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And Scientific Research
Maysan University College of Dentistry

Pathogenesis and Prevention of *Candida albicans* Effects on Dental Implants

Graduation Research Project

Submitted to the Council of the College of Dentistry / University of Misan

As part of the requirements for obtaining the Bachelor's degree in Dentistry

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2025 A.D **1446 A.H**

بِسْمِ اللهِ الرَّحْمَنِ الرَّحِيمِ

(يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)

صَدَّقَ اللهُ الْعَلِيّ الْعَظِيمِ

(من سورة المجادلة، الآية :11)

Certification

I hereby, certify that this research project entitled “**Pathogenesis and Prevention of *Candida albicans* Effects on Dental Implants**" Which is being submitted by

Names of students

1- **Aya Salman Hatem**
2- **Hiba Sammer Badr**

was prepared under my supervision at College of Dentistry / University of Misan, as part of the requirements for obtaining the Bachelor's degree in Dentistry

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Signature:

Date: / 3 /2025

Name: **Muhanad M. Mohammad**

Title: **Assistant Lecturer**

Dedication

In the name of God, the Most Gracious, the Most Merciful

And say, "My Lord, increase me in knowledge."

Praise be to God, who taught man that which he knew not and granted me the strength and patience to complete my academic journey until, with His help and grace, I was able to place this humble research in your hands. To my esteemed professors who never withheld their knowledge, advice, and guidance, to those who served as role models and examples for me in the love of knowledge and learning, to those who instilled in me a love of research and exploration. I dedicate this humble research, of which you are a part, as an expression of my gratitude and appreciation for your generous efforts. I hope that your name and status will be immortalized in scientific and cognitive history.

Researchers

Acknowledgments

First and foremost, we give thanks to God for His boundless mercy, which enabled us to present this project in the best possible form. We would like to extend our gratitude to our project supervisor, (Muhanad M. Mohammed), for his invaluable guidance and support in bringing this project to completion. We are also grateful to our faculty members and professors for providing us with knowledge and resources. Above all, we are deeply thankful to our families for their unwavering love, assistance, support, and encouragement, and to our friends for their understanding and support throughout. this journey

Researchers

Summary

Dental implants are an effective solution for replacing missing teeth, but their success depends on several factors, including the health of the tissues surrounding the implant and the absence of infection. Fungi, particularly Candida albicans, play a pivotal role in causing complications that can affect implant stability. Fungi can multiply on the surface of metal implants, forming a biofilm, making them more difficult to eradicate with conventional treatments.

One of the most prominent problems associated with fungi in dental Implants is peri-implantitis, which, if left untreated, can lead to implant loss. Factors such as weakened immunity, dry mouth, or the use of temporary dentures also increase the risk of infection. Therefore, early detection, meticulous oral hygiene, and regular microbial assessment are essential to maintain the success of dental implants and prevent the negative effects of fbegIt is essential to diagnose fungal Infections in their early stages through clinical examination and microbiological tests, and to use topical or systemic antifungal treatments depending on the severity of the condition.

Patient health education also plays a significant role in reducing the likelihood of infection by promoting regular oral care and avoiding factors that promote fungal growth. This study aims to shed light on the relationship between fungal Infections and dental implants, analyze the biological mechanisms that lead to implant failure, and discuss the latest preventive and therapeutic methods that can be used to reduce the impact of fungi on the long-term success of dental Implants.

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Chapter One
Introduction

1.1. Introduction

Dental implants have become a widely accepted and preferred solution for the replacement of missing teeth, offering functional and aesthetic benefits (Howe *etal*.,2019). However, the success and longevity of these Implants are highly dependent on effective osseointegration – the direct structural and functional connection between living bone and the surface of a load-bearing implant.

Achieving optimal osseointegration is critical for Implant stability and the long-term success of dental prosthetics (Alghamdi and Jansen,2020) To enhance this process, various surface modifications of dental implants have been developd, aiming to improve the interaction between the implant surface and the surrounding biological environment (Tsigarida *etal*.,2020).

In the context of rodent studies, whichh are commonly used in dental implant research, "implant longevity" has generally been as survival beyond 30 days of age In mice, which Is a significant milestone in their lifespan. This definition Is based on the fact that mice have a relatively short median lifespan of around 18–24 months, and 30 days represents a substantial portion of their early life (Scarano *eatal*.,2024; Blanc-Sylvestre *etal*.,2021).

Demonstrated that elastin-like protein coatings on implants in rat tibia and femur reduced micromovements associated with deficient force loads, thereby improving mechanical properties through rapid osseointegration. Additionally, it has also been found that incorporating hyaluronic acid into polyelectrolyte multilayer coatings enhanced osteogenic differentiation of adiposederived stem cells and increased bone mineral deposition (Sabino *etal*.,2021; Accioni *etal*.,2022).

1.2. Aim of the study

- To investigate the pathogenic mechanisms of Candida albicans in relation to dental implants.
- To analyze the role of Candida albicans in biofilm formation and peri-implant infections.
- To identify the factors contributing to implant failure caused by fungal colonization.
- To review current preventive measures and treatment strategies targeting Candida albicans in the context of implant dentistry.

- To emphasize the importance of early detection and proper hygiene in preventing fungal-related complications in dental implants.

Chapter Two
Literature Review

2. Literature Review

2.1. An Overview of *Candida albicans*

Candidiasis is generally provoked by candida species, which is a fungal disease impacting different mucosal surfaces in the human body. This review provide a brief explanation on candidiasis, encircling its epidemiology, pathogenesis, clinical indications, diagnoses, and treatment. (Sharif *etal*.,2024).Annually, 65 million invasive fungal infections occur worldwide, resulting in approximately 3.8 million deaths (Stoia *etal*.,2024; Lu *etal*., 2023; Denning,2024).

Among these fatalities, about 80% is attributed to fungal sepsis from hospital-acquired fungal infections, with Candida albicans being the most prevalent culprit.(Lu *etal*.,2023) Fungal infections in skin are extremely stubborn and seriously threaten human health. In the process of antifungal treatment, it is a huge challenge that the stratum corneum of the skin and fungal biofilms form the drug transport barrier (Ji *etal*.,2021).

