Global Journal of Medicine & Public Health

Invasive fungal infection:A visible menace !

Priti Dave [*1] , *Kevin Bora* [2] , *Sukriti Joshi* [2] , *Yashowardhan Taparia* [2] , *Mayur Patil* [2]

GJMEDPH 2019; Vol. 8, issue 3

[1]Professor, Department of Medicine, Bharati Vidyapeeth to be Deemed University and Medical College, Pune, Maharashtra, India

[2]Post Graduate Student, Department of Medicine, Bharati Vidyapeeth to be Deemed University and Medical College, Pune, Maharashtra, India

***Corresponding Author**
Priti Dave
Professor
Department of Medicine, Bharati Vidyapeeth to be Deemed University and Medical College
H 602, Pride Platinum, Baner, Pune
dave.priti7@gmail.com
Phone No: 9822790490

Conflict of Interest—none

Funding—none

ABSTRACT

Invasive Fungal Infections(IFI) are an upcoming threat in hospitalized patients.We studied the risk factors, etiology, clinical features and outcome in form of survival and death in 30 cases having IFI. This was a prospective observational study. The prevalence of IFI in our study was 0.665%. The associated comorbidities found were diabetes mellitus, neutropenia, chronic kidney disease , malignancy, immunosuppressive therapy including systemic steroids or chemotherapy drugs, and trauma.Some cases underwent major surgeries, used broad spectrum antibiotics ,had sepsis, HIVinfection, were on Total parenteral nutrition (TPN) and had underwent instrumentation or ICU stay .The common IFI were Mucormycosis followed by Candidiasis, Aspergillosis and Cryptococcosis. 76.6% of cases survived while death was seen in 26.6% of cases.

Keywords: Invasive Fungal Infection, Risk Factors, Mucormycosis, Asoergillosis, Candidiasis, Cryptococosis

INTRODUCTION

India is a large tropical country with monsoon season having heavy rains making fungi to inhabitate many regions. There are limited studies done in India and hence precise incidence of invasive fungal infection is not known.[1] Moreover there is alarming rise in fungal infections which adds to the difficulty of getting the latest incidence. According to Invasive fungal infection cooperative group of European origin (IFICG), Invasive fungal infection (IFI) is defined as existence of fungal elements either mould or yeast in biopsy or needle aspiration of deep tissues established by histopathology or culture .[2]

Pathogenicity of fungal infections depend upon host factors and fungal virulence. There are many risk factors in host which favor fungal infections. Fungal virulence depends upon enzymes and toxins produced by them.[3] IFI are sometimes under reported because diagnostic cultures sometimes lack sensitivity as well specificity.[4] Clinical features and management depends upon the type of fungus and the organ involved.

Aim

To evaluate clinical profile of invasive fungal infections in hospitalized patients.

Objectives

1) To determine prevalence of invasive fungal infection in hospitalized patients.
2) To identify risk factors present with invasive fungal infections.
3) To identify fungal species involved in invasive fungal infection.
4) To determine the clinical outcomes of invasive fungal infections at the time of discharge.

METHODS AND MATERIALS

This observational study was done in western Maharashtra in a tertiary hospital. First 30 patients admitted in medicine critical care unit and wards above 18 years of age who met the study definition of IFI were included in the study. Patients with superficial fungal infections were excluded from the study.

Ethics Committee approval and written consent of patients were taken. All patients suspected to have

invasive fungal infections were questioned for history of symptoms and a detailed clinical examination was done. Any suspected risk factor of IFI were noted carefully.

Every patient suspected of having fungal infection was subjected to complete blood cell count, blood sugar levels, renal function test, liver function test, serum electrolytes, blood culture, urine routine and culture. Bronchoscopic alveolar lavage (BAL) routine and culture, sputum culture, tissue scrapings, KOH mount, CSF routine and culture, catheter tip culture, x-ray chest (PA View), HRCT Thorax, MRI brain , X-ray and CT PNS , USG (abdomen+ pelvis), ECG, 2D-echo were done if indicated. Nasal endoscopy or surgical exploration were also done if needed. Probable diagnosis were made by culture from nonsterile site like BAL or sputum etc.

