REVIEW

Clinical and Pathological Spectrum of Oral Tuberculosis: A Systematic Review of Case Reports

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Abstract

Introduction: Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis, primarily affecting the lungs but also capable of affecting extrapulmonary sites. Oral tuberculosis is a rare manifestation of extrapulmonary TB and is frequently underdiagnosed because of its nonspecific clinical presentation and close resemblance to malignant, inflammatory and other granulomatous oral lesions. This systematic review aimed to evaluate published case reports in order to describe the clinical and pathological spectrum of oral tuberculosis and to emphasize diagnostic challenges.

Materials and methods: This systematic review was prepared and carried out following the PRISMA 2020 guidelines. The systematic literature search was performed using the Scopus database to identify case reports of oral tuberculosis involving soft tissues of the oral cavity published between January 2010 and April 2025. The search terms included "oral tuberculosis" and "intra-oral tuberculosis". A total of 71 articles were retrieved. After applying the inclusion and exclusion criteria, 18 full-text case reports were included in the current systematic review. Cases limited to pulmonary tuberculosis or lacking sufficient clinical and histopathological data were excluded. Only full-text case reports were included.

Results: Eighteen case reports from patients aged 23–74 years were analysed. The tongue was the most commonly affected site, followed by the gingiva, palate, lips and buccal mucosa. The most common clinical presentation was a chronic non-healing ulcer, although nodular, fissured, ulceroproliferative lesions were also reported. Oral tuberculosis frequently mimicked oral squamous cell carcinoma (SCC), causing diagnostic delays and initial misdiagnosis. Histopathological examination commonly revealed granulomatous inflammation with epithelioid cells, Langhans giant cells and caseous necrosis, while Ziehl–Neelsen staining demonstrated acid-fast bacilli in many cases.

Conclusion: Oral tuberculosis has a broad range of clinical characteristics, most of which involve the tongue and frequently mimic oral malignancies causing diagnostic delays. Its close resemblance to oral squamous cell carcinoma poses significant diagnostic challenges. Histopathological examination remains essential for accurate diagnosis and increased clinical awareness is crucial for early detection, appropriate management and prevention of disease transmission.

Keywords: Oral Tuberculosis, Acid fast bacilli, Mycobacterium, ulcers, Langhans giant cells

Introduction

Tuberculosis (TB) is a chronic infectious disease principally instigated by Mycobacterium tuberculosis, a slow-growing, acid-fast bacillus that predominantly targets pulmonary system while possessing the capacity to affect virtually all organ systems.[1] A German physician named, Robert Koch identified the Tuberculosis bacillus in the year 1882.[2,3] Despite advancements in preventive and therapeutic strategies, tuberculosis persists as a significant global public health concern, especially within low and middle-income nations.[4]

The World Health Organization has reported the annual identification of millions of tuberculosis (TB) cases, an occurrence that is frequently accompanied by significant rates of morbidity and mortality.[5] Such adverse health outcomes can be attributed to a variety of factors, including delays in diagnostic procedures, the rise of drug-resistant tuberculosis strains and the co-occurrence of other health issues, such as infections caused by HIV. Consequently, the multifaceted challenges linked to tuberculosis necessitate an integrated approach that encompasses prompt diagnostic measures, efficient treatment protocols and targeted public health strategies.

The transmission of tuberculosis (TB) primarily occurs through airborne droplets released by an individual infected with the bacterium during acts such as coughing, sneezing

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or speaking.[6] Following inhalation, the bacilli possess the capacity to either initiate a latent infection or advance to an active disease state, a process influenced significantly by the immune status of the host. Pulmonary tuberculosis is characterized as the most prevalent and communicable form of the disease; however, a considerable percentage of cases are attributed to extrapulmonary tuberculosis. This latter form often poses substantial diagnostic challenges due to its varied and nonspecific clinical manifestations, necessitating prompt recognition of atypical presentations to impede disease progression and further transmission.[7]

Among the various extrapulmonary forms, oral tuberculosis is regarded as an infrequent yet frequently disregarded condition. Owing to its rarity and highly variable clinical presentation, oral tuberculosis is frequently overlooked and often mimics oral squamous cell carcinoma, traumatic ulcers, fungal infections, aphthous ulcers, and other granulomatous disorders. Consequently, diagnosis is often delayed, increasing the risk of disease progression and continued transmission.

