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Tuberculosis in ageing: high rates, complex diagnosis and poor clinical outcomes

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Abstract

Background: worldwide, the frequency of tuberculosis among older people almost triples that observed among young adults.

Objective: to describe clinical and epidemiological consequences of pulmonary tuberculosis among older people.

Methods: we screened persons with a cough lasting more than 2 weeks in Southern Mexico from March 1995 to February 2007. We collected clinical and mycobacteriological information (isolation, identification, drug-susceptibility testing and IS6110-based genotyping and spoligotyping) from individuals with bacteriologically confirmed pulmonary tuberculosis. Patients were treated in accordance with official norms and followed to ascertain treatment outcomes, retreatment, and vital status.

Results: eight hundred ninety-three tuberculosis patients were older than 15 years of age; of these, 147 (16.5%) were 65 years of age or older. Individuals ≥65 years had significantly higher rates of recently transmitted and reactivated tuberculosis. Older age was associated with treatment failure (OR = 5.37; 95% CI: 1.06–27.23; P = 0.042), and death due to tuberculosis (HR = 3.52; 95% CI: 1.78–6.96; P < 0.001) adjusting for sociodemographic and clinical variables.

Conclusions: community-dwelling older individuals participate in chains of transmission indicating that tuberculosis is not solely due to the reactivation of latent disease. Untimely and difficult diagnosis and a higher risk of poor outcomes even after treatment completion emphasise the need for specific strategies for this vulnerable group.

Keywords: tuberculosis, older, ageing, epidemiology, incidence rates, mortality rates, diagnosis, elderly

Introduction

The impact of infectious diseases among older people in low- and medium-resource countries is larger than that observed in developed countries. In the case of tuberculosis, immunosenescence, malnutrition, poverty, decreased access to health services, diabetes mellitus and other comorbidities contribute to a higher risk of tuberculosis among this age group [1]. Worldwide, the frequency of this disease among older people almost triples that observed among young adults [2]. Furthermore, tuberculosis treatment in older individuals is complicated by treatment for associated diseases leading to a consequent increase in adverse drug effects, treatment default and increased rates of retreatment and drug resistance [3–6].

In this study, we report on the epidemiology, diagnosis, clinical manifestations and prognosis of pulmonary tuberculosis among older people. Results will be useful for decision and policy makers.

Methods

Study population and enrolment

The study site and enrolment procedures have been described previously [7]. Briefly, the study area includes 12 municipalities in the Orizaba Health Jurisdiction in Veracruz State, Southern Mexico with an extension of 618.11 km² and a population of 369,235 inhabitants, 14.9% living in rural communities and 68.1% aged 15 years or older [8]. Collaboration was established with local health and political authorities for recruitment of participants at primary care health centres.

Between March 1995 and February 2007, we performed passive case finding, supported by community-based health workers and screened persons 15 years of age or older who reported coughing for more than 2 weeks. Patients with acid-fast bacilli (AFB) or Mycobacterium tuberculosis in sputa were evaluated using a standardised questionnaire, physical exam, and HIV test to determine their epidemiological, clinical and mycobacteriological characteristics. We performed cultures on smear positive sputa from 1995 to 2000; on all sputa (both smear positive and smear negative) from 2000 to 2005; and on sputa from all previously treated TB patients, as well as any new TB patients considered at high risk of having drug-resistant TB from 2005 to 2007. Anteroposterior chest X-rays were interpreted by a radiologist blinded to all patient characteristics.

Treatment was provided using the official norms of Mexico’s National Tuberculosis Control Program. We used the Program’s operational definitions for treatment outcomes except that defaulting and death were defined according to international definitions [9]. We performed annual follow-up to ascertain treatment outcome and vital status, as previously described [7]. We used previously standardised criteria to classify deaths due to tuberculosis [10].

The study was approved by the Ethical Commission of the Instituto Nacional de Salud Pública.

