

The epidemiology and association rules of concurrent pulmonary tuberculosis and extrapulmonary tuberculosis (PTB-EPTB) in China: a large-scale multi-center observational study

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Abstract

Background Tuberculosis (TB) is a multi-systemic disease with a protean presentation and remains a major global health problem. Concurrent pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) are common in clinical practice. However, the information about concurrent PTB-EPTB is scarce. This study aimed to study the epidemiology of concurrent PTB-EPTB by summarizing the diagnostic types of TB and determine the association rules by a large-scale multi-center observational study in China.

Methods The study was performed at 21 hospitals from 15 provinces in China. All the consecutive inpatient with confirmed TB diagnosis during the years from Jan 2011 to Dec 2017 was included in the study. The association rules of concurrent PTB-EPTB were analyzed by Apriori algorithm.

Results Of 438,979 TB inpatients evaluated, the most common were PTB (82.05%), followed by tuberculous pleurisy (23.62%), etc. Concurrent PTB-EPTB occurred in 129,422 cases (29.48%). Concurrent PTB and tuberculous pleurisy was the most common concurrent PTB-EPTB types. In the fully adjusted multivariable logistic models, the odds ratio of concurrent PTB-EPTB was different by gender and age group. In PTB with concurrent EPTB, the strongest association rule was PTB with concurrent bronchial tuberculosis (lift=1.09). In EPTB with concurrent PTB, the strongest association rule was pharyngeal /laryngeal tuberculosis with concurrent PTB (lift=1.11). The confidence and lift of concurrent PTB-EPTB varied with gender and age.

Conclusions There were many types of concurrent PTB-EPTB. The confidence and lift of concurrent PTB-EPTB varied with gender and age. The clinicians should be alert to the presence of concurrent PTB-EPTB and take effective treatment regimen.

Background

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. TB remains a major global health problem. It causes ill-health among millions of people each year worldwide. According to the World Health Organization (WHO), the estimated global incidence of TB cases was 10.0 million in 2018[1]. TB typically affects the lungs (pulmonary TB, PTB) but can also affect other sites (extrapulmonary TB, EPTB), such as pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges, etc [2–5].

In recent years, considerable efforts have been made to gain a deeper understanding of TB [6–8]. TB is a multi-systemic disease with a protean presentation. In clinical practice, PTB and EPTB may be present in the same patient [9, 10]. The treatment of PTB concurrent with EPTB is difficult, and the treatment regimen of some PTB concurrent with EPTB may be different from single PTB or EPTB. However, the information about concurrent PTB-EPTB is scarce. Consequently, summarizing the diagnostic types of TB patients, exploring the epidemiology and association rules of concurrent PTB-EPTB is important. The purpose of the study was to analyze the epidemiology, association rules of concurrent PTB-EPTB, alert clinicians to the presence of concurrent PTB-EPTB and forewarning treatment regimen by a large-scale multi-center observational study.

Methods

Study subjects

The study was performed at 21 Hospitals from 15 provinces in China. All the consecutive inpatient with confirmed TB diagnosis during the years from Jan 2011 to Dec 2017 was included in the study. TB was mainly categorized by the lesion site. Diagnosis of TB was made by WHO guidelines [11] and Clinical Diagnosis Standard of TB issued by Chinese Medical Association [12]. In general, TB has generally been diagnosed by traditional and modern methods that rely on clinical symptoms, physical signs together with the results of bacteriological methods (including sputum smear microscopy, bacterial culture and molecular diagnostic methods), the tuberculin skin test (TST; purified protein derivative (PPD) skin test), X-ray examination results, T-SPOT.TB, Gene Xpert MTB/RIF assay, and successful outcome of treatment with a course of tuberculosis chemotherapy, etc.

Data Management And Statistical Analysis

Measures taken to guarantee the data quality included standardized study protocol and standardized training of research staff. Trained health workers collected medical information by use of a standardized questionnaire. From medical records, we obtained the clinical characteristics of TB inpatients such as age, gender, site of disease etc. The descriptive statistical analysis included frequencies and proportions with 95% confidence intervals (CIs) for categorical variables. Multivariable logistic regression was used to examine the association of gender and age group with the odds ratio of concurrent PTB-EPTB. $P < 0.05$ was the threshold for statistical significance.

