Tuberculosis in Young Adults and the Elderly

A Prospective Comparison Study


Objectives: To compare the clinical, bacteriologic, and radiologic features of pulmonary and pleural tuberculosis in young adults and the elderly and determine if any differences exist between both groups.

Design: Prospective recruitment of all patients diagnosed as having pulmonary and pleural tuberculosis in British Columbia, Canada.

Setting: A population-based sample from a provincial control program TB registry.

Patients: A total of 218 consecutive patients whose conditions were diagnosed between January 1990 and May 1991. We excluded 15 HIV-positive patients whose conditions were diagnosed during this study.

Intervention: Standardized data collection of symptoms, bacteriology, and review of radiology by two readers blind to the clinical and epidemiologic data.

Main results: There were 142 young adult patients and 76 elderly patients. The young adults had a mean age of 41.2 years and the elderly group had a mean age of 75 years of age. Fever (p = 0.002) and night sweats (p = 0.02) were more common in young adults. In culture-proven disease, hemoptysis, fever, and cough were more common in young adult (p = 0.03, 0.02, and 0.01, respectively). There was no difference in the duration of symptoms between the two groups. The odds ratio for cancers other than lung cancer, 3.98 (confidence interval, 1.49, 10.65) in the elderly group was the only significant risk factor to differ between the two groups. Skin test responses to 5TU PPD were positive in 86.2 percent of young adults and 67.6 percent of elderly patients tested (p = 0.03). A total of 79.6 percent of young adults and 88.15 percent of the elderly patients (not significant) were culture positive. Comparison of radiologic findings in young adults vs elderly patients showed no significant differences apart from those with miliary TB 0.7 percent vs 6.7 percent (p = 0.04).

Conclusions: In this population-based study, young adults were more likely to have hemoptysis, fever, and cough and to have a positive PPD response. Cancer was significantly associated as a risk factor in the elderly age group. There was no difference in bacteriologically proven disease or radiologic findings between the two groups, apart from the more common occurrence of miliary TB in the elderly.

CI = confidence interval; IT = isolated tuberculoma; LLZ = lower lung zone;

Tuberculosis (TB) is increasing in prevalence in North America. It is likely that infection with human immunodeficiency virus (HIV) is largely responsible for this increase and is also accounting for significant increases in developing countries. Although infection with HIV is the single greatest risk factor for the development of TB, the elderly are also particularly at high risk for the development of disease, as are aboriginal populations, immigrants from high prevalence countries, and the inner-city poor. It has recently been suggested that TB in the elderly may differ from disease presenting in younger patients and that it should be classified as a separate entity. It has also been suggested that these differences might account for a delay in diagnosis, which in turn leads to avoidable morbidity and mortality in this age group. We therefore decided to prospectively evaluate all cases of pulmonary and pleural TB diagnosed in British Columbia (BC) and compare the patterns of disease in young and old patients. In BC, the overall rate per 100,000 in 1989 was 9.6 in the general population and 28/100,000 in those aged more than 65 years.

METHODS

All cases of pulmonary and pleural TB reported to the Registry, Division of Tuberculosis Control, Ministry of Health, BC, between January 1990 and May 1991 formed the study group. The definition of active TB included disease proved by isolation of Mycobacterium tuberculosis by culture from a patient and disease diagnosed by clinical and radiologic criteria with an appropriate response to therapy but without bacteriologic confir-
mation. The cases in which \textit{M tuberculosis} was isolated are called "bacillary" in this article. The medical records were reviewed and in cases diagnosed in Vancouver the patients were interviewed. The primary care physician or public health nurse was asked to complete the standard data sheet in patients not seen in Vancouver. Data gathered include the following: demographic characteristics, history of previous TB, symptoms, presence of conditions predisposing to TB, bacteriologic status at the time of diagnosis, results of tuberculin test, results of histopathologic examinations, and therapy initiated. Adverse reactions were documented if they were reported as such by the primary physicians and were further analyzed with regard to the need to stop treatment with a particular drug.