Mycobacteriology and genotyping

Sputum samples were processed for M. tuberculosis following standardised procedures and isolates were genotyped and compared using IS6110-based restriction fragment length polymorphisms (RFLP) and spoligotyping, if the isolate’s IS6110 RFLP patterns had fewer than six bands [11]. We used previously standardised criteria to classify cases as ‘clustered’ within 1 year of diagnosis [11, 12].
Statistical analysis

To determine whether older people (≥65 years old) had lesser probability of being screened, we compared the proportion of older people among screened individuals and the proportion of older people among general population, as measured by census data [8].

We estimated the incidence rate of bacteriologically proven pulmonary tuberculosis (total, clustered and reactivated) by age group. The incidence rate of pulmonary tuberculosis cases was calculated using the census data for the population ≥15 years of age as the denominator [8]. An annual population estimate was extrapolated for non-census years assuming a steady annual growth rate in the geographical study area. Rates were evaluated with the $\chi^2$ test for trends. Rates among older people were compared with those observed among the rest of patients with the $\chi^2$ test.

We used bivariate and multivariate analyses to test for age group differences in the patients’ sociodemographic, behavioural, clinical and bacteriological characteristics. To evaluate access to health care, we assessed the severity of symptoms and disease at diagnosis, the distance to health service centres, and the time elapsed between onset of symptoms, diagnosis and starting treatment. We used logistic regression to assess clinical differences between individuals 65 years and older and the other age groups. Using multivariate unconditional logistic regression, we investigated associations between age group and treatment failure first, as defined at treatment completion. Secondly, to include results of follow-up, patients who were re-treated for tuberculosis were classified as retreated and the association between age group and failure was re-analysed. Finally, we constructed Cox proportional hazards models to assess the association of age group with death due to tuberculosis. We used STATA 10.0 (College Station, TX, USA) statistical software for data analysis.

Results

During the 12-year study period, we screened 12,252 persons who reported cough for more than 2 weeks. The proportion of individuals older than 65 years of age among the screened population was higher than the proportion represented by this same age group among the general population [19.6% (2,404/12,252) versus 9.7% (24,365/251,542) $P = 0.022$]. Of all individuals who were screened, 9.1% (1,111/12,252) had AFB or M. tuberculosis in at least one sputum sample and were diagnosed with pulmonary tuberculosis.

We obtained mycobacteriological culture and genotyping results for 80.4% (893/1,111) of the cases. Patients with available M. tuberculosis genotype result were more likely to have more than 10 bacilli per oil immersion field in the sputum smear [25.8% (230/893) versus 8.7% (19/218), $P < 0.001$] and severe clinical symptoms such as fever [74.3% (661/890) versus 64.2% (140/218), $P = 0.003$], than cases whose isolates we were unable to genotype. Age did not have a role to play in being unable to genotype TB [16.5% (147/893) versus 22.0% (48/218) $P = 0.053$].

Incidence and mortality rates, by age group

Distribution of age groups among the 893 pulmonary tuberculosis patients is shown in Table 1. Trends of tuberculosis incidence (both for recently transmitted as for reactivated tuberculosis) and mortality rates (due to all causes and due to tuberculosis) increased with age and were significantly higher among older age groups ($P < 0.001$).

Characteristics of clusters, by age group

Of the 893 tuberculosis cases, 19.3% ($n = 172$) were recently transmitted tuberculosis and 80.7% ($n = 721$) had a unique genotype. There were 85 different clusters, each with 2–18 isolates; 17.7% ($n = 15$) of index cases were 65 years or more.

Characteristics of patients, by age group

The characteristics of the study population, by age group, are shown in Table 2. Individuals 65 years and older were less likely than 15–44 and 45–64-year-old group to have some formal education or to report using alcohol, tobacco

Table 1. Incidence and mortality rates of tuberculosis by age group in Orizaba, Veracruz, 1995–2007

