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Research article

Characterization of non-tuberculous mycobacterial pulmonary disease and pulmonary tuberculosis in patients with AFB smear-positive sputum: A retrospective comparative study

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ABSTRACT

Background: Distinguishing nontuberculous mycobacteria pulmonary disease (NTM-PD) from pulmonary tuberculosis (PTB) is a challenge especially in patients with positive sputum smear of acid-fast bacilli (AFB). This study aimed to compare and identify the clinical characteristics between the two diseases among patients with positive sputum AFB.

Methods: From February 2017 through March 2021, patients with positive sputum AFB were reviewed in two hospitals of China. Among them, clinical data of NTM-PD and PTB patients was collected and compared.

Results: 76 cases of NTM-PD and 92 cases of PTB were included in our study. When compared with PTB, NTM-PD patients were older (59.2 ± 11.4 vs 44.2 ± 19.5 years, $P < 0.001$) and manifested more hemoptysis and dyspnea (28.9 % vs 14.1 %, $P < 0.05$; 48.7 % vs 17.4 %, $P < 0.001$ respectively). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for Xpert were 85.9 %, 96.1 %, 96.3 %, 84.9 %, respectively, compared to 94.2 %, 81.1 %, 83.1 %, 93.5 %, respectively for T-spot in diagnosing PTB. In radiological features, NTM-PD affected more lobes (4.53 ± 0.89 vs 3.61 ± 1.41, $P < 0.001$) and showed more consolidation (50 % vs 32.6 %, $P < 0.05$), destroyed lung (22.7 % vs 9.8 %, $P < 0.05$), honeycomb lung (26.7 % vs 6.5 %, $P < 0.001$) but less nodules (80.3 % vs 95.7 %, $P < 0.05$), tree-in-bud sign (49.3 % vs 87 %, $P < 0.001$), and satellite nodules (14.5 % vs 90.2 %, $P < 0.001$) than PTB. Age (odds ratio [OR], 1.043; 95 % confidence interval [CI], 1.018–1.069, $P < 0.05$), hemoptysis (OR, 3.552; 95% CI, 1.421–8.729, $P < 0.05$), and dyspnea (OR, 2.631; 95%CI, 1.151–6.016, $P < 0.05$) were independently correlated with NTM infection.

Conclusions: NTM-PD and PTB share similar clinical manifestations. Among them, advanced age, hemoptysis, and dyspnea are the independent predictors for NTM infection. Xpert is an efficiency analysis in discriminating between NTM-PD and PTB in patients with positive sputum AFB.

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1. Introduction

Non-tuberculous mycobacteria (NTM), which refer to all mycobacterial species other than *Mycobacterium tuberculosis* and *Mycobacterium leprae* are ubiquitous and widely found in soil, water, and residential environment [1]. They can cause lung, pleura, lymph nodes, soft tissue, skin, central nervous system and disseminated infection [2]. Since it is not a reportable disease, the exact burden of NTM disease is unclear globally. However, data from different regions demonstrated that the incidence and mortality of NTM disease have been steadily increasing in both developing and developed countries over the last two decades [3–5].

Non-tuberculous mycobacteria pulmonary disease (NTM-PD) is the most common clinical phenotype of NTM infection. With positive sputum smear of acid-fast bacilli (AFB), it is usually misdiagnosed as pulmonary tuberculosis (PTB) and treated with the first line anti-tuberculosis drugs empirically [6]. As a result, acquired drug resistant NTM species may generate, of which situation was forecasted to worsen [7]. Not only that, the global burden of drug-resistant tuberculosis is still high. As reported in 2021, it increased by 3 % (including 450 000 rifampicinresitant tuberculosis cases) when compared to 2020 [8]. Anti-mycobacterial drug resistance (AMR) is becoming a major challenge in the management of TB and NTM [9]. Promptly identification and standardized therapy for NTM-PD and PTB is essential for reducing the generation of drug resistance mycobacteria species.

Until now, the methodologies used to discriminate between NTM and TB are complicated and underdeveloped. Distinguishing NTM-PD from PTB in the patients with positive sputum smear of AFB is challenging especially in the regions lacking of facilities. In this study, we compared clinical manifestations of NTM-PD and PTB among patients with positive AFB sputum smear aimed to find the specific characteristics that identify the one from the other.

