ORIGINAL ARTICLE

Chest X-ray findings in relation to gender and symptoms: A study of patients with smear positive tuberculosis in Vietnam

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Abstract

The aim of the study was to analyse chest X-ray (CXR) findings among men and women with smear positive pulmonary tuberculosis (TB). All new cases of smear positive pulmonary TB diagnosed during 6 months in 23 districts in Vietnam were included in a cross-sectional study. 366 cases fulfilled the inclusion criteria. Pleuritis was demonstrated in 17% of the men’s CXR versus 3% of the women’s, \( p < 0.002 \). A miliary pattern was seen in 11% of the men’s CXR versus 3% of the women’s, \( p = 0.04 \). Hilar adenopathy was common and equally distributed among men and women (65% vs 61%). Dyspnoea was common among patients with pleuritis (67%) and a miliary pattern (65%). The radiological findings were more advanced in men than women, despite a similar time from symptom onset to diagnosis. The primary manifestations of TB found among men were unexpected in this setting with an HIV prevalence \(< 0.1\%\) at the time. The association with other risk factors for TB in men needs further investigation. The less advanced CXR findings in women may correspond to a slower rate of progression to smear positive disease, which would have implications for the possibilities of women to obtain a timely TB diagnosis.

Introduction

Tuberculosis (TB) is 1 of the major global infectious health threats today, particularly in low-income countries [1]. Vietnam ranks number 13 of 22 TB high-burden countries identified by the WHO. The incidence of smear positive TB in Vietnam was estimated at 86/100,000 population in 2002 [1]. Although Vietnam reached the stipulated WHO targets for TB control by 1996, and currently reports an 82% case detection rate for new smear positive TB cases, there is no evidence of a decreasing TB incidence [2,3]. In contrast to adjacent countries, the HIV epidemic in Vietnam has not yet had a major impact on the TB situation [3–5]. The estimated HIV prevalence among new TB cases was 0.5% at the time of the study [5].

The most common manifestation of TB in adults is post-primary pulmonary TB. According to earlier reports, the typical chest X-ray (CXR) in such a patient involves lesions in the apical and/or posterior segments of the upper lobe and the superior segments of the lower lobes. Cavities are found in about 50% of these patients [6–9]. Most studies on CXR findings in TB patients have been performed in high-income countries, and it is not known whether the findings are valid in a low-income, high-TB incidence country such as Vietnam.

Key symptoms of pulmonary TB have likewise been identified. Cough of more than 3 weeks duration, sputum production with or without haemoptysis as well as general symptoms such as weight loss and fever are commonly described. There is, however, evidence of gender differences in the response to both TB infection and disease [10]. In a study from Vietnam, self-reported symptoms among male and female TB patients diverged; sputum production and haemoptysis were significantly less common among women [11]. It has also been suggested that CXR findings may differ among men and women [12]. In a study from Turkey, female TB cases more commonly had involvement of lower lung fields [13]. The aim of this study was thus to analyse CXR findings among men and women.
with new smear positive pulmonary TB and to analyse CXR findings in relation to gender and symptoms.

Methods

Study population

This study was part of a larger project, in which different aspects of TB epidemiology and gender in Vietnam were studied [14]. A stratified random sampling procedure selected 23 out of 66 districts by probability proportional to size in 4 provinces of Vietnam. Stratification was based on districts being urban or rural, and having high or low TB prevalence. All new adult (15–49 y) cases of sputum smear positive pulmonary TB diagnosed during January – June 1996, at the district TB units, were eligible as study participants. Diagnosis of TB was performed according to the Vietnamese National TB Programme (NTP) standard procedure and the WHO, which included 3 sputum smear microscopy examinations and a CXR. A total of 366 cases, 299 men and 67 women, fulfilled the inclusion criteria of having provided 3 sputum samples and a CXR, and all of them agreed to participate in the study. The mean age among the study subjects was 34 y (range 15–49 y) for men, and 31 y (16–48 y) for women. An additional 174 cases were diagnosed with pulmonary TB, but did not fulfil our inclusion criteria of providing 3 sputum smear samples and a CXR. A comparative analysis stratified by gender was performed to check for significant differences between the included cases (366 cases) and those who did not fulfil the criteria (174 cases). The following variables were used: age, socioeconomic status and major symptoms at diagnosis. The analysis showed no significant differences between the groups.

