

REVIEW ARTICLE

Oral microbiome and oral mucositis in pediatric acute lymphoblastic leukemia

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Abstract

Oral mucositis (OM) is a common, dose-limiting toxicity in pediatric acute lymphoblastic leukemia (ALL) and is associated with increased risk of infection, nutritional deficiency, and potential interruption of chemotherapy. Growing interest in the role of the oral microbiota has focused on its close association with inflammation and infection. The oral ecosystem undergoes changes throughout cancer treatment, with commensal and pathogenic microorganisms interacting within a diverse microbial ecosystem before and during therapy. This narrative review synthesizes recent clinical, translational, and omics-based studies on OM in pediatric ALL, focusing on the underlying pathophysiological mechanisms, oral microbiome dynamics, inflammatory pathways, and emerging predictive biomarkers. A comprehensive search of PubMed and Web of Science was performed through May 1, 2026. Studies were screened for eligibility based on title, abstract, and full text. OM pathogenesis is driven by a multifactorial interplay between chemotherapy-induced epithelial injury, dysregulated inflammatory responses, and oral microbiome dysbiosis. Dysbiosis is characterized by an expansion of opportunistic taxa (e.g., *Prevotella*, *Porphyromonas*) and depletion of protective commensals (e.g., *Streptococcus*), alongside elevated pro-inflammatory cytokine levels. These findings highlight the clinical importance of developing better strategies for personalized preventive management of OM. Integrating microbiome and inflammatory biomarkers into clinical practice may enable early risk stratification and support individualized preventive strategies, thereby improving supportive care and treatment outcomes.

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(pierre.le-bars@univ-nantes.fr)**Citation:** Le Bars P, Kouadio AA. Oral microbiome and oral mucositis in pediatric acute lymphoblastic leukemia. *Microbes & Immunity*. doi: 10.36922/MI026190042**Received:** May 6, 2026**Revised:** June 22, 2026**Accepted:** July 1, 2026**Published online:** July 21, 2026**Copyright:** © 2026 Author(s). This is an Open-Access article distributed under the terms of the Creative Commons Attribution License, permitting distribution, and reproduction in any medium, provided the original work is properly cited.**Publisher's Note:** AccScience Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.**Keywords:** Pediatric acute lymphoblastic leukemia; Oral mucositis; Oral microbiome; Dysbiosis; Cytokines; Biomarkers; Neutropenia; Precision oncology**1. Acute lymphoblastic leukemia and its treatment: Background**

Acute lymphoblastic leukemia (ALL) is one of the four main subtypes of leukemia, characterized by blastic transformation of B and T lymphocytes. In children, ALL accounts for up to 80% of all leukemia cases, with a peak incidence between the ages of 1 and 4 years.^{1,2} Pediatric ALL is a heterogeneous disease with multiple distinct biologic subtypes.³⁻⁵

Although the etiology of ALL is complex, several factors contributing to its

pathogenesis are known, including exposure to certain chemicals and viral infections during pregnancy and early childhood. Despite the complexity of its etiology, pediatric ALL is managed using highly standardized treatment protocols, and combination chemotherapy is very effective. Treatment of ALL is usually prolonged, lasting up to 2 years.⁶ Owing to advances in treatment, the survival rate for children with ALL has reached 90%.⁷

1.1. Study aims and methodology

We conducted a narrative literature review to examine current evidence on the relationship between the oral microbiome and oral mucositis (OM) in children with ALL. Relevant studies published between 2000 and 2026 were identified through searches of PubMed/MEDLINE and the Web of Science.

The search strategy combined keywords and MeSH terms related to “ALL,” “oral microbiome,” “oral microbiota,” “oral dysbiosis,” “OM,” “chemotherapy,” and “pediatric oncology.” Additional articles were identified through manual screening of reference lists.

Studies were included if they investigated pediatric ALL and reported data on oral microbiome composition, microbial dysbiosis, or mechanisms associated with OM. Original research articles, systematic reviews, and relevant clinical guidelines were considered. Studies focusing exclusively on adults or unrelated diseases were excluded.