Analysis by association rules is used for discovering relationships hidden in large databases. The technique was developed in computer science and has been used in a variety of fields [13–15]. The Apriori algorithm provides a way of applying a set of association rules in data mining. The principle of Apriori is based on two steps. The first step searches for item sets that exceed the minimum support, while in the second step, association rules are generated and filtered by selecting “confidence” item sets (based on a threshold) from those found in the first step [16, 17]. If the association rule of A concurrent with B, support, confidence and lift were defined as: Support = $P(A)$, Confidence = $P(B|A)$, Lift = $P(A \cap B) / [P(A) * P(B)]$. A is antecedent and B is consequent. Lift was used to evaluate the magnitude of association rules. Lift > 1 indicate a positive association rule. The association rules for concurrent PTB and the diverse types of EPTB were analyzed by Apriori algorithm through setting the minimum support degree and the minimum confidence degree.

All data were collected in MS Office Excel (Microsoft, Redmond, WA, USA) datasheets and all analyses were conducted using SPSS software for Windows, version 13 (Chicago, USA) and SPSS modler14.1 (IBM Corp, Armonk, NY, USA).

Results

TB patient characteristics

A total of 438,979 TB inpatients were included from Jan 2011 to Dec 2017 at 21 hospitals from 15 provinces in China, most of which were specialized tuberculosis hospitals (Fig. 1). The ratio of male: female was 1.83. There were 83 kinds of tuberculous lesions involved in 604,114 sites in the 438,979 TB inpatients. On average each TB inpatient had 1.38 TB lesion types. Among the 438,979 TB inpatient cases, the most common types of TB were PTB (82.05%, 95%CI: 81.94%-82.16%), followed by tuberculous pleurisy (23.62%, 95%CI: 23.49%-23.74%), bronchial tuberculosis (7.01%, 95%CI: 6.94%-7.09%), etc. The types of TB proportion $\geq 0.1\%$ cases were shown in Table 1.

Table 1
The proportion of TB diagnosis (proportion $\geq 0.1\%$)

TB types	Frequency	Proportion(95%CI) (%)
pulmonary tuberculosis	360187	82.0511(81.9372–82.1645)
tuberculous pleurisy	103680	23.6184(23.4929–23.7444)
bronchial tuberculosis	30779	7.0115(6.9361–7.0874)
tuberculous meningitis	15711	3.5790(3.5242–3.6344)
tuberculous lymphadenitis of the neck	15282	3.4813(3.4272–3.5359)
tuberculous peritonitis	10059	2.2915(2.2474–2.3362)
tuberculous empyema	7341	1.6723(1.6346–1.7107)
lumbar vertebra tuberculosis	7190	1.6379(1.6006–1.6759)
tuberculous pericarditis	5842	1.3308(1.2971–1.3652)
thoracic vertebra tuberculosis	5317	1.2112(1.1791–1.2440)
tuberculous polyserositis	4870	1.1094(1.0786–1.1408)
intestinal Tuberculosis	4711	1.0732(1.0429–1.1041)
chest wall tuberculosis	4639	1.0568(1.0267–1.0875)
tuberculosis of mediastinal lymph nodes	3482	0.7932(0.7672–0.8199)
renal tuberculosis	2793	0.6362(0.6129–0.6602)
pharyngeal and laryngeal tuberculosis	2382	0.5426(0.5221–0.5648)
pelvic tuberculosis	1835	0.4180(0.3991–0.4376)
tuberculosis of axillary lymph nodes	1521	0.3465(0.3293–0.3643)
knee joint tuberculosis	1179	0.2686(0.2535–0.2843)
tuberculosis of hilar lymph nodes	1117	0.2545(0.2398–0.2698)
hip joint tuberculosis	989	0.2253(0.2115–0.2398)
pleural tuberculoma	917	0.2089(0.1956–0.2229)
cutaneous tuberculosis	871	0.1984(0.1855–0.2120)
epididymal tuberculosis	794	0.1809(0.1685–0.1939)
tuberculosis of abdominal lymph nodes	651	0.1483(0.1371–0.1601)
sacroiliac joint tuberculosis	574	0.1308(0.1203–0.1419)
tuberculous abscess of psoas major	528	0.1203(0.1102–0.1310)
cervical vertebra tuberculosis	513	0.1169(0.1070–0.1274)
testicular tuberculosis	495	0.1128(0.1031–0.1231)
Note: proportion = frequency*100%/438979		

