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ORIGINAL RESEARCH

Predictive Value of Nutritional Status in Sputum Culture Conversion Among Patients with Nontuberculous Mycobacterial Pulmonary Disease: A Retrospective Cohort Study

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Background: Nutritional status has been increasingly recognized as an important determinant of outcomes in nontuberculous mycobacterial pulmonary disease (NTM-PD), but its predictive value for sputum culture conversion remains unclear.

Methods: This retrospective cohort study included 416 patients with NTM-PD between January 2016 and September 2024. Patients were categorized based on nutritional status and sputum culture conversion. Logistic regression was used to identify independent predictors, and a combined predictive model was evaluated using ROC curves. Kaplan–Meier analysis assessed time to culture conversion. Internal validation was performed using bootstrap resampling.

Results: Among 416 patients, 109 (26.2%) achieved sputum culture conversion. Malnourished patients had significantly lower conversion rates. Multivariable analysis showed age (OR=1.048, 95% CI: 1.012–1.085), BMI (OR=0.746, 95% CI: 0.668–0.835), hemoglobin (OR=0.936, 95% CI: 0.906–0.967), and total protein (OR=0.920, 95% CI: 0.853–0.992) were independent predictors. The combined model demonstrated strong predictive performance (AUC=0.925, sensitivity=89.3%, specificity=78.0%).

Conclusion: Nutritional status is significantly associated with sputum culture conversion in NTM-PD. A combined model incorporating nutritional indicators may assist in risk stratification, although further validation is required.

Keywords: nontuberculous mycobacteria, pulmonary disease, nutritional status, sputum culture conversion, Kaplan–meier analysis

Introduction

The incidence of nontuberculous mycobacterial pulmonary disease (NTM-PD) has been increasing worldwide in recent years,[1] becoming an important public health concern.[2,3] Its clinical manifestations commonly include chronic cough, sputum production, abnormal chest imaging findings,[4] and repeated positive sputum cultures. In severe cases, NTM-PD can lead to structural lung damage and functional decline, thereby significantly impairing patients' quality of life and prognosis.[5] With population aging and the growing number of individuals with impaired immunity, the diagnosis and treatment of NTM-PD are becoming increasingly challenging.[6,7]

Previous studies have primarily focused on pathogen distribution and antimicrobial susceptibility.[8] For example, in Europe and North America, *Mycobacterium avium* complex (MAC) and *Mycobacterium kansasii* (*M. kansasii*) are the predominant pathogens,[9] whereas in Asian countries, *Mycobacterium intracellulare* (*M. intracellulare*) and *Mycobacterium abscessus* are more prevalent.[10] In recent years, however, researchers have proposed that beyond microbiological factors, host-related characteristics, particularly nutritional status, may play a critical role in disease progression and sputum culture conversion. Previous studies have suggested that nutritional status, particularly body mass index (BMI), is associated with disease severity and treatment outcomes in NTM-PD.[11–15]. There is a lack of integrative analyses incorporating multiple nutritional parameters.

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Despite increasing recognition of the role of nutritional status in NTM-PD, existing studies have primarily focused on single indicators such as BMI, with limited integration of multiple nutritional parameters. Moreover, the relationship between nutritional status and sputum culture conversion, a key indicator of treatment response, remains insufficiently characterized. We therefore hypothesize that a combination of nutritional indicators, including BMI, hemoglobin, albumin, and total protein, may provide improved predictive value for sputum culture conversion compared with individual markers. Accordingly, the present study aimed to (1) characterize the distribution of pathogenic species in NTM-PD, (2) evaluate the association between nutritional status and sputum culture conversion, and (3) explore the predictive performance of a multivariable model incorporating nutritional indicators. This study seeks to provide additional evidence to support risk stratification in clinical practice.

Methods

Study Design and Participants

This study was a single-center retrospective cohort study. Patients diagnosed with and treated for NTM-PD at Weifang Second People's Hospital between January 2016 and September 2024 were consecutively included. All cases were diagnosed based on clinical symptoms, chest imaging findings, and the isolation of nontuberculous mycobacteria from sputum or bronchoalveolar lavage fluid (BALF), in accordance with the diagnostic criteria of the American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and Infectious Diseases Society of America (IDSA).[16,17] The study was conducted in compliance with the principles of the Declaration of Helsinki (2013 revision) and was approved by the Ethics Committee of Weifang Second People's Hospital (approval number: KY2023-010-01).[18] As this was a retrospective cohort study, all data were obtained from the electronic medical record system and laboratory results. No identifiable personal information was included, and the Ethics Committee approved a waiver of informed consent.

Inclusion criteria were: (1) age ≥18 years, and (2) complete clinical and follow-up data. Exclusion criteria were: (1) co-infection with Mycobacterium tuberculosis or other confirmed pulmonary fungal infections; (2) severe hepatic or renal insufficiency or hematological disorders; and (3) incomplete follow-up data or loss to follow-up.

Sample Size Calculation

The primary outcome of this study was sputum culture conversion. Sample size estimation was based on the principle of events per variable (EPV) for logistic regression analysis. According to the method proposed by Riley et al, at least 10–15 outcome events per candidate predictor variable are required to ensure model stability.[19] In this study, approximately 12 candidate predictors were planned (including age, body mass index [BMI], hemoglobin, albumin, total protein, erythrocyte sedimentation rate [ESR], smoking history, place of residence, and comorbidities). Therefore, at least 120–180 outcome events (sputum conversion or non-conversion) were required. Based on previous literature and pilot data from our center, the sputum conversion rate in NTM-PD patients is estimated at 25–30%.[20] Accordingly, the total sample size required was estimated to be over 400 cases. Ultimately, 416 patients were enrolled, including 109 in the sputum conversion group and 307 in the non-conversion group, thereby meeting the prespecified statistical power requirements.

Data Collection

Data were extracted from the electronic medical record system, including demographic characteristics, nutritional indicators, inflammatory markers, microbiological findings, and comorbidities. Demographic and clinical data included age, sex, marital status, place of residence, and history of smoking or alcohol consumption. Nutritional indicators included BMI, hemoglobin, albumin, total protein, lipid profile, and blood glucose. Inflammatory markers included ESR and lymphocyte count. Microbiological analyses included all nontuberculous mycobacterial isolates isolated from sputum or BALF cultures, and their distribution frequencies were recorded. Clinical symptoms assessed included cough, sputum production, hemoptysis, fever, night sweats, fatigue, anorexia, and weight loss. Radiological follow-up was performed using chest computed tomography (CT) to compare lesion changes before and after treatment, evaluating absorption or progression.

