Am J Transl Res 2025;17(2):951-960
www.ajtr.org /ISSN:1943-8141/AJTR0161099

Original Article

Characteristics and risk factors of pulmonary fungal infection in patients with pulmonary tuberculosis

Yan Wu[1,2], Yanna Yang[3], Yao Lu[3]

[1]Department of Disease Control and Prevention, Beijing Luhe Hospital Affiliated to Capital Medical University, Tongzhou District, Beijing 101149, China; [2]Department of Infectious and Endemic Disease Control, Center for Disease Control and Prevention, Beijing 100176, China; [3]Preventive Health Care Section, Zhangjiawan Health Center, Tongzhou District, Beijing 101100, China

Received October 12, 2024; Accepted January 6, 2025; Epub February 15, 2025; Published February 28, 2025

Abstract: Objective: To investigate the characteristics of and the risk factors for pulmonary fungal infection in patients with pulmonary tuberculosis (PT). Methods: A retrospective analysis was conducted on the clinical data of 218 PT patients treated at Beijing Luhe Hospital Affiliated with Capital Medical University from May 2022 to May 2024. Based on the presence or absence of fungal infection, these 218 patients were assigned to an infection group (n=87) or a non-infection group (n=131). Clinical baseline data, pulmonary fungal infection status ten days after admission, clinical symptoms on the first day of admission, and serum protein and hemoglobin levels were compared between the two groups. Logistic regression analysis was conducted to identify independent risk factors for pulmonary fungal infection in PT patients. A receiver operating characteristic (ROC) curve was generated to evaluate the predictive performance of these independent risk factors. Results: Among the 218 PT patients included, 87 (39.91%) had fungal infections. A total of 210 fungal strains were isolated and cultured from the infection group, with Candida albicans accounting for the highest proportion (42.65%), followed by candida tropicalis (20.59%) and Candida glabrata (17.65%). The infection group exhibited significantly higher rates of cough, fever, anemia, and pulmonary rales compared to the non-infection group (all P<0.05). The infection group showed significantly lower levels of serum protein and hemoglobin than the non-infection group (P<0.0001). Multivariate analysis identified history of smoking, disease course, duration of corticosteroid use, invasive procedure, serum protein level, and hemoglobin level as independent factors for fungal infection in PT patients. ROC curve analysis indicated that serum protein levels had the highest accuracy and area under the curve (AUC) value, while smoking history and hemoglobin levels performed less well in the model. Conclusion: This study found a high rate of pulmonary fungal infections among PT patients, with *Candida albicans* being the most prevalent, followed by *candida tropicalis* and *Candida glabrata*. A history of smoking, a prolonged disease course, invasive procedures, extended corticosteroid use, and low serum protein and hemoglobin levels are independent factors for fungal infection in PT patients.

Keywords: Tuberculosis, pulmonary infection, fungus, symptoms, risk factors

Introduction

Pulmonary tuberculosis (PT), commonly known as pulmonary consumption, is a chronic infectious disease caused by *Mycobacterium tuberculosis*, which significantly affects global public health [1, 2]. Recent epidemiological studies have shown a notable improvement in the incidence of PT in China. However, with the acceleration of the aging population, there is a growing trend of PT cases in older individuals [3]. The symptoms of PT are diverse, commonly including cough, sputum production, fever, night sweats, and in some cases, hemoptysis, which can be life-threatening when severe [4]. When the disease affects the pleura, chest pain may occur, often presenting as stabbing or dull pain [5].

Given its high incidence and mortality rates in China, PT poses significant treatment challenges and is highly contagious [6]. Treatment for PT typically involves antibiotics and anti-tuberculosis drugs. However, excessive antibiotic use can lead to the development of drug-resistant fungi infection, disrupting the microbial balance [7]. Pulmonary fungal infection is a severe complication in PT patients [8]. Fungi are considered

opportunistic pathogens, meaning that under normal conditions, they do not cause infection, even if present in the body [7]. However, when immune function is compromised, normally harmless fungi can become activated, leading to infections. Individuals with PT are particularly susceptible to fungal invasion [8]. On one hand, inflammation and tissue damage at PT lesions provide a favorable environment for fungal growth; on the other hand, the long-term use of anti-tuberculosis drugs may induce dysbiosis, further increasing the risk of fungal infection [9]. Symptoms of pulmonary fungal infections are relatively subtle, making them prone to misdiagnosis and delayed treatment, which severely impacts patient prognosis [10]. Reports indicate that pulmonary fungal infections not only worsen the disease condition and complicate treatment but also significantly elevate the risk of mortality [11]. Among various fungal infections, Candida is the most common co-infection with PT, and its presence can severely affect the treatment of tuberculosis [12]. Therefore, understanding the characteristics of pulmonary fungal infections in PT patients and taking preventive measures is crucial. Nonetheless, the characteristics and risk factors associated with pulmonary fungal infections among PT patients remain insufficiently understood.

