



Risk Factors of Oral Candidiasis Post Teeth Extraction: Scoping Review

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Abstract

Introduction: Tooth extraction can lead to several complications; therefore, it is essential to assess the patient's condition to prevent potential complications carefully. Candida infection is one type of complication triggered by tooth extraction. Oral candidiasis is a common fungal infection in humans caused by the overgrowth of *Candida albicans*, the primary etiological agent. Tooth extraction can increase a person's risk of developing oral candidiasis due to environmental changes in the oral cavity that can increase fungal growth so that the post-extraction wound area becomes prone to candida infection. This scoping review aims to analyze risk factors for oral candidiasis in patients after tooth extraction. **Methods:** The writing followed the PRISMA-ScR guidelines. Articles are searched using electronic databases, namely PubMed, ScienceDirect, and Elsevier. The population in this review was patients diagnosed with oral candidiasis after tooth extraction. Full-text journals in English published from 2013 to 2023 non-literature review research method. **Results:** Seven articles were obtained that met the inclusion criteria. The study design used, namely 2 experimental articles and 5 case report articles, showed the occurrence of oral candidiasis after tooth extraction due to immunocompromised conditions which caused the body to experience decreased immunity, causing a delay in the wound healing process and failure to fight *Candida* infection. Positive fungal culture results for *Candida* spp. confirmed the diagnosis of oral candidiasis. **Conclusion:** The act of tooth extraction increases the risk of oral candidiasis, which is triggered by the patient's underlying condition, rendering the commensal fungus *Candida albicans* pathogenic. This is proven based on research findings in the last 10 years, post-extraction oral candidiasis occurs, accompanied by Immunocompromised conditions such as diabetes, HIV, grave diseases, hypertensive conditions, and also found due to abuse of heroin, opioids, and marijuana.

Keywords: teeth extraction, oral candidiasis, *Candida Albicans*, delayed wound healing.

INTRODUCTION

Tooth extraction is the process of removing a tooth from its socket, a procedure routinely performed in dental practices worldwide.¹ In developing countries, 12.30 to 33.40% of tooth extractions are recorded in daily dental practice.² The results of the 2018 basic health research reported that the tooth extraction rate in Indonesia reached 7.9% and in Central Java tooth extraction reached 5.2% with the main cause of tooth extraction being damaged/cavities/ painful teeth reaching 42.83%.² Extraction is carried out due to the condition of the tooth which can no longer receive treatment with the main indications such as caries, periodontal disorders, traumatic orthodontic treatment, indications for prosthesis, impacted teeth.^{3,1}

This tooth extraction treatment is related to several post-operative complications so it must be based on an examination of the patient's condition to prevent the possibility of complications after tooth extraction.^{1,3} Miclote, et al (2018) reported the 3

most common post-extraction complications, namely wound infection (2%), pain without a clear cause (1%), and *oroantral communication*(1%).⁴ Cochrane research through trials randomized controlled trial (*randomized control trial*), the risk of post-surgical infection after tooth extraction in young, physically healthy patients is about 10%, but the risk increases to 25% in patients with a low immune system.⁵

Candida spp infection is one example of an infection triggered by tooth extraction especially in *immunocompromised* patients and there were no previous clinical signs and symptoms.⁶ Candidiasis is a common fungal infection in humans caused by the overgrowth of fungal microorganisms in the form of candida with the main etiology being *Candida albicans*.⁷ *Candida albicans* is a normal flora in the oral mucosa.⁸ In a state of low immune system, *C. albicans* in the oral cavity will turn into a pathogen and cause infection in the form of candidiasis.⁷ Oral candida is reported to be present in 30-45% of the general healthy adult population.⁹ According to the

Report *World Health Organization* (WHO) in 2001 the prevalence of oral candidiasis was between 5.8% and 98.3%.¹⁰ The prevalence of oral candidiasis in Indonesia reached 84% reported in 2009.