Grouping and Primary Outcome

Nutritional status was assessed using BMI, serum albumin, total protein, and hemoglobin. Malnutrition was defined as the presence of at least one of the following: BMI <18.5 kg/m^2, serum albumin <40 g/L, or hemoglobin <120 g/L.[21–23] Patients were divided into malnutrition and well-nourished groups accordingly, and further stratified into sputum conversion and non-conversion groups based on follow-up sputum smear or culture results. The primary endpoints included the distribution of pathogenic species, differences by nutritional status, and predictors of sputum culture conversion, with subsequent development of a predictive model. This simplified definition was adopted due to the retrospective nature of the study and the limited availability of standardized nutritional assessment tools such as GLIM criteria. Although this approach may introduce potential misclassification bias, it reflects routinely available clinical indicators in real-world settings.

Statistical Analysis

All statistical analyses were conducted using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA) and R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as median (interquartile range, IQR) and compared between groups using the Mann–Whitney *U*-test. Categorical variables were expressed as frequency and percentage, and compared using the chi-square (χ^2) test. Variables with p <0.05 in univariable analysis were entered into multivariable logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs), identifying independent predictors of sputum conversion (This threshold was predefined based on conventional statistical practice). Given the exploratory nature of the study, no formal adjustment for multiple comparisons was performed. Receiver operating characteristic (ROC) curves were generated to compare predictive performance between single factors and the combined model, evaluated by area under the curve (AUC), sensitivity, and specificity. The combined model was constructed using multivariable logistic regression, incorporating age, BMI, hemoglobin, and total protein as independent predictors identified in the analysis. Internal validation was performed using bootstrap resampling (1000 iterations) to assess model stability and potential overfitting.

Kaplan–Meier analysis was performed to evaluate the time-dependent pattern of sputum culture conversion according to nutritional status. Sputum culture conversion was defined as the first documented negative sputum culture during follow-up. The median follow-up time was 9.0 months (interquartile range [IQR]: 6.0–12.0 months). Time to conversion was calculated from the initiation of treatment to the date of sputum culture conversion. Patients who did not achieve culture conversion were censored at the date of last follow-up. Kaplan–Meier curves were constructed to estimate the probability of remaining culture-positive over time, and differences between groups were compared using the Log rank test. A lower curve indicated an earlier and higher probability of sputum culture conversion. All time-to-event analyses were conducted with a two-sided significance level of 0.05. Cumulative sputum culture conversion at clinically relevant time points during follow-up was derived from the Kaplan–Meier estimates. All statistical analyses were conducted following standard methodological practices to ensure robustness and reproducibility.

Results

Pathogen Spectrum in NTM-PD

A total of 423 NTM pathogenic isolates were identified from all enrolled patients. Among them, *M. intracellulare* was the most common species (317 isolates, 78.6%), representing the dominant pathogen. The next most frequent species were *M. kansasii* (43 isolates, 10.7%) and *M. abscessus* (24 isolates, 6.0%).

Less frequently detected species included *Mycobacterium terrene* (*M. terrene*, 12 isolates, 3.0%), *Mycobacterium fortuitum* (*M. fortuitum*, 10 isolates, 2.5%), and *Mycobacterium avium* (*M. avium*, 10 isolates, 2.5%). In addition, *Mycobacterium colombiense* (*M. colombiense*), *Mycobacterium chimaera* (*M. chimaera*), *Mycobacterium malmoense* (*M. malmoense*), *Mycobacterium margaritense* (*M. margaritense*), *Mycobacterium szulgai* (*M. szulgai*), *Mycobacterium scrofulaceum* (*M. scrofulaceum*), *Mycobacterium aarhusense* (*M. aarhusense*), and *Mycobacterium lentiflavum* (*M. lentiflavum*) were each isolated only once (0.2%), considered sporadic species (Table 1). Overall, the pathogen spectrum

Table 1 Distribution of Pathogen Species Isolated from Clinical Samples

Mycobacterial Species	Frequency (n)	Percentage (%)
Mycobacteriu intracellulare	317	78.6
Mycobacterium. kansasii	43	10.7
Mycobacterium. abscessus	24	6
Mycobacterium. chelonae	12	3
Mycobacterium. fortuitum	10	2.5
Mycobacterium. avium	10	2.5
Mycobacterium. colombiense	1	0.2
Mycobacterium. chimaera	1	0.2
Mycobacterium. malmoense	1	0.2
Mycobacterium. marinum	1	0.2
Mycobacterium. szulgai	1	0.2
Mycobacterium. scrofulaceum	1	0.2
Mycobacterium. aurum	1	0.2
Mycobacterium. gordonae	1	0.2
Total	423	100.0

Notes: Values are presented as number of isolates (n) and percentage (%). Percentages were calculated based on the total number of isolates (n = 423). Species names are reported using standard taxonomic nomenclature. Each isolate represents a culture-positive NTM identification from enrolled patients.

was highly concentrated, with *M. intracellulare* predominating, whereas other species were sporadically distributed, suggesting specific pathogen characteristics in this population or environment.

Association Between Nutritional Status and Pathogen Distribution

In the well-nourished group (n = 137, Figure 1A), 120 isolates were identified. *M. intracellulare* remained dominant (94 isolates, 78.3%), followed by *M. kansasii* (19 isolates, 15.8%) and *M. abscessus* (11 isolates, 9.2%). Other species, such as *M. terrene*, *M. fortuitum*, *M. avium*, *M. malmoense*, and *M. colombiense*, were rare (≤2 isolates). In the malnourished group (n = 279, Figure 1B), 303 isolates were isolated, with *M. intracellulare* still predominant (223 isolates, 73.6%), followed by *M. kansasii* (24 isolates, 7.9%) and *M. abscessus* (13 isolates, 4.3%). Other species such as *M. terrene*, *M. fortuitum*, and *M. avium* accounted for <3%. Comparison between groups indicated a relatively higher proportion of