Definitive diagnosis of IFI was done either by positive culture from sterile site like needle aspirate /tissue biopsy or pleural fluid or histopathological evidence of fungus. Aspergillus antigen test and galactomanan levels were tested if needed. Mucormycosis was treated with liposomal Amphotericin b (Amb) or combinations with caspifungin or anidulafungin, Aspergilosis was treated with voricanazole ,Candida were treated by Flucanozole or Echinocandins or Amphotericin as required,in therapeutic dose and duration. Cryptococus was treated with Amphotericin B followed by fluconazole. Prevalence, etiolgy, risk factors organ involved and clinical outcome was studied.

RESULTS

30% of patients were in age group between 51-60 yrs followed by 20% each in 31-40 yrs and 41 to 50 yrs. In age group between 61-70 yrs 16.7% cases were there, while 6.7% in each 71-80 yrs and <30 yrs. 56.67% were male and 33.33% were female. The prevalence of IFI in our study was 66.5%.

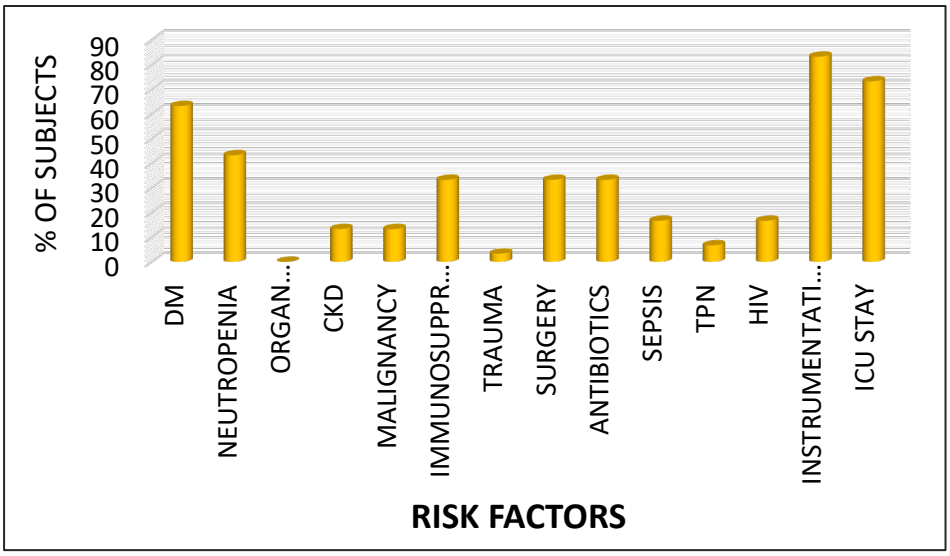

Fig 1 Risk Factors Associated with IFI

As far as clinical features are concerned 50% patients had fever, 35% had breathlessness ,32% cough, 21% nasal discharge, 20% nasal block, 20% had headache, 21% altered sensorium, 18% facial swelling, 16% had cranial nerve palsy, 13% had proptosis and 8% abdominal pain. Weight loss and loss of vision were seen in 3% and 6%.

