Original Article

THE ASSOCIATION BETWEEN CHRONIC ORAL CANDIDIASIS AND EARLY CHILDHOOD CARIES: RESULTS OF A CLINICAL-LABORATORY STUDY

Elima Ruslanovna Tsitsaeva[1], Ayub Albekovich Geshkaev[1], Maryam Vakhaevna Isaeva[1], Ayna Alievna Khutueva[1], Khedi Ruslanovna Gadieva[1], Petimat Osmanovna Dzhamaldinova[1], Yunus Shchamsudievich Dukaev[1], Magomed Anvarovich Medzhidov[2], Samur Edikovich Mirzoev[2], Musa Magomedovich Bayrambekov[2]

[1]*Faculty of Pediatrics, Chechen State University named after A.A.Kadyrov, Grozny, Republic of Chechnya, Russia. Etsitsayeva@inbox.ru*
[2]*Faculty of Dentistry, Saratov State Medical University named after V.I. Razumovsky, Saratov, Russia.*

Received: 25 November 2025; **Revised:** 05 February 2026; **Accepted:** 09 February 2026 https://doi.org/10.51847/0FPw3VkGzj

ABSTRACT

This study aimed to assess the relationship between chronic oral candidiasis and the development of early childhood caries (ECC) in preschool-aged children. A prospective comparative clinical-laboratory study included 70 children aged 3-6 years, divided into two groups: a main group (n=35) with verified chronic oral candidiasis and a control group (n=35). All participants underwent a comprehensive dental examination to determine caries intensity indices (DMFT, DMFS) and oral hygiene status (OHI-S), parental questionnaire-based analysis of dietary habits, and microbiological culture for the detection and quantitative determination of *Candida albicans*. The results showed that caries intensity was significantly higher in children with candidiasis: the DMFT index was 6.4 ± 3.1 compared to 2.3 ± 1.9 in controls ($p<0.001$). *Candida albicans* was isolated from all children in the main group with a mean concentration of $4.2*10^4$ CFU/mL, while carriage in the control group was detected in only 22.9% of children at a substantially lower concentration. Statistical analysis revealed a strong direct correlation between fungal concentration and the DMFS index ($rs=0.82$, $p<0.001$), and multiple regression confirmed that *C. albicans* colonization is an independent predictor of caries intensity. Therefore, severe forms of ECC are linked to persistent oral candidiasis. Because a high concentration of Candida albicans is a substantial biological risk factor, comprehensive caries prevention programs for preschoolers should incorporate microbiological diagnostics and, if needed, antifungal medication.

Key words: Early childhood caries, Oral candidiasis, *Candida albicans*, Preschool children, Oral microbiology, Risk factors.

Introduction

Oral health in early childhood is a cornerstone of overall physical development, social skill formation, and quality of life [1-3]. Among numerous pathologies in this domain, two hold particular clinical and epidemiological significance for preschoolers: early childhood caries (ECC) and oral candidiasis [4, 5]. Traditionally viewed within different paradigms (dental and pediatric), modern evidence suggests these conditions may be closely linked by shared pathogenic pathways. Their combined influence creates a vicious cycle, exacerbating the course of each condition and posing a complex therapeutic challenge that requires a multidisciplinary approach.

Oral candidiasis, or candidal stomatitis, is an infectious lesion of the oral mucosa caused by opportunistic yeast-like fungi of the genus *Candida* (predominantly *C. albicans*) [6-8]. Epidemiological data in the Russian Federation indicate a consistently high prevalence of this pathology among young children. It accounts for 30% to 45% of all infectious-inflammatory diseases of the oral cavity in children under 3 years of age. The average national incidence rate among children aged 0-6 years is 5-7 cases per 1000 children of the corresponding age, with notable regional variability. In regions with warm, humid climates and high population density, this rate can increase by 15-20%. Children in their first year of life are the most vulnerable; however, chronic and recurrent forms, which are of greatest interest for studying long-term consequences, are also actively diagnosed in the preschool period.

Infection occurs both endogenously against a background of dysbiosis and exogenously: vertically (during childbirth from a mother with urogenital candidiasis) or via contact-household routes [9-12]. The classic acute pseudomembranous form ("thrush") with characteristic curd-like plaques is well-known. However, atypical, attenuated, and chronic forms are increasingly encountered in practice: angular cheilitis (perlèche), atrophic candidiasis (manifesting as painful erythema), and hyperplastic candidiasis with dense plaques [13, 14]. It is precisely these forms that often remain undiagnosed, perpetuating a constant inflammatory process.

The high-risk group for developing chronic oral candidiasis comprises children with factors disrupting immune homeostasis or microbial balance: those born prematurely or with perinatal pathology; receiving long-term antibacterial or inhaled corticosteroid therapy; with nutritional disorders,

hypovitaminosis (especially of B vitamins and iron), endocrinopathies (e.g., diabetes mellitus); and those with congenital or acquired immunodeficiencies [15-18]. A key unifying risk factor for both studied diseases is a high-carbohydrate diet. Frequent consumption of readily fermentable sugars not only directly stimulates cariogenic microflora but also serves as a powerful trophic factor for the growth, adhesion, and pathogenicity of *Candida spp* [19, 20].

The consequences of chronic fungal infection extend beyond local discomfort. The prolonged persistence of *Candida* sustains chronic inflammation, impairs the mucosal barrier function, and, most importantly in the context of caries pathogenesis, can radically alter the ecosystem of dental plaque [21, 22]. Modern research has revealed that *C. albicans* exhibits high adhesiveness to enamel hydroxyapatite, can actively ferment sugars producing organic acids (lactic, acetic), and synthesize extracellular polysaccharides that strengthen the biofilm matrix [23, 24]. Furthermore, fungi demonstrate high tolerance to acidic environments, allowing them not only to survive but also to actively participate in establishing a low pH within dental plaque [25]. A model of synergy emerges where *C. albicans* and classic cariogenic bacteria (e.g., Streptococcus mutans) mutually enhance each other's pathogenicity, creating a more aggressive and resilient biofilm [26, 27].