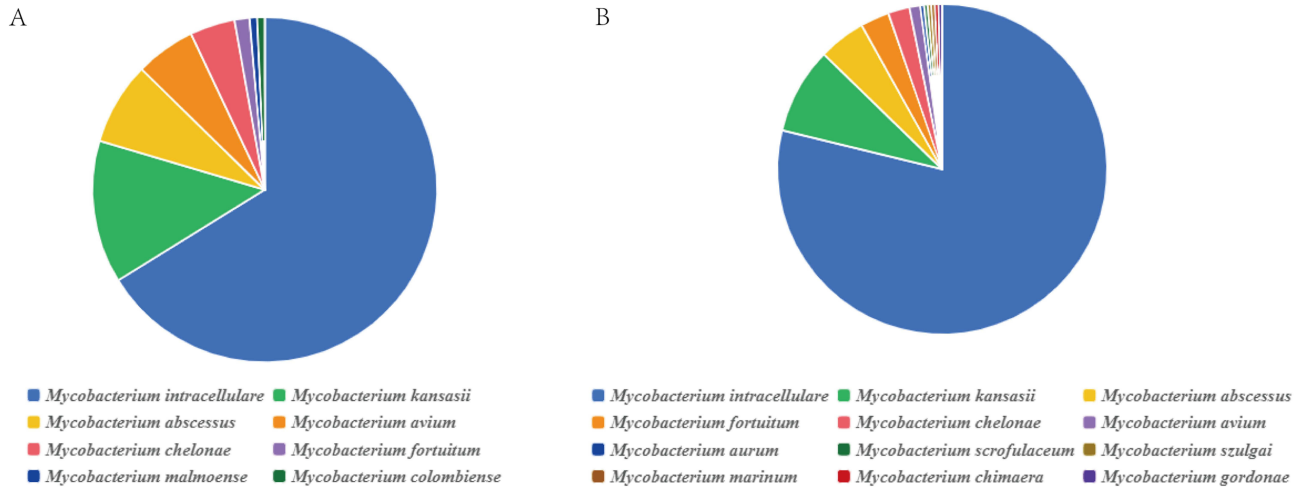

Figure 1 Distribution of pathogenic species stratified by nutritional status. (**A**) Well-nourished group (n = 137); (**B**) Malnourished group (n = 279). The distribution of Mycobacterium species is shown for each group. *M. intracellulare* was the predominant species in both groups, followed by *M. kansasii* and *M. abscessus*.

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M. intracellulare in malnourished patients, whereas low-frequency species (*M. terrene*, *M. fortuitum*, *M. avium*) were slightly more frequent in the well-nourished group. A trend toward differences in pathogen distribution was observed between groups; however, these findings should be interpreted with caution.

Baseline Characteristics of Patients by Nutritional Status

Among 416 patients, 279 were malnourished and 137 were well-nourished (Table 2 and Table 3). Compared with the well-nourished group, the malnourished group was older (65 vs. 57 years, $P < 0.001$), had a higher proportion of males (62.7% vs. 46.0%, $P = 0.001$), and more often lived in rural areas (74.9% vs. 55.5%, $P < 0.001$). Nutritional indices including BMI, hemoglobin, albumin, and total protein were significantly lower in the malnourished group (all $P < 0.001$). ESR was markedly higher (36 vs. 10 mm/h, $P < 0.001$), suggesting greater inflammation. In terms of pathogens, both groups were dominated by *M. intracellulare*, but its proportion was higher in malnourished patients (78.8% vs. 66.2%, $P = 0.043$), whereas *M. avium* and *M. kansasii* were more frequent in well-nourished patients. Regarding comorbidities, the malnourished group showed higher rates of hyperlipidemia, malignancy, rheumatic immune diseases, chronic bronchitis, and interstitial pulmonary fibrosis (all $P < 0.05$).

Clinical Symptoms by Nutritional Status

Significant differences were observed between groups (Table 4). Malnourished patients more frequently had sputum production (87.5% vs. 79.6%, $P = 0.035$), fever (39.8% vs. 13.9%, $P < 0.001$), fatigue (32.3% vs. 18.3%, $P = 0.003$), anorexia (46.2% vs. 18.3%, $P < 0.001$), and weight loss (11.5% vs. 2.2%, $P = 0.001$). No significant differences were found for cough, hemoptysis, night sweats, chest tightness, or chest pain (all $P > 0.05$). Overall, malnourished patients presented with more wasting symptoms (anorexia, weight loss, fatigue) and infection-related manifestations (fever, sputum production), suggesting that poor nutrition may aggravate susceptibility and clinical presentation.

Comparison of Nutritional Indices by Sputum Culture Conversion

Sputum culture conversion was primarily assessed at 3 months after treatment initiation, with extended follow-up up to 12 months to evaluate cumulative conversion over time. As shown in Figure 2, during the 3-month follow-up, patients achieving sputum culture conversion had significantly higher BMI, albumin, and hemoglobin levels compared with non-converters (all $P < 0.001$).

Table 2 Baseline Characteristics of Patients Stratified by Nutritional Status (Continuous Variables)

Variables	Malnourished Group (n=279)	Well-Nourished Group (n=137)	*Z*	*P*
Age (years)	65.00(57.00,72)	57.00(48.00,65.00)	−6.506	< 0.001
Blood pressure (systolic) (mmHg)	122.00(110.00,136.00)	129.00(116.00,140.00)	−2.669	0.008
Blood pressure (diastolic) (mmHg)	75(70,82)	80(70,86)	−3.251	0.001
BMI (kg/m^2)	19.14(17.30,21.45)	22.41(20.20,24.42)	−8.822	< 0.001
Hemoglobin (g/L)	120.00(109.00,131.00)	137.00(127.00,148.00)	−10.318	< 0.001
Albumin (g/L)	36.30(33.00,38.80)	43.50(41.40,45.75)	−14.421	< 0.001
ESR (mm/h)	36.00(17.00,71.00)	10.00(6.00,21.00)	−8.94	< 0.001
Lymphocyte count ($\times 10^9$/L)	1.37(0.97,1.73)	1.64(1.13,2.10)	−3.876	< 0.001
Total protein (g/L)	64.3(59.8,68.3)	71.90(67.35,74.65)	−9.467	< 0.001
Creatinine (μmol/L)	58.60(54.20,67.00)	59.90(52.85,68.40)	−0.442	0.658
Blood glucose (mmol/L)	5.16(4.77,5.85)	5.47(5.04,5.98)	−3.568	< 0.001
Cholesterol (mmol/L)	3.94(3.36,4.63)	4.72(3.86,5.38)	−5.835	< 0.001
Triglyceride (mmol/L)	0.75(0.58,0.99)	0.98(0.69,1.34)	−5.272	< 0.001

Notes: Data are presented as median (IQR). Z values from Mann–Whitney *U*-test.
Abbreviations: BMI, body mass index; ESR, erythrocyte sedimentation rate; BP, blood pressure.

