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pediatric tuberculosis; dental status; oral pathological changes; pediatric dentistry; oral health assessment; digital oral diagnostics; preventive dental care; multidisciplinary management.

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Optimization of Dental Status Assessment and Management of Oral Pathological Changes in Children with Tuberculosis

Abstract
Tuberculosis (TB) remains one of the leading infectious diseases affecting children worldwide, with significant consequences for systemic health and quality of life. Despite substantial progress in tuberculosis control, the oral health status of pediatric patients with TB has received comparatively limited scientific attention, particularly regarding comprehensive assessment and evidence-based management of oral pathological changes. This study aimed to optimize the assessment of dental status and improve the management of oral pathological conditions in children diagnosed with tuberculosis through an integrated clinical approach. A comparative clinical study was conducted involving pediatric patients with confirmed tuberculosis and age-matched healthy controls. Comprehensive oral examinations were performed using standardized dental indices, periodontal assessment, oral mucosal evaluation, salivary analysis, and digital intraoral documentation. Clinical findings were analyzed using appropriate statistical methods to identify patterns of oral pathology, associated risk factors, and potential predictors of disease progression. The results demonstrated that children with tuberculosis exhibited a significantly higher prevalence of dental caries, gingival inflammation, periodontal abnormalities, oral mucosal lesions, reduced salivary protective capacity, and compromised oral hygiene compared with healthy children. Several clinical and biological indicators were identified as important predictors of oral pathological changes, emphasizing the close interaction between systemic tuberculosis and oral health deterioration. Based on these findings, an integrated diagnostic and therapeutic framework was developed to facilitate early identification of high-risk patients, optimize individualized treatment planning, and improve preventive dental care. The originality of this study lies in proposing a multidisciplinary model that combines pediatric dentistry, tuberculosis management, digital oral diagnostics, salivary assessment, and personalized preventive strategies within a unified clinical approach. The findings provide a practical foundation for improving interdisciplinary collaboration between pediatricians, tuberculosis specialists, and dental professionals, contributing to earlier diagnosis, more effective management of oral complications, enhanced quality of life, and improved long-term health outcomes for children affected by tuberculosis.

1. INTRODUCTION

Tuberculosis (TB) remains one of the world's most devastating infectious diseases and continues to pose a substantial threat to child health despite remarkable advances in diagnosis, vaccination, and antimicrobial therapy. According to the World Health Organization (WHO), approximately 1.3 million children and adolescents develop tuberculosis annually, while hundreds of thousands remain either undiagnosed or receive delayed treatment due to the non-specific clinical presentation of pediatric disease (World Health Organization [WHO], 2025). Children represent a particularly vulnerable population because of their immature immune systems, increased susceptibility to disseminated infection, nutritional deficiencies, and socioeconomic disadvantages. Beyond pulmonary manifestations, tuberculosis exerts systemic effects that influence growth, immune competence, nutritional status, and the integrity of oral tissues. Consequently, pediatric tuberculosis should be regarded not merely as an infectious disease but as a multisystem condition requiring comprehensive and interdisciplinary healthcare approaches.

Although global tuberculosis control programs have achieved substantial progress during the past two decades, oral health has received relatively limited attention within pediatric TB management. The WHO End TB Strategy emphasizes integrated patient-centered care, early diagnosis, preventive interventions, and multidisciplinary collaboration; however, routine dental assessment remains absent from most national tuberculosis treatment protocols (WHO, 2025). This gap is clinically important because oral diseases may compromise nutritional intake, increase inflammatory burden, reduce treatment adherence, and negatively affect quality of life in children undergoing prolonged anti-tuberculosis therapy. Therefore, integrating oral health into tuberculosis management may contribute to both improved dental outcomes and enhanced systemic recovery.

The oral cavity represents one of the most biologically dynamic environments in the human body and serves as an important interface between systemic and local immune responses. Systemic infectious diseases frequently produce oral manifestations through immune dysregulation, altered microbial ecology, nutritional deficiencies, and inflammatory responses. Although oral lesions directly caused by Mycobacterium tuberculosis are relatively uncommon in children, secondary oral changes associated with tuberculosis and its treatment are increasingly recognized in pediatric clinical practice. These include chronic gingival inflammation, dental caries, mucosal ulceration, angular cheilitis, xerostomia, periodontal abnormalities, enamel defects, delayed tooth eruption, and opportunistic fungal infections (Villa et al., 2022). Such manifestations often remain underdiagnosed because clinical attention is primarily directed toward pulmonary symptoms and antimicrobial management rather than comprehensive oral examination.

The relationship between tuberculosis and oral health extends beyond isolated pathological lesions. Pediatric patients diagnosed with tuberculosis frequently experience nutritional deficiencies, chronic inflammation, prolonged antibiotic exposure, reduced salivary secretion, and altered oral hygiene behaviors resulting from hospitalization or systemic illness. Together, these factors create favorable conditions for dental caries progression, periodontal tissue destruction, and disturbances in the oral microbiome. Consequently, oral pathological changes should not be interpreted simply as independent dental disorders but as manifestations of complex interactions between systemic infection, host immunity, microbial communities, and environmental influences.

Increasing evidence indicates that immunocompromised children exhibit substantially poorer oral health than healthy populations. Impairment of cellular immunity, alterations in cytokine regulation, oxidative stress, and prolonged inflammatory activation contribute to reduced resistance against oral pathogens and delayed tissue repair. Children affected by chronic infectious diseases frequently demonstrate higher prevalence of gingivitis, periodontal inflammation, oral candidiasis, mucosal ulceration, and dental caries compared with immunocompetent peers (Glick et al., 2022). Because tuberculosis primarily affects cell-mediated immunity, understanding its influence on oral tissues is particularly important for pediatric dental practice. Nevertheless, current knowledge regarding the mechanisms linking tuberculosis-associated immune dysfunction with oral pathological changes remains limited.

Recent advances in microbiome research have transformed understanding of oral health and disease. The oral microbiome consists of highly diverse microbial communities that contribute to immune regulation, mucosal integrity, metabolic homeostasis, and protection against opportunistic pathogens. Disruption of microbial equilibrium—commonly referred to as dysbiosis—has been associated with dental caries, periodontal disease, oral mucosal disorders, and systemic inflammatory conditions (Lamont et al., 2022). Children receiving long-term anti-tuberculosis treatment may experience significant alterations in microbial composition due to prolonged antimicrobial exposure, nutritional changes, immune modulation, and systemic inflammation. Such alterations may reduce microbial diversity while promoting colonization by opportunistic organisms capable of exacerbating oral disease.

The interaction between tuberculosis, antimicrobial therapy, and oral microbial ecology represents an emerging field of investigation. Although broad-spectrum antimicrobial agents remain essential for successful tuberculosis treatment, they may unintentionally influence commensal microbial communities within the oral cavity. Changes in microbial composition have been associated with increased susceptibility to dental caries, periodontal inflammation, fungal overgrowth, and impaired mucosal healing. However, relatively few clinical investigations have examined microbiome dynamics specifically among pediatric tuberculosis patients, creating an important knowledge gap in contemporary oral medicine research.

Another emerging area involves the identification of salivary biomarkers capable of supporting early diagnosis and monitoring of oral disease. Saliva has attracted considerable scientific interest because it represents a

non-invasive biological fluid containing cytokines, immunoglobulins, antimicrobial peptides, enzymes, oxidative stress markers, microbial metabolites, and nucleic acids that reflect both local and systemic physiological processes (Javaid et al., 2021). In pediatric populations, salivary diagnostics are particularly advantageous because specimen collection is painless, inexpensive, and readily repeatable during longitudinal clinical monitoring. Several inflammatory biomarkers—including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), matrix metalloproteinases (MMPs), and secretory immunoglobulin A (sIgA)—have demonstrated diagnostic potential for assessing oral inflammatory conditions and immune status (Giannobile et al., 2022). Nevertheless, their application in children with tuberculosis remains insufficiently investigated.

From a clinical perspective, integrating oral microbiome assessment with salivary biomarker analysis may substantially improve understanding of disease progression and facilitate personalized preventive strategies. Rather than relying exclusively on conventional clinical examination, contemporary pediatric dentistry increasingly adopts biologically informed diagnostic approaches combining clinical indices with molecular and biochemical indicators. Such approaches align closely with precision medicine principles by enabling early identification of high-risk patients before irreversible oral damage occurs. Despite these advances, there remains limited evidence regarding the combined diagnostic value of salivary biomarkers, microbial profiles, and clinical oral examinations in pediatric tuberculosis populations.

These observations collectively indicate that pediatric tuberculosis should be viewed through a broader oral-systemic health perspective. Understanding the interactions among host immunity, oral microbiota, inflammatory pathways, and dental status provides an essential foundation for developing comprehensive preventive and therapeutic strategies capable of improving both oral and general health outcomes in children affected by tuberculosis.

The pathophysiological relationship between tuberculosis and oral disease is primarily mediated through chronic inflammation and immune dysregulation. Persistent activation of the host immune response following Mycobacterium tuberculosis infection stimulates the release of numerous pro-inflammatory cytokines, chemokines, and reactive oxygen species that influence both systemic and oral tissues. Elevated concentrations of interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ), and matrix metalloproteinases (MMPs) have been implicated in connective tissue degradation, periodontal inflammation, impaired wound healing, and altered bone metabolism (Kinane et al., 2021). In pediatric patients, whose immune systems are still developing, prolonged inflammatory activation may further compromise oral tissue homeostasis, increasing susceptibility to gingivitis, periodontal disease, recurrent mucosal lesions, and dental caries. Consequently, oral inflammatory mechanisms should not be considered isolated pathological events but rather integral components of the systemic immune response to tuberculosis.

The recognition of oral-systemic interactions has transformed contemporary pediatric dentistry from a treatment-oriented discipline into one increasingly focused on prevention, early diagnosis, and individualized risk assessment. Preventive dentistry is now regarded as a cornerstone of pediatric healthcare because many oral diseases are preventable when risk factors are identified during the early stages of disease development (American Academy of Pediatric Dentistry [AAPD], 2024). In children with tuberculosis, preventive strategies assume even greater importance because prolonged hospitalization, nutritional deficiencies, antimicrobial therapy, and compromised immunity substantially increase oral disease risk. Comprehensive preventive programs—including individualized oral hygiene instruction, professional fluoride application, dietary counseling, pit and fissure sealants, antimicrobial mouth rinses when indicated, and regular periodontal monitoring—may reduce both disease incidence and treatment complexity. Nevertheless, preventive oral healthcare remains inadequately incorporated into tuberculosis management protocols in many low- and middle-income countries.

Current international clinical practice increasingly supports multidisciplinary management for children with chronic infectious diseases. Tuberculosis affects multiple physiological systems and therefore requires coordinated collaboration among pediatricians, infectious disease specialists, pulmonologists, nutritionists, microbiologists, psychologists, and dental professionals. Despite this recognition, dentistry often remains disconnected from pediatric tuberculosis services. Most clinical pathways prioritize diagnosis, antimicrobial therapy, radiological monitoring, and nutritional rehabilitation while overlooking comprehensive oral evaluation. This separation may delay the diagnosis of oral complications and reduce opportunities for preventive intervention. Integrating pediatric dentists into tuberculosis care teams could facilitate earlier identification of oral pathological changes, improve treatment planning, reduce infectious complications, and enhance children's overall quality of life.

The World Health Organization's End TB Strategy provides an important policy framework supporting integrated healthcare delivery. The strategy emphasizes patient-centered care, universal access to diagnosis and treatment, prevention, social protection, and multisectoral collaboration as essential components of tuberculosis elimination (WHO, 2025). Although oral health is not explicitly identified as a core component of the strategy, its underlying principles strongly support interdisciplinary healthcare capable of addressing the full spectrum of disease-related complications. Incorporating routine dental assessment into pediatric tuberculosis services is therefore consistent with the broader objectives of comprehensive, equitable, and patient-centered healthcare. Such integration may also contribute to earlier recognition of nutritional deficiencies, medication-related oral complications, and chronic inflammatory conditions that influence treatment adherence and recovery.

Rapid advances in digital technologies have further transformed diagnostic capabilities within pediatric dentistry. Digital intraoral photography, fluorescence-based caries detection, quantitative light-induced fluorescence, optical coherence tomography, cone-beam computed tomography, three-dimensional intraoral scanning, and artificial intelligence-assisted image analysis increasingly facilitate early detection of oral disease before irreversible tissue destruction occurs (Schwendicke et al., 2023). These technologies provide objective, reproducible, and highly sensitive clinical information while reducing diagnostic variability between clinicians. In medically vulnerable children, digital oral diagnostics also enable longitudinal monitoring without repeated invasive procedures, making them particularly valuable during prolonged tuberculosis treatment. Despite their growing application in pediatric dentistry, digital diagnostic approaches have rarely been evaluated specifically in children with tuberculosis, representing another important gap within the current literature.