Early childhood caries, defined as the presence of one or more decayed, filled, or missing (due to caries) teeth in a child under 71 months of age, remains one of the most common chronic diseases of childhood [28, 29]. Its etiology is multifactorial, yet the central role belongs to the microbial factor under specific dietary conditions. The hypothesis regarding the involvement of fungal microflora in cariogenesis is gaining increasing support in vitro; however, clinical studies, particularly those focused on preschoolers and chronic forms of candidiasis, are scarce and contradictory. Most research is centered on acute manifestations in infants, overlooking the potentially more significant, in terms of long-term dental consequences, chronic persistence of the fungus [30-32]. A visual representation of this complex interrelationship is presented in **Figure 1**, integrating key risk factors and pathogenic pathways.

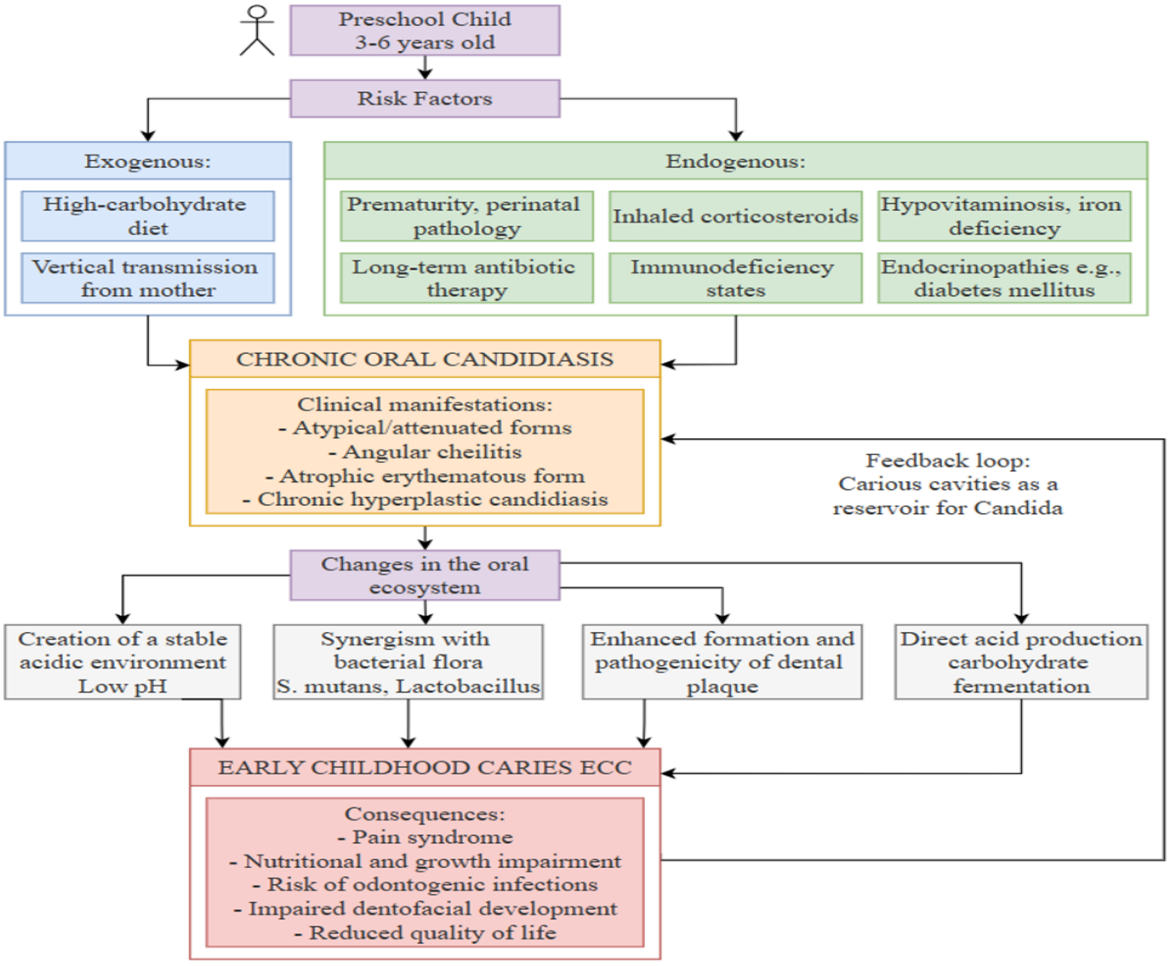

Figure 1. Conceptual model of the relationship between risk factors, chronic oral candidiasis, and early childhood caries in preschool children

The diagram clearly illustrates how diverse exogenous and endogenous risk factors can lead to the development of chronic oral candidiasis, which, in turn, through a series of interrelated mechanisms (creation of an acidic environment, synergy with bacteria, direct acid production), creates the conditions for the onset and aggressive course of early childhood caries. It is important to note the presence of a feedback loop: formed carious cavities serve as ideal anatomical reservoirs for the persistence and protection of *Candida* from the action of saliva and antifungal agents, closing the pathological cycle [33].

Thus, the existing scientific basis allows us to hypothesize that chronic oral candidiasis is a significant biological risk factor for the development and progression of ECC in preschool children. However, targeted studies combining thorough dental diagnostics with modern microbiological methods are necessary to confirm this hypothesis at the clinical level.

The present study aimed to assess, based on a comprehensive clinical-laboratory analysis, the relationship between the presence of chronic oral candidiasis and the prevalence and intensity of early childhood caries in preschool children (3-6 years).

Materials and Methods

This study is a prospective comparative clinical-laboratory investigation, jointly organized at the clinical facilities of the Chechen State University named after A.A. Kadyrov and the Saratov State Medical University named after V.I. Razumovsky. The study was conducted from September 2023 to May 2024. Its design was developed for a comprehensive assessment of dental status, dietary patterns, and microbiological indicators in preschool children with chronic oral candidiasis.

Seventy kids, ages three to six, participated in the study and were split into two observation groups. The main group consisted of 35 children with a verified diagnosis of chronic oral candidiasis, confirmed clinically and microbiologically. The control group, comparable in age and sex, consisted of 35 children without clinical signs of oral candidiasis and with no history of the condition. Acute infectious diseases at the time of examination, severe somatic pathologies in the decompensation stage, congenital maxillofacial malformations, systemic antifungal or antibacterial drug use within the previous four weeks, and documented diabetes mellitus were common exclusion criteria for all participants.