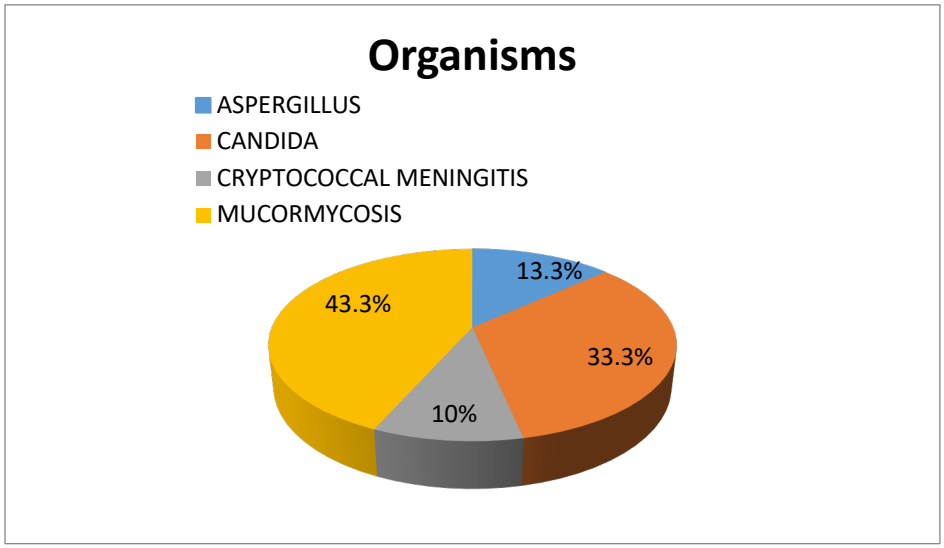

Fig 2 Distribution of Organisms in the Study Group

Table 1 Distribution of Organs Involved in the IFI in the Study Group

Organ Involved	Frequency	Percent
Blood	9	30
CNS-Meninges	3	10
Lungs	7	23.3
Maxillary Sinus or / with Eyes , Nasal Mucosa and Cavity	9	30%
Renal Abscess	1	3.3
CNS +Right Eye	1	3.3
Total	30	100

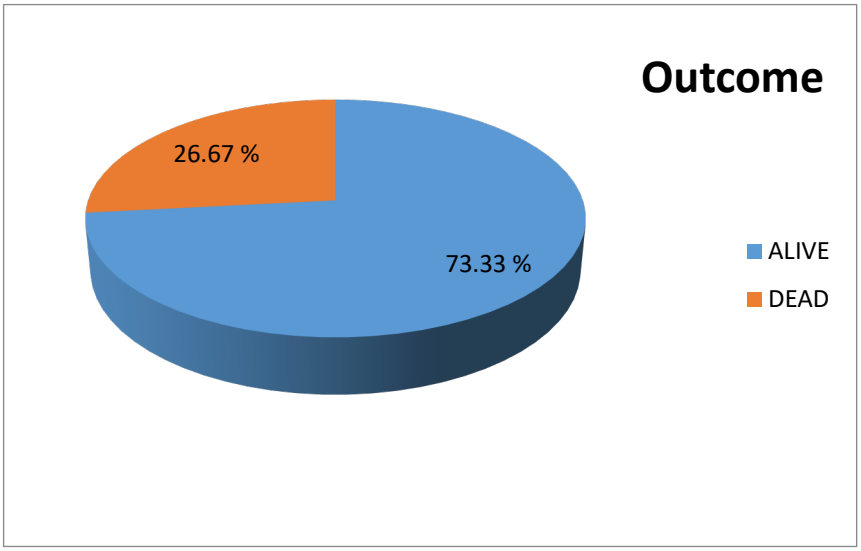

Fig 3 Distribution of Outcome in the Study Group

DISCUSSION

The incidence of invasive fungal infections in our study was .665 per 100 patients. Various studies done to find incidence or prevalence of IFI are in different patient groups like patients on mechanical ventilation, haematological malignancies and intensive care settings. Moreover independent fungal infections are studied separately.[5,6] There are not much studies to compare incidence in general hospitalized patients but we all know that IFI is a upcoming menance in our country in hospitalized patients.

In our study, out of 30 subjects, maximum (43.33%) had 'Mucormycosis' followed by 'Candidiasis' (33.3%). The percentage of subjects with 'Aspergillosis' and 'Cryptococcosis' were nearly similar (13.3 % and 10%). Prevalence of Mucormycosis differ in developed and developing countries. In Europe and United states its prevalence is 1to2 per 100,000 population while in India it is much higher 14 per 100,000 population[7].The commonest (43.3%) mucormycosis was Rhino orbital (30%) followed by pulmonary (10%) and CNS involvement (3.33%). Bala in his study in north India also found rhinoorbital mucormycosis (61.5%) to be the commonest followed by cutaneous (31%), gastrointestinal (5%) and pulmonary involvement (2.5%).[8] In global registry pulmonary mucor was found to be 58.5 % followed by rhinocerebral or rhino-orbital to be 19.5%. However in an Italian study the most common infection site was rhino orbital cerebral.[9] Isolated renal mucormycosis are also seen in India now a days,[7] however we did not have any. Mucormycosis are angioinvasive fungi which further complicates the picture. The commonest risk factor in mucormycosis in our study was Diabetes (72%). Diabetes is linked with faulty neutrophil function and microvascular insufficiency which allows fungal growth.[9] Kl Peterson[10] in his study of 28 cases of mucormycosis found that 64% cases where diabetic. In an Indian study, 56.8 % were diabetic. Warning signs of Rhinocerebral Mucormycosis in diabetics are diplopia, cranial nerve palsy, proptosis and swelling around orbit. Pulmonary mucormycosis radiologically shows multiple nodules and CT scan of chest shows Reverse Halo sign which is more commonly seen in Mucor then in Aspergilosis.[7] Apart from the common risk factors deferaxone therapy for decreasing iron load also is a risk factor as iron removed by it is taken by sideropores of mucour for their growth however this is not the case with newer iron chelators like Deferasirox.[11] In our study no patient was on deferaxone.

