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Study on Risk Factors and Epidemiological Characteristics of Tuberculosis in the Elderly Population

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Abstract: To analyze the epidemiological characteristics and major risk factors of tuberculosis (TB) among the elderly population in China, providing a basis for formulating targeted TB prevention and control strategies. This study comprehensively analyzed recent epidemiological surveys, cohort studies, and literature reports on TB in China to investigate the influencing factors of TB incidence among the elderly. These factors include population aging, gender differences, smoking, alcohol consumption, diabetes, malnutrition, household economic status, living environment, history of close contact with TB patients, and HIV infection. Although the incidence rate of TB among the elderly has shown a decreasing trend over the years, their proportion among all TB patients has been increasing. Factors such as male gender, low income, smoking, diabetes, and poor nutritional status were found to be closely associated with an increased risk of TB among the elderly. Additionally, environmental factors (e.g., poor ventilation) and a history of TB or close contact with TB patients significantly heightened the likelihood of TB occurrence in the elderly. TB prevention and control among the elderly should comprehensively consider trends in population aging, biological factors, and socioeconomic factors. Regular screening, nutritional improvements, and health education for high-risk groups are crucial to effectively reducing the incidence of TB in this population.

1. Introduction

Tuberculosis (TB) is a chronic infectious disease caused by infection with Mycobacterium tuberculosis, primarily transmitted through the respiratory tract, posing a serious threat to human health [1]. Currently, TB remains a significant public health issue both in China and globally. According to the 2023 Global TB Report released by the World Health Organization (WHO), China ranked third among the 30 high TB burden countries in 2022, following India and Indonesia [2]. Simultaneously, the intensifying trend of population aging has highlighted challenges in the social and public health domains. The results of the 2020 Seventh National Population Census indicated that China's elderly population aged 60 and above reached 264 million, accounting for 18.7% of the total population, an increase of 8.7% compared to 2002 [3]. Due to factors such as declining immunity, malnutrition (potentially resulting from poverty or illness), chronic diseases (e.g., diabetes), and limited access to healthcare services, the elderly population has become a high-risk group for TB [4]. Studies have shown that from 2011 to 2020, the reported incidence rate of

pulmonary TB among the elderly in China was 2.4-2.9 times higher than that of the non-elderly population. Elderly TB has gradually become a focal and challenging area in TB prevention and control efforts in China [5]. Therefore, analyzing the epidemiological characteristics and influencing factors of elderly TB is essential for causal prevention, formulating effective control strategies, and reducing TB incidence among the elderly population. This study aims to explore the risk factors for elderly TB and provide valuable references for the formulation and research of future prevention and control strategies.

2. Epidemiological Characteristics of Tuberculosis in the Elderly Population

The results of the Fifth National Tuberculosis Epidemiological Sampling Survey conducted in 2010 revealed that the elderly population (aged ≥60 years) accounted for a significant proportion of pulmonary tuberculosis (PTB) cases, reaching 48.8%, with a prevalence rate of 1,105.2 per 100,000. The peak prevalence was observed in the 75–79 age group [6]. In comparison, the Fourth National Tuberculosis Epidemiological Sampling Survey in 2000 reported that active PTB cases among individuals aged ≥60 years constituted 40.9% of the total, with a prevalence rate of 1,286.0 per 100,000. By comparing age-specific prevalence rates across surveys conducted in 1979, 1990, and 2000, it was observed that the peak prevalence age shifted from 65 years to 70 years and then to 75 years, indicating a 5-year delay in peak age with each decade [7].

Further analysis of national pulmonary tuberculosis (PTB) incidence monitoring data from 2011 to 2020 revealed that the reported incidence rate of tuberculosis among the elderly population (≥65 years) declined from 158.7 per 100,000 in 2011 to 98.3 per 100,000 in 2020. However, the risk of PTB among the elderly remained 2.4–3.1 times higher than that of individuals aged <65 years. In terms of regional differences, the reported incidence rates of PTB among the elderly in eastern, central, and western China during this period were 95.9 per 100,000, 159.0 per 100,000, and 184.4 per 100,000, respectively. The risk of PTB among the elderly in the central and western regions was 1.7 times and 1.9 times higher than in the eastern region, respectively.