Each child underwent a comprehensive examination consisting of three key components. The first stage was a structured questionnaire for parents or legal guardians to assess the child's dietary habits. The questionnaire, developed based on validated surveys, included questions about the frequency and type of consumption of major food groups, with an emphasis on readily fermentable carbohydrates: frequency of sweet beverage consumption (juices, soft drinks), confectionery, sweet baked goods, and the history of nocturnal feeding habits. Responses were coded and analyzed to calculate a total cariogenic dietary index.

The second stage was a detailed dental examination conducted under standard conditions using dental instruments. The condition of hard tooth tissues was assessed using a visual-tactile method under artificial lighting. The number of decayed, filled, and extracted primary teeth was recorded with the calculation of caries intensity indices (DMFT for teeth and DMFS for surfaces). To objectively assess oral hygiene status, the simplified Oral Hygiene Index (OHI-S) by Green-Vermillion was determined by staining six key teeth with fuchsin solution and calculating plaque scores on vestibular and lingual surfaces. Additionally, the presence and location of white spot lesions (enamel demineralization) were assessed.

The third, laboratory stage, involved the diagnosis of oral candidiasis and the quantitative assessment of fungal contamination. Using a sterile spatula, scrapings were taken from the buccal mucosa in the affected area (or from the dorsal surface of the tongue) and from supragingival dental plaque on the approximal surfaces of the first and second primary molars. The obtained material was transported in Amies transport medium. Microbiological investigation included culture on selective chromogenic CHROMagar™ Candida medium with subsequent incubation under aerobic conditions at 37°C for 72 hours. Identification of *Candida albicans* was based on colony morphology and characteristic color, and semi-quantitative assessment was performed to determine colony-forming unit (CFU/mL) concentration. For all children in the main group and for a portion of the control group with positive growth, additional microscopy of a native preparation with potassium hydroxide was performed to confirm the presence of fungal elements.

Statistical analysis of the obtained data was performed using the IBM SPSS Statistics 26.0 software package. Quantitative parameters with a normal distribution are presented as mean ± standard deviation (M ± SD). For comparing mean values between two independent groups, Student's t-test was used; for three or more groups, one-way analysis of variance (ANOVA) with Tukey's post-hoc test was applied. Data with a non-normal distribution are described as median and interquartile range (Me [Q25; Q75]), and the non-parametric Mann-Whitney U test was used for their comparison. Analysis of qualitative characteristics was performed using the chi-square (χ^2) test or Fisher's exact test. For multivariate analysis and assessment of the independent contribution of various factors (presence of candidiasis, dietary index, hygiene) to caries intensity, multiple linear regression was used. To

assess the strength and direction of relationships between parameters, Spearman's rank correlation coefficient (rs) was calculated. In all analyses, differences were considered statistically significant at a significance level of $p < 0.05$.

The study was conducted in strict accordance with the ethical principles of the Helsinki Declaration. The study protocol was approved by the local ethics committees of the participating universities. Parents or legal guardians of all participating children were informed about the study's aims and methods and provided voluntary written informed consent.

Results and Discussion

The clinical-laboratory examination was completed for all 70 children included in the study. The groups were comparable in terms of basic demographic indicators. The mean age of children in the main group was 4.7 ± 1.1 years, and in the control group, 4.5 ± 1.2 years ($p>0.05$). The sex distribution also showed no statistically significant differences: there were 54.3% boys in the main group and 51.4% in the control group ($p>0.05$).

Questionnaire data, presented in **Table 1**, revealed significant differences in dietary patterns between the groups. The cariogenic dietary index was significantly higher in the main group (6.8 ± 2.1 points versus 3.9 ± 1.8 points in the control, $p<0.001$). The most significant differences concerned the frequency of sweet beverage consumption between main meals and the history of nocturnal feeding with sweet products, which was reported for the vast majority of children with chronic candidiasis.

Table 1. Dietary characteristics of children in the compared groups (n=70)

Parameter	Main Group (n=35)	Control Group (n=35)	p-value
Mean Cariogenic Dietary Index (points, M±SD)	6.8 ± 2.1	3.9 ± 1.8	<0.001
Frequency of sweet beverage consumption >2 times/day, n (%)	28 (80.0%)	10 (28.6%)	<0.001
History of nocturnal feeding (sweet), n (%)	23 (65.7%)	7 (20.0%)	<0.001
Daily consumption of confectionery, n (%)	30 (85.7%)	18 (51.4%)	0.002

The results of the dental examination, summarized in **Table 2**, demonstrated a pronounced difference in oral health status. Caries intensity in the main group was 2.8 times higher than in the control group for the DMFT index (6.4 ± 3.1 versus 2.3 ± 1.9, $p<0.001$) and 3.1 times higher for the DMFS index (11.2 ± 6.5 versus 3.6 ± 3.1, $p<0.001$). Oral hygiene was also significantly worse in the group of children with candidiasis (OHI-S 2.5 ± 0.7 versus 1.4 ± 0.5, $p<0.001$).

Table 2. Dental status of children in the compared groups (n=70)

Parameter	Main Group (n=35)	Control Group (n=35)	p-value
DMFT index (teeth, M±SD)	6.4 ± 3.1	2.3 ± 1.9	<0.001
DMFS index (surfaces, M±SD)	11.2 ± 6.5	3.6 ± 3.1	<0.001
OHI-S Index (points, M±SD)	2.5 ± 0.7	1.4 ± 0.5	<0.001
Children with enamel demineralization foci, n (%)	22 (62.9%)	8 (22.9%)	<0.001

Microbiological data **(Table 3)** confirmed not only the presence but also a high level of fungal contamination in the children of the main group. *Candida albicans* was isolated from the mucosa in 100% of children in this group with a mean concentration of $4.2*10^4$ CFU/mL. In the control group, *C. albicans* carriage was detected in only 22.9% of children, and the concentration was two orders of magnitude lower ($1.5*10^2$ CFU/mL). Moreover, fungi were detected in the dental plaque of children in the main group in 88.6% of cases, indicating their integration into the cariogenic biofilm.

