

# Tuberculosis of Tonsil and Its Diagnosis



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## Abstract

Tuberculosis (TB) is the common communicable disease worldwide. Extrapulmonary tuberculosis (EPTB) is found in only 10-15% of all TB cases. Tuberculosis of oral cavity and upper airway is rare, and TB of palatine tonsils is even rarer. Diagnosing EPTB such as tuberculosis of tonsil remains challenging because clinical samples obtained from relatively inaccessible sites may be paucibacillary which decreases the sensitivity of diagnostic tests. The tonsillar specimens should be obtained for both mycobacteriological and histopathological examinations. The measurement of biochemical markers in TB-affected pleural fluids such as adenosine deaminase or gamma interferon could be supportive tests for diagnosis. Molecular biology techniques such polymerase chain reaction may be helpful in rapid diagnosis as well as in paucibacillary cases.

**Keywords:** Biochemical markers; Diagnosis; Molecular biology techniques; Tuberculosis

**Abbreviations:** TB: Tuberculosis; EPTB: Extrapulmonary tuberculosis; HIV: human immunodeficiency virus; WHO: World Health Organization; AIDS: Acquired immune deficiency syndrome; PTB: pulmonary TB; ATDs: Antitubercular drugs; PCR: Polymerase Chain Reaction; ADA: Adenosine Deaminase; TST: Tuberculin Skin Test; IGRA: IFN- $\gamma$  Releasing Assay; IFN- $\gamma$ : Gamma Interferon

## Introduction

Tuberculosis (TB) is the common communicable disease worldwide. It was identified in early 4th century as phthisis, lupus, and scrofula. In 1882, Koch's described the bacillus. There was an estimated 10.4 million new (incident) TB cases worldwide in 2015. Among these, 5.9 million (56%) were men, 3.5 million (34%) women and 1.0 million (10%) children. People living with human immunodeficiency virus (HIV) accounted for 1.2 million (11%) of all new TB cases. About 1.4 million TB deaths was estimated in 2015 and an additional 0.4 million deaths resulting from TB disease among people living with HIV. According to WHO, the majority of new cases of TB was reported from South East Asia. Six countries accounted for 60% of the new cases: India, Indonesia, China, Nigeria, Pakistan and South Africa [1]. Incidence of TB is in rising tendency in developed world because of the increasing incidence of drug resistance [2] among Tubercle bacilli, wide prevalence of acquired immune deficiency syndrome (AIDS) [3,4] and transglobal migration [4].

Although the number of TB deaths fell by 22% between 2000 and 2015, TB remained one of the top 10 causes of death worldwide in 2015 [1]. There are two types of clinical manifestation of tuberculosis- pulmonary TB (PTB) and

extrapulmonary TB (EPTB). Most of the patients suffer from PTB. EPTB is known for TB involving organs other than the lungs (e.g., pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, or meninges) [5]. EPTB is found in only 10-15% of all TB cases [6]. Tuberculosis of oral cavity and upper airway is rare, and TB of palatine tonsils is even rarer.

## Incidence and route of infection of tonsillar TB

Tonsillar tuberculosis is rare with an incidence of less than 5% [7]. The incidence of tonsillar TB was relatively high in the pre-pasteurization era due to Mycobacterium bovis infection through the ingestion of unpasteurized milk of cow [8]. In 1963, Miller [9] concluded that with the advent of pasteurized milk the incidence of TB decreased. Tonsil is a lymphoid tissue located in a site where it is constantly exposed by infected sputum / saliva but the incidence of tonsillar TB has remained rather low. The probable reasons behind this low incidence could be [10]:

- The antiseptic and cleansing action of saliva.
- Presence of saprophytes in oral cavity making colonization of tuberculous bacilli rather difficult.
- Thick protective stratified squamous epithelial surface

covering of tonsil resistant to colonization by mycobacterium tuberculosis.

d) Inherent resistance of tonsil to tuberculosis.

