ORIGINAL RESEARCH

Correlation between Water Environment and Prevalence of Nontuberculous Mycobacteria Pulmonary Disease: A Case-Control Study

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ABSTRACT

Objective • Nontuberculous mycobacteria (NTM) prevalence in water systems has raised concerns about Nontuberculous Mycobacteria Pulmonary Disease (NTM-PD). Understanding the relationship between NTM-PD, drinking water distribution systems (DWDS), and other epidemiological factors is crucial for public health.

Methods • A case-control study was conducted at the Inpatient Department of Tuberculosis Department of Shanghai Pulmonary Hospital. Subjects were divided into the NTM-PD group (n = 314) and pulmonary tuberculosis (PTB) group (n = 308) at a 1:1 ratio. Data was collected through questionnaires covering general information, depression (Self-Rating Depression Scale, SDS), and anxiety (Self-Rating Anxiety Scale, SAS). Multivariate unconditional logistic regression analysis was employed for the study.

Results • The average age of NTM-PD patients was 55.26±14.44, with clinical symptoms including chest tightness, shortness of breath, hemoptysis, fever, and expectoration. Risk factors for NTM-PD included age (>60 years old, OR=1.042), gender (female, OR = 3.089), secondary water supply system (OR = 7.813), occupation (farmer/flower farmer, OR=2.676), depression (OR = 2.956), recurrent bronchiectasis (OR = 6.314), chronic obstructive pulmonary disease (COPD, OR = 2.704), and autoimmune disease (OR = 13.588) ($P < .05$). Use of household water purifiers was identified as a protective factor (OR = 0.128, $P < .001$).

Conclusion • DWDS, drinking water mode, soil-related occupation, bronchiectasis, COPD, age, sex, and depression were closely related to the risk of NTM-PD. It is suggested to pay attention to water hygiene and illness progress and regulate mood to prevent NTM-PD in daily life. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Nontuberculous mycobacteria (NTM) refers to the general term of a large class of mycobacterium except for mycobacterium tuberculosis complex and mycobacterium leprosy, so far, more than 190 NTM strains have been found, most of which are saprophytic parasites, and only a few are pathogenic to humans.[1] NTM can invade human lungs, lymph nodes, bones, joints, skin and other tissues and organs and can cause systemic disseminated diseases.[2] In recent years, the incidence rate of nontuberculous mycobacteria disease (NTMD) around the world has increasing year by year, of which nontuberculous mycobacteria pulmonary disease (NTM-PD) is the most common.[3,4] The incidence rate of NTM-PD showed an obvious upward trend, and it had a trend of surpassing the incidence rate of pulmonary tuberculosis (PTB), which has garnered significant attention worldwide.[5] The distribution of NTM in nature is affected by many factors, such as temperature and humidity, so the distribution of NTM has regional differences. The prevalence of NTM-PD varies greatly in different regions of China. Compared with other regions, the proportion of NTM infection in the eastern and southern regions is higher, which may be related to geographical distribution; that is, coastal areas are higher than inland areas, areas with mild climate are higher than cold areas, and plains and coastal areas are higher than mountains.[6]

In addition to the natural environment, NTM can also be detected in the living environment, such as water distribution

systems, soil, and bathtubs.[7] Due to its resistance to chloramine, NTM continues to exist in water systems, leading to the prevalence of NTM-PD.[8] Although the raw water of many water supply factories contains NTM, the detection rate of NTM before and after treatment in the water factories usually decreases significantly by reducing the turbidity and the content of absorbable organic matter and taking effective disinfection methods.[9] Microorganisms can enter the water supply pipe network at the inlet of the pipe network and during the installation and maintenance of the pipe, and finally survive in the pipe network and form biofilm on the pipe wall, so the detection rate of NTM in drinking water transported through the pipe network has generally increased.[10,11] Compared with the above two water supply modes, the water quality of secondary water supply systems (SWSS) is more vulnerable to pollution.[12] Research showed that the detection rate of NTM in some SWSS was even more than 50%.[13,14] In addition, some researchers investigated the NTM in the building hot water system, and the research showed that the concentration of NTM in the water samples taken at the end of the building hot water system (such as shower nozzle and faucet) was higher than that of the pipe network.[15] It was also reported that the NTM isolated from soil was similar to that studies have shown in the respiratory tract of patients with NTM-PD, which proved that the soil was closely related to the occurrence of NTM-PD.[16]

