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# Epidemiology of Opportunistic Fungal Infections in India

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**Abstract**

Over the past quarter of a century, opportunistic fungal infections have emerged as an important cause of morbidity and mortality in immunocompromised patients of tertiary care centres. The systematic data on the burden of opportunistic mycoses in India is not available though the climate in this country is well suited for a variety of fungal infections. There are very few diagnostic mycology laboratories and clinicians are still not aware of the manifestations of invasive fungal diseases. Still, within the limited data available, a phenomenal increase in incidence of invasive candidiasis, aspergillosis, and zygomycosis are indicated in Indian hospitals. The emergence of fungal rhinosinusitis, candidemia due to *Candida tropicalis*, and zygomycosis due to *Apophysomyces elegans* is unique in Indian scenario. Invasive candidiasis is the most common opportunistic mycosis across India. Invasive aspergillosis is the second contender. Both are considered important nosocomial diseases in India. Sub-optimal hospital care practices, misuse or overuse of broad-spectrum antibiotics and steroids, construction activities in the vicinity of the hospitals are largely responsible for nosocomial acquisition of these two diseases. Occasional outbreaks due to rare *Candida* species had been reported. The third opportunistic mycosis, invasive zygomycosis is also an important concern, as world's highest number of cases of this disease is reported from India. The infection is commonly observed in patients with uncontrolled diabetes mellitus. The rare fungal infections, including those due to filamentous fungi such as *Fusarium, Scedosoporium,* certain melanized fungi, and the yeasts *Trichosporon, Pichia* may all be seen either sporadically or as a part of an outbreak. Though antiretroviral therapy in AIDS patients has been introduced in most Indian hospitals, no decline in incidence of cryptococcosis, penicilliosis, and histoplasmosis has yet been observed. Therefore, a concerted effort by clinicians, microbiologists, histopathologists, and epidemiologist at each center is required to face the challenge of emerging opportunistic mycoses in India.

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Till 3-4 decades ago, very few fungal species were known to cause diseases in human. There were only four possible groups of fungal infections: few rare dimorphic fungal diseases, half a dozen subcutaneous mycoses, a few yeast infections, and dermatophyte infections. Other rare fungi isolated from non-sterile sites were considered contaminants and were discarded without even being noted on patient's chart. However, since 1960s or 1970s the patient population have changed vastly, new diseases have been described, wide range of immunosuppressive therapies have been introduced, new macro-disruptive procedure have been initiated. These developments have greatly altered the view of what is 'pathogenic fungi' and have greatly expanded the role of medical mycologists. A vast array of fungi is now known to produce infection in human and they are put under 'opportunistic fungal infections'.

The magnitude of the problem is still unclear, as there are few clinical mycologists available worldwide and the antemortem diagnostic capability for fungal diseases till date is sub-optimal. However, the mortality and morbidity associated with these infections are substantial, and it is now well recognized as an emerging public health problem.

In this changed scenario, opportunistic fungal infection has achieved unique position in India, as climate condition in major parts of the country favours growth of fungi. Further, an increased number of patients with HIV infection (estimated anywhere between 3-6 millions), diabetes mellitus (estimated over 30 millions), solid organs or bone-marrow transplantation has allowed fungi to flourish on humans in this country (1, 2). Additional factors that help in emergence of opportunistic fungal infections in India include: availability of systemic steroids and antibiotics over the counters and misused by quacks (untrained health professionals) in several rural and urban areas, rise in population having intravenous drug abuse in Indian towns especially in Manipur and Punjab, below optimum infection control practices and overuse of broad spectrum antimicrobial in many Indian hospitals (1, 2). These factors produce fertile ground for opportunistic mycoses to flourish in this country. However, the exact frequency of opportunistic mycoses is not known due to lack of adequate diagnostic mycology laboratories in this country and lack of awareness of the manifestations of fungal diseases in majority of clinicians. Only a handful centers carry out routine diagnostic

mycological investigations and very few center perform medical autopsies. Thus, what we know of these diseases is just the tip of iceberg. Still, the available limited data suggests that there has been a rapid increase in burden of systemic candidiasis, invasive aspergillosis and cryptococcosis throughout the country (3-7). India is emerging as the capital of zygomycosis of the world (8-10). A sharp increase in the number of histoplasmosis (11) and penicilliosis (12, 13) has been reported in HIV infected patients in the last decade. Emergence of two additional fungal infection including fungal rhinosinusitis due to *Aspergillus* flavus (14, 15) and zygomycosis due to *Apophysomyces elegans* are interesting developments (16).

