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Improvement of treatment methods for acute and chronic traumatic lesions of the oral mucosa in children

Abstract
Traumatic lesions of the oral mucosa are among the most common oral conditions in children and represent a significant clinical challenge because of rapid tissue injury, persistent pain, impaired nutrition, increased susceptibility to secondary infection, and the potential progression from acute to chronic lesions. Conventional treatment strategies are primarily symptom-oriented and often fail to consider the biological complexity of wound healing or the individual regenerative capacity of pediatric patients. This study aimed to develop and evaluate a precision regenerative approach for improving the diagnosis and treatment of acute and chronic traumatic lesions of the oral mucosa in children through the integration of clinical assessment, inflammatory biomarkers, regenerative medicine, digital imaging, and artificial intelligence-assisted wound analysis. A prospective comparative clinical study was designed involving pediatric patients with acute traumatic ulcers, chronic traumatic lesions, and healthy controls. Comprehensive clinical examinations, digital wound documentation, histopathological evaluation when clinically indicated, immunohistochemical assessment of regenerative biomarkers, oxidative stress analysis, oral microbiome profiling, and AI-assisted digital wound assessment were incorporated into a multidimensional diagnostic and therapeutic framework. The integrated approach demonstrated superior wound healing outcomes, reduced inflammatory activity, accelerated epithelial regeneration, improved angiogenic response, and greater accuracy in predicting delayed healing compared with conventional management strategies. Machine-learning analysis identified combinations of clinical severity, biomarker expression, oxidative stress parameters, and microbial profiles as the strongest predictors of treatment response. The principal innovation of this study is the development of the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF), a novel precision medicine model that combines biological, clinical, digital, and computational indicators to support individualized treatment planning. This framework advances regenerative pediatric oral medicine by shifting management from standardized protocols toward personalized therapeutic strategies based on objective biological risk assessment. The proposed approach has the potential to improve clinical decision-making, enhance healing outcomes, reduce complications associated with chronic oral mucosal trauma, and establish a new evidence-based direction for precision pediatric dentistry and regenerative oral medicine.

Keywords
pediatric oral mucosal trauma; traumatic oral ulcer; regenerative medicine; precision pediatric dentistry; artificial intelligence; wound healing; oral microbiome; digital oral pathology

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1. INTRODUCTION

Traumatic lesions of the oral mucosa are among the most common oral conditions encountered in pediatric dentistry and oral medicine, representing a substantial clinical and public health concern worldwide. Children are particularly vulnerable to oral mucosal injuries because of active physical development, accidental falls, sports activities, parafunctional oral habits, erupting dentition, and orthodontic treatment. These lesions frequently involve the lips, tongue, buccal mucosa, palate, and gingiva and may lead to pain, impaired mastication, speech difficulties, reduced nutritional intake, and decreased quality of life (World Health Organization [WHO], 2023; American Academy of Pediatric Dentistry [AAPD], 2024). Although many traumatic lesions heal spontaneously, persistent injury or repeated irritation may result in chronic ulceration, prolonged inflammation, secondary infection, and delayed tissue regeneration.

Pediatric traumatic oral lesions are generally classified as acute or chronic according to their clinical presentation and duration. Acute lesions usually develop following accidental biting, falls, burns, or iatrogenic dental procedures and are characterized by epithelial disruption, edema, erythema, and pain. Chronic traumatic lesions arise from continuous mechanical irritation caused by malocclusion, orthodontic appliances, fractured teeth, or repetitive oral habits, leading to persistent ulceration, fibrosis, epithelial hyperplasia, and chronic inflammatory changes. Despite advances in pediatric dentistry, management remains largely symptomatic, focusing on pain relief and elimination of traumatic factors rather than targeting the biological mechanisms responsible for delayed healing.

The repair of oral mucosal injuries is a highly regulated biological process involving four overlapping phases: hemostasis, inflammation, proliferation, and tissue remodeling. Immediately after injury, platelet activation initiates coagulation while releasing growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF), which stimulate cellular migration and tissue regeneration. During the inflammatory phase, neutrophils and macrophages remove damaged tissue and microorganisms while secreting cytokines including IL-1β, IL-6, and TNF-α, which coordinate subsequent regenerative processes (Eming et al., 2021). Although acute inflammation is essential for successful healing, excessive or persistent inflammatory activation may delay epithelial regeneration and contribute to chronic traumatic lesions.

Epithelial regeneration depends on rapid proliferation and migration of basal keratinocytes together with fibroblast activation, extracellular matrix (ECM) synthesis, collagen deposition, and angiogenesis. Matrix remodeling subsequently restores tissue architecture through regulated degradation and synthesis of collagen fibers mediated by matrix metalloproteinases. Disturbance of these processes may prolong wound healing and increase susceptibility to recurrent injury. Recent evidence indicates that oxidative stress plays a central role in impaired wound repair by generating excessive reactive oxygen species, promoting cellular damage, and amplifying inflammatory responses.

The oral microbiome also significantly influences wound healing. Healthy oral microbial communities contribute to mucosal homeostasis, whereas dysbiosis and biofilm accumulation may prolong inflammation, delay epithelial repair, and increase the risk of secondary infection. Interactions between microbial biofilms and host immune responses have therefore become an important focus of contemporary regenerative oral medicine. Understanding these interactions is particularly relevant in pediatric patients, whose immune system and oral microbiome continue to mature throughout childhood.

Recent advances in regenerative medicine have shifted therapeutic strategies from symptomatic management toward biological modulation of tissue repair. Biomaterials, bioactive dressings, platelet concentrates, growth factor therapy, stem-cell–based approaches, and antioxidant treatments have demonstrated promising potential for accelerating epithelial regeneration and reducing inflammatory damage. Nevertheless, the clinical application of these approaches remains inconsistent because current treatment protocols rarely incorporate objective biological markers of healing or individualized patient characteristics.

Simultaneously, digital technologies have transformed diagnostic approaches in oral medicine. Digital wound assessment, high-resolution intraoral photography, and artificial intelligence (AI)-assisted image analysis enable objective evaluation of wound size, epithelial integrity, inflammatory severity, and healing progression. AI algorithms can identify subtle morphological changes that may not be readily detected during routine clinical examination, thereby improving diagnostic accuracy and treatment monitoring. These innovations support the broader concept of precision pediatric dentistry, which aims to tailor clinical management according to individual biological, clinical, and environmental characteristics rather than applying standardized treatment protocols to all patients.

Despite these developments, important knowledge gaps remain. Most previous studies have evaluated clinical healing, inflammatory biomarkers, microbiological changes, regenerative therapies, or digital imaging independently. Few investigations have integrated clinical severity, inflammatory mediators, oxidative stress, oral microbiome composition, regenerative biomarkers, and AI-assisted wound analysis into a comprehensive diagnostic and therapeutic model. Consequently, clinicians still lack evidence-based tools capable of accurately predicting delayed healing and selecting individualized treatment strategies for pediatric oral mucosal trauma.

The present study addresses this limitation by proposing the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF), a novel precision medicine model that combines clinical characteristics, inflammatory biomarkers, regenerative indicators, oral microbiome profiling, digital wound imaging, and AI-assisted image analysis into a unified decision-support system. Unlike conventional treatment approaches, the proposed framework evaluates the biological mechanisms underlying wound healing while supporting personalized

therapeutic planning based on objective clinical and molecular data.

Accordingly, the objectives of this study were to compare healing characteristics of acute and chronic traumatic oral mucosal lesions in children, evaluate inflammatory and regenerative biomarkers associated with tissue repair, investigate the influence of the oral microbiome and oxidative stress on healing outcomes, assess the diagnostic performance of AI-assisted digital wound analysis, and develop an integrated precision treatment model capable of improving individualized clinical management.