In our study 33.3% cases were candida fungal infections. 30 % were blood stream infection while 3.33% cases had renal abscess. Early picking up of blood stream infection can reduce mortality. An important challenge in candida infection is to differentiate benign candida from deep tissue candida infection. Sputum or urine being positive for candida do not mean a pulmonary or kidney infection. In our study 30% of cases were candida albicans while 70% were candida non albicans. Initially Candida albicans was the most visited candida species but now non candida albicans (NCA) are more frequently recorded. NCA appear to be more virulent and more resistant to antifungal medications.[3] Incidence of Candidaemia in India is 1-12 patients /1000 cases that is 20-30 times more in developed country. Candida tropicalis is more common in India. It also have chances to develop sepsis.[4] Canida Glabrata was commonly a normal inhabitant but now becoming a pathogen and azole resistance is the concern.[12] Third most common fungal involvement in our study was Aspergilosis and in all cases lungs were involved in the form of nodules to consolidation to cavitatory lesions. Vaideeswar P [13] in his study of 39 cases at autopsy of invasive pulmonary aspergilosis found lung involvement in the form of pleural fibrosis, consolidation, abscess and cavitation like ours.

We could not find involvement of sinus, brain, skin, heart and eye by Aspergilosis. Out of 350 species of Aspergillosis only 7 are pathogenic. Neutrophil count less than 500/cumm for greater than 21 days is the most common risk factor of IA. It has 45° dichotomous branching of hyphae which invade tissue, alveolar macrophages produce TNF alpha and macrophage inflammatory protein which resist infection but in neutropenia these are reduced causing invasive Aspergilosis.[14] There are case reports of invasive paranasal Aspergillosis in immunocompetent patients. One was an obese

patient who had Bariatric surgery and the other was a case of chronic dacrocystitis which blocked the lacrimal gland and may have predisposed to Aspergillosis.[15] However, in our case we did not find Aspergilosis in immunocompetent patient. We physicians should try to find out predisposing factors in invasive Aspergillosis even when known immunocompromised history is not available.

We had 3 cases of cryptococcal meningitis (CSF cryptococal antigen positive), all were HIV positive and treated with Amphotericin B for 2 weeks followed by flucanosole 400mg/day for 8 weeks then 200mg/day for 3 months. CSF culture turned sterile at the end of 2 weeks and all 3 cases improved. Early Antifungal, correct time to start ART and proper management of raised intracranial pressure by therapeutic Lumbar puncture are important aspects of management.[16] However high mortality is seen in these infections and IRIS is also a complication. They all presented with fever and headache like in a study done by Atul Patel.[16] One of them had a sluggish course and in these cases we need to have high index of suscpicion. 73.33% of IFI cases were alive while death occurred in 26.66% of cases. Among patients who died, 3 patients were having pulmonary Aspergilosis, 4 blood stream candidiasis and 1 patient had mucormycosis. Out of 4 cases of Pulmonary Aspergilosis, 3 patient died. All patients received Voricanazole in therapeutic doses. Aspergilosis has a mortality rate of 90%.[17] Many times diagnosis of Aspergilosis is made at autopsy. The crude mortality of invasive candidemia is 30-81% in critical ill patients.[18]

CONCLUSION

Prevalence of IFI in our study was .665 per 100 patients.The most common IFI found in our study was mucormycosis followed by Candida, Aspergilosis and Cryptococcus. All study patients had some or the other immunocompromised status commonest being Diabetes mellitus. Candida non albicans were more than Candida albicans. 76.6% of cases survived while death was seen in 26.6% of cases. Pulmonary Aspergilosis had high mortality. Early diagnosis and proper treatment can reduce the mortality.