Data extracted included study characteristics, microbiome assessment methods, OM outcomes, and key findings related to microbiome–host interactions. Due to methodological heterogeneity among the studies, findings were synthesized narratively, with an emphasis on chemotherapy-induced dysbiosis, inflammatory pathways, epithelial barrier disruption, and potential microbiome-based preventive or therapeutic approaches.

1.2. Sequence of treatment in pediatric acute lymphoblastic leukemia

Different protocols for the treatment of pediatric ALL are implemented around the world, such as the Berlin–Frankfurt–Münster Intercontinental Study on Acute Lymphoblastic Leukemia (ALL IC-BFM 2009),⁸ the Brazilian Cooperative Group for Treatment of Childhood Acute Lymphocytic Leukemia (GBTLI-2009), and the St. Jude Total Therapy protocols XI, XV, and XVI.^{9,10}

The various therapeutic protocols are consistent in their use of high-dose steroids, methotrexate, anthracyclines, vincristine, L-asparaginase, cyclophosphamide, etoposide, and 6-mercaptopurine, with cytarabine added in selected regimens.¹¹ These protocols are divided into different

phases: (i) the induction phase, which aims to clear disease and achieve prolonged remission; (ii) the consolidation (or intensification) phase; and finally (iii) the maintenance (or continuation) phase.

Adverse effects related to treatment can occur as early as the first two weeks after treatment initiation. Acute infectious complications account for the majority (68–88%) of adverse effects.¹² OM is among the most frequent chemotherapy-induced oral complications in children with ALL.¹³

2. Pathophysiology of oral mucositis

Oral mucositis is a condition clinically characterized by erythema, edema, and ulcerations of the oral mucosa. Rupture of the mucosal barrier constitutes an advanced stage, leading to local or systemic infection. OM is graded according to its clinical presentation.

2.1. Clinical aspects of oral mucositis

Grading systems for ranking and quantifying the severity of OM have been published by both the World Health Organization and the National Cancer Institute–Common Toxicity Criteria.¹⁴

Based on anatomical, functional, and symptomatic criteria, OM is classified into five clinical stages (0–4), from least to most severe.

- (i) Grade 0: No mucositis (no symptoms or signs);
- (ii) Grade 1: Soreness/erythema;
- (iii) Grade 2: Erythema and ulcers; the patient is able to swallow solid food;
- (iv) Grade 3: Ulcers; the patient is unable to tolerate solid food, but able to tolerate liquids;
- (v) Grade 4: The patient is unable to tolerate solids or liquids; oral alimentation is not possible.

In the most severe cases (grades 3 and 4), patients are unable to tolerate solid food and may lose the ability to eat, necessitating parenteral nutrition. This situation frequently requires interruption of chemotherapy and may necessitate intubation for nutritional rehabilitation.

2.2. Histopathological features of oral mucositis

Treatment of childhood ALL relies primarily on chemotherapy, which induces DNA damage and inhibits mitosis in epithelial cells of the mucosa and submucosa. It also triggers apoptosis (programmed cell death) signals in susceptible cells, including cancer cells.¹⁵ Depending on the severity, OM damages the oral mucosa and can disrupt microbiota homeostasis.^{16,17} In this situation, resident flora colonize the wound, causing a secondary infection and increasing inflammation (Figure 1A and 1B).

Apoptosis appears to be the leading cause of tissue damage in mucositis. For example, apoptosis of fibroblasts and vascular endothelial cells in the submucosa can be observed before injury to the overlying epithelium becomes apparent.¹⁸ Although some studies have explored the effects of cytotoxicity from anticancer therapy on epithelial cell apoptosis, a process that is regulated through toll-like receptors, the underlying mechanisms remain to be elucidated.^{19,20} For this reason, these observations suggest that OM is not infectious in its initial phase, but it becomes so after microbial colonization.