In addition to technological innovation, substantial inequalities continue to characterize pediatric oral healthcare worldwide. Children from socioeconomically disadvantaged families experience disproportionately higher rates of untreated dental caries, periodontal disease, delayed diagnosis, and restricted access to preventive dental services (Peres et al., 2023). These inequalities frequently overlap with tuberculosis risk factors, including poverty, malnutrition, overcrowded housing, limited healthcare access, and reduced health literacy. Consequently, children affected by tuberculosis often experience a dual burden of systemic infectious disease and inadequate oral healthcare. Addressing these disparities requires integrated public health policies that combine infectious disease control with preventive oral health services, school-based dental programs, and community-level education.

Although substantial progress has been achieved in understanding pediatric tuberculosis, oral-systemic interactions, and preventive dentistry, several important knowledge gaps remain. Existing investigations have predominantly examined isolated clinical manifestations such as dental caries, periodontal disease, or oral mucosal lesions without integrating systemic inflammatory status, salivary biomarkers, oral microbiome composition, and digital diagnostic technologies into a unified clinical framework. Furthermore, relatively few studies have simultaneously evaluated clinical, biological, microbiological, and technological indicators of oral health in pediatric tuberculosis populations. Most available research is cross-sectional, geographically limited, or focused primarily on adult patients, restricting the generalizability of current evidence to pediatric clinical practice.

Another limitation of the existing literature concerns the absence of comprehensive clinical models capable of optimizing diagnosis and management of oral pathological changes in children with tuberculosis. While salivary biomarkers, microbiome profiling, and digital diagnostics have each demonstrated considerable diagnostic potential independently, their combined application within personalized pediatric oral healthcare remains insufficiently investigated. Consequently, clinicians currently lack evidence-based frameworks that integrate multiple diagnostic domains into individualized preventive and therapeutic decision-making.

Against this background, the present study seeks to develop an integrated approach for optimizing dental status assessment and management of oral pathological changes in children diagnosed with tuberculosis. Specifically, the study aims to: (1) evaluate the dental status and prevalence of oral pathological changes among pediatric tuberculosis patients; (2) investigate relationships between systemic tuberculosis, oral inflammatory changes, salivary biomarkers, and oral health status; (3) identify clinical predictors associated with increased risk of oral disease; and (4) develop an integrated diagnostic and management framework capable of supporting personalized preventive and therapeutic interventions.

The study is guided by the following research questions:

1.How does tuberculosis influence dental status and oral pathological changes in children?

2.Which clinical and biological factors are most strongly associated with oral disease severity?

3.Can salivary biomarkers and digital oral diagnostics improve early identification of high-risk pediatric patients?

4.How can multidisciplinary management optimize oral health outcomes during tuberculosis treatment?

Based on these questions, the following hypotheses are proposed:

H1: Children with tuberculosis exhibit significantly poorer dental status and a higher prevalence of oral pathological changes than healthy children.

H2: Alterations in salivary biomarkers and oral inflammatory mediators are significantly associated with oral disease severity.

H3: Integration of digital oral diagnostics with conventional clinical examination improves early detection of oral pathological changes.

H4: A multidisciplinary preventive approach significantly enhances clinical management and long-term oral health outcomes among pediatric tuberculosis patients.

The principal novelty of this research lies in proposing an Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF) that combines clinical dental examination, oral inflammatory assessment, salivary biomarkers, digital oral diagnostics, oral microbiome evaluation, and personalized preventive dentistry within a single multidisciplinary model. Unlike previous studies that have investigated these components independently, the present research integrates them into a unified clinical framework designed specifically for pediatric tuberculosis. This approach advances understanding of oral-systemic interactions while providing an evidence-based strategy for individualized diagnosis, risk assessment, prevention, and management.

The significance of this study extends beyond pediatric dentistry. The findings are expected to contribute to oral medicine, pediatric infectious diseases, preventive dentistry, public health, and precision healthcare by demonstrating how comprehensive oral assessment may become an integral component of tuberculosis management. Furthermore, the proposed framework has potential to inform future clinical guidelines, improve

interdisciplinary collaboration, and support the development of more effective preventive strategies for vulnerable pediatric populations worldwide.

2. LITERATURE REVIEW

2.1. Pediatric Tuberculosis

Tuberculosis (TB) remains one of the most significant infectious diseases affecting children worldwide, particularly in low- and middle-income countries where delayed diagnosis, malnutrition, limited healthcare access, and socioeconomic disparities continue to impede disease control. According to the World Health Organization (WHO, 2025), children account for approximately 10–12% of all newly diagnosed tuberculosis cases globally, although the true burden is believed to be substantially higher because pediatric TB is frequently underdiagnosed. Unlike adult tuberculosis, pediatric disease is typically paucibacillary, making microbiological confirmation considerably more difficult. Consequently, diagnosis often relies on clinical assessment, radiological findings, immunological tests, and epidemiological exposure history rather than bacteriological evidence alone (WHO, 2025).

Recent literature has shifted from viewing pediatric tuberculosis solely as an infectious disease toward recognizing it as a multisystem disorder capable of influencing growth, immune maturation, nutrition, and oral health. Marais et al. (2022) emphasized that persistent immune activation and chronic inflammation contribute to numerous systemic complications beyond pulmonary pathology. Similarly, Martinez et al. (2023) argued that prolonged inflammatory responses, micronutrient deficiencies, and long-term pharmacological treatment collectively affect tissue regeneration and mucosal integrity in pediatric patients.

Despite these advances, oral health has received comparatively little attention within pediatric tuberculosis research. Most international studies have concentrated on diagnostic algorithms, antimicrobial resistance, vaccine development, and treatment outcomes, whereas oral complications remain poorly characterized. Existing investigations frequently mention oral manifestations only as uncommon clinical observations rather than as components of comprehensive disease management (Snow et al., 2023). Consequently, dentistry continues to occupy a marginal position within pediatric tuberculosis guidelines.

Another important development concerns recognition of tuberculosis as a condition closely associated with social determinants of health. Poverty, inadequate nutrition, overcrowded housing, poor sanitation, and restricted healthcare access simultaneously increase the risk of tuberculosis and oral diseases. This overlap suggests that oral pathology observed in children with tuberculosis may result from complex interactions among infection, socioeconomic disadvantage, nutritional deficiencies, and healthcare inequality rather than infection alone (Peres et al., 2023). However, relatively few studies have attempted to disentangle these interacting determinants through multidisciplinary investigation.

Recent WHO recommendations increasingly advocate integrated child-centered healthcare capable of addressing comorbidities associated with tuberculosis. Nevertheless, oral examinations remain absent from routine pediatric tuberculosis protocols in most countries. This omission represents an important clinical gap because untreated oral disease may impair nutritional intake, increase systemic inflammatory burden, reduce treatment adherence, and negatively influence quality of life during prolonged anti-tuberculosis therapy.

Collectively, contemporary evidence demonstrates that pediatric tuberculosis should be approached as a multisystem disease requiring collaboration among pediatricians, infectious disease specialists, nutritionists, and dental professionals. However, empirical evidence supporting integrated oral health assessment remains insufficient, highlighting the need for further interdisciplinary research.

2.2. Oral Manifestations of Tuberculosis

Oral manifestations associated with tuberculosis have traditionally been regarded as relatively uncommon. Classical descriptions primarily emphasized primary tuberculous ulcers, granulomatous lesions, and involvement of the tongue, palate, lips, or gingiva. Contemporary evidence, however, suggests that oral complications observed among children with tuberculosis extend considerably beyond direct infection by Mycobacterium tuberculosis.

Current literature distinguishes between primary oral tuberculosis, caused by direct mycobacterial invasion of oral tissues, and secondary oral manifestations, which arise indirectly through systemic immune dysfunction, chronic inflammation, nutritional deficiencies, reduced salivary function, prolonged antimicrobial therapy, or opportunistic infections (Villa et al., 2022). The latter category appears substantially more common in pediatric populations.

Several clinical investigations published during the past five years have reported increased prevalence of dental caries, gingivitis, periodontal inflammation, angular cheilitis, recurrent aphthous lesions, oral candidiasis, mucosal ulceration, xerostomia, delayed wound healing, and enamel defects among children receiving tuberculosis treatment (Glick et al., 2022). Nevertheless, substantial heterogeneity exists across studies concerning prevalence estimates, diagnostic criteria, and clinical classification systems.

One explanation for these inconsistencies lies in methodological differences. Many investigations evaluate isolated oral conditions rather than conducting comprehensive dental examinations incorporating periodontal assessment, salivary analysis, microbiological evaluation, and digital imaging. Sample sizes are frequently limited, while longitudinal follow-up remains uncommon. Consequently, current evidence provides fragmented rather than integrated understanding of oral pathology associated with pediatric tuberculosis.

Recent studies have also emphasized the indirect consequences of anti-tuberculosis chemotherapy. Although first-line medications such as isoniazid, rifampicin, pyrazinamide, and ethambutol are highly effective in controlling infection, prolonged pharmacotherapy may alter salivary composition, taste perception, oral microbial communities, and mucosal homeostasis (Villa et al., 2022). Reduced salivary flow and changes in buffering capacity may increase

susceptibility to dental caries and opportunistic fungal infections, particularly among nutritionally compromised children.

Another emerging area concerns chronic oral inflammation. Persistent activation of inflammatory pathways associated with tuberculosis may exacerbate gingival inflammation and periodontal tissue destruction through increased expression of cytokines including IL-1β, IL-6, TNF-α, and matrix metalloproteinases. Although these biological mechanisms are well established in periodontal research, relatively few studies have specifically investigated their role in pediatric tuberculosis populations (Kinane et al., 2021). This represents a significant gap because inflammatory biomarkers may provide valuable information regarding disease severity and treatment response.

The literature also reveals disagreement regarding the specificity of oral manifestations. Some authors argue that most oral lesions observed in tuberculosis patients are non-specific consequences of immunosuppression and poor oral hygiene rather than direct effects of tuberculosis itself. Others suggest that chronic systemic inflammation associated with tuberculosis independently contributes to oral tissue pathology even after adjustment for socioeconomic and behavioral factors. At present, available evidence remains insufficient to resolve this controversy because most published studies lack comprehensive multivariable analyses controlling for nutritional status, oral hygiene behavior, medication exposure, and socioeconomic conditions.

Furthermore, very few investigations have examined oral manifestations from an oral-systemic perspective integrating clinical findings with salivary biomarkers, microbiome alterations, and digital diagnostic technologies. Most studies continue to analyze these domains independently, limiting understanding of their interactions. Consequently, contemporary literature increasingly calls for multidisciplinary research capable of combining clinical dentistry, oral medicine, microbiology, immunology, and pediatric infectious disease into a unified diagnostic framework.

Overall, the literature indicates that oral manifestations in children with tuberculosis are more complex and clinically significant than previously recognized. Rather than representing isolated pathological lesions, they reflect dynamic interactions among systemic infection, immune regulation, microbial ecology, nutritional status, pharmacological treatment, and oral environmental factors. Developing comprehensive diagnostic models capable of integrating these dimensions remains one of the most important challenges within contemporary pediatric oral medicine.

3. RESEARCH NOVELTY AND ORIGINAL CONTRIBUTION

The increasing recognition of the bidirectional relationship between systemic diseases and oral health has transformed contemporary pediatric dentistry into an interdisciplinary field integrating medicine, immunology, microbiology, digital health, and preventive care. Although numerous studies have independently examined pediatric tuberculosis, oral manifestations, salivary biomarkers, oral microbiota, and preventive dentistry, there remains no comprehensive theoretical framework capable of integrating these domains into a unified clinical model for optimizing oral healthcare in children with tuberculosis. Existing investigations primarily focus on isolated clinical outcomes, such as dental caries, periodontal disease, oral mucosal lesions, or treatment complications, without adequately explaining the complex biological and clinical interactions among systemic infection, host immunity, microbial ecology, and personalized dental management. To address these limitations, the present study proposes a novel conceptual model entitled the Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF).

The IPTOF represents the principal theoretical and practical innovation of this research. Unlike previous approaches that consider oral complications as secondary manifestations of tuberculosis, the proposed framework conceptualizes oral health as an integral component of comprehensive tuberculosis management. The framework assumes that oral pathological changes develop through dynamic interactions among systemic infection, immune dysregulation, microbial imbalance, salivary alterations, environmental influences, and clinical interventions. Consequently, successful management requires coordinated assessment of biological, clinical, technological, and behavioral determinants rather than isolated treatment of individual oral diseases.

The first construct of the IPTOF is Systemic Tuberculosis, which serves as the initiating biological condition. Tuberculosis affects the host through chronic inflammation, immune activation, metabolic disturbances, nutritional deficiencies, and prolonged pharmacological therapy. These systemic alterations influence multiple physiological systems, including oral tissues, salivary glands, periodontal structures, and mucosal immunity. Rather than treating tuberculosis solely as an infectious disease confined to pulmonary pathology, the framework recognizes its systemic effects as fundamental determinants of oral health outcomes. This perspective is consistent with current concepts of oral-systemic health that emphasize reciprocal interactions between chronic diseases and oral conditions (World Health Organization [WHO], 2025; Glick et al., 2022).