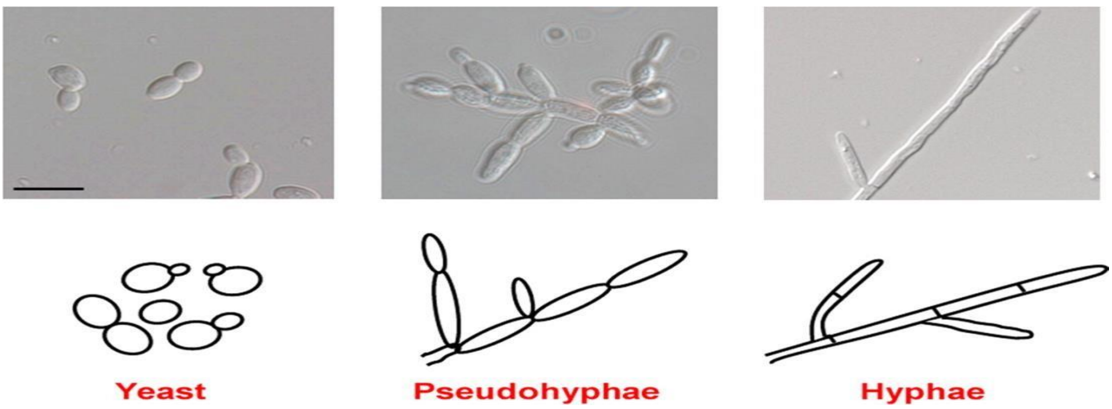

Figure. 1. Major morphologies of human fungal pathogens. (Top) Images of *C. albicans* cells as visualized by differential interference contrast (DIC) microscopy (bar = 10 µm). (Bottom) Schematic representation of each morphology (Egel,2013; Feldmann,2011).

2.1.1. Characteristics and Classification

Candida albicans remains a major fungal pathogen colonizing humans and opportunistically invading tissue when conditions are predisposing (Soll,2024). The last decade has been characterized by a gradual revision of our understanding of microorganisms as single-celled individuals (Lenchenko *etal*.,2020).

In the external environment, about 99.9% of all microorganisms are able to form biofilms (Lenchenko *etal*.,2020; lozovoy *etal*.,2019). The matrix produced by cells in biofilms provides physical protection of the cells from immune system factors such as antibodies and macrophages, and from bacteriophages, and hinders the penetration of antibiotics, contributing to antibiotic resistance. Both bacteria and fungi form biofilms (Rossignol *etal*.,2007; Ramage *etal*.,2002).

2.1.2. Classification of *Candida albicans*

The study aimed to investigate *Candida albicans* presence, antifungal resistance, biofilm formation, putative virulence genes, and molecular characterization in oral samples of dogs and cats (Hizlisoy,2024). *Candida albicans* is a diploid polymorphic yeast that is commonly found on skin and mucosal surfaces as part of the normal human microbiome (Lopes *etal*.,2015; Macias-Paz *etal*.,2023). Additionally, there Is a growing concern about the impact on clinical outcomes of antifungal resistance in IC (Fisher *etal*.,2022).

2.1.3. Role in Oral infections

The genus *Candida* spp. Belongs to the microbiota of the oropharyngeal cavity, gastrointestinal tract, genital system, and skin (Talapko *etal*.,2021). Most of the species of this genus are opportunistic pathogens, and infections caused by them are primarily the result of disturbances in the balance of the normal microbiological flora caused by Immunosuppressants, broad-spectrum antibiotics, or the loss of the protective epithelial barrie (Cczechowic *etal*.,2022).

The principal risk factors for candidiasis are neutropenia following chemotherapy or immunosuppressive treatment (oncological and transplant patients) (Rahi *etal*.,2012). The use of broad-spectrum antibiotic therapy, the presence of a central venous catheter or urinary catheter, parenteral nutrition, renal dialysis, and the use of endoprostheses (Dudakova *etal*.,2022).

2.2. Dental implants

A treatment approach that is widely used as a permanent and natural replacement for missing or extracted teeth is dental implants. VR is a computer-generated simulation that creates a three-dimensional (3D) image or environment (Monaghesh *etal*.,2023).

In recent years, virtual reality and interactive digital simulation have been used in dental education to train dental students before interacting with real patient (Moussa *etal*.,2022). The obtained results showed that the designed touch-based system can simulate different dental implant surgeries with different drill diameter and drill speed, which also takes patient-specific models as input (Rantamaa *etal*.,2022).

Also, based on the results of a study, the virtual surgery system for dental implant training can be used for teaching and learning, with good performance and prediction, to achieve progress in dental implant surgery training (Zhou *etal*.,2021).

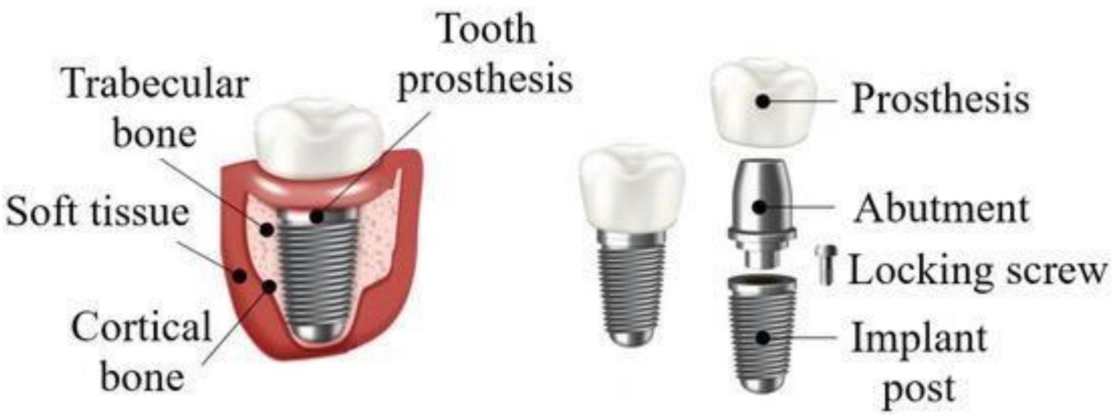

Figure 2. Dental implant with components (kligman *etal*.,2013)

2.2.1. Types of dental implants

The quest for materials suitable for biomedical applications, particularly in dental implants, remains a challenge in Implantology, driven by an aging population and the high incidence of failure rates, thereby increasing the demand for successful rehabilitation treatments (Wong *etal*.,2023; Çallıoğlu and Acar,2020; Wu *etal*.,2022).

Therefore, a deeper insight into the material's composition and structure is crucial for optimizing its performance in biomedical applications (Çallıoğlu and Acar,2020; Santos *etal*.,2023). In the past, precious metals such as gold, and platinum were widely used. However, due to their high cost and limitations such as inadequate mechanical properties and difficulties in manufacturing, these materials have been replaced by more affordable metallic options with more suitable characteristics for the application (Hossain *etal*.,2023).

