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Review Article

Climate Induced, Opportunistic Nosocomial Fungal Infections: Its Prevention and Control

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Abstract

This paper explains recently emerged climate induced opportunistic nosocomial infections in detail with its prevention and control. All these fungal infections have been emerged all of a sudden in hospitalized patients those who are under clinical care, recovered and in home isolation. Recent corona virus pandemic raised this problem as the high dosages of steroids, calcium, zinc and hot vapors inhalation prepared humid a platform on which fungal spores have grown in nasal sacs, eyes, ears, and transferred to internal organ systems lungs, brain and blood, caused septicemia and death of patients. Most of the dermatophytes grow over skin surface and utilize epidermal cells of skin, nails and hair follicles and cause black lesions. Invasive fungal disease mainly mucormycosis and others evoke all of sudden due to immunological defects, use of concomitant immunomodulators or immunosuppressive therapies or steroids to cure Covid-19 patients. For avoiding entry of spores in sinuses or lungs through inhalation of air, double layered mask is essential. This article suggests complete avoidance of steroids by autoimmune or immune deficient patients. For better recovery an early diagnosis, treatment by using fast acting anti-fungal agents and surgery of mucor-mycosis patients are highly important.

Keywords: Invasive Fungal Diseases; Molds; Opportunistic Nosocomial Infections; Aspergillosis; Candidiasis; Mucor-Mycosis

Introduction

Fungi are a diverse and ubiquitous group of organisms that occupy many niches and also perform services for humans, including the fermentation of bread, cheese, wine, and beer, as well as the production of penicillin. As many as a million species of fungi are known to exist; only about 400 are potential agents of human disease. Infections may result from introduction of exogenous organisms due to injury or inhalation, or from endogenous organisms such as the commensals present in the gut and on the skin. Different types of fungus cause a variety of fungal infections. Opportunistic fungal infections are caused by fungi that are nonpathogenic in the immunocompetent host, many of which are part of the normal upper respiratory tract flora. These organisms may cause pulmonary infection in immunocompromised hosts. There are so many invasive fungal diseases which occur due to extra humidity in atmosphere, these are dermatophytoses, *yeast infections*, systemic mycoses, mucormycosis and mycetoma [1]. Recently black fungus disease or mucormycosis is reported in seven states of India where it is declared epidemics. This is rare but serious fungal infection, cause by mycomycetes group of fungi. This is an invasive opportunistic fungal disease caused by a group of molds which found naturally in the environment mainly in soil [2]. This rare black fungus disease or mucormycosis suddenly appear in hospitalized Covid-19 patients under recovery phase. Black fungus disease carted havoc and killed more than 300 people and infected more than 12,000 in India as the country's health system continues to grapple with Covid-19. Recently Rajasthan, Telangana, Maharashtra and Gujarat, M.P., U.P., Jharkhand and Delhi have declared black fungus as epidemic which is fetal. The black fungal infection, triggered by Covid-19, last year caused many of the patients to lose their eyesight. But this year this deadly infection caused a high mortality with many corona virus patients. Life of several patients has been saved by surgical removal of facial, nose and jaw bone fungus. Mostly it was observed in corona virus infected patient who have been treated with oxygen. The deadly fungus moves rapidly in the body, attacking the nose, eyes, jaw and brain. Patients need immediate

surgery to survive, but they are left with disabilities. Among other reasons are high sugar level and most frequent use of steroids and use of infected hospital equipments and weak immunity [2].

Invasive fungal diseases like pneumocystosis, cryptococcosis, histoplasmosis, and coccidioidomycosis also most frequently seen in autoimmune or immune deficient patients. These are also evoked all of sudden due to immunological defects and/or concomitant immunosuppressive therapies [3]. Invasive fungal infections are increasingly common in the nosocomial setting. Furthermore, because risk factors for these infections continue to increase in frequency, it is likely that nosocomial fungal infections will continue to increase in frequency in the coming decades. The predominant nosocomial fungal pathogens include *Candida* spp., *Aspergillus* spp., *Mucorales, Fusarium* spp., and other molds, including *Scedosporium* spp. These infections are difficult to diagnose and cause high morbidity and mortality despite antifungal therapy [4]. Both acquired and congenital immunodeficiency may be associated with increased susceptibility to systemic infections. Fungal infection is difficult to treat because antifungal therapy for *Candida* infections is still controversial and based on clinical grounds and for molds, the clinician must assume that the species isolated from the culture medium is the pathogen [5]. Present article describes important invasive fungal diseases (IFD) including mucor mycosis of black fungal infections with factors associated to its sudden appearance, diagnosis, treatment options, precautions and management.