2. Materials and methods

2.1. Patients

Patients with positive sputum smear for AFB were reviewed in Xinhua Hospital affiliated with Shanghai Jiao Tong University School of Medicine and Weifang Respiratory Disease Hospital in China between February 2017 and March 2021. Among them, patients aged >18 years, and with confirmed diagnosis of NTM-PD or PTB, and with complete clinical information, were included in this study.

According to the American Thoracic Society (ATS)/Infectious Disease Society (IDSA) guidelines in 2007 [10], patients who had clinical symptoms, radiologic findings and at least two positive isolates from sputum or a single NTM isolate from bronchial washing, bronchoalveolar lavage, or lung tissue were defined as NTM-PD cases. PTB cases were defined as patients in whom *M. tuberculosis* were isolated from sputum culture.

2.2. Data collection

According to the electronic medical records, the clinical data included demographic information (age, sex, previous medical history, smoking history), symptoms, the results of laboratory tests (including C-reactive protein [CRP], white blood cell [WBC] counts, lymphocyte counts, erythrocyte sedimentation rate [ESR], procalcitonin [PCT], Xpert, T-spot, isolated NTM species) were collected.

Computer tomography (CT) pictures were reviewed by two pulmonary physicians (XML and DZS) on picture archiving and communication system (PACS). An independent radiologist (CSL) who was blinded to the patients' diagnosis confirmed the results of the imaging analyses. The total affected lobes of each patient and the frequencies of radiological abnormalities such as nodules, consolidation, cavity, pleural effusion, bronchiectasis, destroyed lung, mediastinal lymphadenopathy, intrapulmonary calcification, pleural calcification, opacity, honeycomb lung, stripe shadow, tree-in-bud sign, and satellite nodules were calculated and compared between the two groups.

2.3. Statistical analyses

SPSS version 22.0 (IBM Corporation, Armonk, New York, USA) was used for statistical analysis. Measurement data were presented as mean ± standard deviation (SD). Categorical data were expressed as number and percentage. Comparison of measurement data and categorical data between the two groups were performed by using T-test and chi-squared test respectively. Correlation between the clinical manifestations and NTM infection was analyzed by using univariate and multivariate Logistic regression analysis. Statistical significance was set at $P < 0.05$.

3. Results

A total of 5732 sputum samples were reported positive for AFB smear during the research period. Excluding 3821 repeated samples, samples from 1911 patients were reviewed. Of these, samples from 933 patients (including 698 cases of TB, 214 cases of NTM-PD, and 21 cases of Nocardia) were reported positive for mycobacterium culture. Based on the criteria (patients aged >18 years, and with confirmed diagnosis of NTM-PD or PTB, and with complete clinical information), 76 patients of NTM-PD and 92 patients of PTB were included in our study finally (Fig. 1).

3.1. Patient demographics

NTM-PD patients were older than PTB patients (59.2 ± 11.4 vs 44.2 ± 19.5 years, P < 0.001). No significant difference was found in sex, smoking history, and smoking index between the two groups. NTM-PD patients had more complications than PTB patients (61.8 % vs 28.3 %, P < 0.001). Among the complications, the incidence rates of tumor, post-surgery, and autoimmunity disease in NTM-PD group were significantly higher than that in PTB group (10.5 % vs 2.2 %, P < 0.05; 23.7 % vs 9.8 %, P < 0.05; 11.8 % vs 1.1 %, P < 0.05 respectively). In our study, the most common isolated NTM species was *M. intercelleulare* (82.9 %) followed by *M. avium* (5.3 %), and *M. chelonae* (3.9 %). The isolation rate of remaining NTM species such as *M. kansasii, M. abscessus, M. gordonae, M. scrofulaceum* was rare (Table 1).