Table 3. Results of microbiological investigation (n=70)

Parameter	Main Group (n=35)	Control Group (n=35)	p-value
Isolation of *C. albicans* from mucosa, n (%)	35 (100%)	8 (22.9%)	<0.001
Concentration of *C. albicans* (log CFU/mL, M±SD)	4.62 ± 0.51	2.18 ± 0.91*	<0.001
Detection of *C. albicans* in dental plaque, n (%)	31 (88.6%)	3 (8.6%)	<0.001
***Calculated for positive samples (n=8).**			

A key result of the study was the identified system of strong correlations **(Table 4)**. The closest direct association was observed between the concentration of *C. albicans* on the mucosa and caries intensity (rs=0.82 for DMFS). A strong correlation was also found between the cariogenic dietary index and fungal concentration (rs=0.78), as well as between poor hygiene and caries intensity (rs=0.74). Multiple regression analysis showed that a high level of *C. albicans* colonization is an independent predictor of caries intensity even after accounting for the influence of hygiene and diet (β=0.51, $p<0.01$).

Table 4. Correlation matrix (Spearman's coefficient, rs) of key parameters for the entire sample (n=70)

Parameter	DMFS Index	*C. albicans* Concentration	Cariogenic Dietary Index	OHI-S Index
***C. albicans* Concentration**	0.82**	1	0.78**	0.69**
Cariogenic Dietary Index	0.76**	0.78**	1	0.65**
OHI-S Index	0.74**	0.69**	0.65**	1
Note: ** p < 0.01				

The obtained results provide compelling clinical evidence of a significant association between chronic oral candidiasis and extremely high intensity of early childhood caries [34, 35]. The identified DMFS index values in the main group (11.2 ± 6.5) not only exceed control levels but also meet the criteria for severe ECC, consistent with studies noting a more aggressive nature of the carious process in mixed infections involving fungal flora [36-39]. Our work quantitatively confirms the hypothesis proposed by several researchers that *Candida albicans* is not an incidental "bystander" but an active participant in the cariogenic biofilm, especially under chronic conditions [40-42].

The exceptionally strong positive correlation found between the concentration of *C. albicans* on the mucosa and the DMFS index (rs=0.82) is the central finding of the study. This association proved to be even more pronounced than the correlation of caries with hygiene or diet separately [43-45]. This fact suggests that fungal persistence acts as a powerful catalyst for cariogenesis. The mechanism is likely realized through several pathways described in vitro. First, the ability of *C. albicans* to actively ferment sugars with acid production, directly contributing to enamel demineralization, is well-documented [46, 47]. Second, as experimental studies have shown, fungi can engage in synergy with Streptococcus mutans, enhancing extracellular polysaccharide matrix formation and increasing biofilm acidity and resilience [48, 49]. The high percentage of fungi detected directly in dental plaque (88.6%) in our study serves as clinical confirmation of their integration into these structures.

An important aspect is the identification of common significant risk factors. The high cariogenic dietary index in the main group acts not only as an independent factor but also, likely, as a key condition for maintaining chronic fungal infection. It is known that sucrose significantly enhances the adhesion and growth of *Candida* [50, 51]. Thus, a vicious cycle is formed: a high-carbohydrate diet promotes fungal colonization, which, in turn, enhances the cariogenic potential of the plaque formed under the same dietary conditions. This explains why caries develops more aggressively in children with candidiasis, even with seemingly comparable diets.

Our data on the relationship between colonization (rs=0.69) also finds explanation in the literature [52-54]. Accumulation of dental plaque creates anaerobic niches with low oxidation-reduction potential, which is a favorable environment for fungi. Furthermore, chronic gingival inflammation, concomitant with poor hygiene, may locally suppress the immune response, facilitating the persistence of fungal infection [55, 56].

The results of the multiple regression analysis, indicating the independent contribution of *Candida* colonization to caries intensity, have key practical significance. This means that the very fact of chronic fungal infection substantially increases the risk of developing ECC, even if attempts are made to control diet and hygiene. Consequently, standard preventive measures in this case may be insufficient [57-67]. This conclusion is consistent with studies in which children with recurrent caries often showed an atypical microbial biofilm profile with a high proportion of fungi [68-74].

A limitation of our study is its cross-sectional design, which does not allow establishing a cause-and-effect relationship: whether massive *Candida* colonization leads to caries, or carious cavities become reservoirs for the fungi. However, the strength of the identified associations and existing experimental data on the pathogenic role of fungi in enamel demineralization tips the scales in favor of the former hypothesis. Long-term prospective studies are necessary for its definitive confirmation [75-85].

Thus, the present study allows us to view chronic oral candidiasis not as an isolated local mucosal infection, but as a significant biological marker of high risk for developing severe forms of early childhood caries. The identified systemic interrelationships justify the need to integrate microbiological diagnostics (detection and quantitative

assessment of *Candida*) into the examination algorithm for children with multiple caries, especially in the presence of atypical mucosal lesions. A comprehensive approach, including antifungal therapy, dietary correction, and intensive hygiene, may become a new promising direction in the personalized prevention of ECC for this category of patients.

Conclusion

This comprehensive study allows for the formulation of several significant conclusions supporting the central hypothesis regarding the substantial role of chronic oral candidiasis in the development of severe caries in preschoolers.

The obtained data unequivocally indicate that children with chronic candidiasis constitute a distinct category of high dental risk. It was established that caries intensity in this group is 2.8 times higher than in healthy peers (DMFT index 6.4 ± 3.1 versus 2.3 ± 1.9), reaching criteria for severe and complicated progression. In this context, the key factor associated with such severity of lesions is not merely the presence, but the high concentration of *Candida albicans* on the mucosa, averaging $4.2*10^4$ CFU/mL. The exceptionally strong direct correlation between this microbiological parameter and the DMFS index ($r_s=0.82$, $p<0.001$) indicates that fungal colonization is not a concomitant phenomenon but a significant biological driver of cariogenesis.

