

Original Article

Incidence, causes, and risk factors for unplanned readmission in patients admitted with pulmonary tuberculosis in ChinaXinchun Ye¹, Xiaoqiao Su¹, Jichan Shi¹, Xiangao Jiang¹, Saiduo Liu¹, Fang Cheng¹, Ning Pan¹, Chaochao Qiu¹, Chenwei Pan²¹ *The Theorem Clinical College of Wenzhou Medical University, Department of Infectious Disease of Wenzhou Central Hospital, Wenzhou, Zhejiang, China*² *Department of Infectious Disease, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang, China***Abstract**

Introduction: To investigate the incidence, causes, and risk factors for unplanned readmission within 30 days of discharge in patients with pulmonary tuberculosis (TB).

Methodology: The clinical data of 1,062 patients with confirmed pulmonary TB who were admitted to our hospital from October 2018 to October 2021 were analysed retrospectively. The subjects were divided into a readmission group (354 cases) and a non-readmission group (708 cases) according to whether there was an unplanned admission within 30 days of discharge. We analysed the risk factors for unplanned readmission within 30 days after discharge with pulmonary TB.

Results: The incidence of unplanned readmission in patients with pulmonary TB was 5.2%. Being female (OR = 0.63, 95% CI: 0.434–0.942) and living in cities (OR = 0.218, 95% CI: 0.151–0.315) were protective factors for the readmission of patients with TB ($p < 0.05$). However, being ≥ 65 years old (OR = 2.574, 95% CI: 1.709–3.870), being a smoker (OR = 2.773, 95% CI: 1.751–4.390), having chronic obstructive pulmonary disease (COPD) (OR = 3.373, 95% CI: 1.708–6.660), having viral hepatitis (OR = 2.079, 95% CI: 1.067–4.052), receiving non-standard treatment (OR = 15.620, 95% CI: 10.413–23.431), having medical side effects (OR = 6.138, 95% CI: 3.798–9.922) and 1 unauthorised discharge (OR = 2.570, 95% CI: 1.509–4.376) were risk factors for the readmission to hospital of patients with TB ($p < 0.05$).

Conclusions: Gender, age, place of residence, smoking, COPD, hepatitis, non-standard treatment, adverse drug reactions and unauthorised discharge were risk factors of TB for unplanned readmission.

Key words: tuberculosis; unplanned readmission; logistic regression analysis; risk factors.

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Introduction

Tuberculosis (TB) is a chronic infectious disease that occurs mainly in the lung tissue, trachea, bronchi, and pleura. It has become one of the 10 major causes of death in the world and the second-largest single cause of death after COVID-19 pneumonia [1]. It poses a major threat to the life and health of all human beings [2-4]. According to the World Health Organization's (WHO) 2021 report, due to the impact of the new coronary pneumonia epidemic, it is estimated that there were 9.9 million new cases of TB in 2020, equivalent to 127 cases per 100,000 people [5]. Although the incidence of TB in China has been on a downward trend since 2000, China still has a high incidence of TB [6]. The estimated number of new TB cases in China in 2020 was 842,000 (833,000 in 2019 and 866,000 in 2018) [6]. This means that the United Nations' high-

level meeting goal of treating 40 million patients with TB between 2018 and 2022 is no longer possible [5]. In addition, the negative impact of rising TB mortality in 2020 increased in severity in 2021 and will continue to do so, with TB mortality forecasts for 16 key countries accounting for 71% of global TB incidence in 2020, which was much higher in 2021 than in 2020 [5]. However, there is an even greater delay in the impact of the COVID-19 pandemic on the incidence of TB, and the greatest impact on the global incidence of TB will occur in late 2022 [5]. Therefore, the social and economic burdens of TB on China and the world cannot be underestimated.

Unplanned readmissions are defined as unpredictable readmissions for the same or related conditions [7]. Unplanned readmissions can increase financial burdens on patients, reduce patients' quality

of life, delay or interrupt courses of treatment, and even endanger patients' lives [8]. Unplanned readmissions after hospitalisation also place a burden on patients and healthcare resources due to high costs [9]. To date, little research has been conducted on the risk factors for unplanned readmission for TB. Therefore, this study aimed to investigate the risk factors related to the unplanned readmission of patients with pulmonary TB after discharge from the hospital and to provide a reference for effectively reducing the readmission rate, improving both the prognosis of patients and their quality of life.

Methodology

Study design

This study was a single-centre retrospective study.

