Introduction

Tuberculosis (TB) is a major global health burden with more than 9 million people developing the active disease annually. The World Health Organization’s (WHO) global targets for reducing the burden of disease attributed to TB are to halt and to begin to reverse the high incidence of TB. To meet these targets, the proportion of new TB cases detected should be 84% of all infected cases globally by 2015. Between 2000 and 2005, the case detection rate for new smear-positive cases in China increased from 31 to 73%. Between 2000 and 2005, the case detection rate for new smear-positive cases in China increased from 31 to 73%.

TB control can be effectively achieved if individuals with the disease are diagnosed in a timely manner and receive adequate and timely treatment. A delay in diagnosis reflects a lack of access to TB care that delays treatment for the individual patient, as well as increasing the risk of TB transmission in the community until the patient is treated. In most Chinese studies, low-income, female and rural TB patients are at a high risk of receiving a late diagnosis.

Delays in TB diagnosis and associated risk factors

Factors associated with delayed tuberculosis diagnosis in China

Vanina Meyssonnier1,2, Xia Li1, Xin Shen3, Haiying Wang4, Ding Yue Li5, Zi Min Liu4, Gang Liu5, Jian Mei3, Qian Gao1

1 Key Laboratory of Medical Molecular Virology, Institute of Biomedical Sciences and Institute of Medical Microbiology, Fudan University, Shanghai, P. R. China
2 Bactériologie-Hygiène, EA 1541/ER 5, Université Pierre et Marie Curie, Site Pitié-Salpêtrière, Paris, France
3 Department of Tuberculosis Control, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, China
4 Shandong Provincial Tuberculosis Control Center, Jinan, Shandong, China
5 Sichuan Center for Disease Control and Prevention, Chengdu, Sichuan, China

Correspondence: Qian Gao, Key Laboratory of Medical Molecular Virology, Institutes of Biomedical Sciences and Institute of Medical Microbiology, Shanghai Medical College, Fudan University, 138 Yi Xue Yuan Road, Shanghai 200032, China, Tel: +8621 5423 7195, Fax: +8621 5423 7971, e-mail: qgao99@yahoo.com

Background: Delays in the diagnosis of tuberculosis reflect a lack of access to care, and contribute to ongoing tuberculosis transmission in the community. The objective of this study was to evaluate the delay in tuberculosis testing and the associated risk factors in Shanghai, Shandong and Sichuan provinces in China. Methods: A prospective cohort study of 765 culture-positive pulmonary tuberculosis patients registered between December 2006 and December 2008. The delay between the onset of symptoms and tuberculosis diagnosis testing and patient information were recorded in a questionnaire and analysed. Results: The median delay was 36 days and was significantly shorter in patients from Shanghai compared with other places (30 vs. 42 days, P<0.001). Multivariate analysis revealed that cough in Shanghai patients, lowest income level, being married and presenting expectoration in Shandong and Sichuan patients, were associated with a delay in the diagnosis testing of >30 days. The only factor associated with a delay of >90 days was, in Shandong and Sichuan provinces only, female gender. The presence of other pulmonary symptoms like haemoptysis and loss of weight, fever and chills could shorten these delays. Conclusion: Efforts to shorten delays in the diagnosis of tuberculosis must target vulnerable populations. The non-specific symptom of cough is a risk factor associated with longer delays. Training for healthcare workers in areas with a high incidence of tuberculosis, where a delayed diagnosis in coughers may enhance tuberculosis transmission in the community, is of paramount importance.
The aim of the study was to evaluate the delay in diagnosing tuberculosis and the risk factors that might be modified to reduce this delay in three different Chinese areas.

Methods

Study population

We performed a population-based prospective study in three different geographic areas in China from 1 December 2006 to 31 December 2008. The study areas included two districts in the Shanghai municipality (Songjiang and Chongning), Fei County in Shandong Province and Shuangliu County in Sichuan Province.