An important practical finding is the confirmation of common key modifiable risk factors. 80% of children with candidiasis regularly consumed sweet beverages more than twice a day, and their total cariogenic dietary index (6.8 ± 2.1 points) was significantly higher than in the control group. This creates a pathogenic cycle where a high-carbohydrate diet sustains chronic fungal infection, which, in turn, through synergy with bacterial flora and direct acid production, sharply increases the demineralizing potential of dental plaque. Notably, multiple regression analysis identified *C. albicans* colonization as an independent predictor of caries intensity ($\beta=0.51$, $p<0.01$), even after adjusting for hygiene level and dietary characteristics.

Thus, the results of this work have direct clinical significance and justify the need to revise the standard approach to managing children with aggressive early caries. The detection of a DMFS index exceeding 10 in a child, especially combined with atypical mucosal changes, should be an indication for mandatory microbiological investigation (culture) to detect and quantitatively assess *C. albicans*. High colonization levels (on the order of 10^4 CFU/mL and above) require the prescription of a comprehensive protocol integrating three directions: 1) targeted antifungal therapy to sanitize the focus of chronic infection; 2) strict dietary correction with a reduction in the frequency of sugar consumption to 1-2 times per day; 3) an intensive, controlled hygiene regimen to manage plaque formation.

The implementation of such a differentiated algorithm, based on identifying a specific microbiological risk factor, will allow for a shift from universal recommendations to a personalized strategy for prevention and treatment. This will contribute not only to improved dental health but also to breaking the vicious link between chronic fungal infection and the destruction of hard tooth tissues in the most vulnerable preschool age.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: The study was conducted in strict accordance with the ethical principles of the Helsinki Declaration. The study protocol was approved by the local ethics committees of the participating universities. Parents or legal guardians of all participating children were informed about the study's aims and methods and provided voluntary written informed consent.

References

1. Zou J, Du Q, Ge L, Wang J, Wang X, Li Y, et al. Expert consensus on early childhood caries management. Int J Oral Sci. 2022;14(1):35. doi:10.1038/s41368-022-00186-0
2. Lam PPY, Chua H, Ekambaram M, Lo ECM, Yiu CKY. Risk predictors of early childhood caries increment: A systematic review and meta-analysis. J Evid Based Dent Pract. 2022;22(3):101732. doi:10.1016/j.jebdp.2022.101732
3. Baklanov IS, Baklanova OA, Nesmeyanov EE, Ivashova VA, Kabardokova LA. Comparative analysis of urban and rural environmental quality: the opinions of residents of the region. IOP Conf Ser: Mater Sci Eng. 2020;944:012013. doi:10.1088/1757-899x/944/1/012013
4. Nadeeshani H, Kudagammana ST, Herath C, Jayasinghe R, Liyanage R. Early childhood caries and nutritional status of children: A review. Food Nutr Bull. 2023;44(4):249-64. doi:10.1177/03795721231209358
5. Man VCW, Manchanda S, Yiu CK. Oral Candida-biome and early childhood caries: A systematic review and meta-analysis. Int Dent J. 2025;75(2):1246-60. doi:10.1016/j.identj.2024.08.020
6. Alkhars N, Zeng Y, Alomeir N, Al Jallad N, Wu TT, Aboelmagd S, et al. Oral Candida predicts Streptococcus mutans emergence in underserved US infants. J Dent Res. 2022;101(1):54-62. doi:10.1177/00220345211012385
7. Stoopler ET, Villa A, Bindakhil M, Díaz DLO, Sollecito TP. Common oral conditions: A review.