Overall, the reported incidence rate of tuberculosis (TB) among the elderly in China has shown a declining trend over the years. However, the proportion of elderly patients among all TB cases has been steadily increasing, with the peak prevalence age shifting progressively to older age groups. Additionally, significant differences in incidence rates are observed across genders and regions.

3. Risk Factors for Tuberculosis in the Elderly Population

3.1 Gender

Men are significant risk factors for tuberculosis (TB), a conclusion confirmed in studies across multiple countries [8], including among the elderly population. Cheng et al. [9-13] conducted a cohort study involving 34,076 individuals aged ≥65 years with no history of TB. After a 2-year follow-up, the incidence rate of TB among elderly men in China was 672.7 per 100,000, compared to 317.2 per 100,000 among elderly women. The study revealed that male gender is a risk factor for TB in the elderly population in China (adjusted hazard ratio, aHR=1.78, 95% CI: 1.27–2.49).

The gender differences in tuberculosis risk may be attributed to behavioral and biological factors. Men tend to have higher rates of smoking and alcohol consumption and broader social contact networks, which increase their exposure to Mycobacterium tuberculosis. Additionally, biological factors such as sex steroid hormones, the genetic composition of sex chromosomes, and sex-specific metabolic characteristics may contribute to differences in susceptibility to infection and disease progression between men and women [14-15].

3.2 Smoking

According to conservative estimates, approximately 13% of the global tuberculosis (TB) burden is attributable to smoking (population-attributable risk: 13%, RR=2.09). Leung et al. [16] conducted a study in elderly health service centers in Hong Kong, which found that the annual reported incidence rates of TB among elderly smokers, former smokers, and never smokers were 735 per 100,000, 427 per 100,000, and 174 per 100,000, respectively (P<0.001). Moreover, the risk of active TB increased significantly with the average daily cigarette consumption (P=0.01). Similarly, Nisar et al. [17] conducted a study in residential care homes for the elderly in Liverpool, UK, which concluded that smokers (OR=1.59) had a higher tuberculin skin test positivity rate than former smokers (OR=1.20) and non-smokers.

The potential mechanisms by which smoking increases the risk of tuberculosis (TB) among the elderly include prolonged exposure to tobacco smoke, which can impair the phagocytic function of alveolar macrophages and weaken the clearance ability of respiratory mucociliary cells, thereby increasing host susceptibility to Mycobacterium tuberculosis infection [18]. Additionally, smoking may alter immune responses and lead to functional deficiencies in immune cells such as macrophages, monocytes, and CD4+ T lymphocytes, making smokers more prone to TB infection and progression [19].

3.3 Diabetes

Extensive epidemiological evidence indicates that diabetes is a significant risk factor for tuberculosis (TB) [20-23], with approximately 15% of global TB cases attributable to diabetes [24]. A cross-sectional study by Zhang et al. [25] involving individuals aged ≥65 years in China found that the incidence of active pulmonary TB was significantly higher among diabetic patients compared to non-diabetic individuals (OR=1.83, 98% CI: 1.08–3.10). Similarly, a TB screening conducted by Chen Danshan et al. [26] in Huangpu District, Guangzhou, reported a TB detection rate of 0.83% among elderly diabetic patients, which was higher than that of their non-diabetic counterparts.

Furthermore, studies have demonstrated a clear age gradient in the association between diabetes and tuberculosis (TB) [27-28]. For instance, a study conducted by Kim et al. [27] on Korean civil servants reported that the relative risk (RR) of diabetes for TB was highest in the 30-39 age group (RR=4.54), decreased in the 40-49 age group (RR=2.21), and further declined in the ≥60 age group (RR=1.76; 95% CI: 1.07–5.92) [29]. Similarly, research by Lee et al. [30] found that poor glycemic control was significantly associated with TB among the elderly population (≥65 years, aHR=1.63; 95% CI: 1.05–5.09), indicating that age may influence the relationship between glycemic control and TB risk.

