



PROPORTION OF INVASIVE FUNGAL INFECTIONS AMONG PATIENTS OF HAEMATOLOGICAL MALIGNANCIES RECEIVING CHEMOTHERAPY

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ABSTRACT

Background: The epidemiology of invasive fungal infections (IFI) in haematological malignancies patient have changed substantially in recent years and its incidence varies nation wise. Invasive fungal infections term is used to describe a severe systemic infection with yeast, yeast like fungi, moulds and dimorphic fungi. They are leading cause of morbidity & mortality. **Objective:** To find out the proportion of Invasive Fungal Infection among patients receiving chemotherapy for haematological malignancies. **Methodology:** The study was conducted in the Department of Microbiology, MGM Medical College Indore in association with Radiotherapy Department. Hematological malignancies patients receiving chemotherapy. It was a one year study from October 2021 to September 2022. Blood/sputum/urine were received for fungal culture as per the advice of treating physician. **Results:** Out of 218 clinically suspected & diagnosed fungal infections, 09 samples were positive and confirmed for fungal growth by culture. Candida species were the most common. It was isolated in 08 samples followed by *Aspergillus fumigatus* in 01 sample. The rate of Candida infection caused by non albicans Candida species were higher than *Candida albicans*. Acute myeloid leukemia (AML) was observed as most commonly associated haematological malignancy. **Conclusion:** Patients with AML were at higher risk of invasive fungal infections. Yeast-like fungi was the most common pathogen isolated. Non albicans *Candida* were higher than *C. albicans*.

KEYWORDS : Invasive fungal infections, haematological malignancies, candida, non albicans *Candida*, acute myeloid leukemia.

INTRODUCTION

With increase in use of broad spectrum antimicrobial agents in patients with Haematological malignancies; there has been significant reduction in mortality and morbidity among these patients. At the same time with control of bacterial infections among these patients, Invasive fungal infections have now become a threat. It poses even a greater risk among patients who have undergone chemotherapy and now presenting themselves with reduced Neutrophil counts. Several research works have showed the increasing pattern of invasive fungal infections among the individuals suffering from haematological malignancies^[1]. It is one of the interesting fact that almost half of the incidence of invasive fungal infection occurs at the time of starting the remission chemotherapeutic inductive cycle^[2].

There are few risk factors which affect the course of disease progression such as- geriatric age group, use of steroid excessively, a reduced neutrophil count in blood, multiple sites of infection etc^[3]. Theoretically, due to availability of encouraging environment in Tropical and Sub tropical regions for fungal growth; there should be more prevalence of invasive fungal infections, but concrete supportive evidence in lacking, however, genetics of the population belonging to these geographical terrains, use of the chemotherapeutic regimen, other environmental setting also play role in epidemiology of invasive fungal infections^[4]. Among various hematological malignancies fungal infections of invasive nature are mostly due to *Aspergillus* and *Candida*.^[2] other opportunistic moulds for example- *Fusarium*, *Zygomycetes* species are also there. This study is therefore aimed at providing information on prevalence of invasive fungal infection among individuals suffering from hematological malignancy at a tertiary care hospital setting.

METHODOLOGY-

- It was an observational cross-sectional study, which was conducted at a tertiary care hospital, MGM Medical College and M.Y. Hospital, Indore, Madhya Pradesh (India). A total of 218 patients diagnosed with hematological malignancies and receiving chemotherapy were included in the study after taking an informed consent.
- Duration of study was between October 2021 to September 2022.
- Samples : urine/blood/ sputum was collected .
- The data was collected which included unique Id, age, gender, type of malignancy, chemotherapeutic regimen, sample processed and growth shown etc. were included.

Inclusion Criteria

- All patient receiving chemotherapy for less than 6 months for hematological malignancy
- Patients giving consent for the study.

Exclusion Criteria

- Unsatisfactory sample

Microbiological Processing of Samples

Each sample was cultured on two Sabouraud chloramphenicol dextrose agar (SDA) tubes incubated at 37°C and 25°C each (for yeast and moulds isolation) and examined daily for 10 days. Identification of yeasts was performed with colony morphology and Gram stain and further speciation is done by germ tube test, colours on candychrome plates and final diagnosis with dalmau culture. Filamentous fungi were identified on the basis of macroscopic and microscopic morphological features, in accordance with slide culture.

RESULTS-

During the one year period, 218 adult & paediatrics haematological malignancy patient's samples were collected and processed in our Department. Fungal infection were suspected clinically & diagnosed by culture in 09 cases(4.12%). Patients age ranged between 5 and 72 years with mean age 32.66 and SD of 19.24 (Table -1). It was seen that pure fungal growth was observed in 09 patients. *Candida* species was found to be most commonly encountered fungi. It was present in 08 samples followed by *Aspergillus fumigatus* in 01 sample. The rate of *Candida* infection caused by *non albicans Candida* species(55.55%) was higher than *Candida albicans* (33.33). The various NAC species isolated were: *Candida tropicalis*(11.11%),*Candida glabrata*(33.33%),*Candida krusei*(11.11%).(Image-1) The prevalence of infection with non albicans *Candida* species was encountered more than expected which show mean of 26.4 years with SD of 14.48 . AML, Chronic Myeloid Leukamia(CML), B cell Non Hodgkin's Lymphoma(B Cell NHL) & B cell Acute Lymphoid Leukamia(B Cell ALL) were found to be associated with fungal infections in our study , among them AML was observed as most commonly associated(37.15%) haematological malignancy (Table-2).

