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Review article

Management of the fungal infections and challenges associated with it

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Abstract

Fungal infections are becoming more common at an alarming rate, which poses a significant challenge to medical experts. This growth is directly linked to the rise in the number of people with impaired immune systems as a result of modifications to medical practice, including the use of immunosuppressive medications and intense chemotherapy. HIV and other illnesses that impair immunity have also had a role in this issue. Mucous membranes, keratinous tissues, and the skin are all impacted by superficial and subcutaneous fungal infections. This class includes some of the most common skin conditions that impact millions of people globally. They can have crippling consequences on a person's quality of life and, in certain cases, spread to other people or become invasive, even though they are rarely life-threatening. Fungal pathogens employ several tactics to compromise the immune system of the host and escalate infections. The range of antifungal drugs available is used to treat a number of superficial and systemic diseases. The well-established evidence of fungal resistance to most antifungal medicines complicates antifungal therapy and makes disease control challenging. Fungal resistance is caused by a range of genetic alterations, physiological alterations, and selection in the presence of antifungal drugs. The lack of a wide range of antifungal drugs, resistance building, and biofilm-conferred resistance are the main reasons for the need for novel therapeutics and other approaches to enhance treatment outcomes against mycoses.

Introduction

Topical drug delivery is the process of applying a medication-containing formulation to the skin in order to treat a cutaneous condition. This method is utilized when other routes of medication administration are ineffective. When oral, sublingual, rectal, and parental methods fail, or when there is a local skin illness, such as a fungal infection happens. Topical medication administration a frequent way of treatment for both local and systemic conditions. In the topical administration system, the medication is absorbed through the skin and reaches the target spot of action to generate a therapeutic effect. The percentage of the medication release from a topical preparation is affected by directly on the carrier's physiological characteristics. The main advantage of a topical delivery system is that it bypasses first-pass metabolism [1]. A serious problem for public health is fungal diseases. Fungal infections are connected with life threatening mycoses and mortality in individuals with various disorders, especially Covid-19. Fungal infections can range in severity from superficial to cutaneous, subcutaneous, mucosal, and systemic [2]. The human microbiota contains organisms like the Candida species, which can cause invasive candidiasis, a potentially fatal infection, in immunocompromised individuals such as HIV patients, cancer patients undergoing chemotherapy, and

patients taking immunosuppressive medications, in addition to opportunistic infections in healthy individuals.

Furthermore, in people with underlying medical conditions, fungal pathogens as molds, Aspergillus, Fusarium, Candida, and Mucorales can result in healthcare-associated infections (HAI) [3]. In some regions of the world, endemic fungal pathogens can cause fatal conditions such blastomycosis, coccidiodomycosis, histoplasmosis, talaromycosis, and paracoccidiodomycosis [4].

Types of fungal infections

Superficial fungal infections

Superficial fungal infections can damage your skin, nails, and mucous membranes, including your mouth, throat, and vagina. These are a few instances of fungal infections that are superficial [5-7].

Dermatophytosis (Ringworm)

A kind of fungus known as dermatophytes causes ringworm by feeding on the cells of the skin, hair, and nails. They can infect your hands (tinea magnum), scalp (tinea capitis), facial hair and surrounding skin (tinea barbae), feet (tinea pedis/athlete's foot), groin and inner thighs (tinea cruris/jock itch), and other parts of your body (tinea corporis) [8]. A fungal infection that affects the skin and nails is called ringworm. The infection is called "ringworm" because it can result in a round, red, itchy rash. There are other names for ringworm, such as "tinea" or "dermatophytosis." The various ringworm variations are often named after the bodily part that is infected.

The following body parts are susceptible to ringworm infection:

Feet (tinea pedis, also referred to as "athlete's foot").

Buttocks, inner thighs, or groin (tinea cruris, sometimes referred to as "jock itch".

Scalp (tinea capitis).

Beard (tinea barbae).

Hands (tinea magnum).

Fingernails or toenails (tinea unguium, commonly known as "onychomycosis").

Additional body components, such the arms and legs (tinea corporis).