<table>
<thead>
<tr>
<th></th>
<th>Total cases (no. of cases)</th>
<th>15–44 years old (no. of cases)</th>
<th>45–64 years old (no. of cases)</th>
<th>65 years or older (no. of cases)</th>
<th>P-value*</th>
<th>P-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence rates*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactivated cases</td>
<td>25.7 (721)</td>
<td>18.6 (355)</td>
<td>40.7 (248)</td>
<td>42 (118)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clusters*</td>
<td>6.1 (172)</td>
<td>5.3 (101)</td>
<td>6.9 (42)</td>
<td>10.3 (29)</td>
<td>0.001</td>
<td>0.006</td>
</tr>
<tr>
<td>Total cases</td>
<td>31.9 (893)</td>
<td>23.8 (456)</td>
<td>47.6 (290)</td>
<td>52.3 (147)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mortality rates*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality due to tuberculosis</td>
<td>2.5 (70)</td>
<td>1.5 (28)</td>
<td>3.6 (22)</td>
<td>7.1 (20)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>8.2 (229)</td>
<td>3.8 (72)</td>
<td>15.4 (94)</td>
<td>22.4 (63)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*a* Per 100,000 person/years.

*Clustering within 1 year of diagnosis.

*χ² for trend.

*χ² comparing 65 years and older versus rest.
or illegal drugs and to have clinical symptoms such as fever or haemoptysis. Older individuals were more likely to have negative AFB smears with *M. tuberculosis* in sputa than the rest of patients [16.3% (24/147) versus 10.5% (79/746), *P* = 0.04].

By multivariate analysis, individuals 65 year or older were found to be less likely to have night sweats (OR = 0.60, 95% CI: 0.39–0.94, *P* = 0.026); haemoptysis (OR = 0.64, 95% CI: 0.42–0.97, *P* = 0.036); fever (OR = 0.60, 95% CI: 0.38–0.95, *P* = 0.029) and 10 or more bacilli per oil immersion field in sputum smear (OR = 0.49, 95% CI: 0.30–0.82, *P* = 0.006), adjusting by body mass index, diabetes and HIV infection.

### Treatment outcomes

Nineteen patients refused treatment. Of 874 patients for whom treatment completion could be evaluated, 71.3% (623/874) had initiated treatment within 10 days after diagnosis and 97.7% (854/874) received directly observed therapy, short-course (DOTS). Treatment outcomes overall and according to age group are shown in Table 3. By multivariate analyses, it was found that the middle-age group and older people were more likely than the youngest age group to fail at treatment completion (Table 4).

Patients were followed for a median of 71.6 months [inter-quartile range (IQR) 39–98 months. Follow-up time for the 45–64 years old and 65 years or older age groups was significantly shorter than for the younger age group. During follow-up, there were 69 patients who developed symptoms and were re-treated for tuberculosis. Patients who were retreated were reclassified as such; of these, treatment outcomes of the first episode were as follows: 62.3% (43/69) had been declared cured without bacteriological confirmation, 20.3% (14/69) had defaulted, 15.9% (11/69) had failed treatment and 1.5% (1/69) had been transferred from the study area.

When patients were reclassified considering those who were retreated as an additional category, older individuals were more likely than the youngest age group to fail treatment (Table 4). As all HIV-infected patients failed treatment, the odds ratio is not shown in the table.

There were 229 tuberculosis patients who died during the study period and death was due to tuberculosis in 70 of 229 instances (30.6%). The Cox adjusted hazard ratio for mortality from tuberculosis was higher among older individuals (Table 4).

### Discussion

The older population is increasing more rapidly than any other age group due to both increased survival and decreased fertility rates. This can be recognised as a success story for public health policies, but it also represents a great challenge for society to ensure healthy and functionally able older people as well as their social participation and safety [13].

Data from our population-based study indicate that older individuals suffer both from the progression of recent infection as well as reactivation of latent disease; bacteriological and clinical characteristics make diagnosis more complex and treatment failure and mortality due to tuberculosis during and after treatment are considerable.

Tuberculosis has been identified as one of the most frequent infections among older people [14]. Immunological control of tuberculosis is based on CD4+ produced gamma interferon and subsequent macrophage activation [15]. Immunosenescence includes progressive dysfunction of both humoral and cellular immune functions thus contributing to increased host susceptibility to tuberculosis [16].