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Table 3 Baseline Characteristics of Patients Stratified by Nutritional Status (Categorical Variables)

Variables n (%)		Malnourished Group (n=279)	Well-Nourished Group (n=137)	χ^2	P
Sex	Male	175(62.72%)	63(45.99%)	10.516	0.001
	Female	104(37.28%)	74(54.01%)		
Pathogen species	*Mycobacterium. intracellulare*	223(78.8%)	94(66.2%)	22.853	0.043
	Mycobacterium. kansasii	24(8.48%)	19(13.38%)		
	Mycobacterium. abscessus	13(4.59%)	11(7.75%)		
	Mycobacterium. fortuitum	8(2.83%)	2(1.41%)		
	Mycobacterium. chelonae	6(2.12%)	6(4.23%)		
	Mycobacterium. avium	3(1.06%)	8(5.63%)		
	Mycobacterium. aurum	1(0.35%)	0(0.0%)		
	Mycobacterium. scrofulaceum	1(0.35%)	0(0.0%)		
	Mycobacterium. szulgai	1(0.35%)	0(0.0%)		
	Mycobacterium. marinum	1(0.35%)	0(0.0%)		
	Mycobacterium. chimaera	1(0.35%)	0(0.0%)		
	Mycobacterium. gordonae	1(0.35%)	0(0.0%)		
	Mycobacterium. malmoense	0(0.0%)	1(0.7%)		
	Mycobacterium. colombiense	0(0.0%)	1(0.7%)		
Marital status	Widowed	27(9.68%)	5(3.65%)	16.201	0.001
	Married	246(88.17%)	119(86.86%)		
	Single	6(2.15%)	11(8.03%)		
	Divorced	0(0.0%)	2(1.46%)		
Smoking	Quit smoking	54(19.35%)	9(6.57%)	13.585	0.001
	No	146(52.33%)	92(67.15%)		
	Yes	79(28.32%)	36(26.28%)		
Alcohol consumption	Quit alcohol	16(5.73%)	2(1.46%)	6.936	0.031
	No	201(72.04%)	113(82.48%)		
	Yes	62(22.22%)	22(16.06%)		
Dust exposure history	No	270(96.77%)	135(98.54%)	1.113	0.352
	Yes	9(3.23%)	2(1.46%)		
Residence	Rural	209(74.91%)	76(55.47%)	16.088	<0.001
	Urban	70(25.09%)	61(44.53%)		
Diabetes mellitus	No	255(91.4%)	129(94.16%)	0.988	0.320
	Yes	24(8.6%)	8(5.84%)		
Hypertension	No	240(86.02%)	118(86.13%)	0.001	0.976
	Yes	39(13.98%)	19(13.87%)		
Hyperlipidemia	No	276(98.92%)	126(91.97%)	13.662	<0.001
	Yes	3(1.08%)	11(8.03%)		
Coronary heart disease	No	251(89.96%)	125(91.24%)	0.172	0.678
	Yes	28(10.04%)	12(8.76%)		
Chronic liver disease (chronic viral hepatitis, fatty liver, cirrhosis)	No	265(94.98%)	123(89.78%)	3.959	0.047
	Yes	14(5.02%)	14(10.22%)		
Cerebrovascular disease (cerebral hemorrhage, cerebral infarction)	No	267(95.7%)	135(98.54%)	2.281	0.131
	Yes	12(4.3%)	2(1.46%)		
Chronic kidney disease	No	276(98.92%)	137(100.0%)	1.484	0.223
	Yes	3(1.08%)	0(0.0%)		
Chronic obstructive pulmonary disease	No	217(77.78%)	115(83.94%)	2.166	0.141
	Yes	62(22.22%)	22(16.06%)		
Interstitial pulmonary fibrosis	No	262(93.91%)	137(100.0%)	8.703	0.003
	Yes	17(6.09%)	0(0.0%)		
Pulmonary aspergillosis	No	270(96.77%)	131(95.62%)	0.352	0.553
	Yes	9(3.23%)	6(4.38%)		
Bronchiectasis	No	210(75.27%)	100(72.99%)	0.251	0.617
	Yes	69(24.73%)	37(27.01%)		
Malignancy	No	260(93.19%)	135(98.54%)	5.487	0.019
	Yes	19(6.81%)	2(1.46%)		

(*Continued*)

Table 3 (Continued).

Variables n (%)		Malnourished Group (n=279)	Well-Nourished Group (n=137)	χ^2	P
Pulmonary tuberculosis	No	265(94.98%)	127(92.7%)	0.880	0.348
	Yes	14(5.02%)	10(7.3%)		
Rheumatic immune diseases	No	262(93.91%)	136(99.27%)	6.384	0.012
	Yes	17(6.09%)	1(0.73%)		
Chronic bronchitis	No	245(87.81%)	130(94.89%)	5.180	0.023
	Yes	34(12.19%)	7(5.11%)		
COVID-19 infection	No	275(98.57%)	135(98.54%)	0.000	0.983
	Yes	4(1.43%)	2(1.46%)		
History of gastric disease (gastritis)	No	28(10.04%)	16(11.68%)	0.262	0.609
	Yes	251(89.96%)	121(88.32%)		
Inflammatory markers	Positive	216(77.42%)	60(43.8%)	46.524	<0.001
	Negative	63(22.58%)	77(56.2%)		

Note: Data are presented as median n (%). χ^2 from Chi-square test.
Abbreviations: BMI, body mass index; ESR, erythrocyte sedimentation rate; BP, blood pressure.

Table 4 Comparison of Clinical Symptoms Between Malnourished and Well-Nourished Groups

Variables n (%)		Malnourished Group (n=279)	Well-Nourished Group (n=137)	χ^2/Z	P
Cough	No	22(7.89%)	15(10.95%)	1.064	0.302
	Yes	257(92.11%)	122(89.05%)		
Sputum production	No	35(12.54%)	28(20.44%)	4.455	0.035
	Yes	244(87.46%)	109(79.56%)		
Hemoptysis	No	225(80.65%)	114(83.21%)	0.401	0.526
	Yes	54(19.35%)	23(16.79%)		
Fever	No	168(60.22%)	118(86.13%)	28.725	<0.001
	Yes	111(39.78%)	19(13.87%)		
Night sweats	No	270(96.77%)	134(97.81%)	0.352	0.553
	Yes	9(3.23%)	3(2.19%)		
Chest tightness	No	142(50.9%)	82(59.85%)	2.967	0.085
	Yes	137(49.1%)	55(40.15%)		
Chest pain	No	244(87.46%)	118(86.13%)	0.143	0.706
	Yes	35(12.54%)	19(13.87%)		
Fatigue	No	189(67.74%)	112(81.75%)	9.016	0.003
	Yes	90(32.26%)	25(18.25%)		
Anorexia	No	150(53.76%)	112(81.75%)	30.871	<0.001
	Yes	129(46.24%)	25(18.25%)		
Weight loss	No	247(88.53%)	134(97.81%)	10.268	0.001
	Yes	32(11.47%)	3(2.19%)		

Notes: Data are presented as n (%). χ^2 values are from Chi-square test. $P < 0.05$ was considered statistically significant.