Ringworm is caused by approximately 40 different kinds of fungi. These fungi are known by their scientific names, i.e. Microsporum, Epidermophyton and Trichophyton [9]. When applied topically for two to four weeks, over-the-counter antifungal creams, lotions, or powders work well for treating ringworm on the skin, including jock itch (tinea cruris) and athlete's foot (tinea pedis). Numerous over-the-counter medications are available to treat ringworm, such as:

Clotrimazole (Mycelex, Lotrimin)

Terbinafine (Lamisil)

Miconazole (Aloe Vesta Antifungal, Azolen, Baza Antifungal)

Ketoconazole (Xolegel)

Onychomycosis

The infections caused by fungus in your fingernails or toes (onychomycosis). This can result in discolored or damaged nails [5-7]. Fungal infections of the nail unit, including non-dermatophyte yeasts, dermatophytes and molds cause onychomycosis, which manifests as onycholysis, nail discolouration, and thickening of the nail plate [10, 11]. It can impact the nail matrix, nail bed and nail plate among other parts of the nail unit [12]. The term "onychomycosis" is derived from the Greek terms "onyx," which means nail, and "mykes," which means fungus [13]. At least half of all nail illnesses are caused by onychomycosis, which is the most common disorder affecting the nail unit [11,14,15]. Prior to beginning treatment, it is recommended and cost-effective to obtain laboratory validation of the clinical diagnosis of onychomycosis [15]. Newer methods that allow for a sensitive and accurate diagnosis of onychomycosis as well as innovative treatments for this illness have surfaced in recent years.

Oral therapy

When treating onychomycosis, the most typically given oral drugs are griseofulvin, terbinafine, itraconazole, and ketoconazole. Oral antifungal medications, such as terbinafine (Lamisil®), have more adverse effects and necessitate a longer course of treatment. For 8 weeks for nail fungus in the fingers and 12 weeks for toenail fungus, this medication is used daily. Headache, gastrointestinal disruption (diarrhoea and/or dyspepsia), rash, and increased liver enzymes are the most common side effects of Lamisil® [16].

Sporanazole (Itraconazole) For two or three months, this is frequently administered in "pulse doses," or one week per month. Certain regularly used medications, including the antibiotic erythromycin or various asthma treatments, may interact with it. Increased liver function tests, skin rash, elevated triglycerides, and gastrointestinal side effects (diarrhoea, bloating, and nausea) are the most common adverse effects of Sporanox®. For a few months, ketoconazole (Diflucan®) may be used once a week. Headache, skin rash, and/or gastrointestinal (GI) upset (nausea, vomiting, diarrhoea, and/or abdominal discomfort) are the most frequent adverse effects [16].

Griseofulvin, also known as Gris-Peg®, Gifulvin®, and Fulvicin®, has long been the cornerstone of oral antifungal treatment. This medication is safe, but it doesn't do anything to treat toenail fungus [16].

Topical therapy

Nail fungus is typically not treatable with creams or other topical drugs. The reason behind this is that external applications cannot penetrate the hardness of nails. A new medicated nail lacquer that does not damage the ulnula, or white part of the nail, has been approved to treat toenail or finger fungus in those with healthy immune systems. Fungal infections like onychomycosis can be effectively treated or

prevented using the nail lacquers that are already on the market: ciclopirox and amorolfine. In a clear, stable lacquer vehicle, the nail lacquer contains a water-insoluble film-forming polymer, 2-n-nonyl-1,3-dioxolane or a similar penetration enhancer, volatile solvent, and fungicidally effective quantities of ciclopirox, amorolfine, or another antifungal agent [16].

Candidiasis

Candida causes candidiasis, an infection of the skin and mucous membranes (mostly caused by Candida albicans). Among them include esophageal candidiasis, candidal intertrigo, vaginal yeast infections (vulvovaginitis), oral thrush, and various forms of diaper rash [17]. Candida albicans is the most prevalent species of fungal infection that causes candidiasis. An opportunistic fungal pathogen called Candida albicans usually lives on human skin and mucous membranes in the mouth, intestines, or vagina. It can lead to a variety of mucocutaneous barrier and systemic infections, as well as serious health issues in HIV/AIDS patients and immunocompromised people following chemotherapy, immunosuppressive medication treatment, or antibiotic-induced dysbiosis. Unfortunately, there are few therapeutic antifungal medications for candidiasis, and those that do exist have drawbacks that restrict their clinical use. Furthermore, it is unclear how the host's immune system protects against a C. albicans infection.