The most important finding in our study is that although most cases were still due to reactivation, almost a fifth of older individuals participated in chains of tuberculosis transmission. Older individuals have been described as suffering mainly from reactivation of tuberculosis, favoured by comorbidities, malnutrition, poverty and other common conditions among this age group [17, 18]. Tuberculosis outbreaks have been reported in nursing homes and other environments where crowding and exposure to tuberculosis patients are likely to occur [19]. In contrast, the increased rates of tuberculosis among older people in this study occurred among un-institutionalised individuals, most of them living at home. In our study, both rates of recent transmission and rates of reactivated latent infection among older individuals were higher than among younger age groups. Furthermore, in almost a fifth of clusters, individuals aged 65 years or more were identified as the index case, therefore confirming that they may be sources of infection [20]. Two recent studies have shown that the risk of reactivation decreased with increasing age [21], while the incidence of disease due to recently acquired infection remained stable [22]. Interpretation of our results is complex. Most likely, the effect of ageing on the immune system increases a person’s susceptibility to suffer from reactivation of latent disease, and as immunosuppression becomes more profound, patients rapidly progress from recently acquired infection to active disease, as described for HIV-infected individuals [23].

Our results showing lower frequency of positive smears among patients older than 65 years of age differ from a meta-analysis that did not find differences between older and younger TB patients regarding positive acid-fast bacilli in sputum [3]. However, it is likely that lack of culture confirmation in most studies did not allow detection of differences. This hypothesis is supported by a study showing improvement of diagnosis when performing bronchoscopy and culture [24].

Our data indicate that clinical manifestations are less evident among older patients who suffer a lower frequency of cardinal tuberculosis symptoms such as fever and
A lower frequency of haemoptysis is probably related to a lower frequency of pulmonary cavities associated with consolidation. The hypothesis that less frequent febrile episodes among older mammals postulates a reduced response of the hypothalamic thermoregulatory centre to prostaglandin E2 [25].

Table 2. Characteristics of tuberculosis patients by age group in Orizaba, Veracruz, 1995–2007

