

Risk Factors and Management of Adolescent Tuberculosis

Qingfeng Lai

Gannan Health Vocational College, Ganzhou, China

laiqingfeng@ldy.edu.rs

Abstract. Tuberculosis (TB) is an acute or chronic pulmonary infectious disease caused by *Mycobacterium tuberculosis* and transmitted through the air, which is one of the major infectious diseases threatening human life and health. It is a communicable disease primarily spread via respiratory droplets. TB can affect individuals of any age, this study refers to TB occurring in individuals aged 10-19 (inclusive) as adolescent TB. Despite the overall good control of tuberculosis in China, the incidence rate among adolescents has been rising. Adolescent TB is influenced by both genetic and environmental factors, presents with atypical clinical symptoms, has a low recognition rate, and poor treatment adherence. This not only affects the physical health of adolescents but may also impact the psychological health and academic development. This paper reviews the related influencing factors of the adolescent TB and discusses diagnostic and treatment strategies to provide better approaches for managing and preventing adolescent TB.

Keywords: Adolescents, tuberculosis, factors.

1. Introduction

Pulmonary tuberculosis (TB) is an acute or chronic infectious disease primarily affecting the lungs, caused by the *Mycobacterium tuberculosis* complex (MTBC). However, it can also infect other parts of the body, such as the kidneys and vertebrae. Adolescents, being in a critical stage of growth and development, have an immature immune system, which heightens their risk of contracting pulmonary tuberculosis. The younger the age, the higher the risk of developing the disease. Consequently, the infection and incidence rates of TB in this group should not be underestimated.

As adolescents age, the immunity conferred by the Bacille Calmette-Guérin (BCG) vaccine, administered during childhood, gradually wanes, diminishing its protective effect. Domestic research indicates a significant surge in TB incidence among the 15-19 age group between 2005 and 2010 [1]. Further studies have shown that the peak age for TB incidence has shifted from ≥ 65 years (with 9,694 cases in 2011) to the 15-24 age group (with 8,688 cases in 2020), indicating an increasing trend in TB incidence among individuals under 25, including children and adolescents [1, 2].

The World Health Organization (WHO) 2019 report highlighted that approximately 10 million new TB cases were reported globally, with 1.4 million deaths attributed to the disease. Among these cases, about 200,000 children under 15 years of age die annually. The 2023 WHO report estimated that in 2022, there were 7.5 million new TB cases worldwide, with over one-tenth of these occurring in children aged 0-14 years [3]. Data from the Chinese Center for Disease Control and Prevention (CDC) revealed that between 2004 and 2021, a total of 908,171 student TB cases were reported nationally, with 48,289 cases reported in 2018 alone [4, 5]. Furthermore, the TB incidence rate among children and adolescents shows an upward trend across different age groups [6].

This paper summarizes the factors influencing adolescent pulmonary tuberculosis and discusses relevant diagnostic and treatment strategies to provide better insights for the diagnosis, treatment, and prevention of TB in this population.

2. Epidemiological Characteristics of Adolescent Tuberculosis

According to estimates by the World Health Organization (WHO), more than 1 million children under the age of 15 are diagnosed with tuberculosis (TB) each year globally. Research indicates that poverty, malnutrition, and overcrowded living conditions contribute to a higher incidence of adolescent pulmonary tuberculosis in Asia and Africa. In contrast, developed countries experience

relatively lower rates of TB among adolescents due to high vaccination coverage and better healthcare conditions.

In China, the reported incidence of pulmonary tuberculosis in children and adolescents, particularly during the school age, is approximately one-third of the overall population's incidence. Among these, the age group around 18 years old has the highest proportion. Data from the Global Burden of Disease Study in 2019 shows that from 2000 to 2019, the prevalence of tuberculosis and its various subtypes was notably high among male adolescents aged 15 to 19 in China [7]. This suggests that the incidence of adolescent pulmonary tuberculosis is closely related to a country's economic development, public health policies, and distribution of healthcare resources, with significant variations observed globally.