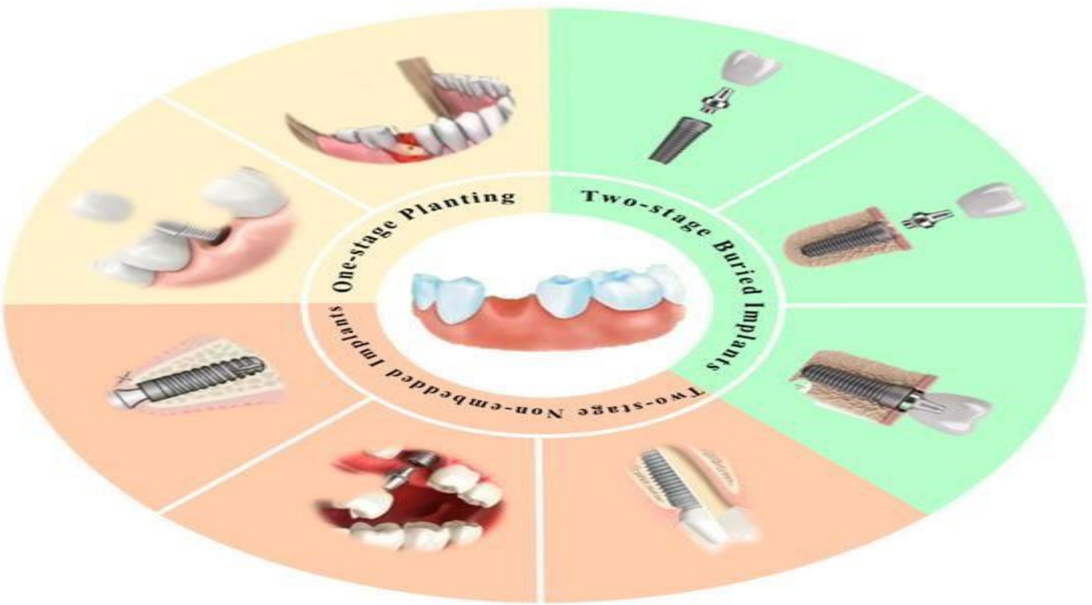

Figure 3. Implant modeling with three types of implants: one-stage implant, two stage non-embedded implant, and two-stage embedded implant. Created through Adobe Photoshop (PS) CS 8.0 drawing software (sailer *etal*.,2022).

2.2.2. Materials used in Dental Implant

Biocompatibility, the ability of the material to be integrated into the body without clinical complications and to Induce the required cellular or tissue response (Zhang *etal*.,2023). Osseointegration, or the fusion of the implant surface with the bone (Wang *etal*.,2023). Or by forming bioactive coatings on the surface, which, according to the authors (Mishra and Chowdhary,2019).

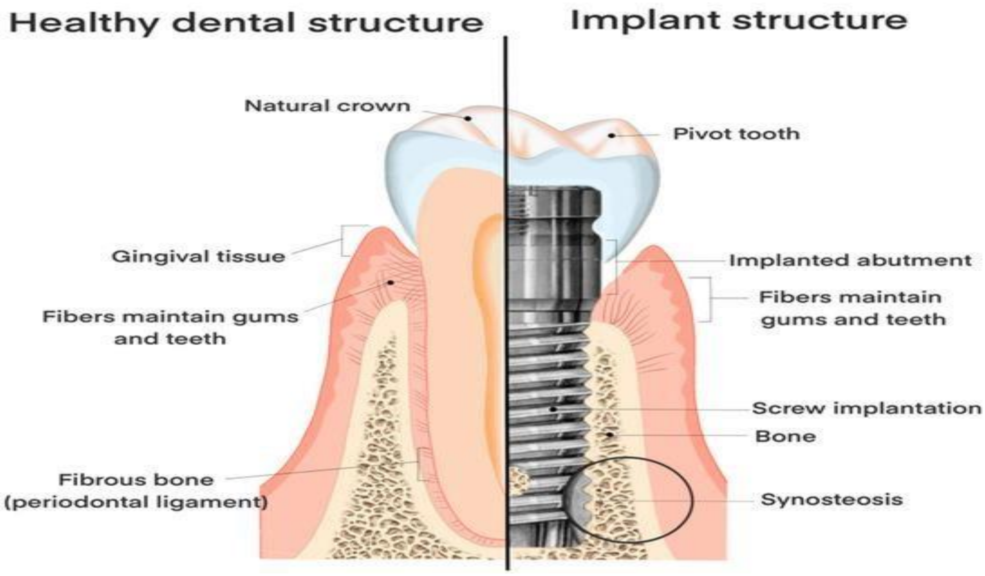

Figure 4. Comparison of healthy tooth structure and dental Implant structure. Natural teeth Include natural crowns, gums, and fibrous bone; dental implants include artificial crowns, abutments, and the implant. Created through Adobe Photoshop (PS) CS 8.0 drawing software (peng *etal*.,2021).

2.3. Osseointegration

Today the focus Is on modulation of the osteoimmune microenvironment at the bone-implant interface (Zhou etal.,2020; Wang *etal*.,2022). In addition, it is known that once macrophages acquire a functional polarization, they still retain the ability to continue changing in response to new environmental stimulation (Liu *etal*.,2020).

Therefore, a balanced inflammatory environment around a biomaterial is critical, since both downregulated and excessive inflammatory responses lead to suboptimal bone regeneration clinical (Ghadami *etal*.,2022) In the case of oral implants where a failing process has already been initiated for other reasons (Albrektsson *et al*.,2022).

2.4. Significance of Dental Implants in Modern Dentistry

Sandblasting involves using a high-speed jet beam created by compressed air to spray materials of different Particle sizes onto the implant surface, changing the surface roughness (Menhall *etal*.,2024). Plasma spraying, a thermal process that utilizes an electrical-driven arc to create high temperature ionized Gas, is a crucial technique in biomaterials and dental implants (Ghadami *etal*.,2022).

In the texturing application, the laser prepares specific Surface topographies on the implant, resulting in a textured surface that can significantly improve Osseointegration (Onder *etal*.,2024), an Alternative electrochemical deposition method has gained prominence recently as an innovative approach For creating sol-gel films (Jaafar *etal*.,2020).

2.5. Interaction Between *Candida albicans* and Dental Implants

2.5.1. Dherence mechanism

C. albicans has a specialized set of proteins(adhesins) which mediate adherence to other C. albicans cells to other microorganisms, to abiotic surfaces and to host cells (Verstrepen &kils*,2006*; Garcia *etal*.,2011).
Arguably the best studied C. albicans adhesins are the agglutinin-like sequence (ALS) proteins which form a family consisting of eight members (Als1–7 and Als9). The ALS genes encode glycosylphosphatidylinositol (GPI)-linked cell surface glycoproteins. Of the eight Als proteins, the hypha-associated adhesin Als3 is especially important for adhesion (Murciano *etal.,* 2012).

ALS3 gene expression is upregulated during infection of oral epithelial cells in vitro and during in vivo vaginal infection (Cheng *etal*.,2005; Wächtler *etal*., 2011). Another important adhesin of C. albicans is Hwp1, which is a hypha associated GPI-linked protein (Sundstrom *etal*., 2002). Hwp1 serves as a substrate for mammalian transglutaminases and this reaction may covalently link C. albicans hyphae to host cells. An hwp1Δ/Δ mutant displayed reduced adherence to buccal epithelial cells and displayed attenuated virulence in a mouse model of systemic candidiasis (Sundstrom *etal.,* 2002).