The occurrence of NTM-PD is also related to the immune ability of the body; that is, when the body has chronic basic disease and consumes energy for a long time, it is easy to suffer from NTM-PD.[17] Suska et al.[18] found that NTM infection was common in patients with bronchiectasis, indicating that bronchiectasis is related to the existence of NTM-PD. Prevots et al.[19] showed that the incidence of bronchiectasis was 44.6% in NTM-PD group (n = 35 444) and 17.7% in control group (n = 65 467), at the same time, in the NTM-PD group and the control group, the rate of chronic obstructive pulmonary disease (COPD) was 81.1% and 17.7% respectively, which fully demonstrated that bronchiectasis and COPD are risk factors of NTM-PD. Research also showed that cystic fibrosis,[20] trauma,[21] rheumatoid arthritis[22] and other diseases are related to NTM-PD. In addition to disease factors, Kim et al.[23] found that >65 years is a risk factor for NTM-PD. Research also showed that females were more prone to the NTM-PD than males, especially menopausal females.[24,25] The Study found that the rate of depression patients suffering from PTB increased, but the relationship between depression patients and NTM-PD still needs to be studied.[26]

Although Nontuberculous Mycobacteria Disease (NTM-PD) is considered a rare disease, an increasing number of NTMs have been identified in clinical practice. The clinical manifestations of NTM-PD typically include cough, expectoration, hemoptysis, chest pain, chest tightness, asthma, night sweats, fever, fatigue, emaciation, and discomfort.[27] There are many uncertainties in the treatment of NTM-PD, thus, identifying its risk factors and initiating prevention as early as possible is of significant importance. NTM infects humans through environmental contact, with water being the most important medium of transmission, serving as one of the most crucial factors in maintaining daily life and essential activities. Therefore, the primary objectives of this study are explicitly stated as follows: to analyze the relationship between the Drinking Water Distribution System (DWDS), drinking water mode, bathing habits, and the prevalence of NTM-PD. Simultaneously, the study will also explore the relationships between autoimmune diseases, depression, anxiety, demographic characteristics, and NTM-PD. These research objectives will aid in deepening our understanding of the risk factors and preventive measures for NTM-PD.

METHODS

Study design and sampling

This cross-sectional study was conducted from October 2019 to October 2021, and 650 questionnaires were collected from the Inpatient Department of the tuberculosis Department of Shanghai Pulmonary Hospital in the form of questionnaires. 639 questionnaires were successfully recovered; two patients with NTM-PD and PTB were excluded; 15 questionnaires were filled with errors and omissions. Finally, a total of 622 patients were included in the analysis. We conducted a case-control study and divided the subjects into the NTM-PD group (n = 314) and the PTB group (n = 308) according to the ratio of 1:1.

Inclusion criteria of patients: (1) Patients diagnosed with NTM pulmonary disease have unlimited pathogenic bacteria in the NTM-PD group; (2) Patients with lung diseases (tuberculosis, other lung infections) without NTM-PD in the PTB group; (3) Patient age: 16-80 years old, gender unlimited. Exclusion criteria for patients: (1) Those who cannot obtain sputum/bronchial lavage fluid samples; (2) Patients in the control group were subsequently diagnosed as NTM-PD according to the relevant examination results after filling in the form; (3) Patients in the treatment group who were found to have tuberculosis at the same time after filling in the form; (4) Those who are unable to cooperate, refuse to fill in or truthfully fill in the questionnaire; (5) People with HIV infection. The rationale behind these criteria was to identify individuals with significant depression or anxiety symptoms and exclude individuals with potential confounding factors that could influence the results.