Bacteriologic investigations were done by the Division of Laboratories, Centre for Disease Control, Ministry of Health, BC. This is the reference laboratory for mycobacteriology in BC and is a level 3 laboratory by the criteria of the American Thoracic Society. The tuberculin test with 5 PPD TU was considered positive at a cut-point of 10 mm induration.

The initial chest radiographs were reviewed by two radiologists aware of the patient's diagnosis but unaware of the clinical and epidemiologic history.

In this article, a chest radiograph with infiltrates predominantly in the upper lobes with or without cavitation is defined as "usual" for postprimary TB. Findings such as isolated pleural effusion, intrathoracic lymphadenopathy alone or with infiltrate, infiltrate exclusively in the lower lung zone defined as the lung below the hilar level (LLZ TB), isolated tuberculosis defined as a well-circumscribed nodular lesion 1 cm or more in diameter (IT), or miliary TB were qualified either as primary TB or as an "unusual" form of postprimary TB when superimposed on residual changes consistent with the previous diagnosis of TB. These changes included those such as calcified primary focus, calcified hilar or mediastinal lymphadenopathy, fibrocalfic changes, pleural fibrosis and calcification, or if they occurred in a person previously treated for TB or if that person had positive results with a PPD skin test in the past. The term "unusual" was also applied to a cavity with a fluid level and to infiltrates involving predominantly the anterior segment of the upper lobes. During the study period, HIV seroprevalence was not routinely obtained but was recommended if the patient had recognized risk factors for HIV infection. Subjects with confirmed HIV infection were excluded from the analysis.

Patients aged between 16 and 64 years of age were considered young adults and those aged 65 years of age or older were considered elderly. To further define the contribution of different age groups, the young adults were further broken down into ages 16 to 44 years and 45 to 64 years. The analyses were also completed across the major ethnic groups to ensure no confounding by ethnicity. The study protocol was approved by the University of British Columbia Human Ethics Committee prior to the study commencing.

\section*{Statistical Analysis}
Statistical analysis was done using a software package (SPSS). Differences between means were compared using a one-way analysis of variance. The \( \chi^2 \) test was also used to determine the significance of relationships between measurements on the nominal scale.

\section*{Results}

\section*{Demographics}
During the study period, there were 233 cases of TB. One hundred forty-two cases occurred in young adults and 76 cases occurred in the elderly patients. Fifteen patients with confirmed HIV positive serologic tests were also diagnosed during the study period but were excluded. The mean age of the young adults was 41.6 years (median, 40.5 years; range, 16 to 64 years; SD \( \pm 13.45 \)). The elderly group had a mean age of 75 years (median, 74 years; range, 65 to 96 years; SD \( \pm 8.09 \)). The major ethnic groups included in young adult patients were as follows: Asians, 68 (48.2 percent); Whites 47 (33.3 percent); and aboriginal Canadians, 25 (17.7 percent). In the elderly, the major ethnic groups included the following: Whites, 35 (47.3 percent); Asians, 29 (39.2 percent); and aboriginal Canadians, 10 (13.5 percent). Data on ethnicity on one young adult and two elderly patients were not available. Results did not differ across ethnic groups.

\section*{Associated Diseases}
Cancer, other than lung cancer 9 (11.8 percent) vs 4 (2.8) \( (p=0.01) \), and malnutrition 4 (5.3 percent) vs none \( (p=NS) \) were more common in the elderly group. The odds ratio for nonlung cancer in the old compared with the young group was 3.98 (95 percent confidence interval [CI], 1.49, 10.65) and lymphoma was 4.91 (CI, 0.87, 27.85).

