

ORIGINAL ARTICLE

## The dynamics of pulmonary tuberculosis in Colima, Mexico (1999–2002)

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### Abstract

Tuberculosis is a public health problem in Mexico. From 1999 to 2002, we assessed retrospectively the epidemiological, clinical, and treatment characteristics of pulmonary tuberculosis in the hospitals of the Mexican Institute of Public Health in the state of Colima (Mexico). We included 184 cases diagnosed with pulmonary tuberculosis. A database containing demographic, epidemiological, and clinical information was constructed and analyzed. We estimate a median patient delay of 83 d and a mean treatment delay of 2.3 d. Of 14 cases suspected for multiresistance and microbiologically assayed, 5 were found to carry a multi-drug-resistant strain. We also found a significant association between a short patient delay and the presence of hemoptysis ( $p = 0.002$ ) or dyspnea ( $p < 0.001$ ). 86 patients (46.8%) were sputum smear microscopy negative at the end of treatment and 40 (21.7%) completed treatment giving an overall success rate of 68.5%, which compares unfavorably with the World Health Organization target success rate of 85%. Five (2.7%) patients failed treatment, 10 (5.4%) died, 39 (21.2%) interrupted treatment, and 4 (2.2%) transferred to another reporting unit. A 2002 strategic change in drug distribution seemed to prove successful.

### Introduction

It is estimated that there were 8.8 million new tuberculosis (TB) cases in the world in 2003, with a prevalence of 15.4 million and 1.7 million deaths from TB [1]. TB is the major cause of death from a single infectious agent among adults in developing countries [2]. The World Health Organization (WHO) estimates 1000 million individuals infected by *Mycobacterium tuberculosis* [3].

In Mexico, tuberculosis is a public health problem, even though Mexico has had a national TB control program since 1973 [4]. The TB mortality rate in Mexico from 1990 to 1998 has experienced a sustained and slow decline, with an average annual decrease of 6.7% [5]. In 1996, the TB mortality rate in Mexico was 4.3 deaths per 100,000 inhabitants [6]. On the other hand, the incidence rate has been growing from 14.4 cases per 100,000 inhabitants in 1986, 18.2 per 100,000 inhabitants in 1996, to 19.1 per 100,000 inhabitants in 1998 [7]. In Mexico,

every year about 17,000 new cases are notified, of which 80% are pulmonary [8]. In this paper, we analyze the epidemiological, clinical, and treatment aspects of pulmonary tuberculosis in the state of Colima, Mexico, from 1999 to 2002. To the best of our knowledge, this is the first study to report on the situation of pulmonary tuberculosis in the state of Colima.

### Materials and methods

The data used in this study were obtained from the 3 hospitals of the Mexican Institute of Public Health (IMSS) in the state of Colima, Mexico. The hospitals are located in the municipalities of Colima, Manzanillo, and Tecoman. Located on the Pacific coast, the state of Colima has a tropical climate and a population of approximately 488,028 inhabitants [9]. The IMSS hospitals provide service to 60% of the total state population.

Tuberculosis treatment is provided free of charge and in accordance with the official Mexican norm for preventing and controlling tuberculosis (NOM-006-SSA2-1993), which is consistent with the WHO strategies for TB control, including case detection, standardized short-course chemotherapy, good case management and regular and uninterrupted supply of all essential anti-TB drugs. In the hospitals in which the study was conducted, patients are provided with their medications every 2 weeks during a 6-month treatment period (self-administered treatment). Moreover, patients are required to undergo monthly sputum smear microscopies during their treatment period. The definition of terms agrees with those of the WHO global tuberculosis control program [10], unless otherwise indicated.

We included all cases of pulmonary tuberculosis diagnosed in the hospitals of the Mexican Institute of Public Health in the state of Colima from January 1999 to December 2002. We analyzed retrospectively the epidemiological, clinical, and treatment elements of tuberculosis. The clinical record included age, gender, date of diagnosis, date of onset of symptoms, date of start of treatment, method of diagnosis, list of close contacts, symptoms, follow-up of monthly sputum microscopies, and treatment outcome. We defined patient delay as the number of d between the date of onset of symptoms and the date of diagnosis. Similarly, we defined treatment delay as the time interval from diagnosis until treatment begins. We classified a patient as 'delayed' when diagnosis was made after 30 d of onset of symptoms. This 30-d period includes 3 weeks of cough during which tuberculosis would not be considered as a diagnosis unless hemoptysis was present [10,11].

