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# ULOGA I ZNAČAJ GLJIVICE *CANDIDA ALBICANS* U NASTANKU I RAZVOJU KARIJESA RANOG DETINJSTVA

# THE ROLE AND SIGNIFICANCE OF THE FUNGUS *CANDIDA ALBICANS* IN THE FORMATION AND PROGRESSION OF EARLY CHILDHOOD CARIES

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***Sažetak***

**Uvod**: Karijes ranog detinstva je *prema definiciji Američke akademije za dečiju stomatologiju iz 2021. svaki karijesni zub, zub koji nedostaje (zbog karijesa) ili plombirana površina na bilo kom mlečnom zubu kod dece do šest godina. To je multifaktorska bolest, koja podrazumeva sinhronizovanu aktivnost kariogenih mikroorganizama, osetljivost domaćina i fermentabilnih ugljenih hidrata. Streptococcus mutans je glavni kariogeni mikroorganizam. Nedavna otkrića pokazuju da se Candida albicans, oportunistička gljivica, često otkriva u većem broju kod dece sa karijesom ranog detinjstva. Istraživanja ukazuju da postoji sinergistički efekat C. albicans i S. mutans, što povećava patogenost, a samim tim i težinu kliničke slike.*
***Cilj studije*** *je da pokaže uticaj gljivice C. albicans na nastanak, tok i prognozu karijesa ranog detinjstva..*
***Materijal i metode****: Pretraživanjem PubMed baza podataka, uz korišćenje ključnih reči Candida albicans, Streptococcus mutans i karijes ranog detinjstvu, analizirano je 17 studija koje su uključene u ovaj rad.*
***Rezultati:*** *Studije pokazuju da interakcija između C. albicans i S. mutans utiče na etiologiju, tok i prognozu karijesa ranog detinjstva.*
***Zaključak****: Neophodna su dodatna longitudinalna istraživanja kako bi se ispitao uticaj sinergističkog dejstva ova dva mikroorganizma na pojavu karijesa ranog detinjstva.*

***Ključne reči****: candida albicans, streptococcus mutans, karijes ranog detinjstva.*

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***Abstract***

***Introduction****: Early childhood caries is defined by the 2021 American Academy of Pediatric Dentistry as any decayed tooth, missing tooth (due to decay), or filled surface on any baby tooth in children under six years of age. It is a multifactorial disease, which involves synchronized activity of cariogenic microorganisms, sensitivity of the host and fermentable carbohydrates. Streptococcus mutans is the main cariogenic microorganism. Recent findings show that Candida albicans, an opportunistic fungus, is often detected in higher numbers in children with early childhood caries. Research indicates that there is a synergistic effect of C. albicans and S. mutans, which increases the pathogenicity and thus the severity of the clinical picture.*
***The aim*** *of the study is to show the influence of the fungus C. albicans on the onset, course and prognosis of early childhood caries.*
***Material and methods:*** *By searching PubMed databases, using the keywords Candida albicans, Streptococcus mutans and early childhood caries, 17 studies included in this paper were analyzed.*
***Results****: Studies show that the interaction between C. albicans and S. mutans affects the etiology, course and prognosis of early childhood caries.*
***Conclusion****: llongitudinal studies are necessary in order to examine the influence of the synergistic effect of these two microorganisms on the occurrence of caries in early childhood. Key words: candida albicans, streptococcus mutans, early childhood caries.*

***Key words:*** *candida albicans, streptococcus mutans, early childhood caries*

## *Introduction*

Early childhood caries (ECC) is an infectious, destructive disease of hard dental tissues, which occurs in babies and young children in the first few years of life and is characterized by rapid carious destruction of milk teeth. According to Voss, it is the most common chronic childhood disease with almost one billion and eight hundred million new cases per year worldwide[1]. Any sign of caries in children under six years of age is considered ECC. Early childhood caries affects children's quality of life. Pain and swelling lead to greater absenteeism from school, treatment costs and the possibility of hospitalization increase, sleep disorders occur, and growth, height and weight parameters can slow down[2,3].

The prevalence of ECC is significantly high in many parts of the world, although it varies by geographic area, socioeconomic status, and access to dental care. Statistics show that ECC is a common phenomenon in poor countries as well as in developing countries. The fact that in a period of twenty years (1998-2018), 72 studies which only dealt with the prevalence of ECC in preschool children were published, shows that ECC preoccupies researchers. The average prevalence of ECC in one-year-olds was 17%, in two-year-olds 36%, and in three, four and five-year-olds it was 43%–63%[4].

The results of the research on the average prevalence are worrying, because the percentage of children with ECC increases with the increase in the age of children of preschool age. According to the research of some authors, ECC is cited as the most common oral disease that especially affects children[5]. The etiology of ECC is multifactorial and includes a combination of biological factors and behavioral habits. It is known that the main etiological factors for ECC are microorganisms, fermentable carbohydrates, host factors and time. The human oral microbiome includes more than 700 different microorganisms, including bacteria, fungi, viruses, protozoa and mycoplasmas as stated by Marshi and Zaura[6].