\section*{Symptoms}
A total of 104 subjects had physician-completed questionnaires at the time of diagnosis. The remainder had data sheets completed by public health nurses. There were no significant differences in data collected between patients interviewed by a physician vs the public health nurse. The proportion of patients with different symptoms are compared in Table 1. The data shown are for all cases. When comparisons were made in bacillary disease (data not shown), there was significantly more hemoptysis \( (p=0.03) \), fever \( (p=0.02) \), night sweats \( (p=0.01) \), and cough \( (p=0.04) \) in young adult patients compared with older patients. There was no significant difference in duration of symptoms between both groups.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Symptoms} & \textbf{Adults, N (%)} & \textbf{Old, N (%)} & \textbf{p Value} \\
\hline
Cough & 77 (57) & 31 (45) & 0.113 \\
Hemoptysis & 25 (18.5) & 4 (6) & 0.025 \\
Weight loss & 62 (45.9) & 24 (35) & 0.169 \\
Fever & 49 (36.3) & 15 (22) & 0.05 \\
Anorexia & 24 (17.8) & 13 (19) & 0.052 \\
Night sweats & 45 (33.3) & 9 (13) & 0.003 \\
Chest pain & 33 (24.4) & 10 (15) & 0.130 \\
Dyspnea & 29 (21.5) & 16 (23) & 1.920 \\
Nonrespiratory & 44 (32.6) & 23 (33) & 0.970 \\
Chills & 19 (14.1) & 8 (12) & 0.782 \\
Asymptomatic & 7 (4.9) & 7 (9.2) & 0.348 \\
\hline
\end{tabular}
\caption{The Frequency of Symptoms in 142 Adults and 76 Elderly Subjects}
\end{table}
When the young adult group was broken down into its two subgroups, the significant differences in hemoptysis, night sweats, and fever remained only for those subjects aged 16 to 44 years and 64 years and older.

Mantoux Skin Testing

Mantoux skin testing was carried out using 5TU PPD in 87 (61.3 percent) of 142 young adults and in 37 of 76 elderly patients (48.7 percent) (p=NS). The results for all cases are shown in Table 2.

Bacteriology

Sputum samples were positive on smear in 68 young adults (69.4 percent) and culture positive in an additional 30 patients. Similar proportions of the elderly group had smear-positive and culture-positive disease with 66 percent being positive on smear (p=0.68).

Radiologic Findings

Results are shown for 136 adults (six radiographs not available) and 75 elderly patients (one radiograph not available). Results are shown in Table 3. Except for the higher proportion of patients with miliary TB in the elderly group, there were no significant differences between the two groups. Where more than one atypical finding was present, the prevalence of such abnormality was compared.

Therapy and Outcome

Three young adults and seven elderly patients were not treated for TB. Of the three young adults, one died of TB and two died of other causes. Two elderly patients died of untreated TB and five died of other causes. The majority of patients received isoniazid, rifampin, and pyrazinamide and there was no significant difference in the type of treatment given to both groups. The total number of specific adverse reactions is shown in Table 4.

**Table 2—Mantoux Skin Test Reactions to 5TU PPD With a Negative Reaction Considered 0 to 9 mm and a Positive Reaction 10 mm or Greater in 57 Adults and 37 Elderly Subjects**

<table>
<thead>
<tr>
<th></th>
<th>Positive Reaction, N (%)</th>
<th>Total No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative Reaction, N (%)</td>
<td>Adults</td>
<td>12 (13.8)</td>
</tr>
<tr>
<td></td>
<td>Old</td>
<td>12 (32.4)</td>
</tr>
</tbody>
</table>

*p=0.031 for the proportion of subjects with a positive PPD.