Variable measurement

Self-made basic information questionnaire. The general demographic characteristics, lifestyle and disease characteristics of patients, including age, gender, marital status, education level, annual household income, occupation, smoking, alcohol drinking, eating habits, residential environment, drinking water mode, DWDS, bathing times, recurrent bronchiectasis, history of tuberculosis, complication, and disinfection of skin trauma were measured. We also recorded the clinical symptoms of NTM-PD, including chest tightness and shortness of breath, hemoptysis, fever, and expectoration.

Assessment of depression and anxiety. Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS) contained both emotional and physical symptoms, including 20 items, respectively.[28] Add all the items together to form a rough score, which is multiplied by 1.25 and rounded to get the standard score to evaluate depression and anxiety. The index score of 50 (original score) was set as the cut-off point for clinically significant depression and anxiety in this research. The Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS) are commonly used in research studies to assess depression and anxiety symptoms, respectively. These scales are easy to administer and score, making them practical for use in large-scale studies. The SDS and SAS have both been shown to have good reliability and validity. Reliability refers to the consistency of the scale's measurements, while validity refers to the accuracy of the scale's measurements. High reliability and validity are important for ensuring that the scales are measuring what they are intended to measure. In terms of reliability, the SDS and SAS have both been found to have high internal consistency, meaning that the items within the scale are measuring the same construct. Additionally, the scales have been found to have good test-retest reliability, meaning that they produce consistent results when administered multiple times. In terms of validity, the SDS and SAS have been found to have good convergent validity, meaning that they correlate well with other measures of depression and anxiety. Additionally, the scales have been found to have good discriminant validity, meaning that they can distinguish between individuals with different levels of depression and anxiety. Overall, the SDS and SAS are widely used and have been found to be reliable and valid measures of depression and anxiety symptoms, making them valuable tools for researchers studying these conditions.

Statistical analysis

Statistic Package for Social Science (SPSS) 26.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. The χ^2 test was used for single factor analysis, and the multivariate unconditional logistic regression analysis was used. $P < .05$ was statistically significant.

RESULTS

Basic information about patients

A total of 622 patients were included in the analysis. 314 (50.5%) patients were in the NTM-PD group, and 308 were (49.5%) in the PTB group. The average age of PTB patients was 41.81±16.95, and the average age of NTM-PD patients was 55.26±14.44. The clinical symptoms of 314 cases of NTM-PD in this study mainly included chest tightness and shortness of breath, hemoptysis, fever, and expectoration. More patients with NTM-PD showed expectoration symptoms. Table 1 shows the details.

Table 1. Clinical symptom data

Clinical symptoms	Chest tightness and shortness of breath	Hemoptysis	Fever	Expectoration
PTB	67	52	82	233
NTM-PD	102	112	94	280
χ^2	9.200	28.263	0.796	19.672
P value	.002	<.001	.372	<.001

Table 2. Relationship between demographic characteristics and NTM-PD (N = 622)

Variables	n (%)	PTB n (%)	NTM-PD n (%)	χ^2	*P* value
Age				115.46	<.001
≤17	11(1.8)	7(1.1%)	4(0.6)		
18-44	225(36.2)	174(28.0)	51(8.2)		
45-59	184(29.6)	68(10.9)	116(18.6)		
≥60	202(32.5)	59(9.5)	143(23.0)		
Gender				52.148	<.001
Male	315(50.6)	201(32.3)	114(18.3)		
Female	307(49.4)	107(17.2)	200(32.2)		
Marital status				51.713	<.001
Unmarried	137(22.0)	105(16.9)	32(5.1)		
Married	485(78.0)	203(32.6)	282(45.4)		
Education level				28.933	<.001
None	42(6.8)	15(2.4)	27(4.3)		
Primary school	62(10.0)	28(4.5)	34(5.5)		
Junior high school	167(26.8)	61(9.8)	106(17.0)		
High school	154(24.8)	84(13.5)	70(11.3)		
Undergraduate	176(28.3)	104(16.7)	72(11.6)		
Graduate student	21(3.4)	16(2.6)	5(0.8)		
Annual household income (CNY)				9.830	.043
≤50,000	186(29.9)	83(13.3)	103(16.6)		
50,000-100,000	203(32.6)	91(14.6)	112(18.0)		
100,000-200,000	162(26.0)	93(15.0)	69(11.1)		
200,000-400,000	52(8.4)	29(4.7)	23(3.7)		
400,000-800,000	19(3.1)	12(1.9)	7(1.1)		
Occupation				30.142	<.001
Other	431(69.3)	245(39.4)	186(29.9)		
Farmers/Flower farmers	191(30.7)	63(10.1)	128(20.6)		
Depression				17.720	<.001
No	499(80.2)	268(43.1)	231(37.1)		
Yes	123(19.8)	40(6.4)	83(13.4)		
Anxiety				1.963	.161
No	501(80.5)	255(41.0)	246(39.5)		
Yes	121(19.5)	53(8.6)	68(10.9)		