Hwp1 and Als3 were also demonstrated to contribute to biofilm formation by acting as complementary adhesins (Nobile *etal*.,2008). Morphology-independent proteins can also contribute to adhesion. These include GPI linked proteins (Eap1, Iff4 and Ecm33), non-covalent wall associated proteins (Mp65, a putative β-glucanase, and Phr1, a β-1,3 glucanosyl transferase), cell-surface associated proteases (Sap9 and Sap10) and the integrin like surface protein Int1.(Zhu & filler,2010; Naglik *etal.,* 2011).

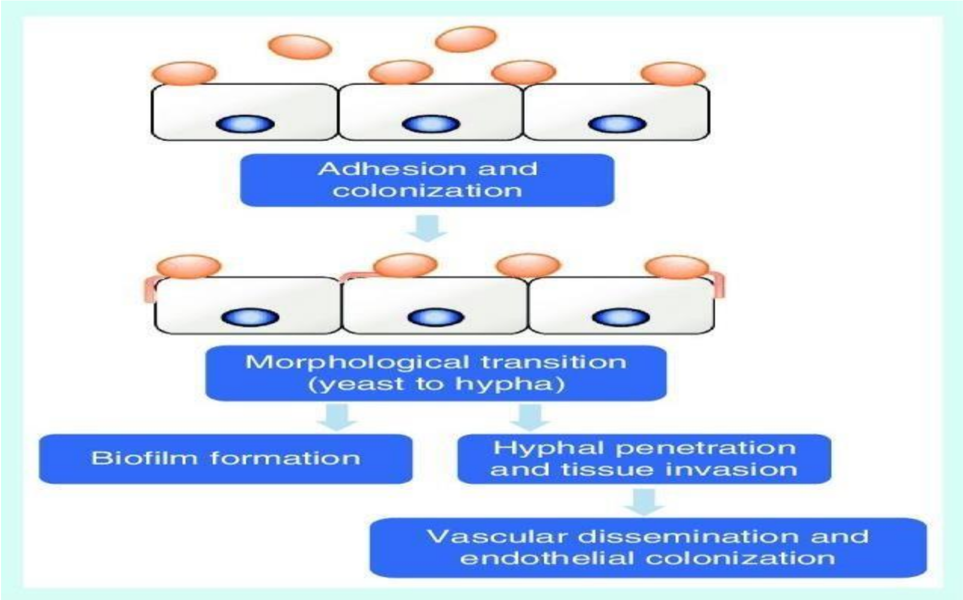

Figure 5. ***Candida albicans*** **adherence and morphogenesis lead to biofilm formation and tissue invasion: adherence of yeast cells to epithelial cell surface is the initial step for C. Albicans colonization; subsequent yeast-to-hypha transition facilitates biofilm formation, tissue invasion and spread of systemic infection (Gow** ***etal*****.,2011).**

2.5.2. Biofilm Formation

A further important virulence factor of C. albicans is its capacity to form biofilms on abiotic or biotic surfaces. Catheters, dentures (abiotic) and mucosal cell surfaces (biotic) are the most common substrates (Fanning & Mitchell, 2012). Biofilms form in a sequential process including adherence of yeast cells to the substrate, of these yeast cells, formation of hyphal cells in the upper part of the biofilm, accumulation of extracellular matrix material and, finally, dispersion of yeast cells from the biofilm complex (Finkel & Mitchell,2011).

Mature biofilms are much more resistant to antimicrobial agents and host immune factors in comparison to planktonic cells.(Finkel & Mitchell,2011;Fanning &Mitchell,2012).The factors responsible for heightened resistance include the complex architecture of biofilms, the biofilm matrix, increased expression of drug efflux pumps and metabolic plasticity (Fanning & Mitchell, 2012).Dispersion of yeast cells from the mature biofilm has been shown to directly contribute to virulence, as dispersed cells were more virulent in a mouse model of disseminated infection (Uppuluri *etal*., 2010).

The major heat shock protein Hsp90 was recently identified as a key regulator of dispersion in C. albicans biofilms (Robbins *etal*., 2011). In addition, Hsp90 was also required for biofilm antifungal drug resistance (Robbins *etal*., 2011).Several transcription factors control biofilm formation.

These include the transcription factors Bcr1, Tec1 and Efg1 (Fanning & Mitchell,2012). In a recent study, investigated the transcriptional network regulating biofilm formation and identified further, previously unknown regulators of biofilm production (Nobile *etal*., 2012). These novel actors include Ndt80, Rob1 and Brg1. Deletion of any of these regulators (BCR1, TEC1, EFG1, NDT80, ROB1 or BRG1) resulted in defective biofilm formation in in vivo rat infection models (Nobile *etal*., 2012). Extracellular matrix production is controlled by additional factors. The zinc-responsive transcription factor Zap1 negatively regulates β-1,3 glucan, the major component of biofilm matrix (Nobile *etal*.,2009).

Glucoamylases (Gca1 and Gca2), glucan transferases (Bgl2 and Phr1) and the exo-glucanase, Xog1, are positive regulators of β-1,3 glucan production (Nobile *etal*.,2009;Taff *etal*.,2012). While expression of GCA1 and GCA2 are controlled by Zap1, the enzymes Bgl2, Phr1 and Xog1 function independently of this key negative regulator (Taff *etal*.,2012).

Biofilms formed by mutants lacking BGL2, PHR1 or XOG1 were shown to be more susceptible to the antifungal agent, fluconazole, both in vitro and in vivo (Taff *etal*., 2012). Furthermore, recent studies indicate that C. albicans biofilms are resistant to killing by neutrophils and do not trigger production of reactive oxygen species (ROS) (Xie *etal*.,2012). Evidence suggests that β-glucans in the extracellular matrix protect C. albicans from these attacks (Xie *etal*.,2012).

