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Original Article

Microbiology Section

Invasive Fungal Infections in Acute Haematological Malignancies: A Cross-sectional Study

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ABSTRACT

Introduction: Fungal infections are common complications of acute haematological malignancies i.e. acute myeloid and acute lymphoblastic leukaemia. The cells in these two groups are different morphologically and immunologically. Hence, the interaction with the different types of fungi may vary.

Aim: To identify the acute leukaemia cases and fungal infection among myeloid and lymphoid groups and to find out association of types of invasive fungal infection according to cell line affected.

Materials and Methods: A cross-sectional observational hospital-based prospective study was conducted in a risk group of acute haematological malignancy over a period of six months from July 2021 to December 2021 in a tertiary care Hospital, Medical College, Kolkata, West Bengal, India. Study tools were questionnaire based on European Organisation for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) criteria, clinical reports and standard laboratory procedures were practiced in Microbiology laboratory. The data was entered in excel spreadsheet and analysed using Statistical Package for the Social Sciences (SPSS) 28.0 version.

Results: A total of 24 cases of Invasive Fungal Infections (IFI) were observed, out of the 78 patients included in the study. This corresponds to an IFI prevalence of 30.77%. Patients with proven IFI constituted 8 (33.33%), probable IFI accounted for 15 (62.5%) where as those with possible IFI accounted for 1 (4.2%) of total IFI cases. There were age and sex wise variation in IFI. The prevalence of IFI was found to be higher in Acute Myeloid Leukaemia (AML) (48.5%) patients as compared to Acute Lymphoblastic Leukaemia (ALL) (19.14%). Of all AML patients, invasive candidiasis was the most common type followed by aspergillosis. In ALL patients, invasive candidiasis also constituted 44.44% followed by dematiaceous mycosis, followed by aspergillosis.

Conclusion: AML patients suffer more from IFI than ALL ones. Invasive non albicans candidiasis affected both types, but more incidence was seen in AML affected group. *Aspergillus* spp. affected lungs of both groups, but dematiaceous fungi were isolated only from ALL affected paediatric patients and in samples other than pulmonary or blood sample.

Keywords: Acute lymphoblastic leukaemia, Acute myeloid leukaemia, Yeasts and moulds

INTRODUCTION

The IFI are common complications of the acute haematological malignancy i.e. AML and ALL. As a result of IFI the morbidity and mortality of primary disease increases along with expenditure of treatment and hospital stay [1]. The development of immunocompromised state predisposing fungal infection cannot be avoided in different phases of these diseases. So, the use of prophylactic antifungal is necessary to prevent the fungal invasion. For this purpose, knowledge of species of invading fungus is necessary to select right medicine (s). Neutrophils, plays a crucial role in the resistance to Candida infection may become dysfunctional in AML patients, making them susceptible to these opportunistic infections [2]. Cell mediated immunity by lymphocytes is also an important factor for containment of the said infection. On the other hand, the reduction in alveolar macrophages (which prevents germination of conidia to tissue-invasive hyphae) leads to Aspergillosis [3]. Antineoplastic drugs induce a neutropenic and lymphocytopenic state which predisposes patients to opportunistic mycoses [4,5]. Severe neutropenia is termed when the absolute neutrophil count is less than 500 cells/mm^3 [6,7]. Opportunistic fungal infections tend to appear during this stage. Febrile neutropenia which includes severe neutropenia along with oral temperature >38.5°C or two consecutive readings of >38°C for two hours typically marks the onset of fungal infections [6]. Studies have shown that older patients (≥65 years) with haematological malignancy have an increased risk of invasive fungal infections [7,8]. The critically ill patients, being treated with broad spectrum antimicrobials, and those on total parenteral nutrition, sepsis, renal insufficiency, prolonged stay in Intensive Care Unit (ICU), current stage of the malignancy (for patients not in remission) are more prone to contract such infections [3,9]. Prolonged ICU stay makes the patient more susceptible to such infections [9-11].

Increasing use of antifungal prophylaxis has led to a significant change in the mycological profile of infections [11]. The data on IFI among paediatric population with ALL are still scarce in comparison to AML as has been reported [12]. Inadequacy of diagnostic procedures in patients with unstable clinical situations or with a bleeding tendency (due to thrombocytopenia resulting from induction chemotherapy) delays treatment, and therefore might interfere with the patient's survival. The aim of present study was, to identify the acute leukaemia cases among admitted patients in hospital ward from clinical and laboratory record. To identify phenotypically the fungus causing IFI in such cases. To determine the association between a particular type of fungus and affected cell line.

MATERIALS AND METHODS

A cross-sectional observational hospital-based prospective study was done for six months (July 2021 to December 2021) in haematology indoor wards and Microbiology Departments of Medical College, Kolkata. The permission required to conduct the study was given by the Institutional Ethics Committee. (IEC) with letter number- Ref No: MC/KOLIECNON-SPON/809/09/20. Study included the patients suffering from acute haematological malignancies and admitted in hospital.

Inclusion criteria

- Consecutive non repetitive febrile patients of ALL and AML admitted in hospital were included in the study.

- Willingness to participate in the study after giving informed written consent was considered in the study.

Exclusion criteria

- Chronic cases of lymphoid and myeloid leukaemia.
- Cases of acute promyelocytic leukaemia.
- Cases of haematogical diseases other than malignancy.
- Unwillingness to participate in the study.

Sample size calculation: A total of 78 patients were studied as proposed.

Sample size $n_0=z^2pq/e^2$ (p is the prevalence and q is 1-p.) The prevalence of fungal infections is taken to be 11% (rounded-off) [12]. The value for Z was found in statistical table, which contains area under the normal curve. Here Z=1.96 for 95% confidence. The margin of error here is taken to be 5%.