Therefore, this study aimed to investigate the characteristics of pulmonary fungal infections in PT patients and to identify the risk factors associated with these infections, with the goal of providing a foundation for developing targeted prevention and treatment strategies. The findings aim to support early, targeted interventions to reduce the incidence of pulmonary fungal infections in this patient population.

Data and methods

Case selection

With the approval of the Ethics Committee of Beijing Luhe Hospital Affiliated with Capital Medical University, a retrospective analysis was conducted on the clinical data from 250 PT patients treated at the hospital from May 2022 to May 2024. Based on the following inclusion and exclusion criteria, 218 eligible cases were finally included in this study. The 218 patients were divided into two groups based on the presence of fungal infections: the infection group (n=87) and the non-infection group (n= 131).

Inclusion criteria: 1) Patients diagnosed with PT according to the "*Guidelines for Primary Care Diagnosis and Treatment of Pulmonary Tuberculosis*" [13], who met the following criteria: a. Presence of typical respiratory symptoms such as cough, sputum production, chest pain, and systemic symptoms like fever, weight loss, and fatigue; b. Chest X-ray or CT scan showing characteristic tuberculosis-related lung abnormalities like infiltrates, cavities, nodules, or other changes indicative of tuberculosis infection; 2) Patients without pulmonary fungal infections prior to hospitalization; 3) Patients aged 18 to 60 years; 4) Patients with detailed clinical data.

Exclusion criteria: 1) Patients with severe liver or kidney failure; 2) Patients with malignant tumors; 3) Patients with systemic infections; 4) Patients with immune system deficiencies; 5) Pregnant or breastfeeding women.

Criteria for diagnosing pulmonary fungal infections

The diagnosis of pulmonary fungal infections was based on the following criteria [14]: (1) The patient showed typical clinical symptoms, including cough, increased sputum production, or worsening of pre-existing respiratory symptoms, and had purulent or blood-tinged sputum, with or without chest pain. In cases with extensive lesions, the patient may have experienced dyspnea and respiratory distress; (2) Physical examination revealed significant moist rales in the lungs; (3) Blood tests showed abnormalities, including elevated procalcitonin levels; (4) Imaging changes indicated pulmonary parenchymal infiltration.

Data collection

Clinical and laboratory data were collected for all patients. Clinical data included patient age, disease course, sex, body mass index (BMI), history of smoking and alcohol use, underlying health conditions (such as diabetes and hypertension), place of residence, clinical symptoms, invasive procedures, sputum smear microscopy results, and duration of glucocorticoid and broad-spectrum antibiotic use. Laboratory data

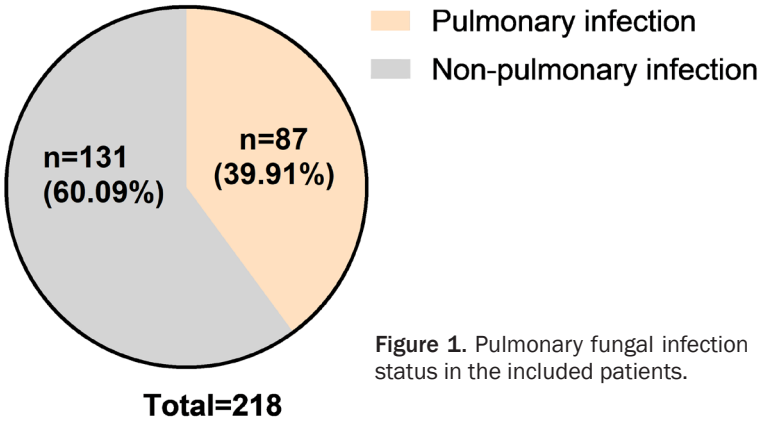

Figure 1. Pulmonary fungal infection status in the included patients.

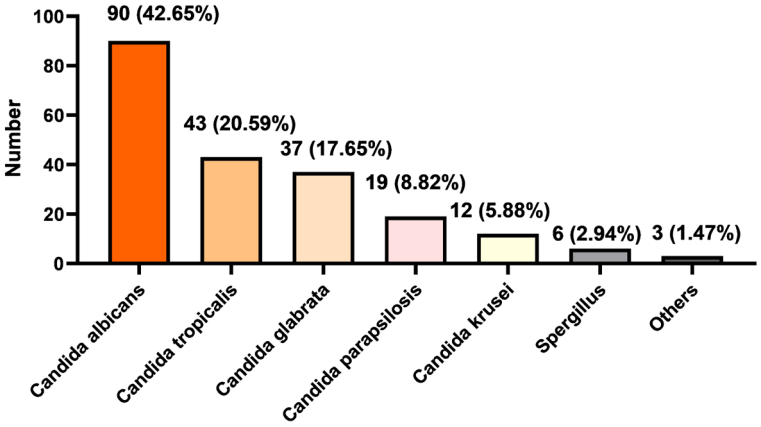

Figure 2. Analysis of fungal species.

included serum albumin and hemoglobin levels.

