

## Oral Lesions in Patients with Tuberculosis: A Cross-Sectional Study

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### Abstract

Tuberculosis (TB) is one of the world's deadliest infectious diseases and predominantly affects the lungs. TB could also occur in other sites of the body, such as the oral cavity. The oral manifestation incidence of TB is approximately 0.05%–5%. Despite being a rare occurrence, oral TB remains a challenging issue because of its nonspecific clinical presentation.

This study aims to assess and determine the oral lesions of patients with TB.

In this cross-sectional study, we examined the oral cavity of patients with TB to assess the appearance of oral lesions in each patient.

In 30 patients with pulmonary TB, we identified 29 oral lesions on the tongue. One patient was suspected with oral tubercular lesion, and four patients had *Candida* infection-related lesions. Most lesions were classified as normal variant lesions of the oral mucosa, with the coated tongue exhibiting the highest incidence. The tongue is often affected by patients' systemic condition.

**Conclusion:** Results suggest that although most patients with TB have oral lesions, the oral TB incidence remains rare. Considering that some lesions might be asymptomatic, dentists could play a vital role in the early diagnosis of lesions for further management.

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### Introduction

Regarded as the “captain of the men of death” by John Bunyan and “white plague” by Oliver Wendell Holmes in the eighteenth century, tuberculosis (TB) remains one of the deadliest infectious diseases in the world. In 2016, nearly 1.3 million HIV-negative people died because of TB, with additional deaths of 374,000 HIV-positive people. Indonesia has the second highest number of TB cases after India, followed by China, the Philippines, and Pakistan (together accounting for >50% of global TB cases in 2016).<sup>1</sup> Poor hygiene conditions and the escalation of HIV/AIDS cases are associated with the increasing number of TB cases in developing countries.<sup>2</sup>

TB predominantly affects the lungs and is categorized as pulmonary TB. However, it could also occur in other sites of the body, such as the

joints, meninges, bones, and lymph nodes; this type of TB is categorized as extrapulmonary TB. The oral cavity could also be one of the body sites affected by TB; however, its incidence is approximately 0.05%–5% of total TB cases.<sup>2</sup> To date, several studies have reported oral lesions of TB with varied clinical presentations, such as oral ulcer, nodules, tuberculomas, periapical granulomas lesions, or gingival, periodontal, and osteomyelitis TB; these lesions could be both painful or painless.<sup>3-5</sup> Oral TB could present in various forms, such as painless and painful ulcer, patches, indurated soft tissue lesion, or even osteomyelitis on the jaws.<sup>6</sup> Oral TB could be either primary or secondary. The primary form of oral TB usually presents as a single painless ulcer accompanied by regional (submandibular, submental, and cervical) lymph node enlargement; this form usually occurs in younger patients, such as children. Conversely, the secondary form of oral TB commonly presents in middle-aged and elderly patients as irregular painful ulcers with induration and inflammatory exudates.<sup>3,7</sup> Some oral TB lesions were reported to be present as gingival enlargement with or without any periodontal involvement instead of an ulcer as a common manifestation.<sup>5,8,9</sup>

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However, the oral lesions of TB could be overlooked in the differential diagnosis because of their nonspecific clinical presentation. Moreover, the onset of oral lesions precedes the systemic signs and symptoms of TB. All of these factors could result in misdiagnosis. Dentists could play a vital role in the early detection of oral TB lesions to ensure its prompt management. Hence, this study aims to assess and identify the oral lesions (both tubercular and nontubercular) of patients with pulmonary TB.

### Materials and methods

This is a cross sectional study and all measurements for study participant are obtained at a single point in time. Study was done at TB outpatient unit of Dr. Soetomo General Hospital Surabaya, East Java, Indonesia. Data collecting was performed in July 2017 - January 2018. Ethics Committee Clearance was taken at the Dr. Soetomo General Hospital, Indonesia. A total of 30 patients of pulmonary tuberculosis, both males and females that were visiting TB outpatient unit of Dr. Soetomo General Hospital were selected with the exclusion children/teenage under 17 years old, pregnancy/lactating females, using corticosteroids, and patients unwilling for sampling.