Risk factors for oral candidiasis can be local, systemic, or physiological.¹¹ Local factors include the use of dentures with poor oral hygiene, the use of corticosteroid drugs, xerostomia, and smoking.¹² Systemic factors include diabetes mellitus, HIV-AIDS, autoimmune, and nutritional deficiencies.¹² Physiological factors in the form of stress, pregnancy, in children and the elderly.¹² The severity of oral candidiasis can occur due to decreased oxygen and saliva flow to the oral tissues, resulting in the production of an acidic and anaerobic environment that supports the overgrowth of fungus *Candida albicans*.¹³ The virulence of the infection can cause death when the pathogen reaches the blood circulation.⁷

Various laboratory procedures can be used to identify *Candida albicans* in diagnosing the cause of candidiasis, such as *fluorescence test*, fungal culture through Sabouraud dextrose agar media, eosin methyl blue agar (EMB), CHROMagar, *cornmeal candida agar*.¹⁴ Species *Candida albicans* grows smooth, shiny, creamy-white, and has a yeasty odor on the culture medium, Oval bud-shaped cells form the surface growth. Pseudomycelium, or pseudohyphae mass, shows the development with blastospores at the tip.¹⁴

The selection of antifungal drugs must take into account the patient's immune status, characteristics of the lesion and pharmacological characteristics of the drug. Three large groups of antifungal drugs are most often used, namely polyenes (amphotericin B and nystatin), echinocandins (anidulafungin, caspofungin, and micafungin), and azoles.¹⁵ Topical medications are applied to the infected area and provide limited relief, with minor side effects. Systemic medications are prescribed when the infection is more extensive and topical therapy has not responded adequately.¹⁶

Tooth extraction can increase a person's risk of developing oral candidiasis due to changes in the environment in the oral cavity which can increase the growth of fungi so that the wound area after extraction becomes susceptible to infection *Candida spp*.^{6,17} This condition can occur when the post-extraction wound fails to heal, leading to contamination of the socket by microorganisms.⁶ The delayed wound infection that causes this open wound is opportunistic, occurring when the organism is exposed to enter the body through an invasive procedure, such as a tooth extraction.^{18,19}

It has been proven that *Candida spp* plays an important role as an opportunistic component and especially a pathogen in wounds.²⁰ Wounds can be colonized by commensal fungi developing into local

infections.^{20,21} Exposure to microorganisms *Candida spp* in post-tooth extraction wounds causing patients to experience oral candidiasis.²² Decreased immunity directly affects the prevention of mucosal infections by *Candida spp* which is mediated primarily by the innate immune response function.²³ The aim of this *scoping review* is to analyze the risk factors for oral candidiasis after tooth extraction.

METHOD

The design of this research is *scoping review*. Reviews are based on guidelines *Preferred Reporting for Scoping Review and Meta-Analysis* (PRISMA-ScR). This topic is structured using the PCC format, namely population, concept, and context. The population in this study were tooth extraction patients. The concept in this study is the occurrence of oral candidiasis. The context is the risk factors for oral candidiasis in tooth extraction patients.

The inclusion criteria are English language articles published between 2013 and 2023 (10 years) obtained through the PubMed, Science Direct and Elsevier databases with articles that can be accessed in full. Articles are ignored if they are included in the exclusion criteria, namely articles with a research design in the form of a *literature review*, and the same articles found in different databases (duplication).

Table 1: Population Concept Context (PCC)

Population	Tooth Extraction Patient
Concept	Oral Candidiasis
Context	Risk Factor of Oral Candidiasis in Tooth Extraction Patient

RESULTS

The search was conducted electronically, identified through a PubMed search of 604 articles, articles identified through a Science Direct search of 2,450 articles, and articles identified through a search on Elsevier of 288 articles, so that the total number of articles obtained was 3,342 articles. The first screening was carried out through selection based on inclusion and exclusion criteria, there were 1,557 articles that were eliminated because they were published outside the time span between 2013-2023, 53 articles were eliminated because they were duplicates, and 1,383 articles were eliminated because the research design used was literature review. There were 349 articles selected for the next stage. Next, the second thinning is carried out by means of screening through reading the title and abstract, there were 312 articles that were eliminated because they were irrelevant and did not meet the inclusion criteria. Furthermore, the third elimination was carried out by reading the entire contents then 7 articles were obtained that met the inclusion criteria. Figure 1 shows the PRISMA-ScR article search results.

