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# Factors associated with delayed recognition of pulmonary tuberculosis in emergency departments in Taiwan



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#### ABSTRACT

*Objective:* To identify and evaluate factors associated with delayed recognition of pulmonary tuberculosis (TB) in the emergency department (ED).

Background: Delayed recognition of pulmonary TB in ED may precipitate mortality and morbidity.

*Methods:* Medical records of newly diagnosed TB patients admitted to four hospitals in Taiwan were retrospectively reviewed. Patients were divided into two groups based on ED physicians' recognition or not of TB and statistically compared to identify differences in their characteristics.

*Results:* 310 newly diagnosed TB patients were identified; 150 were unrecognized in the ED. Cough, chest tightness, general malaise, and body weight loss were more common for those with recognized TB. Older age ( $\geq$ 65 yrs, *P* = 0.035) and chronic renal insufficiency (*P* = 0.005) were associated with delayed TB recognition.

*Conclusion:* Older age and chronic renal insufficiency are risk factors for delayed TB while in the ED. Typical symptoms should heighten alertness for recognizing TB.

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#### Introduction

Delayed diagnosis of active pulmonary tuberculosis (TB) is a significant problem because it can affect disease prognosis and disease transmission.<sup>1–3</sup> Longer delays in TB diagnosis are associated with increased numbers of bacilli on sputum smears and patients can become more infectious.<sup>4</sup> In addition, patients, their relatives, and public health systems are burdened by increased financial costs as a patient's health and disease outcome can be impacted by a delayed TB diagnosis.<sup>5</sup>

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In geographic areas with low-to-moderate incidence, TB may not be immediately recognized, particularly among more recently trained physicians, due to a lack of clinical experience.<sup>6</sup> Complicating this is the multi-faceted presentation of TB that may mimic other disease entities.<sup>7</sup> In addition, rapidly aging populations with increased numbers of elderly people pose another unique problem in that, due to age-related immunosenescence, there may be an increased incidence of latent TB infection activation.<sup>8</sup>

An emergency department (ED) is often the main entry point to a health care system for hospitalized patients and ED physicians provide a first line of defense against nosocomial transmission of infectious diseases, including TB, SARS, and other aerosolized diseases.<sup>9</sup> Patients with undiagnosed active pulmonary TB with variable clinical features contribute to the difficulties for early suspicion in the ED.<sup>10,11</sup> Thus, it is important to identify those factors that are important for increasing the suspicion of TB while patients are still in the ED.

In this study, we retrospectively identified patients who were initially seen in an ED, were then hospitalized, and subsequently diagnosed to have pulmonary TB. Our purpose was to investigate the demographic data and clinical characteristics of patients who

Abbreviations: TB, tuberculosis; ED, emergency department; OR, odd ratio; CI, confidence interval; SARS, Severe Acute Respiratory Syndrome; AFB, Acid-fast bacilli; IQR, interquartile ranges; COPD, Chronic obstructive pulmonary disease; DM, diabetes mellitus; CRI, chronic renal insufficiency; ICU, Intensive Care Unit.

Conflict of interest statement: There were no conflicts of interest associated with this study.

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were and were not suspected of having TB by ED physicians in order to identify those factors that contributed to a delayed recognition of active pulmonary TB in the ED.

#### Methods

#### Study population

This was a retrospective, multi-center study for non-trauma patients older than 18 years of age who were admitted to a hospital after being seen in an emergency department (ED). Fig. 1 shows the flowchart used for patient enrollment (initial N = 5781). As described below, we collected data on newly-diagnosed active pulmonary tuberculosis patients who were admitted to the hospital via ED's in four hospitals from March 1, 2011 to February 28, 2012. Our exclusion criteria were: (1) previous history of pulmonary TB; (2) active pulmonary TB under treatment; (3) referral from other hospitals with a suspected or confirmed diagnosis of pulmonary TB; and (4) patient refusal for hospital admission.

This study was conducted at four university affiliated teaching hospitals located in northern Taiwan (Keelung and Linkou Chang Gung Memorial Hospitals), central Taiwan (Chiayi Chang Gung Memorial Hospital), and southern Taiwan (Kaohsiung Chang Gung Memorial Hospital). Two sites were medical centers (Linkou and Kaohsiung) and two were regional hospitals (Keelung and Chiayi).

This study was approved by each hospital's Institutional Review Board (serial number 98-2245B) and was exempted from obtaining informed consents.