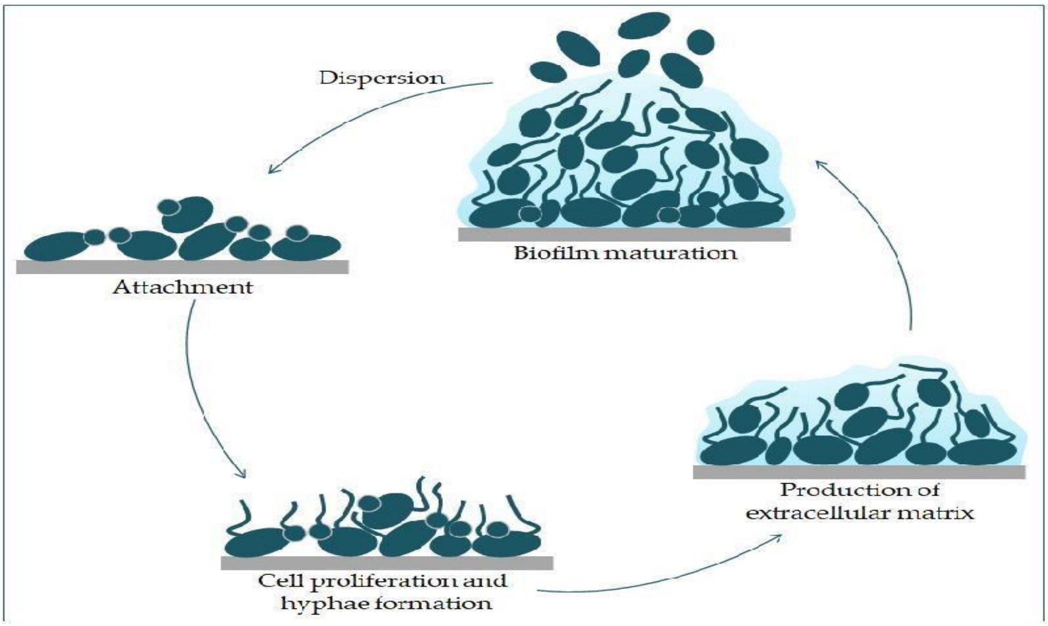

Figure 6. Phases of *C. albicans* biofilm formation (Cavalheiro & Teixeira,2018; McCall *etal*.,2020).

2.5.3. Implants failure

Implant failure is most likely the result of multiple factors. Age and sex, smoking, systemic diseases, maxillary implant site, quantity and quality of bone, and implant surface treatments and features are some of the statistically examined parameters linked to implant failure. The most frequent and avoidable cause of dental implant failure is infection. At any moment over the course of implant therapy, a bacterial infection that results in implant failures can happen. Peri-implantitis is a term used to describe an inflammatory response with bone loss in the soft tissues surrounding implants. The concept of peri-implantitis could include plaque-induced infection caused by plaque building up on the exposed surfaces of the biomaterial (Sánchez Garcés *etal*.,2004).

In connection with loose prosthetic components, fistulas and hyperplastic mucositis are frequently observed. Food particles stuck in the peri-implant crevice can occasionally cause abscesses (McCracken *etal*., 2012). Overload-related implant failures occur when the functional load placed on the implants is greater than what the bone can bear (Hinode *etal*.,2006).

Infection and impaired healing are the two major mechanisms responsible for dental implant failure. Bacterial infection may cause implant failure and can occur at any time during the implant treatment, but it is quite important in early healing period. Impaired healing may be due to the surgical trauma (insufficient irrigation, overheating), micromotions, and the patient's related local and systemic factors, which play an imperative role in dental implant failure related to impaired healing (Sakka *etal*.,2011).

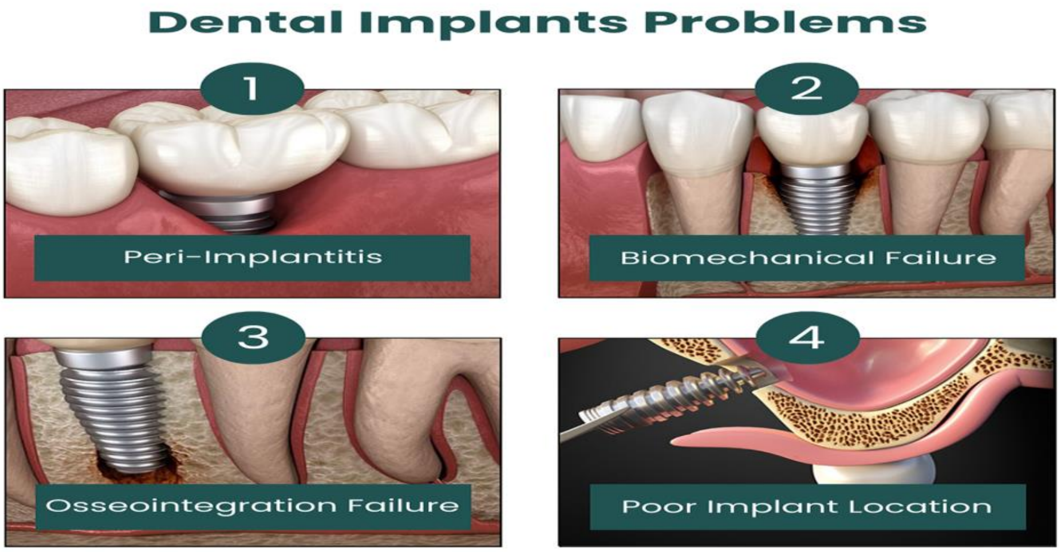

Figure 7. Dental Implants Problems (Sakka *etal*.,2011).

2.6. Pathogenesis of *Candida albicans* Effects on Dental Implants

Inflammation is a protective response of cells to Pathogens, infection or tissue damage. It involves the Coordinated communication of different immune cells and blood vessels through an intricate cascade of Molecular signals. The inflammatory response has four Phases: inflammatory inducers (infection or tissue Damage), inflammatory sensors (mast cells and ,Macrophages), inflammatory mediators (cytokines Chemokines, etc.) and the tissues that are affected (Medzhitov , 2010).

Initially, peri-implant mucositis is a condition that affects the mucosa surrounding dental implants, similar to gingivitis. Preimplant mucositis is a reversible inflammation with clinical signs of redness, swelling, and bleeding upon probing (HeitzMayfield & salvi,2018). Secondly, peri-implantitis is comparable to periodontitis. It is characterized by loss of bone, and infection in the vicinity of the implant (Schwarz etal., 2018).