There were pulmonary tuberculosis patient and oral lesions as variables. Pulmonary tuberculosis patient was defined as patient came to TB outpatient unit of Dr. Soetomo General Hospital and was diagnosed suffering pulmonary tuberculosis by pulmonologist of the unit. Oral lesion belongs to any intra oral finding related to oral mucosa, which is could be pathogen or intra oral varians, classified according to Langlais *et al.* textbook (2009).<sup>10</sup> Oral tubercular lesion defined as tuberculosis that is occurred in oral cavity, appears in various form, ranging from both painless and painful ulcer, patches, indurated soft tissue lesion, or even osteomyelitis on jaws.<sup>6</sup>

We collected data about TB diagnosis, including clinical symptoms assessment and supportive examination results, from the patient's medical records. All enrolled patients had consented to oral cavity examination to assess the appearance of oral lesions. Oral examination of all patients was performed by team of dental practitioners. This study investigation primarily relied on the clinical appearance of lesions and

the related details of oral tubercular lesions in the literature. Any suspected TB-related oral lesion was swabbed by a disposable cotton stick to detect the presence of *Mycobacterium tuberculosis* in the bacteriological examination. *M. tuberculosis* detection and culture examination was performed by Ziehl Neelsen.

Minimal sample size was obtained from formula for qualitative variable, based on previous study that suggested oral tuberculosis lesion ranged between 0.05 – 5 % of tuberculosis cases ( $P < 0.05$ , and precision/absolute error = 0.1).<sup>11</sup> The data were analyzed with descriptive statistic (frequency and percent) using Microsoft Excel 2016.

$$\text{Sample Size} = \frac{Z_{1-\alpha/2}^2 p (1 - p)}{d^2}$$

### Results

There were 30 participants, consisted of 13 males, and 17 females. Patient's ages were ranging between 18 and 69 years old. Nineteen cases were new pulmonary TB case, and haven't receive any anti-tuberculosis therapy, whereas 6 patients were old cases (have received anti-tuberculosis therapy) and 5 patients were relapse cases. Human Immunodeficiency Virus (HIV) positivity status of subjects were unknown, but three patients have Diabetes Mellitus as systemic disease comorbid. Researcher could not determine HIV status of subjects since HIV infection has a window period, as a period of time after a person is infected during which they won't detected positive. Among 37 lesions found from the subjects, 21 lesions were identified in oral cavity of new pulmonary tuberculosis cases. Nine were found in old cases, and 7 lesions in relapse cases. About 43.2% of lesions were presented in male, but of all patients, 4 male subjects (13.3%) did not present any oral manifestation. On the other hand, 2 female patients (6.7%) who didn't have any oral lesion (Table. 1).