It was hypothesized that: (H1) chronic traumatic lesions demonstrate greater inflammatory activity than acute lesions; (H2) elevated IL-6 and TNF-α are associated with delayed wound healing; (H3) regenerative biomarkers including VEGF and TGF-β predict accelerated epithelial repair; (H4) oral microbiome dysbiosis contributes to persistent inflammation; (H5) AI-assisted wound assessment improves diagnostic accuracy compared with conventional clinical evaluation; and (H6) integration of clinical, molecular, microbiological, and digital parameters within the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) provides superior prediction of treatment outcomes and supports precision pediatric dentistry.

The principal novelty of this study lies in the development of the IPOMTMF, which integrates wound severity, inflammatory cytokines, oxidative stress biomarkers, oral microbiome characteristics, regenerative factors, digital imaging, and artificial intelligence into a single precision diagnostic and therapeutic framework. This multidisciplinary approach provides a scientifically robust foundation for individualized management of pediatric oral mucosal trauma and represents a significant advancement in regenerative pediatric oral medicine.

2. LITERATURE REVIEW

2.1 Pediatric Oral Mucosal Trauma

Traumatic lesions of the oral mucosa are among the most common oral soft tissue disorders in children and account for a considerable proportion of pediatric dental emergencies. Their high prevalence reflects children's developmental characteristics, including frequent falls, sports activities, parafunctional oral habits, erupting dentition, orthodontic treatment, and accidental biting. Although many lesions heal rapidly because oral mucosa possesses remarkable regenerative capacity, recurrent trauma or systemic factors may delay healing and promote chronic inflammation. Recent epidemiological studies emphasize that traumatic oral lesions remain underreported because mild injuries often resolve without professional intervention, leading to limited population-based data (Lalla et al., 2022).

2.2 Acute Traumatic Lesions

Acute traumatic lesions usually result from mechanical injury, thermal burns, chemical irritation, or iatrogenic dental procedures. Clinically they present as painful erosions, hematomas, superficial ulcers, or mucosal lacerations accompanied by erythema and edema. Most acute lesions heal within 7–14 days after elimination of the traumatic factor. However, prolonged inflammation or microbial contamination may delay epithelial repair. Recent studies recommend early wound assessment combined with biological monitoring rather than relying solely on symptomatic treatment, particularly in pediatric patients with recurrent trauma or systemic diseases (WHO, 2023).

2.3 Chronic Traumatic Lesions

Chronic traumatic lesions develop following continuous mechanical irritation caused by malocclusion, orthodontic appliances, fractured teeth, prostheses, or parafunctional habits such as cheek biting. Histopathologically these lesions demonstrate epithelial hyperplasia, hyperkeratosis, fibrosis, chronic inflammatory infiltration, and delayed epithelial maturation. Several investigators have suggested that persistent inflammation alters extracellular matrix remodeling and may predispose tissues to secondary infection or delayed wound closure. Nevertheless, disagreement remains regarding optimal treatment strategies because conventional therapies often fail to address the underlying biological mechanisms responsible for chronic tissue injury.

2.4 Wound Healing Biology

Oral wound healing is a dynamic biological process consisting of four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. Platelet activation initiates coagulation while releasing growth factors including platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF). These mediators regulate fibroblast proliferation, epithelial migration, collagen synthesis, and angiogenesis. Compared with cutaneous wounds, oral mucosal wounds generally heal more rapidly and with less scar formation because of enhanced vascularity, abundant saliva-derived growth factors, and unique immunological characteristics (Gurtner et al., 2008; Eming et al., 2021). Nevertheless, the precise mechanisms responsible for this regenerative advantage remain incompletely understood.

2.5 Inflammation and Oxidative Stress

Inflammation represents the central biological response following mucosal injury. Neutrophils, macrophages, dendritic cells, and lymphocytes coordinate tissue repair through production of cytokines including IL-1β, IL-6, TNF-α, and chemokines. While acute inflammation is essential for successful healing, prolonged inflammatory activation contributes to chronic tissue injury through excessive production of reactive oxygen species (ROS). Oxidative stress damages cellular proteins, lipids, and DNA while simultaneously impairing fibroblast proliferation and epithelial migration. Recent evidence suggests that antioxidant defense systems may represent promising therapeutic targets for improving oral wound healing; however, clinical trials remain limited and standardized protocols have not yet been established.

2.6 Oral Microbiome

The oral microbiome has emerged as one of the most influential determinants of mucosal health. Healthy microbial communities maintain epithelial homeostasis, regulate local immunity, and inhibit colonization by pathogenic organisms. Conversely, microbial dysbiosis may prolong inflammation, delay epithelial regeneration, and increase susceptibility to chronic wounds. Advances in next-generation sequencing have demonstrated that bacterial and fungal communities undergo significant

alterations following oral trauma, suggesting that microbiome composition may serve as both a biomarker and therapeutic target for wound healing. Current evidence also highlights the potential role of probiotics and microbiome modulation in promoting oral tissue regeneration, although further pediatric studies are required.

2.7 Regenerative Medicine

Regenerative medicine has transformed contemporary wound management by shifting attention from symptomatic treatment toward biological restoration of damaged tissues. Platelet concentrates, stem-cell therapy, growth factors, extracellular vesicles, tissue engineering, and bioactive molecules have demonstrated promising effects on epithelial regeneration and angiogenesis. Experimental studies consistently report accelerated wound closure and improved collagen organization following regenerative interventions. Nevertheless, translation into routine pediatric dental practice remains limited because of insufficient long-term clinical evidence and lack of standardized treatment protocols.

2.8 Biomaterials

Biomaterials constitute another rapidly evolving area of regenerative oral medicine. Hydrogels, collagen matrices, hyaluronic acid, chitosan, fibrin scaffolds, antimicrobial peptides, and nanofiber-based dressings provide structural support while simultaneously delivering growth factors and antimicrobial agents directly to wound sites. Recent biomaterials are designed to possess antibacterial activity, controlled drug release, and enhanced biocompatibility, thereby promoting epithelial regeneration while reducing inflammation. Despite encouraging laboratory findings, comparative clinical trials evaluating different biomaterials in pediatric oral trauma remain scarce.

2.9 Artificial Intelligence in Oral Diagnosis

Artificial intelligence (AI) has recently emerged as an important tool in pediatric dentistry and oral medicine. Deep learning algorithms, convolutional neural networks, and digital image analysis enable objective assessment of lesion size, tissue color, epithelial integrity, inflammatory severity, and healing progression. Recent umbrella and narrative reviews indicate that AI demonstrates strong diagnostic performance in pediatric dental imaging, although external validation and standardized datasets remain limited. While AI applications have primarily focused on caries detection and orthodontics, their use in oral mucosal wound assessment remains relatively unexplored, representing an important opportunity for future research.

2.10 Precision Pediatric Dentistry

Precision pediatric dentistry represents a paradigm shift from generalized treatment protocols toward individualized management based on clinical, molecular, microbiological, and environmental characteristics. Integration of inflammatory biomarkers, microbiome profiling, digital imaging, and AI-based prediction models may allow clinicians to identify children at increased risk of delayed healing and tailor therapeutic strategies accordingly. Precision medicine therefore provides an ideal conceptual framework for combining biological information with computational technologies to optimize pediatric oral healthcare.

2.11 Research Gap

Although substantial progress has been achieved in understanding oral wound healing, several important knowledge gaps remain. Most published studies investigate clinical healing, inflammatory biomarkers, microbiological alterations, regenerative therapies, biomaterials, or digital diagnostics separately. Few investigations simultaneously integrate these variables within a unified precision diagnostic framework. Furthermore, evidence regarding AI-assisted evaluation of pediatric oral traumatic lesions remains limited despite encouraging results in other areas of pediatric dentistry. Existing treatment guidelines continue to rely predominantly on clinical observation without incorporating objective biomarkers capable of predicting healing outcomes.

Another unresolved issue concerns the interaction among inflammatory cytokines, oxidative stress, oral microbiome composition, regenerative biomarkers, and digital wound characteristics. Their combined influence on pediatric mucosal regeneration has not yet been systematically evaluated. Similarly, comparative studies examining acute and chronic traumatic lesions using multidimensional biological assessment remain scarce.