Data collection

TB physicians of the NTP interviewed all cases at the time of diagnosis. A structured interview form was used to collect socioeconomic and demographic variables, initial clinical symptoms, clinical symptoms at the point of diagnosis and time lag between symptom appearance and diagnosis. The CXR examinations were performed at the district TB units and were used in the regular clinical procedure in the diagnosis of the new sputum smear positive TB cases. A standardized form was used to describe the CXR findings. The form included localization (left or right side, upper-middle-lower lobes) and extent of major CXR findings. CXR outcomes were classified into categories: 1) a miliary pattern; 2) pleuritis; 3) adenopathy; 4) cavitation; 5) calcification; and 6) fibrosis, and each patient could have several findings. A senior lung specialist in Sweden read all the original CXRs, blinded for gender, as well as non-blinded. Blinding was performed by covering the lower half of the CXR with a standardized paper cover. In total, all CXRs were read twice.

Intra-reader agreement

A kappa test evaluates the level of agreement between ‘tests’, or in this case radiology readings. It assumes that agreement between tests/readings is evidence of validity, whereas disagreement suggests that the tests are not reliable. The kappa test thus measures the level of agreement beyond that which may be obtained by chance. The kappa statistic lies within a range between −1 and +1 and the values are evaluated according to arbitrary ‘benchmarks’[1]. The kappa test is commonly used to assess levels of agreement between radiology readings.

In this study intra-reader agreement between blinded and non-blinded readings was very good, with kappa values between 0.87 and 1.00. The non-blinded/unmasked readings were therefore used in the analyses.

Data analyses

Epi info, version 6 and SPSS, version 10 were used for statistical analyses. In order to test differences between proportions, \( \chi^2 \) testing was used. Possible confounding factors were evaluated in logistic regression models. A kappa analysis was performed to assess intra-reader agreement. ANOVA testing was used to examine differences between means.

Ethics

All TB cases included were provided with oral information, and the study was approved by the ethical committee at the Karolinska Institute, as well as by the Ministry of Health, and the National Institute of Tuberculosis and Lung Disease, Hanoi, Vietnam.

<table>
<thead>
<tr>
<th>Kappa value</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.81</td>
<td>Almost perfect agreement</td>
</tr>
<tr>
<td>0.61–0.80</td>
<td>Substantial agreement</td>
</tr>
<tr>
<td>0.41–0.60</td>
<td>Moderate agreement</td>
</tr>
<tr>
<td>0.21–0.40</td>
<td>Fair agreement</td>
</tr>
<tr>
<td>0.01–0.20</td>
<td>Slight agreement</td>
</tr>
<tr>
<td>0.00</td>
<td>Poor agreement</td>
</tr>
</tbody>
</table>
Results

Demographic characteristics

A majority (83%) of the 366 TB cases was living in an urban area, and 40% of the men and 50% of the women were poor or very poor. The median number of family members in each household was 6. No women were pregnant at the diagnosis of TB, but 12 (20%) of the women had been pregnant during the last 3 y prior to the TB diagnosis.

Clinical symptoms

At the time of diagnosis, women reported general symptoms more often than men. Weight loss (94 vs 88%) and lack of appetite (79 vs 66%), were more frequently reported by women, whereas men more commonly reported local symptoms such as chest pain (74 vs 68%) and dyspnoea (52 vs 48%). The mean time to TB diagnosis from the first symptom was 13 weeks for men as well as for women.

Correlation of clinical symptoms and chest X-ray findings

Weight loss and cough were the most commonly reported symptoms associated with any of the CXR findings. Haemoptysis was reported by 27% of the patients with cavities. Dyspnoea was more common among patients with pleuritis (67%) and miliary findings (65%) than among those with cavities (50%) (Table I).

Radiological findings

The gender distribution of the major CXR findings is presented in Table II. Pleuritis and/or a miliary pattern were significantly more common among men than women. Men presented with cavities more often than women, although among those patients who presented with cavities, there was no significant gender difference in the mean number of cavities (men: 1.73, women: 1.86, p = 0.70). Hilar adenopathy was prevalent among both men (65%), and women (61%) (Table II).