Patients With Concurrent PTB-EPTB

A total of 129,422 (29.48%, 95%CI: 29.35%-29.62%) concurrent PTB-EPTB inpatients were found in all the TB inpatients. An age-gender pyramid figure of concurrent PTB-EPTB was shown in Figure S1 in the Supplementary Appendix. In each age group, the number of concurrent PTB-EPTB cases in males was

more than in females. In the fully adjusted multivariable logistic models, female (OR = 1.119, 95%CI:1.104–1.134), < 15years(OR = 1.602,95%CI:1.521–1.686), 15–24 years (OR = 1.831, 95%CI:1.792–1.871), 25–34 years (OR = 1.700, 95% CI: 1.664–1.738), 35–44 years (OR = 1.358, 1.327–1.391), 45–54 years (OR = 1.084, 95%CI: 1.059–1.109) were more likely to have concurrent PTB-EPTB, while 55–64 years (OR = 0.971, 95%CI: 0.949–0.994) was less likely to have concurrent PTB-EPTB (Table 2).

Table 2
The associations between PTB concurrent with EPTB and gender, age group

Characteristics	No. of PTB concurrent with EPTB (%)	aOR (95%CI)	P
gender			
female	49209(31.7)	1.119(1.104–1.134)	< 0.001
male	80213(28.3)	Reference	
Age group(years)			
< 15	2417(34.2)	1.602(1.521–1.686)	< 0.001
15–24	27094(37.2)	1.831(1.792–1.871)	< 0.001
25–34	26806(35.6)	1.700(1.664–1.738)	< 0.001
35–44	17193(30.5)	1.358(1.327–1.391)	< 0.001
45–54	18154(25.8)	1.084(1.059–1.109)	< 0.001
55–64	16835(23.7)	0.971(0.949–0.994)	0.014
≥ 65	20923(24.3)	Reference	

The most common of concurrent PTB–EPTB types

According to the association rules analysis of concurrent PTB-EPTB, the TOP 20 most common of concurrent PTB-EPTB were listed in Table S1 in the Supplementary Appendix, sort by cases. Concurrent PTB and tuberculous pleurisy (15.35%, 95%CI: 15.25%-15.46%), concurrent PTB and bronchial tuberculosis (6.28%, 95%CI: 6.20%-6.35%) were more than others concurrent PTB-EPTB types.

The association rules analysis of concurrent PTB-EPTB

In order to find most of the possible association rules with Antecedent = PTB, the minimum confidence degree was set as 1.00%. After executing the association model, six association rules were obtained. The association rules were shown in Table 3, sorted by confidence. The first rule row (ID = 1) in Table 3 was interpreted as showing that with PTB totaling 360,187 cases (Instances), PTB accounted for 82.05% of all TB cases (Support), PTB with concurrent tuberculous pleurisy accounting for 18.71% of PTB cases (Confidence). The confidence of concurrent bronchial tuberculosis in PTB cases was the next highest (7.65%), followed by tuberculous meningitis (2.72%), etc. The strongest association rule in PTB with concurrent EPTB was PTB with concurrent bronchial tuberculosis (lift = 1.09). The lift value of 1.09 means PTB was positively associated with bronchial tuberculosis.

Table 3
The association rules of PTB with concurrent EPTB where Antecedent = PTB, Minconfidence = 1.00%

Consequent	Antecedent	ID	Instances	Support (%)	Confidence (%)	Lift
tuberculous pleurisy	pulmonary tuberculosis	1	360187	82.05	18.71	0.79
bronchial tuberculosis	pulmonary tuberculosis	2	360187	82.05	7.65	1.09*
tuberculous meningitis	pulmonary tuberculosis	3	360187	82.05	2.72	0.76
tuberculous lymphadenitis of neck	pulmonary tuberculosis	4	360187	82.05	1.93	0.56
tuberculous peritonitis	pulmonary tuberculosis	5	360187	82.05	1.59	0.69
tuberculous empyema	pulmonary tuberculosis	6	360187	82.05	1.05	0.63