Although several individual case reports describing oral tuberculosis have been published over the past decade, the available evidence remains scattered across the literature. Till date, there is a lack of recent systematic synthesis focusing specifically on the clinical presentation, anatomical distribution, histopathological features and diagnostic challenges of oral tuberculosis involving the soft tissues of the oral cavity. This represents an important knowledge gap, particularly for dental practitioners, oral pathologists and clinicians who may encounter these lesions in routine practice. Therefore, the objective of this systematic review was to evaluate published case reports of oral tuberculosis involving the soft tissues of the oral cavity in order to characterize its demographic, clinical and histopathological features, identify the most commonly affected sites and clinical presentations, assess patterns of misdiagnosis and highlight the diagnostic challenges associated with this rare manifestation of tuberculosis.

Materials and Methods

Search Strategy

The PRISMA 2020 guidelines formed the basis for the preparation and execution of this systematic review's procedure. A comprehensive literature search was carried out in the Scopus database to identify case reports of oral tuberculosis involving the soft tissues of the oral cavity published between January 2010 and April 2025. The search strategy was designed to identify records containing the terms "oral tuberculosis" or "intra-oral tuberculosis" in the title, abstract, or keywords. The search was limited to articles published in English and classified as case reports. Only studies with full-text availability were considered to include in this review.

Eligibility Criteria

Inclusion Criteria

Studies were included if they:

1. Were published as case reports or case series.
2. Reported oral tuberculosis involving the soft tissues of the oral cavity (tongue, gingiva, palate, lips, buccal mucosa, floor of mouth, etc.).
3. Provided sufficient clinical and/or histopathological information for analysis.
4. Were published in English between January 2010 and April 2025.
5. Had full-text articles available.

Exclusion Criteria

Studies were excluded if they:

1. Reported only pulmonary tuberculosis without oral manifestations.
2. Involved exclusively osseous lesions of the jaws without soft tissue involvement.
3. Lacked adequate clinical or histopathological details.
4. Were review articles, editorials, conference abstracts, letters to the editor or non-case-report publications.
5. Had unavailable full-text articles.

Study Selection

The initial search retrieved 71 documents from the Scopus database. Titles and abstracts were screened for relevance, followed by full-text assessment of potentially eligible articles. After applying the inclusion and exclusion criteria, 18 case reports were included in the final review and subjected to qualitative analysis.

Data Extraction

The following data were extracted from each of the included case reports: author and year of publication, patient age and sex, site of oral involvement, clinical presentation, provisional diagnosis, histopathological findings and results of Ziehl–Neelsen staining or other relevant investigations. The extracted data were subsequently analysed descriptively to identify patterns in demographic characteristics, anatomical distribution, clinical manifestations, histopathological features and diagnostic challenges associated with oral tuberculosis.

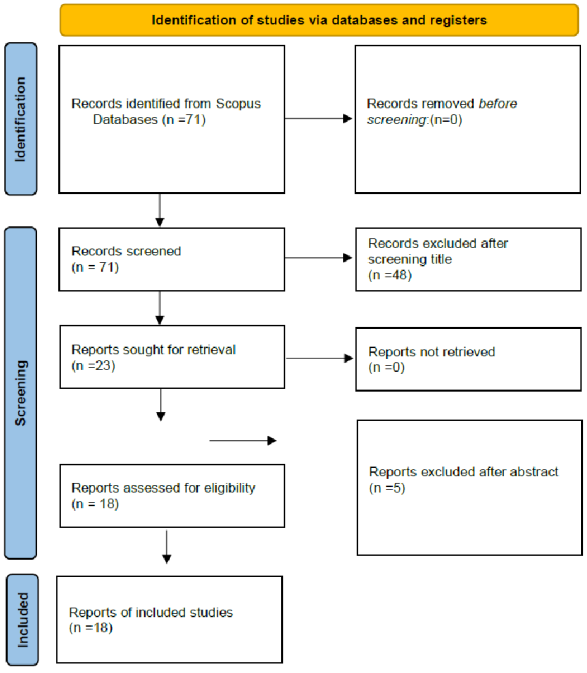

Chart 1- Screening Process

Table 1- Reported Cases of Oral Tuberculosis with clinical presentation and histological findings from the year 2010-2025