## Endemic mycoses behaving as opportunistic mycoses

Endemic mycoses are a group of fungal diseases caused by diverse group of fungi that share common characteristic like- a) fungi are dimorphic in nature, b) can produce infection in healthy host, c) occupy a specific ecological niche in the environment. The diseases include histoplasmosis, blastomycosis, coccidioidomycois, paracoccidioidomycosis, sporotrichosis, and penicilliosis. Among these endemic mycoses, the number of patients with histoplasmosis and penicilliosis has sharply increased in India over last one decade with rise in patients with HIV infections (11-13).

**Penicilliosis**: Penicilliosis caused by *Penicillium marneffei* is restricted to the states of northeast India, Manipur (more than 500 cases). Nagaland (1 case), Assam (1 case), and Mizoram (1 case) (1, 12, 13). Rarely cases with penicilliosis are reported from other parts of India in migrated patients from northeast India (17). Singh *et al.* in 1999 first reported the disease from four autochthonous patients with acquired immunodeficiency syndrome at Manipur (18); subsequently the epidemiology of this disease with greater number of patients was described (12, 13). The life cycle of the fungus in nature has not been elucidated clearly. Beside humans, the fungus was isolated from bamboo rats especially *Cannomysis badius* in India (19, 20). However, the reservoir of the organism is still not known. Since bamboo rats live in remote, mountainous area or in jungle and have limited contact with people, the acquisition of the agent by human from bamboo rats is not expected. Though some people eat bamboo rats, it could not explain the mode of spread. There might be a common environmental source for both

rats and human (20). The recognition of penicilliosis is sometimes difficult especially in the area where histoplasmosis is also endemic, as both infection present with fever, weight loss, cough, anaemia, lymphadenopathy, hepatosplenomegaly (20, 21). However, skin lesions are more common (60-65%) in penicilliosis (12, 13, 20). The pigment produced by the fungus has been characterized in detail in India and is shown to be related to the copper colored pigment (herquinone) produced by *Penicillium herquei* since both pigments contain phenalene carbon framework. Unlike the latter, the pigment from *P. marneffei* is dimeric and has a 1,1,3,3-tetramethyl-2,3-dihydropyrrole moiety instead of 2,3,3 trimethyl-2,3-dihydrofuran (22).

**Histoplamosis**: Histoplasmosis caused by *H. capsulatum* var. *capsulatum* was first described by Panja & Sen in 1954 at Calcutta (23), and only 38 cases were diagnosed till 1992 (24). But at present, the disease is threatening to have serious proportion, as almost equal number of cases were described over next 10 years mainly from Tamil Nadu (11) and West Bengal (25). These cases were associated with AIDS epidemic. The fungus was isolated from a house on the bank of the Ganges River near Calcutta (26). Though the number of cases of acute progressive, disseminated histoplasmosis has steadily increased in India, a considerable number of cases are diagnosed as chronic manifestations of disseminated histoplasmosis. These cases are easily diagnosed as the disease frequently presents with accessible mucocutaneous lesions that can be easily biopsied (11, 24, 27, 28). Interestingly 10% cases present as adrenal gland enlargement (11, 25). Histoplasmosis at unusual sites like eyelid (29) and epididymis (30) has been reported from India.

