

Factors Associated with Healthcare Delay of Active Pulmonary Tuberculosis after Hospitalization

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Revised Abstract

Background: Hospitals are undesirable reservoirs for transmission of respiratory disease outbreak. Active pulmonary tuberculosis (TB) can readily be infected among hospitalized patients. Early recognition of active pulmonary TB is an essential priority against transmission. The aim of this study was to evaluate factors associated with delayed isolation of pulmonary TB patients in a hospital setting.

Methods: Medical records of newly diagnosed TB patients admitted to a referral hospital from January 2015 through December 2017 were reviewed. Delayed recognition of pulmonary TB was defined as failure to initiate airborne isolation within the first three days of admission. We analyzed clinical, microbiological, radiological and healthcare factors associated with delayed isolation of pulmonary TB. Multivariate logistic regression analysis was performed including significant factors.

Results: A total of 134 patients were analyzed who had positive sputum acid-fast bacilli (AFB) cultures. Of these, 44 (33%) patients were isolated three days after admission. Patients with old age (odds ratio [OR] = 1.04, 95% confidence interval [CI] 1.01-1.07, $p = 0.01$), patients who were admitted to departments other than infectious diseases or pulmonology (OR = 4.03, 95% CI 1.52-10.74, $p < 0.01$) and patients with malignancy (OR = 4.75, 95% CI 1.30-17.39, $p = 0.02$) were associated with delayed isolation. Patients with radiologic diagnosis of active pulmonary TB findings were likely to show early isolation (OR = 0.22, 95% CI 0.08-0.66, $p = 0.01$). Patients who were isolated after three days had longer hospital days in comparison to the patients who were isolated within three days (19 days vs. 10 days, $p < 0.001$).

Conclusion: In a country with intermediate TB prevalence, better awareness for pulmonary TB is required for all hospitalized patients who are admitted to departments other than infectious diseases or pulmonology, especially in old age or patients with comorbidity of malignancy. Chest radiographic diagnosis of TB and suggestion of activity is an important parameter for further diagnostic efforts and early isolation.

Introduction

Tuberculosis (TB) is a major global health problem, 6.4 million new cases were notified in 2017 and more than 1.3 million deaths were caused by it [1]. Moreover, TB outbreaks in institutional settings including hospitals have been reported [2]. In Korean health care systems, patient care during hospital stay is often communal and TB can spread easily. Transmission of TB to immunocompromised patients who are hospitalized might lead to severe form of disease which can be critical. The World Health Organization policy on TB infection control recommends administrative measures aimed to reduce exposures of presumptive TB patients [3]. Prompt diagnosis of active pulmonary TB is critical in order to achieve early treatment and to suppress disease transmission among other patients or healthcare workers [4]. In a previous study [5], initial diagnosis of active pulmonary TB for almost half of hospitalized patients was missed and the treatment was delayed as long as 7 days or more for 30% of the patients. According to one systematic review, time delay in diagnosis of pulmonary TB was 68 days for low and middle income countries and 61 days for high income countries [6]. In a previous study, factors associated with delayed diagnosis of active pulmonary TB have been well reported [7]. However, there is a lack of knowledge about factors associated with delayed isolation of active pulmonary TB patients. During hospitalization, there is a discrepancy between factors associated with delayed diagnosis and isolation. Therefore, we conducted this study to figure out factors leading to prolonged exposures before isolation in our healthcare setting.

Methods

Study setting and population

We conducted a retrospective study on patients who were diagnosed with culture positive active pulmonary TB in a university affiliated referral center in Seoul, Republic of Korea between January 2015 and December 2017. At our institution, patients with respiratory diseases such as pulmonary TB are mostly admitted to pulmonology or infectious diseases department. If a patient is initially suspected of having active pulmonary TB, preemptive airborne isolation with negative room air pressure is performed at admission until sputum smear results are reported. If it is unclear whether the patient has active pulmonary TB or not, the patient can be isolated under suspicion depending on the physician's clinical decision. Electronic medical records were reviewed for patients with diagnosis of active pulmonary TB, who were confirmed AFB culture positive with *Mycobacterium tuberculosis* by respiratory specimen. We focused on factors that might contribute to delayed isolation after 3 days of admission that led to continued exposure during hospital stay. We included patient related demographics, admission course, microbiological results, and radiological findings as potential confounders. This study was approved by Institutional Review Board (serial number 2018-04-033) of the hospital and was waived from obtaining informed consents.