Demographic characteristics and prevalence of NTM-PD

Table 2 shows the relationship between demographic characteristics and the prevalence of NTM-PD. 32.5% (202) of the participants were ≥60 years old, and the prevalence of NTM-PD was significantly higher than that of other age groups ($P < .001$). 49.4% (307) of the participants were female, who showed a significantly higher prevalence of NTM-PD than males ($P < .001$). The prevalence of NTM-PD in the unmarried group was significantly lower than that in the married group ($P < .001$). Participants with junior high school education had a significantly higher prevalence of NTM-PD than that of other groups ($P < .001$). Participants who had an annual income of ≤50 000 CNY showed a higher prevalence of NTM-PD higher than that of other groups ($P = .043$). 30.7% (191) of the participants were farmers/flower farmers who mainly worked in contact with soil, and the prevalence of NTM-PD was significantly higher than that of other occupations ($P < .001$). Participants with depression showed a significantly higher prevalence of NTM-PD ($P < .001$). There was no significant difference in the prevalence of NTM-PD among anxiety groups ($P > .05$).

Lifestyle characteristics and prevalence of NTM-PD

The relationship between lifestyle characteristics and NTM-PD is displayed in Table 3. The results showed that participants without alcohol drinking showed a higher prevalence of NTM-PD ($P < .001$). 64.8% (403) of the participants drank water from tap water, and the prevalence of NTM-PD was significantly higher than that of the participants who used BWDs (bottled water dispensers) and HWPs (Household Water-purifiers) ($P <$

Table 3. Relationship between lifestyle characteristics and NTM-PD

Variables	n (%)	PTB n (%)	NTMPD n (%)	χ^2	*P* value
Smoking				4.576	.101
Yes	98(15.8)	58(9.4)	40(6.5)		
No	472(75.9)	225(36.5)	247(40.1)		
Passive smoking	46(7.4)	21(3.4)	25(4.1)		
Alcohol Drinking				16.543	<.001
No	387(62.2)	168(27.0)	219(35.2)		
Occasionally	205(33.0)	125(20.1)	80(12.9)		
Often	30(4.8)	15(2.4)	15(2.4)		
Keeping pets				0.747	.387
Yes	61(9.8)	27(4.3)	34(5.5)		
No	561(90.2)	281(45.2)	280(45.0)		
Eating habits				2.260	.323
Vegetarian	51(8.2)	21(3.4)	30(4.8)		
Regular diet	549(88.3)	274(44.1)	275(44.2)		
Other	22(3.5)	13(2.1)	9(1.4)		
Residential floor				4.797	.091
1st floor	153(24.6)	64(10.3)	89(14.3)		
2-8 floors	369(59.3)	192(30.9)	177(28.5)		
8th floor and above	100(16.1)	52(8.4)	48(7.7)		
Residential environment				0.012	.913
Good lighting	585(94.1)	290(46.6)	295(47.4)		
Dark and damp	37(5.9)	18(2.9)	19(3.1)		
Drinking water mode				103.556	<.001
Tap water	403(64.8)	140(22.5)	263(42.3)		
BWDs	99(15.9)	69(11.1)	30(4.8)		
HWPs	120(19.3)	99(15.9)	21(3.4)		
DWDS				60.854	<.001
Pipe network water system	454(73.0)	268(43.1)	186(29.9)		
SWSS	168(27.0)	40(6.4)	128(20.6)		
Bathing times				13.317	.004
1/One day	323(51.9)	159(25.6)	164(26.4)		
2/One day	63(10.1)	38(6.1)	25(4.0)		
1/Two day	90(14.5)	54(8.7)	36(5.8)		
Bathing habit				9.976	.007
Bath tub	34(5.5)	8(1.3)	26(4.2)		
Shower bath	563(90.5)	286(46.0)	277(44.5)		
Both	25(4.0)	14(2.3)	11(1.8)		