Using standard-case definitions, TB cases were classified as new, relapse, failure, return after default, and transfer-in [10]. Diagnosis was achieved by 1 of the following means: sputum microscopy, mycobacterial culture, histopathology, radiologic, or clinical-epidemiological means. The treatment outcomes were classified as cured (sputum smear negative at end of treatment), treatment completed, treatment failure, death, defaulter (for 30 d or more), and transfer-out [10].

Patients diagnosed with TB were asked to identify any family members or close contacts who had a cough or had possessed a cough in the previous 15 d for whom further assessment in a hospital clinic was required.

The statistical analysis was carried out using Fisher's exact test and the  $\chi^2$  test of independence [12]. Fisher's test is exact and uses a hypergeometric sampling distribution for cell frequencies [12].

## Results

We included 184 cases diagnosed with pulmonary tuberculosis. Of these, 149 were new, 27 relapsed, 2 failed treatment, 5 returned after default, and 1 case transferred-in. 43 cases (23.4%) were diagnosed in 1999, 51 cases (27.7%) in 2000, 51 cases (27.7%) in 2001, and 39 (21.2%) cases in 2002. The mean age of the patients was  $45.5 \pm 20.5$  (SD) y. 108 patients were males (59.7%) and 73 patients were females (40.3%), giving a male/female ratio of 1.5:1. For males, the mean age was  $50.1 \pm 19.9$  y, whereas for females the mean age was  $38.8 \pm 19.5$  y.

### *TB epidemiology and diagnosis*

The most common symptoms observed in TB patients were cough (73.3%), weight loss (68.8%), fatigue (66.1%), and fever (61.54%), whereas the least common symptom was hemoptysis (27.2%) (Figure 1). 164 patients (89.1%) were diagnosed by sputum smear microscopy, 6 (3.3%) by chest X-ray, 2 (1.1%) by bacteriological culture, and the rest (6.5%) by clinical and epidemiological means. The median delay from symptom onset to diagnosis was 83 d (IQR: 39–122). We found a significantly shorter patient delay in patients presenting hemoptysis ( $p = 0.002$ ) or dyspnea ( $p < 0.001$ ) but not with cough ( $p = 0.13$ ), weight loss ( $p = 1$ ), fatigue ( $p = 0.28$ ), fever ( $p = 1$ ), anorexia ( $p = 0.54$ ), thorax pain ( $p = 0.30$ ), sweating ( $p = 0.68$ ), or somnolence ( $p = 0.29$ ). However, we did not find a significant association between patient delay and gender ( $p = 0.12$ , Fisher's exact test) or age (age groups of size-10 y,  $p > 0.5$ ;  $\chi^2$  test). Mean delay from diagnosis to the start of chemotherapy (treatment delay) was 2.3 d (IQR: 0–2), with most of the patients starting treatment immediately after diagnosis.

### *Monthly compliance of sputum smear microscopies*

All patients were under monthly bacteriological surveillance via sputum smear microscopy during their treatment period. However, the compliance of patients for their monthly bacteriological surveillance was very low, as can be seen in Table I. Only 56.5% of the patients complied with at least 3 monthly sputum smear microscopies.

### *Multi-drug-resistant tuberculosis (MDRTB)*

A drug susceptibility test was carried out whenever a patient was suspected of multi-drug-resistant TB, including patients who had received more than 1 treatment, relapse cases, all cases with positive sputum smear microscopy after the fourth month