3.2. Symptoms and laboratory examinations

According to Table 2, the most common symptoms were cough (86.8 % vs 82.6 %) and expectoration (80.3 % vs 79.3 %) in both NTM-PD and PTB patients. NTM-PD patients had more hemoptysis (28.9 % vs 14.1 %, P < 0.05) and dyspnea (48.7 % vs 17.4 %, P < 0.001) than PTB patients. No significant difference was found in other symptoms such as cough, expectoration, chest pain, fever, night sweat, or weight loss between the two groups. The proportion of patients with positive Xpert and T-spot in NTM-PD group was significantly lower than that of PTB group (3.94 % vs 85.9 %, P < 0.001 and 18.9 % vs 94.2 %, P < 0.001 respectively). No significant difference was found in other biomarkers such as CRP, WBC counts, lymphocyte counts, ESR, and PCT between the two groups.

Among patients with positive sputum AFB, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for Xpert were 85.9 %, 96.1 %, 96.3 %, 84.9 %, respectively, compared to 94.2 %, 81.1 %, 83.1 %, 93.5 %, respectively for T-spot in diagnosing PTB (Table 3).

3.3. Imaging features

NTM infections affected more lung lobes than TB (4.53 ± 0.89 vs 3.61 ± 1.41, P < 0.001). NTM-PD patients showed more consolidation (50 % vs 32.6 %, P < 0.05), destroyed lung (22.7 % vs 9.8 %, P < 0.05), and honeycomb lung (26.7 % vs 6.5 %, P P < 0.001) than PTB patients, while PTB patients showed more nodules (95.7 % vs 80.3 %, P P < 0.05), tree-in-bud sign (87 % vs 49.3 %, P < 0.001), and satellite nodules (90.2 % vs 14.5 %, P < 0.001) than NTM-PD patients (Table 4).

3.4. Risk factors for NTM infection

To clarify the correlation between clinical manifestations and NTM infection, we analyzed variables which were significantly different between the two groups by using logistical regression analysis. As shown in Table 5, age (odds ratio [OR], 1.043; 95 % confidence interval [CI], 1.018–1.069, P P < 0.05), hemoptysis (OR, 3.552; 95%CI, 1.421–8.729, P < 0.05), and dyspnea (OR, 2.631; 95%CI, 1.151–6.016, P < 0.05) were independently correlated with NTM infection.

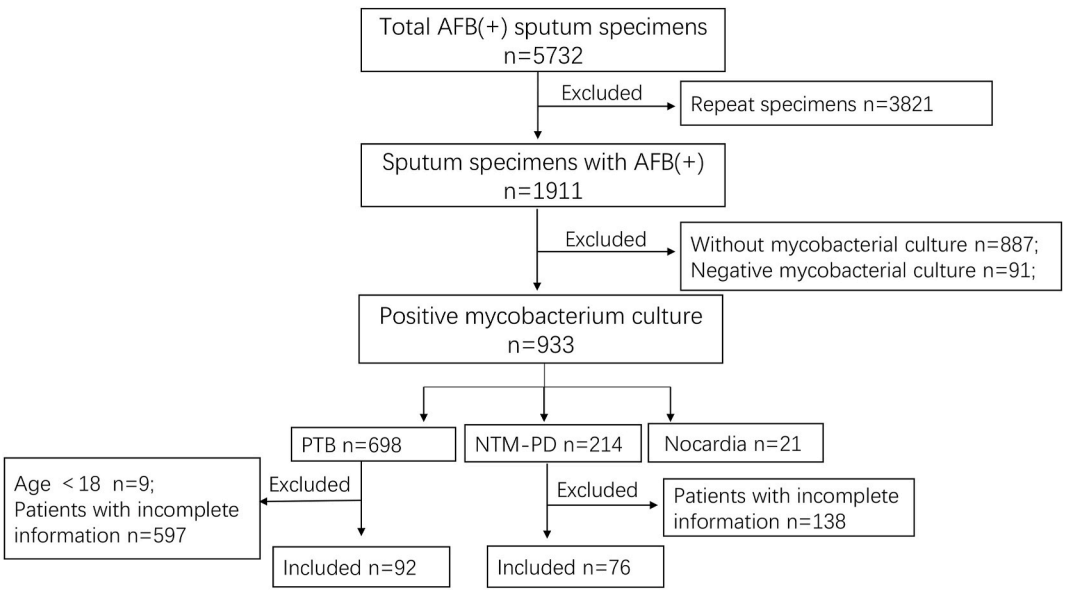

Fig. 1. Flow chart of patient enrollment. AFB = acid fast bacilli, PTB = pulmonary tuberculosis, NTM-PD = non-tuberculosis mycobacteria pulmonary disease.