JAMA. 2024;331(12):1045-54. doi:10.1001/jama.2024.0953
8. Taylor M, Brizuela M, Raja A. Oral candidiasis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. 2023 Jul 4
9. Hon KLE, Chan VP, Leung AK, Leung KKY, Hui WF. Invasive fungal infections in critically ill children: epidemiology, risk factors and antifungal drugs. Drugs Context. 2024;13:2023-9-2. doi:10.7573/dic.2023-9-2
10. Man VCW, Neelakantan P, Yiu CKY. The prevalence of Candida albicans and Malassezia globosa in preschool children with severe early childhood caries: A case-control study. Healthcare (Basel). 2024;12(13):1359. doi:10.3390/healthcare12131359
11. Lopes JP, Lionakis MS. Pathogenesis and virulence of Candida albicans. Virulence. 2022;13(1):89-121. doi:10.1080/21505594.2021.2019950
12. Lu Y, Lin Y, Li M, He J. Roles of Streptococcus mutans-Candida albicans interaction in early childhood caries: A literature review. Front Cell Infect Microbiol. 2023;13:1151532. doi:10.3389/fcimb.2023.1151532
13. Siddaiah SB, Sinha S, Archana BR. Microbiological evaluation of herbal extracts against Candida albicans in early childhood caries patients: An in vitro study. Int J Clin Pediatr Dent. 2024;17(1):26-30. doi:10.5005/jp-journals-10005-2733
14. Yao Y, He LT. Relationship between oral Candida albicans and flora in children with severe early childhood caries. Shanghai Kou Qiang Yi Xue. 2021;30(2):156-61. [Chinese]
15. Zeng Y, Fadaak A, Alomeir N, Wu Y, Wu TT, Qing S, et al. Effect of probiotic Lactobacillus plantarum on Streptococcus mutans and Candida albicans clinical isolates from children with early childhood caries. Int J Mol Sci. 2023;24(3):2991. doi:10.3390/ijms24032991
16. Miyamori A, Oishi M, Kobayashi S, Nagano H, Muramatsu T, Kushiyama A. Factors involved in the detection and development of oral candidiasis in a palliative-care unit. Am J Hosp Palliat Care. 2025;10499091251403093. doi:10.1177/10499091251403093
17. Li P, Yu X, Chen C, Zhao Z, Lu X, Fan Y. Efficacy of probiotics for oral candidiasis management: A systematic review. BMC Oral Health. 2025;25(1):1067. doi:10.1186/s12903-025-06468-3
18. Kaur G, Chawla S, Kumar P, Singh R. Advancing vaccine strategies against Candida infections: exploring new frontiers. Vaccines (Basel). 2023;11(11):1658. doi:10.3390/vaccines11111658
19. Liu Y, Daniel SG, Kim HE, Koo H, Korostoff J, Teles F, et al. Addition of cariogenic pathogens to complex oral microflora drives significant changes in biofilm compositions and functionalities. Microbiome. 2023;11(1):123. doi:10.1186/s40168-023-01561-7
20. Butera A, Maiorani C, Morandini A, Simonini M, Morittu S, Trombini J, et al. Evaluation of children's caries risk factors: A narrative review of nutritional aspects, oral hygiene habits, and bacterial alterations. Children (Basel). 2022;9(2):262. doi:10.3390/children9020262
21. Alkhars N, Al Jallad N, Wu TT, Xiao J. Multilocus sequence typing of Candida albicans oral isolates reveals high genetic relatedness of mother-child dyads in early life. PLoS One. 2024;19(1):e0290938. doi:10.1371/journal.pone.0290938
22. Gharaghani M, Rezaei-Matehkolaei A, Hardani AK, Zarei Mahmoudabadi A. Pediatric candiduria, epidemiology, genotype distribution, and virulence factors of Candida albicans. Microb Pathog. 2021;160:105173. doi:10.1016/j.micpath.2021.105173
23. Turska-Szybka A, Olczak-Kowalczyk D, Twetman S. Probiotics, prebiotics, synbiotics, and postbiotics against oral Candida in children: A review of clinical trials. Nutrients. 2025;17(14):2253. doi:10.3390/nu17142253
24. Jin P, Wang L, Chen D, Chen Y. Unveiling the complexity of early childhood caries: Candida albicans and Streptococcus mutans cooperative strategies in carbohydrate metabolism and virulence. J Oral Microbiol. 2024;16(1):2339161. doi:10.1080/20002297.2024.2339161
25. Pereira R, Dos Santos Fontenelle RO, de Brito EHS, de Morais SM. Biofilm of Candida albicans: formation, regulation, and resistance. J Appl Microbiol. 2021;131(1):11-22. doi:10.1111/jam.14949
26. Kumar D, Kumar A. Molecular determinants involved in Candida albicans biofilm formation and regulation. Mol Biotechnol. 2024;66(7):1640-59. doi:10.1007/s12033-023-00796-x
27. Ponde NO, Lortal L, Ramage G, Naglik JR, Richardson JP. Candida albicans biofilms and polymicrobial interactions. Crit Rev Microbiol. 2021;47(1):91-111. doi:10.1080/1040841X.2020.1843400
28. Uribe SE, Innes N, Maldupa I. The global prevalence of early childhood caries: A systematic review with meta-analysis using the WHO diagnostic criteria. Int J Paediatr Dent. 2021;31(6):817-30. doi:10.1111/ipd.12783
29. Paglia L. Early childhood caries: A family-centred disease. Eur J Paediatr Dent. 2025;26(2):87. doi:10.23804/ejpd.2025.26.02.01
30. Yu C, Li D, Chen D, Zheng C, Qian Y, Qiu X, et al. Temporal variation in the oral microbiome and the prediction of early childhood caries in different ethnicities. J Clin Pediatr Dent. 2024;48(5):144-53. doi:10.22514/jocpd.2024.114
31. Lif Holgerson P, Esberg A, West CE, Johansson I. The breast milk and childhood gastrointestinal microbiotas and disease outcomes: A longitudinal study. Pediatr Res. 2023;93(3):570-8. doi:10.1038/s41390-022-02328-w
32. Rajasekaran JJ, Krishnamurthy HK, Bosco J, Jayaraman V, Krishna K, Wang T, et al. Oral microbiome: A review of its impact on oral and systemic health. Microorganisms. 2024;12(9):1797. doi:10.3390/microorganisms12091797