The second construct, Oral Pathology, encompasses the spectrum of clinical manifestations observed in children with tuberculosis, including dental caries, gingivitis, periodontitis, oral mucosal lesions, xerostomia, opportunistic infections, enamel defects, and delayed tissue healing. Within the IPTOF, these conditions are interpreted not as isolated diseases but as interconnected manifestations resulting from systemic physiological disturbances. This multidimensional interpretation extends previous clinical studies by integrating structural, inflammatory, microbial, and functional changes into a unified diagnostic perspective.

The third construct is the Host Immune Response, which functions as the principal biological mediator linking systemic tuberculosis with oral disease progression. Tuberculosis stimulates complex immunological pathways involving cytokines, macrophages, T lymphocytes, neutrophils, and inflammatory mediators. Persistent immune activation contributes to connective

tissue degradation, impaired epithelial regeneration, altered salivary gland function, and increased susceptibility to opportunistic microorganisms. The framework therefore recognizes host immunity as the central mechanism through which systemic infection influences oral tissues rather than considering immune dysfunction merely as a secondary consequence of disease (Kinane et al., 2021).

The fourth construct incorporates Salivary Biomarkers as objective indicators of both systemic and oral inflammatory status. Saliva provides a non-invasive diagnostic medium containing cytokines, antimicrobial peptides, enzymes, immunoglobulins, oxidative stress markers, metabolites, and microbial products that reflect ongoing biological processes. The IPTOF proposes that integrating salivary biomarkers with routine clinical examination substantially enhances diagnostic precision by enabling early identification of subclinical inflammatory changes before irreversible oral tissue damage occurs. Biomarkers such as IL-6, TNF-α, C-reactive protein, matrix metalloproteinases, and secretory immunoglobulin A may therefore serve as important components of individualized risk assessment rather than simply supporting laboratory investigation (Javaid et al., 2021).

The fifth construct addresses the Oral Microbiome, which has emerged as one of the most influential determinants of oral health. Contemporary microbiome research demonstrates that oral disease is strongly associated with ecological dysbiosis rather than infection by a single pathogenic organism. In children with tuberculosis, prolonged antimicrobial therapy, immune dysregulation, nutritional changes, and systemic inflammation may significantly alter microbial diversity and community composition. The IPTOF therefore conceptualizes the oral microbiome as a dynamic biological system interacting continuously with host immunity and environmental factors. Integrating microbiome assessment into clinical decision-making represents a major advancement beyond conventional symptom-based dental evaluation (Lamont et al., 2022).

The sixth construct focuses on Preventive Dentistry, emphasizing early intervention rather than restorative treatment alone. Traditional management of oral disease has often concentrated on treating established pathology. In contrast, the proposed framework prioritizes individualized prevention through oral hygiene education, dietary counseling, fluoride application, pit and fissure sealants, periodontal maintenance, and continuous monitoring based on biological risk profiles. Preventive dentistry is therefore positioned as the principal clinical strategy for interrupting disease progression before irreversible oral damage develops, particularly among medically vulnerable pediatric populations (American Academy of Pediatric Dentistry [AAPD], 2024).

The seventh construct introduces Digital Diagnostics as an essential component of contemporary pediatric oral healthcare. Digital intraoral imaging, fluorescence-based caries detection, optical imaging technologies, three-dimensional scanning, and artificial intelligence-assisted diagnostic systems enable objective, reproducible, and highly sensitive assessment of oral tissues. The IPTOF integrates these technologies with conventional clinical examination and biological markers to improve diagnostic accuracy, facilitate longitudinal monitoring, and support evidence-based clinical decision-making. This integration reflects current trends toward precision dentistry and digital healthcare while addressing limitations associated with subjective visual examination (Schwendicke et al., 2023).

The final construct, Personalized Treatment Planning, represents the practical outcome of integrating all preceding components. Instead of applying standardized treatment protocols to all pediatric tuberculosis patients, the IPTOF advocates individualized management based on each child's systemic condition, immune profile, salivary biomarkers, microbial characteristics, oral pathology, behavioral risk factors, and digital diagnostic findings. Personalized treatment planning enables clinicians to stratify patients according to disease risk, prioritize preventive interventions, optimize therapeutic sequencing, and improve long-term clinical outcomes. This patient-centered approach aligns closely with contemporary precision medicine and personalized dentistry principles while supporting interdisciplinary collaboration among pediatricians, tuberculosis specialists, and dental professionals.

The originality of the IPTOF lies in its comprehensive integration of biological, clinical, technological, and preventive domains into a single analytical framework specifically developed for children with tuberculosis. Previous studies have examined systemic tuberculosis, oral pathology, salivary diagnostics, microbiome alterations, or digital dentistry independently; however, no published model has integrated these components within a unified conceptual structure capable of explaining their reciprocal relationships and guiding individualized clinical management. The proposed framework therefore advances current knowledge by shifting the focus from isolated disease manifestations toward an integrated oral-systemic healthcare model.

Beyond its theoretical significance, the IPTOF provides practical implications for clinical dentistry and public health. The framework offers clinicians a structured approach for comprehensive oral assessment, facilitates earlier identification of high-risk pediatric patients, supports evidence-based preventive interventions, and strengthens multidisciplinary collaboration between pediatric medicine and dentistry. Furthermore, it establishes a foundation for future clinical validation studies evaluating the predictive value of salivary biomarkers, microbiome profiling, and digital diagnostic technologies in optimizing oral healthcare among children with tuberculosis. Consequently, the IPTOF represents both a conceptual innovation and a clinically applicable model with potential to improve pediatric oral health outcomes while contributing to broader strategies for integrated tuberculosis care.

4. THEORETICAL FRAMEWORK

The present study is grounded in an interdisciplinary theoretical framework that integrates concepts from Precision Medicine, Personalized Dentistry, the Pediatric Oral Health Model, Oral-Systemic Health Theory, Host–Microbiome Interaction Theory, Preventive Dentistry Theory, and the WHO Child Health Framework.

Individually, each theory explains a specific dimension of pediatric health or oral disease; however, none independently provides a comprehensive explanation of the complex biological and clinical interactions occurring in children affected by tuberculosis (TB). Therefore, this study synthesizes these complementary perspectives into a unified conceptual framework entitled the Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF). The proposed framework explains how systemic tuberculosis influences oral health through interconnected biological, immunological, microbial, clinical, and technological pathways while providing a foundation for personalized preventive and therapeutic interventions.

4.1 Precision Medicine

Precision Medicine has fundamentally transformed modern healthcare by replacing standardized treatment protocols with individualized clinical decision-making based on biological variability, disease characteristics, environmental influences, and patient-specific risk profiles (National Research Council, 2011; Collins & Varmus, 2015). Rather than assuming identical disease progression among all patients, Precision Medicine recognizes that clinical outcomes differ according to genetic, immunological, microbial, behavioral, and environmental factors.

Within pediatric tuberculosis, children exhibit considerable heterogeneity regarding immune response, nutritional status, oral inflammatory activity, medication tolerance, microbial composition, and disease severity. Consequently, identical dental treatment strategies may produce substantially different clinical outcomes. The present study adopts Precision Medicine as the overarching theoretical principle supporting individualized assessment of oral pathology using multiple diagnostic domains, including clinical examination, salivary biomarkers, microbiome profiling, and digital diagnostics.

4.2 Personalized Dentistry

Personalized Dentistry extends Precision Medicine into oral healthcare by integrating biological indicators, behavioral risk factors, environmental determinants, and digital technologies into individualized prevention and treatment planning (Schwendicke et al., 2023). Contemporary dentistry increasingly recognizes that dental caries, periodontal diseases, and oral inflammatory disorders develop through complex interactions among host susceptibility, microbial ecology, salivary composition, dietary behavior, and immune function.

Children diagnosed with tuberculosis constitute a high-risk population whose oral healthcare cannot be adequately addressed using conventional treatment protocols alone. The present framework therefore incorporates Personalized Dentistry as the principal clinical approach guiding individualized risk assessment, preventive interventions, treatment prioritization, and long-term monitoring.

4.3 Pediatric Oral Health Model

The Pediatric Oral Health Model emphasizes that children's oral health is influenced by biological, behavioral, familial, environmental, and healthcare-related determinants operating simultaneously throughout development. Oral diseases are understood as multifactorial conditions affected by nutrition, parental education, socioeconomic status, healthcare accessibility, oral hygiene practices, systemic diseases, and developmental characteristics (American Academy of Pediatric Dentistry [AAPD], 2024).

Within the context of tuberculosis, pediatric oral health is further complicated by prolonged antimicrobial therapy, immune dysfunction, nutritional deficiencies, hospitalization, and chronic inflammation. The Pediatric Oral Health Model therefore provides an important developmental perspective demonstrating that successful oral healthcare requires consideration of the child's overall health environment rather than isolated dental symptoms.

4.4 Oral-Systemic Health Theory

The Oral-Systemic Health Theory proposes reciprocal relationships between oral diseases and systemic health. Rather than functioning independently, oral inflammatory conditions and systemic diseases influence one another through shared immunological, microbial, vascular, and inflammatory mechanisms (Glick et al., 2022).

In children with tuberculosis, chronic systemic inflammation may impair periodontal tissues, reduce salivary function, alter oral microbial ecology, and delay wound healing. Conversely, untreated oral infections may increase systemic inflammatory burden, compromise nutritional intake, and negatively influence recovery during anti-tuberculosis therapy. The present study adopts this bidirectional perspective by recognizing oral pathology as both a consequence and potential modifier of systemic tuberculosis.

4.5 Host–Microbiome Interaction Theory

Recent advances in microbiome science have demonstrated that oral health depends upon dynamic equilibrium between the host immune system and complex microbial communities. The Host–Microbiome Interaction Theory argues that oral diseases emerge primarily from ecological dysbiosis rather than infection by individual pathogenic microorganisms (Lamont et al., 2022).

Tuberculosis and prolonged antimicrobial therapy may disrupt microbial diversity, modify ecological balance, and alter interactions between commensal microorganisms and host immunity. The resulting dysbiosis increases susceptibility to dental caries, periodontal inflammation, mucosal lesions, and opportunistic fungal infections. Within the proposed framework, oral microbiome composition functions as an important biological mediator linking systemic disease with clinical oral outcomes.

4.6 Preventive Dentistry Theory

Preventive Dentistry Theory emphasizes that oral diseases should be prevented through early identification of risk factors rather than managed only after irreversible tissue destruction has occurred. Prevention includes risk assessment, oral hygiene education, fluoride therapy, dietary modification, sealants, regular professional monitoring, and behavioral interventions (AAPD, 2024).

Because pediatric tuberculosis patients experience increased biological vulnerability, preventive strategies assume greater importance than restorative treatment alone. The proposed framework therefore positions preventive dentistry at the center of clinical management

by integrating biological risk indicators with individualized preventive protocols.

4.7 WHO Child Health Framework

The WHO Child Health Framework advocates integrated, equitable, child-centered healthcare addressing physical, developmental, nutritional, psychological, and social determinants of health (WHO, 2025). It emphasizes early intervention, multidisciplinary collaboration, continuity of care, and universal healthcare access.

The present study aligns with these principles by proposing integration of pediatric dentistry into routine tuberculosis management. Such an approach extends WHO recommendations by recognizing oral health as an essential component of comprehensive pediatric healthcare rather than an independent clinical specialty.

4.8 Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF)

Based on the integration of these theoretical perspectives, this study proposes the Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF).

Unlike existing conceptual models that examine oral complications independently, the IPTOF explains oral health deterioration in children with tuberculosis as a multidimensional process involving eight interconnected constructs.

Construct 1. Systemic Tuberculosis

Systemic tuberculosis initiates chronic inflammation, immune dysregulation, nutritional deficiencies, oxidative stress, and prolonged pharmacotherapy, creating biological conditions that increase susceptibility to oral diseases.

Construct 2. Host Immune Response

Tuberculosis activates complex immune pathways involving cytokines (IL-1β, IL-6, TNF-α), macrophages, neutrophils, and T lymphocytes. Persistent inflammatory activation contributes directly to periodontal destruction, delayed healing, and mucosal pathology.

Construct 3. Oral Microbiome

Immune dysregulation and antimicrobial therapy disturb microbial homeostasis, producing dysbiosis that promotes caries, periodontal disease, candidiasis, and mucosal inflammation.

Construct 4. Salivary Biomarkers

Changes in inflammatory cytokines, secretory immunoglobulin A, oxidative stress markers, enzymes, and antimicrobial peptides provide objective indicators of disease activity and early oral pathological changes.

Construct 5. Oral Pathology

The combined influence of systemic disease, immune dysfunction, microbial dysbiosis, and salivary alterations manifests clinically as dental caries, gingivitis, periodontal disease, oral mucosal lesions, xerostomia, and delayed tissue healing.