Obesity is an endocrine and heritable disorder, which results in excessive or abnormal adipose tissue/fat accumulation in the body. It is a complex and a multifactorial disease that can cause health impairment. Imbalance between daily energy intake and expenditure leads to excessive weight gain. [1, 2].

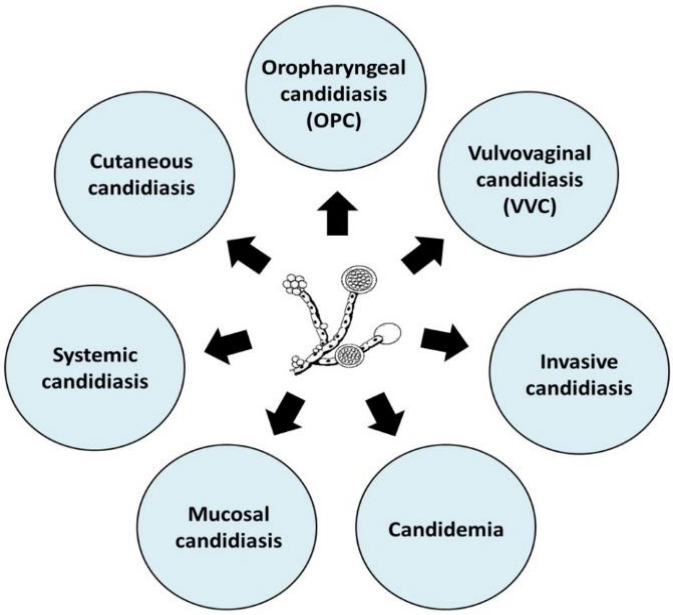

Figure 1. Types of candidiasis [4].

Treatment

Treatments for candida infections include antifungal medications such as amphotericin B, clotrimazole, nystatin, and miconazole. Treatment for mild to moderate genital Candida infections is an antifungal vaginal cream. Antifungal creams are available in treatments of 1, 3, or 7 days. One-time oral doses of 150 mg of fluconazole or econazole may also be administered [18]. Azole derivatives are the most widely used antifungals in the treatment of candidiasis. They are separated into two subfamilies: Imidazoles (ketoconazole, miconazole, etc.) and triazoles (fluconazole, itraconazole, etc.). Their fungistatic activity mainly targets the process involved in the formation of ergosterol. Azole compounds produce a buildup of harmful methyl sterols and modify the pathogen's cell membrane by inhibiting the expression of the Erg11 gene, which genes for 14α-lanosterol demethylase, the enzyme that converts lanosterol into ergosterol [19].

1.d) Tinea versicolor: Another name for it is Pityriasis versicolor. The Malassezia fungus is responsible for the tinea versicolor or Pityriasis versicolor skin discoloration [5-7]. A common skin condition called tinea versicolor, also known as pityriasis versicolor, is brought on by a superficial fungus. On the trunk and upper arms, patients with tinea versicolor usually exhibit asymptomatic hypopigmented or hyperpigmented, finely scaled oval or circular macules/patches [20]. Pruritus is sometimes reported by patients, especially in cases where the illness is more severe. The name "versicolor" describes the range of colors that can appear in skin lesions associated with this disorder. There are numerous clinical signs of tinea versicolor, thus there are numerous possible diagnoses. Pityriasis versicolor (PV) is a chronic fungal infection of the skin caused by lipophilic yeast (Malassezia species) growing in the stratum corneum [21, 22]. The species most frequently associated with PV is Malassezia globosa, while M. sympodialis and M. furfur are also frequently seen [23]. Malassezia, a typical skin flora component, is generally not harmful unless it takes on a mycelial form in PV instances [22]. Numerous things, such as high temperatures and humidity, hyperhidrosis, inherited vulnerability, and immunosuppression, might cause this [21, 22]. PV thus occurs up to 40% more frequently in tropical than in temperate regions [23]. PV is hard to cure because up to 80% of patients relapse within two years of starting treatment [24].