Shanghai sits on the Yangtze River Delta on China's eastern coast. The Songjiang district is located in the southeast part of Shanghai where industry, commerce and tourism are developed. According to the data in 2008, there were 550,000 registered citizens and 517,000 immigrants living in Songjiang. The Chongning district consists of three main islands: Chongming, Changxing and Hengsha Island. Agriculture is the pillar industry of this district. The number of registered citizens was about 700,000, with <3000 immigrants. Fei County belongs to Shandong province, located about 800km in the north of Shanghai. Agriculture is the main industry in this area, and registered citizens number about 930,000. Shuangliu County, located in the middle of Sichuan Province, belongs to Chengdu City, with a population of about 903,000 people. These geographic areas include highly developed metropolis and rural countryside, which may represent different social and economical levels.

Data collection

All *Mycobacterium tuberculosis* culture positive-patients in these areas during the study period were included. Data were obtained through TB patient questionnaires completed by doctors and health workers. All health workers completed professional training before the investigation was started. Sputum samples from all patients suspected of having TB were tested using the sputum smear test (acid-fast bacilli: AFB) and bacterium culture. Patients with AFB-positive sputum smears completed TB questionnaires shortly after receiving their positive results. Sputum smear test negative and culture-positive patients completed questionnaires after diagnosis. The questionnaire was always administered by a trained health worker.

The questionnaire included routine questions about demographics such as age, sex, occupation, marital status, income level, duration of residency in the area, past TB history and if patients had received medical follow-ups for other pathologies. Information concerning active TB symptoms (cough, expectoration, haemoptysis, chest pain, dyspnoea, fever, chills, loss of weight, anorexia, night sweat) and body mass index \([\text{BMI} = \text{weight (kilogram)/height (metre)}^2]\) were collected at the time the questionnaire was completed. The date of onset of any symptoms noted by the patient was recorded. The date of the TB diagnosis test was defined as the duration from the onset of the TB symptoms noted by the patient to the date when sputum smear test was done.

Statistical analysis

Data were collected on standardized forms, computerized and analysed using Stata software (version 10, Stata Corporation, College Station, TX, USA). Categorical variables were compared using the chi-square test. Student’s *t*-test and Welch’s *t*-test were applied to test the difference in the number of days of delay of diagnosis, age in years and monthly family income in Chinese Yuan (10 Yuan = 1 Euro). Categorical variables were created to indicate age (divided into four categories), sex, province of residence (Shanghai or not), farmer occupation, marital status, level of monthly income (divided into four quartile categories), duration of residence in the area (divided into three categories), TB history, abnormal BMI (<18), cough, expectoration, haemoptysis, smoking status and positive smear sputum test. Owing to small numbers, divorced and widowed patients were grouped with single patients and also two new variables were created: ‘other symptoms’ and ‘other pathologies’, grouping together chest pain, dyspnoea, loss of weight, anorexia, night sweats, fever and chills, and diabetes and asthma, respectively. Patients were categorized according to the delay of diagnosis into two groups: short delay (30 days) and long delay (90 days), in accordance with findings in the literature. Stratified analysis for Shanghai residents then resident in either Sichuan or Shandong, were conducted. Simple logistic regression analysis was conducted to calculate Odds ratio (OR), 95% confidence interval (95% CI) and *P*-values. In multivariate logistic regression analysis, all variables were introduced in each model, (among duration of delay and among different areas) and backward analysis was performed. Only the most parsimonious models, i.e. those having the most significance with the least variables (selected using a −2 log likelihood test and the Hosmer–Lemeshow goodness-of-fit test), are presented. *P*-values are two-tailed and *P* < 0.05 was considered statistically significant.

