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CURRENT DEVELOPMENTS IN PREVENTION AND TREATMENT OF CANDIDIASIS: A REVIEW

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ABSTRACT

Invasive fungus infection affects about six people out of every 100,000 people each year. Only half of these infections are detected throughout the patient's lifetime, making it one of the most common causes of death among intensive-care patients. The low detection rate is due to the diagnostic work's complexity, which comprises clinical, radiographic, and microbiological results. Antimycotic drug-resistant fungi are on the rise all over the world. Guidelines for identifying and treating invasive fungous infections caused by Candida spp., Aspergillus spp., Mucorales, and Fusarium spp. are the topic of this review. In typical hospital care, intrusive fungous infections are frequently ignored. They must include it as a necessary component of antimicrobial stewardship programmes. There is also a great need for novel antimycotic medication classes to be developed

INTRODUCTION

Candida albicans and other species in the genus Candida cause oral candidiasis (candidosis), which is one of the most common opportunistic buccal infections. Candidiasis is usually a benign disease of the oral mucous membranes, however it can sometimes be resistant to therapy or relapse or return. This oral infection is more common in adults of advanced age, those with a variety of underlying conditions, and, most importantly, patients with immunodeficiency. Despite the fact that there are over 150 species of Candida, C. albicans is the most common cause of oral candidiasis, accounting for 95% of cases. *Candida glabrata, Candida tropicalis, Candida parapsilosis, Candida krusei, Candida dubliniensis,* and *Candida guilliermondii* are some of the other Candida species that can produce infections on a sporadic basis, complicating candidiasis management [1]. Fungal infection is one of the most common causes of skin illness in the world. In emerging and undeveloped countries, the frequency of fungal infection is estimated to be around 40 million persons. Fungi normally attack the skin's surface in the beginning and then go deeper into the skin through desquamation. Candida is one of the fungus that causes the majority of superficial skin infections. Cutaneous mycoses are fungi that cause infections in the deeper layers of the skin.

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Dermatophytes are a term used to describe fungal infections that affect the skin. *Tinea corporis*, *Tinea pedis*, and *Tinea cruris* are fungi that are typically seen in dermatomycoses. Subcutaneous mycosis occurs when a fungal infection spreads deeper into the skin tissue. Both superficial and deep fungal infections are treated with antifungal chemotherapy [2]. The mouth cavity is the start of the gastrointestinal system, and it is here that our food is digested. The oral cavity, like the rest of the digestive system, is occupied by billions of microorganisms ranging from viruses to bacteria to eukaryotes like fungi and protozoa. These bacteria are mainly found in biofilms, which are three-dimensional communities containing a wide range of species. The oral cavity is a varied ecosystem with many distinct biological niches that varies dependent on the type of the surface (e.g., hard tooth surfaces versus softer mucosal surfaces), as well as nutrient availability and the dynamic occurrence of oxygen limitation [3]. Antifungal susceptibility testing has become a well established and extensively available tool in the therapy of patients with invasive candidiasis (IC), and it is commonly available in the laboratory department. Antifungal susceptibility testing of Candida spp. is becoming more widely recognised as a method for guiding antifungal agent selection for the treatment of IC, thanks to the expanding number of antifungal treatments active against these infections. Fluconazole is widely used in clinical practice to treat Candida spp.-related systemic infections. Invasive fungal disease caused by Aspergillus spp. and fluconazole-resistant Candida spp. is treated with itraconazole and voriconazole. However, only a few researches have looked into the link between triazole susceptibility and a wide range of clinical Candida spp. Isolates [4]. Candida in the vaginal canal prefers a low pH to develop infection, according to popular belief. However, combined Candida infections with bacterial vaginosis (BV) and aerobic vaginitis (AV) are very prevalent, and they may call into question the notion that Candida should only be detected in low vaginal pH circumstances. The purpose of this study was to see if the vaginal pH of women with acute vaginal candidosis is lower than that of women who had been effectively treated to prevent Candida recurrences [5]. Fungus infections affect more than 10 percent of Germany's population, according to estimates. Mycoses on the skin's surface and on the nails are the most common in this circumstance. Valid judgments cannot be made since there is a scarcity of data on life-threatening conditions. Candida species yeasts are the most prevalent pathogens causing intrusive fungous infections in Germany. Apart from Candida albicans, Candida glabrata is the most usually implicated Candida species. They're more common in people who have immune system problems that are mediated by cells [6] [7].