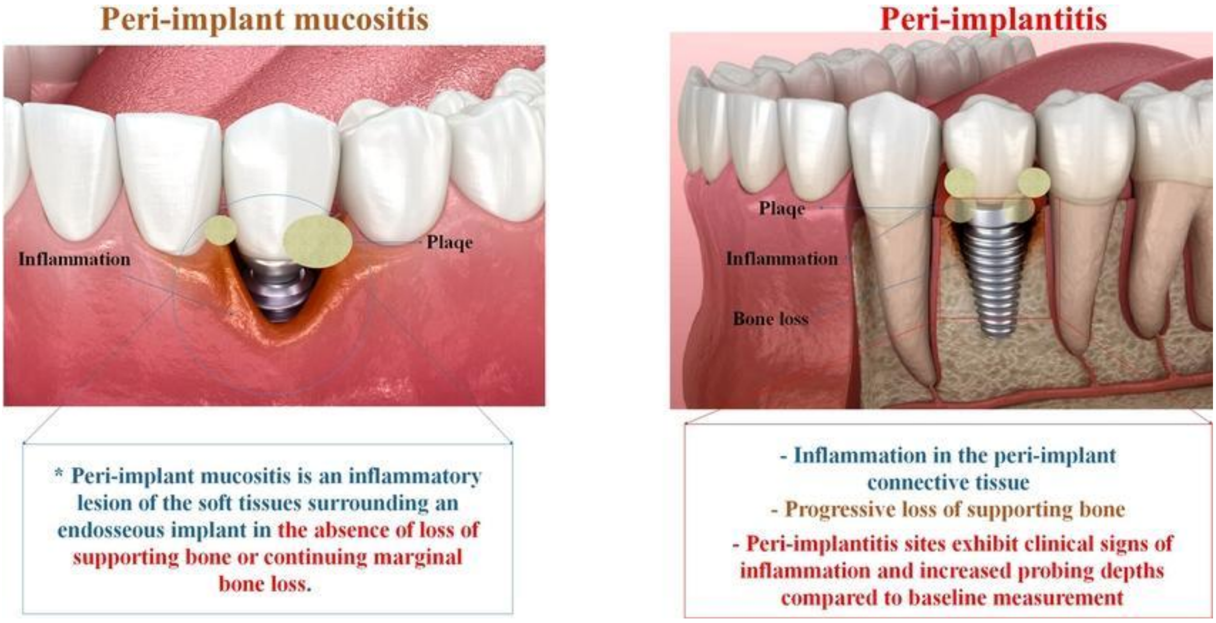

Figure 8. The essential characteristics of per-implant diseases (PIDs), including peri-implant mucositis (PW) and peri-implantitis (Alves *etal*.,2022)

2.7. Prevention and Treatment Strategies

2.7.1. Antifungal Agents

Investigating the five antifungal drug classes that have been approved for use on humans requires an understanding of the structural differences between pathogenic fungus and normal cells. The creation of antifungal drugs frequently targets the mannans, glucans, and chitins, as well as a few of the enzymes of the ergosterol biosynthesis pathways that are exclusive to fungal cells (Georgiev, 2000).

The azoles, polyenes, echinocandins, pyrimidine analogues, allylamines, thiocarbamates, and morpholines are the most widely used antifungal medications, along with a few newly developed antifungal medicines (Castelli *etal*.,2014).

Azoles are the largest class of antifungal drugs and is used for topical treatment of dermatophytic infection. Subsequently, triazole-based drugs, including fluconazole and itraconazole were developed, exhibiting a broader spectrum of activity. Triazoles are taken for both systemic and mucosal infections, whereas imidazole’s are mostly utilised for mucosal fungal infections (Sanglard& Coste,2016).

Polyenes such as amphotericin B (AMB), initially isolated from Streptomyces, are macrolides, amphipathic organic compounds (Vandeputte *etal*.,2012). Amphotericin B (AmpB), natamycin, and nystatin are the three major polyenes. Because of its poor absorption, natamycin and nystatin are favoured for topical infections, whereas AmpB is most effective against Cryptococcus, Candida and Aspergillus species in systemic invasive fungal infections (Lemke *etal*., 2005).

The pyrimidine analogues, such as 5-fluorocytosine (5-FC) and 5-fluorouracil, are synthetic analogues of the nucleotide cytosine (5-FU). Cytidine deaminase transforms the pyrimidine analogue 5-FC into 5-FU, which is then incorporated into DNA and RNA during their synthesis and suppresses cellular activity by either preventing protein synthesis or preventing DNA replication. These medication analogues exhibit anti-Candida and anti-Cryptococcus action (Sanglard *etal*., 2009).

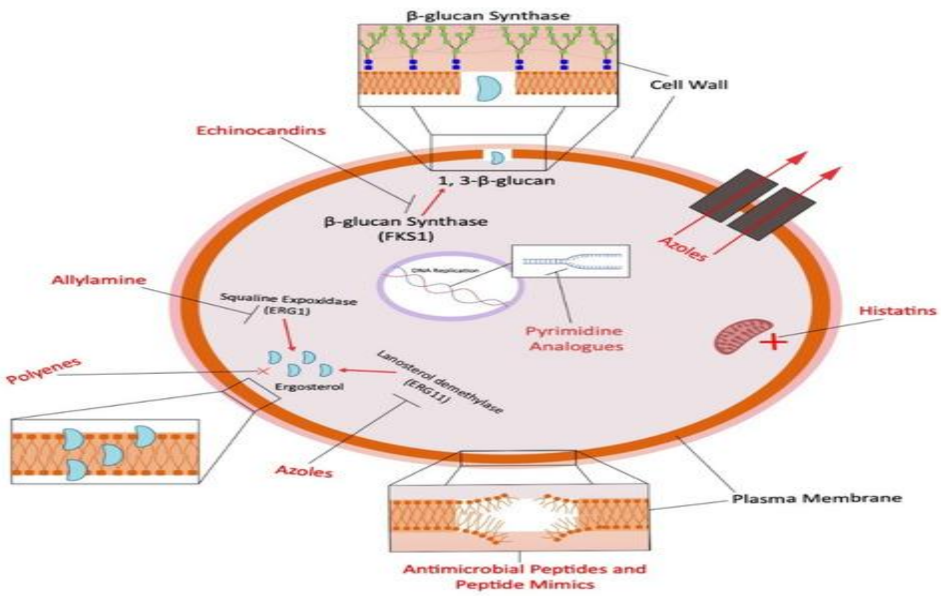

Figure 9. Classes of Antifungal Drugs and Their Overall Mechanism of Action. Drug class names are indicated in red (Castelli *etal*.,2014).

2.7.2. Surface Modifications

Dental implants have become a widely accepted and preferred solution for the replacement of missing teeth, offering functional and aesthetic benefits (Howe *etal.,* 2019). However, the success and longevity of these implants are highly dependent on effective osseointegration – the direct structural and functional connection between living bone and the surface of a load-bearing implant. Achieving optimal osseointegration is critical for implant stability and the long-term success of dental prosthetics (Alghamdi & Jansen*,* 2020). To enhance this process, various surface modifications of dental implants have been developed, aiming to improve the interaction between the implant surface and the surrounding biological environment (Tsigarida *etal*.,2020).

Surface modifications can be broadly categorized into physical, chemical, and biochemical alterations. Physical modifications include changes in surface topography and roughness, which have been shown to influence cell behavior and improve mechanical interlocking between the implant and bone (Chopra *etal*.,2021).

Chemical modifications involve the alteration of surface chemistry to enhance biocompatibility and promote bone cell attachment and proliferation. Biochemical modifications typically include the incorporation of bioactive molecules, such as growth factors, peptides, and proteins, which can further enhance bone regeneration and integration (Christenson *etal*.,2007; Jimbo etal.,2012).