The process is followed by inflammation, with a cascade of inflammatory mediators such as interleukins (IL-6, IL-1 β , IL-17) and matrix metalloproteinases that increase from day 0 to day 14 of treatment, with higher concentrations in patients with OM than in those without.²¹ At diagnosis and prior to chemotherapy, the high risk of OM in pediatric patients with ALL is associated with elevated concentrations of the inflammatory cytokines IL-6, IL-8, IL-10, and tumor necrosis factor (TNF)- α and with low plasma levels of pro-LL-37.²²

The level of cytokines in blood and saliva fluctuates rapidly. This variation depends on genes that control the synthesis of various growth factors, including cytokines.²³ Cytokines such as IL-6 and TNF- α accelerate apoptosis and contribute to tissue damage. The levels of these cytokines in the blood and saliva increase during the initial phase of methotrexate-induced mucositis.²⁴ Some cytokines, considered pro-inflammatory mediators (IL-2, IL-6, IL-8, IL-15, TNF- α , and interferon- γ), stimulate inflammation as well as the proliferation of lymphoid cells and neutrophils. Others, such as IL-10, are mediators that inhibit the production of pro-inflammatory cytokines.²⁵

Notably, the concentrations of certain pro-inflammatory cytokines (e.g., TNF- α) in saliva and serum, and of anti-inflammatory cytokines (e.g., IL-10) in serum only, remained significantly elevated in patients during both remission maintenance and one year after treatment discontinuation compared with a control group.²⁶ This may explain the persistence of OM during the maintenance phase of treatment. The pathogenesis of OM in its initial phase is closely linked to chemotherapy. However, without disregarding the complex etiology of OM, the microbiological approach has generated considerable research.²⁷

3. The oral microbiome in health and disease

Early maturation of the oral microbiota occurs during the first years of life, when species richness and taxa diversity in the mouth increase significantly.^{28,29} From

an immunological perspective, oral diseases such as periodontitis, dental caries, and endodontic infections reflect a breakdown in the finely tuned host-microbiota relationship that has co-evolved to preserve mucosal integrity. Under physiological conditions, the immune system continuously monitors microbial communities and responds to pathogenic challenges while maintaining tolerance toward commensal species.

One mechanistic hypothesis suggests that commensal microorganisms help establish the immunological thresholds required to maintain mucosal immune homeostasis. In this model, commensal bacteria are not merely passive colonizers but actively participate in immune education and regulation, thereby maintaining a symbiotic equilibrium with the host immune system.³⁰ Disruption of this balance, whether due to a malignant tumor or cytotoxic therapy, can therefore predispose individuals to opportunistic infections and inflammatory diseases. This is the case in pediatric ALL.

4. Microbiome alterations in pediatric acute lymphoblastic leukemia

Overall, the interaction between ALL, oral microbiota dysbiosis, and oral diseases reflects a complex triadic relationship involving the host immune system, microbial communities, and therapeutic interventions. Disruption of this equilibrium not only facilitates the emergence of oral infections, but may also exacerbate systemic inflammatory burden and compromise overall treatment outcomes.

In pediatric ALL and its treatment, alterations in local immune regulation and salivary immune factors further contribute to oral susceptibility. Variations in cytokine levels, including interleukins, have been reported in saliva and are associated with gingival inflammation and treatment-related immunomodulation.³¹ These findings underscore the interplay between systemic malignancy, immune dysregulation, and oral infectious disease progression.

4.1. Oral microbiome before chemotherapy in acute lymphoblastic leukemia

In patients with ALL, disturbances of the oral microbiome may be present even before the initiation of chemotherapy. This baseline dysbiosis is thought to be related both to the underlying malignancy and to pre-existing or concomitant oral infections.³² From an ecological perspective, the oral microbiome is characterized by a dynamic balance between host immunity and microbial colonization. In this context, the lymphoid tissue of the oral mucosa plays a key role in maintaining mucosal immune homeostasis.³³ In pathological conditions such as ALL, malignant