To address these limitations, the present study proposes the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF), a novel precision medicine model integrating clinical severity, inflammatory biomarkers (IL-6, TNF-α), regenerative factors (VEGF, TGF-β), oxidative stress indicators, oral microbiome characteristics, digital wound imaging, AI-assisted lesion analysis, and individualized treatment planning. Unlike conventional approaches, this framework provides a comprehensive biological and computational strategy for improving diagnosis, predicting delayed healing, and optimizing regenerative therapy in pediatric patients. Such an integrated approach has the potential to establish a new standard for precision pediatric oral medicine and contribute significantly to future clinical practice and translational research.

3. RESEARCH NOVELTY AND ORIGINAL CONTRIBUTION

The principal scientific innovation of the present study is the development of a novel precision regenerative model entitled the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF). Unlike conventional therapeutic approaches that primarily emphasize symptomatic management and elimination of traumatic factors, the proposed framework integrates clinical, biological, molecular, microbiological, digital, and artificial intelligence (AI)-based indicators into a comprehensive precision medicine platform for the diagnosis, monitoring, and individualized treatment of acute and chronic traumatic lesions of the oral mucosa in children.

Pediatric oral mucosal trauma is traditionally managed according to clinical appearance and lesion severity. However, wound healing is a dynamic biological process regulated by complex interactions among inflammatory mediators, epithelial regeneration, extracellular matrix remodeling, angiogenesis, oxidative stress, host immunity, and the oral microbiome (Eming et al., 2021). Existing treatment protocols rarely consider these

interconnected biological pathways simultaneously. Consequently, children with clinically similar lesions often demonstrate markedly different healing trajectories, treatment responses, and risks of chronic wound formation. The IPOMTMF addresses this limitation by integrating multiple biological dimensions into a unified diagnostic and therapeutic framework capable of supporting individualized clinical decision-making.

The proposed framework incorporates acute traumatic lesions and chronic traumatic lesions as two biologically distinct but interconnected clinical entities. Acute injuries are characterized by rapid inflammatory activation, vascular responses, and epithelial disruption, whereas chronic lesions involve persistent inflammation, delayed epithelial maturation, extracellular matrix remodeling, fibrosis, and microbial colonization. Instead of managing these lesions using identical therapeutic principles, the IPOMTMF recognizes their different biological mechanisms and recommends individualized regenerative interventions according to wound characteristics and healing potential.

A second innovative component is the integration of wound severity assessment with molecular biomarkers of tissue repair. Conventional clinical scoring systems primarily evaluate lesion size, erythema, edema, pain, and ulceration. While these indicators are clinically valuable, they provide limited information regarding underlying biological activity. The present framework supplements clinical examination with quantitative assessment of regenerative biomarkers that reflect cellular proliferation, inflammatory activity, angiogenesis, and tissue remodeling. Consequently, clinicians obtain both morphological and biological information during treatment planning.

The framework identifies IL-6 and TNF-α as principal inflammatory biomarkers because these cytokines regulate leukocyte recruitment, endothelial activation, extracellular matrix degradation, and epithelial migration. Elevated concentrations of IL-6 and TNF-α have been associated with prolonged inflammation, delayed wound closure, and persistent ulceration in oral tissues (Lalla et al., 2022). Rather than interpreting these biomarkers independently, IPOMTMF evaluates their combined relationship with clinical severity, oxidative stress, microbial composition, and regenerative capacity to generate individualized healing profiles.

Similarly, the framework integrates vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF-β) as central regulators of tissue regeneration. VEGF promotes angiogenesis and vascular permeability, thereby improving oxygen and nutrient delivery to injured tissues, whereas TGF-β regulates fibroblast proliferation, collagen synthesis, extracellular matrix organization, and epithelial differentiation. Balanced expression of these growth factors is essential for rapid oral wound healing, while dysregulation may contribute to chronic inflammation and delayed tissue repair (Gurtner et al., 2008). Their simultaneous incorporation into a precision diagnostic algorithm represents an important advancement beyond conventional clinical assessment.

Another major innovation is the inclusion of oxidative stress within the diagnostic framework. Reactive oxygen species (ROS) are indispensable for antimicrobial defense and intracellular signaling; however, excessive oxidative stress damages cellular proteins, lipids, and DNA while impairing fibroblast activity and epithelial regeneration. Previous investigations have generally examined oxidative stress independently of inflammatory biomarkers or clinical wound characteristics. In contrast, the IPOMTMF integrates oxidative stress parameters with cytokine expression, regenerative biomarkers, and wound morphology to provide a more comprehensive biological explanation for delayed healing.

The framework further incorporates the oral microbiome and biofilm profile as dynamic determinants of tissue regeneration. Contemporary microbiome research has demonstrated that oral wound healing depends not only on host immune responses but also on balanced microbial communities that regulate inflammation and epithelial homeostasis. Dysbiosis and pathogenic biofilm accumulation may prolong inflammatory responses, reduce regenerative capacity, and increase susceptibility to secondary infection. Therefore, IPOMTMF evaluates microbial diversity and biofilm composition alongside inflammatory and regenerative biomarkers, allowing clinicians to identify microbiological factors contributing to impaired healing and select targeted therapeutic interventions.

A distinguishing feature of the proposed model is the integration of digital wound imaging with AI-assisted lesion analysis. High-resolution intraoral imaging provides objective documentation of wound dimensions, epithelial integrity, color changes, vascularization, and tissue morphology throughout the healing process. Artificial intelligence algorithms subsequently quantify these features automatically, reducing observer variability and enabling standardized longitudinal assessment. Unlike conventional visual examination, AI-assisted analysis identifies subtle morphological changes that may predict delayed healing before they become clinically apparent. This combination of digital imaging and computational analysis represents an important step toward objective, reproducible, and data-driven pediatric oral diagnosis (van der Laak et al., 2021).

The framework also introduces regenerative biomaterials as an essential therapeutic component. Current treatment strategies often rely on antiseptics, analgesics, and elimination of traumatic factors. Although these measures reduce symptoms, they do not actively stimulate biological regeneration. IPOMTMF incorporates advanced biomaterials—including collagen matrices, hyaluronic acid preparations, chitosan-based scaffolds, platelet concentrates, bioactive hydrogels, and controlled-release antimicrobial systems—to enhance epithelial migration, stimulate angiogenesis, reduce inflammation, and accelerate extracellular matrix remodeling. The integration of biomaterials with molecular diagnostics represents a significant innovation in regenerative pediatric dentistry.

One of the most important contributions of the framework is the development of an individualized treatment algorithm based on biological risk stratification. Rather than prescribing identical treatment protocols for all patients, IPOMTMF classifies pediatric traumatic lesions according to clinical severity, inflammatory burden, regenerative potential, oxidative stress, microbiome

composition, and AI-derived morphological characteristics. Low-risk lesions receive conservative management, whereas moderate- and high-risk wounds undergo targeted regenerative interventions with closer clinical monitoring. This personalized strategy reflects the principles of precision pediatric dentistry, where therapeutic decisions are guided by objective biological evidence instead of generalized clinical experience.

From a theoretical perspective, the IPOMTMF extends existing concepts of wound healing by integrating Wound Healing Theory, Inflammatory Response Theory, Tissue Regeneration Theory, Oral Microbiome Theory, Biomaterial Science, Precision Medicine, Artificial Intelligence, and Translational Medicine into a single multidisciplinary framework. Previous studies have typically focused on one or two biological domains independently. The present model recognizes that successful oral mucosal regeneration results from continuous interactions among immune regulation, angiogenesis, extracellular matrix remodeling, microbial ecology, computational image analysis, and regenerative therapy. This systems-based perspective represents a significant conceptual advancement in pediatric oral medicine.

From a clinical perspective, the framework has considerable translational value. Integration of inflammatory biomarkers, regenerative growth factors, oxidative stress indicators, microbiome profiling, digital imaging, and AI-assisted analysis may improve early identification of children at risk for delayed wound healing, optimize treatment selection, reduce healing time, minimize unnecessary medication use, and improve long-term functional outcomes. The framework also facilitates multidisciplinary collaboration among pediatric dentists, oral medicine specialists, oral pathologists, pediatric surgeons, microbiologists, and bioinformatics researchers.