Abbreviations: BWDs, bottled water dispensers; HWPs, Household Water-purifiers; DWDS, drinking water distribution system; SWSS, secondary water supply system.

Table 4. Relationship between disease characteristics and NTM-PD

Variables	n (%)	PTB n (%)	NTMPD n (%)	χ^2	*P* value
Recurrent bronchiectasis				137.995	<.001
No bronchiectasis	273(43.9)	199(32.0)	74(11.9)		
Yes	164(26.4)	25(4.0)	139(22.3)		
No	185(29.7)	84(13.5)	101(16.2)		
History of tuberculosis				23.368	<.001
No	446(71.7)	248(39.9)	198(31.8)		
Yes	176(28.3)	60(9.6)	116(18.6)		
Complication				104.688	<.001
No	159(25.6)	120(19.3)	39(6.3)		
COPD	240(38.6)	63(10.1)	177(28.5)		
Stomach trouble	23(3.7)	11(1.8)	12(1.9)		
Tumour	37(5.9)	20(3.2)	17(2.7)		
Autoimmune disease	16(2.6)	5(0.8)	11(1.8)		
Diabetes	31(5.0)	20(3.2)	11(1.8)		
Others	116(18.6)	69(11.1)	47(7.6)		
Disinfection of skin trauma				1.596	.450
Yes	167(27.0)	78(12.6)	89(14.4)		
No	123(19.9)	58(9.4)	65(10.5)		
No skin trauma	329(53.2)	171(27.6)	158(25.5)		

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease.

.001). Compared with participants with SWSS, the prevalence of NTM-PD was significantly higher than that of patients with pipe network water system ($P < .001$). The prevalence of of NTM-PD in participants who took a bath once a day was higher than that of the other two groups ($P = .004$), and the prevalence of NTM-PD in participants who used a bathtub for a long time was higher ($P = .007$). There was no significant difference in the prevalence of NTM-PD among smoking, pet keeping, eating habits, and residential floors environment groups ($P > .05$).

Table 5. Multivariable logistic regression of factors affecting NTM-PD

Factors	*β*	S.E.	Wald χ^2	*P value*	OR	95%CI
Age	0.041	0.009	21.514	<.001	1.042	1.024-1.060
Gender (Female vs. Male)	1.128	0.254	19.747	<.001	3.089	1.878-5.079
DWDS						
SWSS vs. Pipe network water	2.056	0.346	35.353	<.001	7.813	3.968-15.387
Drinking water mode			30.291	<.001		
BWDs vs. Tap water	-0.722	0.355	4.144	.042	0.486	0.242-0.973
HWPs vs. Tap water	-2.055	0.379	29.362	<.001	0.128	0.061-0.269
Farmer/Flower farmer vs. Others	0.984	0.182	29.238	<.001	2.676	1.873-3.824
Depression (Yes vs. No)	1.084	0.336	10.380	.001	2.956	1.529-5.716
Recurrent bronchiectasis			20.747	<.001		
Yes vs. No bronchiectasis	1.843	0.410	20.159	<.001	6.314	2.825-14.114
No vs. No bronchiectasis	0.899	0.305	8.705	.003	2.458	1.352-4.468
Complication			19.583	.003		
COPD vs. No	0.995	0.388	6.570	.010	2.704	1.264-5.787
Stomach trouble vs. NO	-0.365	0.617	0.350	.554	0.694	0.207-2.327
Tumour vs. NO	0.193	0.614	0.098	.754	1.212	0.364-4.039
Autoimmune disease vs. NO	2.609	0.829	9.901	.002	13.588	2.675-69.024
Diabetes vs. NO	0.763	0.641	1.419	.234	2.145	0.611-7.530
Constant	-6.301	0.702	80.648	<.001	0.002	

