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Original Research Article

To Determine the Clinic-Mycological Spectrum of Fungal Diseases: A Retrospective Study

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Abstract

Aim: To determine the clinical and mycological characteristics of fungal diseases in the Bihar area.

Material and Methods: This retrospective study was conducted in the Department of Pulmonary Medicine, Holy Promise Hospital, Patna, Bihar, India for one year. Patients with suspected fungal infections were included and detailed history was recorded. Various Samples like blood, body fluids, respiratory samples, pus, tissue, skin scrapings, corneal scrapings, biopsy etc. were included in the study. Microscopic examination with KOH mount was done for all samples except blood samples. The samples were inoculated on two tubes of Sabouraud dextrose agar (SDA) with antibiotics and cycloheximide and two tubes of SDA with antibiotics but without cycloheximide. The growth obtained was identified on the basis of colony morphology, pigment production and microscopic examination with KOH mount and lactophenol cotton blue (LCB). Isolation of candida species from respiratory samples (sputum, endotracheal aspirate, bronchoalveolar lavage, suction tip) and urine were considered as fungal colonization.

Results: Most common fungal infection was Candidiasis 131(60.6%) followed by Aspergillosis 63(29.2%) and Mucormycosis 13(6.0%) and Cryptococcosis 5(2.3%). Among 2 cases of Trichosporon infection, 1 was trichosporonemia and other was Trichosporon pneumonia. 1 case of Fusarium keratitis was observed. Among 131 patients with candidiasis, invasive candidiasis was seen in 128(97.7%) patients & cutaneous candidiasis seen in 3(2.3%) patients. Candida tropicalis 86(62.7%) was most common isolate followed by Candida albicans 17(12.4%) & Candida Guillermin 12(8.7%). In C. albicans 100% susceptibility was seen to Fluconazole and Echinocandins. In NAC, maximum susceptibility was seen to Amphotericin-B (89.2%) followed by Voriconazole (82.5%). Out of 5 cryptococcus species, 4 isolates of Cryptococcus neoformans and 1 Cryptococcus Laurentis was seen.

Conclusions: Fungal infections are associated with significant morbidity and mortality. Candidiasis was the most common infection followed by aspergillosis. Candidemia is the major factor associated with fatal outcome with C.tropicalis, C.gulliermondii and C. parapsilosis being predominant pathogens.

Keywords: C.tropicalis, C.gulliermondii and C. parapsilosis, KOH

Introduction

Fungal infections have emerged as a significant global health concern, affecting millions of people worldwide. These infections range from superficial mycoses, such as dermatophytosis, to invasive and life-threatening diseases like candidiasis and aspergillosis. The clinic-mycological profile of fungal infections encompasses the clinical presentation, epidemiology, risk factors, diagnostic methods, and the spectrum of causative fungal pathogens. Understanding this profile is crucial for timely diagnosis, effective treatment, and improved patient outcomes. Fungal infections can present with a wide range of clinical manifestations depending on the site of infection and the immune status of the host. Superficial fungal infections typically affect the skin, hair, and nails, causing conditions like tinea pedis (athlete's foot), tinea corporis (ringworm), and onychomycosis (nail fungus). In contrast, systemic fungal infections such as invasive candidiasis, aspergillosis, and cryptococcosis predominantly occur in immunocompromised individuals, including those with HIV/AIDS, cancer, or undergoing organ transplantation. Epidemiologically, fungal infections are more prevalent in tropical and subtropical regions due to the warm and humid climate that favours fungal growth. [1-4] However, with the increasing use of immunosuppressive therapies and the rising prevalence of chronic diseases, fungal infections are becoming more common in temperate regions as well. Several factors predispose individuals to fungal infections. These include: Immunosuppression: Patients with weakened immune systems, such as those with HIV/AIDS,