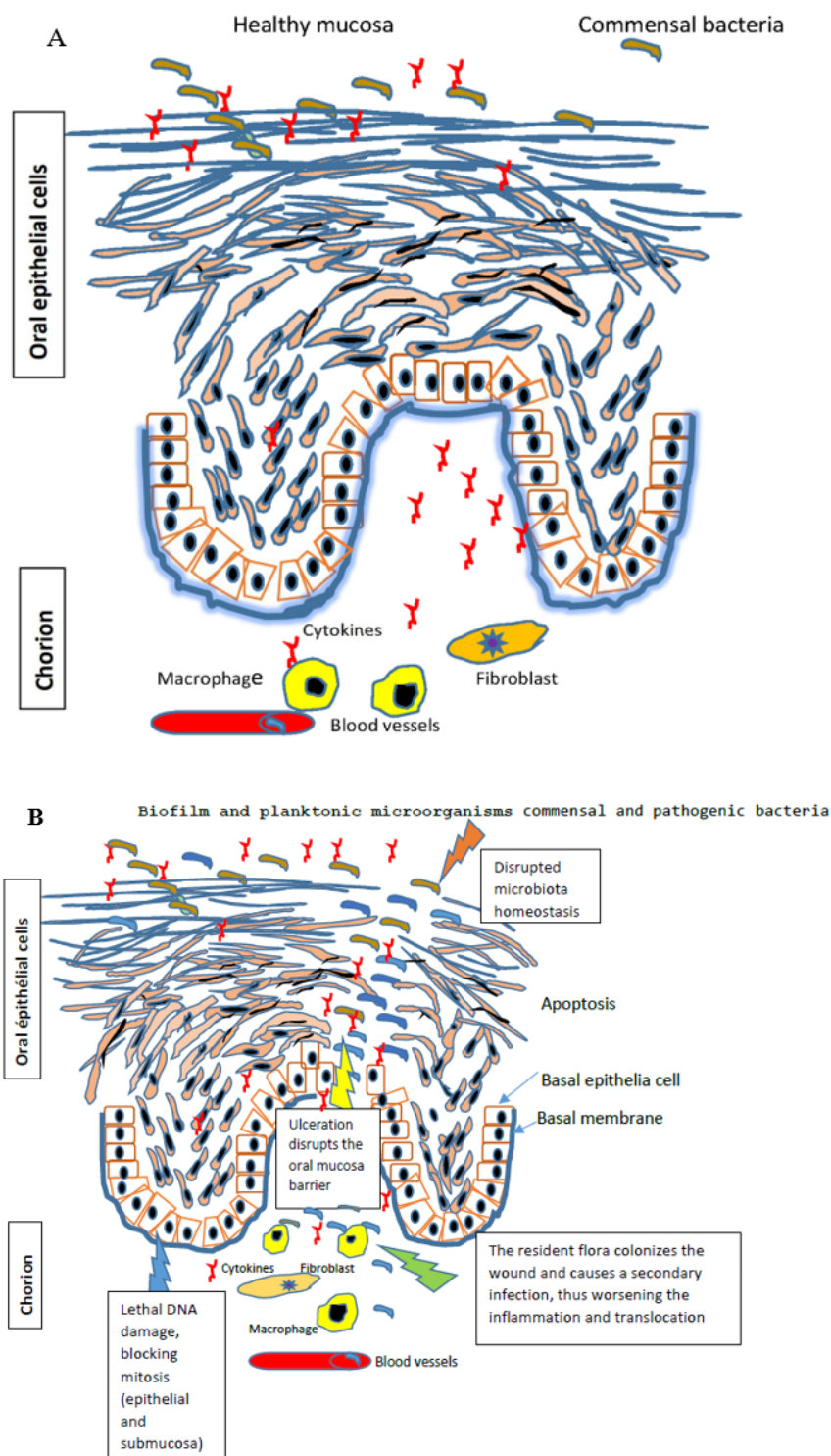


Figure 1. Pathogenesis of cytotoxic chemotherapy-induced oral mucositis. Under normal conditions, the oral immune system naturally maintains homeostasis between the host and its microbiota (A). In patients with ALL, this balance can be disrupted before (orange lightning bolt) and after chemotherapy (blue lightning bolt). These changes affect the oral environment by disrupting the balance between oral microorganisms and the immune system. Local inflammation, in the presence of chemotherapy-induced apoptosis, promotes ulceration of the mucosal barrier (yellow lightning bolt), facilitating microbial translocation (green lightning bolt; B). Source: Created by the authors.