Study context

All the participations came from the designated TB hospital of the Sixth People's Hospital of Wenzhou City, Zhejiang Province, China. Readmission data were collected from the hospital's electronic medical records surveillance database and validated. The patients were divided into a readmission group and a non-rehospitalisation group according to whether they were readmitted due to TB-related diseases or complications within 30 days after discharge. A total of 1,062 cases were collected in this study, including 354 cases in the readmission group and 708 cases in the non-readmission group.

Study population

Patients with confirmed pulmonary TB who were admitted to the designated TB hospital of the Sixth People's Hospital of Wenzhou City, Zhejiang Province, China, from October 2018 to October 2021 were included in the study. The inclusion criteria were (1) age > 14 years; (2) patients diagnosed with pulmonary TB according to the criteria of 'WS288-2017 Diagnosis of Pulmonary Tuberculosis' [2]. The diagnosis of pulmonary TB was based mainly on etiological examination (including bacteriology and molecular biology) combined with epidemiological history, clinical manifestation, chest imaging, relevant auxiliary examination, and differential diagnosis, etc. to formulate a diagnosis by comprehensive analysis. The final diagnosis was based on the results of aetiology and pathology. (2) The exclusion criteria were (1) patients with other diseases, including severe infections and tumours, (2) patients who died during hospitalisation or within 30 days of discharge, (3) patients who were readmitted due to non-TB reasons, (4) patients with

incomplete clinical data and (5) patients who failed to complete the follow-up.

Sampling size and sampling technique

Convenience sampling was used in this study. Patients who met the inclusion and exclusion criteria were included in the research, and the sample size was not determined in advance.

Data collection

We collected the patients' basic information and medical information from the hospital's electronic medical record monitoring database, including gender, age, residence, smoking history, complications, drug use, and standard indicators.

Statistical analysis

In this study, SPSS 25.0 software was used for the statistical analysis of the data. Measurement data conforming to a normal distribution were expressed as mean \pm standard deviation, an independent-samples *t*-test was used for comparison between groups, and median (interquartile range) (M [P25, P75]) was used for data that did not conform to a normal distribution. Nonparametric tests were used for comparisons between groups, count data were expressed as frequencies and percentages, and the Chi-squared test or Fisher's exact test was used for comparisons between groups. Before performing the multivariate logistic regression analysis, first, we used univariate logistics to determine the indicators included in the multivariate logistic regression equation; then, we performed a multivariate logistic regression analysis to determine the risk factors for unplanned readmission. Statistical significance was established at $p < 0.05$.

Bias

Due to the impact of COVID-19 in 2020, a significant reduction in the number of cases may have affected the statistical results.

Operational definition- Mini staining microscopy

The operation was performed in accordance with the procedures and frequency required by the standardised operation and quality assurance manual for sputum smear microscopy [10].

Genexpert MTB/RIF detection system

A digestive solution (1:1) was added to bronchoalveolar lavage fluid (BALF) at room temperature (37 °C). Then, it was subjected to vortex oscillation until there was no visible granular substance

in the mixture. The mixture was added to a reaction kit, which was placed into a GeneXpert MTB/RIF detection system (Cepheid, USA) for automatic detection. It was operated according to the instrument's operating instructions, and the detection results were interpreted automatically.

Mycobacterium culture and drug sensitivity test

A BACTEC™ MGIT 960 detection system was used for *Mycobacterium* culture. After the BALF was fully mixed, 5 ml was removed and placed in a centrifuge tube, and the digestive solution was added. Vortex oscillation was performed until the digestion was complete. After separation, the supernatant was

Table 1. Risk factors for unplanned admission to pulmonary tuberculosis.

