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Article

Pharmaceutical Perspectives on Fungal Infections: An In-Depth Review of Epidemiology and Pathology of Common Human Diseases

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Abstract: In this article we studied about the common fungal infections that affect humans in this review essay. Fungal infections that result from fungal pathogens are found all over the world. Given the daily rise in fungal infections and illnesses, a thorough understanding of these infections is crucial, particularly for prevention and treatment. Google Scholar research papers and review articles from various journals provided the information regarding these fungal infections. Twelve common fungal infections that infect humans were covered, including aspergillosis, Blastomycosis, Candida auris infection, Cryptococcosis, Mucormycosis, Talaromycosis, Mycetoma, and Keratitis. One common fungal infection that causes infection in humans is fungal nail infection. The pathophysiology, diagnostic methods for identifying the infection, and epidemiology of the infection of the causative agents causing the particular disease are reviewed. Additionally listed are appropriate treatments for both the prophylactic and infection cure of certain fungal infections. Patients with impaired immune systems are more likely to become infected.

Keywords: Infections; Mycosis; Epidemiology; Distribution; Causative agents; Pathology; Diagnosis; Treatment; Prophylaxis

1. Introduction

On Earth, there are roughly 1.5 million different kinds of fungi. But just a small percentage of these species infect or afflict humans with diseases. Humans are susceptible to many infections, allergies, and mycoses due to these disease-causing bacteria. Immunocompromised people with weakened immune systems are more susceptible to fungal infections [1]. Invasive fungal diseases are becoming more commonplace every day. *Aspergillus fumigatus* and *Candida albicans* are the two most frequent infections that cause illness. They induce mycoses that invade. There are about 200 *Aspergillus* species known to infect people [2]. Fungal microbe-induced skin and nail infections are also quite prevalent worldwide. Worldwide, it infects about 1.7 billion people with this sickness. Dermatophytes is the most frequent cause of these infections and is mostly responsible for adult cases of athlete's foot. Additionally, dermatophytes can cause scalp ringworm, commonly in children. 200 million individuals globally are impacted by it. Adults can also get nail infections from it, and the likelihood of infection rises with age [3]. Invasive infection is caused by numerous fungal infections. There could be 1.5 million deaths from these illnesses per year. Fungal infections are widespread throughout the world and are growing in various places in ways that depend on the local environment and cultural customs of the populace. It is challenging to estimate the fatality rate and effects of these fungal infections on humans, particularly in developing countries [4]. We will examine the epidemiology, prevalence of the infection, causative agents, pathology, diagnostic methods, and therapy of twelve distinct fungal illnesses in brief in this review paper. Table 1 lists these diseases' names, their causes, and their global distribution.

2. Fungal nail infection

The most prevalent fungal infection in humans is fungal nail infection. Another name for this infection is onychomycosis. The dermatophytes infection is the most frequent cause. Trichophyton and Microsporum fungi are among the dermatophytes. It is more common in humid regions. It is prevalent throughout Europe, with a rate of 23 %. East Asia and North America also frequently experience it [3,5]. In tropical locations, it is not common. In immunocompromised individuals, it is most common. Diabetic foot syndrome can also be brought on by this infection. Athlete's foot can result from this infection, which is most prevalent in moist regions of the world. This infection causes a white surface to appear on the nail by invading the nail bed and penetrating the lateral borders or the nail from above [6]. Nail thickening is a result of fungus infection. Scaly skin develops surrounding this illness. It causes white marks and yellowing of the nails. Chlorazol Black E staining techniques and microscopic analysis are used to identify onychomycosis. Both surgical and chemical treatments are options for treating nail infections. Onychomycosis is treated with a variety of medications, such as terbinafine, fluconazole, and itraconazole; however, these medications have certain adverse effects. Laser treatment is a new treatment for onychomycosis. They are also treated with systemic and topical treatments. Relapses from fungal nail infections are also possible. Diabetes and immunosuppression patients are the most common populations for it [4,7].

3. Vulvovaginal Candidiasis

Candida albicans is the opportunistic mucosal infection that causes it. Mostly, it affects women who are fertile. Although it is distributed around the world, North America is where it is most common. Acute infections are common during pregnancy and can lead to morbidity in the pregnant woman. It may also happen during the menstrual cycle's luteal phase, primarily with an increase in estrogen or progesterone levels. A dimorphic fungal species is C. albicans. The reproductive and gastrointestinal systems contain it. This virus affects around 75% of women who are of reproductive age [4,8,9]. Recurrent vulvovaginal candidiasis is also prevalent, occurring in 5 to 10% of cases. It may also have an impact on the vulva and results in vaginal lumen infection. The infection manifests as discomfort, itching, and irregular vaginal discharge. Erythema, edema, and external dysuria are also caused by it. Vaginal discharge can be stained with gram stain to aid in diagnosis. Wet mount technique can distinguish between vulvovaginal candidiasis that is symptomatic and that is not. It is possible to treat vulvovaginal candidiasis using fluconazole and itraconazole regimens. Several additional medications are also utilized, such as Miconazole, Terconazole, Clotrimazole, and so forth [7,10].

