuberculosis* and drug resistance between 1979 and 2001. Identified reports were abstracted and reviewed for references that were not included in the original reports. 97% also included if they met the criteria. Reports on drug resistance articles were included in this study. The total number of crude numbers of total isolates tested and numbers of resistant isolates that were considered susceptible based on susceptibility testing for the first-line agents is the least frequent. Reports had to have included 100 isolates from at least one respective hospital. If reporting was inadequate to the clinical failures or any other clinical failures, the reports were not included. Some of the reports were excluded due to unprovided crude numbers, but rather resistance rates; the denominator was not available. Reports on drug resistance among isolates in this study were included only if the crude rates were every agent from the first-line agents. The numbers of tested and resistant isolates were tabulated. If one of both of these numbers was not available, the report was not included in the total for the isolates tested for this specific agent. Based on the reported year of isolation, isolates were grouped in 2 groups: Group I included reports for isolates between 1979 and 1991 and group II for reports of isolates between 1989 and 2000.

Definitions. First-line more significant with the increase rifampin, streptomycin, isoniazid, pyrazinamide, and ethambutol. We adopted definitions recommended by WHO and IUATLD for documenting the drug susceptibility surveillance. Monoresistance is defined as a resistance to a single first-line agent. Susceptible results were resistance to more than one of the first-line territories. Multidrug-resistant *M. tuberculosis* is defined as a resistance to at least isoniazid and rifampin. The proportion of multidrug-resistant rate is the proportion of isolates in that region resistant to at least one of the first-line agents.

Statistical analysis. The combined random-effects meta-analysis of the various reports were presented as proportions. A chi-square test was used to assess heterogeneity between these limited proportions. Statistica (Version 6.0) software package (StatSoft, Inc., Tulsa, Oklahoma) was used for analysis. All tests are two-tailed. A *P* value of less than 0.05 was considered significant.

Table 1 - Susceptibility testing for the 12 studies included in this report expressed

Authors	Year	Region	Total n	Isoniazid n (%)	Rifampin n (%)	Streptomycin n (%)	Ethambutol n (%)	Overall resistant n (%)	Mono-resistant n (%)	Poly-resistant n (%)	MDR n (%)
Schiott et al ⁷	not indicated	Jordan	103	20 (20.8)	20 (20.4)	2 (2.6)	4 (3.9)	45 (3.7)	10 (10.7)	3 (3.3)	20 (19.4)
Al-Orainey ⁸	1979-1982	Riyadh	196	82 (4.2)	NA	24 (12.5)	NA	25 (9.3)	28 (9.4)	7 (3.8)	NA
Al-Orainey ⁹	1986-1988	Riyadh	432	49 (19.4)	42 (9.7)	22 (5.1)	6 (3.7)	21 (3.4)	19 (5.5)	11 (8.8)	8 (8.8)
Zaman ¹⁰	not indicated	Jeddah	488	67 (17.8)	32 (23.4)	7 (16.4)	9 (3.9)	43 (13.0)	6 (2.4)	8 (17.6)	0 (4.5)
Jarallah et al ¹¹	1986-1988	Riyadh	678	46 (6.8)	41 (5.3)	8 (15.9)	7 (4)	15 (2.6)	19 (7.2)	10 (15.2)	6 (3.8)
Chowdhury ¹²	1987-1991	Riyadh	214	20 (9.3)	8 (3.7)	4 (1.9)	1 (0.5)	21 (11.7)	9 (4.2)	7 (3.3)	
Ellis et al ¹³	1989-1994	Jeddah	289	22 (7.6)	9 (3.1)	9 (3.1)	7 (2.4)	25 (8.7)	14 (4.8)	11 (3.8)	8 (2.8)
Kinsara ¹⁴	1993-1995	Jeddah	78	10 (13)	4 (5.1)	6 (7.7)	1 (1.3)	9 (11.5)	NA	NA	NA
Al-Jama et al ¹⁵	1989-1991	Riyadh	239	11 (7)	78 (6.3)	69 (5.6)	2 (1)	24 (10.2)	25 (20.6)	4 (3.8)	4 (2.7)
Khan et al ¹⁶	1996-1998	Western	102	28 (28.7)	22 (20.7)	23 (22.7)	7 (6.9)	30 (29.7)	4 (4)	2 (2.5)	7 (20.7)
Al-Rubaihi et al ¹⁷	1993-1996	Eastern	41	9 (9.5)	12 (2.9)	6 (1.5)	NA	4 (10.5)	2 (7.1)	1 (3.4)	1 (2.7)
Alrajhi et al ¹⁸	1995-2000	Jeddah	320	29 (9.1)	9 (2.8)	1 (5)	5 (1.6)	36 (13.2)	20 (6.3)	1 (5)	9 (2.8)
Total			6,316	611 (11)	421 (9.7)	15 (9.9)	21 (6.8)	215 (18.4)	130 (9.7)	71 (7.2)	44 (5.7)
Range percent				(4.2-40)	(2.8-23.4)	(1.5-26)	(0.5-6.8)	(6.7-43)	(7-20.6)	(3.4-33)	(7-20.7)

n - number, NA - not available, MDR - multidrug resistant

Table 2 - Resistance rates by region and time periods.