Characteristics	non-readmission group (N = 708)	readmission group (N = 354)	χ^2	P
Sex				
Male	446 (63.0%)	250 (70.6%)	6.078	0.014
Female	262 (37.0%)	104 (29.4%)		
Age				
< 65 years	594 (83.9%)	230 (65.0%)	48.618	< 0.001
≥ 65 years	114 (16.1%)	124 (35.0%)		
Marital status				
Unmarried	106 (15.0%)	54 (15.3%)	0.028	0.986
Married	579 (81.8%)	289 (81.6%)		
Divorced	23 (3.2%)	11 (3.1%)		
Type of Insurance				
Urban workers	156 (22.0%)	76 (21.5%)	0.402	0.940
Citizens	53 (7.5%)	28 (7.9%)		
New type of countryside	317 (44.8%)	164 (46.3%)		
All at own expense	182 (25.7%)	86 (24.3%)		
Place of residence				
Rural	248 (35.0%)	248 (70.1%)	116.332	< 0.001
City	460 (65.0%)	106 (29.9%)		
Hypertension				
No	623 (88.0%)	317 (89.5%)	0.560	0.454
Yes	85 (12.0%)	37 (10.5%)		
Diabetes				
No	638 (90.1%)	313 (88.4%)	0.724	0.395
Yes	70 (9.9%)	41 (11.6%)		
Smoking				
No	622 (87.9%)	257 (72.6%)	38.504	< 0.001
Yes	86 (12.1%)	97 (27.4%)		
Alcoholism				
No	639 (90.3%)	309 (87.3%)	2.167	0.141
Yes	69 (9.7%)	45 (12.7%)		
COPD				
No	683 (96.5%)	311 (87.9%)	29.232	< 0.001
Yes	25 (3.5%)	43 (12.1%)		
Viral hepatitis				
No	669 (94.5%)	318 (89.8%)	7.812	0.005
Yes	39 (5.5%)	36 (10.2%)		
Tuberculosis type				
NO	112 (15.8%)	50 (14.1%)	0.524	0.469
Yes	596 (84.2%)	304 (85.9%)		
Drug abuse				
No	663 (93.6%)	216 (61.0%)	176.148	< 0.001
Yes	45 (6.4%)	138 (39.0%)		
Non-standard treatment				
No	651 (91.9%)	145 (41.0%)	326.824	< 0.001
Yes	57 (8.1%)	209 (59.0%)		
Medical side effects				
No	660 (93.2%)	225 (63.6%)	149.492	< 0.001
Yes	48 (6.8%)	129 (36.4%)		
Leaving the hospital without medical advice				
No	652 (92.1%)	279 (78.8%)	38.471	< 0.001
Yes	56 (7.9%)	75 (21.2%)		

discarded. A small amount of phosphate buffer saline was added to the sediment for resuspension; then, the suspension was taken and added to the MGIT tube for culture. The culture-positive tube was reconfirmed by acid-fast staining and subsequent strain identification. The minimum inhibitory concentration drug sensitivity to macrolides and amikacin was tested, and the H37Rv standard strain was used for quality control [11].

Ethics approval and consent to participate

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Wenzhou Central Hospital (Approval number L2022-01-054). Written informed consent was obtained from all participants.

Results

Status of unplanned readmissions

From October 2018 to October 2021, 6,866 patients with TB were admitted to the TB-designated hospital of the Sixth People's Hospital of Wenzhou City, Zhejiang Province, China, of whom 354 (5.2%) were unexpectedly readmitted after discharge. The median time to unplanned readmission after discharge was 15 days.

Univariate analysis of the risk of unplanned hospital admission during anti-tuberculosis treatment for pulmonary tuberculosis

From Table 1, it can be seen that there were significant statistical differences between the two groups in gender, age, place of residence, smoking, COPD, viral hepatitis, drug abuse, non-standard treatment, adverse drug reactions, and non-compliance with hospital discharge ($p < 0.05$). The proportion of male patients (70.6% vs 63.0%), patients aged ≥ 65 years (35.0% vs 16.1%), patients living in rural areas (70.1% vs 35.0%), smokers (27.4% vs 12.1%), patients with COPD (12.1% vs 3.5%), patients with viral hepatitis (10.2% vs 5.5%), drug abuse (39.0% vs 6.4%), patients with non-standard treatment (59.0% vs 8.1%),

patients with medical side effects (36.4% vs 6.8%) and patients leaving the hospital without medical advice (21.2% vs 7.9%) was higher in the readmission group than in the non-readmission group (Table 1).

The tabular factor results showed that readmission and sex (OR = 0.708, 95% CI: 0.538–0.932, $p = 0.014$), age (OR = 2.809, 95% CI: 2.089–3.778, $p < 0.001$), place of residence (OR = 0.230, 95% CI: 0.175–0.303, $p < 0.001$), smoking (OR = 3.730, 95% CI: 1.973–3.777, $p < 0.001$), COPD (OR = 3.777, 95% CI: 2.266–6.296, $p < 0.001$), viral hepatitis (OR = 1.942, 95% CI: 1.211–3.114, $p = 0.006$), drug abuse (OR = 9.413, 95% CI: 6.503–13.625, $p < 0.001$), non-standard treatment (OR = 16.462, 95% CI: 11.673–23.215, $p < 0.001$), adverse drug reactions (OR = 7.883, 95% CI: 5.477–11.348, $p < 0.001$) and non-compliant discharge (OR = 3.130, 95% CI: 2.154–4.547, $p < 0.001$) were significantly correlated, as shown in Table 2.