Author/year	Age of the patient	Location	Clinical presentation	Provisional diagnosis	Histological findings
Sun LW et al.[8] (2011)	35 years, Female	Gingiva	Large irregular fiery-red, pebbled, multiple ulcerated gingival lesions extending into buccal vestibule	Chronic granulomatous inflammation (gingival TB) with actinomycetes	Chronic inflammatory infiltrate with angiogenesis; epithelioid granulomas, Langhans giant cells, caseating necrosis, actinomycetes; Ziehl-Neelsen staining was negative for acid-fast bacilli
Chauhan V et al.[9] (2012)	62 years, Male	Lip	Swelling increased in size involving both upper and lower lips	Squamous cell carcinoma	Necrotizing suppurative granulomatous inflammation
Yadav SPS et al.[10](2012)	65 years, Male	Tongue	8×6cm firm swelling over the left side of anterior 2/3rd of tongue with smooth surface and well-defined margins	Submucosal carcinoma of tongue	Granulomatous inflammation. Acid fast bacilli were found in ZN stained sections
Kumar S et al.[11] (2012)	38 years, Male	Tongue	2.5-1.5cm grey-white ulcerated lesion on the lateral border of tongue with irregular margins and whitish patch	Malignancy	Numerous epithelioid cell granulomas with few multinucleated giant cells in a background of mixed inflammatory cells and necrosis. Zeihl Neelsen stain for acid fast bacilli was positive
Bagga P et al.[12] (2012)	31 years, Male	Junction of hard and soft palate	Painful superficial oval ulcers, 2 × 3 cm^2, at the junction of hard and soft palate, with central necrotic base, surrounded by erythematous margins	Infective (bacterial or mycotic), inflammation, or apthous ulcer	Granulation tissue and mixed inflammatory infiltrate
Estomba CMC et al.[13] (2015)	62 years, Female	Base of tongue	Ulcerated hypertrophic lesion in the vallecula of about 2-3 cm in the base of the tongue	--	Acid alcohol resistant bacilli were found through the Ziehl Neelsen method
Nemeş, R. M et al.[14] (2015)	74 years, Male	Tongue	Ulcerated lesion, about 1.5 cm involving right lateral border of tongue, whitish, opaque with smooth surface and well defined margins	Ulcerated tumor	Multiple granulomas with epithelioid cells, Langhans giant cells, central necrosis
Ganesan V et al.[15] (2016)	45 years, Female	Tongue	Painless ulcers in the tip of the tongue	Primary oral tuberculosis of tongue in lepromatous leprosy	Granulomatous reaction with central caseous necrosis and epithelioid and giant cells. Ziehl–Neelsen staining showed acid-fast bacilli.
Khateeb D et al.[16] (2016)	59 years, Female	Tongue	Painful tongue lesion	-	Granulation tissue with non-caseating granulomas; AFB positive
Vučičević Boras V et al.[17](2017)	68 years, male	Tongue	Ulceration on ventro-lateral surface of the tongue, approximately two centimeters in diameter.	Sarcoidosis	Granulomatous inflammation, granuloma with central caseous necrosis
Arora, K. S et al.[18](2018)	25years, Female	Dorsum of the tongue	Ulceroproliferative, rough, irregular-shaped ulcer was seen on the dorsum of the tongue measuring 4 cm × 2 cm in size	Squamous cell carcinoma	Chronic granulation tissue with necrosis; scattered epithelioid cells