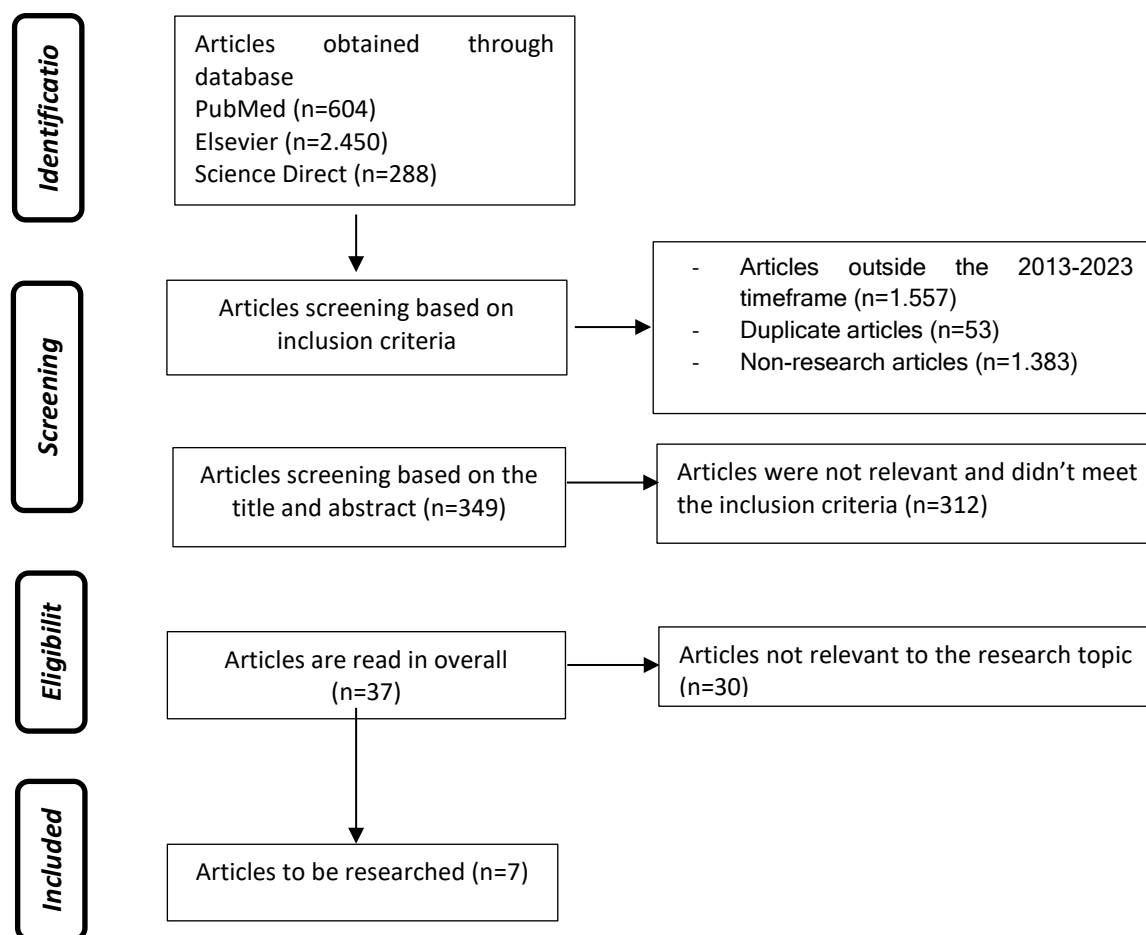


Figure I: PRISMA-ScR Research Flow

Table 2 contains information on the characteristics of the research sample based on the country and the research design used, 3 articles from India, 1 article from South Africa, 1 article from Indonesia, 1 article from the USA, and 1 article from Brunnei Darussalam. The study designs used were experimental and case report.