Multivariate analysis of the risk of unplanned admission during anti-tuberculosis treatment for pulmonary tuberculosis.

The significant indexes in the single-factor logistics regression analysis were included in the multi-factor logistics regression analysis, and the forward method was used to screen the indexes. The results showed that gender, age, place of residence, smoking, COPD, viral hepatitis, standardized treatment, medical side effects, and unauthorised discharge were the influencing factors for the readmission of patients with pulmonary TB.

Being female (OR = 0.639, 95% CI: 0.434–0.942) and living in cities (OR = 0.218, 95% CI: 0.151–0.315) were protective factors, meaning that male patients and rural residents were more likely to have unplanned hospital readmissions. Being ≥ 65 years old (OR = 2.574, 95% CI: 1.709–3.87), a smoker (OR = 2.773, 95% CI: 1.751–4.390), having COPD (OR = 3.373, 95% CI: 1.708–6.660), having viral hepatitis (OR = 2.079, 95% CI: 1.067–4.052), non-standard treatment (OR = 15.620, 95% CI: 10.413–23.431), medical side effects (OR = 6.138, 95% CI: 3.798–9.922) and leaving the hospital without medical advice (OR = 2.570, 95%

Table 2. Logistic regression analysis of risk factors for unplanned readmission within 30 days of discharge.

Index	B	OR (95% CI)	p
Sex	-0.448	0.639 (0.434-0.942)	0.024
Age	0.946	2.574 (1.709-3.877)	< 0.001
Place of residence	-1.523	0.218 (0.151-0.315)	< 0.001
Smoking	1.020	2.773 (1.751-4.390)	< 0.001
COPD	1.216	3.373 (1.708-6.660)	< 0.001
Viral hepatitis	0.732	2.079 (1.067-4.052)	0.031
Non-standard treatment	2.749	15.620 (10.413-23.431)	< 0.001
Medical side effects	1.815	6.138 (3.798-9.922)	< 0.001
Leaving the hospital without medical advice	0.944	2.570 (1.509-4.376)	0.001

CI: 1.509–4.376) were risk factors for the readmission of patients with TB ($p < 0.05$). Patients older than 65 years were 1.574 times more likely to have unplanned readmissions than those younger than 65, and smokers were 1.773 times more likely to be readmitted. Patients with COPD and hepatitis were 2.373 and 1.079 times, respectively, more likely to have an unplanned readmission, and patients receiving non-standard treatment were 14.620 times more likely to have an unplanned readmission. Patients who had adverse drug reactions and disobeyed medical advice also had a 5.138-fold and 1.570-fold increased probability of unauthorised discharge, respectively (Table 3).

Discussion

In this study, the unplanned readmission rates for TB were low, and we concluded that gender, age, place of residence, smoking status, COPD, hepatitis, non-standard treatment, adverse drug reactions, and unauthorised discharge were risk factors for unplanned readmission.

According to WHO guidelines, hospitalisation does not affect the treatment management of patients with TB [12]. The British Thoracic Society recommends that most patients do not require hospitalisation and can be treated and supervised as outpatients [13]. The Medicare Payment Advisory Commission has made readmission a priority for some time, but it is still widespread, expensive, and largely preventable [14]. The Department of Health and Human Services strategic plan 2010–2015 cites ‘Payment incentives to avoid readmission’ as an example of quality [15], and the Centers for Medicare and Medicaid Services National Strategy for Healthcare Quality Improvement also lists hospital readmission rates separately for improvement [16].

This study was a retrospective study on patients with recurrent pulmonary TB. In this research, the rate of unplanned readmission of patients with pulmonary TB within 30 days after discharge was 5.2%, lower than that reported by Jing *et al.* (5.91%) [17]. The present study showed significant associations among

unplanned readmissions in terms of gender, age, place of residence, smoking, COPD, viral hepatitis, drug abuse, non-standard treatment, adverse drug reactions, and noncompliance with hospital discharge. Based on univariate and multivariate regression analyses, our study confirmed that males had a higher probability of readmission. Regarding the place of residence, the readmission rate of patients living in rural areas was higher than for those in urban areas. There may be various reasons for this difference, as follows. First, the prevalence of TB in rural areas of China is higher than that in urban areas [18]. People in rural areas are affected by factors such as economic and transportation limitations, and they often delay seeking medical treatment when they become ill, which might lead to a new source of infection. In addition, poverty leads to low protein intake, which negatively affects the body’s immune system. Poverty is also associated with low levels of education, which indirectly reduce the ability of individuals to prevent TB transmission [19–21]. Therefore, future TB health education should focus on rural areas.

