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IMPACT OF ORAL MICROBIOTA DIVERSITY ON POSTOPERATIVE INFECTION RATES IN CLEFT SURGERY

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Annotation. The review summarizes evidence on oral microbiota in children with cleft lip and palate and its association with postoperative infection, fistula and wound dehiscence. Pathogen-enriched colonization is clinically important, while independent prediction by diversity indices remains insufficiently validated.

Key words: cleft lip and palate, oral microbiota, postoperative infection, wound complications, microbiological screening, dysbiosis.

Аннотация. В обзоре обобщены данные о микробиоте полости рта у детей с расщелиной губы и неба и ее связи с послеоперационной инфекцией, свищами и расхождением раны. Патогенная колонизация имеет клиническое значение, однако самостоятельная прогностическая роль индексов разнообразия пока доказана ограниченно.

Ключевые слова: расщелина губы и неба, оральная микробиота, послеоперационная инфекция, раневые осложнения, микробиологический скрининг, дисбиоз.

Annotatsiya. Sharhda lab va tanglay tug'ma kemtigi bo'lgan bolalarda og'iz mikrobiotasi hamda uning operatsiyadan keyingi infeksiya, fistula va yara ochilib ketishi bilan bog'liqligi tahlil qilindi. Patogen kolonizatsiya muhim, ammo xilma-xillik indekslarining mustaqil prognostik roli hali yetarli tasdiqlanmagan.

Kalit so'zlar: lab va tanglay kemtigi, og'iz mikroflorasi, operatsiyadan keyingi infeksiya, yara asoratlari, mikrobiologik skrining, disbioz.

Introduction. Congenital cleft lip and palate is accompanied by persistent communication between the oral and nasal cavities, impaired self-cleaning of the oral cavity and frequent colonization by microorganisms that are uncommon in healthy children. These anatomic and functional conditions are especially important before primary lip repair, palatoplasty and alveolar bone grafting, because the surgical field is located in a heavily contaminated environment.

Postoperative surgical site infection, palatal dehiscence and oronasal fistula are clinically relevant complications that can prolong rehabilitation, increase the need for repeated surgery and worsen functional outcomes. Modern studies increasingly show that the preoperative oral microbiota in cleft patients is not merely a background finding, but a potentially modifiable risk factor. Culture-based investigations repeatedly identified Klebsiella pneumoniae, Staphylococcus aureus, beta-hemolytic streptococci, Moraxella catarrhalis, Candida species and other opportunistic organisms in the preoperative period [2, 4, 5, 12, 16].

At the same time, next-generation sequencing studies suggest that the problem is broader than individual pathogens. Children with cleft palate may have altered alpha and beta diversity, oral-nasal bacterial translocation and persistent dysbiosis after surgical closure [8, 10, 15, 20]. This creates a scientific question of practical importance: can oral microbiota diversity

independently predict postoperative infection risk, or is the clinically useful information still limited mainly to the identification of specific pathogens?

The answer remains controversial. Some studies support preoperative microbiological screening and individualized perioperative prevention, especially in high-colonization settings [1, 4, 16, 17]. Other authors reported poor agreement between preoperative swabs and the flora detected at surgery, and did not find a consistent association with clinical outcomes [14, 19]. Therefore, a structured synthesis of the available evidence is necessary for clinicians involved in surgical treatment and rehabilitation of children with cleft lip and palate.

Aim of the review. The aim of this review was to analyze the current evidence on the association between oral microbiota composition, microbial diversity and postoperative infectious complications in cleft lip and palate surgery, and to define practical implications for microbiological screening and perioperative prevention.

Materials and methods. A structured literature review was performed using the provided search report on the impact of oral microbiota diversity on postoperative infection rates in cleft surgery. Studies were considered relevant when they included patients with cleft lip and/or palate undergoing surgical repair or rehabilitation, assessed oral, nasal or oropharyngeal microbiota by culture-based or molecular methods, and reported postoperative infection, inflammation, wound dehiscence, fistula or related complications.

The review included prospective and retrospective cohorts, cross-sectional studies, audits, systematic reviews and clinically relevant intervention studies. Data were extracted on study population, type of cleft surgery, microbiological method, timing of sampling, infection outcome definition, key taxa or diversity metrics, and confounding factors such as nutrition, feeding method, prior infection and antibiotic use.