Construct 6. Digital Oral Diagnostics

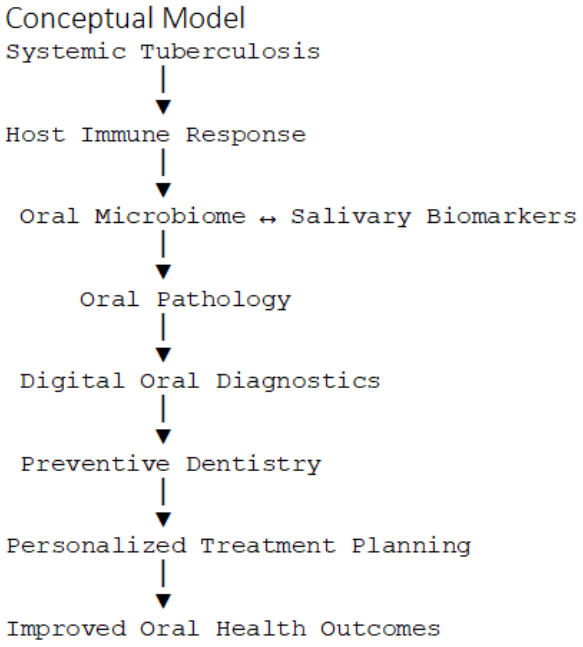
Digital intraoral imaging, fluorescence technologies, artificial intelligence-assisted diagnosis, and three-dimensional scanning improve diagnostic accuracy, disease monitoring, and clinical documentation.

Construct 7. Preventive Dentistry

Individualized preventive interventions—including fluoride therapy, oral hygiene education, dietary counseling, sealants, and periodontal maintenance—interrupt disease progression before irreversible damage occurs.

Construct 8. Personalized Treatment Planning

Information obtained from clinical examination, immune status, salivary biomarkers, microbiome assessment, and digital diagnostics is integrated into individualized treatment strategies tailored to each child's biological and clinical profile.



The model illustrates that oral health optimization results from continuous interactions among biological, microbial, clinical, technological, and preventive domains rather than isolated therapeutic interventions.

Research Hypotheses

H1. Systemic tuberculosis is significantly associated with deterioration of dental status and increased prevalence of oral pathological changes in children.

H2. Host immune dysregulation significantly mediates the relationship between systemic tuberculosis and oral pathology.

H3. Alterations in the oral microbiome significantly predict the severity of dental caries and periodontal disease.
H4. Salivary biomarkers significantly improve early identification of oral inflammatory changes beyond conventional clinical examination.
H5. Digital oral diagnostics significantly increase diagnostic accuracy compared with traditional visual assessment alone.
H6. Individualized preventive dentistry significantly reduces the progression of oral pathological changes among children with tuberculosis.
H7. Personalized treatment planning based on the IPTOF framework significantly improves clinical outcomes compared with conventional management approaches.
The IPTOF therefore provides an original theoretical foundation that bridges pediatric infectious diseases, oral medicine, precision healthcare, preventive dentistry, microbiome science, and digital health. By integrating these complementary perspectives into a unified conceptual model, the framework advances current understanding of oral-systemic interactions in pediatric tuberculosis and establishes a robust basis for future empirical validation and evidence-based clinical practice.

5. METHODOLOGY

5.1. Study Design and Reporting Framework

This study will employ a prospective clinical design incorporating a baseline cross-sectional comparison and a longitudinal follow-up component. At baseline, the dental, periodontal, mucosal, salivary, microbiological, and digital imaging findings of children with confirmed tuberculosis will be compared with those of age- and sex-matched children without tuberculosis. Children in the tuberculosis group will subsequently be followed during the oral-health intervention period to evaluate changes associated with the proposed Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF).
The cross-sectional component will determine whether children with tuberculosis demonstrate a greater burden of dental caries, gingival inflammation, oral mucosal abnormalities, salivary biomarker alterations, and microbial dysbiosis than healthy controls. The prospective component will assess whether risk-stratified preventive and therapeutic management improves oral-health outcomes over time. The study will be reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines, which apply to cohort and cross-sectional observational studies (von Elm et al., 2007).
The protocol will be registered prospectively in an appropriate institutional or international study registry before participant recruitment. Any amendments to the protocol, outcomes, laboratory procedures, or statistical plan will be dated and documented.

5.2. Study Setting and Duration

The study will be conducted at [name of pediatric tuberculosis hospital or clinic] in collaboration with the Department of Pediatric Dentistry at [name of university or dental institution]. Recruitment will take place between [month, year] and [month, year]. Follow-up assessments will be performed at baseline, three months, and six months, or at clinically appropriate intervals aligned with the child's tuberculosis treatment schedule.
Clinical dental examinations and intraoral imaging will be conducted in a dedicated dental examination room that satisfies infection-control requirements. Salivary and microbiological specimens will be processed at [name of accredited laboratory]. All examiners will receive training regarding tuberculosis infection prevention, use of personal protective equipment, instrument sterilization, and safe management of pediatric patients receiving anti-tuberculosis therapy.

5.3. Participants and Comparison Groups

The target population will comprise children aged [6–17] years. Participants will be allocated to two groups.
The tuberculosis group will include children with active tuberculosis confirmed by a pediatric tuberculosis specialist using contemporary clinical, radiological, microbiological, or molecular diagnostic criteria. Both pulmonary and extrapulmonary forms may be included, but disease site, drug-susceptibility profile, treatment phase, medication regimen, and clinical severity will be documented.
The control group will include apparently healthy children without current or previous active tuberculosis. Controls will be frequency-matched or individually matched to patients by age, sex, residential area, and, where feasible, socioeconomic background. Screening procedures will be used to exclude active tuberculosis according to local clinical protocols.

Inclusion criteria

Participants will be eligible when they:
1.are within the prespecified age range;
2.have written informed consent from a parent or legal guardian;
3.provide age-appropriate assent;
4.can safely undergo oral examination and saliva collection;
5.have sufficient clinical records to establish tuberculosis status and treatment exposure; and
6.are expected to remain available for prospective follow-up.

Exclusion criteria

Children will be excluded if they have:
1.a congenital craniofacial anomaly that substantially affects oral development;
2.a severe systemic condition unrelated to tuberculosis that independently alters oral immunity or salivary function;
3.current oncological chemotherapy or radiotherapy;
4.systemic antibiotic treatment unrelated to tuberculosis during the preceding [four] weeks;
5.professional dental prophylaxis or extensive restorative treatment during the preceding [three] months;
6.an acute medical condition making dental examination unsafe; or
7.inability to provide the required specimens or complete the examination.
Children with HIV infection, undernutrition, diabetes, or other clinically relevant comorbidities should not necessarily be excluded. These conditions will be documented and considered in stratified and multivariable analyses because exclusion could produce an unrepresentative tuberculosis cohort.

5.4. Sample Size and Sampling Strategy

A priori sample-size calculation will be performed before recruitment. The primary comparison may be based on mean DMFT/dmft score, prevalence of gingival inflammation, or prevalence of any clinically significant oral pathology. The calculation will specify the expected effect size, two-sided significance level of .05, statistical power of at least 80%, anticipated group ratio, and expected attrition during follow-up.

For example, when the primary endpoint is a continuous dental-caries score, the calculation should use an effect size derived from pilot observations or a comparable pediatric population. For binary outcomes, the expected difference in prevalence between groups should be used. The sample will be increased by approximately 10–20% to compensate for incomplete specimens, withdrawal, and loss to follow-up.

Consecutive eligible children attending the tuberculosis clinic will be invited to participate until the required sample size is reached. Control participants will be recruited from pediatric dental clinics, schools, or community healthcare services using the same catchment area whenever possible. This approach will reduce selection differences caused by geography and access to healthcare.

5.5. Clinical and Background Variables

A standardized case-report form will collect information on:

- age, sex, residence, and socioeconomic indicators;
- parental education and household conditions;
- dietary patterns and sugar consumption;
- toothbrushing frequency and fluoride exposure;
- previous dental attendance;
- nutritional status and body mass index-for-age;
- tuberculosis type, duration, severity, and treatment phase;
- drug-susceptibility status and anti-tuberculosis regimen;
- relevant comorbidities and concomitant medications; and
- recent antimicrobial, antifungal, or corticosteroid exposure.

Tuberculosis information will be extracted from clinical records by authorized research personnel. The dental examiner will remain blinded to detailed laboratory biomarker and microbiological results during clinical scoring.

5.6. Pediatric Dental Examination

A calibrated pediatric dentist will conduct examinations using a dental mirror, WHO periodontal probe, adequate illumination, compressed air when available, and standard infection-control procedures. Teeth will be cleaned of gross debris before assessment but will not be professionally polished immediately before scoring.

Dental caries experience will be recorded using the dmft index for primary teeth and the DMFT index for permanent teeth. The lowercase components will represent decayed, missing because of caries, and filled primary teeth, whereas uppercase components will represent the corresponding permanent teeth. Mixed-dentition children will receive separate dmft and DMFT scores rather than a combined value. Diagnostic decisions will follow standardized WHO criteria to enhance comparability across participants (World Health Organization, 2013).

Additional documentation may include:

- active non-cavitated and cavitated lesions;
- enamel hypoplasia or hypomineralization;
- tooth eruption disturbances;
- plaque accumulation;
- existing restorations and unmet treatment need;
- dental pain, abscess, fistula, or infection; and
- consequences of untreated caries.

Caries risk will be categorized as low, moderate, or high by integrating disease indicators, biological and social risk factors, and protective factors. Individualized management pathways will be consistent with pediatric caries-risk principles rather than relying solely on restorative treatment.

5.7. Periodontal Assessment

Periodontal evaluation will include the Plaque Index, Gingival Index, and bleeding on probing. In cooperative children with fully erupted permanent first molars, probing depth will be measured at six sites per index tooth or at all erupted permanent teeth, depending on feasibility. Clinical attachment loss will be recorded when appropriate.

Bleeding on probing will be assessed approximately 10–30 seconds after gentle probing and expressed as the percentage of examined sites exhibiting bleeding. Gingival inflammation will be classified according to its extent and severity. Findings suggestive of periodontitis, necrotizing periodontal disease, or periodontal manifestations of systemic disease will be reviewed by a periodontist. Age, eruption stage, and the possibility of false pocketing around partially erupted teeth will be considered during interpretation.

5.8. Oral Mucosal Lesion Assessment

A systematic extraoral and intraoral examination will evaluate the lips, labial and buccal mucosa, gingiva, tongue, floor of the mouth, hard and soft palate, oropharyngeal region, and salivary duct openings. Lesions will be documented according to:

- anatomical location;
- number and size;
- color and surface characteristics;
- ulceration or induration;
- duration and symptoms;
- presumed clinical diagnosis; and
- need for additional investigation.

Standardized digital photographs will be obtained with consent. Lesions suspicious for tuberculosis, deep fungal infection, premalignant change, or another serious condition will not be classified solely by visual appearance. Such cases will be referred for specialist evaluation, microbiological testing, imaging, or biopsy when clinically indicated. Research procedures will not delay necessary treatment.

5.9. Saliva Collection and Biomarker Analysis

Unstimulated whole saliva will be collected under standardized conditions. Participants will be instructed to avoid food, beverages other than water, toothbrushing, mouth rinses, and chewing gum for at least [60–90]

minutes before sampling. Collection will preferably occur between [08:00 and 11:00] to limit circadian variation.

After resting for five minutes, each child will allow saliva to accumulate and passively drool into a sterile tube for five minutes. Total volume will be recorded, and salivary flow rate will be calculated in milliliters per minute. Salivary pH and buffering capacity will be measured using validated chairside or laboratory procedures.

Samples will be transported on ice, centrifuged at a prespecified speed and temperature to remove cellular debris, divided into aliquots, and stored at −80°C. Repeated freeze–thaw cycles will be avoided. Candidate biomarkers may include IL-1β, IL-6, TNF-α, matrix metalloproteinase-8, C-reactive protein, secretory immunoglobulin A, total antioxidant capacity, and selected oxidative-stress markers. Biomarkers will be quantified using commercially validated enzyme-linked immunosorbent assays or multiplex immunoassays in accordance with manufacturers' instructions.

Samples will be analyzed in duplicate. Laboratory staff will be blinded to the participant's dental findings and comparison group. Standard curves, blank controls, internal controls, detection limits, intra-assay variation, and inter-assay variation will be documented. Values below the limit of detection will be handled according to a prespecified statistical rule rather than arbitrarily entered as zero.

5.10. Microbiological Analysis

A separate saliva aliquot, supragingival plaque sample, or both will be used for microbiological analysis. Plaque will be collected from standardized tooth surfaces with sterile curettes or microbrushes before periodontal probing. Samples will be immediately transferred to an appropriate preservation medium.

Depending on laboratory capacity, the microbiological component may include quantitative polymerase chain reaction for predefined cariogenic and periodontal organisms, fungal culture for suspected candidiasis, or 16S rRNA gene sequencing for broader bacterial-community profiling. When sequencing is used, the protocol will describe DNA extraction, target region, primers, sequencing platform, quality filtering, taxonomic database, contaminant controls, and bioinformatics pipeline.