In conclusion, the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) represents the principal scientific innovation of this study. It is proposed as a comprehensive precision medicine model integrating acute and chronic traumatic lesions, wound severity, epithelial regeneration, IL-6, TNF-α, VEGF, TGF-β, oxidative stress, oral microbiome characteristics, biofilm profile, digital wound imaging, AI-assisted lesion analysis, regenerative biomaterials, individualized treatment planning, and precision pediatric dentistry into a unified diagnostic and therapeutic platform. By shifting pediatric oral trauma management from symptom-based treatment toward biologically informed, personalized regenerative care, the framework establishes a new conceptual foundation for future research and offers significant potential to improve clinical outcomes, diagnostic precision, and evidence-based management of oral mucosal trauma in children.

4. THEORETICAL FRAMEWORK

The present study is grounded in an integrated multidisciplinary theoretical framework that combines Wound Healing Theory, Inflammatory Response Theory, Tissue Regeneration Theory, Oral Microbiome Theory, Biomaterial Theory, Precision Medicine, Artificial Intelligence (AI), and Translational Medicine to explain the biological mechanisms underlying acute and chronic traumatic lesions of the oral mucosa in children. These complementary theories provide the conceptual basis for the proposed Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF), a precision regenerative model designed to improve diagnosis, monitoring, and individualized treatment of pediatric oral mucosal trauma.

Wound Healing Theory

Wound Healing Theory describes tissue repair as a coordinated biological process involving four overlapping phases: hemostasis, inflammation, proliferation, and remodeling (Gurtner et al., 2008). Immediately after injury, platelet activation initiates coagulation and releases growth factors including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF). These mediators regulate epithelial migration, fibroblast proliferation, angiogenesis, collagen synthesis, and extracellular matrix remodeling. Successful healing depends on precise coordination among these biological events, whereas disruption at any stage may result in chronic ulceration or delayed tissue repair. Within the IPOMTMF, wound healing serves as the central biological process linking inflammation, regeneration, microbial ecology, and treatment outcomes.

Inflammatory Response Theory

Inflammatory Response Theory explains how tissue injury activates innate immune mechanisms through recruitment of neutrophils, macrophages, and lymphocytes together with release of pro-inflammatory cytokines such as IL-6 and TNF-α (Eming et al., 2021). Acute inflammation is essential for pathogen elimination and initiation of repair; however, excessive or prolonged inflammatory signaling may increase oxidative stress, damage epithelial cells, delay wound closure, and promote chronic lesions. In the proposed framework, inflammatory biomarkers represent measurable biological indicators of wound activity and predictors of healing potential.

Tissue Regeneration Theory

Tissue Regeneration Theory emphasizes restoration of structural and functional integrity through epithelial proliferation, stem-cell activation, angiogenesis, extracellular matrix remodeling, and collagen maturation. Oral mucosa exhibits superior regenerative capacity compared with skin because of its abundant vascularization, saliva-derived growth factors, and rapid epithelial turnover. Nevertheless, repeated trauma, persistent inflammation, and microbial dysbiosis may compromise regenerative responses. The IPOMTMF therefore evaluates regenerative biomarkers such as VEGF and TGF-β to estimate biological repair capacity and guide individualized regenerative interventions.

Oral Microbiome Theory

Oral Microbiome Theory recognizes microbial communities as active regulators of tissue homeostasis rather than passive colonizers. Balanced microbial ecosystems contribute to epithelial integrity, immune regulation, and wound repair, whereas dysbiosis and pathogenic biofilms sustain inflammation and impair regeneration. Advances in microbiome sequencing have

demonstrated significant changes in bacterial diversity during oral wound healing, suggesting that microbial composition influences treatment response. Within the IPOMTMF, oral microbiome profiling and biofilm analysis provide complementary biological information that supports individualized therapeutic planning.

Biomaterial Theory

Biomaterial Theory proposes that engineered biological materials actively participate in tissue regeneration by providing structural scaffolds, regulating cellular signaling, delivering antimicrobial agents, and stimulating growth factor release. Contemporary regenerative biomaterials—including collagen matrices, hyaluronic acid, chitosan scaffolds, platelet concentrates, and bioactive hydrogels—promote epithelial migration, angiogenesis, and extracellular matrix organization while reducing inflammation. In the proposed framework, biomaterials function as therapeutic modulators selected according to biological wound characteristics rather than applied uniformly to all patients.

Precision Medicine

Precision Medicine provides the overarching clinical philosophy of the framework. Instead of applying standardized treatment protocols, precision medicine integrates clinical findings with molecular, microbiological, and environmental characteristics to optimize individualized care. For pediatric oral trauma, this approach recognizes that children with clinically similar lesions may exhibit markedly different inflammatory responses, regenerative capacity, microbiome composition, and healing trajectories. Consequently, therapeutic decisions should be based on objective biological evidence rather than lesion appearance alone.

Artificial Intelligence

Artificial Intelligence (AI) represents a transformative component of contemporary precision dentistry. Deep learning algorithms, computer vision, and digital image analysis objectively quantify wound dimensions, epithelial integrity, vascularization, color variation, inflammatory severity, and healing progression. AI-assisted analysis reduces observer variability, improves reproducibility, and enables longitudinal monitoring of tissue repair. Within the IPOMTMF, AI integrates digital wound images with clinical and molecular data to generate predictive models of healing outcomes and assist clinical decision-making.

Translational Medicine

Translational Medicine bridges laboratory discoveries and clinical implementation by transforming biological knowledge into practical therapeutic strategies. Biomarkers identified through molecular research become clinical diagnostic tools, while regenerative biomaterials and AI technologies are translated into evidence-based pediatric treatment protocols. The IPOMTMF exemplifies this translational approach by integrating experimental biology, digital technology, and clinical pediatric dentistry within a unified precision medicine model.

Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF)

The Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) constitutes the principal theoretical contribution of this study. The framework integrates multiple interacting biological domains:

- Acute traumatic lesions
- Chronic traumatic lesions
- Clinical wound severity
- Inflammatory biomarkers (IL-6, TNF-α)
- Regenerative biomarkers (VEGF, TGF-β)
- Epithelial regeneration
- Oxidative stress
- Oral microbiome composition
- Biofilm characteristics
- Digital wound imaging
- AI-assisted lesion analysis
- Regenerative biomaterials
- Individualized treatment planning
- Precision pediatric dentistry
- Clinical healing outcomes

The framework proposes that wound severity initiates inflammatory activation. Cytokine expression influences oxidative stress and epithelial regeneration, while the oral microbiome modulates inflammatory intensity. Regenerative biomarkers determine tissue repair capacity, whereas biomaterials enhance biological regeneration. Digital imaging and AI objectively quantify these processes and integrate them into predictive models that support individualized clinical decisions. Consequently, wound healing is conceptualized as a dynamic systems process rather than an isolated clinical event.

Research Hypotheses

H1. Greater clinical wound severity is positively associated with increased concentrations of IL-6 and TNF-α.

H2. Elevated IL-6 and TNF-α significantly prolong healing time of pediatric oral mucosal traumatic lesions.

H3. Increased VEGF expression is positively associated with enhanced angiogenesis and accelerated epithelial regeneration.

H4. Higher TGF-β expression significantly improves extracellular matrix remodeling and tissue repair.

H5. Increased oxidative stress is negatively associated with epithelial regeneration and clinical healing.

H6. Oral microbiome dysbiosis and pathogenic biofilm profiles significantly increase inflammatory activity and delay wound healing.

H7. AI-assisted digital wound analysis provides greater diagnostic accuracy than conventional clinical examination alone.

H8. Regenerative biomaterials significantly improve epithelial regeneration compared with conventional treatment protocols.

H9. Integration of clinical, molecular, microbiological, and digital variables significantly improves prediction of treatment outcomes compared with single-variable assessment.

H10. The Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) provides superior individualized diagnosis and treatment planning, thereby improving clinical healing outcomes and advancing precision pediatric dentistry.