Table 1
Demographics, comorbidities of patients and NTM species isolated in this study.

	NTM-PD (n = 76)	PTB (n = 92)	P value
Age (years)	59.2 ± 11.4	44.2 ± 19.5	**<0.001**
Sex (female, %)	40 (52.6 %)	35 (38 %)	0.058
Smoking (yes, %)	25 (32.9 %)	34 (37 %)	0.583
Smoking index (pack-year) (n = 30/25)	34.5 ± 22.1	28.4 ± 20.8	0.96
Previous chronic disease history (have, %)	47 (61.8 %)	26 (28.3 %)	**<0.001**
Diabetes mellitus (n, %)	5 (6.6 %)	10 (10.9 %)	0.332
Hypertension (n, %)	11 (14.5 %)	7 (7.6 %)	0.152
Atherosclerosis Coronary heart diseases (n, %)	4 (5.3 %)	2 (2.2 %)	0.283
COPD (n, %)	8 (10.5 %)	6 (6.5 %)	0.35
Tumor (n, %)	8 (10.5 %)	2 (2.2 %)	**<0.05**
Post-surgery (n, %)	18 (23.7 %)	9 (9.8 %)	**<0.05**
Cerebral apoplexy (n, %)	2 (2.6 %)	1 (1.1 %)	0.452
Autoimmunity disease (n, %)	9 (11.8 %)	1 (1.1 %)	**<0.05**
NTM species (n,%)			
Mycobacterium intercelleulare	63 (82.9 %)		
M. avium	4 (5.3 %)		
M. chelonae	3 (3.9 %)		
M. kansasii	2 (2.6 %)		
M. abscessus	2 (2.6 %)		
M. gordonae	1 (1.3 %)		
M. scrofulaceum	1 (1.3 %)		

Note: COPD, chronic obstructive pulmonary disease; NTM, nontuberculous mycobacteria; NTM-PD, nontuberculous mycobacteria pulmonary disease; PTB, pulmonary tuberculosis. P value less than 0.05 were in bold. NTM species were showed in italicized type.

Table 2
Symptoms and laboratory tests of NTM-PD and PTB patients.

	NTM-PD (n = 76)	PTB (n = 92)	P value
Symptoms			
Cough (n, %)	66 (86.8 %)	76 (82.6 %)	0.45
Expectoration (n, %)	61 (80.3 %)	73 (79.3 %)	0.883
Chest pain (n, %)	8 (10.5)	14 (15.2 %)	0.37
Hemoptysis (n, %)	22 (28.9 %)	13 (14.1 %)	**<0.05**
Fever (n, %)	24 (31.6 %)	31 (33.7 %)	0.77
Dyspnea (n, %)	37 (48.7 %)	16 (17.4 %)	**<0.001**
Night sweat (n, %)	3 (3.9 %)	6 (6.5 %)	0.461
Weight loss (n, %)	7 (9.2 %)	7 (7.6 %)	0.708
Laboratory tests			
CRP (mg/L)	18.26 ± 17.8	20.22 ± 19.06	0.343
WBC (*10^9/L)	7.09 ± 2.83	6.93 ± 2.43	0.353
Lymphocyte (*10^9/L)	1.56 ± 0.75	1.56 ± 0.70	0.267
ESR (mm/h)	34.36 ± 30.11	28.51 ± 26.02	0.065
PCT (mg/L)	0.076 ± 0.10	0.077 ± 0.11	0.732
Positive Xpert	3 (3.94 %)	79 (85.9 %)	**<0.001**
Positive T-spot (n = 53/52)	10 (18.9 %)	49 (94.2 %)	**<0.001**

Note: NTM-PD, nontuberculous mycobacteria pulmonary disease; PTB, pulmonary tuberculosis. CRP, C-reactive protein, WBC, white blood cell, ESR, erythrocyte sedimentation rate, PCT, procalcitonin; P value less than 0.05 were in bold.

Table 3
Diagnostic performance of Xpert and T-spot for PTB.