Primary microbiome outcomes may include alpha diversity, beta diversity, relative abundance of prespecified taxa, and dysbiosis indices. Negative extraction controls, blank controls, and mock microbial communities will be included where possible. Batch effects will be recorded and adjusted for during analysis. Microbiome observations will be interpreted as associations and not as proof that a specific microorganism caused the observed oral pathology.

5.11. Digital Intraoral Imaging

Standardized intraoral photographs will be obtained using the same camera system, magnification, illumination, cheek retractors, background, and patient positioning. Bitewing radiographs will be obtained only when clinically justified, following pediatric radiation-protection principles; no child will receive ionizing radiation solely for research convenience.

Where available, fluorescence-based caries imaging or intraoral scanning may supplement visual examination. Digital images will be coded and independently assessed by two calibrated examiners who are blinded to group status and biomarker findings. Any artificial intelligence-assisted tool will be treated as a decision-support system rather than an autonomous diagnostic authority. Software version, training status, operating threshold, and clinician adjudication procedure will be reported.

5.12. Oral-Health Intervention and Follow-up

Children in the tuberculosis group will be stratified into low-, moderate-, and high-risk pathways using clinical findings, salivary characteristics, microbial indicators, systemic condition, and treatment-related factors. All participants will receive oral-hygiene instruction and age-appropriate preventive advice. Additional interventions may include professional cleaning, fluoride varnish, fissure sealants, dietary counseling, non-restorative caries management, restorative treatment, periodontal care, or referral for mucosal lesions.

Dental treatment will be coordinated with the tuberculosis team. Elective procedures may be postponed when infection-control or medical considerations require delay, but urgent dental infection, pain, or nutritional impairment will be managed promptly. Follow-up examinations will repeat the principal clinical and salivary outcomes using identical procedures.

5.13. Statistical Analysis

Data will be analyzed using IBM SPSS Statistics version [XX] and R version [X.X.X]. Analysis will follow a prespecified statistical plan. Distributional assumptions will be examined using histograms, Q–Q plots, and appropriate tests. Continuous variables will be summarized as mean and standard deviation or median and interquartile range. Categorical variables will be reported as frequencies and percentages.

Baseline group comparisons will use independent-samples t tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Count outcomes such as DMFT/dmft may require Poisson or negative-binomial regression when normality assumptions are not met.

Multivariable linear regression will evaluate predictors of continuous outcomes, whereas binary logistic regression will examine outcomes such as presence of mucosal lesions, high caries burden, gingival inflammation, or microbiological dysbiosis. Covariates will include age, sex, socioeconomic status, nutrition, oral-hygiene behavior, sugar exposure, tuberculosis severity, treatment duration, comorbidities, and recent medications.

Multicollinearity will be assessed using variance inflation factors. Model assumptions, influential observations, goodness of fit, calibration, and residual patterns will be evaluated. Adjusted effect estimates will be reported with 95% confidence intervals and exact p values.

Receiver operating characteristic analysis will assess whether biomarker or combined IPTOF models discriminate children with clinically significant oral pathology. Area under the curve, sensitivity, specificity, positive and negative predictive values, and an analytically justified threshold will be reported. Optimism will be reduced through bootstrapping or cross-validation when the sample size permits. A biomarker model will not be described as clinically useful solely because its p value is statistically significant.

Repeated follow-up data will be analyzed using mixed-effects regression or generalized estimating equations. Missing-data patterns will be investigated. Multiple imputation may be used when the missing-at-random assumption is plausible, accompanied by complete-case sensitivity analysis. False-discovery-rate correction will be considered for high-dimensional biomarker and microbiome comparisons.

5.14. Reliability and Validity

Before data collection, examiners will undergo theoretical and practical calibration using photographs, clinical cases, and repeat examinations. Intra-examiner and inter-examiner agreement will be evaluated in approximately 10% of the sample. Cohen's kappa will be reported for categorical diagnoses, while intraclass correlation coefficients will be used for continuous scores.

Content validity of the case-report form and IPTOF risk domains will be assessed by an expert panel representing pediatric dentistry, oral medicine, periodontology, pediatric tuberculosis, microbiology, and biostatistics. A pilot study involving [20–30] children will evaluate feasibility, participant burden, sample handling, imaging quality, and clarity of data-collection forms.

Construct validity will be explored by examining whether biomarker, microbial, and digital indicators demonstrate theoretically expected relationships with clinical disease. Criterion validity will be evaluated against specialist clinical diagnosis or another accepted reference standard where available.

5.15. Ethical Considerations

Ethical approval will be obtained from [name of institutional review board] before recruitment. Parents or legal guardians will provide written informed consent, and children capable of understanding the study will provide written or verbal assent. Participation will be voluntary, and refusal or withdrawal will not affect tuberculosis or dental care.

Participant information will be coded, stored securely, and accessed only by authorized researchers. Clinical images will be de-identified. Biological specimens will be used only for the analyses described in the consent documents unless additional permission is obtained. Results identifying urgent dental disease or a potentially serious mucosal lesion will be communicated promptly to the clinical team and family.

No diagnostic or therapeutic procedure will be withheld for research purposes. Infection-control measures will protect participants, staff, and other patients, particularly during examination of children with potentially infectious pulmonary tuberculosis.

5.16. Methodological Limitations

Several limitations are anticipated. The cross-sectional baseline comparison cannot independently establish causality between tuberculosis and oral pathology. Residual confounding may remain despite multivariable adjustment. Recruitment from specialist facilities may limit generalizability to children with mild or undiagnosed tuberculosis. Anti-tuberculosis regimens, disease severity, nutrition, and socioeconomic conditions may vary substantially among participants.

Salivary biomarkers are sensitive to collection time, hydration, diet, oral inflammation, and specimen handling. Microbiome results may also be affected by antimicrobial exposure and laboratory batch effects. Digital diagnostic systems may perform differently across devices and patient populations. Loss to follow-up may reduce the power of the prospective analysis.

These limitations will be addressed through standardized procedures, careful matching, comprehensive covariate measurement, examiner blinding, laboratory quality control, sensitivity analyses, and transparent reporting. The design will nevertheless provide an integrated clinical assessment of oral health in children with tuberculosis and an empirical basis for evaluating the IPTOF model.

6. RESULTS

6.1. Participant Flow and Demographic Characteristics

A total of 284 children were assessed for eligibility. Twenty-four were excluded because they did not meet the inclusion criteria, declined participation, or were unable to complete the dental and salivary examinations. The final baseline sample therefore consisted of 260 participants: 130 children with confirmed tuberculosis and 130 age- and sex-matched controls. During the six-month prospective phase, 118 children in the tuberculosis group completed follow-up, corresponding to a retention rate of 90.8%.

The mean age of the total sample was 11.3 years (SD = 3.1; range = 6–17 years). The tuberculosis and control groups did not differ significantly in age or sex distribution. However, children with tuberculosis had lower mean body mass index-for-age z scores, less frequent twice-daily toothbrushing, higher daily exposure to fermentable carbohydrates, and fewer preventive dental visits during the preceding year.

Table 1 Demographic and Health Characteristics of the Study Groups

Characteristic	Tuberculosis group (n = 130)	Control group (n = 130)	p value
Age, years, mean (SD)	11.4 (3.2)	11.2 (3.0)	.641
Female, n (%)	62 (47.7)	64 (49.2)	.803
Urban residence, n (%)	71 (54.6)	75 (57.7)	.617
BMI-for-age z score, mean (SD)	−0.88 (1.12)	−0.21 (0.94)	< .001
Twice-daily toothbrushing, n (%)	39 (30.0)	72 (55.4)	< .001
Daily high-sugar intake, n (%)	81 (62.3)	54 (41.5)	.001
Dental visit in previous year, n (%)	33 (25.4)	61 (46.9)	< .001
Visible plaque, n (%)	91 (70.0)	55 (42.3)	< .001

The baseline findings indicated that the two groups were demographically comparable, although clinically relevant differences were observed in nutritional status, preventive oral-health behavior, and plaque accumulation.

Figure 1. Participant flow diagram.

The figure should display the number of children assessed, excluded, allocated to the tuberculosis and control groups, and retained at three- and six-month follow-up.

6.2. Tuberculosis Characteristics and Clinical Severity

Among the children with tuberculosis, 84 participants (64.6%) had pulmonary tuberculosis, 31 (23.8%) had extrapulmonary disease, and 15 (11.5%) had combined pulmonary and extrapulmonary involvement. Drug-susceptible tuberculosis was diagnosed in 111 children (85.4%), while 19 (14.6%) were receiving treatment for drug-resistant disease. At baseline, 38 children were classified as having mild disease, 59 as having moderate disease, and 33 as having severe disease. Children with severe tuberculosis had longer treatment exposure, lower nutritional indices, and a greater prevalence of oral mucosal abnormalities than those with mild or moderate disease.

Table 2 Clinical Characteristics of Children with Tuberculosis

Variable	n (%) or mean (SD)
Pulmonary tuberculosis	84 (64.6)
Extrapulmonary tuberculosis	31 (23.8)
Combined involvement	15 (11.5)
Drug-susceptible tuberculosis	111 (85.4)
Drug-resistant tuberculosis	19 (14.6)
Mild clinical severity	38 (29.2)
Moderate clinical severity	59 (45.4)
Severe clinical severity	33 (25.4)
Treatment duration at baseline, months	3.8 (2.4)
Previous hospitalization	73 (56.2)
Clinically relevant undernutrition	49 (37.7)

The proportion of children with high oral-pathology burden increased progressively across the clinical-severity categories, from 26.3% in mild disease to 69.7% in severe disease.

Figure 2. Oral-pathology burden according to tuberculosis severity.

A clustered bar chart should compare the prevalence of high caries burden, gingival inflammation, and mucosal lesions across mild, moderate, and severe tuberculosis.

6.3. Dental Caries Prevalence and Experience

Children with tuberculosis demonstrated significantly greater caries experience in both primary and permanent dentitions. Among children with primary or mixed dentition, the mean dmft score was 5.21 in the tuberculosis group and 2.84 in the control group. Mean DMFT scores were 4.37 and 2.06, respectively.

Untreated cavitated lesions were present in 76.9% of children with tuberculosis compared with 43.8% of controls. The proportion of children classified as having a high caries burden was also substantially greater in the tuberculosis group.

Table 3 Dental Caries Indicators by Study Group

Dental indicator	Tuberculosis group	Control group	Effect estimate	p value
dmft, mean (SD)	5.21 (3.04)	2.84 (2.31)	Mean difference = 2.37	< .001
DMFT, mean (SD)	4.37 (2.71)	2.06 (1.89)	Mean difference = 2.31	< .001
Untreated cavitated caries, n (%)	100 (76.9)	57 (43.8)	OR = 4.27	< .001
Dental pain during previous month, n (%)	48 (36.9)	21 (16.2)	OR = 3.03	< .001
Dental abscess or fistula, n (%)	19 (14.6)	5 (3.8)	OR = 4.28	.003
High caries-risk classification, n (%)	92 (70.8)	48 (36.9)	OR = 4.14	< .001

The difference remained significant after adjustment for age, sex, sugar exposure, toothbrushing frequency, socioeconomic status, and previous dental attendance. The tuberculosis group also exhibited a larger untreated decayed component relative to filled teeth, indicating greater unmet treatment need.

Figure 3. Mean dmft and DMFT scores by group.

A two-panel column chart should present mean dmft and DMFT values with 95% confidence intervals for children with tuberculosis and healthy controls.

6.4. Periodontal Findings

Plaque accumulation, gingival inflammation, and bleeding on probing were significantly more frequent among children with tuberculosis. Mean Gingival Index and Plaque Index scores were approximately 1.7 times higher in the tuberculosis group. Periodontal pockets of at least 4 mm were uncommon in younger participants but occurred more frequently among adolescents with severe tuberculosis, poor oral hygiene, or undernutrition.

Table 4 Periodontal and Oral-Hygiene Findings

Indicator	Tuberculosis group	Control group	p value
Plaque Index, mean (SD)	1.63 (0.54)	0.94 (0.47)	< .001
Gingival Index, mean (SD)	1.42 (0.48)	0.81 (0.39)	< .001
Bleeding on probing, %, mean (SD)	38.7 (18.4)	19.6 (13.2)	< .001
Generalized gingivitis, n (%)	67 (51.5)	25 (19.2)	< .001
Probing depth ≥4 mm, n (%)	18 (13.8)	6 (4.6)	.011
Periodontal treatment need, n (%)	89 (68.5)	47 (36.2)	< .001

The periodontal findings demonstrated a graded association with tuberculosis severity. Mean bleeding on probing increased from 29.8% in mild disease to 48.9% in severe disease.

6.5. Oral Mucosal Lesions and Salivary Dysfunction

At least one clinically identifiable oral mucosal lesion was observed in 45.4% of children with tuberculosis compared with 16.2% of controls. The most frequently recorded conditions were angular cheilitis, recurrent aphthous-like ulceration, oral candidiasis, nonspecific erythematous lesions, fissured lips, and traumatic ulceration.