From a biological mechanism perspective, diabetes can impair the immune function of the body against Mycobacterium tuberculosis infection. An animal model study demonstrated that diabetic mice had a higher bacterial load after experimental infection with Mycobacterium tuberculosis compared to normoglycemic mice. This was accompanied by significantly reduced production of IFN-γ and IL-1β, as well as decreased ESAT-6-responsive T cells, indicating impairment of the critical Th1 adaptive immune response [31]. Moreover, compared to normoglycemic individuals, diabetic patients, particularly those with poor glycemic control, exhibit reduced neutrophil chemotaxis and oxidative killing capacity [32], as well as diminished leukocyte bactericidal activity [33], which facilitates the proliferation and dissemination of Mycobacterium tuberculosis within the body.

3.4 Nutritional Status

Chen et al. [34] conducted a large prospective cohort study in China to analyze the relationship between body mass index (BMI) and tuberculosis (TB) incidence. The results demonstrated a negative logarithmic linear relationship between BMI and TB incidence (adjusted R^2=0.76). Among individuals with a BMI of 17.5–18.4, the TB incidence was significantly higher (aHR=2.01; 95% CI: 1.29–3.14). Age-stratified analysis revealed that, among the elderly population (≥65 years), overweight or obese individuals had a 64% lower risk of TB compared to those with a normal BMI (aHR=0.36; 95% CI: 0.12–1.22), while underweight individuals had a significantly higher risk (HR=2.33; 95% CI: 1.32–4.12) compared to the normal BMI group.

Malnutrition, as a risk factor for tuberculosis (TB), is associated with impaired innate and adaptive immune responses. Malnutrition can suppress cellular immunity and inhibit the release of cytokines such as tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), and interleukin-2 (IL-2) [35]. Nutritional status may also influence vaccine immune responses, thereby increasing the risk of TB. Studies have shown that malnutrition is associated with delayed immune responses following Bacillus Calmette–Guérin (BCG) vaccination [36]. Beyond malnutrition characterized by reduced BMI, micronutrient deficiencies are also common among TB patients. Vitamin D, due to its immunomodulatory properties, has garnered attention as its deficiency is considered a risk factor for respiratory infections, including Mycobacterium tuberculosis [37]. Similarly, deficiencies in zinc and copper may limit the host's bactericidal response to mycobacteria [38].

Currently, there is insufficient epidemiological research to establish a causal relationship between various micronutrient deficiencies and tuberculosis (TB) incidence, with studies focusing on elderly populations being particularly scarce. Against this backdrop, Aibana et al. [39] conducted a case-control study within a longitudinal cohort of household contacts of pulmonary TB patients, demonstrating a negative correlation between vitamin E levels and TB incidence, providing new directions for future research.

3.5 Alcohol Consumption

Alcohol consumption, particularly excessive drinking, is one of the significant risk factors for tuberculosis (TB) [40-42]. It is estimated that approximately 10% of global TB cases can be attributed to alcohol consumption [43]. A meta-analysis conducted by Lönnroth et al. [44] revealed that individuals who consume more than 40 g of alcohol daily or have alcohol use disorders have nearly a threefold increased risk of TB (OR=3.50, 95% CI: 2.01–6.11). In a study investigating Mycobacterium tuberculosis infection among rural elderly individuals aged 50–70 years, it was found that moderate alcohol consumption (<10 g/day) was associated with a lower risk of Mycobacterium tuberculosis infection compared to non-drinkers (OR=0.82, 95% CI: 0.71–0.96). Additionally, a comparison of clinical characteristics between TB patients aged 18–59 years and those aged ≥60 years indicated that the proportion of patients with a history of alcohol consumption was significantly higher in the younger group (20%) compared to the elderly group (3%), suggesting that the association between alcohol consumption and TB risk may be weaker in older populations. However, studies specifically focusing on the relationship between alcohol consumption and TB risk in elderly populations remain limited.