After invent of highly effective antitubercular drugs (ATDs), incidence of tonsillar TB is reduced to zero, but its incidence is increasing nowadays as mentioned above. Tonsillar TB are commonly found in patients with poor host reaction due to alcoholism, HIV infection, and so forth. Poor dental hygiene, dental extraction, periodontitis, and leukoplakia are the predisposing factors for primary oral TB. It has been postulated that such infections are acquired by inhalation, with harbouring of disease in Waldeyer's ring as secondary form rather than primary form [11].

### Classification of tonsillar tuberculosis [12]:

Irwin Moore's classified tonsillar TB into:

- a) Primary tuberculosis of tonsil- TB of tonsil occurs without involvement of lungs
- b) Secondary tuberculosis of tonsil- There is pulmonary involvement with presence of positive sputum smear in addition to tonsillar TB.

### Diagnosis

#### i. Mycobacterial stain and culture

The culture of Mycobacterium tuberculosis organisms from a tonsillar specimen of the patient can make a definitive diagnosis of TB. However, Mycobacterial culture usually takes 2-8 weeks to receive the results, which is too slow to help treatment decisions [13]. Despite normal chest radiography findings, some EPTB patients have positive sputum culture results [14]. Bronchoscopic evaluation or sputum induction with nebulized hypertonic saline can increase diagnostic sensitivity [15,16].

#### ii. Biopsy

The diagnosis of tonsillar TB depends on the histological evidence. There should be presence of epithelioid granulomas, caseous necrosis, Langhan giant cells and AFB positive test for histopathologic diagnosis. However, loss of host immune function can result in demonstrating greater suppurative response and less well-formed granulomas in histopathologic findings [17]. Diagnostic accuracy can be increased if the results of the histology and polymerase chain reaction (PCR) assays are combined with those of culture. Moreover, formalin used for preservation of biopsy specimens destroys the mycobacteria and prevents further culture confirmation. Hence, biopsy material for mycobacterial culture should be submitted fresh or in a small amount of sterile saline.

#### iii. Examination of body fluid

Tissue biopsy is the most effective method of diagnosing tonsillar TB but it is invasive. The more easily accessible body fluid, such as pleural fluid can be studied if the patient has

associated primary pulmonary TB, then it can often provide valuable diagnostic clue for diagnosis. Exudative fluid is found in tuberculous pleural fluid study with predominance of lymphocytes in about 90% of cases. Adenosine deaminase (ADA) measurement is one of the most widely used biomarkers in body fluids for the diagnosis of EPTB. ADA is an enzyme involved although possible false-negative and false-positive results should be considered [18-20].

#### iv. Nucleic acid amplification test

The nucleic acid amplification test, such as PCR has a major advantage, i.e., a rapid diagnosis can be made. The sensitivity could be improved by PCR because EPTB is a paucibacillary disease, as it can detect as few as 10 mycobacteria [21].

#### v. Immunological tests

There are some supportive methods for diagnosing tonsillar TB, such as Tuberculin skin test (TST) and IFN- $\gamma$  releasing assay (IGRA), but these have a limited diagnostic value. Interpretation of the result of TST reactivity can be complicated by cross-reactivity with previous Bacille Calmette-Guerin vaccination or latent TB infection in countries where TB is common. Other factors like HIV infection, poor nutritional status, recent viral or bacterial infections, or vaccination with live virus can also reduce response to the TST. Similarly, IGRA cannot distinguish between latent infection and active pulmonary TB or EPTB. Thus, negative results cannot entirely exclude the disease [22].

### Conclusion

The tonsillar specimens should be obtained for both mycobacteriological and histopathological examinations. The measurement of biochemical markers in TB-affected pleural fluids such as ADA or IFN- $\gamma$  releasing assay could be supportive tests for the diagnosis. Molecular biology techniques such PCR may be helpful in rapid diagnosis as well as in paucibacillary cases.

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