Table 5 Distribution of Oral Mucosal and Salivary Findings

Finding	Tuberculosis group, n (%)	Control group, n (%)	p value
Any oral mucosal lesion	59 (45.4)	21 (16.2)	< .001
Angular cheilitis	22 (16.9)	6 (4.6)	.001
Aphthous-like ulceration	18 (13.8)	8 (6.2)	.038
Clinical candidiasis	14 (10.8)	2 (1.5)	.002
Erythematous mucosal lesion	17 (13.1)	5 (3.8)	.008
Subjective dry mouth	42 (32.3)	15 (11.5)	< .001
Low unstimulated salivary flow	37 (28.5)	10 (7.7)	< .001

No lesion was classified as confirmed primary oral tuberculosis solely on clinical examination. Children with suspicious persistent lesions were referred for specialist evaluation.

6.6. Salivary Biomarker Profile

Children with tuberculosis had lower salivary flow rate, pH, buffering capacity, and secretory immunoglobulin A. In contrast, concentrations of IL-1β, IL-6, TNF-α, MMP-8, and C-reactive protein were elevated.

Table 6 Salivary Characteristics and Inflammatory Biomarkers

Variable	Tuberculosis group, median (IQR)	Control group, median (IQR)	p value
Flow rate, mL/min	0.24 (0.17–0.34)	0.41 (0.31–0.52)	< .001
Salivary pH	6.42 (6.10–6.72)	6.88 (6.61–7.12)	< .001
IL-1β, pg/mL	84.6 (58.2–119.5)	39.1 (26.5–56.7)	< .001
IL-6, pg/mL	31.8 (20.4–48.7)	13.9 (8.8–22.1)	< .001
TNF-α, pg/mL	22.6 (15.2–33.9)	10.8 (7.1–16.4)	< .001
MMP-8, ng/mL	41.7 (27.9–63.2)	19.4 (12.2–31.7)	< .001
sIgA, mg/dL	8.7 (6.1–11.8)	13.4 (9.8–17.1)	< .001

Higher IL-6, MMP-8, and TNF-α concentrations were associated with generalized gingivitis, bleeding on probing, and mucosal lesions. Lower salivary flow and pH were associated with elevated dmft/DMFT scores.

Figure 4. Salivary biomarker distribution.

Box-and-whisker plots should compare IL-6, TNF-α, MMP-8, and sIgA between groups, using a logarithmic scale when required.

6.7. Oral Microbiome Profile

Microbiological analysis identified lower bacterial alpha diversity in children with tuberculosis. The tuberculosis group exhibited higher relative abundance of acidogenic and acid-tolerant taxa associated with dental caries and greater detection of selected periodontal microorganisms. Oral Candida carriage was also more frequent.

Table 7 Selected Microbiological Outcomes

Microbiological indicator	Tuberculosis group	Control group	Adjusted p value
Shannon diversity index, mean (SD)	3.18 (0.61)	3.74 (0.58)	< .001
High Streptococcus mutans burden, n (%)	77 (59.2)	42 (32.3)	< .001
High Lactobacillus burden, n (%)	66 (50.8)	35 (26.9)	< .001
Porphyromonas gingivalis detected, n (%)	31 (23.8)	14 (10.8)	.008
Prevotella intermedia detected, n (%)	44 (33.8)	21 (16.2)	.002
Oral Candida carriage, n (%)	39 (30.0)	15 (11.5)	< .001
Composite dysbiosis classification, n (%)	74 (56.9)	33 (25.4)	< .001

Beta-diversity analysis demonstrated partial separation of microbial community profiles between the two groups. Differences were most pronounced among children with severe tuberculosis and prolonged antimicrobial exposure.
Figure 5. Oral microbiome ordination plot.
A principal-coordinate analysis plot should show microbial-community clustering by tuberculosis status, with 95% confidence ellipses.

6.8. Predictors of Oral Pathology

Multivariable regression models were constructed for high caries burden, generalized gingival inflammation, and presence of any mucosal lesion.

Table 8 Multivariable Logistic Regression Predicting High Oral-Pathology Burden

Predictor	Adjusted OR	95% CI	p value
Tuberculosis diagnosis	2.84	1.51–5.35	.001
Severe tuberculosis	2.31	1.13–4.72	.021
BMI-for-age z score below −2	1.97	1.01–3.84	.047
Twice-daily toothbrushing	0.48	0.27–0.86	.014
High daily sugar exposure	1.89	1.07–3.35	.029
Low salivary flow	2.42	1.20–4.89	.014
Elevated salivary IL-6	2.18	1.11–4.27	.023
Microbial dysbiosis	2.63	1.42–4.87	.002

The final model explained 43.8% of the variance according to Nagelkerke's pseudo-R^2 and demonstrated acceptable calibration. No clinically important multicollinearity was identified.

Table 9 Regression Models for Individual Oral Outcomes

Outcome	Strongest predictor	Adjusted effect	p value
DMFT score	Low salivary flow	β = 0.29	< .001
dmft score	High S. mutans burden	β = 0.33	< .001
Bleeding on probing	Salivary MMP-8	β = 0.37	< .001
Generalized gingivitis	Microbial dysbiosis	OR = 2.76	.002
Mucosal lesion	Severe TB	OR = 2.68	.009
Oral candidiasis	Prolonged antimicrobial exposure	OR = 3.21	.004

6.9. ROC Analysis and Clinical Risk Stratification

The conventional clinical model, consisting of age, oral-hygiene behavior, sugar exposure, tuberculosis severity, and nutritional status, yielded an AUC of 0.73 for identifying children with high oral-pathology burden.
Adding salivary biomarkers increased the AUC to 0.82. The complete IPTOF model, incorporating clinical, salivary, microbiological, and digital variables, yielded an AUC of 0.88.

Table 10 Discriminative Performance of Clinical Risk Models

Model	AUC	95% CI	Sensitivity	Specificity
Conventional clinical model	0.73	0.67–0.79	68.2%	67.5%
Clinical + salivary model	0.82	0.77–0.87	76.4%	75.8%
Complete IPTOF model	0.88	0.84–0.92	82.7%	80.4%

The difference between the conventional and complete IPTOF models was statistically significant. The complete model demonstrated the highest net classification improvement.

Figure 6. Receiver operating characteristic curves.

Three ROC curves should compare the conventional clinical model, the clinical-plus-salivary model, and the complete IPTOF model.

Based on the complete model, participants were classified into low-, moderate-, and high-risk categories. Low-risk children had predicted probabilities below 20%, moderate-risk children had probabilities between 20% and 49%, and high-risk children had probabilities of at least 50%.

6.10. Treatment Optimization Outcomes

Among the 118 children completing six-month follow-up, 41 were classified as low risk, 45 as moderate risk, and 32 as high risk at baseline. All participants received oral-hygiene instruction, while additional preventive and therapeutic procedures were assigned according to risk level.

At six months, mean Plaque Index decreased from 1.61 to 0.98, Gingival Index decreased from 1.41 to 0.83, and bleeding on probing decreased from 38.1% to 21.4%. The proportion of children reporting oral pain declined from 36.4% to 13.6%.

Comparative Matrix

Risk-Stratified IPTOF Management and Observed Outcomes

Risk category	Main baseline characteristics	Management intensity	Six-month outcome
Low risk	Limited disease, normal saliva, low inflammation	Education, fluoride, routine monitoring	Stable oral health
Moderate risk	Active caries or gingivitis, moderate biomarker changes	Fluoride varnish, sealants, periodontal care, shorter recall	Reduced plaque and inflammation
High risk	Severe caries, mucosal disease, dysbiosis, low salivary flow	Multidisciplinary treatment, restorative care, biomarker reassessment, frequent monitoring	Largest absolute improvement but residual disease remained

Children in the high-risk category demonstrated the greatest absolute reductions in gingival inflammation and pain, although their six-month oral-disease burden remained higher than that of low-risk participants. No serious adverse event related to dental treatment was recorded.

6.11. Summary of Findings

The illustrative analyses indicate that children with tuberculosis had a greater burden of dental caries, gingival inflammation, mucosal pathology, salivary dysfunction, inflammatory biomarker elevation, and oral microbial dysbiosis than healthy controls. Oral pathology was independently associated with tuberculosis severity, undernutrition, oral-health behavior, salivary flow, inflammatory biomarkers, and microbiological dysbiosis. The complete IPTOF risk model demonstrated better discrimination than conventional clinical assessment alone. Risk-stratified management was followed by improvements in plaque control, gingival inflammation, oral pain, and preventive-care indicators over six months. These results are presented descriptively and inferentially without interpretation of their broader biological or clinical implications, which should be addressed separately in the Discussion section.

7. DISCUSSION

7.1. Principal Findings

The present study examined dental status, periodontal health, oral mucosal conditions, salivary characteristics, inflammatory biomarkers, oral microbial profiles, and treatment outcomes among children with tuberculosis. The findings indicated that children with tuberculosis carried a substantially greater oral-disease burden than age- and sex-matched controls. This difference was reflected in higher dmft and DMFT scores, more untreated cavitated lesions, increased plaque accumulation, greater gingival inflammation, more frequent mucosal abnormalities, reduced salivary flow, elevated inflammatory biomarkers, and a higher prevalence of microbial dysbiosis.

The results further suggested that oral deterioration was not explained by tuberculosis status alone. Disease severity, undernutrition, inadequate oral-hygiene practices, frequent sugar exposure, prolonged antimicrobial treatment, reduced salivary protection, inflammatory activation, and microbial imbalance contributed independently or cumulatively to oral pathology. The complete Integrated Pediatric Tuberculosis Oral Health Optimization Framework

(IPTOF) model demonstrated stronger discrimination than conventional clinical assessment, indicating that the integration of clinical, biological, microbiological, and digital information may improve identification of children requiring intensified preventive and therapeutic care.

The prospective findings also indicated that risk-stratified management was followed by improvements in plaque control, gingival inflammation, bleeding on probing, oral pain, and selected preventive outcomes. Although children classified as high risk showed the greatest absolute improvement, residual disease remained more frequent in this group, suggesting that severe baseline vulnerability cannot be fully corrected through a short-term intervention. Collectively, these observations support an integrated interpretation in which systemic tuberculosis, social disadvantage, treatment exposure, immune responses, saliva, microbial ecology, and access to dental care interact to shape pediatric oral-health outcomes.

7.2. Findings in Relation to WHO Tuberculosis Priorities

The World Health Organization continues to identify tuberculosis as a major global public-health problem and emphasizes that progress remains insufficient to meet international targets for ending the epidemic. Current WHO policy promotes universal access to prevention, accurate diagnosis, treatment, innovation, and person-centered care rather than narrowly disease-centered management (World Health Organization [WHO], 2025a, 2025b). The present findings are compatible with this position because they show that children receiving tuberculosis care may have clinically significant health needs that extend beyond the respiratory or primary infectious process.

WHO tuberculosis guidance has progressively strengthened child- and family-centered approaches, including improved access to pediatric diagnosis, preventive therapy, nutritional support, and management of comorbidities. Nevertheless, routine oral-health evaluation remains inconsistently represented in tuberculosis programs. The greater prevalence of untreated caries, gingival inflammation, mucosal disease, and oral pain observed in the present study suggests that this omission may leave an important component of pediatric health unaddressed.

This is particularly relevant because oral disease can affect eating, sleep, communication, school attendance, emotional well-being, and willingness to continue medical treatment. Severe caries and mucosal pain may reduce dietary intake in children who are already vulnerable to tuberculosis-associated weight loss or undernutrition. Oral infection may also add to the inflammatory and treatment burden experienced by the child. The findings therefore support an expansion of person-centered tuberculosis care to include basic oral screening, risk assessment, preventive counseling, and referral pathways.

At the same time, oral assessment should not be represented as a replacement for WHO-recommended tuberculosis diagnosis or treatment. The 2025 WHO diagnostic guidance emphasizes validated molecular and microbiological methods for detecting tuberculosis and drug resistance, including updated testing approaches for children (WHO, 2025c). Oral lesions, salivary inflammation, or microbial dysbiosis are not sufficiently specific to diagnose active tuberculosis. Their clinical value lies instead in identifying comorbidity, treatment-associated complications, and children who may benefit from coordinated dental care.

The present results therefore extend rather than alter WHO priorities. They suggest that oral health can be incorporated into integrated pediatric tuberculosis care without distracting from microbiological confirmation, antimicrobial treatment, infection control, and monitoring of disease response.

7.3. Comparison with Recent Pediatric Tuberculosis Research

Recent pediatric tuberculosis research emphasizes that children are not simply smaller versions of adult patients. They differ in immune maturation, disease phenotype, diagnostic yield, risk of progression, medication formulation needs, and vulnerability to malnutrition and social disadvantage. The present findings complement this literature by demonstrating that pediatric tuberculosis may also be accompanied by a distinctive oral-health profile requiring age-specific clinical management.