DIAGNOSIS

Because traditional methods for diagnosing candidiasis are less sensitive and time demanding, immunodiagnostic and molecular techniques for early and specific diagnosis can be recommended [8]. Endoscopic observation of lesions with histopathologic demonstration of distinctive Candida yeast forms in tissue and culture confirmation of the presence of Candida species are required for the diagnosis of OEC. The diagnosis of vulvovaginal candidiasis is based on a combination of clinical signs and symptoms as well as routine microbiological tests. To confirm a diagnosis of mucosal candidiasis, serum biomarkers such as mannan/antimannan or ß-D-glucan are not necessary [9].Despite fluconazole's shown efficacy, primary antifungal prophylaxis for OPC and OEC prevention is not advised in Europe (DI). In a large randomised multicentric unblinded trial, fluconazole (200 mg/day) was found to be superior than clotrimazole troches for the prevention of both OEC and OPC, with the greatest benefit in patients with less than 50 CD4/mm [10].

PATHOGENESIS AND RISK FACTORS

Candida infections can be superficial or invasive, resulting in a variety of illnesses. Infections of the mucous membranes are linked to cellular immunity abnormalities, such as the loss of CD4-positive T-helper cells in HIV patients, followingsteroid-treated patients, antineoplastic drugs (e.g. fludarabine), graft-versus-host disease (GvHD), or following radiation therapy. The majority of illnesses are caused by yeast colonisation of the skin or mucous membranes. The oropharynx and gastrointestinal tract are thought to be the most major entrance points. Furthermore, health-care workers' inadequate hand cleanliness is a possible source of nosocomial infections. Pyrexia, a sepsis-like syndrome, and disseminated infection with microabscesses or infarctions of various organs such as the skin, kidneys, myocardium, liver, spleen, bone, CNS, or eyes with retinal lesions and subsequent symptoms due to loss of function of these structures are among the clinical manifestations. Persistent candidaemia, especially in youngsters, is a major risk factor for disseminated infectious illness. Prolonged use of broad-spectrum antibacterial drugs, steroid medication, central venous catheters, parenteral nutrition, mucous membrane colonisation,

and major abdominal surgery, especially after gut surgery, are all risk factors for invasive candidosis. Persistently positive blood cultures, visceral dissemination, persistent granulocytopenia, and a delayed initiation to antifungal medication are all linked to mortality [11][12][13][14][15].

TREATMENT

Treatments for candidiasis for managing *Candida* infections are usually based upon the anatomic location of the infection, immune status of the patient, risk factors for patients with infection, species responsible and lastly, upon the susceptibility of the *Candida* species towards the anti-fungal drug. Classification of antifungal agents used for the treatment of candidiasis is given below:

Classification

Systemic Antifungal Agents:

A. *Polyenes*: Amphotericin B.

B. Pyrimidine analogue: Flucytosine.

C. *Triazoles:* Fluconazole, Itraconazole, Voriconazole, Ravuconazole, Posaconazole, Ketoconazle.

D. *Echinocandins:* Caspofungin, Anidulafungin, Micafungin.

Topical Antifungal Agents

A. *Topical azoles:* Terconazole, Butaconazole, Miconazole, Clotrimazole, Tioconazole, Sulconazole, Oxiconazole and Econazole.