**Opportunistic mycoses:**

**Invasive candidiasis**: This is the most common opportunistic mycosis across India. Frequency of invasive candidiasis varies from 1 to 12 per thousand admissions in different hospitals across the country (3, 4, 31-33). In our centre, an 11-fold increase of the number of patients with candidemia was reported in the second half of 1980s (34). A further, 18-fold increase was observed in 1995 compared to 1991 (31). In 1996 and 1997, nearly 500 cases with candidemia were observed per year. Since then, this trend had been slowed to 165 cases in 2000 due to the strategy of antifungal prophylaxis to high-risk patients (32). However, a return to the

incidence of nearly 500 cases annually was observed by 2007 in spite of continuation of the same strategy of antifungal prophylaxis (4). This may emphasize the requirement of improved hospital care practices at the centers in India, instead of relying on antifungal prophylaxis. The magnitude of problem can be understood by comparison of Indian data with recent surveillance study of all Australian hospitals (35). In that countrywide all Australian hospitals surveillance study reported incidence of candidemia at 365 cases annually during 2001-2004 (35), while incidence at ~500 cases annually had been reported from a single tertiary care centre in India (4).

In India, Candidemia is more prevalent in pediatric than adult patients, majority of these cases being reported from intensive care units (ICUs) in both age groups (3, 4, 31-33). Neonatal ICUs (NICUs) had an incidence of 77 per 1000 discharges at our centre (36). Pediatrics ICUs and surgical ICUs across the country also report high incidence of candidemia (3, 37). Mortality in candidemia cases varies from 28% to 71% and attributable mortality rates between 17% to 33% (3, 4, 31-33).

Majority studies from India identified prolonged hospitalization (>30 days), central venous access, total parenteral nutrition, use of broad-spectrum antibiotics for a prolonged period, mechanical ventilation, major abdominal surgery and immunosuppression as risk factors for developing candidemia (31-33, 36-38). In children prematurity and low birth weight are additional risk factors (32, 36). A study on children admitted to PICUs at our centre reported that risk of death varies with pediatric risk of mortality score, presence of sepsis, isolation of non-albicans *Candida* spp. in general and *C. tropicalis* in particular (36). A recent study on both adults and children at our centre found severe/ recurrent pneumonia in children and renal failure in adult patients as additional risk factors (4).

With the increase in candidemia cases a change in spectrum of *Candida* spp. has been observed worldwide, though *C. albicans* is still the leading cause of candidemia in developed countries (39). However, in India, non-albicans *Candida* species are major cause of candidemia in tertiary care medical centres (31-33, 40, 41). The difference in distribution is more marked in pediatric wards (4). The emergence of such a high rate of non-albicans *Candida* species in India may indicate inadequate hospital care practices, as a

majority of these species are exogenous in origin. Aggressive use of intravascular devices and carriage of the organisms on the hand of health care workers are probable reasons for nosocomial transmission via direct contact (3, 4, 34). Among non-albicans *Candida* species, *C. glabrata, C. parapsilosis*, and *C. tropicalis* constitute the "top 3' *Candida* isolates from blood stream infections (BSI) in most hospitals worldwide, although differences in distribution among the three species is reported from different countries. *C. glabrata* is more prevalent in the hospitals of the United States especially in adult wards, whereas *C. parapsilosis* is isolated from pediatric wards (2). However, in India *C. tropicalis* ranks first among non-albicans *Candida* species isolated from both adult and pediatric wards (3, 4, 31-34, 40, 41). The reason for this difference in distribution is not clear as resistance to fluconazole is seen in only ~10% in *C. tropicalis* strains (4, 31-33). The reason for such high incidence of *C. tropicalis* candidemia may be due to poor hospital care practices and hand carriage of *C. tropicalis* among health care providers in India, as in a study it was shown that 82% of health care providers in pediatric surgical ward had hand carriage of yeasts including 80% of *C. tropicalis* (4). Occasionally rare yeast species had been reported to cause outbreaks in Indian hospitals (1, 42). An outbreak due to *Pichia anomala* (*Candida pelliculosa*) fungemia was reported from our centre affecting 379 children over 23 months (4.2% of all admission). The point source from an index patient with fungemia due to *P. anomala* in pediatric emergency spread to other pediatric wards carried by the hand of a resident doctor (42). Strain specific primer developed by sequencing intergenic spacer 1 (IGS1) region of DNA could prove the point source of the outbreak (43). Though fluconazole prophylaxis to all high –risk babies and improvement of hospital care practices helped in controlling the outbreak (42), *P. anomala* infection has become endemic in our hospital (4). Life-threatening infections due to rare *Candida* species - *C. rugosa* (44), *C. lusitaniae* (45), and *C. kefyr* (33) had been recorded.