Most common fungal infections

Fungi dermatophytes parasitize the horny cell layer that results dermatophytosis. The most common dermatophytes are *Trichophyton rubrum* and *Trichophyton mentagrophytes*. Because dermatophytes most commonly grow on skin, feed its keratin. These fungi usually infect the epidermal horny cell layer, nails and hair follicles, causing lesions (tinea superficialis). In dermatophytosis dermatophytes penetrate in dermis and proliferate in deep dermal layers (tinea profunda).

Tinea pedis

Tinea pedis is caused *Trichophyton rubrum*, it is also called athlete's foot. Disease shows multiple clinical features and has three clinical subtypes. Inter-digital erosive is the most common of the three subtypes, in which the fourth toe cleft is most commonly affected. Disease begins with erythema and vesicles on the interdigital region and form scales. Red lesions appear on skin which is infiltrative, cause intense itching, and soften to become whitish, then exfoliating and becoming erosive. Erosion results in sharp pain or cellulitis and appears as secondary infection. In vesicular scaling base of the toes are most frequently involved. Multiple vesicles occur and dry, leading to scaling. It tends to appear during the rainy season and subside in autumn. It occurs most frequently on the heels. The third clinical subtype causes hyperkeratosis or roughness of the skin, and cracking of skin cause sharp pain. This clinical subtype is resistant to topical agents; but treatment with oral antifungals found effective [6,7]. Tinea pedis can be treated by using oral antifungal pills i.e. Terbinafine, Itraconazole, Griseofulvin, Fluconazole, Ketoconazole up to 3 - 4 weeks (Table 1).

Tinea unguium

Tinea unguium grow in first toe, as secondary to tinea pedis. Disease appears as tip of the toenail become white or leukonychia, it gradually spreads to the nail matrix [6,7]. After few days nail becomes fragile and pulverizes when cut with clippers. The fungal elements penetrate deeper in nail plate and form hyperkeratotic nail bed. It remains asymptomatic for long period. It also form skin lesion similar to a tinea pedis skin lesion, causes autoinfection and intrafamilial infection. It is sometimes difficult to improve with topical agents. Oral antifungal drugs are more effective [6,7] (Table 1).

Tinea corporis

The same type of skin lesion as in tinea corporis appears, often symmetrically. Itching is intense. Tinea corporis is occasionally caused by *Microsporum canis*, which parasitizes dogs and cats. Tinea corporis caused by *Microsporum canis* is characterized by intense inflammatory symptoms. Topical and oral antifungal agents are the main treatments. As in tinea pedis, the causative dermatophyte in most cases of tinea corporis is Trichophyton rubrum. Trichophyton infection in hair follicles results in sharply edged alopecia of the scalp. Dry pityroid scales and short, broken off hairs in the lesions are formed. This is called scald head. This fungal disease most frequently occur in children [6,7]. Few topical antifungal agents i.e. Terbinafine, Clotrimazole, Miconazole, Econazole, Oxiconazole, Ciclopirox, Ketoconazole, Sulconazole, Naftifine and Butenafine Wehn topical treatment fails oral antifungal pills, Terbinafine, Itraconazole, Griseofulvin, Fluconazole, Ketoconazole are

provided up to 4 - 6 weeks (Table 1).

Tinea capitis

Tinea capitis or ringworm is fungal infection of scalp develop itching and black dot formation at the follicles after the hairs break off is called black dot ringworm. This disease also evoke due to misuse of topical steroid ointments. Tinea capitis is caused by a fungus called *Trichophyton tonsurans*. Fungus target hair follicle, small red lesion appears which spread outward in all directions, causing a large, scaly, circular lesion. Due to fungal growth and invasion hair usually becomes brittle and broken, and the affected area is extremely itchy. If the scalp ringworm is left untreated, the scalp can become soft and very tender as the infection spreads throughout the body. Scalp ringworm causes fever and pain along with enlarged lymph nodes in children. Oral antifungal drugs are provided for the treatment. The affected site should be kept clean and dry [6,7] (Table 1).

Tinea barbae or ring worm of beard

Tinea barbae is an infection that specifically affects the part of the face that is usually shaven, known as the beard distribution. Beard ringworm is contagious and is passed from person to person, animal to person, and from contaminated objects (such as towels and pillows) to person. Infection grows at sites with barbae mainly mustache and beard and sides of upper lip and its periphery. Fungal infection causes reddening and swelling in the entire area with barbae, pus comes out from the hair follicles and hairs pulled out very easily. This infection is caused due to shaving or misuse of steroids. The treatments needs topical antifungal creams or lotions i.e. Terbinafine Clotrimazole, Miconazole. Apply the cream to each lesion and to the normal-appearing skin 2 cm beyond the border of the affected skin for at least 2 weeks [6,7] (Table 1).