#### Survey contents and administration

All non-trauma patients who visited our ED's were monitored prospectively and were enrolled in our study once a diagnosis of TB was confirmed. A diagnosis of pulmonary tuberculosis was based on a positive sputum tuberculosis culture. We reviewed patients' charts and recorded the following items: age, gender, chief complaints, presenting illness, vital signs, radiology findings, laboratory test results, recognition or not of TB by ED physicians, time from ED admission to TB diagnosis, discharge diagnosis, and mortality or survival on discharge. The numbers of health care providers that contacted each patient without adequate precautions (N-95 mask) during the patient's ED stay were also recorded.

Recognition of TB by ED physicians was defined by: (1) Acid fast stain, TB smear, TB culture or TB DNA polymerase chain reaction test of sputum was ordered during a patient's ED stay; or (2) Pulmonary TB was one of the admission diagnoses made by ED physicians.

Suspected TB patients were kept in ED respiratory isolation rooms based on a physician's decision. These decisions were based on chest X-ray findings and clinical presentation. If a patient had clinical symptoms of pulmonary TB and a typical chest X-ray pattern, isolation was in a single-negative pressure room (standard respiratory isolation room). ED physicians ordered AFB sputum smears and culture tests. The time it took to obtain the culture results either for patients in the ED or after being admitted to the hospital resulted in possible delays in the diagnosis of TB.

#### Statistical analysis

Results for continuous variables are given as medians and interquartile ranges (IQR, 25th and 75th percentiles) due to nonnormal distributions. Results for categorical variables are given as frequencies and percentages. Comparisons between patients with delayed-recognition TB and those without delayed-recognition TB were made by Wilcoxon rank-sum tests for continuous variables and by Chi-square test or Fisher's exact test for categorical variables, as appropriate. Univariate and multivariate logistic regression analyses were used to investigate factors possibly associated with delayedrecognition TB. Factors for delayed-recognition TB that were identified using univariate analysis ( $P \le 0.10$ ) were entered into multivariate models. The final model was chosen using backward selection for which factors that did not improve the model fit at P < 0.05 were discarded; however, age and gender were always used in these models for adjustment purposes. These models provided crude and adjusted odds ratios (OR's) with the corresponding 95% confidence intervals (CI's). We used similar subgroup analyses to investigate the factor profiles associated with delayed-recognition TB among patients with and without respiratory co-morbidities. Since chest radiographs play an important role in diagnosing TB, we also performed similar logistic regression analysis to analyze factors that may influence a delay in diagnosis of TB in patients who had chest radiographs performed in the ED as chest radiographs can play a key role in diagnosing TB. All statistical analyses were done using SAS software version 9.2 (SAS Institute Inc., Cary, NC). A 2-tailed *P*-value of <0.05 was considered significant.

#### Results

#### Patient baseline demographic and clinical characteristics in the ED

After applying the exclusion criteria shown in Fig. 1, a total of 310 patients were enrolled who had positive pulmonary TB sputum cultures during their hospitalization. The baseline demographic and clinical characteristics of these patients while they were in the ED are shown in Table 1. There were 202 men (65.2%) and 108 women (34.8%) whose median age was 76 years (IQR: 66–82 years). There were significantly less delayed-recognition of TB for patients who smoke (P = 0.017).

Regarding respiratory diseases, one fifth of these patients had COPD and 14% had emphysema. There were no significant differences between patients with and without delayed-recognition of TB regarding respiratory diseases. Regarding other co-morbidities, diabetes mellitus (DM; 32.3%) and chronic renal insufficiency (CRI; 21.0%) were the most frequently noted. Their median Charlson co-morbidities index value was 5 (IQR: 4–7). Compared to patients without delayed-recognition TB, those with delayed-recognition more frequently had CRI (P = 0.001), higher Charlson comorbidity index values (P < 0.001). The most frequently reported symptoms were cough (68.7%), followed by fever (51.0%) and dyspnea (50.7%). Compared to patients without delayed-recognition TB, patients with delayed recognition TB less frequently had symptoms of cough (P < 0.001), chest tightness (P < 0.001), hemoptysis (P = 0.003), general malaise (P = 0.041), night sweating (P = 0.015), and body weight loss (P < 0.001).

Most patients (87.4%) had chest X-rays taken while in the ED and less than one-fifth of these patients (18.1%) been isolated while in the ED. Among these 310 patients, 150 (48.3%) were not recognized as having pulmonary TB by ED physicians.

The median times from triage to the first TB test and to a TB diagnosis were 1 day (IQR: 0–3 days) and 15 days (IQR: 2–38 days), respectively. Compared to patients without delayed-recognition TB, those with delayed-recognition had a longer period from triage to TB diagnosis (P < 0.001) (Table 1).

#### Factors associated with delayed-recognition TB

Table 2 shows the logistic regression results for factors associated with delayed-recognition TB. After adjusting for significant factors and potential confounders in the multivariate model,

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