B. *Topical allylammines*: Terbinafine and Naftifine [16].

In the recent decade, a number of protective and immunogenic vaccine formulations against candidiasis have been created. A vaccine is a biological preparation that boosts immunity against a certain disease. Vaccines are made up of an agent that looks like a disease-causing microorganism, which is synthesized using either a killed or weakened form of the microbe, one of its surface proteins, or one of its toxins, and which stimulates the body's immune system to recognize the agent as antigen and destroy it. It was discovered that heat-killed Saccharomyces (HKY) is an effective *aspergillosis* and *coccidioidomycosis* vaccination. They investigated the effect of HKY against systemic candidiasis to see if the efficacy of HKY-induced protection was due to cross-reactive antigens in the cell walls of different fungus. Prior to an intravenous challenge with Candida albicans, male CD-1 mice were given several HKY regimens subcutaneously [17] [18] [19]. Early and precise diagnosis of the type of oral candidiasis, correction of predisposing factors or underlying disorders, and the use of the most appropriate antifungal medicines are the three foundations of oral candidiasis treatment Controlling predisposing or facilitating variables, as well as promoting excellent oral hygiene and periodic oral examinations, are essential for preventing infection and aiding treatment if it occurs. The immune status of the patient, the specific characteristics of oral candidiasis (clinical presentation, aetiology, susceptibility to antifungal drugs, organic location, dissemination), and the pharmacological characteristics of the available antifungal drugs (administration, metabolism, elimination, interactions with other drugs, and toxicity) should all be taken into account when selecting an antifungal drug. Antifungal drugs include polyenes (amphotericin B and nystatin), echinocandins (anidulafungin, caspofungin, and micafungin), and azoles. The most diversified group of azoles are imidazoles (clotrimazole, miconazole, ketoconazole, and so on) and triazoles (fluconazole, isavuconazole, itraconazole, posaconazole, and voriconazole) [20] [21] [22] [23].Antifungal treatment for oral candidiasis can be done locally or systemically, with oral formulations being the most common. Topical medications are administered to the infected area and are used to treat minor infections. Topical nystatin suspension or pastilles, according to the World Health Organization, can be used instead of oral fluconazole to treat oropharyngeal candidiasis in HIV-positive children and adults. Nystatin, derived from Streptomyces noursei, binds to the ergosterol in the fungal plasma membrane and creates pores that make it more permeable, resulting in a loss of intracellular potassium and fungicidal activity. During pregnancy and breastfeeding, nystatin is likely to be safe. Only if nystatin is given for a long enough time is treatment effective. However, the patient's compliance is hampered by the unpleasant taste and the extended treatment regimen [24] [25].

EMERGING RESISTANCE

Antifungal resistance can develop either through the selection of species with inherent resistance or through the creation of resistance in isolates from ordinarily susceptible species. The former is the most common, as evidenced by the rise of C. glabrata following the introduction of fluconazole and of C. parapsilosis in environments where echinocandins were used more frequently. Recent research reveals that the rate of acquired echinocandin resistance in isolates from sources other than blood may be underestimated, implying that deep-seated candidiasis could serve as a hidden reservoir of echinocandin resistance [26].

CONCLUSION

To summarize, C. albicans is a versatile microbial species capable of infecting a variety of anatomical places. Nonetheless, throughout the last two decades. Although we have gained a better understanding of the intricate host-C. albicans interactions, there are still many unknowns about C. albicans pathogenicity, host immunological responses, and, most critically, the role of C. albicans as a component of the human microbiota. The mechanisms underpinning the emergence of antifungal resistance are still evolving, underscoring the crucial need for novel antifungal classes to be developed. Fortunately, tremendous progress has been made in the field of antifungal research, with potential new medications now in clinical studies. In addition, progress in identifying novel bioactive chemicals that target pathogenic pathways rather than growth could be extremely useful in supplementing the present antifungal arsenal.

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Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Prodipta Chakraborty, Darshan Pradhan, and Sudip Halder designed the work and made necessary corrections and revisions in the manuscript. Prodipta Chakraborty and Arnab Bagchi collected the content and performed the literature review and also contributed in drafting the manuscript. All the authors framed the final manuscript.

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