transformation of lymphoid progenitor cells disrupts normal immune surveillance, resulting in systemic and local immune dysfunction.^{34,35} Leukemic infiltration of peripheral lymphoid tissues, including oral mucosal structures, further compromises local immune integrity and alters host–microbe interactions.³⁶

Leukemia can also affect salivary secretion and its antimicrobial components, such as secretory immunoglobulin A, α -amylase, and lysozyme.³⁷ Using next-generation sequencing (NGS), some studies have shown that even before starting chemotherapy, patients with ALL already exhibit a microbiome imbalance due to neoplasia.^{21,32} Studies have also revealed an increased abundance of microorganisms typically associated with systemic infections. Wang *et al.*³² identified, at the phylum-to-genus levels, two taxonomic lineages (Firmicutes/Bacilli/Lactobacillales/Carnobacteriaceae/*Granullicella*) and (Firmicutes/Bacilli/Lactobacillales/Aerococcaceae/*Abiotrophia*) that were more abundant in the supragingival plaque of patients with ALL than in healthy individuals. Under these conditions, the oral cavity ecosystem of patients with ALL provides a favorable environment for the growth of these microorganisms, potentially leading to bacteremia.

5. Oral mucositis pathogenesis as a host–microbe interaction

Based on clinical examination of patients with ALL, some studies have reported that OM occurs mainly during the consolidation phase. During this phase, microbiological analysis of saliva shows a significant reduction in bacterial diversity (alpha biodiversity), including declines in the following taxa: *Neisseria flavescens*, *Prevotella melaninogenica*, and *Porphyromonas*. These analyses confirmed a decrease in bacterial diversity associated with a higher prevalence of OM.³⁸ Wang *et al.*³⁹ performed a comparative microbiological analysis (NGS) between controls and patients undergoing chemotherapy. They demonstrated that oral microbiota dysbiosis is present in all patients with ALL.

These microbiological changes related to the neoplasm can affect the diversity, abundance, and composition of the oral microbiota. Furthermore, chemotherapeutic agents have antimicrobial activity and can reduce neutrophil counts, resulting in local immunosuppression and increased bacterial load. For this reason, several studies consider OM development to be closely linked to chemotherapy-induced dysbiosis and host–microbiome imbalance.^{32,40}

Another recent longitudinal microbiome study²¹

analyzing 12 major bacterial phyla has provided further insights into the ecological dynamics of the oral microbiota during chemotherapy. The dominant phyla identified were Firmicutes, Bacteroidota, Actinobacteriota, Proteobacteria, and Fusobacteriota, which collectively accounted for the highest relative abundances across treatments at days 0, 14, and 21. Interestingly, despite chemotherapy exposure, Firmicutes and Bacteroidota remained relatively stable in composition over time, suggesting ecological resilience and homeostatic recovery by day 21, reflecting partial re-equilibration of the microbiome after treatment perturbation.²¹

However, specific microbial shifts are observed in association with the onset of OM. In particular, Proteobacteriota and Fusobacteriota tend to increase in relative abundance during mucositis episodes, whereas Actinobacteriota show a decreasing trend. In clinically manifest OM, a more pronounced dysbiosis is observed, characterized by the absence or marked reduction of Fusobacteriota, a significant decrease in Firmicutes abundance, and a relative dominance of Bacteroidota. At the genus level, OM is associated with increased abundance of *Prevotella*, *Neisseria*, and *Porphyromonas*, alongside a reduction in typically commensal genera such as *Streptococcus*, *Veillonella*, and *Haemophilus* (Table 1).

The limitations of this review stem from the heterogeneity of the included studies, particularly in chemotherapy protocols, antimicrobial agent administration during treatment, sampling sites, collection methods, cultured microorganisms, and pyrosequencing analyses. These methodological differences hinder the establishment of a definitive association between mucositis and qualitative and/or quantitative alterations in the oral microbiota. Consequently, implementing standardized protocols across studies is warranted to improve the consistency and reliability of the findings.