Topical treatment for Tinea versicolor

It is possible to use creams, lotions, and shampoos as topical treatments for PV. Depending on how long they are used for, they can be taken once or twice day to quickly improve clinical symptoms. Minor skin discomfort or the need for several, time-consuming applications may have an impact on patient compliance. Topical therapies for PV that are not species-specific do not particularly target Malassezia species. Instead, they eradicate the dead, contaminated tissue either chemically or physically [22]. Photovoltaic cell

damage can be effectively treated with non-specific treatments including Whitfield's ointment, propylene glycol, zinc pyrithione, and selenium sulphide (available in creams, lotions, and shampoos) [25, 26].

Many topical drugs, including miconazole, clotrimazole, and bifonazole, have been demonstrated to be successful in treating PV due to their direct fungistatic action [26]. Studies frequently use these and non-specific drugs to show that the more recent oral and topical antifungals are equally effective [27,28]. 1% ciclopirox olamine cream, for example, was much more effective than 1% clotrimazole cream when applied twice daily for 14 days (mycological cure 77% vs. 45%, $p < 0.001$) [29]. Ketoconazole and terbinafine are the topical antifungals that have undergone the most current in-depth research.

Ketoconazole

Ketoconazole, an imidazole, was the first broad-spectrum antifungal used to treat superficial and systemic mycoses. Ketoconazole inhibits the enzyme lanosterol 14α-demethylase, which hinders the formation of ergosterol, hence restricting cell growth and function [30]. Many cream, shampoo, and foam formulations have shown promise in treating PV; nevertheless, the most widely used regimen calls for using cream or foam once daily for a period of 14 days. While ketoconazole shampoo was demonstrated to be as effective as 2.5% selenium sulphide [31] and 1% flutrimazole shampoo [32] ketoconazole cream was shown to be as effective as 1% clotrimazole [33] and 1% terbinafine cream.

Terbinafine

The allylamine terbinafine has fungicidal properties against molds, yeasts, and dermatophytes [34] Terbinafine inhibits squalene epoxidase, a process that alters the integrity of fungal cell membranes and stops the synthesis of sterols [35]. Terbinafine cream is similar to topical ketoconazole and bifonazole cream in that it showed mycological and complete cures ranging from 88% to 100% [27, 32]. Additionally, compared to using 1% bifonazole cream twice daily, the mean treatment period (maximum 4 weeks) for mycological cure with 1% terbinafine cream was noticeably shorter [27].

Oral therapy for Tinea versicolor

While systemic, or oral, antifungals are useful in treating a range of infections, they can also have major side effects. When treating severe or resistant infections, like PV, oral antifungals are utilized as a second line of treatment. When it comes to terbinafine in PV, oral treatment is ineffective [36]. It is possible that terbinafine does not sweat like other antifungals do, and that its concentration in the stratum corneum is insufficient to have fungicidal effects on Malassezia species [37, 38]. However, as previously mentioned, topical terbinafine is not limited in this way and can be beneficial.

Itraconazole

Triazole antifungal itraconazole, like ketoconazole, modifies fungal cell activity by preventing cytochrome P450-dependent ergosterol production [30]. Itraconazole dosages of at least 1000 mg were required for PV patients to experience a meaningful improvement in their mycological response throughout treatment. A 200 mg once-daily itraconazole prescription is advised to treat PV for five days because it shows great effectiveness for a month following therapy. The typical itraconazole treatment regimen lasts for 7 days [39].

Fluconazole

Like itraconazole and ketoconazole, fluconazole is a triazole antifungal that inhibits cytochrome P450-dependent ergosterol production [30]. Research indicates that fluconazole is just as beneficial as oral ketoconazole, if not more so, in treating PV. A large-scale randomized trial carried out 2 by Amer (1997) demonstrated the efficacy of weekly fluconazole regimens: 150 mg or 300 mg for four weeks, or 300 mg twice a week for four weeks [40]. The mycological cure for regimens of 300 mg fluconazole (weekly 93%, biweekly 87%) was substantially higher than that of 150 mg fluconazole (73%, $p < 0.0001$) four weeks following the last therapy [40]. For PV, two weekly dosages of 300 mg of fluconazole are advised.