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; DWDS, drinking water distribution system; SWSS, secondary water supply system; BWDs, bottled water dispensers; HWPs, Household water purifiers.

Disease characteristics and prevalence of NTM-PD

Table 4 shows the relationship between disease characteristics and the prevalence of NTM-PD. The prevalence of NTM-PD in participants with recurrent bronchiectasis was significantly higher than that of participants without recurrent bronchiectasis or bronchiectasis ($P < .001$). Participants with a history of tuberculosis had a significantly higher prevalence of NTM-PD than the other group ($P < .001$). Compared with other groups, participants who had COPD showed a significantly higher prevalence of NTM-PD ($P < .001$). There was no significant difference in the prevalence of NTM-PD among disinfection of skin trauma groups ($P > .05$).

The results of multivariable logistic regression analysis

We included the variables ($P < .1$) in the χ^2 test in the multivariate logistic regression equation. The Hosmer-Lemeshow test showed the model had good goodness of fit (χ^2=12.479, $P = .131 > .05$), and the Nagelkerke-R^2 was 0.649. Table 5 shows the results of multivariate logistic regression analysis to determine which factors contributed most to the possibility of the NTM-PD. The results showed that >60 years old (OR = 1.042), female (OR = 3.089), SWSS (OR = 7.813), farmer/flower farmer (OR = 2.676), depression (OR = 2.956), recurrent bronchiectasis (OR = 6.314), COPD (OR = 2.704), and autoimmune disease (OR = 13.588) were risk factors for NTMPD ($P < .05$), and the HWPs (OR = 0.128) was protective factors for NTM-PD ($P < .001$).

DISCUSSION

Correlation between water-related factors, soil-related factors and NTM-PD

The content of bioassimilable substances in the pipeline system is very low, and the residual chlorine in the pipeline network also has an inhibition and killing effect on microorganisms, which makes it difficult for ordinary microorganisms to proliferate in the pipeline network.[29,30]

SWSS is the last link of the four major links of the urban water supply system (water source, water factory, water pipe network and SWSS). In many cases, the pipe network water was qualified, but the faucet of SWSS had problems. Research on SWSS showed that different pipe materials form biofilms on the surface, and long-term retention will lead to higher microbial indicators of faucets.[31] The study also confirmed that the concentration of NTM in the water sample collected by the faucet was higher than that of the pipe network.[15] Therefore, the prevalence of NTM-PD using SWSS was significantly higher than that of using pipe network water system, similar to previous studies.[8,13]

A study in the US reported that the mycobacterium abscess complex in NTM mainly exists in tap water.[32] Long-term drinking of tap water will increase the risk of NTM-PD. Although compared with tap water, the prevalence of NTM-PD of BWDs was lower due to the remaining days before the bottle expires and the impact of exposure to sunlight during storage; microorganisms can proliferate in bottled water and diffuse in BWDs.[33] Compared with BWDs, the radiation of HWPs can effectively disinfect the microbial pollutants in drinking water, which is more suitable for direct drinking.[34] Therefore, the prevalence of NTM-PD using HWPs was significantly lower than that of using BWDs and tap water. This study fully illustrated the risk of water-related factors to NTM-PD from different angles and suggested that we should pay more attention to drinking water and water use in our daily lives to prevent NTM-PD. Our study also showed that farmers/flower farmers who mainly worked in contact with soil were high-risk groups of NTM-PD. NTM is widely distributed in the soil, dust and river water in nature.[35] Besides water factors, it may also be infected by contacting the surrounding soil.[16] This suggested that we should wash and disinfect in time to keep clean after contact with soil.