**Table 3—Chest Radiographic Findings Among 136 Adults and 75 Elderly Patients**

<table>
<thead>
<tr>
<th>Description</th>
<th>Adults, N (%)</th>
<th>Elderly, N (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper lobe changes, including upper lobe changes without any other findings</td>
<td>69 (50.7)</td>
<td>45 (57.3)</td>
<td>0.438</td>
</tr>
<tr>
<td>Cavitration</td>
<td>19 (14.0)</td>
<td>11 (14.7)</td>
<td>0.890</td>
</tr>
<tr>
<td>Anterior segment of upper lobe involved</td>
<td>7 (5.1)</td>
<td>4 (5.3)</td>
<td>0.953</td>
</tr>
<tr>
<td>Cavity with fluid level</td>
<td>3 (2.2)</td>
<td>2 (2.7)</td>
<td>0.833</td>
</tr>
<tr>
<td>Adenopathy</td>
<td>24 (17.6)</td>
<td>11 (14.7)</td>
<td>0.716</td>
</tr>
<tr>
<td>Lower lung zone TB</td>
<td>8 (5.9)</td>
<td>5 (5.3)</td>
<td>0.869</td>
</tr>
<tr>
<td>Isolated tuberculosis</td>
<td>11 (8.1)</td>
<td>5 (6.7)</td>
<td>0.919</td>
</tr>
<tr>
<td>Isolated pleural effusion</td>
<td>12 (8.8)</td>
<td>4 (5.3)</td>
<td>0.519</td>
</tr>
<tr>
<td>Pleural effusion with parenchymal disease</td>
<td>15 (11.0)</td>
<td>15 (20)</td>
<td>0.114</td>
</tr>
<tr>
<td>Miliary TB</td>
<td>1 (0.7)</td>
<td>5 (6.7)</td>
<td>0.040</td>
</tr>
<tr>
<td>Normal radiographs</td>
<td>3 (2.2)</td>
<td>—</td>
<td>0.491</td>
</tr>
</tbody>
</table>

*A total of seven (six adult and one elderly) patients had missing chest radiographs.

**Table 4—Adverse Reactions to All Drugs Given in Both Age Groups**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Adult, N (%)</th>
<th>Old, N (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity</td>
<td>14 (10.1)</td>
<td>10 (14.5)</td>
<td>0.478</td>
</tr>
<tr>
<td>Skin reactions</td>
<td>22 (15.8)</td>
<td>6 (8.7)</td>
<td>0.229</td>
</tr>
<tr>
<td>GI upset</td>
<td>11 (7.9)</td>
<td>4 (5.8)</td>
<td>0.876</td>
</tr>
<tr>
<td>Others</td>
<td>11 (7.9)</td>
<td>6 (8.7)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Discussion

Although recent attention has focused on TB associated with HIV infection,5 TB continues to cause significant disease in the elderly, such that in 1988 the incidence of cases in patients older than 65 years was close to twice as high as any other age group.16,17 Prior to the recent onset of HIV-associated TB, the elderly, newly arrived immigrants, and minority populations were the groups in North America whose rates of disease continued to rise.6 The elderly have documented very high rates of disease, particularly in nursing homes.18-20 In Arkansas, rates of disease of over 1,000/100,000 in men and 376/100,000 in women have been reported in those aged 65 years or older.20 The potential for significant ongoing transmission of TB infection within such enclosed communities has been described.19 The importance of considering the diagnosis of TB in this age group lies in the potential for such index cases to infect many others in nursing homes18,19 as well as transmitting infection to caregivers and relatives.

Tuberculosis in the elderly is most often associated with reactivation of endogenous infection.21 The delay in diagnosis of TB causing avoidable morbidity and mortality22,23 has often been assumed, particularly in the elderly, to be related to atypical, clinical, and radiologic features. A recent study and editorial suggested that the pattern of disease in the elderly was so characteristic that it should be given a separate classification.11,12
Our data suggest that although younger patients were more likely to have hemoptysis, fever, and night sweats, there was no difference in most symptoms and also no difference in duration of symptoms between the two groups. These differences in symptoms have been reported previously in a smaller, hospital-based, retrospective series but were lacking in another study that had similar methodologic limitations. Both series consisted only of male subjects and were of hospitalized patients. The small but significant minority of patients in our series who are asymptomatic probably in part related to the fact that this is a registry-based series and therefore a number of cases would have been diagnosed in the process of contact evaluation. As might be expected, Mantoux skin testing with 5TU PPD was a relatively inefficient adjunct in the diagnosis of active TB.