3. Biological Factors of Adolescent Tuberculosis

3.1. Genetic Factors

The occurrence and progression of tuberculosis (TB) are the results of interactions between genetic and environmental factors. Research indicates that susceptibility genes for TB can be classified into two categories: HLA (human leukocyte antigen) genes and non-HLA genes, such as VDR (vitamin D receptor) genes [8]. Specific genetic variations, such as certain alleles in the HLA complex, may increase an individual's susceptibility to *Mycobacterium tuberculosis*. For example, the HLA-DQB1 0201 allele is associated with a higher incidence of TB in some populations [9].

A study involving 40 adolescents aged 15-19 found that polymorphisms in the VDR gene were linked to increased susceptibility to TB in adolescents [10]. Additionally, low vitamin D levels are associated with a higher risk of developing TB [11]. However, research on susceptibility genes and potential mechanisms for TB is still not fully developed, and the relationship between genetic factors and adolescent TB needs further investigation to control for individual and environmental factors.

3.2. Immune System Development in Adolescents

Some researchers have noted that tuberculosis (TB) is a genetically regulated infectious disease caused by *Mycobacterium tuberculosis*, with an underdeveloped immune system being a significant factor for susceptibility in adolescents [12]. The immune system's incomplete maturation means that adolescents have weaker resistance to TB compared to adults. For instance, T-cell-mediated immune responses in adolescents may not be as effective as in adults, allowing *Mycobacterium tuberculosis* to survive and proliferate more easily within the body.

Studies have highlighted that the development and progression of TB are closely related to the dynamic imbalance between CD4⁺ T-cell subsets, specifically the ratio of Th1 to Th2 cells and the ratio of Th17 to regulatory T cells [13]. Elevated levels of CTLA4 and Tim3 on peripheral blood T cells have been identified as risk factors for TB in patients [14].

4. Environmental Factors in Adolescent Tuberculosis

4.1. Natural Environment

A statistical analysis of 2,989 cases of TB among students in Enshi Prefecture from 2013 to 2022 revealed that the number of cases was lowest in February each year and highest in April and June, indicating a peak in spring and summer [15]. Climate is a significant factor influencing infectious diseases. Research conducted from 2012 to 2016 in Ganzhou District found a positive correlation between TB incidence across seasons and the number of consecutive dry days ($r = 0.543$, $P = 0.013$), suggesting that arid weather impacts TB incidence [16]. This study also highlighted that children under 15 years old are a key population for local infectious disease prevention and control.

4.2. School Environment

Adolescent patients are often in a collective living environment, such as a school setting. A study conducted on tuberculosis among teachers in Jilin Province from 2012 to 2021 revealed that 70.51% of teachers with tuberculosis experienced delays in seeking medical attention [17]. Given that students frequently interact with teachers, who often teach multiple classes, delays in diagnosis among teachers significantly increase the risk of tuberculosis transmission to adolescents. Active tuberculosis patients can spread the disease to approximately 10-15 people annually through close contact, highlighting the importance of preventive measures and protection for adolescents as a vulnerable group in schools [18].

5. Clinical Symptoms of Adolescent Tuberculosis

The symptoms of pulmonary tuberculosis primarily include fever, coughing, fatigue, night sweats, loss of appetite, and weight loss or failure to gain weight. According to the World Health Organization (WHO), approximately 1 million adolescents are infected with tuberculosis each year worldwide, with about 10% of these patients exhibiting the aforementioned symptoms. A study conducted in India on adolescent tuberculosis patients revealed that over 60% reported persistent coughing and sputum production, while hemoptysis was observed in approximately 20% of the patients. Adolescent tuberculosis typically presents with acute onset, high fever, rapid disease progression, pronounced systemic toxicity, a tendency towards dissemination, fewer complications, and a generally favorable prognosis. In contrast, symptoms of tuberculosis in the elderly are atypical, with low-grade fever, and are often complicated by multiple underlying conditions, making the clinical presentation more complex. In many cases, the clinical manifestations are dominated by comorbidities such as chronic obstructive pulmonary disease, which not only increases the difficulty of treatment but also results in a high rate of missed diagnoses and a lack of timely and standardized treatment.