Correlation between disease-related factors and NTM-PD

Patients with autoimmune diseases are at higher risk to NTM-PD, similar to previous studies.[17] Because the invasion and pathogenicity of NTM pathogens into the human body are affected by congenital and acquired resistance and various living environment factors when NTM invades the body, the cellular immune function plays a major role in anti-NTM infection.[36] Many risk factors of NTM-PD have been identified, among which the common ones are structural lung disease, including bronchiectasis and COPD.[19] Our study also proved that patients with recurrent bronchiectasis and COPD had a higher risk of NTM-PD. Long-term NTM lung infection can lead to bronchiectasis, increasing the risk of NTM-PD.[18] After suffering from bronchiectasis and COPD, the rate of pulmonary function decline will accelerate, seriously affecting the functions of ventilation, ventilation immunity and defense, fluid transport, hematopoiesis, angiotensin conversion and regulation; therefore, patients are more susceptible to NTM and more prone to NTM-PD.[37]

Correlation between demographic characteristics and NTM-PD

This study showed that patients over 60 years old were risk for NTM-PD, similar to previous studies.[25] Respiratory muscle atrophy will increase with age, and the aging immune system will show the decline of macrophage function, lung migration and poor homing of dendritic cells, the promotion of abnormal inflammatory response, the acceleration of aging-related inflammation and the increase of immune aging, all of which increase the susceptibility of the elderly to NTM and are more prone to NTM-PD.[37] In our study, the female was the risk factor for NTM-PD, similar to the previous study.[24] The possible reason is that menopausal status and hormone level contribute to the susceptibility to NTM infection.[37] For example, the lack of estradiol (the main estrogen of reproductive age) was associated with the development of NTM-PD.[38] Finally, our research results showed that depression may be a potential risk factor for NTM-PD, although it is rare in previous studies. Patients with depression have nervous system dysfunction and decreased immune function, which makes them susceptible to tuberculosis infection, and depression such as fatigue, laziness, and social avoidance can be considered inflammatory states.[39] All the above immune system abnormalities may increase the risk of NTM-PD.

Strengths and limitations

First, this study included over 30 influencing factors, which was relatively comprehensive and fully illustrated the relationship between the water environment and NTM-PD. Second, compared with previous studies, our study included as many as 600 patients and more than 300 patients in the case group, and the results were feasible. Third, we included mental factor which was not designed in previous studies to verify the relationship between depression and NTM-PD. The limitation of this study was that the clinical indicators of patients were not measured, and different water sources were not tested, which will be improved in future studies.

CONCLUSION

Our study primarily unveiled the impact of water environment factors, including drinking water distribution system, modes of water consumption, and soil-related occupations on Nontuberculous Mycobacteria Pulmonary Disease (NTM-PD). We also determined the effects of autoimmune diseases, age, sex, and depression on NTM-PD. It is recommended to maintain water hygiene, monitor illness progression, and regulate mood in everyday life to prevent NTM-PD. Our research identified specific risk factors for NTM-PD, including aspects of the water environment, autoimmune diseases, age, sex, and depression. Maintaining water hygiene and mood regulation in daily life emerged as protective factors against NTM-PD. The findings of our study have broader implications for public health and policy. How can this research contribute to raising public awareness and informing strategies for the prevention of

NTM-PD? We acknowledge that our study has its constraints. No research is without limitations, and acknowledging them demonstrates our awareness of potential shortcomings and areas for further investigation. Based on the gaps or unanswered questions from our study, we suggest areas for future research or investigations. This guidance can assist other researchers in building upon our work.

ETHICAL COMPLIANCE

The ethics committee of Shanghai Pulmonary Hospital approved this study. Signed written informed consent were obtained from the patients and/or guardians.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

XS and WS designed the study and performed the experiments, XS and RY collected the data, WS and RY analyzed the data, XS and WS prepared the manuscript. All authors read and approved the final manuscript.

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