Baseline Features Associated with Sputum Culture Conversion

Compared with the non-conversion group (n = 307), the sputum conversion group (n = 109) was younger (55 vs. 65 years, $P < 0.001$) and had higher blood pressure (SBP: 127 vs. 122 mmHg, $P = 0.018$; DBP: 80 vs. 75 mmHg, $P = 0.001$). Nutritional indices, including BMI, hemoglobin, and albumin, were all significantly higher in converters (all $P < 0.001$). Total protein, cholesterol, and triglyceride levels were also higher, whereas ESR was lower (10 vs. 33 mm/h, $P < 0.001$), indicating a milder inflammatory response. Comorbidity analysis showed lower rates of malignancy (0.9% vs. 6.5%, $P = 0.022$), rheumatic immune diseases (0% vs. 5.9%, $P = 0.010$), and chronic bronchitis (4.6% vs. 11.7%, $P = 0.032$) in converters. Rural residence was more frequent in non-converters (73.0% vs. 56.0%, $P = 0.001$). Positive inflammatory markers were also more common in non-converters (73.3% vs. 46.8%, $P < 0.001$, Table 5).

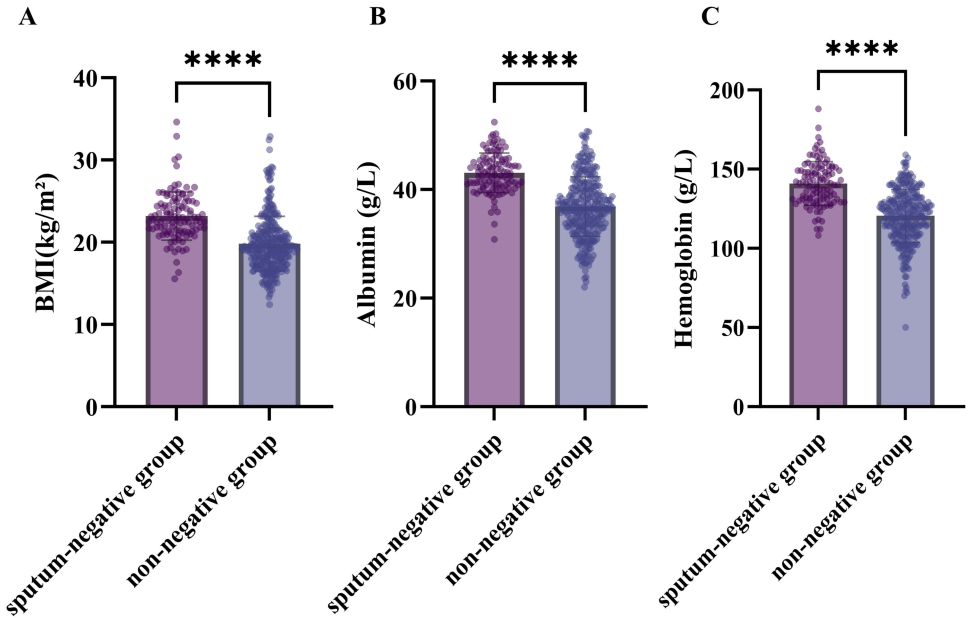

Figure 2 Comparison of nutritional indices between sputum conversion and non-conversion groups. (**A**) BMI (kg/m^2); (**B**) Albumin (g/L); (**C**) Hemoglobin (g/L). ****P < 0.0001.

Independent Risk Factors for Sputum Culture Non-Conversion

Malnutrition (OR ≈ 2.0–2.5), diabetes (OR ≈ 1.8–2.2), and age >65 years (OR ≈ 1.5–2.0) were independent risk factors for sputum non-conversion. Multivariate logistic regression (Tables S1 and 6) identified age (OR = 1.048, 95% CI: 1.012–1.085, P = 0.009), BMI (OR = 0.746, 95% CI: 0.668–0.835, P < 0.001), hemoglobin (OR = 0.936, 95% CI: 0.906–0.967, P < 0.001), and total protein (OR = 0.920, 95% CI: 0.853–0.992, P = 0.031) as independent predictors of sputum conversion. Advanced age was a risk factor, whereas higher BMI, hemoglobin, and total protein were protective. Other factors, including blood pressure, albumin, ESR, smoking, residence, and comorbidities, were not significant (all P > 0.05).

Table 5 Baseline Characteristics and Clinical Features Between Sputum-Negative and Non-Negative Groups

Variables		Sputum Conversion Group (n=109)	Non-Conversion Group (n=307)	t/Z/χ^2	P
Age (years)		55(41.5,65)	65(56,71)	−6.517	<0.001
Blood pressure (systolic) (mmHg)		127(117.5,140)	122(110,137)	−2.368	0.018
Blood pressure (diastolic) (mmHg)		80(70,86)	75(70,82)	−3.247	0.001
BMI (kg/m^2)		19.47(17.58,21.3)	141(131,149.5)	−9.561	<0.001
Hemoglobin (g/L)		141(131,149.5)	122(110,132)	−10.333	<0.001
Albumin (g/L)		43.10 ± 3.64	36.87 ± 5.51	13.245	<0.001
ESR (mm/h)		10(5.5,20)	33(12,68)	−7.979	<0.001
Lymphocyte count (×10^9/L)		1.59(1.15,2.22)	1.38(0.96,1.77)	−3.496	<0.001
Total protein (g/L)		71.09 ± 6.34	65.37 ± 7.50	7.115	<0.001
Creatinine (μmol/L)		61.1(54.5,70)	58.3(52.8,66.1)	−2.207	0.027
Blood glucose (mmol/L)		5.46(4.95,5.94)	5.26(4.87,5.91)	−1.698	0.09
Cholesterol (mmol/L)		4.54(3.77,5.28)	4.03(3.44,4.80)	−3.595	<0.001
Triglyceride (mmol/L)		0.98(0.65,1.31)	0.77(0.59,1.01)	−4.005	<0.001
Sex, n (%)	Male	59(54.13%)	179(58.31%)	0.574	0.449
	Female	50(45.87%)	128(41.69%)		

(*Continued*)

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Table 5 (Continued).