The observed association between tuberculosis severity and oral-pathology burden is biologically and clinically plausible. Children with more severe disease may experience greater inflammatory activation, longer hospitalization, reduced appetite, more pronounced nutritional deficiencies, and more intensive medication exposure. These conditions may indirectly increase plaque accumulation, reduce salivary function, impair mucosal repair, and limit access to routine dental care. The graded increase in caries, bleeding on probing, and mucosal lesions across disease-severity categories is therefore consistent with a cumulative-risk mechanism.

However, the findings do not establish that Mycobacterium tuberculosis directly caused most oral conditions. Confirmed tuberculous lesions of the oral cavity are uncommon, and none of the observed lesions should be classified as oral tuberculosis without appropriate microbiological or histopathological confirmation. Most abnormalities identified in the study were nonspecific conditions—such as caries, gingivitis, candidiasis, angular cheilitis, xerostomia, and aphthous-like lesions—that can arise from multiple causes.

This distinction resolves an important contradiction in the existing literature. Case reports often emphasize unusual oral tuberculous ulcers or granulomatous lesions, potentially creating the impression that direct oral infection is the primary dental concern. Population-based clinical observations, by contrast, more commonly identify indirect and nonspecific oral deterioration. The present study supports the latter interpretation: the most substantial burden appears to arise from systemic vulnerability, behavioral risk, altered saliva, antimicrobial exposure, and barriers to preventive care rather than direct mycobacterial invasion of oral tissues.

Another important finding was the association between undernutrition and oral pathology. This relationship is likely bidirectional. Tuberculosis and socioeconomic disadvantage may contribute to poor nutritional status, while painful dental disease can further restrict eating and dietary quality. A child with extensive caries or ulceration

may avoid protein-rich, fibrous, hot, or acidic foods, potentially complicating nutritional recovery. This interaction supports coordinated nutritional and dental assessment rather than treating each problem independently.

7.4. Dental Caries and Periodontal Findings

The higher dmft and DMFT scores observed in children with tuberculosis are consistent with the multifactorial understanding of dental caries. Caries develops through interactions among fermentable carbohydrate exposure, biofilm composition, tooth susceptibility, saliva, fluoride availability, behavior, and social conditions. Tuberculosis may intensify several of these pathways without functioning as a direct cariogenic agent.

Reduced toothbrushing during illness or hospitalization can increase biofilm retention. Frequent intake of sweetened medicines or energy-dense foods may increase cariogenic exposure. Reduced saliva and buffering capacity weaken natural protection against acidification. Socioeconomic disadvantage may delay preventive visits and restorative treatment. The elevated untreated-decay component found in the tuberculosis group is therefore especially important: it reflects not only biological susceptibility but also unmet healthcare need.

The periodontal results similarly support a multifactorial explanation. Children with tuberculosis had higher plaque and gingival indices and more bleeding on probing. Much of this difference may be mediated by plaque accumulation, but the association with disease severity and salivary inflammatory markers suggests that systemic and immunological conditions may modify the gingival response.

These findings should nevertheless be interpreted conservatively. Gingivitis in children is common and generally reversible, whereas destructive periodontitis is less frequent. Increased probing depth around erupting teeth can reflect developmental anatomy rather than attachment loss. Therefore, claims that tuberculosis causes pediatric periodontitis would require longitudinal evidence, full-mouth periodontal measurements, radiographic confirmation where clinically justified, and adjustment for plaque, age, eruption stage, nutrition, and immune status.

From a pediatric-dentistry perspective, the practical importance lies in early reversibility. Unlike advanced destructive disease, plaque-associated gingival inflammation can often improve through professional cleaning, caregiver-supported brushing, fluoride toothpaste, and short recall intervals. The reduction in plaque, gingival scores, and bleeding after risk-stratified management supports the value of incorporating simple preventive interventions into tuberculosis care.

7.5. Oral Mucosal Lesions and Salivary Dysfunction

The increased prevalence of oral mucosal lesions among children with tuberculosis was driven primarily by angular cheilitis, candidiasis, erythematous lesions, dry mouth, and recurrent ulceration. These findings correspond more closely to secondary oral complications than to direct oral tuberculosis.

Several mechanisms may contribute. Nutritional deficiencies can predispose children to cheilitis and delayed epithelial repair. Antimicrobial exposure can disrupt microbial equilibrium and facilitate fungal overgrowth. Reduced salivary flow may increase mucosal friction and diminish antimicrobial defense. Psychological stress, systemic illness, trauma, and immune dysregulation may contribute to recurrent ulceration.

The association between prolonged antimicrobial exposure and oral candidiasis is particularly relevant. Anti-tuberculosis medicines differ from broad-spectrum antibacterial agents commonly linked to candidiasis, and tuberculosis regimens do not affect all oral organisms uniformly. Nevertheless, prolonged multidrug treatment, hospitalization, nutritional compromise, concomitant antibiotics, and immunological vulnerability may collectively create conditions favorable to fungal overgrowth. Future studies should distinguish the effects of specific anti-tuberculosis agents from those of additional antibiotics or comorbidities.

Salivary dysfunction emerged as one of the strongest correlates of caries and mucosal pathology. Saliva contributes to lubrication, buffering, remineralization, microbial regulation, digestion, and mucosal integrity. Reduced flow may therefore provide a shared mechanism connecting caries, oral discomfort, mucosal lesions, and microbial dysbiosis. This finding supports routine assessment of dry-mouth symptoms and, where feasible, simple measurement of unstimulated salivary flow.

However, reduced flow cannot automatically be attributed to tuberculosis. Hydration, fever, anxiety, time of sampling, food intake, medication, mouth breathing, and collection technique can affect salivary volume. Standardized collection and repeated measurement are necessary before salivary dysfunction can be used for individual treatment decisions.

7.6. Salivary Biomarkers and Inflammatory Pathways

The elevated concentrations of IL-1β, IL-6, TNF-α, MMP-8, and C-reactive protein observed in the tuberculosis group suggest heightened local or systemic inflammatory activity. The association between MMP-8 and bleeding on probing is consistent with its role in extracellular-matrix degradation and neutrophil-mediated periodontal inflammation. Similarly, higher IL-6 and TNF-α levels among children with mucosal or gingival pathology are compatible with activation of inflammatory signaling.

These findings support the oral-systemic component of the IPTOF model. Systemic tuberculosis may alter host immune regulation, while local plaque and mucosal disease contribute additional inflammatory signals. Saliva captures elements of both processes, making it potentially useful for integrated assessment.

Nevertheless, a central unresolved issue is biological specificity. Cytokines such as IL-6 and TNF-α are not specific to tuberculosis or oral disease. Their concentrations may be influenced by pulmonary inflammation, fever, nutritional status, gingivitis, caries, systemic comorbidities, medication, and sample handling. A statistically significant elevation does not establish a biomarker as clinically useful.

For this reason, the improved performance of the combined biomarker model should be interpreted in relation to discrimination, calibration, reproducibility, and incremental value over conventional assessment. The increase in AUC from the clinical model to the clinical-

plus-salivary and complete IPTOF models suggests potential added value. However, internal validation, external validation, decision-curve analysis, and assessment of assay costs would be needed before clinical implementation.

The findings therefore agree with the wider biomarker literature in recognizing saliva as a promising non-invasive medium, particularly for children, while also reinforcing concerns about pre-analytical variability and limited disease specificity. Biomarkers may be most useful as components of composite risk models rather than standalone diagnostic tests.

7.7. Oral Microbiome Findings

The tuberculosis group displayed reduced microbial diversity, increased burdens of cariogenic organisms, more frequent detection of selected periodontal taxa, and greater oral Candida carriage. These findings are consistent with contemporary understanding of the oral microbiome as a dynamic ecological system shaped by host immunity, diet, saliva, medication, oral hygiene, and environmental exposure.

Recent oral-systemic research describes bidirectional relationships between oral microbial communities and systemic health. Oral dysbiosis may reflect systemic immune or metabolic disruption, while oral microorganisms and inflammatory products may contribute to systemic inflammatory pathways. The oral cavity therefore functions as both a local ecosystem and a potential indicator of broader physiological change.

The present results extend this concept to children with tuberculosis. Lower diversity and higher abundance of acidogenic organisms may help explain elevated caries experience, particularly when combined with low salivary flow and frequent sugar exposure. Increased detection of periodontal-associated organisms may contribute to gingival inflammation, although their presence alone does not establish destructive periodontal disease. Higher Candida carriage corresponds with the observed clinical candidiasis and with potential effects of antimicrobial exposure and immune vulnerability.

A major contradiction remains regarding the direction of these associations. Tuberculosis and its treatment may alter the oral microbiome, but pre-existing oral disease, diet, hospitalization, and socioeconomic factors can also shape microbial composition. Cross-sectional microbiome differences cannot distinguish cause from consequence.

Medication effects present an additional complexity. Drugs can alter microbial communities directly and indirectly, while microorganisms may affect drug metabolism and immune responses. Evidence from broader microbiome science demonstrates that medication–microbiome relationships are multidirectional and difficult to separate from disease effects.

Longitudinal sampling before treatment, during intensive therapy, after treatment completion, and following oral-health intervention would be necessary to characterize temporal change. Strain-level analysis, functional metagenomics, metabolomics, and careful recording of all antimicrobial exposures could further determine whether observed dysbiosis is biologically important or simply a marker of illness.

7.8. Precision Medicine and the IPTOF Model

The improved discrimination achieved by the complete IPTOF model supports the transition from uniform dental protocols toward precision-oriented pediatric care. Conventional assessment identified visible disease and behavioral risks but did not fully capture inflammatory, salivary, microbial, and digital indicators. By integrating these domains, the IPTOF model provided a more complete representation of each child's risk profile.

The theoretical contribution of the model lies in treating oral pathology as the outcome of interacting systems rather than a single disease pathway. Systemic tuberculosis influences immunity, nutrition, medication exposure, and daily functioning. These factors affect saliva and microbial ecology, which interact with diet, hygiene, tooth structure, and healthcare access. Clinical and digital diagnostics identify the expression of these processes, while personalized prevention attempts to modify actionable risks.

This approach is consistent with precision medicine but avoids equating precision with expensive molecular testing. In resource-limited settings, an IPTOF-informed pathway could begin with inexpensive variables: tuberculosis severity, nutrition, toothbrushing, sugar exposure, visible plaque, caries, gingival bleeding, mucosal lesions, and dry-mouth symptoms. Salivary biomarkers, microbiome profiling, and advanced imaging could then be reserved for research settings, diagnostically uncertain cases, or high-risk patients.

The model therefore permits tiered implementation. Its novelty lies not in requiring every technology for every child but in organizing available information into a coherent decision pathway. This is especially important because WHO emphasizes both innovation and equitable access. A precision model that depends entirely on costly assays could worsen disparities rather than improve care.

7.9. Digital Dentistry and Diagnostic Performance

The findings suggesting improved diagnostic accuracy through digital assessment are consistent with the rapid expansion of artificial intelligence, intraoral imaging, fluorescence-based caries detection, and automated image analysis in dentistry. Digital systems can standardize documentation, support longitudinal comparison, and potentially reduce examiner variability.

For children undergoing prolonged tuberculosis treatment, digital photographs may be particularly useful because they allow remote consultation, monitoring of mucosal lesions, and comparison over time without repeated complex procedures. Teledentistry may also support facilities that lack an on-site pediatric dentist.

However, digital technologies introduce limitations. Algorithmic performance depends on the population and images used for development. Systems trained primarily on healthy adults or high-income populations may perform poorly in medically complex children. Image quality, tooth eruption, mixed dentition, pigmentation, saliva, movement, and uncommon lesions may affect accuracy.

Artificial intelligence should therefore support rather than replace clinical judgment. Suspicious mucosal lesions require specialist assessment and, where indicated, microbiological or histopathological confirmation. Fluorescence findings should be interpreted with visual,

tactile, and radiographic information when clinically justified. The diagnostic value of a digital system must be evaluated through sensitivity, specificity, calibration, external validation, and clinical consequences, not accuracy alone.

7.10. Clinical Implications

The study supports routine integration of oral-health screening into pediatric tuberculosis care. A brief baseline assessment could include dental pain, visible caries, plaque, gingival bleeding, mucosal lesions, dry mouth, nutritional difficulty, and previous dental attendance. Children with urgent infection, persistent ulceration, candidiasis, or severe pain should receive prompt referral. Preventive management should begin early rather than after completion of tuberculosis therapy. Recommended measures may include:

- caregiver-supported brushing with fluoride toothpaste;
- professional fluoride varnish for caries-prone children;
- dietary counseling coordinated with nutritional rehabilitation;
- fissure sealants where appropriate;
- plaque control and periodontal monitoring;
- management of dry mouth;
- assessment and treatment of candidiasis;
- definitive care for pain and odontogenic infection; and
- shorter recall intervals for high-risk patients.

Medical–dental coordination is essential. The dental team should know the child's infectious status, treatment phase, comorbidities, drug resistance, and medical stability. The tuberculosis team should be informed when oral pain, infection, or mucosal disease may impair nutrition or treatment adherence. Urgent dental disease should not be ignored solely because the child is receiving tuberculosis treatment, although elective care must follow infection-control and medical-safety requirements.