Pramiconazole

A relatively recent triazole called pramiconazole prevents fungal cells from synthesizing ergosterol. It has demonstrated efficacy in vitro against species of Malassezia, Candida, and dermatophytes. Pramiconazole demonstrated Itraconazole's efficacy against Candida species is doubled and ten times the potency of ketoconazole against Malassezia species at doses less than 1 μg/mL [41]. In a Phase II study, 19 PV patients were divided into groups and followed for 30 days (Days 4, 10, 30) to assess the efficacy and safety of 200 mg of pramiconazole given once daily for three days [42]. Over the duration of the trial, there was a substantial decrease in clinical signs and symptoms (such as erythema, itching, and desquamation) in compared to the baseline, with a p-value of less than 0.001 [42].

Subcutaneous fungal infections

If a fungus enters a cut or wound, it can cause a fungal infection subcutaneously, or beneath the skin's surface. This usually happens after working with plants and causes an accident, same to rubbing yourself against a thorn. They result in ulcers, rashes and other skin problems. Subcutaneous fungal infections are more common in tropical and subtropical areas of the world. Here are several examples:

Sporotrichosis: It is sometimes known as rose gardener's disease. Sporothrix fungus is the cause of sporotrichosis. Sporotrichosis can also occur in the lungs or other regions of the body.

Chromoblastomycosis: Many types of fungi can cause chromoblastomycosis. It can result in long-term (chronic) skin infections. It only rarely spreads to other sections of your body.
Eumycetoma: Numerous types of fungi can produce eumycetoma. It usually affects your feet [5-7].

Deep fungal diseases

Deep fungal infections can occur in organs other than the skin, such as the blood, urinary system, brain or lungs. Some illnesses are categorized as opportunistic, which implies that they exclusively affect individuals with compromised immune systems.
Invasive or Deep fungal diseases include the following:
Histoplasmosis: Your lungs, brain, or other organs may get infected with Histoplasma, the fungus that causes histoplasmosis. The Mississippi and Ohio River valleys are where it is most prevalent [5-7].

Valley fever (coccidioidomycosis): Coccidioidomycosis is caused by the fungus Coccidioides, which your lungs could contract and, in rare cases, spread to other parts of your body [43]. In California and Arizona, it is extremely typical.

Blastomycosis: The fungus Blastomyces, which causes blastomycosis, usually affects the bones, lungs, and skin It can occasionally infect your brain and spinal cord [5,6,7].

Aspergillosis: Aspergillus, the mold that causes aspergillosis, can induce both chronic pulmonary aspergillosis (CPA) and allergic bronchopulmonary aspergillosis (ABPA), among other lung conditions. It could spread to other bodily areas and develop into a fungus ball known as an aspergilloma [44-46].

Urinary tract infection caused by Candida: While the majority of urinary tract infections (UTIs) are caused by bacteria, some are also caused by yeasts like Candida [5-7].

Invasive Candidiasis: Invasive candidiasis is caused by a variety of species of the yeast Candida. It can cause infections in the brain, eyes, heart, blood, bones, and other organs (candidemia, ophthalmitis, and retinitis) [47].

Pneumocystis pneumonia (PJP): One kind of pneumonia is this. A fungus called Pneumocystis jirovecii pneumonia (PJP) can infect your lungs.

Mucormycosis: Mucormycosis is caused by a type of molds known as Mucormycetes. Mucormycetes may result in infections in the skin (cutaneous mucormycosis), sinuses and brain (rhino cerebral mucormycosis), intestines (gastrointestinal mucormycosis), lungs (pulmonary mucormycosis), or many body areas at once (disseminated mucormycosis) [5-7].

Cryptococcosis: The microbes that cause cryptococcosis are Cryptococcus gatti and Cryptococcus neoformans. Although they typically target the lungs, they can also infect the brain and spinal cord (cryptococcal meningitis) [48].