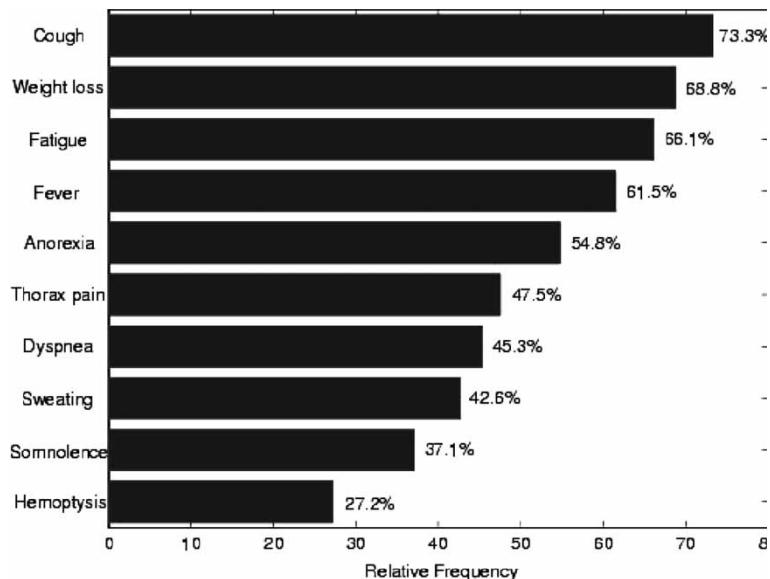


Figure 1. Relative frequency of symptoms developed by the patients diagnosed with pulmonary tuberculosis.

of treatment, and all probable or confirmed cases that were contacts of MDRTB cases. MDRTB is caused by a bacillus that is resistant to at least isoniazid and rifampicin, the most powerful anti-TB drugs. 14 patients underwent a drug susceptibility test to isoniazid (H), rifampicin (R), streptomycin (S), ethambutol (E), or pyrazinamide (T). Four individuals were resistant to the 5 drugs, 1 resulted resistant to H-R-S-T, and 1 patient resulted resistant to H-T. Thus, a total of 5 MDRTB cases were identified.

*Contact tracing*

A mean of  $4 \pm 3$  (SD) contacts was declared by the patients. Figure 2 shows the distribution of the number of declared contacts by each patient. A total of 949 contacts was declared, of which 856 (90%) were examined for TB infection (Table II). 17 contacts were diagnosed with TB and 30 contacts underwent chemoprophylaxis to prevent infection. Chemoprophylaxis with isoniazid administered orally with a dose of 10 mg per d per kg weight (up to 300 mg) is strictly supervised to contacts younger

than 5 y of age (6-month treatment under strictly supervised treatment), contacts between 5 and 14 y of age who had not received BCG vaccine (6-month treatment), and contacts older than 15 y infected with HIV (12-month treatment).

*Treatment outcome*

Table III shows treatment results. The treatment success (patients who showed sputum smear negative in the last month of treatment or completed treatment) was significantly lower in 2000 and 2001, but it improved significantly in 2002. A possible explanation for such an apparent improvement is given in the Discussion section of this paper.

Overall, 86 patients (46.8%) were sputum smear microscopy negative at the end of treatment, 40

Table I. The results of monthly sputum smear microscopies during the patients' treatment period.

Month	Positive	Negative	Skipped
1	26 (14.1%)	76 (41.3%)	82 (44.6%)
2	14 (7.6%)	75 (40.8%)	95 (51.6%)
3	13 (7.1)	69 (37.5%)	102 (55.4%)
4	4 (2.2%)	58 (31.5%)	122 (66.3%)
5	5 (2.7%)	64 (34.8%)	115 (62.5%)
6	4 (2.2%)	74 (40.2%)	106 (57.6%)

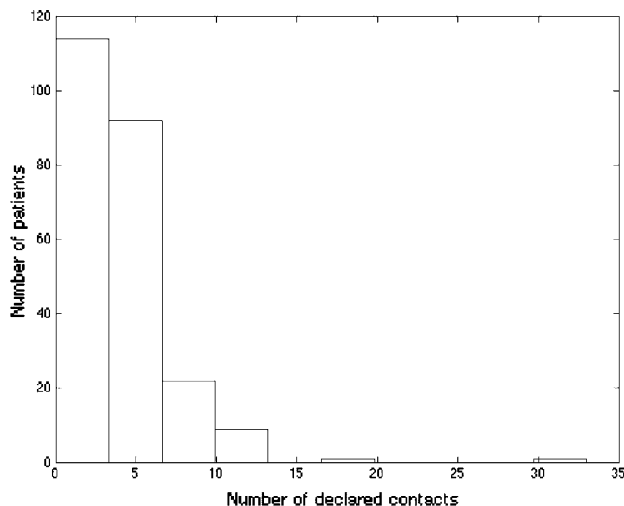


Figure 2. The distribution of the number of declared contacts. The mean number of contacts is  $4 \pm 3$  (SD) contacts.

Table II. Results of the contact tracing study by age groups.