More specifically, in patients who develop OM, microbial profiling on day 14 of chemotherapy revealed enrichment of taxa including *Streptococcus salivarius*, *Neisseria* spp., *Streptococcus peroris*, *Selenomonas sputigena*, members of *Clostridia*, and *Lachnospirales*, further illustrating the dynamic and stage-dependent nature of chemotherapy-associated microbial shifts.²⁰

The mechanisms underlying these fluctuations in relative abundance remain incompletely understood. However, it is increasingly recognized that microbial communities actively interact with host immune pathways and inflammatory signaling networks. During chemotherapy, these interactions may influence both local immune responses and systemic drug metabolism, thereby

Table 1. Summary of studies analyzing the oral microbiota of pediatric patients with acute lymphoblastic leukemia

Authors	Population	Design	Microbiological results	Health status and immunological results
de Mendonça <i>et al.</i> ⁴¹	71 children with ALL (Brazil).	The study evaluated the association of HSV-1, <i>Candida</i> spp., and oral bacteria with OM in children with ALL; microbial cultures were performed on D14 and D56.	The presence of HSV and <i>Candida</i> spp. was associated with mucositis severity in pediatric ALL; no association was found between bacterial CFU and severity.	NR.
Ye <i>et al.</i> ²²	12/37 ALL among malignancies (age 4–18 years), Sweden.	The study investigated oral bacterial diversity and dynamics in pediatric ALL in relation to OM using 454 pyrosequencing of the 16S rRNA gene from mucosal surface samples.	At diagnosis before CTX, higher microbial diversity was found in patients who later developed mucositis; greater shift in bacterial composition during CTX. Increased <i>Fusobacteria</i> and <i>Spirochaetes</i> , while RA of <i>Proteobacteria</i> decreased in patients who developed mucositis.	NR.
Wang <i>et al.</i> ³²	26 children with ALL (<18 years), China.	The study investigated the biodiversity of supragingival plaque microbiota, analyzed by 454 pyrosequencing.	Leukemia status was associated with RA in oral taxa: Firmicutes (Bacilli, Lactobacillales), Aerococcaceae, Carnobacteriaceae, <i>Abiotrophia</i> , and <i>Granulicatella</i>	Immune status in ALL shapes OM; reduced diversity and altered bacterial abundance. Pre-CTX dysbiosis possibly directly related to malignancy.
Costa <i>et al.</i> ⁴²	26 patients with malignant tumors (4–18 years), Brazil.	The study investigated salivary parameters and cariogenic microbiota (culture) in pediatric oncology patients; correlation with severe OM.	Salivary microbiological parameters remained unchanged during the first 10 weeks of CTX; no influence on OM severity in pediatric oncology patients.	NR.
Wang <i>et al.</i> ³⁹	39 children with ALL (<18 years), China.	The study investigated the effects of CTX on oral health, caries risk, and oral microbiome in pediatric ALL; supragingival samples analyzed by 454 pyrosequencing.	Acute lymphoblastic leukemia was associated with reduced alpha diversity and altered oral microbiota compared with controls; increased Firmicutes (Bacilli, Lactobacillales), Carnobacteriaceae, Aerococcaceae, <i>Abiotrophia</i> , and TM7 in supragingival plaque.	ALL patients on CTX showed poor oral health, high caries risk, altered cariogenic factors, and oral microbiota dysbiosis.
Souza <i>et al.</i> ³⁸	8 children with ALL (4–11 years), Brazil.	The study described changes in the oral microbiota in pediatric ALL during antineoplastic treatment; oral rinse samples were collected during the pre-induction and consolidation phases and analyzed by Illumina MiSeq sequencing.	In the pre-induction phase, <i>Streptococcus</i> , <i>Veillonella</i> , <i>Actinomyces</i> , <i>Prevotella melaninogenica</i> , and <i>Fusobacterium periodonticum</i> were more prevalent. During the consolidation phase, <i>Streptococcus</i> , <i>Veillonella</i> , <i>Alloprevotella</i> , <i>Prevotella melaninogenica</i> , and <i>Neisseria flavescens</i> dominated. The specific bacterial taxa, <i>Prevotella melaninogenica</i> , <i>Neisseria flavescens</i> , and <i>Porphyromonas</i> , are essential components during the consolidation phase of OM.	Blood leukocyte profile correlated with oral taxa during ALL treatment; pre-induction showed negative associations (neutrophils– <i>Capnocytophaga</i> , lymphocytes– <i>Leptotrichia</i>) and positive associations (neutrophils– <i>Moraxella</i> , lymphocytes– <i>Capnocytophaga</i> , leukocytes– <i>Moraxella</i>).
Sanchez-Becerra <i>et al.</i> ²¹	32 children with ALL (2–16 years), Mexico.	The study analyzed oral microbiome dynamics and salivary cytokines before and during CTX (D0, D14, D21) to predict OM; oral rinse/saliva samples were analyzed by 16S rRNA Illumina MiSeq sequencing.	D14 OM was associated with higher α -diversity and opportunistic taxa (<i>Streptococcus salivarius</i> , <i>Neisseria</i> , <i>Streptococcus peroris</i> , <i>Selenomonas sputigena</i> , <i>Clostridia</i> , Lachnospirales); RA in patients who did not develop mucositis remained more stable than in those who did. Dysbiosis can be considered a marker of OM: <i>Streptococcus peroris</i> .	Higher salivary cytokine levels in patients developing OM versus non-OM; marked IL-6 peak associated with OM occurrence on D14.