Kerion

A kerion is a scalp ringworm (tinea capitis) infection, the affected site inflamed, thickened, pus-filled area, and fever. Kerion is most common on the scalp but can be produced in other sites. The most common causative agent of kerion celsi is *Microsporum canis*, which infects humans through their pets. Infants are most frequently affected. Infection starts with barbae mustache and beard, near to upper lip and its periphery. Inflammation soon occurs, leading to erythema, follicular papules, pustules and flat or dome-shaped abscesses. The lesions are accompanied by sharp pain, mild pulsation and discharge of pus. The hairs in the lesion fall out. There are systemic symptoms such as swelling of the regional lymph node and fever. Most cases are caused by misuse of steroid ointments on tinea capitis of the scalp and the incidence has been increasing in recent years. *Trichophyton tonsurans* infection is found in hairs; inflammatory cellular infiltration occurs in peripheral follicles [6,7]. For treatment oral antifungal medicines are used because the fungus grows deep into the hair follicle where topical creams and lotions cannot penetrate (Table 1).

Trichophytic granuloma

It causes the disease tinea superficialis in which a nodule appears intradermally, subcutaneously, or in a skin lesion [8]. On skin surface flat infiltrative plaques or tumorous plaques are formed. At later stage localized or whole body granuloma trichophyticum appears [9]. Localized granuloma trichophyticum may be associated with misuse or abuse of topical steroids. Oral antifungal drugs are provided for treatment. This fungal infection occurs in immunocompromised individuals such as organ transplantation recipient [10]. Fungal infections penetrate deep into tissues and form trichophytic granulomas (Table 1).

Candidiasis

Candidiasis is an infection caused by a yeast (a type of fungus) called *Candida*. *Candida* normally lives inside the body (in places such as the mouth, throat, gut, and vagina) and on skin without causing any problems. Sometimes *Candida* can multiply and cause an infection if the environment inside the vagina changes in a way that encourages its growth. Candidiasis in the vagina is commonly called a "vaginal yeast infection [11]". Other names for this infection are "vaginal candidiasis," "vulvovaginal candidiasis," or "candidal vaginitis [12]". It is an infection of the skin or mucous membrane caused by yeasts of the genus Candida. Based on location and clinical features different subtypes of candidiasis have been reported. Moreover, these subtypes are cutaneous candidiasis (e.g. candida intertrigo, erythema mycoticum infantile, candidal paronychia), mucosal candidiasis (thrush, genital candidiasis), and atypical candidiasis (e.g., chronic mucocutaneous candidiasis). It may also occur as an occupational disease in industry workers whose hands are in frequent contact with water. It is also mostly happen in sexually transmitted patients as disease or an opportunistic infection due to immunodeficiency. The affected site should be kept clean

and dry. The antifungal imidazole is topically applied [12]. Symptoms of vaginal candidiasis include [11]: Vaginal itching or soreness, Pain during sexual intercourse, Pain or discomfort when urinating and Abnormal vaginal discharge, diabetic, pregnant, using hormonal contraceptives, Have a weakened immune system (for example, due to HIV infection or medicines that weaken the immune system, such as steroids and chemotherapy mainly recently taken antibiotics (Table 1).

Scientists estimate that about 20% of women normally have *Candida* in the vagina without having any symptoms. Sometim es, *Candida* can multiply and cause an infection if the environment inside the vagina changes in a way that encourages its growth. This can happen because of hormones, medicines, or changes in the immune system. Vaginal candidiasis is usually treated with antifungal medicine [13]. For most infections, the treatment is an antifungal medicine applied inside the vagina or a single dose of fluconazole taken by mouth. Other treatments may be needed for infections that are more severe, that don't get better, or that keep coming back after getting better. These treatments include more doses of fluconazole taken by mouth or other medicines applied inside the vagina, such as boric acid, nystatin, or flucytosine [14] (Table 1).

Aspergillosis

Aspergillosis is an infection that affects the respiratory system. It is caused by a type of mold (fungus) *Aspergillus*. It evokes in weakened immune systems, underlying lung disease or asthma patient who inhale fungal spores. In some people, the spores trigger an allergic reaction. Few people develop mild to serious lung infections [15]. Two forms of aspergillosis have been identified invasive aspergillosis that occurs when the infection spreads to blood vessels and beyond. Some people with asthma or cystic fibrosis have an allergic reaction to aspergillus mold, while few show allergic bronchopulmonary followed by fever, cough comes out with blood or plugs of mucus [15] (Table 1).

Aspergilloma starts with growth of fungus in lung cavities, fungus fibers may find their way into the cavities and grow into tangled masses (fungus balls) known as aspergillomas. It also causes chronic lung (pulmonary) conditions such as emphysema, tuberculosis or sarcoidosis. The symptoms of disease are dry cough with hemoptysis, wheezing, Shortness of breath and weight loss [16]. Invasive aspergillosis is most severe diseases; it appears as the infection spreads rapidly from the lungs to the brain, heart, kidneys or skin. It also occurs in weaker immune systems, mainly patients taking cancer chemotherapy, bone marrow transplantation or a disease of the immune system. Untreated, this form of aspergillosis may be fatal [17]. It important symptoms are headaches, skin lesion**,** ever**,** chills hemoptysis, shortness of breath, chest and joint pain**.** Aspergillus also grow in lungs mainly in sinuses, fungus can cause a stuffy nose sometimes accompanied by drainage that may contain blood. Fever, facial pain and headache may also occur (Table 1).