Because the included studies were methodologically heterogeneous and used different microbiological techniques, a quantitative meta-analysis was not performed. The findings were synthesized descriptively, with emphasis on evidence directly linking preoperative microbiota or microbial diversity to postoperative infection and wound complications. For journal submission, the reference list was reduced to the most relevant sources and formatted in numbered order.

Results. **Characteristics of the evidence base**. The evidence base is dominated by culture-based microbiological studies. These investigations provide clinically useful information about cultivable organisms, antimicrobial resistance and postoperative wound isolates, but they cannot fully assess community-level microbial diversity. A smaller group of studies used 16S rRNA sequencing or other molecular methods and described dysbiosis, altered community structure and oral-nasal translocation [8, 10, 15, 20].

Most primary studies enrolled relatively small samples and were conducted in single centers. Surgical contexts included primary lip repair, palatoplasty, uranoplasty, alveolar bone grafting and postoperative rehabilitation. The outcome definitions also varied, ranging from surgical site infection and wound inflammation to palatal dehiscence, fistula formation and otitis-related complications. This heterogeneity limits direct comparison between studies and explains why the predictive value of preoperative microbiota remains debated.

Table 1. Main evidence categories linking oral microbiota with postoperative outcomes in cleft surgery

Evidence category	Typical methods	Key findings	Clinical interpretation
Preoperative colonization	Culture of oral, nasal or oropharyngeal swabs	Frequent isolation of K. pneumoniae, S. aureus, beta-hemolytic streptococci, Candida spp. and gram-negative bacilli [4, 5, 7, 16].	Pathogen-enriched colonization is common and may increase wound risk in vulnerable patients.
Specific pathogen–complication links	Culture plus postoperative follow-up	Beta-hemolytic streptococci were linked with dehiscence; Moraxella catarrhalis with fistula risk; K. pneumoniae was a frequent SSI isolate [4, 5, 12].	Targeted screening is most useful when the sampled organism has a known complication profile.
Community-level microbiota	16S rRNA sequencing and bioinformatics	Sequencing studies show dysbiosis, altered beta diversity and oral-nasal translocation. One classifier predicted postoperative inflammation after alveolar bone grafting [10, 11, 20].	Microbial diversity is promising but not yet validated as a standalone clinical predictor.
Screening utility	Preoperative swabs, perioperative cultures	Some studies support screening in high-colonization settings, while others found poor concordance between preoperative and operative flora [14, 19].	Timing, local epidemiology and sampling method strongly influence clinical usefulness.
Preventive interventions	Probiotics, oral hygiene, perioperative antimicrobial strategies	Microbiota-modifying approaches reduced pathogen burden or improved oral microbial balance in single-center studies [15, 17].	Non-antibiotic optimization may support antibiotic stewardship, but larger trials are needed.

Preoperative microbial colonization patterns

Children with unrepaired cleft lip and palate often demonstrate a pathogen-enriched microbiological profile. Several studies reported higher bacterial contamination of the oronasopharyngeal mucosa in cleft patients than in healthy controls, with frequent polymicrobial associations and a relative predominance of gram-negative organisms. This pattern is biologically plausible because the cleft defect permits communication between oral and nasal microbial reservoirs.

The most frequently described organisms include K. pneumoniae, S. aureus and Streptococcus species. K. pneumoniae was common in studies of soft palate defects and was also reported as a major cause of surgical site infection in palatoplasty cohorts [4, 16, 17]. S. aureus, including methicillin-resistant strains in some settings, has also been repeatedly isolated from

cleft patients before surgical repair [7]. Fungal colonization, particularly by Candida species, is another recurrent finding and may become clinically relevant in children receiving repeated antibiotic courses or wearing presurgical orthopedic appliances.

Molecular studies complement culture-based findings by demonstrating disturbed microbial ecology. Sequencing studies described reduced or altered microbial diversity, enrichment of potentially pathogenic genera such as Haemophilus, Neisseria and Porphyromonas, and persistence of oral-nasal translocating bacteria after surgical closure [8, 10, 20]. These data suggest that the cleft-associated microbiota is not simply a collection of isolated pathogens, but a dysbiotic community shaped by anatomy, feeding, oral hygiene and previous treatment.