Data collection and definitions

The patients were separated into two groups depending on the date of isolation and time of 3 hospital days. We reviewed patients' medical charts and the following were statistically analyzed: age, gender, chief complaints, presenting symptoms, signs of illness, past medical history, admission date, isolation date, discharge date, admission department, radiologic findings of chest radiograph, findings of chest computed tomography (CT), AFB stain, AFB culture results and TB DNA polymerase chain reaction test results. The time from admission to adequate airborne isolation was defined as the exposure period. Respiratory symptoms such as cough, purulent sputum, dyspnea, hemoptysis and pleuritic chest pain were included. Weight loss of 10% of the body weight or 5 kilograms or more during the last six months was considered. Malignancies included all solid and hematologic types.

Evaluation of radiologic findings

Two chest radiologists retrospectively reviewed initial chest radiographs (134/134) and chest CT scans (122/134) of the enrolled patients. Radiologic diagnosis including TB and also evaluation for disease activity were performed without clinical information to eliminate preconceived impressions. Final decisions were reached by consensus. Radiologic findings of active pulmonary TB included cavities, nodules and micronodules with segmental distribution, airspace consolidation, diffuse miliary nodules and newly appeared or progression of findings described above on follow-up exams compared to previous ones. Findings of stable or inactive pulmonary TB included absent findings of active disease, mostly calcified small granulomas or lymph nodes, fibronodular scars stable for at least 6 months. Radiologic diagnosis of TB activity was assigned as active, inactive or indeterminate. Typical and relatively atypical radiologic manifestations of TB in adults were also evaluated. Typical findings included upper lung involvement, cavities with nodules or micronodules and unilateral pleural effusion suggesting TB pleurisy. Atypical findings included middle or lower lower lung involvement, lobar or segmental airspace consolidation, diffuse miliary disease, bilateral pleural effusions, lymphadenopathy with no definite lung disease and airway involvement [8].

Results

Patient baseline demographics and clinical characteristics

Total of 134 patients with positive sputum AFB cultures were identified. Of these patients, 44 (33%) were classified as the delayed isolation group. An extracted comparison of the baseline characteristics of patients between early and delayed isolation groups is presented in table 1. Mean age of patients with delayed isolation was older (72 years vs. 55 years, $p < 0.001$). Patients with early isolation revealed less disease comorbidity (38% vs. 14%, $p < 0.01$), such as hypertension (32% vs. 52%, $p = 0.03$), chronic obstructive pulmonary disease (2% vs. 14%, $p = 0.02$) and malignancy (7% vs. 23%, $p < 0.01$). Patients who were isolated early seemed to have more clinical symptoms and features related to pulmonary TB such as cough, sputum, night sweat and weight loss. These patients were mostly admitted to infectious diseases or pulmonology department compared to others (76% vs. 41%, $p < 0.001$). Both the median hospitalization days (10 days vs. 19 days, $p < 0.001$) and the days before isolation (<1 day vs. 9 days, $p < 0.001$) were longer in those who had delayed isolation. The in-hospital mortality was 13% (17/134) for all patients. The difference of in-hospital mortality between the two groups was not significant (12% vs. 14%, $p = 0.82$).