33. Garcia BA, Acosta NC, Tomar SL, Roesch LFW, Lemos JA, Mugayar LRF, et al. Association of Candida albicans and Cbp+ Streptococcus mutans with early childhood caries recurrence. Sci Rep. 2021;11(1):10802. doi:10.1038/s41598-021-90198-3
34. Vernon JJ. Modulation of the human microbiome: probiotics, prebiotics, and microbial transplants. Adv Exp Med Biol. 2025;1472:277-94. doi:10.1007/978-3-031-79146-8_17
35. Chowdhry A, Kapoor P, Bhargava D, Bagga DK. Exploring the oral microbiome: An updated multidisciplinary oral healthcare perspective. Discoveries (Craiova). 2023;11(2):e165. doi:10.15190/d.2023.4
36. Reis RM, Carlo HL, Dos Santos RL, Sabella FM, Parisotto TM, de Carvalho FG. Possible relationship between the oral and gut microbiome, caries development, and obesity in children during the COVID-19 pandemic. Front Oral Health. 2022;3:887765. doi:10.3389/froh.2022.887765
37. Gomersall JC, Slack-Smith L, Kilpatrick N, Muthu MS, Riggs E. Interventions with pregnant women, new mothers, and other primary caregivers for preventing early childhood caries. Cochrane Database Syst Rev. 2024;5(5):CD012155. doi:10.1002/14651858.CD012155.pub3
38. Shrestha P, Graff M, Gu Y, Wang Y, Avery CL, Ginnis J, et al. Multiancestry genome-wide association study of early childhood caries. J Dent Res. 2025;104(3):280-9. doi:10.1177/00220345241291528
39. Tuan DA, Masak J. Natural-compound adjuvants dismantle Candida biofilms: mechanisms, design rules, and biofilm-aware pharmacology. Curr Microbiol. 2026;83(2):131. doi:10.1007/s00284-025-04713-0
40. Li Y, Huang S, Du J, Wu M, Huang X. Current and prospective therapeutic strategies: tackling Candida albicans and Streptococcus mutans cross-kingdom biofilm. Front Cell Infect Microbiol. 2023;13:1106231. doi:10.3389/fcimb.2023.1106231
41. Du Q, Ren B, He J, Peng X, Guo Q, Zheng L, et al. Candida albicans promotes tooth decay by inducing oral microbial dysbiosis. ISME J. 2021;15(3):894-908. doi:10.1038/s41396-020-00823-8
42. Xiong K, Zhu H, Li Y, Ji M, Yan Y, Chen X, et al. The arginine biosynthesis pathway of Candida albicans regulates its cross-kingdom interaction with Actinomyces viscosus to promote root caries. Microbiol Spectr. 2022;10(4):e0078222. doi:10.1128/spectrum.00782-22
43. Colombo S, Paglia L. Childhood obesity, sugar, and early childhood caries: the sweet trap. Eur J Paediatr Dent. 2024;25(4):254-5. doi:10.23804/ejpd.2024.25.04.01
44. Jha K, Abdul NS, Baldev KC, Satyarth S, Mandal NB, Mogla S, et al. Correlation of body mass index to oral hygiene and dental caries in school students: An original research. J Pharm Bioallied Sci. 2022;14(Suppl 1):S298-300. doi:10.4103/jpbs.jpbs_758_21
45. Kapil D, Saraf BG, Sheoran N, Srivastava P, Singh S, Singh R. To assess the prevalence of dental caries and its association with body mass index, socioeconomic status, dietary habits, and oral hygiene among 6–12-year-old children in Faridabad. Int J Clin Pediatr Dent. 2023;16(4):626-32. doi:10.5005/jp-journals-10005-2637
46. Yang H, Ma Y, Xie X, Wang H, Li X, Fang D, et al. Candida albicans enriched in orthodontically derived white spot lesions and shaped focal supragingival bacteriome. Front Microbiol. 2023;14:1084850. doi:10.3389/fmicb.2023.1084850
47. Kim HE, Liu Y, Dhall A, Bawazir M, Koo H, Hwang G. Synergism of Streptococcus mutans and Candida albicans reinforces biofilm maturation and acidogenicity in saliva: An in vitro study. Front Cell Infect Microbiol. 2021;10:623980. doi:10.3389/fcimb.2020.623980
48. Francis AB, Settem RP, Jeyamoorthy M, Nuthangi VH, Sharma A, Rajasekharan SK. Multifaceted roles of Candida albicans and Streptococcus mutans in contributing to polybiofilm infections in early childhood caries. Front Cell Infect Microbiol. 2025;15:1625103. doi:10.3389/fcimb.2025.1625103
49. Wu R, Cui G, Cao Y, Zhao W, Lin H. Streptococcus mutans membrane vesicles enhance Candida albicans pathogenicity and carbohydrate metabolism. Front Cell Infect Microbiol. 2022;12:940602. doi:10.3389/fcimb.2022.940602
50. Xiang Z, Wakade RS, Ribeiro AA, Hu W, Bittinger K, Simon-Soro A, et al. Human tooth as a fungal niche: Candida albicans traits in dental plaque isolates. mBio. 2023;14(1):e0276922. doi:10.1128/mbio.02769-22
51. Brito ACM, Bezerra IM, Borges MHS, Cavalcanti YW, Almeida LFD. Effect of different salivary glucose concentrations on dual-species biofilms of Candida albicans and Streptococcus mutans. Biofouling. 2021;37(6):615-25. doi:10.1080/08927014.2021.1946519
52. McReynolds DE, Moorthy A, Moneley JO, Jabra-Rizk MA. Denture stomatitis: An interdisciplinary clinical review. J Prosthodont. 2023;32(7):560-70. doi:10.1111/jopr.13687
53. Abuhajar E, Ali K, Zulfiqar G, Al Ansari K, Raja HZ, Bishti S, et al. Management of chronic atrophic candidiasis (denture stomatitis)–a narrative review. Int J Environ Res Public Health. 2023;20(4):3029. doi:10.3390/ijerph20043029
54. Pisano M, Romano A, Di Palo MP, Baroni A, Serpico R, Contaldo M. Oral candidiasis in adult and pediatric patients with COVID-19. Biomedicines. 2023;11(3):846. doi:10.3390/biomedicines11030846
55. Pawar S, Markowitz K, Velliyagounder K. Effect of human lactoferrin on Candida albicans infection and host response interactions in experimental oral candidiasis in mice. Arch Oral Biol. 2022;137:105399. doi:10.1016/j.archoralbio.2022.105399