Kim S Y et al.[19] (2019)	57 years, Male	Tip of the tongue	Round ulcer measuring approximately 0.7 cm in diameter on the tip of the tongue	Major aphthous ulcer, traumatic ulcer, granulomatous diseases, and infections	Epithelioid cells and multiple Langhans giant cells and ZN staining demonstrated acid-fast bacilli
Fragoso J et al.[20] (2020)	44 years, Male	Posterior third of the dorsum of tongue	Papillomatous, hardened and painful lesion measuring about three centimeters in the posterior third of the tongue	Squamous cell carcinoma	Numerous epithelioid granulomas, some with central necrosis and frequently accompanied by giant multinucleated cells of the Langhans type. Ziehl-Neelsen staining revealed the presence of acid-fast bacillary structures
Hamid R et al.[21] (2020)	37 years, Female	Gingiva	Gingiva was red, irregular, pebbled and granular in appearance with surface ulceration	Ulcerative gingivitis	Clusters of epithelioid cells, caseating necrosis and numerous Langhans-type giant cells surrounded by a chronic inflammatory type of infiltrate
Hamid R et al.[21] (2020)	45 years, Female	Gingiva and hard palate	Indurated, irregular ulcerations with undermined margin and a yellowish granular necrotic base	Malignant lesion	Caseating granulomas surrounded by lymphocytes, epithelial cells and Langhans-type giant cells. Ziehl–Neelsen staining was negative.
Hamid R et al.[21] (2020)	49 years, Male	Tongue	Ulcer measuring 1.5 cm × 1.0 cm on the dorsolateral border of anterior part of tongue.	Oral squamous cell carcinoma	Granulomatous inflammation with Langhans giant cells and caseous necrosis; sputum AFB negative
Hamid R et al.[21] (2020)	23 years, Female	Gingiva	Gingival swelling	Gingival overgrowth	Epithelioid cells with Langhans giant cells; no caseation
Razem, B et al.[22] (2021)	36 years, Female	Undersurface of tongue	1 cm long fissure in the undersurface of the tongue (left side) and a regular induration of the retromolar trigone	Locally advanced carcinoma	Clusters of epithelioid cells, caseating necrosis and numerous Langhans-type giant cells surrounded by a chronic inflammatory type of infiltrate
Martins-de-Barros AV et al.[23] (2021)	36-years, Male	Tongue apex	Ulcerative lesion affecting the tongue apex	--	Granulomatous inflammation, Positive Ziehl-Neelsen staining for acid-fast bacilli
Barragán YA et al.[24] (2022)	55 years, Male	Lateral tongue	3 × 1.5 cm tender ulcer with irregular, raised, firm edges on lateral tongue	---	Granulomatous infiltrate, with acid-fast rods on Ziehl-Neelsen stain
Sriram S et al.[25](2023)	43 years, Male	Buccal and labial mucosa of the lower lip	Nonhealing ulcer on the labial mucosa of the lower lip measuring 1 5 cm× 1 cm and an ulcer of 1 cm× 0 8cm in diameter, on buccal mucosa	Aphthous / traumatic / malignant ulcer, drug reaction, and infections (bacterial, fungal, and viral)	Caseating granulomas, encircled by epitheloid cells, Langhan's giant cells, and chronic inflammatory cells. Ziehl-Neelsen staining positive for acid-fast bacilli

Results

Through Scopus database search, 71 documents were obtained. Out of which, only applicable 18 case reports with oral tuberculosis were included. Cases of exclusive pulmonary tuberculosis and those of which full article was not available were excluded. After qualitative synthesis all 18 case reports were included for systematic review. The screening process is depicted in Chart 1. The characteristics of the included 18 case reports comprising 21 individual cases are summarized in Table 1.

A total of 18 case reports with 21 individual cases of oral tuberculosis were included in this systematic review. The age of patients ranged from 23 to 74 years, with most cases occurring in the fourth to seventh decades of life. Of the total cases, 12 (57.1%) were male and 9 (42.9%) were female. The tongue was the most frequently affected site, observed in 13 cases (61.9%), followed by gingiva (4 cases, 19.0%), lips (2 cases, 9.5%), palate (1 case, 4.8%) and buccal mucosa (1 case, 4.8%). Clinically, chronic non-healing ulcer was the most common presentation, observed in 15 cases (71.4%), followed by ulceroproliferative lesions (3 cases, 14.3%), nodular/swelling presentations (2 cases, 9.5%) and fissure-type lesions (1 case, 4.8%). (Table 2)

Table 2- Summary of demographic, clinical and histopathological characteristics of included case reports of oral tuberculosis

Variable	Category	n (%)
Sex	Male	12 (57.1)
	Female	9 (42.9)
Site	Tongue	13(61.9)
	Gingiva	4 (19.0)
	Lips	2 (9.5)
	Palate	1 (4.8)
	Buccal mucosa	1 (4.8)
Clinical presentation	Chronic ulcer	15 (71.4)
	Ulceroproliferative	3 (14.3)
	Swelling/nodule	2 (9.5)
	Fissure	1 (4.8)
Histopathology	Granulomas present	19 (90.5)
	Caseous necrosis	16 (76.2)
Disease type	Primary TB	11(52.4)
	Secondary TB	10 (47.6)

Histopathologically, granulomatous inflammation with epithelioid cells and Langhans giant cells was seen in 19 cases (90.5%), while caseous necrosis was reported in 16 cases (76.2%). Regarding disease classification, 11 cases (52.4%) were primary oral tuberculosis and 10 cases (47.6%) were secondary oral tuberculosis. (Table 2)

Discussion

Oral tuberculosis (TB) remains as a rare manifestation of extrapulmonary tuberculosis, accounting for a small percentage of TB cases globally. In India, the prevalence of tuberculosis (TB) is 3.2 million, with 2.7 million new cases recorded annually. Oral tuberculosis accounts for 0.5-1% of all tuberculosis cases.[1]