For diagnosis of aspergilloma or invasive aspergillosis imaging test such as chest X-ray or computerized tomography (CT) scan usually reveal a fungal mass and confirm any sign of invasive aspergillosis and allergic bronchopulmonary aspergillosis. Respiratory secretion (sputum) test is also performed to know the presence of *Aspergillus* filaments in specimens. Skin testing, as well as sputum and blood tests, also found helpful in confirming allergic bronchopulmonary aspergillosis. Biopsy is also done to confirm invasive aspergillosis. For the treatment of Aspergillosis Prednisone (Deltasone), prednisolone (Orapred), and methylprednisolone (Medrol) are provided. These drugs are established standard treatment of invasive pulmonary aspergillosis. Other medicines which are commonly used for the treatment of Aspergillosis voriconazole (VFEND) and amphotericin B (Amphocin, Fungizone) [18] (Table 1).

Mucormycosis

Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection [19]. This is an invasive opportunistic fungal disease caused by a group of molds (mucormycetes) *Rhizopus* species, *Mucor* species, *Rhizomucor* species, *Syncephalastrum* species, *Cunninghamella bertholletiae*, *Apophysomyces* species and *Lichtheimia* (formerly *Absidia*) species [20]. These different types of fungi which cause mucormycosis belong to the order Mucorales. It is also known as zygomycosis is serious but rare fungal infection caused by molds (CDC). The most common types that cause mucormycosis are *Rhizopus* species, *Syncephalastrum* species and *Mucor* species [21]. Other examples include *Rhizomucor* species, *Cunninghamella bertholletiae*, *Apophysomyces, Lichtheimia* (formerly *Absidia*)*, Saksenaea* and *Rhizomucor* [20]. Fungal diseases, or mycoses have been categorized on the basis of site of infection;

it may be superficial, cutaneous, subcutaneous, or deep and systemic. Second parameter is route of acquisition, either it may be exogenous or endogenous, third parameter is disease generated virulence, it may be primary or opportunistic (Table 1). For example, coccidiomycosis progresses from a cutaneous lesion to a systemic infection of the lungs. Cutaneous infections include attacks on skin, hair, and nails; examples are ringworm, athlete's foot, and jock itch. Subcutaneous infections are normally introduced by trauma and accompanied by inflammation; if inflammation is chronic, extensive tissue damage may ensue. Deep mycoses involve the lungs, the central nervous system, bones and the abdominal viscera. These infections can occur through ingestion, inhalation, or inoculation into the bloodstream. A very rare and deadly outbreak of fungal meningitis in 2012 was linked to *Exserohilum rostratum*, a fungal contaminant in a preparation of corticosteroids used for epidural injections. Virulence can be divided into primary, indicating the rare agents with high pathogenicity, and opportunistic, denoting weakly virulent agents that primarily infect individuals with compromised immunity. Most fungal infections of healthy individuals are resolved rapidly, with few clinical signs. The most commonly encountered and best-studied human fungal pathogens are *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Coccidioides immitis*, *Histoplasma capsulatum*, and *Blastomyces dermatitidis*. Diseases caused by these fungi are named for the agent; for example, *C. neoformans causes* cryptococcosis and *B. dermatitidis* causes blastomycosis. In each case, infection with these environmental agents is aided by predisposing conditions that include AIDS, immunosuppressive drug treatment, and malnutrition (Table 1).

Fungi belong to Mucormycetes usually grow on decaying organic matter, such as leaves, compost piles, and animal dung in soil. These more commonly found in soil in all weather condition i.e. summer, winter or spring season [22-24]. People are infected with these fungi when come in contact with the fungal spores. Fungal spores also found entry inside the lung or sinus, due to breathing air, spores start growing and infection evokes all of a sudden. Mucormycosis usually occur in people who have health problems, hospitalized and taking steroids which lower the body's ability to fight germs and sickness [25,26]. Mucormycosis also develop on the skin after the fungus enters the skin through a cut, scrape, burn, or other type of skin trauma (Table 1).

Symptoms

There are several forms of mucor-mycosis and each one of them is characterized by different symptoms. Rhinocerebral mucormycosis that occurs particularly in sinuses and brain patient feel fever, cough, chest pain and shortness of breath. One-sided facial swelling, excessive redness, or swelling appears with severe headache, nasal or sinus congestion, black lesions appear on upper side of mouth or nasal bridge. In skin mucormycosis blisters or ulcers form in infected area that become black after some time. In case of gastro-intestinal fungal attack patient feel severe abdominal pain, problem of nausea and vomiting, gastrointestinal bleeding also starts. Disseminated mucormycosis typically occurs in people who are already sick from other medical conditions; hence, it is difficult to understand because apparent symptoms not displayed related mucormycosis. But internally fungus grown inside brain and invade nerve cells and change the mental status or generates coma. Pulmonary or lung mucormycosis is characterized by fever, cough, chest pain and shortness of breath (Table 1).