In order to find most of the possible association rules with Consequent = PTB, the minimum support degree was set as 0.1% and the minimum confidence degree was set as 40%. After executing the association model, 22 association rules were obtained, including five rules with confidence above 70%. The association rules were shown in Table 4, sorted by confidence. The first rule row (ID = 1) in Table 4 was interpreted as showing that 2,382 cases (Instances) of pharyngeal/laryngeal tuberculosis accounted for 0.54% of all TB cases (Support), pharyngeal /laryngeal tuberculosis with concurrent PTB accounted for 91.23% of pharyngeal/laryngeal tuberculosis cases (Confidence).The confidence of concurrent PTB in bronchial tuberculosis cases was the next highest

(89.51%), followed by tuberculosis of mediastinal lymph nodes (77.57%), etc. The strongest association rule in EPTB with concurrent PTB were pharyngeal/laryngeal tuberculosis (lift = 1.11). That means pharyngeal/ laryngeal tuberculosis were positively associated with PTB.

Table 4
The association rules of EPTB with concurrent PTB where Consequent = PTB, Minsupport = 0.1%, Minconfidence = 40%

Consequent	Antecedent	ID	Instances	Support (%)	Confidence (%)	Lift
PTB	pharyngeal/laryngeal tuberculosis	1	2382	0.54	91.23	1.11*
PTB	bronchial tuberculosis	2	30779	7.01	89.51	1.09*
PTB	tuberculosis of mediastinal lymph nodes	3	3482	0.79	77.57	0.95
PTB	tuberculosis of hilar lymph nodes	4	1117	0.25	74.93	0.91
PTB	intestinal tuberculosis	5	4711	1.07	71.75	0.87
PTB	tuberculosis of abdominal lymph nodes	6	651	0.15	66.36	0.81
PTB	tuberculous pleurisy	7	103680	23.62	65.01	0.79
PTB	tuberculous meningitis	8	15711	3.58	62.43	0.76
PTB	tuberculous polyserositis	9	4870	1.11	59.22	0.72
PTB	tuberculous pericarditis	10	5842	1.33	58.18	0.71
PTB	tuberculous peritonitis	11	10059	2.29	56.99	0.69
PTB	testicular tuberculosis	12	495	0.11	54.75	0.67
PTB	tuberculous empyema	13	7341	1.67	51.53	0.63
PTB	sacroiliac joint tuberculosis	14	574	0.13	50.87	0.62
PTB	chest wall tuberculosis	15	4639	1.06	48.35	0.59
PTB	thoracic vertebra tuberculosis	16	5317	1.21	46.00	0.56
PTB	tuberculous lymphadenitis of the neck	17	15282	3.48	45.58	0.56
PTB	pleural tuberculoma	18	917	0.21	45.37	0.55
PTB	epididymal tuberculosis	19	794	0.18	45.21	0.55
PTB	cutaneous tuberculosis	20	871	0.20	45.01	0.55
PTB	renal tuberculosis	21	2793	0.64	43.04	0.52
PTB	pelvic tuberculosis	22	1835	0.42	42.78	0.52
Notes: The first column represents the consequents (the "then" part of the rule), while the next column represents the antecedents (the "if" part of the rule).						
ID displays the sequence of the association rules.						
Instances display the cases of TB.						
*: lift > 1						

The association rules of concurrent PTB-EPTB types with gender

Most types of TB can be found both in males and females, with obvious exceptions such as tuberculosis of ovary, oviduct tuberculosis etc. We found association rules in males and females through setting the minimum support degree and the minimum confidence degree (Tables S2&3 in the Supplementary Appendix). In males, tuberculous empyema with concurrent PTB was the strongest association rule (lift = 1.20), followed by costal tuberculosis with concurrent PTB (lift = 1.16), etc. In females, bronchial tuberculosis with concurrent PTB was the strongest association rule (lift = 1.64), followed by supraclavicular lymph node tuberculosis with concurrent PTB (lift = 1.56), etc.