cancer, or on immunosuppressive medications, are at higher risk for invasive fungal infections. Chronic Diseases: Diabetes mellitus, chronic obstructive pulmonary disease (COPD), and other chronic illnesses increase the susceptibility to fungal infections. Environmental Exposure: Exposure to contaminated soil, air, and water can lead to infections with environmental fungi like Aspergillus and Histoplasma. Hospitalization: Long-term hospital stays, particularly in intensive care units (ICUs), and the use of invasive devices such as catheters and ventilators can increase the risk of nosocomial fungal infections. The diagnosis of fungal infections involves a combination of clinical evaluation, microscopic examination, culture, histopathology, and molecular techniques. [5] Microscopy and Culture: Direct microscopic examination of clinical specimens (skin scrapings, nail clippings, sputum) with potassium hydroxide (KOH) preparation can reveal fungal elements. Culture on Sabouraud dextrose agar helps in the isolation and identification of fungi. Histopathology: Tissue biopsy followed by histopathological examination can identify invasive fungal infections and the extent of tissue involvement. Serological Tests: Detection of fungal antigens or antibodies in blood can aid in the diagnosis of certain fungal infections like cryptococcosis and aspergillosis. Molecular Methods: Polymerase chain reaction (PCR) and other nucleic acid amplification techniques provide rapid and specific identification of fungal pathogens. A wide variety of fungi are implicated in human infections, with the most common being: Candida species: Cause both superficial (oral thrush, vaginal candidiasis) and invasive infections (candidemia). Aspergillus species: Responsible for allergic bronchopulmonary aspergillosis, chronic pulmonary aspergillosis, and invasive aspergillosis. Dermatophytes: Trichophyton, Microsporum, and Epidermophyton species cause superficial infections of the skin, hair, and nails. Cryptococcus neoformans: Causes cryptococcal meningitis, particularly in immunocompromised individuals. Histoplasma capsulatum: Causes histoplasmosis, a systemic infection acquired through inhalation of spores from contaminated soil. [6-8]

Material and Methods

This retrospective study was conducted in the Department of Pulmonary Medicine, Holy Promise Hospital, Patna, Bihar, India for one year. Patients with suspected fungal infections were included and detailed history was recorded. Various Samples like blood, body fluids, respiratory samples, pus, tissue, skin scrapings, corneal scrapings, biopsy etc. were included in the study. Microscopic examination with KOH mount was done for all samples except blood samples. The samples were inoculated on two tubes of Sabouraud dextrose agar (SDA) with antibiotics and cycloheximide and two tubes of SDA with antibiotics but without cycloheximide. The growth obtained was identified on the basis of colony morphology, pigment production and microscopic examination with KOH mount and lactophenol cotton blue (LCB). Isolation of candida species from respiratory samples (sputum, endotracheal aspirate, bronchoalveolar lavage, suction tip) and urine were considered as fungal colonization. [8] Blood and body fluid culture were done by BAC-T alert or BACTEC automated systems. The blood culture bottles were incubated till the bottle indicate positive by the system for maximum period of 7 days. Identification and antifungal susceptibility for yeasts was done by VITEK-2 technology. Serological correlation was done with (1-3)-β-D Glucan assay with Fungitell Kinetic Assay and value of <60pg/mL was taken as negative, 60 to 79 pg/mL indeterminate and 80 pg/mL positive. Serum galactomannan assay was done using Platelia Aspergillus EIA (enzyme immunoassay) kit (Bio-Rad, France) and value of < 0.50 were considered as negative and 0.50 were considered as positive. Invasive aspergillosis cases were classified according to revised definitions given by Invasive Fungal Infections Co- Operative Group (IFICG) of the European Organization for Research and Treatment of Cancer and Mycoses study group case definitions (EORTC/MSG) into proven, probable and possible invasive aspergillosis based on host, clinical and mycological factors. [8]

Statistical Analysis

The data was recorded on the proforma enclosed. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 25 version statistical program for Microsoft Window.