Outcome measures

Primary outcome measures: (1) The clinical baseline data of the two groups were compared, including age, gender, BMI, history of smoking and alcohol consumption. (2) The status of pulmonary fungal infections in patients was assessed ten days after hospitalization. The patient was instructed to rinse their mouths twice in the morning and then perform a deep cough to collect a second sputum sample for bacterial culture. The sputum was cultured for three consecutive days, with Gram staining performed before culturing. A specimen was considered qualified if there were more than 25 white blood cells and fewer than 10 epithelial cells in each low-power field. The specimens were cultured on blood agar, and any fungi isolated were further identified. (3) Based on the comparative results between the two groups, factors influencing pulmonary fungal infections in patients were identified. Subsequently, logistic regression analysis was conducted to determine the independent risk factors for fungal infections in PT patients.

Secondary outcome measures: (1) Clinical symptoms assessedonthefirstdayofhospitalization, including hemoptysis, cough, fever, anemia, pulmonary rales, and malnutrition, were compared between the two groups. (2) Serum protein and hemoglobin levels quantified on the second day of hospitalization were compared between the two groups. Fasting venous blood (5 mL) were collected from on the second day of hospitalization for measurement of serum protein and hemoglobin levels using an automatic biochemical analyzer. (3) ROC curve analysis was conducted to evaluate the predictive performance of independent risk factors for predicting pulmonary fungal infection in PT patients.

Statistical methods

In this study, statistical analysis was performed using SPSS 20.0 (IBM Corp, Armonk, NY, USA), and graphs were created using GraphPad Prism 7 (GraphPad Software, San Diego, USA). Counting data were expressed as [n (%)] and compared between the two groups using the chi-square test (χ^2 test). Measurement data were expressed as (x±sd) and compared using the t-test. Logistic multivariate regression analysis was conducted to identify factors influencing the occurrence of pulmonary fungal infections in PT patients. ROC curve analysis was used to predict the likelihood of pulmonary fungal infection in PT patients based on independent risk factors. A corresponding Nomogram was generated on the website https://www.zstats.cn/software2/pre01/ to visualize the predictive model. A *P*-value of <0.05 was considered statistically significant.

Table 1. Comparison of baseline data between the infection and non-infection groups

	Infection group (n=87)	Non-infection group (n=131)	χ^2/t	P
Age	47.64±6.91	47.68±6.80	0.0403	0.9679
Sex			1.1541	0.2827
Male	40	71		
Female	47	62		
BMI			0.2805	0.5964
≥23 kg/m^2	49	69		
<23 kg/m^2	38	62		
History of smoking			8.4921	0.0036
Yes	50	49		
No	37	82		
History of alcohol consumption			0.4441	0.5052
Yes	31	41		
No	56	90		
Disease course			46.2510	<0.0001
≥5 years	61	31		
<5 years	26	100		
Comorbid diabetes			0.5691	0.4506
Yes	21	26		
No	66	105		
Comorbid hypertension			1.1771	0.2779
Yes	19	21		
No	68	110		
Place of residence			0.1639	0.6856
Rural area	65	101		
Urban area	22	30		

Note: BMI: Body mass index.

Results

Pulmonary fungal infection status

Statistics revealed that among the 218 included PT patients, 87 cases presented with fungal infections, accounting for 39.91% (**Figure 1**). In the infection group, 210 fungal isolates were cultured from the 87 cases. The most common fungus was *Candida albicans* (42.65%), followed by *Candida tropicalis* (20.59%) and *Candida glabrata* (17.65%). Other fungus types included *Candida parapsilosis*, *Candida krusei*, *Aspergillus*, and unspecified fungi, with proportions ranging from 1.47% to 8.82% (**Figure 2**).

Comparison of clinical baseline data between the two groups

Analysis comparing the clinical baseline data of the two groups revealed no significant differences in terms of age, sex, BMI, history of smoking/alcohol consumption, comorbid diabetes, comorbid hypertension, or place of residence (all P>0.05, **Table 1**).

Comparison of clinical symptoms between the two groups

Comparison of clinical manifestations between the two groups revealed that the infection group had significantly higher incidences of cough (89.66% vs. 62.60%), fever (79.31% vs. 64.12%), anemia (60.92% vs. 35.11%), and pulmonary rales (63.22% vs. 38.17%), and a significantly lower incidence of hemoptysis (10.34% vs. 24.43%) compared to the non-infection group (P<0.05). However, no significant difference was observed in the incidence of malnutrition (77.01% vs. 66.41%) (P>0.05), as shown in **Table 2**.