The association rules of concurrent PTB-EPTB types with age

We found association rules in all age groups through setting the minimum support degree and the minimum confidence degree (Tables S4 ~ S10 in the Supplementary Appendix). In patients < 15 years of age, tuberculous meningitis with concurrent PTB was the strongest association rule (lift = 3.89), followed by tuberculosis of axillary lymph nodes with concurrent PTB (lift = 3.78), cervical vertebra tuberculosis with concurrent PTB (lift = 3.61), etc. In patients aged 15–24 years, splenic tuberculosis with concurrent PTB was the strongest association rule (lift = 2.23), followed by tuberculous myelitis with concurrent PTB (lift = 2.18), etc. In patients aged 25–34, oviduct tuberculosis with concurrent PTB was the strongest association rule (lift = 3.09), followed by endometrial tuberculosis with concurrent PTB (lift = 2.17), etc. In patients aged 35–44 years, the strongest association rule was again oviduct tuberculosis with concurrent

PTB (lift = 1.71), followed by endometrial tuberculosis with concurrent PTB (lift = 1.69), etc. In patients aged 45–54 years, the strongest association rule was vocal cord tuberculosis with concurrent PTB (lift = 1.61), followed by wrist joint tuberculosis with concurrent PTB (lift = 1.57), etc. In TB patients aged 55–64 years, the strongest association rule was ankle joint tuberculosis with concurrent PTB (lift = 1.55), followed by adrenal tuberculosis with concurrent PTB (lift = 1.51), etc. In TB patients aged ≥ 65 years, the strongest association rule was tuberculous pericarditis with concurrent PTB (lift = 1.42), followed by hilar lymph nodes with concurrent PTB (lift = 1.30), etc.

Discussion

TB is spread when people who are sick with PTB expel the bacteria into the air. When a person breathes in TB bacteria, the bacteria can settle in the lungs and begin to grow. From there, they can disseminate through the lymphatic or hematogenous systems and subsequently affect single or multiple extrapulmonary sites, such as the pleura, lymph nodes, meninges, bones and joints, etc. PTB is the most common presentation of TB. However, EPTB contributes considerably to morbidity, lifelong sequelae, and mortality [18]. The mechanisms for EPTB dissemination are complicated [19]. PTB concurrent with EPTB are common in clinical practice, but the information about concurrent PTB-EPTB is scarce. Given the variety of clinical presentations and the nonspecific systemic symptoms of TB, a more profound understanding of the site distribution of TB should be sought. In this study, we summarized the diagnostic types of TB and explored the association rules of concurrent PTB-EPTB so as to alert the clinicians to the presence of concurrent PTB-EPTB by a large TB sample.

Tuberculous pleurisy was one of the most common forms of EPTB [20]. We found tuberculous pleurisy (23.62%) was the second most common types of TB. Tuberculous pleurisy is thought to represent primarily a hypersensitivity reaction to tuberculous protein [21]. Previous studies have also noted that concurrent PTB-EPTB patients [9, 10]. Boonsangskul et al [9]. demonstrated that 12.2% were of concurrent PTB-EPTB (120/986). In this study, concurrent PTB-EPTB occurred in about 30% in TB patients. We also found that the strongest association rule of PTB concurrent with EPTB was PTB concurrent with bronchial tuberculosis (lift = 1.09). In this study, 7.65% PTB had concurrent bronchial tuberculosis. Because bronchi are adjacent to the lung, PTB is prone to cause bronchial tuberculosis. But this is not inevitable, hence the proportion of EPTB with concurrent PTB was different depending on whether patients were primarily viewed as EPTB or PTB patients. Laryngeal tuberculosis was an infrequent manifestation of EPTB. Usually, it was seen as a complication of PTB [22]. The strongest association rule of EPTB concurrent with PTB was pharyngeal/ laryngeal tuberculosis concurrent with PTB (lift = 1.11). In this study, 91.23% of the pharyngeal/laryngeal tuberculosis patients had concurrent PTB. Expulsion of Mycobacterium tuberculosis by PTB patients is liable to affect the larynx. Consistent with this, most of laryngeal tuberculosis patients had concurrent PTB. These findings suggested that once PTB was diagnosed, bronchial tuberculosis should be considered first. Furthermore, once pharyngeal/laryngeal tuberculosis or bronchial tuberculosis was confirmed, attention should be paid to PTB. In essence, the diagnosis of TB must be carefully undertaken to avoid misdiagnosis.