Microorganisms interact with each other and form a biofilm of different content. *S. mutans* is the main microorganism in the development of caries. It is naturally present in the oral cavity immediately after dentition. In order to survive, it forms a biofilm, i.e. organized microbial community[6].

Biofilm formation begins when saliva components are selectively adsorbed on the enamel, forming the acquired dental pellicle. The pellicle provides an attachment site for oral microorganisms, including *S. mutans*, which allows colonization of it. In such conditions, this bacterium begins to multiply and produce exopolysaccharides, forming a community that contains channels for a better distribution of oxygen, nutrients and signaling molecules. Further, sucrose-dependent biofilm metabolism relies on an extracellular, self-secreted glucosyltransferase (GtFB, GtFC, GtFB)[7].

Although many facts are known about the prevention and treatment of ECC, the prevalence of this disease is still high, which leads researchers to look for another potential etiological factor such as the fungus *C. albicans* which is linked to the occurrence and progression of ECC.

A feature of the fungus *C. albicans* which makes it a significant opportunistic pathogen, is its ability to adapt and multiply in different environments, such as acidic environments[8]. In this context, the fungus *C. albicans* can coexist with other oral microorganisms in a biofilm or carious lesion as a natural consequence of an acidic microenvironment.

*C. albicans* is most often associated with mucosal infection (candidiasis), while research in recent years has shown that it may also play a role in the etiology and progression of ECC. Numerous studies deal with the etiology, epidemiology, prevention and interaction between the fungus *C. albicans* and the bacterium *S. mutans* in the development of this disease[9,10].

The fact that immunity in younger children is in the process of formation, and the *C. albicans* species has the potential to increase in concentration during a state of low immunity, may partially explain the rapid progression of ECC in this age group. On the other hand, due to impaired immunity, patients with ECC are often malnourished, which makes them susceptible to *C. albicans* infection. Numerous studies have analyzed the role of *C. albicans* spp. in the biofilm of teeth and gums, as well as its interaction with cariogenic bacteria such as *S. mutans*. These studies also indicated an association between Candida and ECC[11,12]. The study aimed to show the influence of the fungus *C. albicans*, and its interaction with the bacterium *S. mutans* on the occurrence, course and prognosis of ECC.

### ***Relationship of S. mutans and C. albicans spp. in the Development of Early Childhood Caries***

The structure of the cell wall of *C. albicans* is cited as a possible link between bacteria and fungi. The main components of the cell wall are mannins, glucans and chitin.

Mannins are found on the outer layer of the cell wall of *C. albicans*. It is possible that these biomolecules are involved in the binding of glucosyltransferase exoenzymes to the fungal cell surface[13].

The joint presence of *C. albicans* and *S. mutans* in the biofilm produces a higher amount of protein, oxidation and resistance to antibacterial stress, acid resistance, larger microcolonies and a much more complex 3D structure[9].

A possible mechanism of synergistic action is based on the exoenzyme glucosyltransferase B (GtfB) from the microorganism *S. mutans*, which is a key producer of exopolysaccharides. The GtfB exoenzyme binds to the surface of the fungus *C. albicans* in an active form and produces exopolysaccharides that ensure better binding of *S. mutans*, which ultimately leads to the formation of a biofilm containing a large amount of exopolysaccharides of *S. mutans* and *C. albicans* species[9,14].

In the thus formed biofilm with a rich content of exopolysaccharides, a vicious circle is created that limits diffusion and creates good conditions for the growth of *S. mutans* and *C. albicans*9, which also implies an increase in the acidity of the biofilm and ultimately demineralization of teeth[15].

The binding strength of the GtfB enzyme to the surface of *C. albicans* is astonishing, it is 2.5 times greater and 20 times more stable than the adhesion of the enzyme to *S. mutans*.

The strong and highly stable binding of GtfB to *C. albicans* could explain, at least in part, why this exoenzyme efficiently forms a link between *C. albicans* and *S. mutans*[16].

The question arises whether saliva affects the synergistic reaction between S. mutans and *C. albicans*, specifically regarding its effect on the increase in biofilm virulence. It was investigated whether 100% purified saliva (without antimicrobial peptides) could affect the mature biofilm. The results indicate that saliva has no effect in the initial phase of biofilm formation, while it can affect the mature biofilm[17].

There is no interaction between Candida C. albicans and Streptococcus S. mutans in a healthy oral environment, nor is *C. albicans* colonization observed on the tooth surface. In ECC, one of the main factors contributing to the serious destruction of dental tissues is the prolonged consumption of drinks and food rich in sucrose, which allows increased physical adhesion between *S. mutans* and *C. albicans* and colonization of the teeth.

Previous studies suggest the possible influence of *C. albicans* in the development and progression of ECC.

## *Conclusion*

Research results of the last ten years show that the etiology, progression and severity of the clinical picture of caries in early childhood are significantly correlated with the combined colonization of *C. albicans* and *S. mutans* spp. Certainly, additional longitudinal studies are necessary to explain the impact of bacterial–fungal interactions on ECC, which could lead to new perspectives in anticariogenic procedures and therapies.

### *Conflicts of Interest*

The authors declare that they have no conflict of interest.

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