Table I. CXR outcomes in relation to symptoms at diagnosis.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cavitation n = 182 n (%)</th>
<th>Miliary findings n = 35 n (%)</th>
<th>Pleuritis n = 54 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>101 (55)</td>
<td>23 (66)</td>
<td>38 (70)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>164 (90)</td>
<td>32 (91)</td>
<td>51 (94)</td>
</tr>
<tr>
<td>Cough</td>
<td>172 (95)</td>
<td>32 (94)</td>
<td>49 (91)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>131 (73)</td>
<td>26 (76)</td>
<td>42 (78)</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>48 (27)</td>
<td>7 (21)</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>89 (50)</td>
<td>22 (65)</td>
<td>36 (67)</td>
</tr>
</tbody>
</table>

Logistic regression with miliary findings and pleuritis as dependent factors, and gender, age and symptoms duration as independent factors, showed that gender was the only factor significantly associated with these outcomes.

There were no differences in the location of cavities among men and women (48% of the men and 42% of the women had cavities in the upper lobes, and 6% versus 6% in the lower lobes). Hilar adenopathy on the left side was significantly more frequent in the male group (48 vs 34%, p = 0.03); otherwise there were no significant gender differences in right versus left CXR findings.

Discussion

We found that, despite a similar disease duration, men presented with advanced CXR findings at the time of diagnosis of TB more often than women. Our results do not support that CXR findings in women with TB would appear different from what has previously been described as the typical CXR in a pulmonary TB patient. The reported symptoms of TB correlated in general well with CXR findings and with what is known from clinical practice [7,15].

A limitation of this study is the use of a hospital-based sample of patients who have had access to health care services and the National TB Programme. To what extent this has implications for our findings is difficult to assess. Internal validity of this study is increased by the Vietnamese National TB Programme context, which has been recognized for its achievements in terms of outcomes and organization [1,16]. The Vietnamese TB Programme reports about two-thirds male and one-third female sputum positive TB cases, a gender difference which is also reflected in this study [1,16].
Most of the studies of radiological findings in TB have been carried out in high-income countries with a relatively low incidence of TB [6–9,13,17]. In this study population, men had a higher prevalence than women of radiological findings that are associated with primary manifestations of TB, or commonly seen in the immunocompromized hosts [6,8]. In reports from North America, a miliary CXR pattern occurs in about 1–7% of all forms of TB, and is considered a manifestation of primary TB. Pleuritis is reported in 6–7% of the cases of primary TB, and is less prevalent in post-primary TB [7]. Here, a miliary CXR pattern was found in 11% of the men and 3% of the women, and pleuritis in 17% and 3%, respectively. In addition, a majority of men and women frequently presented with hilar adenopathy, another CXR finding which is usually associated with primary TB or the immunocompromized host [18].

In the US, attention has been brought to the shifting pattern in CXR findings among TB patients during recent decades. A higher prevalence of radiological findings as miliary shadowing, adenopathy and pleural effusion has been described. The proposed explanation is a major decrease in childhood infections, and thus a higher prevalence of primary disease in the older population [6,8,9]. In Vietnam there is evidence of a gradually increasing trend in CXR findings among TB patients it was about 0.5% [3–5]; thus, concomitant HIV infections are not a likely explanation of the results. Findings related to ours are presented in a study from South Africa, which showed that pleuritis was more common in adolescent men than adolescent women and could be part of an explanation of our findings [19–22]. The HIV prevalence in the general population at the time was less than 0.1%, and among TB patients it was about 0.5% [3–5]; thus, concomitant HIV infections are not a likely explanation of the results. Findings related to ours are presented in a study from South Africa, which showed that pleuritis was more common in adolescent men than adolescent women owing to the fact that the female sex steroids predispose to the development of post-primary pulmonary TB in adolescent women [23].

In conclusion, the CXR findings differed between men and women, with men presenting more advanced findings despite a similar time from symptom start to diagnosis. The primary manifestations of TB found in the male group were unexpected in this setting, with a high TB incidence and a low HIV prevalence of less than 0.1% at the time. The association with other known and unknown risk factors for TB in men thus needs further investigation in order to target prevention. The less advanced CXR findings in women could correspond to a slower rate of progression to smear positive disease, which would have implications for the possibilities for women to obtain a timely TB diagnosis. The localization and form of the CXR findings correlated well with what has earlier been described in relation to symptoms.

Acknowledgements

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References