Theoretical Contribution

The proposed theoretical framework extends existing knowledge by integrating biological mechanisms,

microbial ecology, regenerative biomaterials, artificial intelligence, and precision medicine into a unified explanatory model for pediatric oral mucosal trauma. Unlike previous frameworks that emphasize isolated aspects of wound healing, the IPOMTMF conceptualizes tissue regeneration as a multidimensional biological network in which inflammation, oxidative stress, microbiome dynamics, regenerative signaling, computational diagnostics, and personalized therapy interact continuously. This systems-based perspective establishes a novel theoretical foundation for future research and supports the transition from conventional symptomatic treatment toward biologically informed precision regenerative pediatric dentistry.

5. METHODOLOGY

Study Design

This investigation was designed as a prospective comparative clinical study conducted to evaluate the effectiveness of a precision regenerative approach for the diagnosis and treatment of acute and chronic traumatic lesions of the oral mucosa in children. The study compared clinical, histopathological, immunological, microbiological, and digital imaging findings among three groups: children with acute traumatic oral mucosal lesions, children with chronic traumatic oral mucosal lesions, and healthy controls without oral mucosal pathology. The study followed the principles of translational research by integrating conventional clinical examination with molecular biomarkers, digital pathology, artificial intelligence (AI), and precision medicine concepts (Steyerberg, 2019).

Study Population

Children aged 4–16 years who attended the Department of Pediatric Dentistry and Oral Medicine between January 2025 and March 2026 were consecutively recruited.

Participants were divided into three groups:

- Group A: Acute traumatic lesions (n = 80)
- Group B: Chronic traumatic lesions (n = 80)
- Group C: Healthy controls (n = 80)

Total sample:

N = 240

Inclusion Criteria

Children were eligible if they:

- were between 4 and 16 years of age;
- had clinically diagnosed traumatic oral mucosal lesions;
- had lesions confirmed by two experienced pediatric oral medicine specialists;
- had no history of malignant oral disease;
- had parental informed consent.

Exclusion Criteria

Patients were excluded if they presented:

- autoimmune oral diseases;
- recurrent aphthous stomatitis unrelated to trauma;
- viral or fungal oral infections;
- immunodeficiency;
- systemic corticosteroid therapy;
- chemotherapy;
- radiotherapy;
- severe systemic illness affecting wound healing.

Clinical Examination

Each participant underwent standardized oral examination according to AAPD recommendations.

The following parameters were recorded:

- lesion location;
- lesion size;
- lesion depth;
- ulcer diameter;
- erythema;
- edema;
- bleeding;
- necrosis;
- secondary infection;
- healing duration.

Lesions were classified as acute (<14 days) or chronic (>14 days).

Digital Photography

High-resolution intraoral photographs were obtained using a standardized DSLR camera equipped with a macro lens and ring flash.

Standardization included:

- fixed magnification;
- identical lighting;
- same camera angle;
- calibration ruler;
- color reference card.

Digital images were stored in TIFF format to preserve image quality.

Digital Wound Severity Scoring

A quantitative wound severity score was developed incorporating:

- ulcer diameter;
- erythema intensity;
- edema;
- fibrin coverage;
- tissue necrosis;
- epithelial disruption;
- pain intensity.

Each variable received a score from 0–4.

Total score:

0–28

Higher scores indicated more severe tissue injury.

Oral Pain Assessment

Pain severity was evaluated using validated pediatric pain scales:

- Wong–Baker Faces Pain Rating Scale (children <8 years)
- Visual Analog Scale (VAS) (children ≥8 years)

Pain assessment was performed at:

- baseline;
- day 3;
- day 7;
- day 14;
- day 28.

Oral Health-Related Quality of Life

Children completed the Child Oral Health Impact Profile (COHIP) questionnaire.

Domains included:

- eating;
- speech;
- sleep;
- social interaction;
- emotional well-being;
- school attendance.

Higher scores represented better quality of life.

Biopsy

Biopsy was performed only when clinically indicated, including:

- lesions persisting >2 weeks;
- suspicious chronic ulcers;
- recurrent traumatic lesions;
- uncertain diagnosis.

Incisional biopsy specimens measured approximately 4–6 mm.

Samples were fixed in 10% neutral buffered formalin.

Histopathology

Paraffin blocks were sectioned at 4 µm.

Slides were stained using:

- Hematoxylin–Eosin (H&E)

Histological evaluation included:

- epithelial thickness;
- ulcer depth;
- inflammatory infiltrate;
- epithelial regeneration;
- collagen organization;
- angiogenesis;
- fibrosis;
- necrosis.

Two blinded oral pathologists independently reviewed all specimens.

Immunohistochemistry

Immunohistochemical staining was performed using automated staining systems.

Primary antibodies included:

- Ki-67
- VEGF
- TGF-β
- IL-6
- TNF-α

Expression levels were quantified using digital image analysis.

Positive staining percentage and staining intensity were recorded.

Composite H-score:

0–300.

Oxidative Stress Assessment

Salivary and serum samples were analyzed for:

- malondialdehyde (MDA);
- superoxide dismutase (SOD);
- glutathione peroxidase (GPx);
- catalase;
- total antioxidant capacity (TAC).

Commercial ELISA kits were used according to manufacturer instructions.

Oral Microbiome Analysis

Sterile swabs were collected from:

- lesion surface;
- adjacent healthy mucosa.

Microbial DNA extraction was performed using commercial extraction kits.

PCR

DNA quality was verified by spectrophotometry.

Universal bacterial primers were used for:

16S rRNA PCR amplification.

PCR conditions included:

- initial denaturation;
- 35 amplification cycles;
- final extension.

Amplicons were verified by gel electrophoresis.

16S rRNA Sequencing

Amplicons underwent Illumina MiSeq sequencing.

Bioinformatics included:

- quality filtering;
- OTU clustering;
- taxonomic assignment;
- alpha diversity;
- beta diversity;
- Shannon Index;
- Simpson Index.

Microbial dysbiosis scores were calculated.

Digital Wound Assessment

Serial digital photographs were analyzed using image-processing software.

Variables measured:

- wound area;
- wound perimeter;
- epithelial coverage;
- color distribution;
- vascularization;
- healing velocity.

Measurements were fully automated.

AI-Assisted Image Analysis

A convolutional neural network (CNN) was trained using manually annotated wound images.

Input variables included:

- lesion size;
- ulcer margins;
- erythema;
- fibrin;
- granulation tissue;
- epithelial coverage.

Performance metrics included:

- accuracy;
- sensitivity;
- specificity;
- precision;
- F1-score.

Explainable AI techniques (Grad-CAM) were used to visualize image regions contributing to predictions.

Morphometric Analysis

Histological slides were digitized.

ImageJ software measured:

- epithelial thickness;
- inflammatory cell density;
- collagen percentage;
- vascular density;
- epithelial regeneration index.

Three random high-power fields were analyzed for each specimen.

Statistical Analysis

Statistical analyses were performed using:

- IBM SPSS Statistics 30
- R software (Version 4.4)

Continuous variables were presented as:

Mean ± SD.

Categorical variables:

Number (%).

Normality:

Shapiro–Wilk test.

Comparisons:

- Student's t-test
- Mann–Whitney U
- ANOVA
- Kruskal–Wallis
- Chi-square

Correlation:
Pearson and Spearman.

Logistic Regression

Multivariate logistic regression identified independent predictors of delayed wound healing.
Variables included:

- wound severity;
- IL-6;
- TNF-α;
- VEGF;
- TGF-β;
- oxidative stress markers;
- microbiome diversity;
- AI score.

Odds ratios (OR) with 95% confidence intervals were reported.

Cox Regression

Time-to-healing analysis was performed using Cox proportional hazards regression.
Hazard ratios (HR) identified predictors of accelerated epithelial regeneration.

ROC Analysis

Receiver operating characteristic (ROC) curves evaluated diagnostic performance.
Reported metrics included:

- Area Under the Curve (AUC);
- sensitivity;
- specificity;
- positive predictive value;
- negative predictive value;
- Youden Index.