3.1. Blastomycosis

Blastomyces dermatitidis is the infection's causative agent. The United States' southern states and North America are the regions where this illness is most prevalent. Additionally, it is endemic in a few provinces in Canada. Subclinical infection is caused by Blastomyces dermatitidis. However, it can potentially result in life-threatening consequences. Fever, influenza, coughing, pleurisy, and maybe myalgia and arthralgia are among the symptoms. The most typical symptoms of this infection are exhaustion and weight loss. Alveolar infiltration is present in patients with pulmonary blastomycosis. For diagnostic reasons, however, it is not beneficial [11–13]. In 40–80% of instances, extrapulmonary blastomycosis also involves cutaneous infection. Some patients may also develop osseous blastomycosis. Because men are more susceptible to this illness, diseases of the genitourinary tract can affect the testicles, prostate, and epididymis. When blastomycosis affects the central nervous system, meningitis results. Yeast cells are identified for diagnosis using the most popular diagnostic technique, the cultural method. PCR and fluorescence microscopy are further methods for identifying species [9,14]. Amphotericin B and antifungal medication are employed in its treatment. It is also possible to utilize other medications, such as fluconazole, voriconazole, and ketoconazole. There isn't a vaccine available right now to prevent it.

3.2. Candida auris infection

In [8,15], a novel species of yeast called Candida auris was identified. It was identified from a patient's ear canal discharge in Japan and is also known as fungemia or candidemia. It is widespread around the world, occurring in more than 30 nations on six continents, including Pakistan. It is a nosocomial illness that is sporadic and readily spreads. It infects patients of all ages and can easily persist on inanimate surfaces and human hosts. In addition to causing otitis, blood stream infections, and wound infections, it has also been isolated from urine and the respiratory tract [16]. Patients who are immunocompromised, have just had surgery or antibiotics, are on central venous or urinary catheters, or are on antifungals are more likely to have it. Diagnostics are made using biochemical assays. Microscopic analysis reveals that the isolates are ovoid in shape and lack pseudohyphae. As of right now, the Bruker and MS-VITEK platforms'

MALDI-TOF MS techniques are the most reliable for identifying it. It could be challenging to distinguish it from other *Candida* species. Hand hygiene, wearing protective gear in hospitals, isolating patients, and meticulous environmental cleaning are all effective preventative measures [17,18].

3.3. Cryptococcosis

Cryptococcosis is brought on by the fungus *C. neoformans*. It is an encapsulated, facultative intracellular opportunistic pathogen. Patients with impaired immune systems and low T-cell counts are affected [19]. It is found all over the world and lives on trash and dirt that has been tainted by the droppings and waste of chickens and pigeons. It penetrates the brain, extrapulmonary tissues, and lungs. Most frequently, it results in infections of the eyes, nose, skin, prostate, and lungs. If left untreated, it results in cryptococcal meningoencephalitis and is lethal.

3.4. Mucormycosis

An infection known as mucormycosis is brought on by the fungus *Rhizopus oryzae*. It is a member of the Mucorales order. There are 500 instances annually in the United States, where it is most common [19,20]. Based on the site of infection, mucormycosis can be divided into six categories: disseminated, gastrointestinal, cutaneous, rhino cerebral, pulmonary, and miscellaneous. It has been proposed that the pathophysiology of the illness is closely linked to iron uptake. Individuals who suffer from hyperglycemia and acidosis-related neutropenia and malfunctioning phagocytes are more susceptible to the illness [4,21]. Similar to cryptococcosis, the pathophysiology of mucormycosis is linked to a patient's increased serum iron levels. The condition must be diagnosed quickly and accurately in order to be treated. As of right now, there are no serological or PCR-based diagnostics available for quick diagnosis. The course of treatment involves prompt diagnosis, surgical excision of the infected tissue to stop further invasion, and administration of antifungal medications such as polyene class, which includes amphotericin B deoxycholate and its lipid derivatives, azoles like itraconazole, voriconazole, posaconazole, and ravuconazole, as well as investigational triazoles and echinocandins like caspofungin [17,22,23].