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total cases, n = 893</th>
<th>15–44 years old, n = 456</th>
<th>45–64 years old, n = 290</th>
<th>65 years or older, n = 147</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index (kg/m²), [median (IQR)]</td>
<td>20.8 (18.3–23.4)</td>
<td>20.1 (17.8–22.5)</td>
<td>21.8 (18.9–24–1)</td>
<td>20.8 (18.3–22.9)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Diabetes [%]</td>
<td>289/893 (32.4)</td>
<td>72/456 (15.8)</td>
<td>162/290 (55.9)</td>
<td>55/147 (37.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HIV infection [%]</td>
<td>19/874 (2.2)</td>
<td>17/449 (3.8)</td>
<td>2/283 (0.7)</td>
<td>0/142 (0.00)</td>
<td>0.003</td>
</tr>
<tr>
<td>Previous TB treatment [%]</td>
<td>101/892 (11.3)</td>
<td>47/455 (10.3)</td>
<td>39/290 (13.4)</td>
<td>15/147 (10.2)</td>
<td>0.380</td>
</tr>
<tr>
<td>AFB negative and M. tuberculosis in sputum [%]</td>
<td>103/893 (11.5)</td>
<td>51/456 (11.2%)</td>
<td>28/290 (9.6)</td>
<td>24/147 (16.3)</td>
<td>0.113</td>
</tr>
<tr>
<td>More than 10 bacilli per oil immersion field [%]</td>
<td>488/893 (54.7)</td>
<td>256/456 (56.1)</td>
<td>168/290 (57.9)</td>
<td>64/147 (43.5)</td>
<td>0.011</td>
</tr>
<tr>
<td>Haemoptysis [%]</td>
<td>295/890 (33.2)</td>
<td>151/456 (33.1)</td>
<td>106/288 (36.8)</td>
<td>38/146 (26.0)</td>
<td>0.079</td>
</tr>
<tr>
<td>Fever [%]</td>
<td>661/890 (74.3)</td>
<td>364/456 (80.4)</td>
<td>210/290 (72.4)</td>
<td>87/147 (59.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fever and more than 10 bacilli per oil immersion field [%]</td>
<td>182/890 (20.5)</td>
<td>62/453 (50.9)</td>
<td>66/290 (32.6)</td>
<td>54/147 (16.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Night sweats [%]</td>
<td>637/891 (71.5)</td>
<td>341/455 (74.9)</td>
<td>215/290 (74.1)</td>
<td>81/146 (55.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight loss [%]</td>
<td>762/870 (87.6)</td>
<td>401/450 (89.1)</td>
<td>243/279 (87.1)</td>
<td>118/141 (83.7)</td>
<td>0.224</td>
</tr>
<tr>
<td>Cavities in chest radiograph [%]</td>
<td>344/822 (41.9)</td>
<td>172/423 (40.7)</td>
<td>118/268 (44.0)</td>
<td>54/131 (41.2)</td>
<td>0.674</td>
</tr>
<tr>
<td>Enlarged throracic lymph nodes in chest radiograph [%]</td>
<td>301/821 (36.7)</td>
<td>136/423 (32.2)</td>
<td>101/268 (37.7)</td>
<td>64/130 (49.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hepatic cirrhosis [%]</td>
<td>7/893 (0.8)</td>
<td>3/456 (0.7)</td>
<td>4/290 (1.4)</td>
<td>0/147 (0.8)</td>
<td>0.390</td>
</tr>
<tr>
<td>Interval between initiation of symptoms and diagnosis, days [median (IQR)]</td>
<td>95 (56–181)</td>
<td>94 (55–185)</td>
<td>93 (57–175)</td>
<td>100 (57–179)</td>
<td>0.971**</td>
</tr>
<tr>
<td>Interval between initiation of symptoms and treatment, days [median (IQR)]</td>
<td>106 (66–185)</td>
<td>107 (62–185)</td>
<td>104 (67–183)</td>
<td>115 (75–186)</td>
<td>0.423**</td>
</tr>
<tr>
<td>Interval between diagnosis and initiation of treatment, days [median (IQR)]</td>
<td>6 (2–11)</td>
<td>6 (2–10)</td>
<td>6 (2.5–10)</td>
<td>7 (2–24)</td>
<td>0.085**</td>
</tr>
<tr>
<td>Mycobacteriology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. tuberculosis resistant to isoniazid and rifampin [%]</td>
<td>37/866 (4.6)</td>
<td>18/404 (4.5)</td>
<td>16/273 (5.9)</td>
<td>3/129 (2.3)</td>
<td>0.282</td>
</tr>
<tr>
<td>Clustered genotype pattern [%]</td>
<td>172/893 (19.3)</td>
<td>101/456 (22.1)</td>
<td>42/290 (14.5)</td>
<td>29/147 (19.7)</td>
<td>0.035</td>
</tr>
</tbody>
</table>

Table 3. Treatment outcomes among tuberculosis patients by age group in Orizaba, Veracruz, 1995–2007

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total cases, n = 893</th>
<th>15–44 years old, n = 456</th>
<th>45–64 years old, n = 290</th>
<th>65 years or older, n = 147</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure [%]</td>
<td>736/874 (84.2)</td>
<td>383/447 (85.7)</td>
<td>230/283 (81.3)</td>
<td>123/144 (85.4)</td>
<td>0.256</td>
</tr>
<tr>
<td>Default [%]</td>
<td>69/874 (7.9)</td>
<td>34/447 (7.6)</td>
<td>25/283 (8.8)</td>
<td>10/144 (6.9)</td>
<td>0.751</td>
</tr>
<tr>
<td>Failure [%]</td>
<td>26/874 (3.3)</td>
<td>7/447 (1.6)</td>
<td>15/283 (5.3)</td>
<td>4/144 (2.8)</td>
<td>0.015</td>
</tr>
<tr>
<td>Death during treatment [%]</td>
<td>33/874 (3.8)</td>
<td>16/447 (3.6)</td>
<td>11/283 (3.9)</td>
<td>6/144 (4.2)</td>
<td>0.943</td>
</tr>
<tr>
<td>Follow-up after treatment completion, days [median (IQR)]</td>
<td>71.6 (39.5–98.7)</td>
<td>74 (45.3–38.1)</td>
<td>61.8 (38.1–86–3)</td>
<td>61.4 (30.8–86)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Retreatment [%]</td>
<td>69/841 (8.2)</td>
<td>30/431 (7.0)</td>
<td>31/272 (11.4)</td>
<td>8/138 (5.7)</td>
<td>0.060</td>
</tr>
<tr>
<td>Death due to TB [%]</td>
<td>70/893 (7.8)</td>
<td>28/456 (6.1)</td>
<td>22/290 (7.6)</td>
<td>20/147 (13.6)</td>
<td>0.013</td>
</tr>
<tr>
<td>All cause mortality [%]</td>
<td>229/893 (25.6)</td>
<td>72/456 (15.8)</td>
<td>94/290 (32.4)</td>
<td>63/147 (42.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IQR, inter-quartile range; TB, tuberculosis.