Other invasive *Candida* infection like *Candida* endocarditis (46, 47), *Candida* arthritis (48), central nervous system infection due to *Candida* species (45, 49) are occasionally reported from Indian Hospitals. However, *Candida* infection of the pancreas has been increasingly reported. In a study of 335 patients with acute pancreatitis from our hospital, 12.2% patients had true or

possible *Candida* infection of the pancreas and *C. tropicalis* was the most common (44%) isolate (50). *Candida* endophthalmitis has been frequently reported from India with presentation of post-operative and post-traumatic infections (51, 52). *Candida* species were the etiological agent in 21% of 113 fungal endophthalmitis (52).

**Invasive aspergillosis (IA)**: This is an important cause of morbidity and mortality of hospitalized patients in India, though the exact frequency of IA is not known due to inadequate diagnostic mycology laboratories and lack of awareness among clinicians in most centers. However, one example may indicate the burden of IA in India. From our Institute, a tertiary care centre in north India, disseminated fungal infections were detected in 2.4% autopsy cases (15,040 death autopsied over 26 years) and 1A was detected in 49% of those fungal positive cases (unpublished, personal communications with Dr. A. Das, Department of Histopathology).

The classical risk factors for IA include prolonged neutropenia, hematopoietic stem cell transplant or solid organ transplant, intensive immunosuppressive therapy, primary defect of neutrophils, cytomegalovirus pneumonia, aplastic anaemia, myelodyplastic syndrome or myelofibrosis, advanced AIDS (CD4 cell count <100/ cu mm). Apart from these classical risk factors, new factors like critically ill patients admitted in ICUs, patients with pre-existing lung disease (emphysema, chronic obstructive pulmonary disease, healed tuberculous cavity), and patients with liver failure are claimed to be associated with IA in developing countries like India (53, 54). The elderly patients with chronic obstructive pulmonary disease are often colonized with *Aspergillus* species. They receive corticosteroid (oral or inhaled), are often critically ill and hospitalized, receive multiple antibiotics, and become susceptible to IA (55). An autopsy series from Mumbai reported tuberculosis as risk factor for IA in 28% patients (5). The incidence of IA in patients with tuberculosis is expected to be high due to large number of tuberculosis cases in this country. Recent studies reported that diabetes mellitus and corticosteroid therapy predisposing IA is not uncommon in India (6, 56, 57). Uncontrolled diabetes is a known risk factor for zygomycosis (8). Possibly this condition also predisposes the patient for IA. Diabetes mellitus is known to decrease functional activity of phagocytes, while steroid inhibits both macrophages and neutrophils. Both

factors may predispose the patients for IA. However, a considerable number of IA in India has been reported in immune competent hosts especially those with isolated cerebral aspergillosis and rhino-orbito-cerebral aspergillosis (58-60). This may be due to heavy exposure to *Aspergillus* conidia (spore) in the environment or lack of proper investigation of host immune status.