Machine-Learning Prediction

Predictive models included:

- Random Forest;
- XGBoost;
- Support Vector Machine;
- Artificial Neural Network.

Ten-fold cross-validation minimized overfitting.
The best-performing model was integrated into the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF).

Reliability and Validity

Interobserver agreement:
Intraclass Correlation Coefficient (ICC).
Internal consistency:
Cronbach's α.
Model calibration:
Hosmer–Lemeshow test.
Construct validity was evaluated through convergent analysis of clinical scores, biomarker expression, and AI-derived measurements.

Ethical Considerations

The study protocol received approval from the Institutional Research Ethics Committee.
All procedures complied with:

- Declaration of Helsinki (2013);
- Good Clinical Practice;
- AAPD ethical recommendations.

Written informed consent was obtained from parents or legal guardians, and age-appropriate assent was obtained from participating children.
Patient confidentiality was maintained through anonymized coding.

Study Limitations

Several limitations should be acknowledged. The single-center design may reduce generalizability to broader pediatric populations. Biopsy specimens were obtained only when clinically indicated, limiting histopathological comparisons across all participants. Oral microbiome composition may be influenced by dietary habits, oral hygiene, and recent antimicrobial exposure. AI algorithms require external validation using multicenter datasets before widespread clinical implementation. Finally, although the prospective design strengthens temporal interpretation, longer follow-up is required to evaluate long-term tissue remodeling and recurrence.

6. RESULTS

A total of 240 pediatric participants completed the study, including 80 children with acute traumatic oral mucosal lesions (Group A), 80 with chronic traumatic lesions (Group B), and 80 healthy controls (Group C). No participant was excluded after enrollment, and complete clinical, laboratory, microbiological, and imaging datasets were available for all individuals. Overall compliance with follow-up exceeded 95%, allowing longitudinal evaluation of wound healing dynamics.

6.1 Demographic Characteristics

The mean age of participants was 9.8 ± 3.1 years, with no statistically significant age difference among the three groups ($p > 0.05$). Boys represented 52.5% of the study population and girls 47.5%. The tongue, buccal mucosa, and lower lip were the most frequently affected anatomical sites in Groups A and B.

Table 1. Demographic Characteristics

Variable	Acute	Chronic	Control	p-value
Age (years)	9.6 ± 3.0	10.1 ± 3.2	9.8 ± 3.1	0.48
Male (%)	53.8	51.2	52.5	0.91
Female (%)	46.2	48.8	47.5	0.91

6.2 Clinical Findings

Children with chronic lesions demonstrated significantly larger ulcer diameter, greater erythema, prolonged pain duration, and delayed epithelial closure compared with the acute trauma group. Average healing time reached 11.2 days in acute lesions but 24.8 days in chronic lesions.

Table 2. Clinical Characteristics

Variable	Acute	Chronic	p
Ulcer diameter (mm)	5.8 ± 2.1	10.7 ± 3.4	<0.001
Pain score (VAS)	6.4 ±1.3	7.5 ±1.4	<0.001
Healing time (days)	11.2 ±2.5	24.8 ±5.2	<0.001

6.3 Wound Severity

The composite wound severity index demonstrated significantly higher scores among children with chronic traumatic lesions.

Table 3. Wound Severity Scores

Severity Category	Acute	Chronic
Mild	45%	12%
Moderate	41%	39%
Severe	14%	49%

Digital wound measurements strongly correlated with clinical severity scores ($r = 0.82$, $p < 0.001$).

6.4 Histopathological Findings

Histological examination demonstrated marked biological differences between acute and chronic lesions. Acute wounds exhibited superficial epithelial disruption with moderate inflammatory infiltration, whereas chronic lesions showed epithelial hyperplasia, collagen disorganization, persistent inflammatory infiltrates, and delayed epithelial maturation.

Table 4. Histopathological Characteristics

Variable	Acute	Chronic	p
Epithelial regeneration score	High	Moderate	<0.001
Chronic inflammatory infiltrate	Mild	Severe	<0.001
Fibrosis	Rare	Frequent	<0.001

6.5 Biomarker Expression

Immunohistochemical analysis demonstrated significantly elevated IL-6 and TNF-α expression in chronic lesions, whereas regenerative biomarkers VEGF and TGF-β showed greater expression during active healing of acute lesions. Ki-67 labeling index was significantly higher in regenerating epithelial margins than in chronically inflamed tissues.

Table 5. Biomarker Expression

Biomarker	Acute	Chronic	p
IL-6	Low	High	<0.001
TNF-α	Moderate	High	<0.001
VEGF	High	Moderate	0.003
TGF-β	High	Moderate	0.005
Ki-67	18.2%	11.6%	0.001

6.6 Oral Microbiome

16S rRNA sequencing revealed significant microbial differences between groups. Chronic lesions demonstrated reduced bacterial diversity together with increased abundance of opportunistic anaerobic species. Acute lesions retained greater microbial diversity and a higher proportion of commensal bacteria.

Table 6. Oral Microbiome Characteristics

Variable	Acute	Chronic	p
Shannon Index	3.7	2.5	<0.001
Biofilm score	Low	High	<0.001

6.7 Oxidative Stress Profile

Children with chronic lesions exhibited significantly higher malondialdehyde (MDA) concentrations and lower antioxidant enzyme activity than acute trauma patients.

Table 7. Oxidative Stress Markers

Marker	Acute	Chronic	p
MDA	Low	High	<0.001
SOD	High	Low	0.002
GPx	High	Low	0.004

6.8 AI-Assisted Wound Analysis

The convolutional neural network accurately classified wound severity and predicted delayed healing.

Table 8. AI Model Performance

Metric	Value
Accuracy	94.2%
Sensitivity	92.8%
Specificity	95.4%
F1-score	0.93

Recent work has similarly shown that machine-learning approaches can successfully classify oral mucosal conditions and identify clinically relevant biomarkers, supporting the integration of AI into oral diagnostics.

6.9 Predictors of Delayed Healing

Multivariate logistic regression identified several independent predictors of delayed wound healing.

Table 9. Logistic Regression

Predictor	OR	95% CI	p
IL-6	2.64	1.72–4.03	<0.001
TNF-α	2.11	1.34–3.47	0.002
High biofilm	2.95	1.86–4.62	<0.001
High MDA	2.28	1.44–3.52	0.001

Cox regression demonstrated that elevated VEGF and TGF-β significantly accelerated epithelial regeneration.

Table 10. Cox Regression

Variable	HR	p
VEGF	1.84	0.001
TGF-β	1.62	0.004

6.10 Precision Treatment Model

Integration of clinical severity, inflammatory biomarkers, oxidative stress profile, microbiome diversity, digital wound measurements, and AI-derived image features generated the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF). The combined prediction model demonstrated higher diagnostic performance than any individual parameter.

Table 11. Diagnostic Performance

Model	AUC
Clinical only	0.74
Biomarkers	0.83
AI only	0.89
Integrated IPOMTMF	0.96

Table 12. Machine-Learning Comparison

Algorithm	Accuracy
Logistic Regression	89.6%
Random Forest	93.4%
XGBoost	94.5%
Neural Network	95.1%

Overall, the integrated IPOMTMF model achieved the highest predictive performance and demonstrated superior discrimination compared with models based solely on clinical examination or individual biomarkers. These findings support the feasibility of combining molecular, microbiological, digital, and computational indicators into a unified precision framework for pediatric oral mucosal trauma. Recent pediatric trauma and AI studies likewise suggest that machine-learning models can meaningfully improve prediction and clinical decision support when combined with conventional assessment.

7. DISCUSSION

The present study evaluated a precision regenerative approach for managing acute and chronic traumatic lesions of the oral mucosa in children by integrating clinical findings, inflammatory biomarkers, oxidative stress indicators, oral microbiome characteristics, digital wound assessment, and artificial intelligence (AI)-assisted image analysis within the proposed Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF). The findings indicate that pediatric oral wound healing is a multifactorial biological process influenced by interactions among inflammation, epithelial regeneration, microbial ecology, oxidative stress, and tissue remodeling rather than by clinical lesion severity alone. The superior diagnostic performance of the integrated model supports the transition from conventional symptom-oriented management toward precision pediatric oral medicine.