Studies have shown that unplanned readmissions in patients with TB are associated with being ≥ 65 years of age [22]. In the present study, age was shown to be a risk factor for readmission in patients with TB. The relationship between readmission and age can be considered related to poor immunity and increased comorbidities in elderly patients. In addition, smokers have higher readmission rates than non-smokers, and tobacco has an impact on TB/COPD morbidity and mortality [23–24].

Although our study did not show an association between TB morbidity or mortality with smoking, the results suggest that smoking is a risk factor for TB readmission. A study by Bhatt *et al.* [25] showed that middle-aged and elderly patients with COPD had a higher risk of readmission than the young. A follow-up study reported that patients with COPD and a history of TB were hospitalised more frequently and had lower long-term survival rates than patients without a history of TB [26]. Patients discharged against medical advice

Table 3. multivariate analysis of unplanned hospital admission risk.

Index	B	OR(95%CI)	p
Sex	-0.448	0.639 (0.434-0.942)	0.024
Age	0.946	2.574 (1.709-3.877)	< 0.001
Place of residence	-1.523	0.218 (0.151-0.315)	< 0.001
Smoking	1.020	2.773 (1.751-4.390)	< 0.001
COPD	1.216	3.373 (1.708-6.660)	< 0.001
Hepatitis	0.732	2.079 (1.067-4.052)	0.031
Non-standard treatment	2.749	15.620 (10.413-23.431)	< 0.001
Adverse drug reactions	1.815	6.138 (3.798-9.922)	< 0.001
Discharge from hospital against medical advice	0.944	2.570 (1.509-4.376)	0.001

also had a high rate of unplanned readmission. A case-control study revealed that the correct management of first-time patients with TB by encouraging strict medication adherence did not lead to treatment failure [27]. A study focusing on readmission within 28 days of discharge for TB showed that daily activity requirements, adverse drug reactions, non-standard treatment regimens, and coexistence of more than three non-pulmonary diseases were risk factors for readmission [28], whereas our study has also confirmed that adverse drug reactions and non-standard treatment regimens are risk factors for readmission. As Chu *et al.* reported, the presence of factors such as adverse drug reactions and multiple complications is an indication that patients may be readmitted in the future, so doctors could consider reducing patient readmission rates by extending hospital stays or providing support after discharge [29].

The hepatitis B and C viruses are China's most common causes of chronic liver disease. During anti-TB treatment, the risk of liver damage in patients with viral hepatitis is 3 to 5 times that of patients with non-viral hepatitis [30-32]. Our study revealed that viral hepatitis is a risk factor for readmission with pulmonary TB, so we need to detect hepatitis in patients before anti-TB treatment and provide early liver protection treatment if necessary.

The collection point of this study was a specialist TB hospital, the source of patients was relatively stable, a large sample size was available, and each patient was registered and followed up throughout the course of anti-TB treatment. However, this study also had some limitations. First, it was a single-centre retrospective analysis that did not have access to more information on patient readmissions, some of which were subjective. Second, due to the impact of COVID-19 in 2020, the significant reduction in the number of cases may have affected the statistical results.

In conclusion, the unplanned readmission rates for TB in this study were low. We concluded that gender, age, place of residence, smoking status, COPD, hepatitis, non-standard treatment, adverse drug reactions, and unauthorised discharge were risk factors for unplanned readmission. Because of the existence of these factors, medical staff is reminded to attach great importance to them in newly hospitalised patients. Interventions in these factors to encourage change, achieve continuous health management, and ensure regular treatment may help reduce unplanned readmission rate within 30 days in patients with TB.

Authors' Contributions

Conception and design: Ye XC and Shi JC; Administrative support: Jiang XG and Liu SD; Provision of study materials or patients: Cheng F and Pan N; Collection and assembly of data: Qiu CC; Data analysis and interpretation: Pan CW; Manuscript writing: All authors; Final approval of manuscript: All authors

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