Comparison of serum proteins and hemoglobin levels between the two groups

Analysis of serum protein and hemoglobin levels revealed that the serum protein levels we-

Table 2. Comparison of clinical symptoms between the two groups

	Infection group (n=87)		Non-infection group (n=131)		P
	Number of patients (person)	Proportion	Number of patients (person)	Proportion	
Hemoptysis	9	10.34	32	24.43	0.0092
Cough	78	89.66	82	62.60	<0.0001
Fever	69	79.31	84	64.12	0.0164
Anemia	53	60.92	46	35.11	0.0002
Pulmonary rales	55	63.22	50	38.17	0.0003
Malnutrition	67	77.01	87	66.41	0.0924

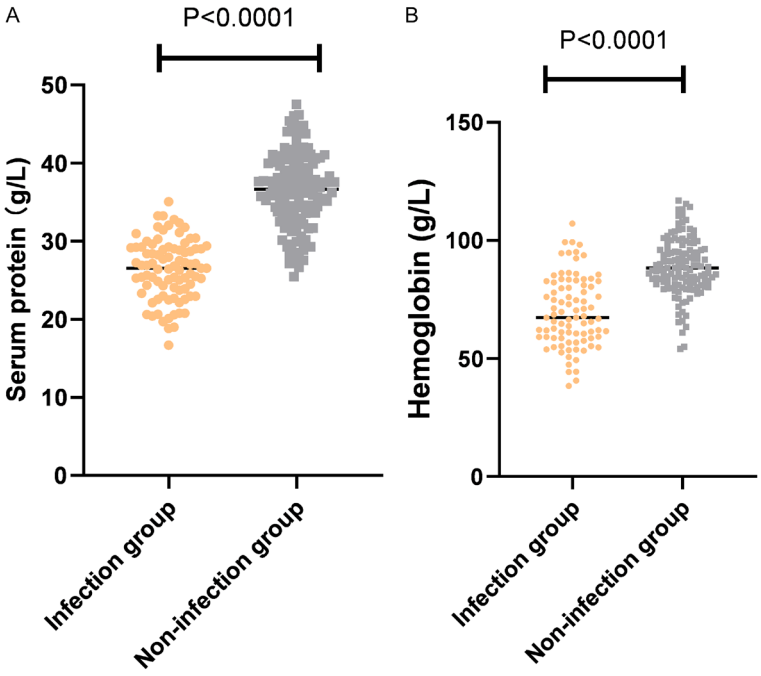

Figure 3. Comparison of serum protein (A) and hemoglobin (B) levels between the two groups.

re significantly lower in the infection group (26.38±3.84 g/L) compared to the non-infection group (36.48±4.78 g/L). Similarly, the hemoglobin levels were significantly lower in the infection group (69.75±14.89 g/L) compared to the non-infection group (88.77±12.01 g/L) (all P<0.0001, **Figure 3**).

Univariate analysis of fungal infection in PT patients

The results of univariate analysis indicated a significant correlation between fungal infection in PT patients and several factors, including history of smoking, disease course, invasive procedures, duration of corticosteroid use, duration of broad-spectrum antibiotics use, serum protein levels, and hemoglobin levels (all P<0.05, **Table 3**).

Multivariate analysis of fungal infection in PT Patients

In the multivariate analysis, the counting data with significant differences between the two groups in the univariate analysis were assigned values (**Table 4**). Subsequently, fungal infection was set as the dependent variable, and the history of smoking, disease course, duration of corticosteroid use, invasive procedures, duration of broad-spectrum antibiotic use, serum protein levels, and hemoglobin levels were considered as independent variables. Logistic regression analysis revealed that history of smoking, disease course, duration of corticosteroid use, invasive procedure, serum protein level, and hemoglobin level were independent factors influencing the occurrence of fungal infection in patients with PT (all P<0.05, **Table 5**).

Predictive performance of independent risk factors for the occurrence of pulmonary fungal infection in patients with PT

ROC curves for the history of smoking, disease course, duration of corticosteroid use, invasive procedures, duration of broad-spectrum antibiotic use, serum protein levels, and hemoglobin levels in predicting the occurrence of pulmonary fungal infection in PT patients were plotted (**Figure 4**). The results revealed that serum protein demonstrated the highest accuracy

Table 3. Univariate analysis of fungal infection in pulmonary tuberculosis patients

	Infection group (n=87)	Non-infection group (n=131)	χ^2/t	P
History of smoking			8.4921	0.0036
Yes	50	49		
No	37	82		
Disease course			46.2510	<0.0001
≥5 years	61	31		
<5 years	26	100		
Duration of corticosteroid use			20.8910	<0.0001
≥7 days	62	52		
<7 days	25	79		
Invasive procedure			44.1210	<0.0001
Yes	60	31		
No	27	100		
Duration of corticosteroid use			4.3181	0.0377
≥14 days	53	61		
<14 days	34	70		
Serum protein level (g/L)	26.38±3.84	36.48±4.78	16.4900	<0.0001
Hemoglobin level (g/L)	69.75±14.89	88.77±12.01	10.3900	<0.0001

Table 4. Assignment table

	Assignment	
	1	0
History of smoking	Yes	No
Disease course	≥5 years	<5 years
Duration of corticosteroid Use	≥7 days	<7 days
Invasive procedure	Yes	No
Duration of broad-spectrum antibiotic use	≥7 days	<7 days
Serum protein	<32.45 g/L	≥32.45 g/L
Hemoglobin	<81.18 g/L	≥81.18 g/L
Fungal infection	Yes	No

and AUC value, while smoking history and hemoglobin showed lower predictive accuracy (**Table 6**). Based on the logistic regression analysis results, we also developed a Nomogram prediction model incorporating the independent factors to predict the risks of pulmonary fungal infection in PT patients (**Figure 5**).