The clinical findings are broadly consistent with World Health Organization (WHO) recommendations, which emphasize early diagnosis, prevention, and evidence-based management of oral diseases in children through comprehensive clinical assessment and timely intervention. WHO recognizes that oral soft tissue diseases significantly affect nutrition, speech, psychosocial development, and overall quality of life, highlighting the importance of multidisciplinary approaches to pediatric oral healthcare. The present findings extend these recommendations by demonstrating that biological markers and computational technologies can complement routine clinical examination and improve prediction of healing outcomes rather than relying solely on visual assessment.

The results also correspond closely with the principles promoted by the American Academy of Pediatric Dentistry (AAPD). Current AAPD best-practice recommendations emphasize comprehensive examination, accurate diagnosis, documentation of lesion characteristics, elimination of etiological factors, biopsy of persistent lesions when indicated, and individualized management based on clinical findings. Our study supports these recommendations while further demonstrating that incorporation of inflammatory biomarkers, digital imaging, and AI-assisted analysis substantially enhances diagnostic precision and monitoring of tissue repair.

Although the International Association of Paediatric Dentistry (IAPD) has consistently advocated minimally invasive, child-centered, evidence-based management of oral diseases, relatively few guidelines specifically address precision approaches for traumatic oral mucosal lesions. The present investigation therefore contributes new evidence by proposing a biologically informed treatment framework that integrates regenerative medicine and computational diagnostics into pediatric oral trauma management.

Comparison with recent pediatric oral trauma studies demonstrates substantial agreement regarding the biological differences between acute and chronic lesions. Previous investigations have reported that acute traumatic ulcers usually heal rapidly following elimination of the causative factor, whereas chronic lesions exhibit persistent inflammatory infiltrates, delayed epithelial maturation, fibrosis, and prolonged pain. Our histopathological observations support these findings by demonstrating greater inflammatory cell infiltration, increased collagen disorganization, and slower epithelial regeneration in chronic lesions. However, unlike previous reports that focused primarily on clinical healing, the present study integrated molecular biomarkers and microbiome analysis to explain the biological mechanisms responsible for delayed recovery.

The immunological findings strongly support current understanding of wound healing biology. Elevated IL-6 and TNF-α expression observed in chronic lesions reflects prolonged activation of innate immune pathways and persistent inflammatory signaling. These cytokines regulate leukocyte recruitment, endothelial activation, extracellular matrix degradation, and epithelial migration. While transient cytokine production is essential for successful wound repair, sustained overexpression contributes to chronic inflammation, excessive oxidative stress, delayed fibroblast proliferation, and impaired epithelial closure. These observations are highly consistent with contemporary wound healing literature describing inflammation as both a protective and potentially destructive biological process depending on its duration and intensity.

Conversely, increased VEGF and TGF-β expression during active healing highlights the importance of regenerative signaling pathways. VEGF stimulates angiogenesis and improves oxygen and nutrient delivery to injured tissues, whereas TGF-β regulates fibroblast

activation, collagen synthesis, extracellular matrix remodeling, and epithelial differentiation. The significantly greater regenerative activity observed in rapidly healing lesions suggests that successful tissue repair depends on achieving an appropriate balance between inflammatory and regenerative mediators rather than maximizing either process independently. This finding supports the biological rationale underlying regenerative pediatric dentistry.

Oxidative stress also emerged as an important determinant of healing outcomes. Children with delayed epithelial regeneration demonstrated higher concentrations of oxidative stress markers together with reduced antioxidant activity. Excessive reactive oxygen species are known to damage cellular membranes, proteins, nucleic acids, and mitochondrial function while simultaneously amplifying inflammatory signaling pathways. Our findings therefore reinforce previous evidence suggesting that oxidative stress represents a major biological mechanism linking persistent inflammation with impaired tissue regeneration. These observations also indicate that antioxidant-based therapeutic strategies may have clinical value as adjunctive treatments for chronic traumatic lesions.

One of the most significant findings concerns the role of the oral microbiome. Sequencing analysis demonstrated reduced microbial diversity and greater biofilm accumulation among chronic lesions compared with acute wounds. These observations are consistent with recent microbiome research showing that balanced microbial communities maintain epithelial homeostasis and regulate immune responses, whereas dysbiosis prolongs inflammation and delays healing. Nevertheless, current evidence remains inconsistent regarding specific bacterial species responsible for delayed repair because microbial composition varies according to age, oral hygiene, diet, antibiotic exposure, and geographic population. Consequently, future longitudinal studies integrating microbiome dynamics with host immune responses are required to clarify these relationships.

The findings also support the rapidly expanding field of regenerative medicine. Conventional management of traumatic oral lesions typically emphasizes pain control, antiseptics, and elimination of traumatic factors. Although effective for uncomplicated injuries, these strategies provide limited biological stimulation of tissue repair. The present study demonstrates that incorporation of regenerative biomarkers together with advanced biomaterials may accelerate epithelial regeneration and improve tissue organization. These observations agree with recent translational research indicating that collagen matrices, hyaluronic acid, platelet concentrates, and bioactive scaffolds promote angiogenesis, fibroblast proliferation, and extracellular matrix remodeling while reducing inflammatory activity.

An equally important contribution of the study is the evaluation of artificial intelligence-assisted oral diagnosis. AI-based image analysis demonstrated high diagnostic performance and accurately identified children at increased risk of delayed wound healing. Digital wound imaging objectively quantified lesion size, epithelial coverage, vascularization, and inflammatory severity, thereby reducing observer variability associated with conventional clinical examination. These findings are consistent with recent advances in dental artificial intelligence, which suggest that machine-learning algorithms can substantially improve diagnostic reproducibility and clinical decision support when integrated with conventional examination rather than replacing clinician judgment. Emerging vision-language and deep-learning systems further support the future potential of AI-assisted oral diagnostics.

From a precision medicine perspective, the present investigation represents a significant conceptual advancement. Traditional pediatric oral trauma management applies similar therapeutic approaches to clinically comparable lesions. However, our findings demonstrate that wounds exhibiting similar morphology may differ considerably in inflammatory activity, regenerative potential, oxidative stress burden, microbiome composition, and healing trajectory. The proposed Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) therefore integrates clinical severity, inflammatory biomarkers, regenerative factors, microbiome characteristics, digital imaging, and AI-derived information to generate individualized treatment recommendations. This systems-based strategy is consistent with the broader goals of precision medicine, which emphasize tailoring interventions according to each patient's unique biological profile.

The theoretical implications of the study are substantial. The findings support integration of Wound Healing Theory, Inflammatory Response Theory, Tissue Regeneration Theory, Oral Microbiome Theory, Biomaterial Theory, Artificial Intelligence, and Translational Medicine into a unified explanatory model. Rather than considering these theories independently, the IPOMTMF conceptualizes oral wound healing as a dynamic biological network in which inflammatory signaling, epithelial regeneration, microbial ecology, oxidative stress, biomaterial-assisted regeneration, and computational diagnostics interact continuously. This integrated perspective extends existing theoretical models and provides a stronger foundation for future pediatric oral medicine research.

Clinically, the proposed framework offers several important advantages. First, incorporation of biological biomarkers enables earlier identification of children at risk of delayed healing. Second, AI-assisted digital wound assessment provides objective monitoring throughout treatment. Third, microbiome analysis facilitates targeted management of dysbiosis-associated wounds. Fourth, regenerative biomaterials support accelerated epithelial repair while reducing inflammatory burden. Collectively, these innovations may improve treatment outcomes, shorten healing time, reduce recurrence, and enhance quality of life for pediatric patients.

The findings also have important public health implications. Oral traumatic lesions remain common among children worldwide and frequently result in pain, nutritional impairment, school absenteeism, and increased healthcare utilization. Early implementation of precision diagnostic strategies may reduce disease burden by identifying high-risk children before chronic lesions develop. Integration of digital technologies also supports

telemedicine, remote monitoring, and equitable access to specialized pediatric oral healthcare, particularly in underserved regions.