DISCUSSION-

The prevalence of fungal infections of invasive nature, also labeled as IFI (invasive fungal infections) has significantly associated now a days as compare to earlier, among population living with haematological malignancies [4]. The Invasive fungal infections were very rare nearly half century ago, but now it is among life threatening conditions especially in those patients who's Immunity has been compromised due to some reasons.

The increased numbers of Invasive fungal infection encounters among Hematological malignancies may be due to availability of modern diagnostic procedures. However exact prevalence will always be challenging and underreported, considering difficulty in laboratory identification and related procedures, such as: nonspecific clinical presentation, inappropriate sample collection and transportation, contamination of samples, long duration required for identification of species [5].

Identification of IFI at appropriate time and its management are crucial in these individuals suffering from Onco hematological disorders in order to decrease in mortality and morbidity.

The present study has 218 total patients of various Hematological malignancies with the mean age of 33.42 years and standard deviation (SD) of 18.32 years. All patients were screened for presence of Invasive fungal infections per se. Our study demonstrated that out of 218 patients, 9 patients were suffering from Invasive fungal infections with the mean age of 32.66 and SD of 19.24. This results in its prevalence of 4.12%. In accordance with our study, a single center study, Bitterman et al [6] shows the prevalence of 5% in Hematological malignancy patient. Another article, Pagano et al [2] shows the prevalence of IFI around 4%. However, a study, Yubhisha dabas [7] et al shows the prevalence of IFI 7.6% which is higher than our study. This difference may be there due to very large sample size as compare to present study. Another study, Yuqian Sun et al [8] shows the prevalence of 1.1% which is lower than the present study. This difference may be because of geographic differences, different sample sizes, and different prevalence of Hematological malignancies and varied reporting of cases. The presentation of disease, the symptoms, the signs, and all changes with the time as the pathogen itself makes change within. The changes also happen in the infectivity and virulence of the fungi. Previous data shows that *Candida albicans* was the most common isolate in case of Invasive fungal infection among Hematological malignant

patients. In our study, the prevalence of Non albicans *Candida* species encountered higher than *Candida albicans* species. Interesting fact that is noted in our study is that the prevalence of non albicans species infection was encountered more than expected which show mean of 26.4 years with SD of 14.48. The similar trend in accordance with our study has been depicted by Shariq Ahmed et al [9]. They also showed that the trend is changing toward more and more cases of Non albicans *Candida* infections.

In present study it is found that acute myeloid leukemia (AML) was the Hematological malignancy more frequently associated with invasive fungal infections. Furthermore, high rates of Invasive fungal diseases have been noted in patients of ALL. The similar trend in accordance with our study has been depicted by Nicola Stefano Fracchiolla, Mariarita Sciume [10] they also showed that among Hematological malignancy, AML is the most commonly associated with IF

CONCLUSION-

Patients with AML were at higher risk of invasive fungal infections. Yeast-like fungi was the most common pathogen isolated. Non albicans *Candida* were higher than *C.albicans*. Early diagnosis of fungal infections provides specific treatment & may prove life-saving or at least stave off the complications produced by the infections. Further studies are expected to provide more insight for early detection and management of these invasive infections.

Table -1 Age wise distribution of participants

Sr.No.	Age Group(in years)	n (%)
1	0-10	24(11)
2	11-20	40(18.34)
3	21-30	42(19.26)
4	31-40	40(18.34)
5	41-50	28(12.84)
6	51-60	24(11)
7	61-70	15(6.88)
8	71-80	5(2.29)

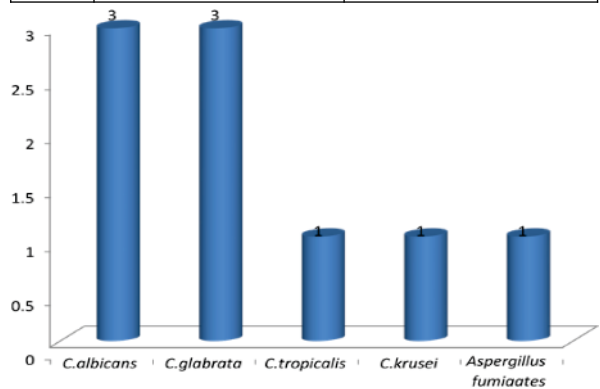


Image -1 Bar diagram showing different fungi isolated

Table -2 Type of malignancy among participants

Sr. No.	Type of malignancy	n (%)
1	Acute myeloid leukemia(AML)	81(37.15)
2	B cell ALL with fibrosis(ALL)	66(30.27)
3	Chronic myeloid leukemia(CML)	54(24.77)
4	Non Hodgkin's lymphoma(NHL)	8(3.66)
5	Anaplastic large cell lymphoma(ALCL)	9(4.12)

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