Children and adolescents, due to their young age, may be unable to clearly describe their discomfort, and the clinical presentation of tuberculosis in this group varies significantly. Mild cases may exhibit no symptoms, and some cases are only detected during routine examinations, often misdiagnosed as a common cold or other pulmonary infections, ultimately leading to delays in the detection and treatment of tuberculosis in children and adolescents.

Globally, the detection rate of tuberculosis in children is less than 50%. According to information from the WHO and the International Union Against Tuberculosis and Lung Disease (IUALTD), approximately 260,000 cases of pediatric tuberculosis are reported annually in China, but only 5,000 to 8,000 cases are officially registered. A multi-center prospective study involving 330 suspected cases of pulmonary tuberculosis in children and adolescents under the age of 15 found that stool Ultra tests for *Mycobacterium tuberculosis* had similar accuracy and consistency to respiratory specimen testing but were more convenient [19]. Pulmonary tuberculosis is primarily transmitted through the air; when an infected person coughs, sneezes, talks, or spits, they release droplet nuclei containing *Mycobacterium tuberculosis*, which healthy individuals may inhale, potentially leading to infection. Adolescents, due to their social behavior patterns, such as frequent social interactions and group living, are a high-risk group for both acquiring and transmitting tuberculosis. Therefore, early identification and diagnosis of tuberculosis in adolescents are crucial.

6. Imaging Features of Adolescent Tuberculosis

Typical radiological manifestations of pulmonary tuberculosis predominantly involve the apical posterior segment of the upper lobe and the dorsal segment of the lower lobe. A study on chest CT scans of adolescent patients aged 15-35 with active pulmonary tuberculosis revealed that adolescent tuberculosis often presents with characteristic imaging features, such as the involvement of a single lung, with infections primarily affecting the apical posterior segment of the upper lobe and the dorsal segment of the lower lobe, often leading to the formation of thin-walled cavities. This is frequently

accompanied by centrilobular nodules, blurred nodules, and the tree-in-bud sign [20]. In contrast to the CT imaging of adolescent tuberculosis, studies have shown that elderly patients exhibit fewer of these typical manifestations, such as nodules and the tree-in-bud sign [21]. Another study found that the radiological features of adolescent tuberculosis vary significantly among different ethnic groups [22]. For instance, Tibetan adolescents with active pulmonary tuberculosis tend to have bilateral lung involvement, affecting multiple lobes and segments (2-4 lobes), with a combination of various signs, including infiltrative pulmonary tuberculosis and cavitary tuberculosis, often associated with extrapulmonary tuberculosis. These differences may be related to the unique living environments, hygiene practices, and medical conditions specific to these ethnic groups.

7. Treatment of Adolescent Tuberculosis

7.1. Pharmacological Treatment

Mycobacterium tuberculosis is an acid-fast, aerobic, non-motile bacillus whose unique cell wall structure confers natural resistance to many antibiotics. Anti-tuberculosis drugs, predominantly chemical agents, are central to the treatment of adolescent pulmonary tuberculosis. The clinical treatment course is typically lengthy; even non-severe pediatric cases often require over four months of medication. During this period, patients must adhere to a regimen of first-line anti-tuberculosis drugs, such as isoniazid, rifampicin, pyrazinamide, or ethambutol. Isoniazid, a small water-soluble molecule, is highly selective and potent against *Mycobacterium tuberculosis*, making it a frontline treatment for pulmonary tuberculosis. However, the use of a single drug has its limitations. Blood drug concentrations in pediatric and adolescent patients tend to be lower, requiring higher doses to reach effective therapeutic levels [23]. This situation can lead to the proliferation of drug-resistant *Mycobacterium tuberculosis*, complicating treatment and prolonging symptoms. Higher doses of isoniazid can reduce vitamin B6 utilization, leading to amino acid metabolism disorders and causing peripheral neuritis. It can also decrease the inhibitory neurotransmitter GABA in the central nervous system, resulting in central nervous system stimulation, insomnia, irritability, and in severe cases, seizures, schizophrenia, or epilepsy.