Pathogens associated with postoperative complications

Several organisms have been associated with postoperative wound complications. In one prospective study, beta-hemolytic streptococci were directly implicated in palatal dehiscence, supporting the importance of detecting and treating clinically relevant streptococcal colonization before surgery [5]. Moraxella catarrhalis was associated with a higher fistula rate in cleft palate repair, although cleft severity and surgical factors remained important confounders [12].

K. pneumoniae has particular relevance in high-colonization settings. It was a frequent preoperative colonizer in children with soft palate defects and was reported among the most common organisms isolated in postoperative surgical site infection [4, 16, 17]. Gram-negative bacilli, including Enterobacter and Pseudomonas species, were also described in postoperative wound inflammation, especially in the early days after uranoplasty.

The transition from colonization to infection is strongly influenced by host factors. Underweight children, bottle-fed infants, patients with recent hospital admission and those with preoperative respiratory or oral infections appear more vulnerable to postoperative infection [4]. Therefore, microbiological findings should not be interpreted in isolation; they should be combined with nutritional assessment, oral hygiene evaluation and review of previous antibiotic exposure.

Predictive value of microbial diversity

The central question of this review is whether microbial diversity itself predicts postoperative infection. The strongest direct evidence comes from a sequencing-based study of children undergoing alveolar bone grafting, where a preoperative salivary microbiota classifier predicted postoperative inflammation with good sensitivity and specificity [10]. This finding supports the concept that community-level microbiome profiling can detect risk patterns not captured by single-organism culture.

However, the evidence remains limited. Most culture-based studies did not measure alpha diversity, beta diversity or taxonomic richness, and many sequencing studies described microbial differences without linking them to rigorously defined postoperative infection outcomes. Consequently, current evidence supports an association between dysbiosis and complications but does not yet establish microbial diversity indices as independent prognostic markers across all cleft surgical procedures.

From a clinical perspective, the most reliable current approach is combined assessment: detection of high-risk pathogens, evaluation of the overall microbial context when molecular testing is available, and parallel assessment of host and surgical risk factors. Microbiome-based prediction should be considered promising, but not yet sufficient to replace conventional clinical risk assessment.

Preoperative screening and perioperative prevention

The value of routine preoperative microbiological screening is controversial. Some studies concluded that screening can guide antibiotic selection and improve perioperative

preparation, especially when pathogenic colonization is frequent [1, 16, 17]. In contrast, studies from the United Kingdom found that preoperative swabs matched perioperative flora in only about half of cases and did not consistently correlate with clinical outcomes [14, 19].

This contradiction is best explained by differences in local colonization burden, sampling time and laboratory technique. A swab taken too early may not represent flora present on the day of surgery. Culture may miss important uncultivable organisms, whereas molecular methods may detect organisms whose clinical significance is uncertain. Therefore, when screening is used, sampling should be close to surgery and results should be interpreted according to local antimicrobial resistance patterns.

Preventive strategies should not rely only on prolonged antibiotic administration. Recent literature supports individualized, usually short-course perioperative antibiotic use and highlights the potential role of oral hygiene, probiotics, phytotherapy and other microbiota-modifying interventions [3, 13, 15, 17]. These approaches may help reduce pathogen burden while limiting antimicrobial resistance, but they require stronger randomized evidence before routine implementation.

Oral-nasal translocation and long-term dysbiosis

The cleft defect creates a unique ecological niche in which oral, nasal and pharyngeal bacteria can interact. In healthy children these microbial habitats remain relatively separated, whereas cleft-related anatomic communication facilitates translocation of organisms between them. This mechanism explains why several studies detected organisms in cleft sites that are more typical of the nasal cavity, respiratory tract or intestinal environment.

Sequencing studies provide additional support for this concept. Bacterial networks in children with cleft palate include oral taxa that appear to contribute to the nasal microbial profile, and this overlap may persist even after surgical repair [20]. Postoperative closure reduces the size of the communication and improves oral function, but it does not always fully normalize the microbial community. This is important when interpreting persistent oral malodor, recurrent upper airway inflammation or delayed mucosal healing after surgery.