Discussion

Tuberculosis is relatively common, characterized by a prolonged course and significant treatment challenges [15]. The chronic nature of tuberculosis results in a decline in patients' nutritional status and immune function. Furthermore, tuberculosis, primarily triggered by *Mycobacterium tuberculosis*, can cause significant damage to lung tissues, further compromising pulmonary resistance and increasing the susceptibility of PT patients to fungal infections [16]. Pulmonary fungal infections are often associated with disruptions in the body's microbial balance and weakened immune defenses [17]. Pulmonary fungal infections are considered opportunistic, with fungi typically coexisting harmlessly in the body but becoming pathogenic when the immune system is compromised or deficient [18]. In tuberculosis patients, the disruption of bronchial and pulmonary structural integrity creates favorable conditions for fungal proliferation in the lungs [19].

The occurrence of fungal infections in PT patients is relatively common, particularly in cases of compromised immunity or prolonged antibiotic use [20]. Research indicates that the incidence of fungal infections among PT patients ranges from 10% to 30% [10]. In our study, 87 out of the 218 tuberculosis patients were found to have fungal infections, accounting for 39.91%, slightly higher than the reported 10-30%. This deviation may be attributed to the relatively small sample size of the study. These results underscore the importance of closely monitoring fungal infections in PT pa-

Table 5. Multivariate analysis of fungal infection in pulmonary tuberculosis patients

	B	S.E,	Wals	df	Sig.	Exp (B)	95% C.I. For EXP(B)	
							Lower limit	Upper limit
History of smoking	1.486	0.700	4.502	1	0.034	4.420	1.120	17.443
Disease course	2.167	0.642	11.383	1	0.001	8.736	2.480	30.772
Duration of corticosteroid Use	1.433	0.638	5.056	1	0.025	4.193	1.202	14.627
Invasive procedure	2.422	0.682	12.622	1	<0.001	11.271	2.962	42.888
Duration of broad-spectrum antibiotic use	0.391	0.613	0.406	1	0.524	1.478	0.444	4.918
Serum protein	5.243	0.966	29.439	1	<0.001	189.296	28.481	1258.113
Hemoglobin	2.687	0.651	17.021	1	<0.001	14.682	4.097	52.610

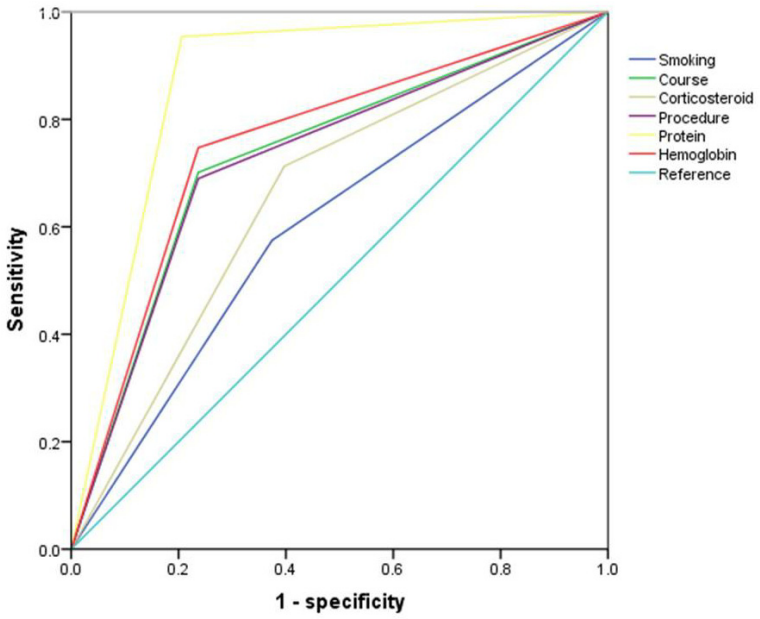

Figure 4. The predictive performance of independent risk factors for the occurrence of pulmonary fungal infection in patients with pulmonary tuberculosis (Receiver operating characteristic curve).

tients and emphasize the need for further research to comprehensively evaluate the incidence and risk factors associated with fungal infections in PT patients. In this study, among the 87 cases of pulmonary fungal infections, the fungal culture results revealed *Candida albicans* as the most prevalent pathogen, followed by *Candida tropicalis* and *Candida glabrata*. This differs from a study by Israel et al. [21], where *Candida albicans* (22.58%) and *Aspergillus* (17.20%) were the most common pathogens in tuberculosis patients with pulmonary fungal infections. This discrepancy may be attributed to differences in regional factors and the time periods of the studies, underscoring the variability and complexity of fungal infections in tuberculosis patients.