Table 2: Characteristics of research samples by country and research design

No	Title	Writer	Country	Year	Research Design
1	<i>Candida Albicans</i> Induced Chorioretinitis and Retinal Vasculitis In An Immunocompetent Adult Following Tooth Extraction	Ali, Nadir & George, J. & Joshi, N	Brunei Darussalam	2014	Case Report
2	Molecular and Histological Association Between <i>Candida Albicans</i> from Oral Soft Tissue and Carious Dentine of HIV-Positive Children	E. Blignaut & W. F. P. van Heerden	South Africa	2015	Experimental
3	Maxillary Osteomyelitis with Candidiasis due tue Extraction in Uncontrolled Diabetes State	Deepak Kulkarni LS, et al	India	2015	Case Report
4	Oral Candidiasis Turns to Oral Cancer - A Rare Clinical Presentation	Kharadi U, Kharadi UA, Parkarwar P, Khairnar S, Reddy S, Arur P, et al.	India	2016	Case Report
5	Oral Candidiasis in Grave's Disease after Dental Surgery	Laihad, F. M. et al.	Indonesia	2018	Case Report
6	Mandibular Osteomyelitis Associated with <i>Candida Albicans</i> in Marijuana and Heroin Abusers	Daya Attie M, Anderson IA, Portnof J	USA	2018	Case Report
7	Microbial Analysis of Dentoalveolar Bone Immediately After Extraction	N. P. Muralidharan, Sahana Kritivasan, Nabeel Nazar	India	2019	Eksperiment al

Table 3 shows the number of samples, the results of the research conducted, accompanied by a description of the conditions experienced by the patient. It was found that all of them showed the occurrence of oral candidiasis with different clinical manifestations based on the conditions of each patient, the findings of oral candidiasis were proven by positive fungal culture results against *Candida spp.*

Table 3: Extraction results based on number of samples, patient conditions, and research results

No	Title	Sample Amount	Patient Condition	Results
1	<i>Candida Albicans</i> Induced Chorioretinitis and Retinal Vasculitis in an Immunocompetent Adult Following Tooth Extraction	1 Patient	Healthy Individual	Growth <i>Candida Albicans</i> in the culture of tooth extraction swab mandibular molar
2	Molecular and Histological Association Between <i>Candida Albicans</i> from Oral Soft Tissue and Carious Dentine of HIV-Positive Children	151 Child Patients	HIV	Candidiasis pseudomembrane findings in dorsal tongue swab obtained 80% isolate <i>C.albicans</i>
3	Maxillary Osteomyelitis with Candidiasis due to Extraction in Uncontrolled Diabetes State	1 Patient	Diabetes Melitus Type 2	Gingival area of extraction tooth 26 & 27 show whitest, smear results cytology found <i>Candida albicans</i>
4	Oral Candidiasis Turns to Oral Cancer - A Rare Clinical presentation	1 Patient	Hypertension	Candidiasis pseudomembrane on palate and hyperplastic chronic and candidiasis on the ventral surface right and left on the tongue
5	Oral Candidiasis in Grave's Disease after Dental Surgery	1 Patient	Grave's Disease (Hyperthyroid)	<i>Candida tropicalis</i> found from culture fungus on the mucosa gingiva of tooth 38
6	Mandibular Osteomyelitis Associated with <i>Candida Albicans</i> in Marijuana and Heroin Abusers	2 Patient	Heroin abuse, opioids, and marijuana	Microbiological culture of the extraction socket was positive for <i>C. albicans</i>
7	Microbial Analysis of Dentoalveolar Bone Immediately After Extraction	20 Patients	Immunocompromised condition	3 Patients show smear test results found <i>Candida albicans</i>

DISCUSSION

Oral candidiasis occurs due to the excessive growth of the fungus *Candida albicans*, caused by an imbalance between the growth of *Candida albicans*, its virulence factors, and host defenses, resulting in decreased immune system function that allows *Candida albicans* to colonize and damage host tissue. Oral candidiasis caused by fungi *Candida albicans* can be detected after fungal culture is performed through a swab process at the location where the lesion was found. Cases of oral candidiasis after tooth extraction are rare; however, several research reports have documented the occurrence of infection after tooth extraction.