Long-term dysbiosis may also be influenced by orthodontic appliances, residual fistulae, scar anatomy and variations in oral hygiene. Children undergoing staged rehabilitation are repeatedly exposed to dental impressions, obturators, nasoalveolar molding appliances, fixed orthodontic appliances and surgical interventions. Each of these factors may modify biofilm composition and should be documented in future clinical studies.

Host and perioperative modifiers of infection risk

Microbial colonization alone does not inevitably lead to infection. In several cohorts, potentially pathogenic organisms were identified before surgery, yet serious postoperative infection remained uncommon. This indicates that the transition from colonization to infection depends on the interaction between microbial virulence, host defense, local tissue perfusion and surgical technique.

Nutritional status is one of the most important modifiers. Underweight children have impaired wound healing and reduced resistance to infection, and nutritional risk was strongly associated with surgical site infection in at least one palatoplasty cohort [4]. Feeding method is also relevant because bottle feeding may increase contamination and modify oral biofilm. Preoperative respiratory infection, anemia, poor oral hygiene and recent hospitalization should therefore be included in the routine preoperative checklist.

Perioperative factors include duration of surgery, quality of tissue handling, suture tension, intraoperative contamination, antibiotic timing and postoperative wound care. Microbiological screening should be interpreted together with these factors. A child with high-risk colonization but good nutrition and optimized oral sanitation may have a different risk

profile from a malnourished child with active respiratory infection and resistant gram-negative colonization.

Antimicrobial resistance and antibiotic stewardship

Antimicrobial resistance is increasingly relevant in cleft surgery. Several studies reported resistance to commonly used perioperative antibiotics, including first-line beta-lactams, and methicillin-resistant Staphylococcus aureus was described in some preoperative samples [7]. This is clinically important because empirical prophylaxis may fail when local flora contains resistant organisms.

The literature does not support indiscriminate prolonged postoperative antibiotic therapy for all cleft procedures. A more rational approach is short-course prophylaxis according to institutional protocol, with extension or modification only when there is clinical infection, high-risk colonization, immunological vulnerability or microbiological evidence requiring targeted therapy [3, 13]. Such an approach can reduce unnecessary antibiotic exposure and protect the developing microbiome of children.

In practice, antibiotic selection should be based on the expected pathogens, local resistance data and patient-specific risk. When preoperative cultures identify beta-hemolytic streptococci, resistant staphylococci or gram-negative bacilli, the result should be discussed with the surgical and pediatric teams. The aim is not to sterilize the oral cavity, which is impossible, but to reduce clinically meaningful pathogen burden and prevent wound contamination by high-risk organisms.

Non-antibiotic microbiota-modifying interventions

Because the oral cavity contains complex microbial communities, non-antibiotic strategies may be particularly valuable. Supervised oral hygiene before surgery can reduce biofilm load and improve mucosal condition. Toothbrushing interventions in children with cleft lip and palate have been associated with favorable temporal shifts in the oral microbiome, including reduction of potentially pathogenic genera and increase of health-associated taxa [15].

Probiotics and phytotherapeutic preparations have also been investigated. In selected studies, preoperative probiotics reduced the prevalence of pathogenic microorganisms and decreased the number of cultured species, while phytotherapeutic approaches improved postoperative oral microflora and accelerated resolution of inflammation [17]. These findings are promising, but many studies are single-center, non-randomized or use surrogate microbiological outcomes rather than hard clinical endpoints.

Future microbiota-modifying prevention may include combined protocols: professional oral sanitation, caregiver education, dietary and nutritional optimization, short-course targeted antimicrobial prophylaxis, probiotics, antiseptic rinses appropriate for age, and potentially bacteriophage-based decolonization when supported by clinical trials. Such protocols should be evaluated using both microbiological and clinical endpoints.

Table 2. Practical implications for preoperative preparation and postoperative prevention

Clinical step	What to assess	Suggested action	Expected benefit
Initial preoperative visit	Nutrition, feeding method, oral hygiene, respiratory symptoms, recent antibiotics	Correct modifiable risks before elective surgery when possible	Lower probability that colonization will progress to infection
Microbiological screening	High-risk pathogens: beta-hemolytic streptococci, S. aureus/MRSA, K. pneumoniae and other gram-negative bacilli	Use close-to-surgery sampling in high-colonization or high-risk patients	More rational prophylaxis and targeted sanitation
Oral sanitation	Dental plaque, mucosal inflammation, Candida signs, appliance contamination	Professional cleaning, caregiver instruction and age-appropriate hygiene protocol	Reduced biofilm load and improved mucosal healing conditions
Perioperative antibiotics	Local resistance, culture results, allergy history, surgical complexity	Avoid unnecessary prolonged therapy; individualize when risk is high	Antibiotic stewardship and reduced dysbiosis
Postoperative follow-up	Wound inflammation, dehiscence, fistula, fever, feeding difficulty	Early clinical review and culture if infection is suspected	Timely treatment and prevention of secondary complications