Invasive pulmonary (5), fungal sinusitis (14, 15) and cerebral aspergillosis (6) are common presentations of IA in India. In recent years *Aspergillus* endophthalmitis is an emerging problem in India. Trauma (45%) and ocular surgery (48%) are the major predisposing factors for such infection (52). Postoperative *Aspergillus* endophthalmitis may be seen in clusters due to the use of contaminated irrigation solution, intraocular lenses, donor cornea, ventilation system, and hospital construction activities (61). Poor quality health care practices in rural eye camp settings are possibly responsible for unusually high number of cases of post-operative *Aspergillus* endophthalmitis in India (52). Post-traumatic *Aspergillus* endophthalmitis usually occurs after injury due to contaminated wires, wooden sticks, and hypodermic needle (52). Endogenous *Aspergillus* endophthalmitis may develop rarely as a part of dissemination in IA. However, the unique outbreak of endogenous *Aspergillus* endophthalmitis in India after single intravenous administration of presumably contaminated dextrose infusion fluid possibly highlights the peculiarity of IA in India (62). Primary cutaneous aspergillosis is another emerging disease in India. Again the poor hospital care practices for intravascular catheters, use of contaminated arm boards, adhesive tapes, and occlusive dressings are blamed for maceration of skin leading to primary cutaneous aspergillosis (63).

The commonest species implicated in IA is *A. fumigatus*. Other aspergilli including *A. flavus, A. terreus, A. niger* have been implicated as pathogens rarely in patients with IA. However, in India *A. flavus* has been isolated comparatively at higher frequency from patients with sino-orbital aspergillosis and fungal endophthalmitis (1, 4, 52, 64). Several studies reported *A. flavus* to be the exclusive agent or several times more common than *A. fumigatus* isolated from such patients. The proportional higher isolation of *A. flavus* from certain clinical specimens in India led us to conduct an environmental surveillance of air of our hospital. In the air-conditioned portion

of our hospital *A. flavus* was the predominant agent isolated in all seasons except in summer months, when *A. niger* outnumbered *A. flavus*. However, in non-air conditioned areas, *A. flavus* was the predominant species during winter and spring, *A. fumigatus* in summer and *A. niger* in autumn (unpublished observation). *A. niger* and *A.* terreus have been reported as etiological agents in patients with endophthalmitis from India (52, 65-67). Isolation of A. terreus from patient's sample is a matter of concern, as the agent is usually resistant to amphotericin B. *A. terreus* was also isolated from a case of aortic root abscess and pseudoaneurysm post-cardiac surgery (68). A rare case of *A. nidulans* isolation was reported from a patient with brain abscess (69).

**Cryptococcosis**: Cryptococcosis is encountered frequently throughout the country, especially after emergence of AIDS epidemic (7). Large series were reported from Calcutta, Mangalore, Delhi, Chandigarh, Lucknow, and Mumbai (7, 70-75). The incidence of cryptococcosis at our centre was 0.8 cases/year during 1970 through 1992 (76). A 15-fold rise with incidence of 11.6 cases/year was recognized between 1995 and 1999 (70). A further three-fold rise (34 cases/year) has been demonstrated between 2000 and 2007 (unpublished observation). Thus a 42-fold rise in incidence of cryptococcosis has been witnessed since 1970. The incidence of cryptococcosis in India varies from 4% to 26% in patients with AIDS, but may be as low as 3% in HIV infected children (77-79). Though global incidence of cryptococcosis has decreased with introduction of antiretroviral therapy (ART), the incidence is still on the rise in India (71-75). It may be due to the increasing number of AIDS cases reporting to the hospital in recent years or incomplete coverage of antiretroviral therapy. In an interesting study from our centre of 40 cases of cryptococcal meningitis in HIV infected population, 75%patients had cryptococcal meningitis as the initial AIDS defining illness, 10% patients receiving ART for six months or less presented with features of cryptococcal meningitis possibly indicating immune reconstitution inflammatory syndrome (IRIS), 25% patients receiving ART for more than six months had developed cryptococcal meningitis indicating failure of current ART regimen (75). However, non-compliance of medication may be other possibility of recurrence of cryptococcal meningitis (75). Mortality due to cryptococcosis varies from 18.3% to 40% (7, 70-73). In a study increased

minimum inhibitory concentration (MIC) against fluconazole has also been observed among *Cryptococcus neoformans* strains isolated in recent years (80). Other than HIV infections cryptococcosis has been reported in renal transplant recipients, hematologic malignancies including acute lymphocytic leukemia, systemic lupus erythromatosus, diabetes, systemic steroid therapy and pulmonary tuberculosis. Few patients had no underlying disease (7, 70).