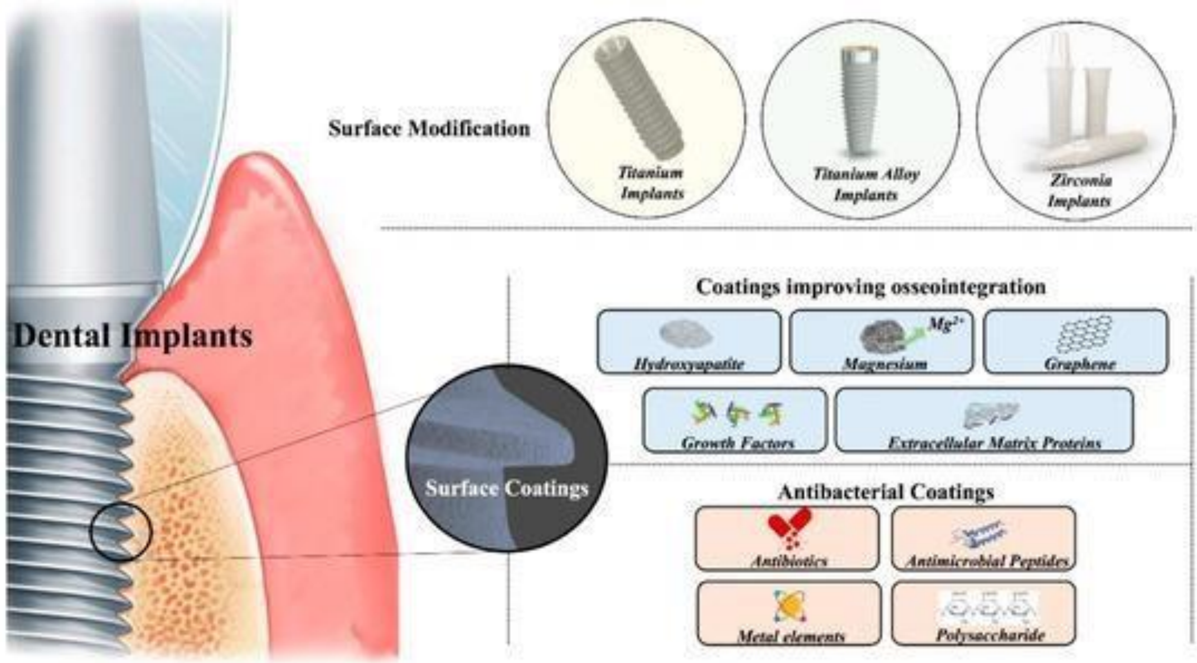

Figure 10. Surface modification and coatings of dental implants (Dong *etal*.,2020).

2.7.3. Clinical Strategies for Preventing *Candida albicans* infections

The concept of protection through antibody has been controversial for quite long time, a large amount of data is coming out in favor of its use to prevent and also to cure the diseases. This alternative method is gaining its importance in the context of growing number of immunocompromised patients who are sensitive to toxic effect of conventional drugs. For treating the Candida infections, antibodies have been generated against cell wall polysaccharides, heat shock protein, secreted proteins, and peptides (Cutler,2005; Yang *etal*.,2005).

The synthetic glycopeptide vaccine against disseminated candidiasis has been found to be quite effective in mice (Xin *etal*.,2008). Furthermore, synthetic glycopeptide conjugates were made by combining fungal cell wall beta-mannan trisaccharide and six 14 mer peptides from six different proteins such as enolase, phosphoglycerate kinase, fructose bisphosphate aldolase, hyphal wall protein-1, methyl tetrahydropteroyltriglutamate, and glyceraldehydes3phosphate dehydrogenase (Xin *etal*., 2008).

Furthermore, it has been demonstrated that vaccine and monoclonal antibody E2-9 (IgM) against peptide, Fba (derived from fructose bis phosphate aldolase), can protect mice from candidiasis (Xin & Cutler,2011).Also, antibodies raised against beta glucan (elicited by peptide conjugate) are able to protect mice that are challenged with C. albicans possibly by inhibiting the fungal growth and its adherence to mammalian cell (Kondori *etal*.,2008; Torosantucci *etal*.,2009).

2.8.Management of *Candida albicans* Infections on Dental Implants

2.8.1. Non-Surgical Approaches

Non-surgical debridement is frequently the initial method employed to address infected tissues in the vicinity of dental implants(Renvert *etal*.,2008). This procedure typically entails the comprehensive removal of debris, plaque, and calculus from the implant surface and the adjacent tissues. Its objective is to reduce inflammation and bacterial infection without necessitating invasive procedures. Nevertheless, in certain instances of advanced or persistent infection, surgical intervention may be required to completely access and clean the area surrounding the implant (Wijesundara *etal*.,2023).

Manual instruments and ultrasonic devices are the primary tools and devices used in the clinical setting for the nonsurgical mechanical debridement (Renvert *etal*.,2008).

Air particle abrasive systems (e.g., air-polishing) can be employed in conjunction with instrument cleaning to eliminate biofilm and calculus from difficult-to-reach regions surrounding the implant. The efficacy of these instruments and devices in managing peri-implant diseases has been the subject of numerous RCTs. These mechanical debridement methods have been demonstrated to decrease peri-implant inflammation, as evidenced by the plaque and bleeding-on probing scores. Nevertheless, there was no discernible effect on the probing depth (PD) (Renvert *etal*.,2008).

In cases where the infection is severe or has spread beyond peri-implant tissues, the administration of local antibiotics can be a critical component of the treatment strategy for periimplantitis (Passarelli *etal*.,2021). Given that the biofilm of peri-implantitis contains a broader spectrum of pathogenic microorganisms, it may be even more crucial to reduce the number of pathogens and alter the bacterial biofilm composition in the management of peri-implantitis. From this perspective, the administration of antibiotics could be advantageous for the management of biofilm dysbiosis (Mombelli & Lang,1992).

Chlorhexidine is frequently employed in periodontology due to its broad-spectrum antimicrobial properties(Sahrmann *etal*.,2019). For dental implants, many clinicians used to prescribe antiseptic mouthwash to patients as part of their daily oral hygiene regimen. This could potentially mitigate the risk of peri-implant diseases by preventing the accumulation of bacterial plaque on implant surfaces and adjacent gingival tissues (Krishnamoorthy *etal*.,2022).

2.8.2. Surgical Interventions

The treatment of peri-implantitis requires surgical intervention to eliminate the pocket, clean the infected defect, and decontaminate the implant surface (Wijesundara *etal*., 2023). The progression of periimplantitis can be effectively treated by resective surgery (i.e., ostectomy and osteoplasty) in combination with the smoothing and polishing of the dental implant surface (Aljohani *etal*.,2020).