Oral TB can affect any area of the oral mucosa; however, it is most usually found on the tongue. Other locations in the oral cavity include the palate, lips, buccal mucosa, gingiva, palatine tonsil and floor of mouth. Salivary glands, tonsils and the uvula are also other affected sites.[26] Clinically, oral tuberculosis can present itself as chronic non-healing ulcers, nodular or granulomatous lesions, fissures or indurated masses. Among these diverse oral lesions, ulcerative forms are most frequently observed.[1,27] These ulcers are characterized by pain and it is noteworthy that caseation of the dependent lymph nodes is typically absent in such presentations. Additionally, lesions localized within the jaw may manifest as TB osteomyelitis or simple bony radiolucency.[28] Such lesions are often painful and may be associated with regional lymphadenopathy, dysphagia or systemic symptoms such as weight loss, fever and night sweats.

The diagnosis of oral tuberculosis is challenging due to its rare occurrence and resemblance to conditions such as squamous cell carcinoma, traumatic ulcers, fungal infections and other granulomatous diseases.[28,29] Several cases clinically mimicked oral malignancy, including those reported by Kumar S et al. (2012), Yadav SPS et al. (2012), Arora KS et al. (2018), Fragoso J et al. (2020), Hamid R et al (2020), and Razem B et al. (2021), underscoring the diagnostic challenge posed by oral TB.[10,11,18,20,21,22]

Histopathological examination typically shows granulomatous inflammation with caseous necrosis and Langhans giant cells, while microbiological and molecular tests help confirm the presence of Mycobacterium tuberculosis. However, as evidenced in this current systematic review of case reports, its clinical and pathological spectrum is remarkably broad, often mimicking malignant, inflammatory or other granulomatous conditions. This diagnostic ambiguity continues to present significant challenges for clinicians and pathologists alike.

Management of oral tuberculosis relies primarily on standard anti-tubercular therapy, which usually results in total resolution of oral lesions. Early diagnosis not only improves patient outcomes but also plays an important role in controlling the spread of tuberculosis within the community.

Demographic and Clinical Characteristics

The cases included in this review span a wide age range (23–74 years), with a majority of middle-aged and older adults, consistent with prior research suggesting that oral TB is more frequently diagnosed in individuals with long term exposure or underlying systemic risk factors. Both sexes were affected, although a slight male predominance was observed, aligning with the known epidemiology of tuberculosis globally.

The tongue was shown to be the most typically involved region, specifically the lateral border, tip, dorsum, and ventrolateral surfaces. This predilection may be explained by repeated

microtrauma, rich vascularity and exposure to infected sputum, which facilitate direct inoculation of Mycobacterium tuberculosis. Less commonly affected locations included the base of the tongue, gingiva, palate and lips, underscoring that oral TB should be considered in the evaluation of persistent oral lesions. Extra-lingual involvement, such as the lip and gingiva, was reported by Sun LW et al. (2011), Chauhan V et al. (2012), Hamid R et al (2020) and Sriram S et al. (2023), highlighting that oral TB is not limited to the tongue.[8,9,21,25]

Clinically, oral tuberculosis was most commonly presented as chronic, non-healing ulcers, typically painful, with irregular, indurated or raised margins. Lesion size varied widely, from small ulcers less than 1 cm to large ulceroproliferative masses exceeding 8 cm. Several cases described papillomatous, hypertrophic or fissured lesions. Importantly, these clinical features strongly resembled oral squamous cell carcinoma, leading to frequent provisional diagnoses of malignancy, especially in older patients or those with indurated lesions.

Diagnostic Challenges and Misdiagnosis

A striking finding of this review is the high rate of initial misdiagnosis, most commonly as squamous cell carcinoma, traumatic ulcers, aphthous ulcers, sarcoidosis or other granulomatous diseases. This reflects the nonspecific clinical appearance of oral TB as well as the condition's rarity, which often results in low clinical suspicion. Some lesions were initially misdiagnosed as aphthous or traumatic ulcers, as described by Bagga P et al. (2012), Kim SY et al. (2019) and Sriram S et al.(2023).[12,19,25]

Several cases were provisionally diagnosed as locally advanced carcinoma or ulcerated tumors, emphasizing that oral tuberculosis can closely resemble malignancy clinically. This misinterpretation can delay appropriate anti-tubercular therapy and subject those patients to unnecessary anxiety or invasive interventions. Therefore, oral TB should be included in the differential diagnosis of chronic oral ulcers, particularly in endemic regions or in patients with relevant systemic symptoms or immunocompromised conditions.