Radiologic findings

The characteristics of radiologic findings of pulmonary TB in our patients are shown in table 2. Pulmonary TB was diagnosed by experienced radiologists by retrospective review of chest radiographs in 70% (94/134) of our patients. Of the remaining 40 patients, chest radiographic diagnoses were pneumonia (n=17), bronchiectasis (n=3), lung cancer (n=2), pleural effusion (n=2), nontuberculous mycobacterial disease (n=1), pulmonary fibrosis (n=1), septic lung (n=1), lung abscess (n=1) and nonspecific features including normal finding (n=12). In the delayed isolation group, chest radiographic diagnosis of TB was made in about half of the patients on retrospective review. Furthermore, chest radiographic findings of active TB and typical findings of TB in adults were observed in only 23% and 34%, respectively. Four patients (3%, 4/134) who had negative finding on chest radiograph were subsequently diagnosed as TB on chest CT scans.

Factors associated with delayed isolation of TB

Table 3 shows the logistic regression results for significant factors between patient groups isolated before and after 3 hospital days. Those with older age, comorbid malignancy and who were hospitalized in departments other than infectious diseases or pulmonology were more likely to have delayed isolation. Patients who were diagnosed as active pulmonary TB on chest radiographs were more likely to be isolated earlier.

Conclusion

Incidents of pulmonary TB outbreak is a burdensome health care concern worldwide causing in hospital transmissions and expensive medical costs. We need to be more careful and aware about the factors associated with delayed isolation. Especially in patients who are older, those with malignancy, those hospitalized to departments other than infectious diseases or pulmonology and patients with uncertain activity of pulmonary TB on chest radiograph.

Results

Table 1. Baseline demographic and clinical profiles of patients divided by isolation period.*

Characteristics	Total number of patients (n=134)	Isolated less than 3 days (n=90)	Isolated after 3 days (n=44)	p value
Age, years, mean (\pm SD)	61 (\pm 22)	55 (\pm 22)	72 (\pm 17)	<0.001
Comorbidity				
None	40 (30)	34 (38)	6 (14)	<0.01
Hypertension	52 (39)	29 (32)	23 (52)	0.03
COPD	8 (6)	2 (2)	6 (14)	0.02
Malignancy	16 (12)	6 (7)	10 (23)	<0.01
Clinical feature				
Cough	69 (52)	54 (60)	15 (34)	0.01
Sputum	43 (32)	35 (39)	8 (18)	0.02
Night sweat	10 (7)	10 (11)	0 (0)	0.03
Weight loss	23 (17)	21 (23)	2 (5)	<0.01
Other pain†	21 (16)	9 (10)	12 (27)	0.01
Laboratory result				
AFB smear	84 (63)	66 (73)	18 (41)	<0.001
TB PCR	107 (80)	78 (87)	29 (66)	<0.01
Hospitalization course				
Admission department‡	48 (36)	22 (24)	26 (59)	<0.001
Hospital days, median (range)	13 (6 - 22)	10 (3 - 17)	19 (12 - 51)	<0.001
Exposure days, median (range)	1 (0-6)	0 (0-1)	9 (6-14)	<0.001
In-hospital mortality	17 (13)	11 (12)	6 (14)	0.82

Table 2. Radiographic findings of patients divided by isolation period.*

Radiographic findings	Total number of patients (n=134)	Isolated less than 3 days (n=90)	Isolated after 3 days (n=44)	p value
TB diagnosed by radiologist	94 (70)	74 (82)	20 (46)	<0.001
Active TB findings	76 (57)	66 (73)	10 (23)	<0.001
Typical findings	76 (57)	61(68)	15 (34)	<0.001
New TB lesions	37 (28)	25 (28)	12 (27)	0.03

Table 3. Multivariate logistic regression results for associated risk factors.

Variables	Adjusted OR	95% CI	p value
Age	1.04	1.01 - 1.07	0.01
Malignancy	4.75	1.30 - 17.39	0.02
Admission department‡	4.03	1.52 - 10.74	<0.01
Radiologic activity of TB	0.22	0.08 - 0.66	0.01

* Data are numbers (%) of patients, unless otherwise indicated. SD standard deviation and PCR polymerase chain reaction. † Other pain includes musculoskeletal pain originating from sites other than thorax. ‡ Admission to departments other than infectious diseases or pulmonology.

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