REFERENCES

1. Chakrabarti A, Chatteerjee SS, Shivaprakash MR. Overview of Opportunistic Fungal Infections in India. Jpn J.Med.Mycol. 2008; Vol.49. (3).
2. Ramana, K V, et al. "Invasive Fungal Infections: A Comprehensive Review." American Journal of Infectious Diseases and Microbiology .2013; 1(4): 64-69.
3. Enoch DA, Ludlam HA, Brown NM. Invasive fungal infections: a review of epidemiology and management options. Journal of medical microbiology. 1 July 2006; 55(7): 809-18.
4. Sunavala AJ, Soman R. Invasive Fungal Infections. The association of physicians of India.76-80
5. Hsu.L.Y,Lee D.G , Yeh.S.P, Bhurani D, etall Epidemiology of Invasive Fungal Diseases among patients with haematological disorders in the Asia – Pacific : a prospective observational study. Clin Microbiol infect 2015 ; 21:59 4e7594e11
6. Chakraboti A, Jaiswal A, Verma .P.K Singhal R. A Prospective study of fungal colonization and Invasive Fungal Diseases in Long term Mechanically Ventilated patients in a Respiratory Intensive Care Unit. Indian J Criti Care Med.2018; 22(8):597-601.
7. Skiada A, Lass-Floerl C,. Klimko N et al. Challenges in the diagnosis and treatment of mucormycosis .Medical Mycology,.2018; 56, S93–S101
8. Bala K, Chander J, Handa U, Punia RS, Attri AK. A prospective study of mucormycosis in north India: experience from a tertiary care hospital. Med Mycol. April 2015; 53 (3): 248-57.
9. Carlos Rodrigo Camara-Lemarroy, Emmanuel Irineo González-Moreno, Rene Rodríguez-Gutierrez, et al., "Clinical Features and Outcome of Mucormycosis," Interdisciplinary Perspectives on Infectious Diseases. 2014; 5.
10. K. L. Peterson, M. Wang, R. F. Canalis, and E. Abemayor, "Rhinocerebral mucormycosis: evolution of the disease and treatment options," Laryngoscope.1997;7(107) : 855–862.
11. Prakash A, Chakrabarti A Global epidemiology of mucormycosisJ, Fungi. 2019; 5(26):
12. Bhattacharjee P, Epidemiology and antifungal susceptibility of candida species in a tertiary care hospital, Kolkata, India curr, Med Mycol. June 2016; 2(2):20-27.

13. Vaideeswar P,Prasd S ,Deshpande JR, Pandit SP.Invasive pulmonary aspergilosis :A study of 39 cases at autopsy .Journal of postgraduate medicine.Jan 2004;50 (1):21.
14. Ana María Garcia-Giraldo, Barbara Lucia Mora, Jorge Mario Loaiza-Castaño, Jorge Andrés Cedano, Fernando Rosso. Diagnosis and treatment of invasive pulmonary aspergillosis in neutropenic patients. Med Mycol Case Rep.March 2019 ; 23: 12–15.
15. Invasive fungal infections by Aspergillus in Immunocompetent hosts: A case series and literature review.
16. Patel AK, Patel KK, Ranjan R, Shah S, Patel JK. Management of cryptococcal meningitis in HIV-infected patients: Experience from western India. Indian J Sex Transm Dis AIDS. 2010;31(1):22–26.
17. David W.Denning Invasive fungal infection by Aspergillus flavus in immunocompetent hosts: A case series and literature review .Aspergilosis,.Harrisons principles of Internal Medicine chapter 212,1536
18. Tak V, Mathur P, Varghese P, Gunjiyal J, Xess I, Misra MC. The epidemiological profile of candidemia at an Indian trauma care center. J Lab Physicians. 2014;6(2):96–101.