Results

Out of 19698 samples received, 372 isolates were obtained from 365 patients. Out of 372 isolates, 97(0.63%) were obtained from 15380 blood sample and 126 (29.2%) from other 4318 samples. Candida isolates (149) from respiratory samples and urine samples were considered as colonizers and rest 223 were labelled as pathogens. (Table 1) These 223 isolates were obtained from 216 patients. Male preponderance was seen 141(65.3%) as compared to females 75(34.7%) Majority of patients belong to 51-60 years (23.1%), followed by 61-70 years (21.8%). Maximum no. of patients with fungal infections were from medicine wards (59.3%) followed by ICU “s (22.7%), Surgery 11.5% and pediatrics 6.5%.Steroid use (21.3%) was the most common risk factor observed followed by diabetes mellitus (18.1%). Majority of patients presented with fever (65.3%) followed by shortness of breath (41.2%) and cough (23.1%). Most common fungal infection was Candidiasis 131(60.6%) followed by Aspergillosis 63(29.2%) and Mucormycosis 13(6.0%) and Cryptococcosis 5(2.3%). Among 2

cases of Trichosporon infection, 1 was trichosporonemia and other was Trichosporon pneumonia. 1 case of Fusarium keratitis was observed. (Table 2). Among 131 patients with candidiasis, invasive candidiasis was seen in 128(97.7%) patients & cutaneous candidiasis seen in 3(2.3%) patients. Candida tropicalis 86(62.7%) was most common isolate followed by Candida albicans 17(12.4%) & Candida gulliermondi 12(8.7%). In C. albicans 100% susceptibility was seen to Fluconazole and Echinocandins. In NAC, maximum susceptibility was seen to Amphotericin-B (89.2%) followed by Voriconazole (82.5%). Susceptibility to fluconazole and micafungin in C. albicans was statistically significant as compared to NAC. (Table 3). Out of 5 cryptococcus species, 4 isolates of Cryptococcus neoformans and 1 Cryptococcus laurentii was seen. All the 4 patients with cryptococcal meningitis were HIV reactive. Out of 63 cases of aspergillosis, most common infection was pulmonary aspergillosis 45(71.4%) followed by sino-nasal aspergillosis 12(19.1%). Aspergillus flavus 49(77.8%) was predominant species followed by Aspergillus fumigatus 14(22.2%). Among the cases of pulmonary aspergillosis, most common radiological findings were consolidation 7(21.9%) and consolidation with ground glass opacity 7(21.9%). Out of 45 cases of pulmonary aspergillosis, galactomannan assay was received in 38 patients, out of which 20 were positive. Percentage positivity of 52.6% was observed. In the present scenario, suspicion of Invasive pulmonary Aspergillosis (IA) were categorized. Cases of A were further classified as probable IA-32 and possible IA-45 and no case was as proven as per European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) criteria. Out of total 13 cases of mucormycosis, most common infection was Sino-nasal mucormycosis 8(61.5 %) followed by cutaneous mucormycosis 4(30.8%). Most common species observed was Rhizopus 8(57.2%) followed by Mucor 6(42.8%). Out of 216 patients with fungal infections, 204(94.4%) patients got discharged and 12(5.6%) expired.

Table 1: Sample wise distribution of fungal isolates(n=223)

Sample	*Candida*	*Cryptococcus*	*Trichosporon*	*Aspergillus*	*Mucor*	Rhizopus	Fusarium	Total
Blood	96	-	1	-	-	-	-	97
Respiratory samples	148	1	1	46	1	1	-	198
Body fluids	37	4	-	1	-	-	-	42
Tissue	2	-	-	4	1	1	1	9
Sino-nasal mucosa	-	-	-	11	3	5	-	19
Pus	1	-	-	-	-	1	-	2
Urine	1							1
Others	1	-	-	2	1	_	-	4
	286	5	2	64	6	8	1	372

Table 2: Clinical categorization of fungal infections. (n=216)

Clinical categorization	n=216	Percentage (%)
Candidiasis	**131**	**60.6%**
Candidemia	93	43.1
Invasive *Candidiasis*	35	16.1
Cutaneous *Candidiasis*	3	1.4
Cryptococcosis	**5**	**2.3%**
Cryptococcal Meningitis	4	1.9
Cryptococcal Pneumonia	1	0.5
Trichosporonosis	**2**	**0.9%**
Trichosporinemia	1	0.5
Trichosporon pneumonia	1	0.5
Aspergillosis	**64**	**29.6%**
Pulmonary Aspergillosis	46	21.3
Sino-nasal Aspergillosis	12	5.5
Cutaneous Aspergillosis	5	2.2
Ocular Aspergillosis	1	0.5
Mucormycosis	**13**	**6.1%**
Sino-nasal Mucormycosis	8	3.6
Cutaneous Mucormycosis	4	1.9
Pulmonary Mucormycosis	1	0.5
Fusarium Keratitis	**1**	**0.5%**