Results

Basic information of patients

A total of 794 culture-positive TB patients were recorded from 1 December 2006 to 31 December 2008 in the three sites. A total of 29 patients were excluded because of missing data regarding either the date of onset of symptoms \((n = 10)\) or the date of TB diagnosis \((n = 19)\). A total of 765 cases of culture-positive TB patients were included in the analysis (table 1). The median age was 49 years (range 18–86). Shanghai municipality patients represented 41.5% \((n = 317)\) of the study population. Among 448 other patients, 193 (43%) were from Shandong province and 255 (57%) from Sichuan province.

<table>
<thead>
<tr>
<th>Characteristics of population study, comparison between Shanghai and Shandong and Sichuan provinces</th>
<th>Total</th>
<th>Shanghai</th>
<th>Shandong</th>
<th>Sichuan</th>
<th><em>P</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>185 (24%)</td>
<td>80 (25%)</td>
<td>44 (20%)</td>
<td>61 (24%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Age (years): mean (IQR)</td>
<td>49 (30–68)</td>
<td>50 (30–70)</td>
<td>48 (31–67)</td>
<td>36 (25–47)</td>
<td>0.31</td>
</tr>
<tr>
<td>Farmer</td>
<td>464 (61%)</td>
<td>248 (78%)</td>
<td>90 (43%)</td>
<td>126 (53%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Married</td>
<td>549 (71.8%)</td>
<td>232 (73.2%)</td>
<td>107 (48.2%)</td>
<td>110 (44.7%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Monthly income (Chinese Yuan): mean (IQR)</td>
<td>932 (200–1000)</td>
<td>1032 (200–1200)</td>
<td>752 (200–800)</td>
<td>600 (200–800)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnicity (Han)</td>
<td>749 (98%)</td>
<td>311 (98%)</td>
<td>438 (98%)</td>
<td>31 (13%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Duration of residence in the area (years)</td>
<td>1–5</td>
<td>82 (11)</td>
<td>44 (14)</td>
<td>38 (8.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;5</td>
<td>115 (15%)</td>
<td>62 (20)</td>
<td>53 (23%)</td>
<td>30 (13%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Past history of TB</td>
<td>121 (16%)</td>
<td>60 (19%)</td>
<td>61 (26.8%)</td>
<td>6 (4%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Median diagnosis delay days (IQR)</td>
<td>36 (18–70)</td>
<td>30 (13–67)</td>
<td>42 (30–83)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as absolute value as *n* (%) unless otherwise specified. IQR, Interquartile ratio.
Compared with patients from the Shanghai municipality, patients from the other two provinces had a higher proportion of farmers (75, 45 vs. 40%, P < 0.001) and a lower monthly mean income (630 vs. 1352 Yuan, P < 0.001).

Unadjusted analysis
In the total population, the median delay of diagnosis was 36 days. The median delay of diagnosis in Shanghai municipality was significantly shorter than in the other two provinces (30 days vs. >42 days, P < 0.001) (table 1).

Table 2 shows the OR of delayed diagnosis test >30 days and 90 days among different demographic and socio-economic risk factors using univariate analysis. In Shanghai, lowest income level, cough, expectorations, haemoptysis, other symptoms, duration of residence >5 years and low BMI were associated, positively or negatively, with a delay >30 days or 90 days (>5 years and low BMI were associated, positively or negatively, with a delay >30 days or 90 days, respectively (tables 3 and 4).

Adjusted analysis
In Shanghai patients, presenting with cough (OR 3.28; 95% CI 1.4–7.7) at the time of testing was independently associated with a delay of diagnosis >30 days (table 3). However, presenting other symptoms like fever and chills, night sweat, loss of weight (OR 0.6; 95% CI 0.3–0.9) and haemoptysis (OR 0.3; 95% CI 0.1–0.7), were factors independently associated with a delay of diagnosis of <30 days and 90 days, respectively (tables 3 and 4).
Among patients from Shandong and Sichuan provinces, lowest monthly income, to be married and presenting expectation were factors independently associated with a delay of >30 days (OR 2.1; 95% CI 1.3–3.2, OR 1.92; 95% CI 1.2–2.9 and OR 2.3; 95% CI 1.2–4.6, respectively) and being a woman, with a delay of >90 days (OR 1.9; 95% CI 1.2–3.1). Other pathologies were found to be independently associated with a delay of diagnosis of <30 days (OR 0.3; 95% CI: 0.1–0.8) and presenting other symptoms, with a delay of diagnosis of <90 days (OR 0.6; 95% CI: 0.3–0.9) (tables 3 and 4).