Challenges associated with the management of fungal infections

Epidemiological Challenges

Owing to an increase in those who are at-risk (growing incidence of diabetes, immunosuppression), the global epidemiology of IFI has changed over time) [49]. It is anticipated that exposure to antifungal agents, patient characteristics, and environmental factors would all have an increasing effect on IFI epidemiology [49,50]. One needs to be knowledgeable about the local epidemiology of fungal infections in a country or region in order to deliver the right care. Appropriate management concerning pharmaceutical therapies, prevention, and control of infections [51].
The most studied IFI is invasive candidiasis (IC), especially candidemia. According to studies conducted in several Middle Eastern countries (United Arab Emirates (UAE), Kuwait, United Arab Emirates (UAE), Qatar, Saudi Arabia, Bahrain and Jordan), C. albicans was demonstrated to be the most often isolated Candida species (22.3%–60%). Blood cultures of Candida glabrata, Candida tropicalis, Candida parapsilosis, and Candida auris were used to diagnose candidemia [52]. Similar situations exist in various regions of the world. Nonetheless, there are regional variations in the epidemiology of IC and candidemia. In the Middle East, certain patient populations—such as those in intensive care units (ICUs) and neutropenic patients—have not been well studied [52, 53]. Additionally, there are few published regional research on the diseases produced by invasive mold, such as invasive aspergillosis (IA), and other invasive mold infections, such as human histoplasmosis [54].

Resistance to antifungals

Global concern over the evolution of antifungal drug resistance is growing. It has been demonstrated that invasive Candida infections are extremely resistant to antifungal therapy (AFT) [55]. Candidiasis has increased in Kuwait. Antifungal resistance emerged quickly, with a 47% related mortality rate [56]. There have been reports of enhanced fluconazole resistance in various Candida species, including C. parapsilosis, C. glabrata and C. albicans [55, 57]. But the biggest worry is Candida auris, a multidrug-resistant strain of the parasite that emerged in Japan in 2009 and is responsible for severe hospital outbreaks in the Middle East [58]. It has been found that reduced sensitivity to azoles, polyenes, and echinocandins in C. auris was linked to elevated antifungal resistance [59]. 70% of the C. auris isolates examined in Qatar were resistant to fluconazole and amphotericin B [60].

Diagnostics challenges

Fungal diagnostic testing's limitations: The diagnostic diagnostics for infections caused by filamentous insects (FIs) include histopathologic examination, radiologic evidence, traditional mycologic techniques (such as culture and susceptibility, serologic methods), serum biomarkers, and molecular approaches based on PCR [61]. Direct inspection under a microscope to identify the etiological agent, clinical samples (tissue, sputum, urine, or blood) are analyzed and cultured. The gold standard for IFI diagnosis is a fungal agent [61, 62]. However, conventional diagnostic techniques are useless because of the material's invasive nature and their lengthy turnaround times. This is essential for testing. Additionally, if patients cannot wait a few days for the results of a fungal culture, they may require antifungal medication (AFT) right away if they are undergoing chemotherapy or are in critical care. Though not proven, early AFT is believed to reduce mortality in high-risk individuals [63].

Management challenges

Inadequate knowledge of fungal diseases and mycology: Healthcare professionals (HCPs) have trouble managing patients with IFI because they are ignorant about the symptoms, diagnosis, and administration of antifungal medications. Mycology is a rare medical specialty that is often neglected in medical school curriculums, leading to a lack of knowledge and expertise even among specialists in respiratory and infectious diseases (ID) [64]. Historically, there has been minimal focus on research, funding, and education on fungal diseases including aspergillosis and other infections [64]. Additionally, managing immunocompromised patients with IFI presents unique challenges with regard to pharmacokinetics and severe drug-drug interactions (DDI) involving a range of co-administered medications [65, 66].

Further, instead of targeted therapy, empiric treatment is being employed more often in high-risk group patients due to inadequate diagnosis and knowledge of DDIs and antibiotic resistance [66, 67]. When there is no radiological or microbiological evidence, antifungal medication is often administered as a consequence of empirical therapeutic techniques [68]. As a result, a lack of knowledge, resources, and experience among healthcare professionals impedes the proper management of IFI, which is already challenging because of inaccurate diagnosis [65].

Insufficient medical records in IFI administration: For important stakeholders like health care professionals and public health authorities, trustworthy epidemiological data and healthcare information are hard to come by. Even though the majority of Middle Eastern nations use electronic health records, there are limitations on updating the database to include data on laboratory markers and medication intake in order to maximize IFI management. Recently, the United States implemented Optum®, a data collection strategy, to gather anonymous data on invasive mucormycosis [69]. The Middle East could benefit from the development of these prediction models in order to collect information on the different types of IFIs, including the causative bacteria, AFT used, and patient outcomes. Descriptive epidemiology, informed public health and patient care therapy, and policy decisions about antifungal usage and IFI diagnosis would all be made possible by a consolidated case record.