When smoking and alcohol consumption coexist, their synergistic effect has been confirmed to be closely associated with the incidence of tuberculosis (TB). Soh et al. [45] analyzed health data from 63,257 middle-aged and elderly Chinese individuals (aged 45–74 years) in Singapore and found that consuming two or more drinks daily synergized with smoking to increase the risk of active pulmonary TB among smokers (HR=1.51). Among individuals who both smoke and drink,

increasing either the amount of smoking or alcohol consumption independently elevated the risk of developing pulmonary TB.

Current mechanistic studies have found that alcohol consumption impairs the host immune system by inhibiting the mobilization and adhesion capacity of alveolar macrophages [46], limiting the production of cytokines by monocytes that regulate inflammation, and reducing the ability of macrophages to present Mycobacterium tuberculosis antigens to lymphocytes, thereby hindering the activation of antigen-specific T cells [47]. Furthermore, alcohol consumption may interact with factors such as malnutrition, liver disease, and hematopoietic disorders, indirectly impacting the immune system and further increasing the risk of tuberculosis (TB) [48].

3.6 History of Close Contact with Tuberculosis Patients and Previous History of Tuberculosis

Compared to the general population, the risk of tuberculosis (TB) is significantly higher among contacts of TB patients [49]. Velen et al. [50] conducted a meta-analysis of 244 studies on close contacts of TB patients published between 2011 and 2019, finding that the prevalence of active pulmonary TB among close contacts was 3.6% (95% CI: 3.3%–4.0%), markedly higher than in the general population. Wang Lili [51] analyzed 893 elderly pulmonary TB patients registered at the Qixia Center for Disease Control and Prevention and 920 healthy individuals as a control group. The results indicated that a history of TB contact is an independent risk factor for TB among the elderly. Zhang Jiayong et al. [52] estimated the detection rate of active pulmonary TB among close contacts across different age groups in China, finding that the detection rate was 6.02% (95% CI: 5.00%–7.25%) in individuals aged ≥60 years, significantly higher than 2.45% (95% CI: 1.76%–3.32%) in those aged <15 years. Additionally, the study by Xie Xin et al. [53] revealed that elderly close contacts aged ≥60 years were 3.9 times more likely to develop latent TB infections compared to contacts aged <60 years.

Zhang et al. [25] conducted a cross-sectional study among individuals aged ≥65 years in China, which demonstrated that a history of close contact with pulmonary tuberculosis (TB) patients (OR=7.30, 95% CI: 2.15–13.83) is a significant risk factor for TB. In this study population, 5.4% (33/606) of previous TB patients experienced relapse. Similarly, Shen et al. [54-55] conducted a retrospective cohort study in Shanghai, China, which revealed that at least 5.3% (710/13,417) of former TB patients had experienced one or more relapses, with a recurrence rate of 7.55 per 1,000 person-years (95% CI: 7.01–8.12).

3.7 Human Immunodeficiency Virus, HIV

HIV infection is a known risk factor for tuberculosis (TB), and TB can occur at any stage of HIV progression [56]. Studies have shown that the risk of developing TB among individuals with HIV is 16 times higher than that of those without HIV (uncertainty interval: 14–18) [57]. In China, approximately one-third or more of individuals with HIV may develop TB [56]. However, research on the impact of HIV infection on the risk of TB in elderly populations remains limited, which may be attributed to the relatively low proportion of elderly individuals within the population co-infected with Mycobacterium tuberculosis and HIV [58-59]. With the increasing number and proportion of elderly individuals among those infected with HIV in China, the issue of HIV in the elderly population is gaining attention [60]. Future research is needed to further explore the relationship between HIV infection and TB risk among the elderly.

Extensive mechanistic studies have demonstrated that HIV infection significantly increases susceptibility to Mycobacterium tuberculosis. Following HIV infection, the host's CD4+ T lymphocyte count decreases, and their function becomes impaired [61]. CD8+ T lymphocyte function is also compromised, exhibiting differentiation abnormalities [62], while macrophage

activation and functionality are similarly impaired [63]. Furthermore, the reduction and functional abnormalities of CD4+ T lymphocytes lead to a decline in B lymphocyte count and weakened antibody responses [64]. This cascade of immune impairments affects both cellular and humoral immunity in individuals with HIV, substantially enhancing their susceptibility to Mycobacterium tuberculosis.