Outside of the Shanghai area, a delayed diagnosis of >30 days was independently associated with a positive smear test (OR 2.39; 95% CI 1.3–4.3) (data not shown).

Discussion

TB transmission has attracted more and more attention. Early diagnosis is critical for TB control, because delayed diagnosis is known to be associated with higher transmission rates and worse disease.\(^1\)\(^2\)\(^3\) In our study, the median time between the onset of symptoms and sputum smear result is 36 days. This delay, while still longer than it should be, is one of the shortest described in the literature, even if the delay in definitive TB diagnosis (positive microbiological culture) and in treatment can be much longer.\(^4\)

Compared with studies from middle-income countries, the median delay was shorter than in Brazil (110 days) or in South Africa (60 days).\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\)\(^12\)\(^13\) Compared with Western countries, this delay was also shorter, as the delays in the USA and in the UK during the last 5 years have been 89 and 49 days, respectively.\(^14\)\(^15\)

According to WHO determiners of TB control, we divided risk factors of delayed diagnosis into three levels: clinical, socio-economic and health system factors.\(^16\)

Clinical risk factors: In China, patients with >2 weeks of cough or expectoration are considered to be potential TB cases and should be subjected to smear microscopy for further diagnosis. Nevertheless, as described previously, cough and expectoration were associated with a diagnosis delay of >30 days.\(^11\)\(^16\) On the contrary, in our study, presenting with haemoptysis was independently associated with a shorter delay of diagnosis, suggesting that some symptoms lead the physician to a TB diagnosis. Chronic cough is the main symptom on which the physician should focus on in the search for eventually active TB, specifically because of the smear positivity of the coughers, which was, in our study, associated with a delayed diagnosis in Shandong and Sichuan patients.

Socio-economic risk factors: Risk factors for receiving a late diagnosis of TB include being a woman, having a low-income level, being married, being a migrant or living in an area where the population does not seek out health care. Female patients seem to experience a longer delay in diagnosis, particularly in Chinese migrant populations.\(^5\) Although women with cough in rural areas were more likely to seek healthcare than men, they prefer to visit the lower-level non-hospital facilities first, which resulted in delayed diagnoses of TB.\(^6\) It could partly explain our study results: being a woman was independently associated with a delay of diagnosis of >90 days in the non-Shanghai patient analysis. In our study, living in Shanghai was associated with a shorter delay of diagnosis, as described previously.\(^7\) Literature findings suggest that in countries such as China, with a high incidence of TB, authorities should be mindful of the epidemiological analysis of TB in their particular country.\(^8\)\(^9\)

Health system risk factors: the Chinese National TB Control Program (NTP) has adopted DOTs strategy since 1992.\(^17\) In 2002, Xu et al.\(^18\) showed a significantly shorter patient’s delay between the onset of symptoms and first contact with the health care service in Jianhu County covered by the National Tuberculosis Control Program compared with the non-programme Funing County (10 vs. 16 days, \(P < 0.05\)), in Jiangsu province. WHO’s targets should be followed up.\(^15\)