Age group	Declared	Examined	TB	
			disease	Chemoprophylaxis
<15 y	318	301	5	19
>15 y	631	555	12	11
Total	949	856	17	30

(21.7%) completed treatment, 5 (2.7%) patients failed treatment, 10 (5.4%) patients died, 39 (21.2%) patients interrupted treatment, and 4 (2.2%) patients transferred to another reporting unit.

## Discussion

The higher proportion of males than females (ratio 1.5:1) diagnosed with TB is in agreement with other studies [11,13,14]. However, the mean age of patients was higher than in other reports [11,13,14]. Cough, weight loss, fatigue, and fever were some of the most common symptoms presented by patients, in agreement with other studies [11,14]. A significant proportion of patients reported anorexia (54.8%), dyspnea (45.3%), sweating (42.6%), and somnolence (37.1%).

Long patient delays not only complicate the clinical state of the patient but also contribute to further transmission of the disease. We found a median patient delay of 11.9 weeks, which is in close agreement with an estimate of 12.5 weeks in Malaysia [15]. A longer patient delay (17 weeks) has been reported in Ghana [16] and shorter patient delays have been reported in Canada (6 weeks) [17], Nigeria (8 weeks) [18], urban Zambia (8.6 weeks) [11], and east London (9 weeks) [19]. We found that patient delay was significantly associated with the presence of hemoptysis or dyspnea, whereby the patient delay among patients presenting hemoptysis or dyspnea was significantly shorter than among patients not presenting these symptoms. This association has been reported in previous reports [13]. We did not find a significant association between patient delay and gender or age. However, other

reports have documented an association of patient delay with female gender and lower education [11].

We estimated a mean of 2.3 d for treatment delay, with most of the treatments starting immediately after diagnosis. Significantly higher estimates for treatment delay have been estimated in Nigeria (1 week) [18] and in east London (median of 5 weeks) [19], and a shorter mean treatment delay of 1.4 d has been reported in Turkey [13].

An overall success rate of 68.5% and annual success rates from 1999 to 2002 (Table III) compare unfavorably with the WHO target success rate of 85%. This discrepancy can be explained by the poor monthly compliance of patients to bacteriological surveillance via sputum smear microscopies (Table II), a problem possibly associated with poor adherence to medications. Hence, appropriate implementation of strictly supervised treatment in hospitals of the Mexican Institute of Public Health is a promising means of increasing the success rate to the target success rate recommended by the WHO.

Before 2002, TB patients subscribing to IMSS hospitals were required to collect their medications at their corresponding hospital clinic. This requirement was a problem for many who lived far from their corresponding hospital. The consequences are observed in the poor monthly compliance of sputum smear microscopies (Table I) and the appearance of 5 cases of multi-drug-resistance tuberculosis. As a result of the arising problem, a significant change in case management was implemented in all IMSS hospitals. Beginning in 2002, each hospital clinic was made responsible for their own patients by sending, when necessary (e.g. difficult transportation to hospital), a medical unit to the patient's house to provide appropriate medications. The treatment success rate in 2002 (Table III) suggested a positive effect from the change in case management, but more data are needed to assess the effect of the change in case management on the treatment success rate.

In general, the most critical component for success in TB control is an appropriate case management that results in treatment completion [20]. Educational campaigns should inform the population on

Table III. The distribution of treatment outcomes from 1999 to 2002. Patients successfully treated are those who showed sputum smear negative in the last month of treatment or completed treatment.

Y	Treatment success	Failed	Death	Defaulter	Transfer-out	Total
1999	32 (74.4%)	0 (0%)	3 (7%)	6 (14%)	2 (4.6%)	43
2000	29 (56.9%)	0 (0%)	3 (5.9%)	18 (35.2%)	1 (2%)	51
2001	33 (64.7%)	4 (7.9%)	2 (3.9%)	12 (23.5%)	0 (0%)	51
2002	32 (82%)	1 (2.6%)	2 (5.1%)	3 (7.7%)	1 (2.6%)	39
Total	126	5	10	39	4	184

how to identify early key symptoms of TB and highlight the importance of early diagnosis. Furthermore, educational campaigns have the potential to significantly decrease patient delays, which in turn would contribute toward reducing the number of secondary cases generated by infectious individuals. Strategies aimed at identifying latent TB cases and tailoring service delivery are also promising means for TB control [21].

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