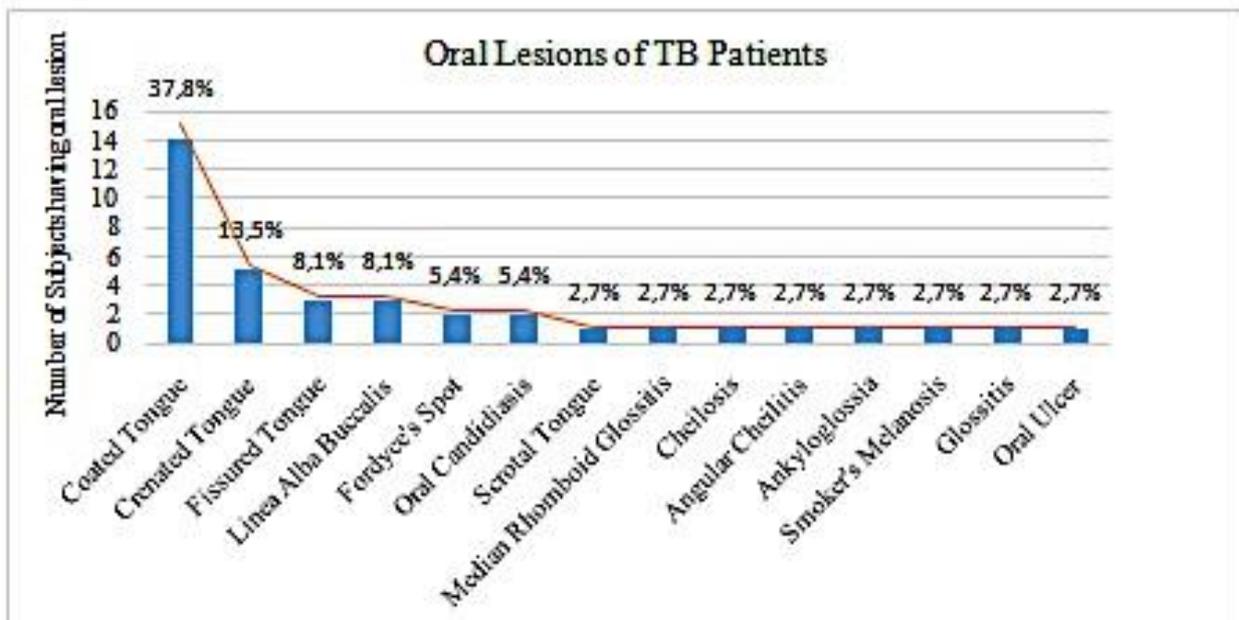
Regarding to anatomical site, we identified 29 (78.4%) oral lesions on the tongue, and the second most prevalent site was buccal mucosa (22.2%). The highest incidence was coated tongue (14 patients) followed by crenated tongue (5 patients). Furthermore, three patients with TB had fissured tongue, three patients had linea alba buccalis, two patients had fordyce's spots, two patients had oral candidiasis, one patient had scrotal tongue, one patient had

median rhomboid glossitis, one patient had cheilosis, one patient had angular cheilitis, one patient had ankyloglossia, one patient had smoker's melanosis, one patient had glossitis, and one patient had oral ulcer (Fig. 1). Median rhomboid glossitis, coated tongue, fissured

tongue, crenated tongue, and linea alba buccalis were lesions identified among three subjects with diabetes mellitus.

Category	Number of Subjects	Number of Lesion
<b>Sex</b>		
Male	9 of 13	16 (43.2%)
Female	15 of 17	21(56.8%)
<b>Total</b>	<b>24 of 30</b>	<b>37 (100%)</b>
<b>TB Cases</b>		
New	15 of 19	21 (56.8%)
Old	5 of 6	9 (24.3%)
Relapse	4 of 5	7 (18.9%)
<b>Total</b>	<b>24 of 30</b>	<b>37 (100%)</b>

**Table 1.** Distribution of Subjects and Lesion based on Sex and TB Case Category



**Figure 1.** The distribution of oral lesions in the study cohort. Most lesions are present in the normal (non-TB) group.

In this study, one lesion was related to TB; it was a single, irregular, yellowish, and painless ulcer on the ventral part of the tongue (approximately 2 cm × 1 cm) with an irregular border and granulomatous surface (Fig. 2).



**Figure 2.** Oral ulcer on the left side of the ventral tongue.

### Discussion

Selvamuthukumar *et al.* reported that the TB organism culture from suspected oral lesions in patients with TB could not be considered diagnostic tools of the lesion because the sputum and saliva might harbor microorganisms, thus resulting in bias. Furthermore, the oral lesion is not tuberculous in origin. Conversely, viable acid-fast microorganisms might remain undetected because of oral cavity washing in patients with TB. Therefore, a definitive diagnosis should be determined by comparing the clinical appearance of lesions and histopathological tissue examination results.<sup>12</sup> Jan *et al.* reported that the sputum-based test was unsuitable for the diagnosis of extrapulmonary TB (e.g., oral TB), and DNA amplification could be highly useful for detecting the TB microorganism in formalin-fixed paraffin-embedded tissue biopsies.<sup>9</sup> In this study, we did not conduct any invasive procedures, such as biopsy, because the patients had a nonoral health-related problem and were not willing to undergo histopathological examination.