56. Paniagua-Contreras GL, Cano-Kobayashi A, Fernández-Presas AM, Ruíz-De la Cruz M, Martínez-Gregorio H, Vaca-Paniagua F, et al. Candida albicans associated with periodontal disease exhibits different clusters of adhesion gene and protease expression. Int J Mol Sci. 2025;26(17):8721. doi:10.3390/ijms26178721
57. Delcea C, Gyorgy M, Siserman C, Popa-Nedelcu R. Impact of maladaptive cognitive schemas on suicidal behavior in adolescents during the COVID-19 pandemic: A predictive study. Int J Soc Psychol Asp Healthc. 2024;4:42-6. doi:10.51847/EHCf9HzLEP
58. Essah A, Igboemeka C, Hailemeskel B. Exploring gabapentin as a treatment for pruritus: A survey of student perspectives. Ann Pharm Educ Saf Public Health Advocacy. 2024;4:1-6. doi:10.51847/h8xgEJE3NE
59. Frost N, Deckert PM, Nolte CH, Kohl R, Schreiber SJ. Challenges and strategies in recruiting patients for a trial on patient-centered navigation in age-associated diseases. Ann Pharm Educ Saf Public Health Advocacy. 2024;4:50-62. doi:10.51847/BLHlqwfTFT
60. Rosellini E, Giordano C, Guidi L, Cascone MG. Creation of a novel surgical suture material designed to inhibit arterial thrombosis formation. J Med Sci Interdiscip Res. 2024;4(1):1-7. doi:10.51847/7denx72XdE
61. Umarova MS, Akhyadova ZS, Salamanova TO, Dzhamaldinova ZI, Taysumova ZD, Bekmurzaeva MR, et al. Influence of vibrations and other negative physical factors of production on protein metabolism and protein dynamics in the body. J Med Sci Interdiscip Res. 2024;4(1):39-44. doi:10.51847/Jk38F1v5XH
62. Constantin VD, Silaghi A, Epistatu D, Dumitriu AS, Paunica S, Bălan DG, et al. Diagnostic and therapeutic insights into colorectal carcinoma. Arch Int J Cancer Allied Sci. 2022;2(1):24-8. doi:10.51847/HojLmKBDvP
63. Mojsak D, Dębczyński M, Kuklińska B, Mróz RM. Ewing's sarcoma in a 58-year-old man: challenges of cancer diagnosis during the COVID-19 era. Arch Int J Cancer Allied Sci. 2022;2(1):37-41. doi:10.51847/J1EMRn8tE2
64. Lee MJ, Ferreira J. COVID-19 and children as an afterthought: establishing an ethical framework for pandemic policy that includes children. Asian J Ethics Health Med. 2024;4:1-19. doi:10.51847/haLKYCQorD
65. Kajanova J, Badrov A. Medical students' perspectives on trust in medical AI: A quantitative comparative study. Asian J Ethics Health Med. 2024;4:44-57. doi:10.51847/36mpdZ9AZ8
66. Sugimori T, Yamaguchi M, Kikuta J, Shimizu M, Negishi S. The biomechanical and cellular response to micro-perforations in orthodontic therapy. Asian J Periodontics Orthod. 2022;2:1-15. doi:10.51847/Z9adSJ59rj
67. Dipalma G, Inchingolo AD, Fiore A, Balestriere L, Nardelli P, Casamassima L, et al. Comparative effects of fixed and clear aligner therapy on oral microbiome dynamics. Asian J Periodontics Orthod. 2022;2:33-41. doi:10.51847/mK28wdKCIX
68. Simonyan R, Babayan M, Yekmalyan H, Alexanyan A, Simonyan G, Alexanyan S, et al. Identification and extraction of superoxide-generating protein assemblies from Helianthus tuberosus, Daucus sativus, and Solanum tuberosum. Spec J Pharmacogn Phytochem Biotechnol. 2023;3:15-20. doi:10.51847/Vj5MeBCcDs
69. Tsiganock AS, Bgantseva AE, Vostrikova VR, Shevel DS, Saidarova AI, Bekbuzarov IM, et al. Exploring the wound healing potential of aqueous extracts from Caucasus herbs in diabetes mellitus. Spec J Pharmacogn Phytochem Biotechnol. 2023;3:31-8. doi:10.51847/Y5Fvcyw12s
70. Sanlier N, Yasan N. Exploring the link between COVID-19 and vitamin D: A concise overview. Interdiscip Res Med Sci Spec. 2024;4(1):23-32. doi:10.51847/skW1PmtWeB
71. Ribeiro A, Martins S, Fonseca T. Progress and gaps in national medicines policy implementation in SADC member states: A comprehensive desktop review. Interdiscip Res Med Sci Spec. 2024;4(1):42-56. doi:10.51847/0eVBxAI8y0
72. Balaji A, Jei JB, Murugesan K, Muthukumar B. Case report on distal extension edentulous rehabilitation using claspless extra-coronal attachments. J Curr Res Oral Surg. 2022;2:16-9. doi:10.51847/OhXCPOyjBp
73. Alhussain BS, Alamri FS, Alshehri FA, Aloraini AA, Alghamdi SM, Alfuhaid NA, et al. Influence of mechanical properties and occlusal fit on the success of CAD/CAM ceramic endocrowns. J Curr Res Oral Surg. 2022;2:20-6. doi:10.51847/2MEMcd7epS
74. Uneno Y, Morita T, Watanabe Y, Okamoto S, Kawashima N, Muto M. Assessing the supportive care needs of elderly cancer patients at Seirei Mikatahara General Hospital in 2023. Int J Soc Psychol Asp Healthc. 2024;4:13-9. doi:10.51847/o4njwxvRSF
75. Ceylan MF, Basal M, Gayretli S. Impact of digital burnout on consumer perceptions of online shopping. Asian J Indiv Organ Behav. 2024;4:7-14. doi:10.51847/D1BR4edNsN
76. Maralov VG, Sitarov VA, Koryagina II, Kudaka MA, Smirnova OV, Romanyuk LV. Neuropsychological and personal factors influencing students' attitudes toward hazards. Asian J Indiv Organ Behav. 2024;4:34-43. doi:10.51847/GmDL98vb2E
77. Oran IB, Azer OA. The evolution of Turkey's role in international development: A globalization perspective. Ann Organ Cult Leadersh Extern Engagem J. 2023;4:1-8. doi:10.51847/oNOPb4T9g1
78. Ncube M, Sibanda M, Matenda FR. The influence of AI and the pandemic on BRICS nations: South Africa's economic performance during crisis. Ann Organ Cult Leadersh Extern Engagem J. 2023;4:17-24. doi:10.51847/lrMvYTE3OF
79. Lee S, Kim J, Byun G. The interplay of political skill, ethical leadership, and leader-member exchange in shaping work outcomes. Ann Organ Cult Leadersh

Extern Engagem J. 2023;4:45-53. doi:10.51847/vAKE892Paf
80. Razhaeva MU, Khuchieva LA, Musaev SA, Rustamov AK, Bicherkaeva KS, Usmanova KS. Environmental impact of the Y-isomer of HCH: unveiling its role in cancer formation. Asian J Curr Res Clin Cancer. 2022;2(2):1-5. doi:10.51847/Rtj57FuF6z
81. Rojas P, Soto M, Vargas I. Influence of patient age on the biological profile and prognosis of operable early-stage breast cancer. Asian J Curr Res Clin Cancer. 2022;2(2):33-42. doi:10.51847/AsL4oopFGu
82. Al Abadie M, Sharara Z, Ball PA, Morrissey H. Pharmacological insights into Janus kinase inhibition for the treatment of autoimmune skin diseases: A literature review. Ann Pharm Pract Pharmacother. 2023;3:1-8. doi:10.51847/lhABjfuIwh
83. Guzek K, Stelmach A, Rożnowska A, Najbar I, Cichocki Ł, Sadakierska-Chudy A. A preliminary investigation of genetic variants linked to aripiprazole-induced adverse effects. Ann Pharm Pract Pharmacother. 2023;3:40-7. doi:10.51847/ZT28xcs95J
84. Sri KB, Fatima MS, Sumakanth M. Development and validation of a stability-indicating UV spectroscopic method for baricitinib in bulk and formulation. Pharm Sci Drug Des. 2022;2:8-13. doi:10.51847/JxHXkcB6tD
85. Adeleke OA. Development and enhancement of liquisolid compact containing rifampicin and quercetin: An in-vitro and in-vivo investigation. Pharm Sci Drug Des. 2022;2:14-25. doi:10.51847/lw1PmMAVuw