Histopathological Spectrum

Across the reviewed cases here, the most consistent findings were granulomatous inflammation composed of epithelioid histiocytes, Langhans-type multinucleated giant cells and variable degrees of central caseous necrosis. Cases reported by Nemeş RM et al. (2015), Ganesan V (2016), then Kim SY et al. (2019), Fragoso J et al. (2020) and Hamid R et al (2020) showed classic tuberculous features such as epithelioid cell granulomas, Langhans-type giant cells and central caseous necrosis histopathologically.[14,15,19,20]

Ziehl–Neelsen staining revealed acid-fast bacilli (AFB) in a majority of cases, confirming its diagnostic value. Ziehl–Neelsen positivity for acid-fast bacilli was frequently reported, including in cases by Kumar S et al. (2012), Estomba CMC et al. (2015), Kim SY et al. (2019) and Allan Vinícius Martins-de-Barros et al. (2021) confirming mycobacterial etiology.[11,13,19,23] However, some reports documented negative AFB staining despite classic granulomatous histology, highlighting the well-recognized limitation of AFB detection in paucibacillary extrapulmonary lesions. This emphasises the importance of correlating histopathology with clinical findings and, when needed, adopting adjunctive diagnostic modalities such as culture, PCR or systemic evaluation for tuberculosis.

Interestingly, both caseating and non-caseating granulomas were noted, which can further complicate differentiation from conditions such as sarcoidosis, Crohn's disease, fungal infections or foreign body reactions. Notably, Sun LW et al. (2011) reported a complex case of gingival TB with concomitant actinomycetes infection, despite Ziehl–Neelsen negativity.8 Non-caseating granulomas with positive acid-fast staining were also observed by Khateeb D (2016), broadening the histological spectrum.[16]

Primary versus Secondary Oral Tuberculosis

Oral tuberculosis lesions can be primary or secondary. Primary lesions are rare and typically occur in younger patients with enlarged cervical lymph nodes. Whereas, secondary oral tuberculosis is often associated with pulmonary disease and can affect persons of all ages, but middle-aged and older individuals are more likely to be affected. Secondary oral TB typically develops due to autoinoculation of infected sputum or hematogenous spread from a primary focus somewhere else in the body.[1,3]

In the current review, among the 21 included cases, 11 were classified as primary oral tuberculosis and 10 as secondary oral tuberculosis. Primary oral tuberculosis was identified in cases with no evidence of pulmonary or systemic involvement at presentation, whereas secondary cases were associated with confirmed pulmonary or disseminated disease. Although secondary oral tuberculosis has traditionally been reported more frequently, the findings of this review demonstrate a nearly equal distribution between primary and secondary forms. This suggests that oral tuberculosis may not always be a secondary manifestation and can, in several instances, represent the initial clinical presentation of infection. Hence, comprehensive clinical, radiological and systemic evaluation is essential in all suspected cases to accurately determine the disease origin and ensure appropriate management.

Clinical Implications

The findings of this systematic review highlight that oral tuberculosis, though uncommon, is a clinically significant disguised disease. Persistent oral ulcers unresponsive to conventional therapy, especially those with induration or ulceroproliferative features, warrant histopathological evaluation. Awareness among dental practitioners, oral surgeons and pathologists is critical for avoiding misdiagnosis and thus ensuring timely initiation of anti-tubercular treatment regimen.

Limitations

This systematic review has several limitations. The literature search was restricted to the Scopus database, which may have resulted in the omission of relevant studies indexed elsewhere. Publication bias may have influenced the findings, as unusual or diagnostically challenging cases are more likely to be reported. Furthermore, the review was based solely on case reports, which represent a low level of evidence and are

subject to limited generalizability. Owing to the small number and heterogeneity of the included cases, statistical analysis and meta-analysis could not be performed.

Conclusion

Oral tuberculosis exhibits a broad clinical and pathological spectrum and frequently resembles malignant and other granulomatous oral diseases. The tongue is the most commonly affected site and histopathological evaluation revealing granulomatous inflammation with or without demonstrable acid-fast bacilli remains the cornerstone of diagnosis. A high level of suspicion, particularly in chronic non-healing oral lesions, is essential to prevent misdiagnosis and ensure appropriate treatment.

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