Table 3: Anti fungal susceptibility profile of *Candida species*.(n=137)

Species	Fluconazole	Voriconazole	Amphotericin-b	Caspofungin	Micafungin
C.albicans (17)	100%	88.20%	94.10%	100%	100%
C.tropicalis (86)	79.90%	87.30%	96..2%	93.60%	89.90%
C.parapsilosis (8)	62.50%	87.50%	100%	100%	87.50%
C.cifferi (4)	-	75%	75%	-	-
C.pelliculosis (3)	66.70%	100%	100%	/	/
C.lusitanie (1)	100%	100%	100%	100%	100%
C.utilis (1)	100%	100%	100%	-	-
C.glabrata (1)	-	100%	100%	100%	100%

Discussion

Out of total, fungal infection was seen in 1.88% (372) samples. Whereas in a study conducted by Ahir HR et al 9 higher positivity (6.7%) of fungal isolates can be seen. 372 isolates were obtained from 365 patients. Out of total isolates, 198 were from respiratory samples, 97 from blood, 42 from body fluids, 19 from sino nasal mucosa, 9 from tissue, 2 from frank pus, 1 from urine and 4 from other samples. Table 1 shows the sample wise distribution of fungal isolates. Out of total samples, positivity of fungal infections in blood was 0.63% and 29.2% from others. [9] Fungal infections were more common in males 141(65.3%) as compared to females 75(34.7%) in our study. This can be explained by the fact that the males are more exposed to fungal spores due to outdoor activities. These findings were more accordant with the study conducted by Lin SJ et al. which showed out of 225, 162 (72%) were males and 63 (28%) were females. [10] Majority of patients belonged to elderly age group 51-60 years (23.1%) in our study. This can be compared with the study done by Marrin K et al [11] where 50-70 years age group was most common age group. (range 20-95 years). Majority of the patients were admitted in medical wards (59.3%) followed by ICU (22.7%). Similarly, Chen S et al [12] reported majority of fungal infections in medical wards 390 [35.6%] followed by critical care units 273 [24.9%] and surgical wards [17.3%]. In contrast to this, some studies showed a significant increase in candidemia incidence in ICU's. [13,14] Chronic steroid use was most common risk factor (21.29%) followed by diabetes mellitus (18.05%). Majority of immunocompromised individuals were started with steroid therapy. Uncontrolled diabetes mellitus is the most important co-morbid condition associated with mucormycosis. This can be associated with lack of regular health checkups in Indian population. Similarly in a study by Ahmadikia K et al [15] in 2021 the use of steroids therapy was a prominent risk factor. In a study by, Singh G et al [16] most common risk factor was diabetes mellitus (41.9%) followed by mechanical ventilation (40.5%). Most common presentation in our study was fever (65.3%) followed by shortness of breath (41.2%) and pain abdomen (25%). Fever without specific signs and symptoms was seen. Similarly Noorifard M et al [17] reported fever(100%) the most common clinical symptom. In our study, most common fungal infection observed was candidiasis (61.4%) followed by aspergillosis (28.7%) and mucormycosis (6.2%). Similarly, Ahir HR et al [9] in 2018 reported candidiasis (97.4 %) as the most common fungal infection. Among all candida isolates, majority of the isolates were non-albicans candida (NAC) (87.6%) followed by Candida albicans (12.4%). Among the 120 NAC, most common species obtained was Candida tropicalis (62.7%) followed by Candida gulliermondi (8.7%) and Candida parapsilosis (5.8%). These findings establish the great importance of NAC as pathogen in clinical samples. In contrast to our study, few studies reported C. albicans as the predominant pathogen (39.42%), followed by C. parapsilosis (34.02%). [18] The distribution of the species are different in various regions and studies. For management of patients, determination of changes in the distribution of candida species is important. Pulmonary aspergillosis (71.9%) was most common manifestation among all the cases of aspergillosis, followed by Sino-nasal aspergillosis (18.8%), cutaneous aspergillosis (7.8%) and ocular aspergillosis (1.6%). Similarly in a study by Swu-Jane Lin et al, [19] 70% of the infections were pulmonary and 9% of patients had disseminated and/or CNS aspergillosis. Aspergillus flavus is prevalent in tropical countries like India, Pakistan, Sudan and leading to majority of cases of aspergillosis. Also in our study, out of 64 cases, Aspergillus flavus (78.13%) was the most common species obtained followed by Aspergillus fumigatus (21.88%). Similarly, JishnuBTet al [20] observed A. flavus was the most predominant species and was identified in 46 (63.80%) cases of Aspergillosis. Unlike to this, Tashiro T et al [21] observed A. fumigatus (41%) and A. niger (32%), as the predominant species. In 1 respiratory sample 2 isolates were obtained, 1 was A. flavus and other was Mucor. In the present study, suspicion of Invasive pulmonary Aspergillosis (IA) was categorized. Cases of IA were further classified as probable IA-32 and possible IA-45 and no case was as proven as per European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses

Study Group (EORTC/MSG) criteria. Whereas, a study categorizes 81 patients as proven IA (14.8%), probable IA (48.2%), possible IA (27.2%), or no IA (8, 9.9%) as per EORTC/MSG criteria. [22] Out of total 13 cases of mucormycosis, most common infection was Sino-nasal mucormycosis (61.5 %) followed by cutaneous mucormycosis (30.8%). Mucorales are present in air community and hospital settings. Most of the infections are nosocomial in origin. Cutaneous mucormycosis was seen after trauma, burns and nosocomial infection after surgery. Out of 13 cases, histopathology was done in 9 cases, which all were co-in siding with the culture reports. Rhizopus arrhizus is the most common agent causing mucormycosis in India and globally. In the present study, among the 13 isolates of mucormycosis, most common species was Rhizopus (57.2%) followed by Mucor (42.8%). Parkash H et al [23] observed Rhizopus the most common cause of mucormycosis. The antifungal susceptibility was studied for azoles (fluconazole, voriconazole) amphotericin-b and echinocandins (caspofungin and micafungin). In our study, in C. albicans 100% susceptibility was seen to Fluconazole and Echinocandins followed by 94.15% to amphotericin-b and least susceptibility was seen to voriconazole (88.2%). Sensitivity to fluconazole and micafungin was statistically significant in C. albicans as compared to NAC.

In NAC isolates, maximum susceptibility was seen to Amphotericin-B (89.2%) followed by Voriconazole (82.5%). Hazrat Bilal et al [24] observed 100% sensitivity of C.glabrata to amphotericin-b. In candidemia, higher susceptibility of voriconazole (84.4%) and amphotericin- b (93.8%) observed, as compared to 78.4% and 81.1%in body fluids respectively. Whereas few studies showed decreased susceptibility to azole agents and resistance to amphotericin-b in candidemia patients. [25] Long term prophylaxis is associated with development of resistant to these drugs. Outcome was observed in terms of discharge and death. Out of 216 patients, 94.1% patients discharged and 5.9% patients had fatal outcome. In a study conducted by TakVet al, very hi 68(43.31%) out of 157 patients had fatal outcome. [26] Some other studies also showed high mortality rate of 30% to 70%In our study, higher mortality (66.7%) was seen in elderly age group (>60 years) than younger age group (<60 years). Maximum patients who were discharged were of younger age group. [27]

Conclusions

Fungal infections are associated with significant morbidity and mortality. Candidiasis was the most common infection followed by aspergillosis. Candidemia is the major factor associated with fatal outcome with C.tropicalis, C.gulliermondii and C. parapsilosis being predominant pathogens. The growing rate of non-albicans candida resistance to azole confirms the monitoring of changes in distribution of pathogenic candida species. Until rapid susceptibility testing is available, empiric therapy should be used based on patients' clinical condition, risk factors, site of infection and local anti-fungal microbiological patterns. In many countries, very effective anti-fungal agents are available. But, in developing countries like ours these are very expensive and not available to all the patients. So, early diagnosis and continuous surveillance of fungal infections is important for better outcome of patients.

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