Based on the case report of Ali, Nadir, et al 2014²⁴, shows the presence of white ulcers on mandibular molar tooth extraction site. Fungal culture was performed through a swab of the extraction site showing fungal growth. *Candida albicans*. Ulcerated lesions are common found in oral diseases with various causes, one of which is fungal contamination. Ulcers can be colonized by commensal fungi, including *Candida albicans* and develop into a local

candidiasis infection. Candidiasis is a common condition that affects individuals with compromised immune systems. However, the patient denied any medical history and stated that he was not taking any medications that could raise suspicions as a cause of the infection. In healthy individuals, *Candida albicans* can be found as one of the commensal microflora in the oral cavity. However, due to changes in the amount and composition of saliva, it can trigger infections due to growth *Candida albicans* which are pathogenic.

In contrast to research conducted by E. Blignaut & WFP van Heerden 2015²⁶, reported pseudomembranous candidiasis in 151 pediatric patients confirmed with HIV was caused by the growth of *Candida albicans* which was found up to 80% based on swab results on the dorsal tongue. Tooth extraction in children is carried out because there is an indication of dentin caries which causes unbearable pain so that it is decided to perform tooth extraction.

Candida albicans and caries are often investigated in healthy and diseased conditions. immunosuppression

conditions. People with HIV/AIDS have a higher risk of caries due to decreased CD4 cells.+causes decreased salivary gland function. Low saliva flow causes fungal colonization. *Candida albicans*. CD4 levels+low levels cause fungal species to experience uncontrolled growth and will become pathogens that invade locally in the oral mucosa, resulting in candidiasis infections.²⁷

This is supported by a case report by Deepak Kulkarni LS, et al, 2015²⁸ A tooth extraction was performed on a 56-year-old patient showing complications of oral candidiasis, indicated by the results of an intraoral examination which found that the socket had not undergone a healing process and that there was a white gingival crust in the extraction area of teeth 26 and 27. The results of the cytology smear showed positive for *Candida albicans*. The patient was known to have uncontrolled diabetes with fasting blood sugar levels reaching 380 mg/dl. Uncontrolled diabetes results in circulatory disorders that cause delayed response to an infection that occurs, so in this case the diabetes condition experienced is considered the cause of impaired wound healing after extraction.

Based on the case report of Kharadi U, Parkarwar P, et al, 2016²⁹ shows the occurrence of pseudomembranous candidiasis on the palatal and chronic hyperplastic candidiasis on the right and left ventral surfaces of the tongue. This condition is based on the finding of white lesions scrapable involving the palatal extending to the maxillary alveolar and on the right and left ventral surfaces of the tongue, occurred 15 days after tooth extraction. The patient had a history of asthma, also had a history of hypertension and Amlodipine treatment since 3 years ago.

Increased blood pressure causes the spread of inflammation.³⁰ This factor can influence the occurrence of delayed wound healing because high blood pressure can make it difficult for blood to flow through the blood vessels that carry oxygen and nutrients to the wound site.³¹ This slows the healing process and increases the risk of infectious complications. Amlodipine is an antihypertensive drug in the calcium channel blockers. The use of the antihypertensive drug Amlodipine acts as a systemic factor calcium channel *blocker* will suppress saliva secretion by blocking Ca²⁺ channels. Side effects include decreased saliva flow by blocking the parasympathetic nerves through the calcium pathway. Calcium ions cannot enter the parasympathetic nerve post-synapses, which are chemical messengers for the parasympathetic nerves to stimulate the salivary glands. Decreased saliva production results in a reduction of anti-candida saliva components, such as lysozyme, histatin, lactoferrin, and calprotectin, allowing *Candida* to grow more easily and increasing the risk of oral candidiasis.

Based on case reports Laiad, FM et al, 2018³², tooth odontectomy 38 was performed on a 40-year-old

patient with a history of Graves' disease, a condition hyperthyroidism. It is known that one month earlier, the patient had an odontectomy on tooth 48, taking the antibiotic cefadroxyl 500 mg, 2 times a day, and mefenamic acid 500 mg, 3 times a day, as a pre-medication. Swelling occurs in the neck, intraoral conditions are not There is swelling of the oral gingiva, normal mucosa, no redness. From the examination microbiology *Candida tropicalis* found from fungal cultures on the gingival mucosa ³⁸.