	Sensitivity% (95 % CI)	specificity% (95 % CI)	PPV% (95 % CI)	NPV% (95 % CI)
Xpert	85.9 (77.2–91.5)	96.1 (88.6–99.1)	96.3 (89.4–99.2)	84.9 (75.7–91.1)
T-spot	94.2 (83.8–98.6)	81.1 (68.4–89.6)	83.1 (71.3–90.7)	93.5 (81.9–98.4)

Note: PPV: positive predictive value; NPV: negative predictive value; PTB, pulmonary tuberculosis.

4. Discussion

The increasing incidence of NTM infection has triggered public health concerns globally [11]. For the limited capability of diagnosing NTM infection, many patients with NTM infection end up receiving treatment for TB or other common infections for months or years especially in the low- or middle-income areas. In order to avoid generation of drug resistance species, it is important to distinguish NTM from PTB promptly among patients with positive sputum smear of AFB. Current study showed that age, hemoptysis,

Table 4
Radiological features of NTM-PD and PTB patients.

	NTM-PD (n = 76)	PTB (n = 92)	P value
Affected lung lobes (Mean ± SD)	4.53 ± 0.89	3.61 ± 1.41	**<0.001**
Nodules (n, %)	61 (80.3 %)	88 (95.7 %)	**<0.05**
Consolidation (n, %)	38 (50 %)	30 (32.6 %)	**<0.05**
Cavity (n, %)	41 (53.9 %)	40 (43.5 %)	0.176
Pleural effusion (n, %)	23 (30.3 %)	28 (30.4 %)	0.981
Bronchiectasis (n, %)	65 (86.7 %)	70 (76.1 %)	0.084
Destroyed lung (n, %)	17 (22.7 %)	9 (9.8 %)	**<0.05**
Mediastinal lymphadenopathy (n, %)	33 (44 %)	53 (57.6 %)	0.08
Intrapulmonary calcification (n, %)	33 (44 %)	37 (40.2 %)	0.622
Pleural calcification (n, %)	4 (5.3 %)	7 (7.6 %)	0.555
Opacity (n, %)	64 (85.3 %)	74 (80.4 %)	0.406
Honeycomb lung (n, %)	20 (26.7 %)	6 (6.5 %)	**<0.001**
Stripe shadow (n, %)	59 (78.7 %)	79 (85.9 %)	0.222
Tree-in-bud sign (n, %)	37 (49.3 %)	80 (87 %)	**<0.001**
satellite nodules (n, %)	11 (14.5 %)	83 (90.2 %)	**<0.001**

Note: NTM-PD, nontuberculous mycobacteria pulmonary disease; PTB, pulmonary tuberculosis. P value less than 0.05 were in bold.

Table 5
Correlation between the clinical manifestations and NTM infection.

	Odds ratio (Univariate)	Odds ratio (Multivariate)
Age (per increase of 1 year)	1.056 (1.034–1.079) (**P<0.001**)	1.043 (1.018–1.069) (**P<0.05**)
Tumor (without as 1.0)	5.294 (1.089–25.733) (**P<0.05**)	2.227 (0.374–13.267) (P = 0.379)
Post-surgery (without as 1.0)	2.862 (1.202–6.815) (**P<0.05**)	1.287 (0.452–3.665) (P = 0.673)
Autoimmunity disease (without as 1.0)	8.575 (2.537–38.071) (P = 0.999)	
Hemoptysis (without as 1.0)	2.476 (1.149–5.337) (**P<0.05**)	3.552 (1.421–8.729) (**P<0.05**)
Dyspnea (without as 1.0)	4.506 (2.233–9.094) (**P<0.001**)	2.631 (1.151–6.016) (**P<0.05**)
Consolidation (without as 1.0)	2.067 (1.105–3.866) (**P<0.05**)	1.839 (0.608–5.559) (P = 0.280)
Destroyed lung (without as 1.0)	2.657 (1.109–6.369) (**P<0.05**)	1.465 (0.482–4.447) (P = 0.501)
Honeycomb lung (without as 1.0)	5.119 (1.936–13.536) (**P<0.05**)	1.326 (0.579–3.038) (P = 0.505)

Note: NTM, nontuberculous mycobacteria. P value less than 0.05 were in bold.

and dyspnea are the independent predictors for NTM infection, while Xpert is an efficiency analysis in distinguishing NTM-PD from PTB among patients with positive AFB for its excellent specificity in diagnosing TB.