3.8 Household Economic Conditions

Household economic conditions directly impact the living standards and healthcare access of family members and are a critical social determinant of tuberculosis (TB) incidence. Numerous studies have shown that poor household economic status is a significant risk factor for TB [65-68]. The results of China's Fifth National Tuberculosis Epidemiological Sampling Survey support this finding, with 82.8% of pulmonary TB patients belonging to households with a per capita annual income below the local average [6]. Zhao Ye et al. [43-44] conducted a case-control study among elderly individuals (≥60 years) in Harbin, revealing that higher monthly per capita household income was associated with a lower risk of TB (OR=0.60, 95% CI: 0.40–0.90).

3.9 Living and Working Environment

The study by Singh et al. [69] highlighted that various risk factors in the residential environment, such as indoor smoke, type of cooking fuel, availability of a separate kitchen, materials of floors, roofs, and walls, the number of residents per room, and shared access to toilets and drinking water, are closely associated with the occurrence of tuberculosis (TB). Further supporting this, Zhao Ye et al. [43] conducted a case-control study among elderly individuals aged ≥60 years in Harbin, demonstrating that ventilation in the residential environment also impacts TB risk. Elderly individuals with better ventilation had a lower risk of TB compared to their peers with average ventilation conditions (OR=0.71, 95% CI: 0.51–1.00).

4. Drug Resistance and Adverse Reactions in Elderly Drug-Resistant Tuberculosis Patients

The Drug Resistance and Adverse Reactions in Elderly Drug-Resistant Tuberculosis Patients are shown in Table 1 and Table 2 below.

Table 1: Incidence Rate of Adverse Reactions in Elderly Drug-Resistant Tuberculosis Patients

Adverse Reaction	Number of Cases	Incidence Rate (%)
Liver function abnormalities	3	15.00
Elevated uric acid	3	15.00
Gastrointestinal symptoms	1	5.00
Nausea, vomiting	1	5.00
Fever	1	5.00
Total	**9**	**45.00**

Table 2: Distribution of Different Drug Resistance Types in Elderly Primary and Retreated Tuberculosis Patients

Drug	Primary Patients (n = 9)		Retreated Patients (n = 11)		Total (n = 20)	
	Number of Cases	Resistance Rate (%)	Number of Cases	Resistance Rate (%)	Number of Cases	Resistance Rate (%)
Single Drug Resistance						
R	3	33.33	0	0	3	15.00
H	1	11.11	0	0	1	5.00
Multidrug Resistance						
R + A	1	11.11	1	9.09	2	10.00
R + S	1	11.11	0	0	1	5.00
H + S	0	0	2	18.18	2	10.00
R + E	0	0	1	9.09	1	5.00
R + H	2	22.22	1	9.09	3	15.00
R + H + S	0	0	2	18.18	2	10.00
R + H + S + E	1	11.11	0	0	1	5.00
R + H + S + Lfx	0	0	1	9.09	1	5.00
R + H + A + K + Pto	0	0	1	9.09	1	5.00
R + H + S + E + Pto + Lfx	0	0	1	9.09	1	5.00
R + H + A + K + P + Pa	0	0	1	9.09	1	5.00

Abbreviations:
R: Rifampicin
H: Isoniazid
E: Ethambutol
A: Amikacin
S: Streptomycin
K: Kanamycin
P: p-Aminosalicylic acid
Pa: p-Aminosalicylate
Lfx: Levofloxacin
Pto: Prothionamide

5. Conclusions

This study revealed that among 20 elderly drug-resistant tuberculosis (TB) patients, 14 were male (70.00%) and 6 were female (30.00%). In the age group of 60–69 years, 18 cases (90.00%) were recorded, of which 13 were male (72.22%) and 5 were female (27.78%). The number of male patients significantly exceeded that of female patients, indicating that elderly men are more susceptible to drug-resistant TB than women, consistent with findings from related studies [9-10]. The predominance of male elderly drug-resistant TB patients in this region may be attributed to

factors such as increased social activities, smoking, alcohol consumption, staying up late, poor hygiene practices, and neglect of personal health [70].

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