Few warning symptoms also appear in patients as he/she feel one-sided facial pain, numbness, pain and redness around the eyes or nose, with fever, headache, coughing, shortness of breath, bloody vomits, cheek bone pain, chest pain, respiratory and mental problems. After two days it convert into sinusitis with blackish nasal discharge, nasal congestion, and black lesions over skin, pleural effusion, Vision becomes blurred and sight form double vision. Thrombosis and necrosis are worst phase of this disease. Fungal spores grow in sinuses or lungs inhaled from the air (Table 1).

Risk factors

Mucormycosis is not spread between people or between people and animals, but it is spread to get in touch of infected surfaces, soil, samples, fungal mucormycosis spores found suspended in air cause in the environment. There is no vaccine to prevent mucormycosis. For people who have weakened immune systems, there may be some ways to lower the chances of developing mucormycosis. A number of factors increase the risk of developing fungal infections. Do not use deodorants or scented tampons; avoid shower baths, swimming pools, and hot tubs/spas in rainy season. Diabetic patient should remain careful and maintain their glucose level to

avoid risk of murcormycosis. HIV/AIDS and corona virus patients, organ transplant recipients or taking steroid medications or chemotherapy, or using broad spectrum antibiotics especially for long periods of time remain at high risk [25,27,28]. It is also true that not all people remain under risk to develop fungal infections.

Other category of patients is cancer affected, skin injury due to surgery, burns, or wounds, or neonatal problems such premature birth weight also remain at high risk of mucormycosis. In these patients, fungal infections can spread throughout the body, and may severally affect vital organs, such as the heart and the brain. Few life-threatening complications such as abscess formation, endocarditis, meningitis, nephritis, and organ failure and transplant rejection also seen in patients affected with black fungus.

Diagnosis and testing

The severe patients of mucormycosis having infection in upper jaw mainly maxillofacial and sometimes even the eye essentially need surgical removal. For better treatment medical history, symptoms, physical examinations, and laboratory tests are used to properly diagnose mucormycosis. Samples are collected secretions from lungs or sinuses might or secreting fluid from respiratory system for testing in agar plate method. Tissue biopsy is also performed collect strong evidence of mucormycosis, by analyzing fungal culture under a light microscope. CT scan or imaging tests of lungs, sinuses, or any other parts of body is done for confirmation of location of the suspected infection site [29]. In case of invasive fungal diseases absence of specific symptoms complicates diagnosis. In case of *Candida, the disease changes its spectrum and r*ecovery of fungi from blood and deep specimens remains an insensitive diagnosis, leading to delayed treatment and high mortality. For better diagnosis certain biomarkers, such as 1,3-β-D-glucan (BG), galactomannan (GM), glucuronoxylomannan (GXM) and mannan, anti-*Candida* antibodies, or fungal DNA are proved useful diagnostic tools. BG is a panfungal marker that can be present early in the blood and other biological fluids of patients suffering from invasive fungal disease (IFD) [30]. GM is a marker of invasive aspergillosis and be positive prior to clinical and radiological suspicions of infection. GXM is used as marker for diagnosis of cryptococcal meningitis. Mannan and anti-*Candida* antibody detection is helpful in the diagnosis of invasive candidiasis [31]. DNA detection is a promising diagnostic tool but it is not recommended for clinical use [32].

Treatment

Mucormycosis is a serious infection, for its treatment certain antifungal medicines i.e. amphotericin B, posaconazole, or isavuconazole are used. These medicines are provided through a vein (amphotericin B, posaconazole, isavuconazole) or orally (posaconazole, isavuconazole). Other medicines, including fluconazole, voriconazole, and echinocandins, do not fund effective against black fungus disease or mucormycosis. In case of infection reached into deep tissue or grow on skin surface and its sub-layers or inside an organ patient essentially need surgical operation to cut away the infected tissue. Recipients of organ transplant or a stem cell transplant remain at high risk and need appropriate and early medication to prevent mucormycosis and other mold infections [33-35]. For a an effective treatment sugar level of patients must be regulated.

There are some dietary use for reducing the chance of fungal infection i.e. eating yogurt or taking acidophilus supplements help to correct the abnormal balance of microorganisms in the mouth and digestive tract, Medications, including prescription topical or oral antifungal medications such as fluconazole, is used to treat thrush in infants. It finishes infection within two weeks and may need no treatment other than watching the progress of the mouth lesions.