*Because there were missing values for the characteristics of some of the tuberculosis patients, several of the numbers below do not sum to the group total.

χ²; P-value.

**Mann–Whitney U test.

haemoptysis as has been previously reported [3]. One hypothesis explaining less frequent fever episodes among older mammals postulates a reduced response of the hypothalamic thermoregulatory centre to prostaglandin E2 [25] or a greater sensitivity to central alpha-MSH which may account for the reduced febrile response seen in the aged [26]. A lower frequency of haemoptysis is probably related to a lower frequency of pulmonary cavities associated with
a modified response to inflammatory cytokines occurring in immunosenescence [27].

When treatment outcomes of patients were reclassified if the patients had developed symptoms and been retreated for tuberculosis, older patients were found to be more likely to fail treatment. Treatment failure among older patients may be due to decreased absorption of drugs associated with age-related physiological changes such as altered gastric pH, modified gastric emptying rates and slower intestinal transit time; and drug intolerance associated with the likelihood of polytherapy [28]. It is likely that older patients, who failed treatment either died, went undiagnosed or refused treatment in the months following treatment completion, therefore explaining why we did not find an association between older age and retreatment.

We observed that even after timely diagnosis and treatment completion, mortality due to tuberculosis among patients older than 65 years of age more than tripled that observed in younger patients. In contrast with previous studies, we documented higher mortality rates from tuberculosis not only at diagnosis or during therapy [29], but also during follow-up after treatment completion. Greater number of comorbid illnesses and adverse effects leading to treatment suspension contribute to explain higher mortality rates associated with tuberculosis among older people [4].

This study has several sources of possible bias. Although the proportion of screened older individuals doubled the proportion represented by this age group among general population, it is highly possible that the proportion of older people with a cough persisting for more than 2 weeks was greater among the older population than among the younger population living in the study area and therefore the rates among the older age group may be underestimated. Our data may not be generalisable to patients with fewer bacilli and less severe symptoms. This would be more relevant in the period 1995–2000 when we only recruited smear positive individuals. Determining the cause of death can be a complex process. In this study, we used a combination of criteria (clinical, bacteriological and caregiver interview, and/or death certificate) that has previously been validated by our group to ascertain the cause of death and allowed us to estimate mortality rates [10].

In conclusion, older pulmonary tuberculosis patients participate in transmission chains, indicating that tuberculosis is not solely due to the reactivation of latent disease. Clinical manifestations among this population make diagnosis more complex (as sputum smears have fewer bacilli, and patients exhibit a lower frequency of fever and haemoptysis). Finally, these patients have a higher probability of failing treatment and of death due to tuberculosis during treatment and after treatment completion. These results have relevant implications for health policies. The globally increasing number of older individuals will magnify this problem, particularly in regions where tuberculosis is endemic. Our findings emphasise the importance of timely diagnosis and treatment in this age group. Secondly, usage of M. tuberculosis cultures in addition to sputum smears is essential given the lack of sensitivity of smears. Thirdly, health care systems need to pay immediate attention to the projected increases in health care needs of the older age group. An integrated approach should take into consideration timely treatment and diagnosis of chronic transmissible and non-transmissible diseases; management of adverse reactions caused by pharmacological interactions and special care to nutritional requirements [30].