Pulmonary fungal infections in PT patients often lack typical clinical manifestations, making them easily confused with other infections [22]. The results of this study indicate that, prior to the onset of pulmonary fungal infections, PT patients experienced significant increases in clinical manifestations such as cough, fever, anemia, and pulmonary rales. Furthermore, in this study, the levels of serum proteins and hemoglobin upon admission in the infected group were significantly lower than those in the non-infected group. These lower levels of serum proteins and hemoglobin likely reflect inadequate nutritional status, compromised immune function, or heightened inflammatory responses. Collectively, these factors may diminish the body's ability to resist fungal infections, creating an environment conducive to their development [23]. Disruptions in protein metabolism and overactivation of the immune system may lead to increased protein breakdown to maintain immune function and repair tissue damage, potentially leading to the loss of trace elements such as iron. These physiological changes contribute to decreased levels of serum proteins and hemoglobin in tuberculosis patients with fungal infections compared to those without infections [24].

To identify the risk factors for fungal infections in PT patients, this study conducted both univariate and multivariate analyses. The univariate analysis revealed that history of smoking,

Table 6. ROC curve analysis for the independent risk factors in predicting pulmonary fungal infection in patients with pulmonary tuberculosis

	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	AUC
History of smoking	0.61 (0.54-0.67)	0.63 (0.54-0.71)	0.57 (0.47-0.68)	0.60
Disease course	0.74 (0.67-0.80)	0.76 (0.69-0.84)	0.70 (0.60-0.80)	0.73
Duration of corticosteroid Use	0.65 (0.58-0.71)	0.60 (0.52-0.69)	0.71 (0.62-0.81)	0.66
Invasive procedure	0.73 (0.67-0.79)	0.76 (0.69-0.84)	0.69 (0.59-0.79)	0.73
Serum protein	0.86 (0.80-0.90)	0.79 (0.72-0.86)	0.95 (0.91-1.00)	0.87
Hemoglobin	0.76 (0.69-0.81)	0.76 (0.69-0.84)	0.75 (0.66-0.84)	0.76

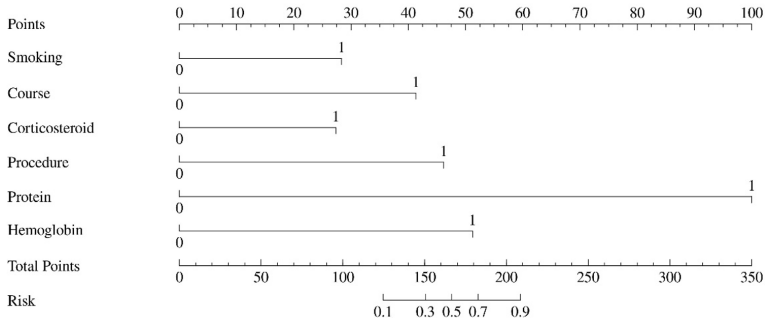

Figure 5. The Nomogram developed based on the identified risk factors.

disease course, duration of corticosteroid antibiotic use, invasive procedures, duration of broad-spectrum antibiotic use, and levels of serum protein and hemoglobin levels were associated with the occurrence of fungal infections in PT patients. Multivariate analysis discovered that a disease duration of ≥5 years, invasive procedures, as well as serum protein levels <32.45 g/L and hemoglobin levels <81.18 g/L were independent risk factors for fungal infections in PT patients. Smokers, due to the persistent inhalation of irritant gases, are particularly susceptible to damage to the sensory nerve endings in the lungs. This damage impedes the clearance of respiratory secretions, increases mucus secretion by glands, reduces the effectiveness of bronchial mucosa cilia, and enhances the vulnerability to fungal infections [25, 26]. During the treatment of PT patients, long-term use of broad-spectrum antibiotics and corticosteroids can also increase the risk of fungal infections. Prolonged use of broad-spectrum antibiotics disrupts the balance of microbial flora in the body, increasing the likelihood of fungal infections [27]. While corticosteroids can effectively control the patient's condition, they also induce immunosuppression, leading to decreased immune function and rendering the patient more susceptible to fungal infections [28]. PT patients are often in a state of intense inflammatory response, which results in a sharp decrease in serum albumin levels, further impairing immune function and increasing susceptibility to pulmonary fungal infections. For PT patients with a disease duration of ≥5 years, malnutrition and immunodeficiency are common. The longer the disease duration, the more severe the body's depletion, weakening its ability to resist external pathogens [29]. Invasive procedures can also compromise lung defense mechanisms, and if proper hygiene protocols are not followed, they may introduce pathogens into lung tissues, heightening the risk of fungal infections [30]. Additionally, low levels of serum protein and hemoglobin reflect a decline in the patient's overall nutritional and immune status, making them more susceptible to fungal infections. Therefore, clinical interventions should focus on addressing these high-risk factors early in order to improve outcomes, reduce the risk of fungal infections, and optimize patient care.