Precautions to avoid mycosis

To avoid infection of molds both personal protection and community protection are quite important from the environment [36,37]. For avoiding inhalation of dust particles and fungal spores wear an N95 respirator (a type of face mask) while you're there. Avoid direct contact with water-damaged buildings and flood water after hurricanes and natural disasters [38]. Do not wearing tight-fitting underwear, T-shirts, thongs, jeans, or other pants. In hot summer and in rainy season wear loose cotton cloths. Wear gloves if you are working in soil, moss, or manure. After work wash your hands with soap, use dettol for cleaning skin injuries. All these actions are important and recommended for prevention of mucormycosis. Among other causes are micro-environment of hospital deficient in oxygen, high in humidity, infected bad sheets, nebulizers, clothes, and any mistake invited unwanted fungal infection. Always wear long-sleeved shirts and gloves while handling soil (gardening), moss or providing manure to the plants. Avoid using deodorants or scented or deodorant tampons, used gloves, shirts

or any other infected item. Maintain personal hygiene including a thorough scrub bath, washing of hands and other body parts by using mild soap and water. Do not wearing tight-fitting because they absorb more sweat that invites infection. Diabetes, HIV/AIDS, cancer and organ transplant recipients should seek regular medical care throughout and appropriate treatment time to time. Thorough drying of body surfaces after washing and taking sun bath is much better for avoiding invasive fungal infection (Table 1).

Pneumocystis pneumonia (PCP)

Pneumocystis jirovecii is an opportunistic fungal pathogen that causes *Pneumocystis* pneumonia (PCP) a serious infection [39]. PCP is usually occurs in immune-deficient patients mainly passing through a long medical treatment like HIV/AIDS. About 30 - 40% of PCP cases were having HIV/AIDS [40,41]. These patients take corticosteroids for treatment that reduce the body's ability to fight microbial and parasitic infection. Now this steroid problem has been solved due to advent of antiretroviral therapy (ART). Now PCP exists as a substantial public health problem [42-44].

Previously *Pneumocystis jirovecii* was grouped in protozoa but now it is identified as a fungal pathogen [45] *Pneumocystis jirovecii* used to be called *Pneumocystis carinii*. Disease appears after few weak of infection, its main symptoms are Fever, Cough, Difficulty breathing, Chest pain, Chills, Fatigue (tiredness) [40,42,46,47]. PCP is extremely rare in healthy people, but the fungus that causes this disease can live in their lungs without causing symptoms. It is a chronic lung disease that also form, cancer, inflammatory diseases or autoimmune diseases (for example, lupus or rheumatoid arthritis) or Solid organ or stem cell transplant (Table 1).

Fungal disease	Causative agent	Mode of Transmission	Climate induced symptoms/effects	Treatment	Precautions
Athlete' foot or Tinea pedis	*Trichophyton rubrum*	Infected skin scales or contact with fungi in damp areas	Redness or blisters, itching, stinging, or burning sensations	Treatment may include topical creams (applied to the surface of the skin) or oral medications	Avoid moist environments mainly soil exposure.
Jock itch or Tinea cruris	*Trichophyton rubrum* and *Epidermophyton floccosum*	Contaminated towels or hotel bedroom sheets,	Chafing, irritation, itching, or burning in the infected area,	over-the-counter medications	Avoid moist environments mainly soil exposure
Tinea unguium	*Trichopyton rubrum, Trichopyton mentagrophytes, Epidermophyton floccosum*	Direct contact with skin or nail lesions of infected people	Tip of the toenail become white or leukonychia, it gradually spreads to the nail matrix	Oral antifungal medication.	Avoid bearing tight cloths, deodorants and take, thorough scrub bath, washing of hands
Tinea corporis	*Microsporum canis*	Fungal spores from infected skin	Skin lesion as in appears, often symmetrically. Itching is intense	Topical and oral antifungal agents	Avoid moist environments mainly soil exposure
Tinea capitis or ringworm	*Trichophyton tonsurans*.	Infected hairs on combs, brushes, hats or pillow cases	Develop itching and black dot formation at the follicles after the hairs break off is called black dot ringworm.	Topical and oral antifungal agents	Avoid moist environments mainly soil exposure
Kerion celsi	*Microsporum canis*	Infected skin touch	Scarring and permanent hair loss.	Griseofulvin (20–25 mg/kg per day	Avoid moist environments mainly soil exposure