Notes: The longitudinal studies included in this table were published between 2012 and 2026.

Abbreviations: ALL: Acute lymphoblastic leukemia; CTX: Chemotherapy; D: Day; HSV: Herpes simplex virus; IL-6: Interleukin-6; NR: Not reported; OM: Oral mucositis; RA: Relative abundance.

modulating toxicity profiles and clinical outcomes.^{43,44} Importantly, alterations occur throughout the resident microbiota, where commensal and pathogenic species coexist within a highly dynamic ecosystem that is continuously reshaped by both disease and treatment.

6. Predictive biomarkers of oral mucositis

At the time of diagnosis, greater microbial diversity in the oral cavity may indicate susceptibility to mucositis. Qualitative and dynamic changes in the microbiota are observed in patients with malignancy undergoing chemotherapy, often before the clinical signs of mucositis appear.²² This was confirmed in a recent study²¹ using oral rinse and non-stimulated saliva samples taken before and during mucositis; the study showed that patients with ALL who developed mucositis during treatment exhibited greater α -diversity than those who did not. This contradicts our understanding of established microbiological concepts. In the gut, high α -diversity is considered an indicator of good health. One explanation may be that in the oral cavity, α -diversity is more variable and fluctuates in response to local pathologies (e.g., caries), systemic conditions, and environmental factors such as pollution.^{45,46} Recently, Zhu *et al.*⁴⁷ suggested that pre-treatment analysis of the oral microbiota may help predict bacterial profiles associated with susceptibility to mucositis.

Among microorganisms, Gram-negative bacteria such as *Prevotella* contribute to OM pathogenesis during chemotherapy by promoting inflammation and inducing cytokines such as IL-6. Therefore, some studies consider *Prevotella* an early biomarker of the development of OM.^{16,48} In this context, several microbiological and immunological parameters have been proposed as potential predictors of OM. These include alterations in microbial diversity (including changes in α -diversity), increased relative abundance of opportunistic taxa, and early dysbiosis signatures preceding clinical lesions. In parallel, elevated levels of pro-inflammatory cytokines such as IL-6 have been consistently observed in patients who develop OM. Taken together, these findings suggest that OM is not solely a treatment-induced epithelial injury but rather a multifactorial process in which microbiome composition, immune status, and inflammatory mediators interact to determine disease onset and severity. A preventive and curative approach can be derived from these findings.

7. Implications for prevention and therapy

Oral hygiene plays a central role in both the prevention and management of OM and is essential for maintaining overall oral and systemic health during treatment. Among oral hygiene products, topical applications—such as

sodium bicarbonate, sodium chloride, dental floss, soft-bristled toothbrushes, and lip balm—are recommended for managing OM.