An increase in NTM isolates was seen with increasing age [12]. According to our data, in patients with positive AFB sputum smear, advanced age was one of the independent risk factors for NTM infections which was accordance with Koh's study [13]. In addition, when compared with PTB, NTM-PD patients had higher prevalence rates of comorbidities (61.8 % vs 28.3 %, $P < 0.001$), such as tumor, surgical history, and autoimmune disease. Disease remission rates and mortality vary depending on NTM species, patient age and comorbidities [14]. The old age and more comorbidities may partly interpret more refractory of NTM-PD when compared to PTB. Direct and indirect evidence has suggested that individuals who had underlying immune dysfunction were prone to NTM infection [11]. For the usage of immunosuppressive agents in the comorbidities mentioned above, our data may indicate more severe immune deficiency in NTM-PD patients than PTB patients. Although structural lung diseases such as chronic obstructive lung disease (COPD) and bronchiectasis have been identified as risk factors for NTM pulmonary disease [15,16], the prevalence of the two diseases had no significant difference between the two groups in our study, which because COPD and bronchiectasis are also risk factors for TB infection [17].

Considerable overlap in the clinical symptoms between NTM-PD and PTB patients has been reported [6,13,18]. According to our data, when compared to PTB, NTM-PD patients showed more hemoptysis and dyspnea, which were independent risk factors for NTM infection in patients with positive AFB smear. These results may attribute to the old age, mycobacterium species, and the radiological features of NTM patients in our study. As the study of Hu and colleagues, old patients manifested more hemoptysis when infected with NTM [19]. Dong and colleagues found that among NTM infections, hemoptysis only occurred in patients infected with *M. intracellulare* and *M. abscessus* [20], which account for most of the cases in our study. However, data should be considered with caution because of the variety of NTM species in different regions. For *M. intracellulare* dominates the NTM infections in China, our findings may only be promoted in North America (such as Canada, USA), South America (Brazil), Europe (such as Ireland, Scotland, UK), Africa (such as Kenya, Nigeria), and Asia (such as Japan, South Korea, India), where *M. intracellulare* is the commonly isolated NTM specie [21]. Other researchers demonstrated a negative correlation between imaging changes on CT and pulmonary function [22]. According to our data, NTM infection affected more lung lobes and showed more consolidation, destroyed lung, and honeycomb lung than TB. The impaired ventilation and diffusion pulmonary function caused by the lung structure destroy may lead to the symptom of dyspnea. While due to the subjectivity of dyspnea, our data may not avoid to have certain bias. Objective parameters associated with dyspnea, such as arterial partial pressure of oxygen (PO2), predicted percentage diffusing lung capacity for carbon monoxide (DLCO%pred), and forced expiratory volume in 1s to forced vital capacity (FEV1/FVC) should be compared between the two diseases in the future studies.

T-spot is an interferon γ release assay to detect an immune response against MTB antigens, but isn't cross-reactive with most non-tuberculosis mycobacteria [23]. Both active and previous infection of TB present positive result. The overall sensitivity of T-spot for diagnosing active TB is reported to be 77%–88 %. In addition, T-spot have been expected to have poor specificity for active tuberculosis especially in regions with a high TB burden, because of a high background prevalence of past or latent TB infection [24,25]. As increasing studies reported, Xpert had a lower sensitivity but a higher specificity than T-spot in TB diagnosis [26,27]. In current study, based on the culture confirmed diagnosis, Xpert had a lower sensitivity (85.9 % vs 94.2 %) while higher specificity and PPV (96.1 % vs 81.1 %; 96.3%vs 83.1 %; respectively) than T-spot in diagnosing PTB among AFB positive patients. China has the world's third heaviest TB burden behind Indian and Indonesia [8]. High rate of past TB infection of the population and none cross-reactive with NTM of T-spot may explain its low specificity and high sensitivity in current study. TB would be excluded in a high probability when patients with positive sputum AFB but negative Xpert. Performing a Xpert test costs 29.8 US dollars averagely and not more than 2 h [28], which is more cost-effective than some rapid molecular diagnosis tests such as metagenomic next-generation sequencing (mNGS) [29,30]. Considering the cost performance, our study highlights the importance of Xpert among patients with positive AFB sputum smear. In regions lacking facilities, starting anti-TB treatment for patients with positive Xpert but waiting for culture results in patients with negative Xpert may be an effective procedure in reducing unreasonable therapy.