Variables		Sputum Conversion Group (n=109)	Non-Conversion Group (n=307)	$t/Z/\chi^2$	P
Pathogen species	Intracellular	70(62.5%)	249(79.05%)	21.800	0.059
	Kansasis	19(16.96%)	24(7.62%)		
	Abscess	8(7.14%)	16(5.08%)		
	Occasional	3(2.68%)	7(2.22%)		
	Turtle	6(5.36%)	6(1.9%)		
	Bird	6(5.36%)	5(1.59%)		
	Aarhus	0(0.0%)	1(0.32%)		
	Scrofula	0(0.0%)	1(0.32%)		
	Suga	0(0.0%)	1(0.32%)		
	Margaret	0(0.0%)	1(0.32%)		
	Chimera	0(0.0%)	1(0.32%)		
	Slow-growing Yellow	0(0.0%)	1(0.32%)		
	Malmo	0(0.0%)	1(0.32%)		
	Colombia	0(0.0%)	1(0.32%)		
Marital status	Widowed	4(3.67%)	28(9.12%)	21.236	<0.001
	Married	93(85.32%)	272(88.6%)		
	Single	12(11.01%)	5(1.63%)		
	Divorced	0(0.0%)	2(0.65%)		
Smoking	Quit smoking	7(6.42%)	56(18.24%)	9.440	0.009
	No	72(66.06%)	166(54.07%)		
	Yes	30(27.52%)	85(27.69%)		
Alcohol consumption	Quit alcohol	2(1.83%)	16(5.21%)	3.855	0.146
	No	89(81.65%)	225(73.29%)		
	Yes	18(16.51%)	66(21.5%)		
Dust exposure history	No	107(98.17%)	298(97.07%)	0.376	0.540
	Yes	2(1.83%)	9(2.93%)		
Residence	Rural	61(55.96%)	224(72.96%)	10.777	0.001
	Urban	48(44.04%)	83(27.04%)		
Diabetes mellitus	No	103(94.5%)	281(91.53%)	0.996	0.318
	Yes	6(5.5%)	26(8.47%)		
Hypertension	No	96(88.07%)	262(85.34%)	0.500	0.479
	Yes	13(11.93%)	45(14.66%)		
Hyperlipidemia	No	102(93.58%)	300(97.72%)	4.243	0.039
	Yes	7(6.42%)	7(2.28%)		
Coronary heart disease	No	100(91.74%)	276(89.9%)	0.314	0.575
	Yes	9(8.26%)	31(10.1%)		
Chronic liver disease (chronic viral hepatitis, fatty liver, cirrhosis)	No	98(89.91%)	290(94.46%)	2.658	0.103
	Yes	11(10.09%)	17(5.54%)		
Cerebrovascular disease (cerebral hemorrhage, cerebral infarction)	No	107(98.17%)	295(96.09%)	1.064	0.302
	Yes	2(1.83%)	12(3.91%)		
Chronic kidney disease	No	109(100.0%)	304(99.02%)	1.073	0.300
	Yes	0(0.0%)	3(0.98%)		
Chronic obstructive pulmonary disease	No	91(83.49%)	241(78.5%)	1.240	0.265
	Yes	18(16.51%)	66(21.5%)		
Interstitial pulmonary fibrosis	No	108(99.08%)	291(94.79%)	3.785	0.052
	Yes	1(0.92%)	16(5.21%)		
Pulmonary aspergillosis	No	107(98.17%)	294(95.77%)	1.333	0.248
	Yes	2(1.83%)	13(4.23%)		
Bronchiectasis	No	81(74.31%)	229(74.59%)	0.003	0.954
	Yes	28(25.69%)	78(25.41%)		
Malignancy	No	108(99.08%)	287(93.49%)	5.258	0.022
	Yes	1(0.92%)	20(6.51%)		
Pulmonary tuberculosis	No	99(90.83%)	293(95.44%)	3.150	0.076
	Yes	10(95.44%)	14(4.56%)		

(*Continued*)

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Table 5 (Continued).

Variables		Sputum Conversion Group (n=109)	Non-Conversion Group (n=307)	t/Z/χ^2	P
Rheumatic immune diseases	No	109(100.0%)	289(94.14%)	6.680	0.010
	Yes	0(0.0%)	18(5.86%)		
Chronic bronchitis	No	104(95.41%)	271(88.27%)	4.615	0.032
	Yes	5(4.59%)	36(11.73%)		
COVID-19 infection	No	107(98.17%)	303(98.7%)	0.160	0.689
	Yes	2(1.83%)	4(1.3%)		
History of gastric disease (gastritis)	No	102(93.58%)	270(87.95%)	2.696	0.101
	Yes	7(6.42%)	37(12.05%)		
Inflammatory markers	Positive	51(46.79%)	225(73.29%)	25.301	<0.001
	Negative	58(53.21%)	82(26.71%)		

Notes: Data are presented as median (IQR), mean ± SD, or n (%). Z values derived from Mann–Whitney *U*-test, χ^2 from Chi-square test.
Abbreviations: BMI, body mass index; ESR, erythrocyte sedimentation rate; BP, blood pressure.

Table 6 Multivariate Logistic Regression Analysis of Factors Associated with Sputum Conversion

Variable	β	SE	Wald	p-value	OR	95% CI (Lower Limit, Superior Limit)
Age	0.047	0.018	6.878	0.009	1.048	1.012–1.085
Blood pressure_systolic	−0.008	0.013	0.33	0.565	0.992	0.967–1.019
Blood pressure_diastolic	−0.015	0.023	0.42	0.517	0.985	0.941–1.031
BMI	−0.292	0.057	26.353	0	0.746	0.668–0.835
Hemoglobin	−0.067	0.017	16.049	0	0.936	0.906–0.967
Albumin	−0.042	0.061	0.485	0.486	0.959	0.851–1.08
ESR	0.017	0.011	2.357	0.125	1.018	0.995–1.04
Lymphocyte count	−0.004	0.223	0	0.986	0.996	0.643–1.542
Total protein	−0.083	0.039	4.675	0.031	0.92	0.853–0.992
Creatinine	−0.013	0.012	1.12	0.29	0.987	0.963–1.011
Cholesterol	−0.307	0.192	2.552	0.11	0.735	0.504–1.072
Triglyceride	−0.153	0.337	0.205	0.651	0.858	0.443–1.663
Marital status			2.657	0.448		
Marital status (1)	−20.309	27986.728	0	0.999	0	0
Marital status (2)	−21.395	27986.728	0	0.999	0	0
Marital status (3)	−19.943	27986.728	0	0.999	0	0
Smoking status			0.461	0.794		
Yes vs Quit	−0.305	0.457	0.444	0.505	0.737	0.301–1.806
Never vs Quit	−0.107	0.689	0.024	0.877	0.899	0.233–3.467
Residence	0.022	0.356	0.004	0.951	1.022	0.508–2.055
Hyperlipidemia	−0.666	0.776	0.737	0.391	0.514	0.112–2.349
Malignancy	−0.975	1.29	0.572	0.45	0.377	0.03–4.727
Rheumatic immune diseases	−16.972	8227.713	0	0.998	0	0
Chronic bronchitis	−0.166	0.685	0.059	0.808	0.847	0.221–3.245
Inflammation-related	0.261	0.401	0.423	0.515	1.298	0.591–2.852
Alliance	63.761	29171.074	0	0.998	490786208657810000000000000.000	–