The cause of infection comes from fungus *Candida tropicalis*. A condition of immunocompromised can trigger fungal infections, Graves' disease is a hyperthyroid (autoimmune) condition, so a compromised immune system can make a person more susceptible to infection with candida. There is a history of antibiotic use in previous operations, as one of the most common cause of candida growth. Overuse of antibiotics.

various reviews in Above, swelling as a symptom of inflammation that occurs indicates a fungal infection.

Based on case reports Daya Attie M, Anderson IA, Portnof J, 2018³³ Two patients who had undergone tooth extraction complained of pain and failure of the extraction site to heal. Microbiological cultures from the surgical site were positive for *C. albicans*. Both had a history of heroin, opioid, and marijuana abuse. The relationship between marijuana and heroin abuse and susceptibility to infection is due to the direct effects of these drugs on the immune response to pathogens.³⁴ Marijuana is the common name given to *Cannabis sativa*; this plant has been widely used for medicinal purposes. An important factor to consider with cannabis use is the increased susceptibility to infection due to its effects on immune cells directly affecting the number, proliferation, and sensitivity of important immune cells such as T cells, B cells, and NK cells by directly inhibiting the migration of immune cells into tissues thereby decreasing the host's defenses against infection.³⁵ On the other hand, heroin and opioids have been associated with increased susceptibility to infection with direct exposure to pathogens through injection.

Heroin disrupts the immune system through direct effects on lymphocyte responses, particularly Natural Killer (NK) cells.³⁵ Opioids suppress the immune system through the release of corticosteroid hormones and immunosuppressive hormones, resulting in suppression of the immune system so that opioid abuse makes individuals susceptible to opportunistic infections such as fungal infections.³⁶

Based on research NP Muralidharan, et al, 2019³⁷, the research was conducted on 20 patients with indications of caries and periodontal disorders. After the extraction procedure was performed, samples were collected via swab from the socket. Growth was examined by solid media culture and smear cytology. The results found *Candida albicans* in 3 patients after tooth extraction. Fungal growth was

found in individuals with this condition. *Immunocompromised patients* are accompanied by poor oral hygiene. This fungus can become a pathogen under certain conditions, particularly in individuals with a weakened immune system. A compromised immune system will cause the colonization of the fungus to increase but the body cannot control its growth and its nature will change to become a pathogen. This will increase the risk of candidiasis infection.

Oral candidiasis as a post-tooth extraction complication due to delayed wound healing in the tooth extraction socket. Species *Candida albicans* is the most common fungus that causes delays in the wound healing process causing infection in the extraction socket area due to the entry of microorganisms *Candida albicans* pathogen.³⁸ The results of the analysis of seven articles found that oral candidiasis is at risk of occurring when tooth extraction is carried out, accompanied by conditions such as immunocompromised conditions, such as diabetes, HIV, Graves' disease, hypertension, and the effects of drug abuse—heroin, opioids, and marijuana. The immune system protects the body against pathogenic microorganisms through the inflammatory process, which aids in wound healing.³⁹ Decreased immunity directly affects the prevention of mucosal infections by *Candida spp* mediated by neutrophils and macrophages, resulting in delayed wound healing, as well as disrupting the body's ability to fight infection.

This study was conducted with limited availability of articles in 3 online databases regarding the incidence of oral candidiasis after tooth extraction. With these limitations, it is hoped that further research can be conducted to support and strengthen these findings as a risk indicator for the occurrence of oral candidiasis following tooth extraction.

CONCLUSION

The research above indicates that tooth extraction may increase the risk of oral candidiasis, which is triggered by the patient's underlying condition, leading to the development of commensal fungal properties. *Candida albicans* becomes pathogenic. These results are based on research findings in the last 10 years, namely the occurrence of oral candidiasis after extraction, accompanied by conditions such as immunocompromised conditions, such as diabetes, HIV, Graves' disease, hypertension, and also found to be the result of drug abuse, heroin, opioids, and marijuana.

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