Moreover, ROC curve analysis was conducted to evaluate the predictive abilities of independent risk factors for pulmonary fungal infection in PT patients. Serum protein level emerged as the most reliable predictor with the highest accuracy and AUC value, while factors like smoking history and hemoglobin performed less effectively. These findings suggest the potential significance of serum protein levels in identifying and managing pulmonary fungal infection in patients with PT, highlighting the importance of comprehensive risk factor assessment in clinical practice.

The study does have some limitations. As a retrospective analysis, the conclusions are based on existing data and statistical analyses, and further research is needed to validate these findings and explore the underlying mechanisms in a greater depth. Additionally, the limited sample size in this study may affect the precision and reliability of the results, suggesting the need for larger, more diverse cohorts in future studies.

Conclusion

In summary, fungal infection has a high prevalence in PT patients, with *Candida albicans* being the most prevalent, followed by *candida tropicalis* and *Candida glabrata*. A history of smoking, prolonged disease course, invasive procedures, extended corticosteroid use, and low levels of serum protein and hemoglobin are independent factors influencing the occurrence of fungal infection in patients with PT.

Disclosure of conflict of interest

None.

Address correspondence to: Yan Wu, Department of Disease Control and Prevention, Beijing Luhe Hospital Affiliated to Capital Medical University, Tongzhou District, Beijing 101149, China. E-mail: spzhang@suda.edu.cn

References

[1] Sossen B, Richards AS, Heinsohn T, Frascella B, Balzarini F, Oradini-Alacreu A, Odone A, Rogozinska E, Häcker B, Cobelens F, Kranzer K, Houben RMGJ and Esmail H. The natural history of untreated pulmonary tuberculosis in adults: a systematic review and meta-analysis. Lancet Respir Med 2023; 11: 367-379.

[2] Goussard P, Eber E, Venkatakrishna S, Frigati L, Greybe L, Janson J, Schubert P and Andronikou S. Interventional bronchoscopy in pediatric pulmonary tuberculosis. Expert Rev Respir Med 2023; 17: 1159-1175.

[3] Goussard P, Eber E, Venkatakrishna S, Frigati L, Janson J, Schubert P and Andronikou S. Complicated intrathoracic tuberculosis: role of therapeutic interventional bronchoscopy. Paediatr Respir Rev 2023; 45: 30-44.

[4] Weldemhret L. Burden of pulmonary tuberculosis and challenges related to tuberculosis detection in Ethiopia. J Infect Dev Ctries 2023; 17: 578-582.

[5] Zhuo Q, Zhang X, Zhang K, Chen C, Huang Z and Xu Y. The gut and lung microbiota in pulmonary tuberculosis: susceptibility, function, and new insights into treatment. Expert Rev Anti Infect Ther 2023; 21: 1355-1364.

[6] Jindal SK. Is pulmonary tuberculosis a true risk-factor for chronic obstructive pulmonary disease? Indian J Tuberc 2022; 69: 131-133.

[7] Pillay S, Steingart KR, Davies GR, Chaplin M, De Vos M, Schumacher SG, Warren R and Theron G. Xpert MTB/XDR for detection of pulmonary tuberculosis and resistance to isoniazid, fluoroquinolones, ethionamide, and amikacin. Cochrane Database Syst Rev 2022; 5: CD014841.

[8] Amiri MRJ, Siami R and Khaledi A. Tuberculosis status and coinfection of pulmonary fungal infections in patients referred to reference laboratory of health centers Ghaemshahr City during 2007-2017. Ethiop J Health Sci 2018; 28: 683-690.

[9] Mohamed A, Obanda BA, Njeri HK, Loroyokie SN, Mashedi OM, Ouko TT, Gatumwa EM, Korir RK, Yaguchi T and Bii CC. Serological evidence of chronic pulmonary aspergillosis in tuberculosis patients in Kenya. BMC Infect Dis 2022; 22: 798.

[10] Teng GL, Huang Q, Xu L, Chi JY, Wang C and Hu H. Clinical features and risk factors of pulmonary tuberculosis complicated with pulmonary aspergillosis. Eur Rev Med Pharmacol Sci 2022; 26: 2692-2701.

[11] Anot K, Sharma S, Gupta M and Kaur D. Disseminated histoplasmosis and tuberculosis: dual infection in a non-endemic region. BMJ Case Rep 2020; 13: e235531.

[12] Cortes T and Cox RA. Transcription and translation of the rpsJ, rplN and rRNA operons of the tubercle bacillus. Microbiology (Reading) 2015; 161: 719-728.

[13] Georghiou SB, de Vos M, Velen K, Miotto P, Colman RE, Cirillo DM, Ismail N, Rodwell TC, Suresh A and Ruhwald M. Designing molecular diagnostics for current tuberculosis drug regimens. Emerg Microbes Infect 2023; 12: 2178243.