### Table 4. Results of the multivariate analysis of the risk factors for treatment failure and death from tuberculosis among bacteriologically confirmed pulmonary tuberculosis patients, Orizaba Veracruz, 1995–2003

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment failure (1)</th>
<th>Treatment failure (2)</th>
<th>Death from TB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR* (95% CI)</td>
<td>P-value</td>
<td>OR* (95% CI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P-value</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–44 years old</td>
<td>1 (reference)</td>
<td></td>
<td>1 (reference)</td>
</tr>
<tr>
<td>45–64 years old</td>
<td>6.71 (1.61–28.00)</td>
<td>0.009</td>
<td>1.93 (0.38–9.58)</td>
</tr>
<tr>
<td>65 years or older</td>
<td>5.79 (1.10–30.40)</td>
<td>0.038</td>
<td>5.37 (1.06–27.23)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>HIV infection</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fever and more than 10 bacilli per oil immersion field</td>
<td>3.36 (1.07–10.46)</td>
<td>0.036</td>
<td>2.95 (0.63–13.86)</td>
</tr>
<tr>
<td>Previous treatment</td>
<td>6.16 (2.25–16.82)</td>
<td>&lt;0.001</td>
<td>3.66 (0.95–14.02)</td>
</tr>
<tr>
<td>Drug resistance (to any drug)</td>
<td>49.51 (11.14–219.97)</td>
<td>&lt;0.001</td>
<td>65.27 (7.48–569.31)</td>
</tr>
<tr>
<td>M. tuberculosis resistant to isoniazid and rifampin</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Two or more treatment schedules</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

OR, odds ratio; HR, hazard ratio; TB, tuberculosis; variable not included in final model.
*Non-conditional logistic regression results.
†Cox model results.
‡HIV infection predicts failure perfectly.

Treatment failure 1, treatment failure at treatment completion; treatment failure 2, treatment failure after reclassifying patients undergoing retreatment.
Older tuberculosis patients have a higher probability of

- Sputum smears are more frequently negative in the face of positive cultures and patients have less fever and haemoptysis.
- Older tuberculosis patients have a higher probability of treatment failure and of mortality due to tuberculosis.

**Key points**

- Reactivation of latency is not the sole mechanism for disease among community-dwelling older individuals.
- Higher tuberculosis rates are due both to recently transmitted disease and to reactivation of latent disease.
- Sputum smears are more frequently negative in the face of positive cultures and patients have less fever and haemoptysis.
- Older tuberculosis patients have a higher probability of treatment failure and of mortality due to tuberculosis.

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**Conflicts of interest**

None declared.

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**References**

Self-efficacy is independently associated with brain volume in older women

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Abstract

Background: ageing is highly associated with neurodegeneration and atrophy of the brain. Evidence suggests that personality variables are risk factors for reduced brain volume. We examine whether falls-related self-efficacy is independently associated with brain volume.

Method: a cross-sectional analysis of whether falls-related self-efficacy is independently associated with brain volumes (total, grey and white matter). Three multivariate regression models were constructed. Covariates included in the models were age, global cognition, systolic blood pressure, functional comorbidity index and current physical activity level. MRI scans were acquired from 79 community-dwelling senior women aged 65–75 years old. Falls-related self-efficacy was assessed by the activities-specific balance confidence (ABC) scale.

Results: after accounting for covariates, falls-related self-efficacy was independently associated with both total brain volume and total grey matter volume. The final model for total brain volume accounted for 17% of the variance, with the ABC score accounting for 8%. For total grey matter volume, the final model accounted for 24% of the variance, with the ABC score accounting for 10%.

Conclusion: we provide novel evidence that falls-related self-efficacy, a modifiable risk factor for healthy ageing, is positively associated with total brain volume and total grey matter volume.

Trial Registration: ClinicalTrials.gov Identifier: NCT00426881.

Keywords: self-efficacy, brain volume, older women, elderly