In this study, two TB cases had oral candidiasis; and both patients complained about white lesions intraorally and burning sensation in the oral cavity. The clinical examination showed that lesions appeared on the palate as a pain-irregular erythematous patch and a white pseudomembranous lesion on the tongue (Fig. 3). Oral candidiasis is often considered one of the most prevalent lesions associated with systemic disorders (incidence rate, 5%-92%).<sup>13</sup> The

occurrence of oral candidiasis as mycotic infection increased with the increased incidence of immunosuppressive diseases; thus, it was reported as the most prevalent lesion in HIV-infected people.<sup>14</sup> The prevalence of pulmonary TB with *Candida* co-infection is approximately 15% - 32%.<sup>15</sup> Another study reported a strong correlation between oral candidiasis and TB diseases independent of CD4<sup>+</sup> cell counts; this finding was supported by another study that reported that TB and oral candidiasis were the only opportunistic infections that commonly occurred among HIV-positive adults in South Africa with CD4<sup>+</sup> cell counts  $\geq 200$  cells/mm<sup>3</sup>.<sup>16</sup> The other intraoral lesions found in this study were associated with *Candida* infection, such as median rhomboid glossitis and angular cheilitis. Median rhomboid glossitis was recognized as manifestation of chronic candidiasis.<sup>17</sup> Other than *Candida* infection, both median rhomboid glossitis and angular cheilitis are associated with different predisposing factors that affect *Candida* multiplication as normal flora; these factors include smoking, denture wearing, and diabetes mellitus in median rhomboid glossitis occurrence and hypovitaminosis, iron deficiency, age-related corner of the mouth tissue sagging, and decreased vertical dimension of occlusion in angular cheilitis.<sup>18,19</sup>



**Figure 3.** Oral candidiasis in a patient. Erythematous patch on palate (a) and whitish pseudomembranous lesion on tongue (b)

In this study, coated tongue cases were predominant. Some previous studies suggested that salivary flow rate is one of important key in tongue coating formation. But, Van Tornout *et al.* (2013) stated that their study did not support any association between accumulation of tongue coating and salivary flow rate.<sup>22</sup> Other than this factor, tongue coating is also associated with some diseases, dietary habits, poor oral hygiene,

and drugs.<sup>23</sup> As it is formed from food and bacteria, tongue coating is a facilitating environment to *Candida* spp. Growth.<sup>24</sup>

More than half of the patients exhibited oral lesions and variations in this study. As study that was conducted by Gemaque *et al.*, patients with tuberculosis did not present typical lesion from this specific disease in oral cavity.<sup>13</sup> Mucosal lesions found oral cavity of pulmonary tuberculosis patients might have association with *Candida* spp, however, since mycological examination was not performed as confirmation of fungal infection in this study, it is still being doubtful. Overall, most of the lesions identified in this study commonly presented in the normal group or are normal variants of the oral mucosa. Different medical conditions, such as febrile condition, dehydration, chronic renal failure, leukemia, and diabetes, could affect the oral cavity, including the tongue,<sup>23,25</sup> thus, almost 78% lesions were found on the tongue.

### Conclusions

To date, the incidence of oral TB remains rare. This study encountered most lesions as coated tongue rather than oral tubercular lesions in patients with TB. Even though coated tongue and other lesions considered as normal variants, they could be related to the presence of systemic diseases, because the systemic condition could result in oral cavity changes. Hence, given that some oral lesions could be asymptomatic, routine oral examination is required to facilitate the early diagnosis of oral lesions for further management.

### Declaration of Interest

The authors declare that there are no conflicts of interest.

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