[14] Liu Z, Fu Z, Dai JH and Niu C. Clinical features of children with bronchial asthma complicated by pulmonary fungal infection and risk factors for pulmonary fungal infection. Zhongguo Dang Dai Er Ke Za Zhi 2019; 21: 431-435.

[15] Cardona PJ. Pathogenesis of tuberculosis and other mycobacteriosis. Enferm Infecc Microbiol Clin (Engl Ed) 2018; 36: 38-46.

[16] Jové N, Masdeu E, Brugueras S, Millet JP, Ospina JE, Orcau À, Rius C, Caylà JA and Sánchez F. Threats and interventions during the treatment of tuberculosis in an inner-city district. Arch Bronconeumol (Engl Ed) 2021; 57: 330-337.

[17] Xu Y, Yang G, Xu X, Huang Y, Liu K, Yu T, Qian J, Zhao X, Zhu J, Wang N and Xing C. IgG4-related nephritis and interstitial pulmonary disease

complicated by invasive pulmonary fungal infection: a case report. BMC Nephrol 2021; 22: 22.
[18] Harada N, Kimura SI, Gomyo A, Hayakawa J, Tamaki M, Akahoshi Y, Ugai T, Kusuda M, Kameda K, Wada H, Ishihara Y, Kawamura K, Sakamoto K, Sato M, Terasako-Saito K, Kikuchi M, Nakasone H, Kako S, Tsubochi H and Kanda Y. Surgical resection for persistent localized pulmonary fungal infection prior to allogeneic hematopoietic stem cell transplantation: analysis of six cases. J Infect Chemother 2020; 26: 175-180.
[19] Gong Y, Li S, Rong R, Chen X and Jiang L. Isolated gastric varices secondary to abdominal tuberculosis mimicking lymphoma: a case report. BMC Gastroenterol 2019; 19: 78.
[20] Chen S, Ye J, Wang Y, Tang X and Xie W. Analysis of clinical characteristics and detection of pathogens in patients with pulmonary tuberculosis complicated with fungal infection. Minerva Med 2023; 114: 754-756.
[21] Njovu IK, Musinguzi B, Mwesigye J, Kassaza K, Turigurwa J, Nuwagira E, Bazira J, Kabanda T, Mpeirwe M, Ampaire L, Mutekanga A, Kiguli J, Achan B and Itabangi H. Status of pulmonary fungal pathogens among individuals with clinical features of pulmonary tuberculosis at Mbarara University Teaching Hospital in Southwestern Uganda. Ther Adv Infect Dis 2021; 8: 20499361211042477.
[22] Sani FM, Uba A, Tahir F, Abdullahi IN, Adekola HA, Mustapha J, Nwofe J, Usman Y and Daneji IM. Spectrum of pulmonary fungal pathogens, associated risk factors, and anti-fungal susceptibility pattern among persons with presumptive tuberculosis at Gombe, Nigeria. Int J Mycobacteriol 2020; 9: 144-149.
[23] Muni S, Rajpal K, Kumar R, Kumari R, Sinha R, Kumar S and Kumari N. Identification of fungal isolates in patients with pulmonary tuberculosis treated at a tertiary care hospital. Cureus 2023; 15: e37664.
[24] Guillet C, Masgrau A, Walrand S and Boirie Y. Impaired protein metabolism: interlinks between obesity, insulin resistance and inflammation. Obes Rev 2012; 13 Suppl 2: 51-57.
[25] Lugg ST, Scott A, Parekh D, Naidu B and Thickett DR. Cigarette smoke exposure and alveolar macrophages: mechanisms for lung disease. Thorax 2022; 77: 94-101.
[26] Ali Hossain M, Asa TA, Rabiul Auwul M, Aktaruzzaman M, Mahfizur Rahman M, Rahman MZ and Moni MA. The pathogenetic influence of smoking on SARS-CoV-2 infection: integrative transcriptome and regulomics analysis of lung epithelial cells. Comput Biol Med 2023; 159: 106885.
[27] Hou S, Wang X, Yu Y, Ji H, Dong X, Li J, Li H, He H, Li Z, Yang Z, Chen W, Yao G, Zhang Y, Zhang J, Bi M, Niu S, Zhao G, Zhu R, Liu G, Jia Y and Gao Y. Invasive fungal infection is associated with antibiotic exposure in preterm infants: a multi-centre prospective case-control study. J Hosp Infect 2023; 134: 43-49.
[28] Thrikawala SU, Anderson MH and Rosowski EE. Glucocorticoids suppress NF-κB-mediated neutrophil control of aspergillus fumigatus hyphal growth. J Immunol 2024; 213: 971-987.
[29] Malavia D, Crawford A and Wilson D. Nutritional immunity and fungal pathogenesis: the struggle for micronutrients at the host-pathogen interface. Adv Microb Physiol 2017; 70: 85-103.
[30] Ferrarese A, Cattelan A, Cillo U, Gringeri E, Russo FP, Germani G, Gambato M, Burra P and Senzolo M. Invasive fungal infection before and after liver transplantation. World J Gastroenterol 2020; 26: 7485-7496.