However, the resective approach is associated with increased postoperative recessions, which is not suitable for esthetic sensitive areas. Consequently, the regenerative approach for the treatment of peri-implantitis is another effective surgical technique, as recommended by numerous recent clinical studies. Mainly, the application of guided bone regeneration (GBR) with various grafting materials and/or resorbable membranes resulted in favorable therapeutic outcomes (Yu *etal*.,2024).

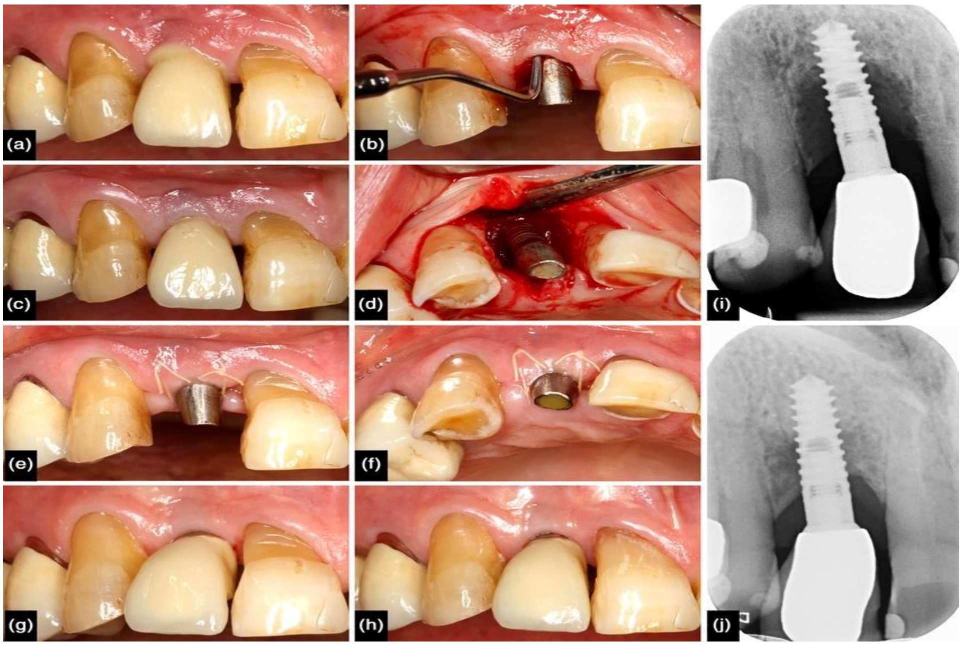

Figure 11. Non-surgical and surgical treatment of peri-implantitis. (a) Purulent peri-implantitis lesion at implant regio 12. (b) Clinical view after removal of the cemented crown. Note the increased probing pocket depth at the buccal aspect of the implant. (c) Clinical situation 2 weeks after non-surgical treatment using an air-polishing device. Note the resolution of inflammation signs. (d) After mobilization of the mucoperiosteal flap, a circumferential infrabony defect was detected. The surgical treatment included decontamination of the implant surface and application of enamel matrix derivatives. (e and f) Apart from a minor soft tissue dehiscence at the mesial papilla, an uneventful wound healing was observed 1 week after surgery. (g and h) Bland mucosal conditions 1 and 2 years after surgery without formation of mucosal recession. (i and j) A pronounced infrabony component was present on the baseline X-ray. A significant bone fill was achieved 2 years after surgery(Günay *etal*.,2013; Adam *etal*.,2019)

2.9. Diagnosis and Management

There are many laboratory methods for the identification of Candida, and the most commonly used is cultural microscopic exam. The presence of clustered pseudo hyphae on Gram stain had a high sensitivity, specificity, positive predictive value, and negative predictive value for *C. albicans*; therefore, the presence of pseudo hyphae clusters on Gram staining is useful in distinguishing *C.albicans* (Harrington *etal*., 2007).

Other than Gram staining, there are many different staining methods, including Wright's–Giemsas, periodic acid Schiff stain (PAS), May–Grünwald Stain, and Liu's stain. In our lab, we adopted the Wright's–Giemsas stain and the Liu’s stain . Both stains clearly show WBC swallowing Candida. The patterns of fungi and mycelium can be directly observed in the blood of patients infected with candidemia and the medical examiner must be highly alert to these features to facilitate differential diagnosis and early treatment.The germ tube test is routinely used for the rapid identification of Candida albicans and its variants, and is generally thought to be specific for these organisms.(Gow, 1997).

There is evidence to demonstrate that hyphae of Candida have a sense of touch that enables them to grow along grooves and through pores (thigmotropism). This may aid infiltration of epithelial surfaces during tissue invasion. Hyphae are also aero tropic and can form helices when contacting solid surfaces. Candida species form germ tubes when incubated in serum up to 3 hours, which can be observed under a microscope. Currently, there are also polymerase chain reaction (PCR) and pulse-field gel electrophoresis analysis methods. PCR of whole blood samples had perfect sensitivity and specificity for patients with candidemia when compared with healthy controls (Avni *etal.,* 2011).

Conclusions

and

Recommendation

2.10. Conclusions and Recommendations

2.10.1. Conclusions

- Fungi, particularly Candida albicans, are opportunistic pathogens that can negatively impact the success of dental implants, especially in cases of immunodeficiency or poor oral hygiene.
- The ability of Candida albicans to form biofilms on the surface of dental implants poses a significant treatment challenge, as the fungi become resistant to conventional medications and antiseptic agents.
- Fungi contribute to infections of the tissues surrounding the implant, such as peri-implant mucositis and peri-implantitis, leading to loss of bone support and long-term implant failure.
- There are major risk factors that increase the likelihood of fungal infections, such as diabetes, dry mouth, smoking, poor dental hygiene, and the use of temporary or permanent dentures.
- Prevention is the best way to preserve dental implants, through awareness, regular checkups, and enhanced oral hygiene practices, along with the use of topical or systemic antifungal treatments when needed.

2.10.2. Recommendations

- The necessity of conducting a comprehensive microbial assessment before and after dental implants, especially for patients at risk of fungal infections, such as those with diabetes or those taking immunosuppressive medications
- Encouraging clinicians to use antimicrobial implant materials and surface techniques that reduce fungal adhesion and biofilm formation
- Developing treatment protocols specifically targeted to combat fungi around the implant, whether topical or systemic, depending on the severity of the condition.
- The importance of continuous patient education about the fungal risks associated with implants and the need to adhere to regular follow-up visits

- Avoiding factors that contribute to fungal growth, such as smoking, poor nutrition, and dry mouth
- Conduct regular post-implant examinations to detect any signs of peri-implant infection early...
- Further clinical studies are still needed to understand the mechanism of fungal interactions with different implants and to develop preventive strategies and implant materials that are resistant to microbial growth.

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2.11. Reference

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