Trichophytic granuloma	*Trichophyton rubrum*	Potent topical steroids on unsuspected tinea	It causes the disease tinea superficialis in which a nodule appears intradermally, subcutaneously,	Terbinafine for 6 weeks	Avoid moist environments mainly soil exposure
Tinea barbae	*Trichophyton mentagrophytes or Trichophyton verrucosum.*	Person to person	Beard ringworm is contagious and is passed from person to person, animal to person, and from contaminated	Griseofulvin, terbinafine, or itraconazole, taken by mouth	Avoid moist environments mainly soil exposure
Tinea versicolar	*Malassizia furfur*	Direct contact	Trunk, neck, face arm	Over-the-counter (OTC) antifungal medications	Avoid moist environments mainly soil exposure
Aspergillosis allergic bronchopulmonary aspergillosis, allergic Aspergillus sinusitis, aspergilloma	*Aspergillosis flavus. A.fumigatus,* A. niger, and A. terreus	Air borne Direct contact	Wheezing, shortness of breath, cough, runny nose, loss of smell	Itraconazole, Voriconazole amphotericin isavuconazole, itraconazole, caspofungin, and micafungin	Bear mask
Blastomycosis	Blastomyces	Through inhalation of spores in breathing. Direct exposure from moist soil and in decomposing matter	Fever, Cough, Night sweats, Muscle aches or joint pain, Weight loss, Chest pain, Fatigue (extreme tiredness)	Amphotericin B is usually recommended for severe blastomycosis in the lungs	Bear mask
Candidiasis	*Candida auris,* Candida albicans	Direct contact	Skin, mucus membrane, Erythema, mycoticum infantile, candidal paronychia, thrush, unusual vaginal discharge	Oral dose of fluconazole	Wash underwear in very hot water
Cryptococcosis	Cryptococcus gattii	Air borne Direct contact	lungs, central nervous system	Antifungal medication.	Bear mask
Coccidioidomycosis	*C. neoformans, C*occidioides	Air borne	Fatigue (tiredness), Cough, Fever, Shortness of breath, Headache, Night sweats, Muscle aches or joint pain, Rash on upper body or legs	Fluconazole or itraconazole at 400 mg daily	try to avoid breathing in large amounts of dust

Superficial mycosis or Piedraia horte	Black piedra, White piedra	Direct contact soils, poor hygiene	Skin or hair shaft	Topical treatments including salicylic acid, benzoic acid or mercury perchloride	Avoid moist environments mainly soil exposure
Cutenous mycoses	*Trichophyton mentagrophytic*	Direct contact, poor hygiene, soil	Beared hair	Systemic terbinafine or fluconazole or topical fixed combination isoconazole nitrate/ diflucortolone valerate	Avoid moist environments mainly soil exposure
Sub-cutneous mycosis	*Phialophora verrucosa*	Direct contact, poor hygiene, soil	Legs, feet	Amphotericin B, itraconazole and terbinafine	Avoid moist environments mainly soil exposure
	Sporothrix schenckii	Direct contact	Puncture bounds	Amphotericin B,	Same as above
Systemic mycosis	*Coccidioidis immitis*	Blood or rarely via direct spread from an overlying ulcer and infected skin	lungs other parts of body	Ketoconazole	Avoid moist environments mainly soil exposure
	Cryptococcus neoformans	Blood or rarely via direct spread	Lungs skin, bones, viscera, cns	Amphotericin B, itraconazole and terbinafine	Same as above
	Histoplasma capsulatum	Inhalation of spores	Within phagocytosis	Amphotericin B, itraconazole and terbinafine	Same as above
Opportunistic mycosis	Aspergillus fumigates, A. flavus	Direct contact	Respiratory system	Use of systemic agents	
Pneumocystis jirovecii	Pneumocystis jirovecii	Direct, immune-deficient patients, autoimmune diseases, solid organ or stem cell transplants	Fever, Cough, Difficulty breathing, Chest pain, Chills, Fatigue (tiredness)	Trimethoprim/sulfamethoxazole (TMP/SMX), or co-trimoxazole.	Avoid contact with infected person, bear mask

Table 1: Climate induced opportunistic invasive fungal diseases of man.

Diagnosis and testing

PCP is diagnosed using a sample from a patient's lungs. The sample is usually mucus that is either coughed up by the patient (called sputum) or collected by a procedure called bronchoalveolar lavage. Sometimes, a small sample of lung tissue (a biopsy) is used to diagnose PCP. The patient's sample is sent to a laboratory, usually to be examined under a microscope. Polymerase chain reaction (PCR) can also be used to detect *Pneumocystis* DNA in different types of samples. A blood test to detect β-D-glucan (a part of the cell wall of many different types of fungi) can also help diagnose PCP [48].

Treatment and outcomes

PCP must be treated by using trimethoprim/sulfamethoxazole (TMP/SMX), or co-trimoxazole. This medicine is given by mouth or through a vein for 3 weeks. TMP/SMX can cause side effects such as rash and fever. Other medicines are available for patients who cannot take TMP/SMX. Without treatment, PCP can cause death. PCP spreads from person to person through the air [49,50].