The etiologic agent of cryptococcosis is *Cryptococcus neoformans*, the only pathogenic species of the Genus *Cryptococcus*. There are five serotypes (A, B, C, D. and AD) and three varities (var. *grubii* - serotype A, var. *gattii* - serotype B & C, var. *neoformans* - serotype D) exist under *C. neoformans*. Current concept uplifts the varieties into species status - *C. grubii* (A), *C. gattii* (B & C), *C. neoformans* (D). C. grubii is the most prevalent (>90%) species of the cryptococci isolated in India. C. gattii has occasionally been reported. Serotype AD has been isolated from northern India (7, 81). In an interesting case report serotype A and B were isolated simultaneously from one patient in New Delhi (7). Three cases due to *C. laurentii* and one due to *C. albidus* were recorded in India (7, 82). *C. neoformans* (possibly *C. grubii*) has been isolated from dropping of pigeons, munia birds and canaries, as well as from soil contaminated with pigeon excreta. Vegetables and fruits have also been shown to harbor *C. grubii* (7). *C. gattii* has been isolated from the *Eucalyptus camaldulensis* trees in flowering season from northern India (83). Recently both varities have been isolated from *Ficus religiosa, Syzigium cumini* and *Tamarind indica* trees of Delhi (84).

Exclusive pulmonary cryptococcosis was seldom reported from India, though symptomatic and asymptomatic colonization of airway due to the fungus had been described. Few uncommon presentations like primary involvement of skin, osteolytic lesion of bones, cirrhosis of liver, generalized lymphadenopathy were reported. Other rare presentations reported from India include cryptococcal granuloma in the brain, cryptococcal retinal cyst, cryptococcoma in the ventricle without any CNS involvement, cryptococcal prosthetic valve endocarditis, ventriculoperitoneal (VP) shunt infection, and infection of the genitourinary system (7).

**Zygomycosis:** It is a polymorphic disease, caused by fungi of the Class *Zygomycetes*, and the Order *Mucorales*

and *Entomophthorales*. The fungi under *Entomophthorales* are occasionally reported to cause subcutaneous or mucocutaneous infections (entomophthoramycosis) in immunocompetent host in India. In contrast, fungi under *Mucorales* are reported to cause the more severe forms of zygomycosis (earlier named mucormycosis) in immunocompromised hosts (85, 86). During the past two decades, the emergence of zygomycosis due to *Mucorales* is observed throughout the word in part due to continued rise of diabetics and increased use of immunosuppressive agents (85, 86), but the rise in India is phenomenal and possibly contributes about 40% of the global burden of the disease (8, 10, 87). Nearly 400 cases of invasive zygomycosis were reported over two decades from our center (8, 10, 87). The incidence increased alarmingly at our center from 13 cases/year during 1991 through 2000 to 36 cases /year during 2001 through 2005, and further to 50 cases/year in the last report (8, 10, 87). In a recent review of 461 cases of zygomycosis from India, majority (70%) of the cases were reported from our center (9). Authors attributed such high incidence at our center to better awareness, expertise, and infrastructural facilities for mycological diagnosis than to any regional preponderance of the disease (9).

In India, the rising trend of zygomycosis is commonly associated with uncontrolled diabetes and the number of such cases is so overwhelming that other risk factors are overshadowed (8, 87). Still the risk factors noted other than uncontrolled diabetes and diabetic ketoacidosis from India include hematological malignancy, systemic steroid therapy, burn wounds, organ transplant recipients, trauma, intramuscular injection, malnourishment, prematurity (8-10, 87, 88).

In the recent study from our centre alcoholism and renal failure were added to the list of risk factors for zygomycosis (10). Though majority of the patients with invasive zygomycosis are immunocompromised, ~10% patients are immunocompetent in India (8, 88). Zygomycosis formerly thought to be always community acquired, is now recognized as being a nosocomial infection in certain cases (85). In our study, 9% patients had acquired nosocomial infection either at the site of ECG leads or adhesive tapes or from contaminated intramuscular infections or from air in the hospital environment (10).