Notes: (1) (2), (3) indicate that when a variable is categorical with more than two levels, one category is selected as the reference group, and the remaining categories are coded as (1), (2), (3)… to represent the effect relative to the reference group. Logistic regression model was applied to identify independent factors for sputum conversion. OR < 1 indicates protective factors, OR > 1 indicates risk factors.Variables with P < 0.05 are considered statistically significant. Large OR values may reflect sparse data and should be interpreted with caution.

ROC Curve Analysis for Predictive Performance

As shown in Table 7 and Figure 3, in single-variable models, hemoglobin (AUC = 0.833, 95% CI: 0.792–0.874) and BMI (AUC = 0.808, 95% CI: 0.764–0.852) had the best predictive performance, whereas total protein (AUC = 0.723, 95% CI:

Table 7 ROC Curve Analysis of Predictors for Sputum Conversion

Variable	AUC	Youden	S.E.	95% CI	Sensitivity (%)	Specificity (%)
Age (years)	0.7099	0.3366	0.02958	0.6520 to 0.7679	70.36	63.3
BMI (kg/m^2)	0.8081	0.4972	0.02249	0.7640 to 0.8522	57.98	91.74
Hemoglobin (g/L)	0.8329	0.5189	0.02115	0.7915 to 0.8744	68.4	83.49
Total Protein (g/L)	0.7227	0.3827	0.02634	0.6711 to 0.7743	55.7	82.57
Combined model (Alliance)	0.9251	0.6723	0.01359	0.8985 to 0.9517	89.25	77.98

Notes: Youden Index = Sensitivity + Specificity – 1. The "Alliance" represents the combined prediction model integrating multiple variables.
Abbreviations: AUC, area under the curve; SE, standard error; CI, confidence interval.

0.671–0.774) and age (AUC = 0.710, 95% CI: 0.652–0.768) were less predictive. The combined model, incorporating age, BMI, hemoglobin, and total protein, demonstrated improved predictive performance compared with individual predictors. By contrast, the combined model integrating multiple indices achieved the highest performance (AUC = 0.925, 95% CI: 0.899–0.952), with sensitivity 89.3% and specificity 78.0%, significantly outperforming any single predictor. This indicates that the combined model has higher clinical utility in predicting sputum culture conversion.

Time-Dependent Sputum Culture Conversion According to Nutritional Status

To further characterize the time-dependent pattern of sputum culture conversion, Kaplan–Meier analysis was performed to assess the probability of remaining culture-positive according to nutritional status (Figure 4). During a median follow-up of 9.0 months (IQR: 6.0–12.0 months), patients in the well-nourished group showed a significantly higher probability of sputum culture conversion. Throughout the 12-month follow-up, patients in the well-nourished group exhibited a significantly lower probability of remaining culture-positive compared with those in the malnourished group, indicating earlier and more frequent sputum culture conversion.

The separation between the two curves became evident within the early months after treatment initiation and progressively widened over time. By 12 months, the proportion of patients remaining culture-positive was markedly higher in the malnourished group, whereas a substantially greater proportion of well-nourished patients had achieved sputum culture conversion. The difference in culture conversion dynamics between the two groups was statistically significant (Log rank test, $P < 0.0001$).

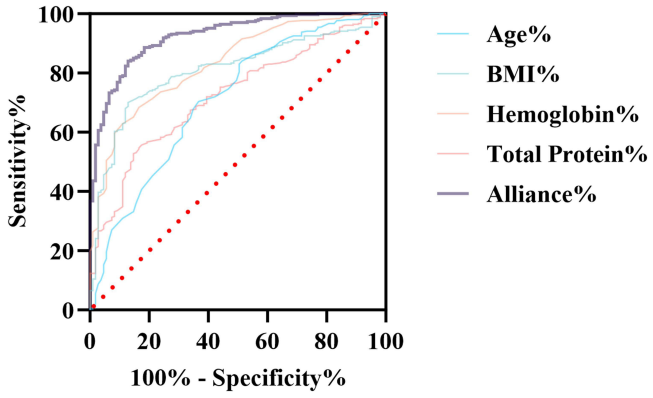

Figure 3 Receiver operating characteristic (ROC) curves for predicting sputum culture conversion. ROC curves were generated for individual predictors (age, BMI, hemoglobin, and total protein) and the combined model. The combined model (Alliance) included age, BMI, hemoglobin, and total protein. The area under the curve (AUC) was used to evaluate predictive performance.

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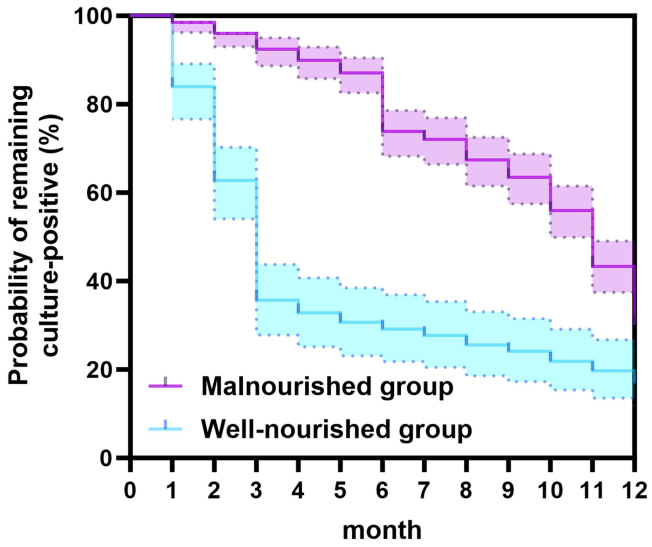

Figure 4 Kaplan–Meier curves showing the probability of remaining culture-positive stratified by nutritional status. Sputum culture conversion was defined as the event. Patients without conversion were censored at the last follow-up. A lower curve indicates a higher and earlier probability of sputum culture conversion.