Challenges associated with guidelines and therapeutic options

Resistance to Antifungal Drugs: A major problem with IFI management in the Middle East is that there are not any regional or local treatment guidelines for IC and IA. For the treatment of both IC and IA, clinicians in this field frequently follow international standards from the Infectious Diseases Society of America (IDSA) and the American Society of Clinical Oncology (ASCO) [70]. IDSA and Middle Eastern experts generally recommended echinocandin (micafungin, anidulafungin, and caspofungin) for invasive Candida infections in individuals who had previously been exposed to azoles [70]. Patients with Candida infections in Saudi Arabia were studied, and it was discovered that those who had previously been exposed to echinocandin were more inclined to become resistant to antifungals [55]. Another Saudi Arabian study testing several Candida species (C. tropicalis, C. parapsilosis, C. glabrata and C. albicans) found 100% susceptibility to echinocandins versus 41.5% for fluconazole [71]. This emphasizes the importance of local epidemiology in developing local guidelines. Moreover, little is understood about the ways in which various fungus species react to antifungal drugs. Additionally, many of the countries in this region lack robust data on medicine resistance, which complicates the process of optimizing IFI therapy management for the region. In order to direct doctors in a manner that is both epidemiologically and practically appropriate with regard to access to diagnostic tests and antifungal drugs, local recommendations created by professionals in the area are essential.

Therapeutic drug monitoring: Understanding the pharmacokinetic and pharmacodynamic characteristics of the antifungal medications on the market is essential for monitoring therapeutic drugs. Nowadays, it is acknowledged that Therapeutic drug monitoring (TDM) is a key strategy for raising antifungal efficacy and reducing toxicity. Not all institutions can do therapeutic drug monitoring for all medications, particularly for therapies that need for prompt responses and analytical methods that are not readily available in typical clinical labs. The two drugs that are most frequently prescribed for TDM are triazoles and flucytosine [66, 72]. But only 53% of Middle Eastern practitioners regularly use TDM for the pertinent indication and sampling period [73]. In the area, there needs to be a greater understanding of the need for TDM and better access to drug level testing.

Accessibility to antifungal medications: Many factors, including as activity, dosage, safety profiles, expenses, underlying medical issues, and surgical consequences, influence when AFT should begin. Better results in middle-class and lower-income countries are further hampered by the cost and accessibility of drugs. For instance, availability to flucytosine, which is mostly used to treat Cryptococcus infections, is limited in many low- to middle-income countries [74]. One significant obstacle is the cost of prescription drugs. Isavuconazole is a new azole that was licensed in the United state in 2015 and is used to treat aspergillosis and mucormycosis as an alternative therapy. Because of its high cost, several centers cannot afford to utilize it.

Conclusion

Fungal infections, both systemic and local, are becoming more common at a startling rate. This is mostly because of improvements in medical treatment, which have led to an increase in the number of hospitalized patients who are critically ill and immunocompromised. This rising pool of people at risk has been made more so by the HIV epidemic and other immune system disorders. Although superficial fungal infections are not severe, they can occasionally spread to other parts of the body or to other people. Less frequently, but more gravely, they could transform into invasive types. Even though they are not fatal, diseases like onychomycosis can seriously impair a patient's self-esteem and quality of life. To reduce the chance of spread, it is therefore preferable to treat localized fungal infections. High death rates are linked to systemic fungal infections in immunocompromised patients, including recipients of solid organ transplants and bone marrow. The most common pathogens in systemic infections are Aspergillus species and Candida albicans, although a recent change in the burden of disease has led to the appearance of several significant non-albicans Candida spp. as well as uncommon infectious agents like M. furfur. While reducing risk factors like inadequate hygiene practices in hospitals can lower the frequency of fungal infections, our inability to consistently prevent these diseases emphasizes the need for better therapies.

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Conflicts of interest

The authors report no financial or any other conflicts of interest in this work.

Ethical approvals

This study does not involve experiments on animals or human subjects.

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Data availability

All data generated or analyzed during this study are included in this published article.

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