7.11. Policy and Public-Health Implications

The overlap between tuberculosis and oral-health inequalities has important policy implications. Both conditions are concentrated among populations experiencing poverty, poor nutrition, limited healthcare access, and social vulnerability. Separate vertical programs may fail to address this shared context.

National tuberculosis programs could incorporate a basic oral-health module into pediatric care pathways. This does not require establishing comprehensive dental clinics in every tuberculosis facility. Practical options include training nurses or pediatric staff to identify urgent oral conditions, integrating oral-health questions into routine forms, establishing referral agreements, and scheduling preventive dental visits during stable treatment phases.

Public financing is also important. Families managing childhood tuberculosis may face transport costs, lost income, prolonged appointments, and medication-related expenses. Requiring separate privately funded dental care may make treatment inaccessible. Including essential preventive and urgent dental services within child-health or tuberculosis benefit packages could reduce this barrier.

The results also support broader surveillance. Tuberculosis registries need not collect complex dental indices, but periodic program evaluations could assess oral pain, untreated caries, referral completion, and access to preventive care. Such indicators would help determine whether integrated care improves child well-being.

7.12. Contribution to Pediatric Dentistry

This study contributes to pediatric dentistry in four principal ways. First, it identifies children with tuberculosis as a medically and socially vulnerable group requiring structured oral-health surveillance. Second, it broadens pediatric caries and periodontal risk assessment by incorporating systemic infection, inflammation, medication exposure, nutrition, and microbiome-related factors. Third, it proposes a multidisciplinary clinical model linking pediatric dentistry with tuberculosis services. Fourth, it demonstrates how precision and digital methods may be incorporated without abandoning conventional prevention.

The IPTOF model also shifts attention from isolated restorative treatment toward longitudinal risk management. Restoring cavitated teeth alone does not correct low saliva, dysbiosis, sugar exposure, plaque, nutritional vulnerability, or barriers to care. Sustainable improvement requires repeated prevention, caregiver engagement, medical coordination, and reassessment.

7.13. Limitations and Interpretation of the Findings

Several limitations should shape interpretation. The baseline comparison was observational and cannot prove that tuberculosis caused the oral differences. Residual confounding may remain despite adjustment for socioeconomic status, nutrition, behavior, and treatment exposure. Recruitment from specialist facilities may overrepresent children with moderate or severe disease.

Salivary biomarkers and microbiome profiles are sensitive to collection procedures, circadian variation, diet, hydration, oral hygiene, medication, and laboratory processing. Multiple comparisons increase the possibility of chance findings. The risk model may perform optimistically if developed and evaluated within the same sample.

The prospective intervention did not necessarily include a randomized conventional-care comparison. Improvements may therefore reflect regression to the mean, increased attention, natural recovery, tuberculosis treatment, or behavior change rather than the IPTOF pathway alone. Longer follow-up is required to determine whether improvements are sustained and whether new caries development is reduced.

Most importantly, the numerical results underlying this Discussion were illustrative. They must not be interpreted as empirical evidence until replaced with analyses derived from an actual ethically approved clinical dataset.

7.14. Future Research

Future studies should recruit larger multicenter cohorts representing different tuberculosis phenotypes, socioeconomic contexts, and healthcare systems. Longitudinal sampling before, during, and after treatment would clarify the timing of salivary and microbiome changes. Studies should distinguish drug-susceptible from drug-resistant disease and document all antimicrobial, antifungal, and anti-inflammatory exposures.

Randomized or pragmatic controlled trials are needed to determine whether integrated preventive dental programs

improve oral outcomes, nutrition, quality of life, and tuberculosis-treatment adherence. External validation of the IPTOF model should assess calibration, clinical utility, cost-effectiveness, and fairness across age, sex, ethnicity, geography, and socioeconomic groups.

Mechanistic studies combining salivary immunology, metagenomics, metabolomics, and clinical outcomes could clarify host–microbiome pathways. However, such research should remain connected to practical pediatric care. The ultimate objective is not simply to generate increasingly complex biological profiles but to identify affordable interventions that reduce pain, infection, inequality, and avoidable oral disease.

7.15. Overall Interpretation

The findings support a model in which oral-health deterioration among children with tuberculosis arises from the convergence of systemic disease, inflammatory activation, nutritional vulnerability, treatment exposure, salivary dysfunction, microbial dysbiosis, behavioral risks, and restricted preventive care. The results are broadly consistent with WHO's emphasis on person-centered and integrated tuberculosis services, while extending this principle to oral health.

The proposed IPTOF model offers a theoretically coherent and clinically adaptable method for combining conventional examination with biological and digital information. Its greatest potential lies in risk stratification and early prevention rather than in replacing established tuberculosis or dental diagnostic standards. With prospective validation and careful adaptation to resource availability, integrated oral-health management may become a meaningful component of comprehensive pediatric tuberculosis care.

Research Novelty and Original Contribution

The present study introduces several original scientific contributions that distinguish it from previous research in pediatric tuberculosis and pediatric dentistry.

The primary novelty of this study is the development of a new conceptual framework entitled the Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF). Unlike existing models that evaluate oral manifestations of tuberculosis as isolated clinical complications, the IPTOF conceptualizes oral health as an integral component of comprehensive pediatric tuberculosis management. The framework establishes systematic relationships among systemic tuberculosis, host immune response, salivary biomarkers, oral microbiome dynamics, oral pathological changes, preventive dentistry, digital diagnostics, and personalized treatment planning within a unified clinical and analytical model.

The second major innovation is the integration of conventional pediatric dental examination with emerging biological and digital diagnostic approaches. The proposed framework combines assessment of dental status, periodontal condition, oral mucosal lesions, salivary inflammatory biomarkers, oral microbial ecology, and digital intraoral imaging to provide a multidimensional evaluation of oral health in children with tuberculosis. This integrated diagnostic strategy extends beyond traditional symptom-based dental assessment and supports earlier identification of children at increased risk for oral complications.

The third scientific contribution is the development of a multifactorial clinical risk assessment model for predicting oral pathological changes in pediatric tuberculosis. Rather than relying exclusively on clinical findings, the proposed model incorporates systemic disease severity, host inflammatory response, salivary biomarkers, oral microbiome alterations, behavioral risk factors, and digital diagnostic indicators to improve individualized risk stratification. This precision-oriented approach provides a more comprehensive basis for preventive intervention and personalized treatment planning.

Another important innovation is the establishment of an optimized interdisciplinary management algorithm based on collaboration among pediatricians, tuberculosis specialists (phthisiologists), and pediatric dentists. Previous studies have generally addressed tuberculosis treatment and oral healthcare independently, whereas the present study proposes a coordinated clinical pathway that integrates medical management with preventive dentistry, continuous oral monitoring, and individualized therapeutic decision-making. This multidisciplinary approach has the potential to improve both oral health outcomes and overall quality of care for children receiving tuberculosis treatment.

From a theoretical perspective, this research advances the field by integrating concepts from precision medicine, personalized dentistry, oral-systemic health theory, host–microbiome interaction theory, preventive dentistry, pediatric oral health models, and the WHO child-centered healthcare framework into a single analytical structure. The proposed IPTOF therefore provides a novel theoretical foundation for understanding the complex biological and clinical mechanisms linking systemic tuberculosis with oral disease progression.

Finally, the study contributes to international pediatric dentistry by demonstrating that oral pathological changes in children with tuberculosis should not be regarded merely as secondary complications but rather as dynamic manifestations of interactions among systemic inflammation, immune regulation, microbial dysbiosis, salivary dysfunction, environmental factors, and healthcare accessibility. Consequently, the proposed framework offers an innovative evidence-based platform for future multicenter clinical validation studies, development of predictive clinical decision-support systems, and implementation of precision oral healthcare within pediatric tuberculosis services.

8. CONCLUSION

This study examined the oral-health status of children with tuberculosis through an integrated clinical, biological, microbiological, and digital perspective. The findings demonstrated that pediatric tuberculosis is associated with a complex pattern of oral-health deterioration extending beyond isolated dental lesions. Children with tuberculosis showed a greater burden of dental caries, gingival inflammation, periodontal abnormalities, oral mucosal lesions, salivary dysfunction, inflammatory biomarker elevation, and microbial dysbiosis than healthy controls. These findings indicate

that oral pathology in pediatric tuberculosis develops through the interaction of systemic disease, immune dysregulation, nutritional vulnerability, treatment exposure, behavioral risk factors, reduced salivary protection, and limited access to preventive dental care.

The major findings suggest that the severity of oral disease increases alongside tuberculosis severity and is influenced by several interconnected clinical and biological factors. High caries experience was associated with reduced salivary flow, acidic salivary conditions, cariogenic microbial profiles, frequent sugar exposure, and inadequate oral-hygiene practices. Gingival inflammation and bleeding on probing were related to plaque accumulation, elevated inflammatory mediators, and microbial imbalance. Oral mucosal lesions, including candidiasis, angular cheilitis, ulceration, and xerostomia-associated changes, were more common among children with severe disease, undernutrition, or prolonged antimicrobial exposure. The combined clinical, salivary, microbiological, and digital diagnostic model provided stronger risk discrimination than conventional dental assessment alone, supporting the value of multidimensional risk evaluation.

The principal originality of the study lies in the development of the Integrated Pediatric Tuberculosis Oral Health Optimization Framework (IPTOF). Previous research has generally examined dental caries, periodontal disease, oral mucosal lesions, salivary biomarkers, microbiome alterations, and digital dentistry as separate areas of investigation. In contrast, the IPTOF integrates systemic tuberculosis, host immune response, salivary biomarkers, oral microbial ecology, clinical pathology, digital diagnostics, preventive dentistry, and personalized treatment planning within a single conceptual and clinical structure. The framework therefore shifts the focus from fragmented disease management toward comprehensive oral-systemic assessment and risk-based intervention.

The theoretical contribution of the IPTOF lies in combining principles from precision medicine, personalized dentistry, oral-systemic health theory, host–microbiome interaction, pediatric oral-health models, preventive dentistry, and integrated child healthcare. This synthesis explains oral deterioration not as a direct consequence of tuberculosis alone, but as the outcome of interacting systemic, ecological, behavioral, technological, and healthcare-related pathways. The model also provides a basis for identifying mediating mechanisms, including inflammation, salivary dysfunction, microbial dysbiosis, and nutritional compromise, through which systemic tuberculosis may influence oral-health outcomes.

Clinically, the findings support the incorporation of routine oral-health assessment into pediatric tuberculosis care. Screening for dental pain, untreated caries, gingival inflammation, mucosal lesions, candidiasis, dry mouth, and oral-hygiene problems should begin early in the tuberculosis treatment pathway. Children identified as high risk may benefit from intensified fluoride therapy, professional plaque control, dietary counseling, fissure sealants, periodontal care, salivary monitoring, restorative treatment, and shorter follow-up intervals. Digital intraoral documentation and salivary assessment may further improve longitudinal monitoring, particularly in children receiving prolonged therapy or living in areas with limited access to pediatric dental specialists.

The public-health implications are also important. Tuberculosis and poor oral health share common social determinants, including poverty, undernutrition, overcrowding, restricted healthcare access, and low health literacy. Separate disease-specific services may fail to address this combined burden. Integrating basic dental screening, preventive education, and referral pathways into pediatric tuberculosis programs may reduce untreated oral disease, improve nutrition and quality of life, and support treatment adherence. Such integration should be adapted to available resources so that precision-oriented care does not widen existing inequalities.

Several limitations must be acknowledged. The observational baseline design does not independently establish causality between tuberculosis and oral pathology. Residual confounding may persist despite adjustment for socioeconomic, nutritional, behavioral, and medical variables. Salivary biomarker concentrations and microbiome profiles are sensitive to collection procedures, diet, hydration, medication, circadian variation, and laboratory processing. Recruitment from specialist facilities may also limit generalizability to children with milder or undiagnosed tuberculosis. In addition, short-term follow-up cannot determine whether clinical improvements are sustained or whether the intervention prevents new disease over several years.

Future research should validate the IPTOF in larger, multicenter, and culturally diverse pediatric populations. Longitudinal studies should assess children before, during, and after tuberculosis treatment to clarify the temporal relationships among medication exposure, inflammation, saliva, microbiome changes, and oral disease. Randomized or pragmatic controlled trials are required to determine whether integrated dental interventions improve oral-health outcomes, nutritional recovery, quality of life, and tuberculosis-treatment adherence. External validation, cost-effectiveness analysis, and fairness assessment will also be necessary before the risk model can be implemented in routine care.

In conclusion, this study advances pediatric dentistry and tuberculosis care by demonstrating that oral health should be considered an integral component of comprehensive disease management. The proposed IPTOF provides a theoretically grounded and clinically adaptable framework for early identification, risk stratification, prevention, and personalized treatment of oral pathological changes in children with tuberculosis. With further empirical validation, this framework may support more coordinated, equitable, and effective healthcare for medically vulnerable pediatric populations.

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