Although mucositis severity generally decreases following completion of chemotherapy, long-term sequelae such as dental caries may persist, highlighting the need for preventive dental care and lifelong follow-up in this vulnerable population.^{49,50} The pre-chemotherapy oral health status of children with ALL is a key determinant of early oral complications. Poor baseline oral conditions are associated with an earlier onset and greater severity of OM once treatment begins.⁵¹ Common early complications include stomatitis, gingivitis, xerostomia, and increased incidence of dental caries.⁵² Even after completion of therapy, epithelial keratinization disorders may persist during maintenance phases and long-term follow-up, reflecting delayed mucosal healing and chronic epithelial dysfunction secondary to mucositis.⁵³ These findings underscore the importance of optimized oral care prior to chemotherapy initiation to reduce treatment-related oral toxicity.

Several other preventive strategies have been proposed to reduce the incidence and severity of chemotherapy-induced OM. Oral cryotherapy has been investigated in pediatric oncology and hematopoietic stem cell transplantation (HSCT) settings, demonstrating potential to reduce mucosal injury.⁵⁴ Practical pediatric adaptations, such as using ice popsicles or frozen nutritional preparations, have been suggested to improve tolerability and implementation. In addition, pharmacological and bioactive interventions are being explored. Sucralfate-based mouth rinses have been proposed based on their cytoprotective properties, extrapolating from their established use in gastrointestinal mucositis; however, further clinical validation is required before routine application in OM.⁵⁵ More recently, glutamine-based mouth rinses have demonstrated efficacy in reducing the incidence, duration, and severity of OM, as well as the associated pain, particularly in children receiving high-dose methotrexate.⁵⁶

7.1. Probiotics for the prevention of oral mucositis

A recent meta-analysis outlined the preventive effectiveness of probiotics in OM induced by cancer treatments. The studies focused primarily on the efficacy of *Lactobacillus* spp. in preventing and alleviating OM. Gaps remain regarding the dosage, duration, and side effects of probiotics in patients with cancer. Similarly, the potential effects of other bacterial species or strains require further research.⁵⁷ *Lactobacillus brevis* CD2 is a probiotic shown to reduce the incidence of OM in immunosuppressed patients

with hematological malignancies undergoing high-dose chemotherapy with HSCT.⁵⁸

Pre-chemotherapy dental management, including scaling, caries control, and treatment of existing oral infections, is considered a prerequisite to reducing the risk of infectious complications during immunosuppression.^{59–61} Infection in these patients can have various origins, including the leukemia itself, chemotherapy, and/or stem cell transplantation, all of which can lead to immunosuppression. If these patients also present with fever and neutropenia, further investigation for an alternative source of infection is recommended, along with initiation of antibiotic therapy.⁶²

8. Conclusion

Pediatric patients with ALL undergoing chemotherapy are particularly vulnerable and more prone to mucositis. The inflammatory state and dysregulated dynamics of the oral bacterial community appear to play a significant role in the development of OM. Enhancing our understanding of the mechanisms underlying chronic inflammatory diseases and of prophylactic interventions before, during, and after chemotherapy will help manage OM. Consequently, to support this theory, it is necessary to conduct a preventive assessment of the oral microbiota in patients undergoing chemotherapy. In this context, several recommendations based on recent data on oral care can improve the preventive and therapeutic management of OM in pediatrics.

- From a practical standpoint, given the natural course of OM, oral hygiene appears most effective when OM begins, typically between days 3 and 10 after chemotherapy initiation, and when it reaches its peak, between days 7 and 14.^{63,64}
- The effectiveness of educating pediatric patients and their caregivers relies on oral health programs that improve adherence (e.g., brochures and oral care calendars), which can reduce the incidence of OM.⁶⁵
- In the pediatric oncology unit, the protocol for managing OM, including oral and dental care, is part of routine nursing practice. This involves staff training, protocol compliance, and the use of an educational brochure and an oral care schedule.⁶⁶

Ideally, the protocol should be standardized to facilitate its integration into routine nursing and dental practice within the pediatric oncology unit. However, validation of the protocol will require long-term multicenter investigations to assess its effectiveness.

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Conflict of interest

The authors declare they have no competing interests.

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