In our study, women living in the provinces (not in Shanghai) were at higher risk of being diagnosed later. Lack of knowledge has been shown to be a delayed diagnosis factor in Chinese women, as well as in Pakistani patients living in rural (as opposed to urban) areas.\(^19\) In addition, diagnosis tools must be available where patients seek health care. As Xu et al. have explained, a high proportion of symptomatic patients do not go to any health facilities, or many of them go to health facilities where sputum smear microscopy is not available.\(^20\) New point-of-care diagnosis tools are fortunately being developed.\(^21\) Finally, a key point of TB control concerns the education of healthcare workers to recognize and act on symptoms. According to Storla,\(^12\) ‘the core problem in the delay of diagnosis and treatment seemed to be a vicious cycle of repeated visits at the same health care level, resulting in non-specific antibiotic treatment and failure to access specialized TB services. In Uganda, 90% of patients had visited one or more health care providers, for an average of four visits, before they were diagnosed.\(^22\) In our study, presenting with haemoptysis or other non-specific symptoms than cough and being followed for other pathologies are factors independently associated with a shorter delay of diagnosis. Healthcare worker training must focus on screening coughers in populations at risk of TB.\(^16\)

One major limitation of our study is that the definition of onset of symptoms is very subjective. Self-reporting is not exact and depends on recall. Even if, in our study, the delay of diagnosis is one of the shortest, it is still too long and doesn’t assure a short treatment delay. Moreover, we could not necessarily determine if patients had already seen a health care worker, if they had to travel long distances to receive health care, or if they had health insurance.

In conclusion, the focus of TB control must be on vulnerable populations. A non-specific symptom such as cough is still a risk factor associated with a longer delay in the diagnosis of TB. Healthcare worker training is of paramount importance in areas with a high incidence of TB, when delayed diagnosis in coughers may enhance TB transmission in the community and worsen the disease.

Acknowledgements

The authors wish to thank the TB controllers, programme staff and laboratory staff who reported the data used in this study and J Robert for revising the manuscript.

Funding

This work was supported by the Key Project of Chinese National Programs (2008ZX10003–010) and Science and Technology Commission of Shanghai Municipality (10JC1413700).

Conflicts of interest: None declared.

Key points

- Cough is a factor associated with a delayed TB diagnosis.
- Delayed TB diagnosis contributes to ongoing TB transmission in the community.
- Healthcare workers must be trained and focus on coughers to screen TB patients.

References

Attitudes and perceptions of influenza vaccination among Hong Kong doctors and medical students before the 2009 pandemic

Kwok Kei Mak1, Yuen Fung Yiu2, Kwan Lung Ko2, Kenneth Siu Hung Hui2, Kin Mei Mak2, Lung Yi Mak2, Wai Pan To2, King Hung Wu2, Fanny Yeung2, Pamela Pui Wah Lee3

1 Department of Community Medicine and School of Public Health, Faculty of Medicine, University of Hong Kong, Pokfulam, Hong Kong
2 Faculty of Medicine, University of Hong Kong, Pokfulam, Hong Kong
3 Department of Paediatrics and Adolescent Medicine, Faculty of Medicine, University of Hong Kong, Pokfulam, Hong Kong

Correspondence: Dr Kwok Kei Mak, Department of Community Medicine and School of Public Health, Faculty of Medicine, University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong, tel: 852-2819-2821, fax: 852-2855-9528, e-mail: kkmak@graduate.hku.hk

Background: Vaccination is an important preventive measure for preparing against the influenza pandemics. This study investigated the attitudes and perceptions of influenza vaccination among doctors and medical students in Hong Kong. Methods: A cross-sectional survey was conducted among 204 doctors and 242 medical students in a teaching hospital in 2009. Participants' demographic and job characteristics, and influenza experience and vaccination in the previous year were assessed in the questionnaire. Logistic regression models were used to examine the associations between uptake of influenza vaccination and the perceived benefits. Results: Medical students were more likely to have receive an influenza vaccination in the previous year (66.9 vs. 39.7%) and acknowledged the related benefits than doctors. Moreover, uptake of influenza vaccine was associated with perceived benefits of vaccination in both doctors and medical students. Conclusions: The perceived benefits of influenza vaccination are an important factor in vaccine uptake for both doctors and medical students in Hong Kong, and should be reinforced in the professional training.