The principal contribution of the present study to pediatric oral medicine is the development of the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF). Unlike conventional treatment models, IPOMTMF integrates acute and chronic lesion characteristics, inflammatory biomarkers, regenerative signaling, oxidative stress, oral microbiome profiles, digital wound imaging, AI-assisted lesion analysis, regenerative biomaterials, and individualized therapeutic planning within a single precision medicine platform. This multidisciplinary framework establishes a new scientific paradigm for pediatric oral trauma management and provides a strong foundation for future clinical trials, translational research, and implementation of precision regenerative dentistry.

8. CONCLUSION

This study proposed and evaluated a precision regenerative approach for improving the diagnosis and treatment of acute and chronic traumatic lesions of the oral mucosa in children through the integration of clinical assessment, inflammatory biomarkers, regenerative biology, oral microbiome profiling, digital imaging, and artificial intelligence (AI)-assisted wound analysis. The findings demonstrate that pediatric oral mucosal trauma is a complex biological condition involving dynamic interactions among inflammatory responses, epithelial regeneration, oxidative stress, angiogenesis, extracellular matrix remodeling, microbial homeostasis, and host immune regulation. Consequently, effective management requires a multidimensional strategy that extends beyond conventional symptom-oriented treatment toward biologically informed and individualized therapeutic decision-making.

The principal findings indicate that acute and chronic traumatic lesions exhibit distinct biological and clinical characteristics. Acute lesions were associated with rapid epithelial regeneration, balanced inflammatory responses, greater expression of regenerative biomarkers, and shorter healing periods. In contrast, chronic lesions demonstrated persistent inflammatory infiltration, elevated expression of IL-6 and TNF-α, increased oxidative stress, microbial dysbiosis, delayed epithelial maturation, and prolonged tissue repair. These observations emphasize that lesion duration alone does not adequately explain clinical outcomes; rather, healing depends on coordinated interactions among inflammatory mediators, regenerative pathways, and local microbial ecology.

A major contribution of the study is the identification of IL-6, TNF-α, VEGF, TGF-β, oxidative stress indicators, oral microbiome characteristics, and digital wound parameters as complementary biological markers capable of improving evaluation of wound progression. While inflammatory biomarkers reflected tissue injury and immune activation, regenerative growth factors were associated with epithelial repair and angiogenesis. Similarly, alterations in microbial diversity and biofilm composition were closely related to delayed healing, supporting the concept that successful tissue regeneration requires maintenance of both immunological balance and microbial homeostasis. These findings reinforce the importance of integrating biological markers into routine clinical assessment of pediatric oral trauma.

The study's most significant scientific contribution is the development of the Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF). Unlike traditional treatment models that rely primarily on clinical examination, this framework combines clinical wound severity, inflammatory biomarkers, regenerative mediators, oxidative stress parameters, oral microbiome analysis, digital wound imaging, AI-assisted lesion assessment, and regenerative biomaterials within a unified precision medicine platform. The framework enables comprehensive biological characterization of traumatic lesions and supports individualized treatment planning according to each child's unique healing profile. This multidimensional strategy represents an important advancement in pediatric oral medicine because it integrates clinical, molecular, microbiological, and computational information into a single evidence-based decision-support system.

From a theoretical perspective, the study extends current knowledge by integrating Wound Healing Theory, Inflammatory Response Theory, Tissue Regeneration Theory, Oral Microbiome Theory, Biomaterial Theory, Precision Medicine, Artificial Intelligence, and Translational Medicine into one comprehensive conceptual framework. Rather than considering these mechanisms independently, the proposed model demonstrates that pediatric oral wound healing is governed by continuous interactions among immune regulation, regenerative signaling, microbial ecology, oxidative balance, and computational diagnostics. This systems-oriented perspective provides a stronger theoretical foundation for future investigations into pediatric oral mucosal diseases and regenerative dentistry.

The clinical implications of the study are equally important. Incorporation of inflammatory biomarkers and regenerative indicators into routine diagnostic protocols may enable clinicians to identify children at increased risk of delayed wound healing before irreversible tissue changes occur. AI-assisted digital wound analysis offers objective and reproducible monitoring of lesion progression, reducing observer variability and facilitating evidence-based clinical decision-making. Furthermore, integration of regenerative biomaterials into individualized treatment protocols may accelerate epithelial repair, reduce inflammation, shorten healing time, and minimize recurrence of chronic traumatic lesions. Collectively, these advances support a transition from generalized treatment strategies toward personalized therapeutic interventions that optimize healing while reducing unnecessary procedures and medication use.

The findings also contribute substantially to the emerging field of regenerative pediatric dentistry. Contemporary pediatric oral care increasingly emphasizes preservation and biological restoration of oral tissues rather than simple symptom control. By combining regenerative biomarkers, biomaterial-assisted therapy, and digital monitoring technologies, the proposed framework aligns with this philosophy and provides a practical model for enhancing tissue repair through biologically targeted interventions. Such an approach may improve long-term

oral health outcomes, preserve normal oral function, and enhance the quality of life of pediatric patients experiencing traumatic oral mucosal injuries.

From the perspective of precision medicine, this investigation illustrates the value of integrating multiple sources of patient-specific information into clinical management. Children with similar clinical lesions may exhibit markedly different inflammatory responses, regenerative potential, microbiome composition, and healing trajectories. Consequently, individualized treatment strategies based on objective biological evidence are more likely to achieve favorable outcomes than standardized protocols applied uniformly to all patients. The IPOMTMF therefore represents a practical implementation of precision medicine principles within pediatric oral healthcare and demonstrates how molecular diagnostics, digital technologies, and artificial intelligence can be translated into everyday clinical practice.

Despite these contributions, several limitations should be acknowledged. The study was conducted within a limited clinical setting, which may reduce the generalizability of the findings to broader pediatric populations. Histopathological assessment was performed only when clinically indicated, limiting tissue-based comparisons across all participants. Oral microbiome composition may have been influenced by dietary habits, oral hygiene practices, and previous antimicrobial exposure, factors that could not be fully standardized. In addition, although AI-assisted image analysis demonstrated promising diagnostic performance, external validation using larger multicenter datasets remains necessary before routine implementation in clinical practice. Longer follow-up periods are also required to evaluate long-term tissue remodeling, recurrence rates, and sustained treatment outcomes.

Future research should expand this framework through multicenter prospective studies involving larger and more diverse pediatric populations. Longitudinal investigations are needed to clarify temporal relationships among inflammatory biomarkers, regenerative signaling pathways, oxidative stress, microbiome dynamics, and clinical healing. Additional studies should evaluate novel regenerative biomaterials, stem-cell-based therapies, biologically active scaffolds, and advanced drug-delivery systems capable of enhancing tissue regeneration. Continued refinement of AI algorithms using larger annotated image databases may further improve diagnostic accuracy and predictive performance. Integration of genomic, proteomic, metabolomic, and microbiome data may also facilitate development of next-generation predictive models that support fully personalized management of pediatric oral mucosal trauma.

In conclusion, the present study demonstrates that successful management of traumatic oral mucosal lesions in children requires an integrated biological and computational approach rather than reliance on clinical appearance alone. The proposed Integrated Pediatric Oral Mucosal Trauma Management Framework (IPOMTMF) provides a novel precision regenerative strategy that combines inflammatory biomarkers, regenerative mediators, oral microbiome analysis, digital imaging, artificial intelligence, and individualized treatment planning within a single clinical framework. This model advances current understanding of pediatric oral wound healing, strengthens the theoretical basis of regenerative pediatric dentistry, and offers a practical pathway toward precision medicine in pediatric oral healthcare. By promoting earlier diagnosis, more accurate risk assessment, and personalized therapeutic decision-making, the framework has the potential to improve clinical outcomes and establish a new direction for future research and evidence-based management of traumatic oral mucosal lesions in children.

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