The 2022 Guidelines further standardize the management of tuberculosis in children and adolescents, introducing integrated treatment decision pathways. For example, a combination of two or more anti-tuberculosis drugs is recommended to eliminate the pathogen. For adolescents with drug-sensitive tuberculous meningitis, a six-month (6H-R-Z-Eto) or twelve-month (2H-R-Z-E/10H-R) intensive regimen is advised [24]. However, prolonged treatment with multiple anti-tuberculosis drugs in adolescents is likely to impact other organ functions and growth, potentially causing adverse reactions such as liver and kidney dysfunction, skin allergies, and hearing loss. Long-term medication can also damage the gastric mucosa [25]. Thus, treatment adherence is a significant challenge for adolescent patients. A study on adolescent pulmonary tuberculosis patients found that over one-fifth of them failed to adhere to standardized drug therapy, which not only affects treatment outcomes but also increases the risk of developing drug-resistant strains.

Therefore, it is crucial to strengthen the management of potential adverse reactions at different stages of treatment in adolescents. This approach will help ensure standardized treatment, reduce the occurrence of drug-resistant strains, and ultimately improve treatment outcomes.

Recent animal studies have shown that after administering pure INHT Fe₃O₄/CS/INH magnetic nanocomposite microspheres to mice, there was significant drug accumulation in the lungs. This finding suggests that nanoparticles can precisely target pulmonary lesions, enhance drug delivery efficiency, and significantly reduce drug dosage, thereby minimizing adverse reactions. Nanotherapy holds promise as a future therapeutic option [26].

7.2. Surgical Treatment

Due to the lower level of cooperation and weaker sputum expectoration abilities in children and adolescents, the positive rate of *Mycobacterium tuberculosis* in their sputum is relatively low.

However, a positive or persistent positive sputum test for *Mycobacterium tuberculosis* remains a crucial indicator for surgical intervention. With the continuous development of surgical treatments for pulmonary tuberculosis in China, the approach has evolved from thoracoplasty and lobectomy to minimally invasive procedures. These advancements have shifted the focus from traditional surgery to minimally invasive techniques. For instance, in cases where pulmonary tuberculosis is complicated by endobronchial tuberculosis, medication treatment can be complemented by bronchoscopic procedures. These procedures can address bronchial stenosis, ulcers, and necrotic lesions through direct drug instillation.

Some experts in China have suggested that the timing of surgical intervention for pulmonary tuberculosis could be advanced appropriately. Utilizing precise imaging to accurately locate lesions, minimally invasive surgical treatment of localized conditions such as pulmonary tuberculosis cavities or nodules may offer advantages such as reduced trauma, faster recovery, and fewer complications.

8. Conclusion

The current diagnosis of pulmonary tuberculosis primarily relies on the clinical symptoms and signs exhibited by the patient, as well as the detection of *Mycobacterium tuberculosis* in body fluid samples such as saliva and feces through rifampin sensitivity testing. However, radiological changes, which often take a longer time to develop, are needed to aid in diagnosis. The precision and specificity of early tuberculosis diagnosis are not yet optimal. Thus, the future development of rapid, accurate, and cost-effective diagnostic tools is crucial to shorten the detection time and narrow the diagnostic window, which represents a significant challenge in the field of adolescent pulmonary tuberculosis diagnosis.

The severity of tuberculosis in most adolescents is generally lower than in adults. However, since adolescents are in a critical stage of growth and development, shorter treatment durations may be considered, though this requires more evidence-based support. Simultaneously, combining pharmacotherapy with minimally invasive surgical interventions to control symptoms early, reduce lesions, and facilitate earlier surgical intervention presents a challenge for both medical and surgical disciplines. Achieving precise treatment with fewer side effects necessitates a multidisciplinary approach to the treatment of adolescent tuberculosis.

Adolescence is a transitional period between childhood and adulthood, characterized by unique social behaviors and developmental stages, making adolescents a high-risk group for tuberculosis infection. This paper summarizes the factors influencing adolescent pulmonary tuberculosis, outlines relevant diagnostic and treatment strategies, and provides insights into the early identification, diagnosis, and treatment of adolescent pulmonary tuberculosis, contributing to the goal of eliminating tuberculosis in China by 2035.

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