Immune defense against fungal infection

Innate immunity controls most fungal infections. The barriers of innate immunity control most fungi. Phagocytosis by neutro-

phils maintain strong defense against most fungi. Resolution of infection in normal, healthy individuals is often rapid and initiated by recognition of common fungal cell wall PAMPs. There are three most medically relevant cell wall components include-glucans (polymers of glucose), mannans (long chains of mannose), and chitin (a polymer of N-acetylglucosamine). To recognize PMPs certain pattern recognition receptors (PRRs) resolving fungal infection. Commensal mirco-organisms also assist in controlling the growth of potential pathogens, as most of them died after long-term treatment with broad-spectrum antibiotics. Oral or vulvovaginal candidiasis is an opportunistic infection caused by Candida albicans. It generally occurs due to destruction of mucosal bacterial flora. Further, an increased susceptibility to mycoses is seen in individuals with defects certain molecular variants of dectin 1 a C-type lectin receptor that also results into chronic mucocutaneous candidiasis.

In addition, Toll-like receptors 2, 4 and 9, as well as complement receptor 3 (CR3), also found involved in the innate response to fungi. More often, recognition of these cell wall components leads to the activation of complement via both alternative and lectin pathways along with the induction of phagocytosis and destruction of fungal cells. More specially CR3, recognizes complement deposited on the glucans of fungal cells. It was tested in mice with *Cryptococcus* increased after an antibody to CR3 was administered after induction of fungal infection. Like other microbes, fungi have evolved mechanisms to evade the innate immune response. These include production of a capsule, as in the case of *C. neoformans*, which blocks PRR binding. Further, pre-exposure of fungal pathogens or infection shows presence of memory responses. For examples a granulomatous inflammation controls spread of *C. neoformans* and *H. capsulatum*, is a good sign of generation of acquired cell-mediated immunity. The presence of antibodies is another sign of prior exposure and lasting immunity, and antibodies against C. neoformans are commonly found in healthy subjects.

More especially TH2 and TREG cell responses, or their products, are associated with susceptibility to mycoses. Same has been observed in patients displaying distinct T helper responses to coccidioidomycosis, where TH1 immune activity is associated with a mild, asymptomatic infection and TH2 responses result in a severe and often relapsing form of the disease. However, the organism may remain in a latent state within the granuloma, reactivating only if the host becomes immunosuppressed. The presence of antibodies is another sign of prior exposure and lasting immunity, and antibodies against *C. neoformans* are commonly found in healthy subjects. However, probably the most convincing argument for preexisting immunity against fungal pathogens comes from the frequency of normally rare fungal diseases in patients with compromised immunity. AIDS patients suffer increased incidences of mucosal candidiasis, histoplasmosis, coccidiomycosis, and cryptococcosis. These observations in T-cell compromised AIDS patients and data showing that B-cell-deficient mice have no increased susceptibility to fungal disease indicate that cell-mediated mechanisms of immunity likely control most fungal pathogens. The study of immunity to fungal pathogens has become more pressing with the advent of AIDS and the increase in individuals receiving immunosuppressive drugs for other conditions. In AIDS patients those who are receiving immunosuppressive drugs generate strong TH1 responses. It induces production of IFN-α important that results in macrophage activation, which provide protection against fungi.

Conclusion

From diagnosis it is clear that opportunistic nosocomial fungal infection caused in hospital admitted patients seeking clinical care. Due to corona virus attack immunity of most of the patients become weaker, and most of the patients in recovery phase are invaded by opportunistic nosocomial fungal strains. These fungal invasive diseases are also caused in healthy persons after having exposure from contaminated soil, swimming pools, shower facilities, hot tubs/spas. These invasive fungal diseases (IFDs) are serious complications in hematological and surgical patients. Among them most are caused by *Candida, Aspergillus and* but other emergent fungi. The absence of specific symptoms complicates diagnosis. Most of these cases have reported in diabetic and immune compromised patients treated with high doses of steroids. Invasive fungal infection also develops in weak immunity patients system in HIV/AIDS patients, or taking steroid medications or chemotherapy, and recipients of organ or stems transplant. Fungal infection mostly occurs due poor personal hygiene, and use of heavy doses of strong antibiotics, for long periods of time. For treatment of fungal early sensitive diagnosis and timely treatment can ensure better recovery. For instant treatment antifungal drugs either oral or topical are used on the advice of doctors. All ecological and climatic factors are responsible diseases and other associating complex cultural factors should study. Management of Covid patients with mucormycosis microbiologists, clinical specialists, neurologists, ENT specialists, ophthalmologists, dentists, surgeons (maxillofacial/

plastic) and other stake holders should come on same plate form to save the life of the people. Important precautions such as sun shine drying, sunbath and fresh hygienic environment also provides good protection and recovery in fungal infection. Regular medical care health care is required for developing fungal infections followed by prompt diagnostic testing. These measures greatly increase the chances of recovery from fungal infections in their earliest stages.

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Disclosure of Conflict of Interest

The authors declare no competing financial interests.

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Volume 2 Issue 7 July 2021