Previous data from BC have shown the presence of a similar proportion of positive reactors in bacteriologic proven TB of all ages. The radiologic pattern of pulmonary TB in non-HIV series of patients has usually been reported in retrospective series and even when it has been prospective it has been institutional based. The recent HIV epidemic has further complicated the radiologic pattern of disease. In a recent review, we have noted the relatively high proportion of atypical radiologic findings in HIV-associated TB. To our knowledge, this is the first, in recent years, population-based prospective evaluation of the radiologic pattern of pulmonary TB in North America. Our data confirm that a relatively high proportion of patients in all age groups have atypical radiologic findings and confirm previous retrospective series showing no major differences between younger and elderly patients.

Our failure to confirm the findings of Morris of atypical disease in the elderly may be due to his series being related solely to hospitalized or nursing home patients and possibly the very high proportion of black patients. In addition, he failed to include a control population of younger patients. The one exception to our failure to find a difference between the younger and older adults was the occurrence of a statistically significant higher number of cases of miliary TB in the elderly (five vs two). The difficulties of making this diagnosis in the elderly, particularly when the "cryptic" form of disease occurs, have been documented. Only a minority of our patients had HIV infection, and we excluded them to ensure they did not contribute to differences between both groups. Although normal chest radiographs occurred in only five patients, as previously shown, the absence of radiologic changes, in an appropriate setting of symptoms, a history of contact, and a positive PPD skin test should suggest the possibility of the diagnosis and should be pursued with the examination of sputum for acid-fast bacilli. The occurrence of pleural effusions in the presence of radiologic evidence of previous disease, until recently thought to be an uncommon occurrence, was found to be relatively common in both our study groups.

There was no difference in the proportion of patients with bacteriologically proven disease between the two age groups. This is in keeping with the radiologic findings where there was no difference in the presence of cavitation or in the extent of disease in terms of the number of zones involved. Thus, in elderly patients, as in HIV-infected patients, delay in diagnosis relates to physician failure to consider the diagnosis and obtain bacteriologic specimens for diagnosis rather than unusual radiologic features.

It has been suggested previously that adverse reactions to antituberculous drugs are more likely in the elderly and although there was not a statistically significant difference between both groups, there was a tendency for more hepatotoxic reactions in the elderly.

In conclusion, we have shown that TB in the elderly is associated less often with classic symptoms of night sweats, hemoptysis, and fever but is similar to disease in the young in terms of the risk factors, with the exception of cancers other than lung cancer in older patients. In terms of diagnosis, radiologic appearances are similar and bacteriologic confirmation is as likely in both age groups. These data therefore confirm, yet again, the importance of considering TB as a diagnosis in the elderly even in the absence of classic symptoms, and the appropriate collection of sputum or bronchial washings will yield the diagnosis as effectively as in younger patients. In an era when our attention is focused on HIV-associated TB, we should continue to be alert to the possibility of the diagnosis in the elderly who continue to contribute a significant number of cases and in particular, deaths.

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REFERENCES

5. Schulzer M, FitzGerald JM, Enasar D, Grzybowski S. A mathematical model to predict the future impact of HIV
infection on tuberculosis in sub-Saharan Africa. Tuber Lung Dis 1992; 73:52-8
7 Stead WW, Lofgren JP. Does the risk of tuberculosis increase in old age? J Infect Dis 1983; 147:951-55
16 Stead WW, Dutt AK. Tuberculosis in the elderly. Semin Respir Infect 1989; 4:189-97
25 Katz PR, Reichman WE, Dube D. Clinical features of pulmonary tuberculosis in young and old veterans. JAGS 1987; 35:512-15
27 Battershill JH. Cutaneous testing in the elderly patient with tuberculosis. Chest 1980; 77:188-89
33 Schmidek HH, Hardy MA. Pulmonary tuberculosis with normal chest x-rays. Can Med Assoc J 1967; 97:178-80
34 Miller WT, McGregor RR. Tuberculosis: frequency of unusual radiographic findings. AJR 1978; 130:867-75
35 Farman OP, Speir WA. Initial roentgenographic manifestation of bacteriologically proven mycobacterium tuberculosis: typical or atypical. Chest 1986; 89:75-7

Tuberculosis in Young Adults and Elderly (Korzeniewska-Kosela et al)