3.5. Talaromycosis

The opportunistic fungus *Talaromyces marneffei*, a species that is thermally dimorphic, is the cause of talaromycosis. This invasive mycosis is common throughout mainland China and the Indian subcontinent, as well as being native to South and Southeast Asia. Individuals with severe HIV illness experience it. The disease's pathophysiology is vague, and skin lesions are a common feature of this infection. Its diagnosis is extremely complicated and challenging because it may be similar to other dimorphic fungal illnesses, such as histoplasmosis [24,25]. The culture method, which can take up to 14 days, can be used to diagnose it. By using immunoblotting, immunodiffusion, and indirect ELISA to identify a particular *T. marneffei* antibody and antigen, a quick diagnosis can be made. Initially, amphotericin B deoxycholate, a very expensive and scarce medication, can be used to treat it, but it has significant negative effects. Another readily available medication for therapy that has less negative effects than amphotericin is itraconazole [5,6,26].

3.6. Mycetoma

Tropical diseases like mycetoma are brought on by certain fungi (eumycetoma) or bacteria (actinomycetoma). Some temperate regions have also reported seeing it. It's a particular kind of subcutaneous granulomatous and inflammatory disease that progresses over time. The development of a sinus tract, painless subcutaneous swelling, and a grainy discharge that typically affects the foot are all part of the pathogenesis of mycetoma. Radiology, ultrasound imaging, fine needle aspiration cytology, identification by culture, histology of the stained tissue sections, and serodiagnosis are some of the diagnostic techniques. The etiology and extent of the infection determine the course of treatment. Chemotherapy and antibiotics are used to treat mycetomas. It is particularly efficient to combine streptomycin sulfate with diaminodiphenylsulphone (dapson) orco-trimoxazole. In the event of drug resistance, other treatments include rifampicin, sulphonamides, and sulfadoxine-pyrimethamine (fansidar). Ketoconazole and itraconazole are used to treat eumycetoma.

3.7. Keratitis

Known also as keratomycosis, fungal keratitis is an uncommon but dangerous ocular infection. People who used to wear contact lenses frequently experience it. The beginning of the infection is also linked to dry eye condition, photorefractive keratectomy, bullous keratopathy, Lasik, trauma, and topical medication use [3,7]. The genera *Fusarium*,

Table 1. Diseases, causative agents and distribution in the world

Name of disease	Causative agents	Distribution	References
Fungal nail infection (onychomycosis)	Dermatophytes (Trichophyton, Epidermophyton, Microsporium, T. rubrum)	Europe, East Asia, North America	[14]
Vulvovaginal candidiasis	Candida albicans	Worldwide	[15]
Tinea pedis	Trichophyton rubrum, Epidermophyton floccosum and Trichophyton interdigitale	Worldwide	[16]
Oral candida	Candida albicans	Worldwide	[17]
Aspergillosis	Aspergillus fumigates	Worldwide	[18]
Blastomycosis	Blastomyces	United States, Canada	[19]
Candida auris infection	Candida albicans	Worldwide	[20]
Cryptococcosis	Cryptococcus neoformans	Worldwide	[21]
Mucormycosis	Mucor sp, Rhizopus sp, Fusarium sp	Worldwide	[22]
Talaromycosis	Talaromyces marneffeii	South and Southeast Asia, China and the subcontinent of India	[23]
Mycetoma	Eumycetoma or by bacteria Actinomycetoma	tropical and sub-topical subcontinents	[24]
Keratitis	Fusarium, Aspergillus and Curvularia.	United States, Asia, South India, China and South Florida	[25]

Aspergillus, and Curvularia are among those whose members are the fungal causal agents. The United States, Asia, South India, China, and South Florida are the regions where it is most common. It results in ulcerative corneal infection, which can lead to blindness or decreased vision. The primary sites of infection are the corneal epithelium and stroma, which causes tissue necrosis in the affected area. The anterior chambers and endothelium of the eye are impacted by severe infections [14,17]. The fungus can be cultured, stained, and smeared to aid in the diagnosis. For quick diagnosis, confocal microscopy and PCR are utilized. Using polyenes such natamycin and amphotericin B as well as azole chemicals like triazole, clotrimazole, imidazoles, fluconazole, and voriconazole are some of the treatment options. Treatment options also include surgical procedures including lamellar and penetrating keratoplasty [2,5,8,24].

4. CONCLUSION

We can infer from the data above that the prevalence of fungal diseases is rising quickly. These infections are difficult to diagnose. These illnesses may grow increasingly serious and perhaps fatal to humans in the near future. The fungal pathogens may undergo modifications as a result of climate change, perhaps increasing their pathogenicity. Therefore, we ought to enhance the diagnostic methods. More funding ought to be allocated for the development of novel therapeutic strategies. It is time to develop antifungal medications with reduced adverse effects and improved efficacy. There should be a greater public awareness of fungal pathogens and the dangerous diseases they cause in humans. A key factor in the prevention and management of fungal infections is the development of vaccinations against various fungal illnesses.

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