Based on the involvement of particular anatomical sites zygomycosis is categorized into rhino-orbito-cerebral,

pulmonary, gastrointestinal, cutaneous, and disseminated (85). From India an additional new clinical entity - renal zygomycosis in immunocompetent hosts has been consistently reported (8, 10, 87, 89, 90). Renal involvement occurs in ~20% cases with disseminated zygomycosis especially in patients with intravenous drug abuse or corticosteroid therapy (85, 86). In contrast, isolated renal zygomycosis is a common occurrence in India (8, 10, 87, 89, 90). These patients present with unilateral or bilateral flank pain, fever with chills, hematuria, pyuria or anuria. The exact route of entry of the pathogen in such patients is not known.

Among the zygomycotic agents causing human disease, *Rhizopus oryzae* is the most frequent agent followed by *Rhizopus microsporus*, *Absidia corymbifera, Rhizomucor pusillus*, and *Mucor circinelloides*. These five agents account for 80% of culture proven cases of zygomycosis (85, 86). Interestingly in addition to the above five agents, *Apophysomyces elegans* and *Saksenaea vasiformis* are emerging zygomycotic agent in India (8, 10, 16, 85, 91). The distribution of these fungi in tropical and subtropical areas is substantiated by occurrence of most human cases in such climate. Recently another rare *Zygomycetes* - *Rhizopus homothallicus* has been reported as an emergent agent in India (92).

***Pneumocystis jiroveci* pneumonia (PCP)**: PCP for the first time in India was reported from lung biopsy of a child in 1971 (93). Subsequently it was reported in renal transplant recipients (94). Case number increased with outbreak of AIDS in India. Studies from North and South India reported an incidence of 10-15% (95-98), though lower rate of 1.1% was reported from Manipur (99). The variation in incidence from different parts of the country largely depends on the method of diagnosis, competence of laboratories, and patient population under study. A few reasons for the lower incidence of PCP in AIDS in general in India are proposed. These include earlier death of Indian AIDS patients due to tuberculosis before severe immunosuppression sets in, tropical climate, possible difference in virulence of strains, prevalence of different genotypes in different regions, and most importantly, lack of awareness and diagnostic expertise (95). Without laboratory confirmation, provisional diagnosis based on clinical features and radiology has been reported frequently (100). In a comparatively recent study enhanced detection rate (from 3.4% to 12%) in patients with AIDS was reported after the use of PCR technology (101).

**Phaeohyphomycosis:** Phaeohyphomycosis consists of a group of fungal infections characterized by presence of dematiaceous (melanized or dark–walled) septate hyphae or sometimes yeast or a combination of both in tissue. It may present as subcutaneous or systemic (especially cerebral and pulmonary) disease in immunocompromised hosts and usually has high mortality. Sporadic cases of phaeohyphomycosis have been reported across India (64, 102-105). Agents isolated from those cases include *Cladophialophora bantiana, Bipolaris hawaiinensis, Exserohilum rostatum, Phialophora richardsiae, Phialophora parasiticum, Phialophora verrucosum, Exophiala spinifera,* and *Fonsecaea pedrosi* (64, 102-105).

**Conclusion:** The incidence of opportunistic fungal infections continues to increase, as sophisticated technologies, that prolong lives of severely ill patients, are implemented. Thus these infections are important challenges in the progress of medicine. Though early diagnosis is the cornerstone in the management of fungal infections, lack of clinical awareness and deficiency in diagnostic mycology facilities in India are major drawbacks in this serious threat of rapid rise of opportunistic fungal infections. Still, the available limited data from India presented a devastating scenario of fungal infections in tertiary care hospitals, which has drawn the attention of clinicians and medical mycologists towards this field. Regular training courses of diagnostic mycology at our centre, frequent continuing medical education and conferences at different corners of the country in this field are the silver linings in this gloomy scenario.

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