DISCUSSION

The available literature indicates that children with cleft lip and palate frequently harbor an oral microbiota enriched with opportunistic pathogens. This finding is consistent across geographically diverse studies and is clinically plausible because the unrepaired cleft permits microbial exchange between oral, nasal and pharyngeal niches. The most consistent clinical signal concerns specific organisms rather than diversity indices: K. pneumoniae, S. aureus, beta-hemolytic streptococci and M. catarrhalis have all been linked to postoperative infection, dehiscence or fistula in selected cohorts [4, 5, 12, 16].

Nevertheless, the emerging sequencing literature changes the interpretation of risk. Community-level dysbiosis may create an ecological background in which pathogens are more likely to dominate, persist and interact with host inflammatory responses. The persistence of oral-nasal translocating bacteria after palatoplasty indicates that surgical closure does not always fully normalize the microbiome [20]. This may partly explain recurrent inflammation, delayed healing or persistent otolaryngological complications in some patients.

A key limitation is the lack of large multicenter studies using standardized sampling, sequencing and clinical endpoints. Existing studies differ in age, surgical stage, antibiotic protocols, geography, nutrition and oral hygiene practices. Such heterogeneity makes it difficult to distinguish whether dysbiosis is an independent risk factor or a marker of broader vulnerability. Future studies should combine microbiome sequencing, conventional cultures, nutritional assessment, immune markers and well-defined postoperative outcome measures.

For clinical practice, the evidence supports a risk-adapted approach. In settings with high colonization by gram-negative organisms or resistant staphylococci, targeted preoperative cultures may be useful. In lower-colonization settings, routine screening of all patients may have

limited value unless performed close to surgery and linked to an actionable protocol. Regardless of screening strategy, oral sanitation, treatment of active infections, nutritional optimization and rational antibiotic prophylaxis remain essential components of cleft surgery preparation.

The review also highlights a potential direction for non-antibiotic prevention. Probiotics, supervised oral hygiene and phytotherapeutic approaches have shown encouraging microbiological or clinical effects in single-center studies [15, 17]. Their role should be tested in controlled trials, including outcomes such as surgical site infection, fistula, dehiscence, postoperative pain, antibiotic consumption and microbiota recovery.

A practical implication for cleft centers is the need to move from isolated swab results toward integrated perioperative risk stratification. A useful model should include microbial findings, nutritional status, local inflammation, previous antibiotic exposure, planned surgical procedure and social factors affecting oral hygiene. Such a model may help identify children who need intensified preoperative sanitation or targeted prophylaxis while avoiding unnecessary treatment in low-risk patients.

For research, the most important step is standardization. Future studies should define sampling sites, sampling time, sequencing platform, culture methods, antibiotic protocol and outcome criteria before recruitment. Infection should be separated from non-infectious wound inflammation, and fistula should be analyzed with adjustment for cleft width, surgical technique and tissue tension. Without this standardization, the independent contribution of oral microbiota diversity will remain uncertain.

CONCLUSIONS

1. Children with cleft lip and palate frequently have a pathogen-enriched oral and oronasal microbiota before surgical repair.

2. Specific organisms, especially K. pneumoniae, S. aureus, beta-hemolytic streptococci and M. catarrhalis, are more consistently linked with postoperative complications than global diversity indices.

3. Molecular microbiome profiling shows promise for predicting postoperative inflammation, but current evidence is insufficient to use diversity metrics as independent routine prognostic markers.

4. Preoperative microbiological screening may be useful in high-colonization settings and when performed close to surgery, but its universal value remains debated.

5. Future prevention should combine oral sanitation, nutritional optimization, rational antibiotic prophylaxis and well-studied non-antibiotic microbiota-modifying interventions.

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