Discussion

Current Status of Research on NTM-PD

NTM-PD has shown an increasing trend globally and in China in recent years.[24] The pathogen spectrum is complex, primarily including *Mycobacterium avium* complex (MAC), *M. intracellulare*, *M. abscessus*, and *M. kansasii*, with geographic and environmental exposure differences.[25] Previous studies have mainly focused on pathogen identification, drug susceptibility, imaging features, and immunophenotypes, whereas the relationship between nutritional status (eg, BMI, serum protein/albumin levels) and sputum culture conversion or treatment outcomes has been less frequently reported. In several studies in China, elderly or malnourished patients were noted to have lower treatment or microbiological sputum conversion rates compared with well-nourished patients, though specific indicators and predictive models vary widely.[26] For example, Kang et al[27] noted in a systematic review that "elderly and malnourished" patients represent a population with lower microbiological cure rates after treatment completion.

Comparison with Existing Literature

Consistent with our findings, Kang et al reported that malnourished NTM-PD patients in multiple regions of China had lower treatment or microbiological sputum conversion rates, and elderly patients had reduced cure rates.[27–29] Moon et al[30] found that lower BMI in MAC-PD patients was associated with failure to achieve sputum conversion, although hemoglobin and other indicators did not emerge as strong independent factors in their sample. Regarding nutritional assessment tools, Chung et al[31] recently evaluated the utility of the short-form Mini Nutritional Assessment (MNA-SF) in elderly NTM-PD patients, finding moderate correlations with BMI, CT lesion severity, and other disease severity indicators, supporting the link between nutritional status and disease severity/outcomes. In our study, Follow-up imaging showed that improved cases exhibited lesion shrinkage and absorption of inflammatory consolidation, whereas progression cases demonstrated lesion enlargement and aggravation of fibrotic strands (Figure S1). Total protein and hemoglobin were included in the model as protective factors, consistent with previous studies, but we additionally found that their combined predictive performance was superior, a finding rarely reported in prior literature.

Potential Mechanistic Explanations

The strong association between malnutrition and failure to achieve sputum conversion may reflect multiple mechanisms. First, malnutrition is associated with insufficient protein and energy intake, resulting in decreased serum proteins (including albumin and total protein) and impaired immune function, particularly cell-mediated immunity, reducing pathogen clearance.[32]

Second, decreased hemoglobin may cause tissue hypoxia, impairing local pulmonary immune responses, including macrophage phagocytosis and reactive oxygen species-mediated bacterial killing.[33] Third, advanced age contributes to immunosenescence and a higher prevalence of comorbidities (eg, chronic bronchitis, interstitial lung disease), which may further delay or hinder pathogen clearance. Additionally, recent experimental and basic research suggests that protein-energy restriction can exacerbate MAC-PD progression by disrupting lipid metabolism and impairing immune and pulmonary tissue repair functions.[34] Collectively, these mechanisms may explain the lower sputum conversion rates in malnourished patients.

The observed predominance of *Mycobacterium intracellulare* in malnourished patients may reflect a potential interaction between host nutritional status and pathogen susceptibility. Malnutrition has been associated with impaired immune responses, which may influence host–pathogen dynamics and contribute to differential pathogen distribution. Although this relationship requires further investigation, it suggests that nutritional status may play a role in shaping the microbial profile in NTM-PD.

Clinical Significance and Applications

This study provides additional insight into the association between nutritional status and sputum culture conversion in NTM-PD. Our study highlights that nutritional status in NTM-PD patients not only reflects overall health but is closely associated with sputum culture conversion. Early screening of nutritional indices may help identify high-risk patients and guide individualized treatment and care management.[35] In particular, routine monitoring of BMI, hemoglobin, and total protein can serve as important supplemental prognostic indicators. The combined predictive model demonstrated high sensitivity and specificity in our study, suggesting its potential application in clinical risk stratification and follow-up management; however, further validation is required before clinical application. These findings may assist clinicians in identifying patients at higher risk of delayed sputum culture conversion and support individualized risk stratification in NTM-PD.

Limitations and Future Directions

Despite a comprehensive analysis of nutritional indices, pathogen spectrum, clinical symptoms, and sputum outcomes, this study has limitations. Some regression coefficients appeared relatively large, which may reflect sparse data or quasi-separation, a known issue in multivariable logistic regression when certain categories have limited observations. However, the direction and statistical significance of the key predictors remained consistent. First, it was a single-center retrospective study, which may introduce selection bias. The study population was derived from a single-center cohort, which may limit the generalizability of the findings to other regions or healthcare settings. Second, follow-up was limited to short-term sputum culture conversion, without systematic evaluation of long-term outcomes such as recurrence, pulmonary function decline, or mortality. Third, some confounding factors were not fully included, such as differences in treatment regimens, medication adherence, environmental exposures (eg, water and soil pathogens), and immune cell function (eg, T-cell subsets). Future research could adopt prospective, multicenter designs with larger sample sizes, incorporating immune function indices, microbiome analysis, and genetic susceptibility, to establish more dynamic and generalizable predictive models. Interventional studies on nutritional support (dietary or supplementation) to improve sputum conversion rates are also warranted. The use of a simplified nutritional classification may have introduced misclassification bias. Important treatment-related factors, including regimen selection, duration of therapy, and treatment adherence, were not consistently available and therefore were not included in the analysis. These variables may act as potential confounders influencing sputum culture conversion. Although internal validation was performed, external validation was not conducted, which may limit the generalizability and robustness of the predictive model. The model should be considered exploratory and hypothesis-generating rather than definitive. The model requires further validation before clinical application.

Conclusion

The observed predominance of *M. intracellulare* in malnourished patients in this cohort may indicate a potential association between host nutritional status and pathogen distribution. Malnutrition has been associated with impaired immune responses, which may alter host–pathogen interactions and influence susceptibility to specific mycobacterial species. However, given the observational design of this study, this finding should be interpreted with caution and does not imply a causal relationship. Further studies are required to clarify the underlying mechanisms. Nevertheless, these findings suggest that nutritional status

may be a contributing factor in shaping the microbial profile in patients with NTM-PD. The model demonstrates potential utility for risk stratification; however, further validation is required before clinical application.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was conducted in compliance with the principles of the Declaration of Helsinki (2013 revision) and was approved by the Ethics Committee of Weifang Second People's Hospital (approval number: KY2023-010-01). As this was a retrospective cohort study, all data were obtained from the electronic medical record system and laboratory results. No identifiable personal information was included, and the Ethics Committee approved a waiver of informed consent.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there is no competing interests.

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