Most types of tuberculous lesions can be found both in males and females. But female (OR = 1.119, 95%CI: 1.104–1.134) was more likely to have concurrent PTB-EPTB than male in this study. Jung et al. [23] also found female gender was an independent predictor of concomitant EPTB in patients with active PTB (OR = 4.35, 95%CI: 1.78–10.63). The magnitude of association rules of concurrent PTB-EPTB varied with gender. In males in this study, tuberculous empyema with concurrent PTB was the strongest association rule (lift = 1.20). The proportions of tuberculous empyema with concurrent PTB in male were more than 70%. In females, bronchial tuberculosis with concurrent PTB was the strongest association rule (lift = 1.64). The proportion of bronchial tuberculosis with concurrent PTB in females was more than 55%. Cellular immunity, hormones, access to health care, socio-economic factors and cultural factors had been linked to these differences [24–26].

TB affects all age groups, but overall the best estimate for 2018 was that about 90% of cases were adults (aged ≥ 15 years). The prevalence of TB is strongly associated with age [1]. Our research found that the strongest association rule in children and adolescents (< 15 years) were PTB with concurrent tuberculous meningitis (lift = 3.89). This may be also related to the particular physiological characteristics and the immunological mechanisms in children and adolescents. We also found that the strongest association rule in 15–24 year group of TB patients was splenic tuberculosis with concurrent PTB (lift = 2.23). Splenic tuberculosis is mostly caused by hematogenous dissemination and a small number of the bacteria can directly spread to the spleen via the lymphatic pathway and adjacent organs [27]. Our study showed that oviduct tuberculosis with concurrent PTB was the strongest association rule in the 25–34 (lift = 3.09) and 35–44 (lift = 1.71) year groups. The age range of 25–44 years is the main child-bearing age and is thought to be the most risky time to get genital tuberculosis. Oviduct tuberculosis is an important chronic pelvic disease and etiology of infertility. Spread of the infection is usually through the hematogenous systems, while direct spread from other abdominal organs and the peritoneum is also possible [28]. Isolated vocal cord tuberculosis and ankle tuberculosis were rarely reported; vocal cord tuberculosis with concurrent PTB was the strongest association rule in ages 45–54 years (lift = 1.61); ankle joint tuberculosis with concurrent PTB was the strongest association rule in ages 55–64 years (lift = 1.55). Tuberculous pericarditis refers to an infection of the membrane that covers the heart (pericardium) by the Mycobacterium tuberculosis. In endemic areas, tuberculous pericarditis has been found in 1–2% of people who have pulmonary tuberculosis [29]. We found that tuberculous pericarditis with concurrent PTB was the strongest association rule in ≥ 65 -year-old TB patients (lift = 1.42).

This study had several strengths including its large-scale multi-center representative sample, and detailed analysis of the diagnostic types of TB and the confidence/lift of concurrent PTB-EPTB for the first time in the world. There were several limitations to our study. First, our study may have been subject to Berkson bias. The study population was hospitalized TB patients. There is a high likelihood that the concurrent PTB-EPTB would have more possibility to be hospitalized, which may overestimate the proportions in the population at large. Therefore, data collected from whole population-based studies will be needed to clarify the associations. Secondly, most of the hospitals in our study were TB-specialized hospitals. Therefore, these findings may not represent the general TB patient population and may not apply to settings elsewhere in the country. Thirdly, some TB-specialized hospitals in our country do not admit pediatric TB. Therefore the results may underestimate the proportion of pediatric TB. Lastly, the analysis did not consider disease complications and comorbidities such as HIV; which was low in China.

Conclusions

In conclusions, our present study found many types of concurrent PTB-EPTB and analyzed the association rules between PTB and EPTB for the first time in the world by a large sample. The concurrent PTB and tuberculous pleurisy was the most common types of concurrent PTB-EPTB. The strongest association rule in PTB with concurrent EPTB was PTB with concurrent bronchial tuberculosis. The strongest association rule in EPTB with concurrent PTB was pharyngeal/laryngeal tuberculosis with concurrent PTB. The confidence and lift of concurrent PTB-EPTB varied with gender and age. The clinicians should be alert to the presence of concurrent PTB-EPTB and take effective treatment regimen to treat the patients.

Declarations

Ethical Approval and Consent to participate: Given that the medical information of inpatients was recorded anonymously by case history, which would not bring any risk to the participants, the Ethics Committee of Beijing Chest Hospital, Capital Medical University approved this study with a waiver of informed consent from the patients.

Consent for publication: Not applicable.

Availability of supporting data: Data are not publicly available. However, de-identified data can be obtained on a reasonable request to correspondence.

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Figures



Figure 1

Geographical distribution of TB inpatient enrolled in this study (*) Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

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