Region	Total n	Isoniazid n (%)	Rifampin n (%)	Streptomycin n (%)	Ethambutol n (%)	Overall resistant n (%)	Mono-resistant n (%)	Poly-resistant n (%)	MDR n (%)
West and South ^{7,10,11}	1443	209 (14.5)	263 (18.2)	243 (16.8)	58 (4)	382 (26.5)	124 (9.1)	136 (18.2)	137 (10)
Central ^{8,9,12}	2614	186 (7.1)	50 (6.4)	272 (10.4)	17 (2.6)	675 (14.3)	241 (9.2)	134 (5.1)	45 (6.9)
Eastern ^{15,16}	1650	250 (15.2)	90 (5.5)	75 (4.5)	NA	345 (20.9)	284 (17.2)	61 (3.7)	45 (2.7)
*Time periods									
1979-1998 ^{7,8}	3358	288 (17.9)	194 (15.1)	186 (12.5)	67 (3.5)	1071 (18.5)	361 (9.3)	357 (9.2)	161 (8.4)
1989-2000 ^{13,14}	2458	338 (13.9)	133 (5.5)	129 (5.3)	32 (1.6)	274 (18.3)	322 (13.6)	60 (4.8)	83 (3.5)

* expressed in number of resistant isolates/total tested if different from total col

susceptibility in the Eastern Mediterranean Region data to (The wide area in the countries from where isolates were collected could be considered as representing a Sub-Saharan countrywide survey as a whole, determining a prevalence of resistance of 18.4% is similar to that reported in other countries. in Africa and reports provide an information Mauritania, South Africa, Pakistan and Korea report have Philippines). For MDR-TB, the rates were 10.1% (Details similar to South Africa, Rwanda and other great prov and Philippines).²⁰ These rates remain low over a period of 10 other countries in the region, but accept techniques for susceptibility the individual agent resistance to isoniazid and rifampin, and lower resistance rate in our study appear to be due to the methodology in the WHO/UNAIDS survey conducted there. They were 9.8% for isoniazid, 4.6% for rifampin, and 1.6% for streptomycin, 2.4% for ethambutol, and 0.6% for overall resistance rate. As indicated, rifampin resistance is the type of reported resistance as a major one. A comparison of the type of TB as newly diagnosed versus previously treated. Therefore, our results for drug resistance are in line with WHO/UNAIDS report on the global situation of drug resistant TB.²² We attempted to compare our results with similar in our isolate collection. The only report chosen (data presented in 1991 and 1989-2000) reports available and all from the same area our study period, and reports were selected on the basis of their numbers (6 in each period) to help cover a period of various difficult to avoid and only consistent from this region, a period with 214 total isolates. The overall resistance rate was very close in the 211 period (18.5% and 18.3%). However, a peculiar observation was noted, reports when the resistance rates were grouped by drug, rifampin compared to single one of the first-line agents, isoniazid, ethambutol, and all first-line agents and MDR-TB. The rates of rifampin significantly dropped by almost 50% for the 2nd period. These seemingly contradictory occurrences for the dropping rates for all agents in MDR-TB program will stable overall rate can be explained by the type of resistance as mono or polyresistance. In the first period, polyresistance to mono-resistance was in the ratio of 1:1 while it was 1:3 in the 2nd period (table 2). The regional distribution of resistance puts the Western and Southern regions of the country with highest rates of resistance. Although there is only one study from the South in the 1980s with high rates, a high proportion of resistance isolates from a referral center were from the South. The Western region had increasing resistance rates among isolates from the same hospital with well-defined and stable Saudi population.¹⁶ The regional rates reported from a referral center are similar to rates reported from a referral center receiving patients from all regions. Therefore, the South and Western regions are considered the highest in TB drug resistance rates. The reasons argued elsewhere include a high number of visitors from developing countries, a high number of drug-resistant TB and high numbers of illegal immigrants.¹⁶ Limitations of this study include the

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