Regarding radiological features, TB infections are prone to occur in upper lobes, while NTM infections are disseminated and without a location predilection [31], which may explain the more lobes affected by NTM than TB. We found nodules including satellite nodules and tree in bud pattern were more frequently in PTB than NTM-PD patients, while honeycomb lung which represents severe cystic changes was more frequently in NTM-PD than PTB patients. These results were consistent with Yuan and Lee's studies from Taiwan and South Korea respectively [32,33]. Additionally, in Yuan's study, a strongly association between cystic appearances and NTM infection were found, which was consistent with our results. Fibrocavitary changes is one of the classical imaging types of *M. avium intracellulare complex* (MAC) especially in the elderly patients who with preexisting lung disease such as emphysema and interstitial lung disease [31]. The similar findings of radiological features in our and others' studies may attribute to the MAC which dominates the NTM infections in Asia. According to our data, univariate logistic regression analysis also showed correlation between NTM infection and destroyed lung as well as consolidation. Destroyed lobe of the lung is always secondary to chronic or recurrent lung infections with irreversible damage of pulmonary parenchyma. TB, NTM and aspergillus infections are the most common cause. Being consistent with Kabiri's study [34], destroyed lung were found more frequency in NTM-PD than in PTB patients. The long time without effective treatment before accurate diagnosis for NTM may be the reason. Consolidation is a common imaging feature of PTB and NTM-PD. According to the literature, the comparative incidence of consolidation between NTM and PTB is still controversial [33,35]. Based on radiomics analysis, characteristics but not only incidence of consolidation have been considered to be helpful in distinguishing NTM and PTB in a recent study [36]. Inspired by this research, more typical lung lesions should be deep analyzed by radiomics to differentiate NTM from PTB.

To the literature, this is the largest comparative study of NTM-PD and PTB in terms of sample size. All the patients with culture confirmed diagnosis. Our study compared clinical manifestations of the two diseases comprehensively which may enrich the research in this filed and provide clues for clinicians to distinguish NTM-PD from PTB among patients with positive sputum AFB. However, there are several limitations to our study that must be addressed. First, in order to review and compare the clinical characteristics of the two diseases comprehensively, we excluded lots of patients from outpatient department without completely information, which may generate certain bias. This problem would be addressed by prospective and randomized controlled trials. Our research findings may be more presentative among hospitalized patients. Second, *M. intercelleulare* is the main NTM species isolated in our study. Our findings may only be promoted in the regions mentioned above, where *M. intercelleulare* causes NTM infection commonly [21]. Third, most patients had received whether correct or not therapy before the research began. That may limit the study on the benefit of differentiating between NTM-PD and PTB on patient management. So, we didn't explore the treatment outcomes in current study. These limitations should be solved and the findings may be validated in prospective, multi-centered, ideally designed studies in the future.

5. Conclusion

Similar clinical manifestations between NTM-PD and PTB were still found in patients with positive AFB smear. Among them, advanced age, hemoptysis, and dyspnea are independent risk factors of NTM infection. Xpert combined with AFB smear is an efficiency method for differential diagnosis between NTM-PD and PTB in the regions lacking of facilities.

Ethics statement

This study was approved by the Ethics Committee of Xinhua Hospital, affiliated with Shanghai Jiao Tong University School of Medicine. (Approval NO. XHEC-D-2022-154). Due to the retrospective nature, the study had no impact on the existed treatment. The confidentiality of patients' privacy and identity information was guaranteed, and there was no commercial interest involved, so that the informed consent was waived. All research studies on humans have been performed in accordance with the principles stated in the Declaration of Helsinki.

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Data availability statement

Due to ethical limitations, the electronic medical record data used in this research is not publicly available. The generated synthetic data set discussed in this paper will be made available on request.

CRediT authorship contribution statement

Xiaoming Li: Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Dezhi Sun:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Changsheng Liang:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Wen Gu:** Writing – review & editing, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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