Putting the values p=0.11, q= 0.89

Sample size=150 (for unlimited population).

However, sample size of 150 in case of period prevalence of 12 months, 75 comes for six months (from modified Cochran's formula for smaller population).

Study tools:

- Questionnaire form prepared beforehand (Based on EORTC/MSG criteria of IFI) [13] [Annexure:1].
- Laboratory diagnostic tools for clinical and mycological assessment.

Study Procedure

Questionnaire proforma was prepared by authors, the research workers [Annexure:1]. After getting written consent, subjects were first interrogated using questionnaire prepared beforehand for selecting the cases of AML and ALL and obtaining information about fungal infection. No cell line was used for research work in the laboratory. The target population was identified from records of involved myeloid or lymphoid cell line and questionnaire helped in categorising patients to proven, probable and possible IFI (or no IFI cases) [Table/Fig-1] [13]. Empirical antifungal was given in cases of febrile neutropenia for more than four days not responding to broad spectrum antibiotics. Prophylactic antifungals used in our setting was posaconazole and it was given only in selected patients (33 patients).

Clinical assessment

- The baseline data of each patient like the age, gender, the type of acute leukaemia, chemotherapeutic stage of the patient, complete blood count and drugs received by the patient were collected.
- A febrile episode is defined as oral temperature >38.5°C or two consecutive readings of >38°C for two hours. Fever was considered due to chemotherapy, if it occurred within 12 hours of starting chemotherapy and resolved spontaneously in the next 24-hour period [6].
- The febrile episode was investigated for any possible source of fungal infection by taking the sample, from the clinically suspected site of infection.
- Neutropenia is defined as an absolute neutrophil count less than 500 cells/mm^3 [6,7].
- The High Resolution Computed Tomography (HRCT) of chest was done for the radiological evidence of invasive fungal infection.

Sample types

- Blood sample: Biphasic blood culture medium by using Sabouraud Dextrose Agar (SDA) slant and trypticase soy broth was used.
- Sputum sample: It was induced by using nebulised sterile hypertonic saline solution.
- Urine sample: Few paediatric patients were examined.
- Bone marrow: One bone marrow sample was examined.
- Nasal mass: Evacuated mass from maxillary sinus was examined.

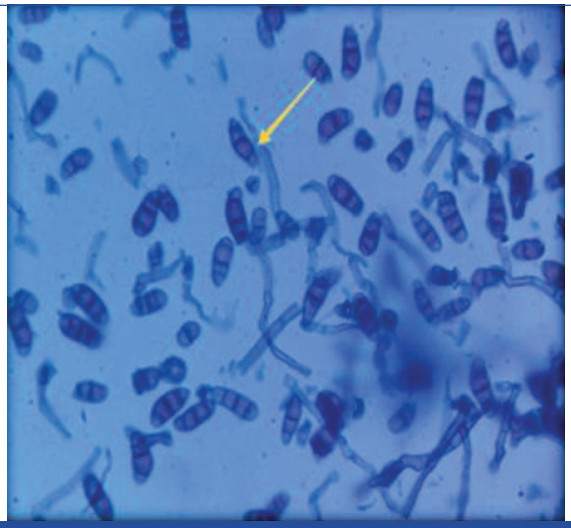
Potassium Hydroxide (KOH) mount: The samples were examined for fungal element under light microscope preparing 10% or 20% KOH mount [Table/Fig-2].

Fungal culture: Samples were inoculated in SDA/Sabouraud Dextrose Chloramphenicol Agar in two sets to incubate one at 37°C and another at 25°C. For the yeasts isolates, speciation was done by VITEK 2 YST ID card. For the moulds, Lacto Phenol Cotton Blue (LPCB) tease mount was examined for morphological study [Table/Fig-3].

Definitions of invasive fungal diseases [13]		
Proven invasive fungal disease	Microscopic analysis of normally sterile material	By histopathological, cytopathological or direct microscopic means demonstrating fungal infection and in case of mold accompanied by evidence of tissue damage.
	Culture of normally sterile material	Including blood culture demonstrating fungal growth.
	Serological analysis of Cerebrospinal Fluid (CSF)	Positive for cryptococcal antigen.
Probable invasive fungal disease	Host factors	Neutropenia >10 days associated temporarily with invasive fungal disease.
		Recipient of an allogenic stem cell transplant.
		Steroids (0.3 mg/kg/day for >3 weeks.
		Treatment with T-cell immunosuppressant.
		Inherited severe immunodeficiencies.
	Clinical criteria	Lower respiratory tract diseases- air crescent, cavity, lesion and/or halo on Computed Tomography (CT).
		Tracheobronchitis-ulcer, nodule, plaque, pseudomembrane or eschar on bronchoscopy.
		Sinonasal disease-acute localising pain radiating to eye, nasal ulcer with black eschar or extension of lesion across bony barriers.
		Disseminated candidiasis- small target-like abscess in liver or spleen or progressive retinal exudates.
		Central Nervous System (CNS) disease-focal lesion or meningeal enhancement.
	Mycological criteria	Direct test (cytology, direct microscopy, culture).
		Indirect test (Biomarkers)-galactomannan in plasma, serum and bronchoalveolar lavage, CSF or β-D Glucan (fungal infection other than zygomycosis or cryptococcosis) in serum.
Possible invasive fungal disease	Cases that meet the criteria for a host factor and a clinical criterion, but for which mycological criterion is absent.	

[Table/Fig-1]: European organisation for research and treatment of cancer/mycoses study group [13].

[Table/Fig-2]: KOH mount of sputum sample with 10% KOH showing pseudohyphae with budding yeast cells.



[Table/Fig-3]: Lactophenol cotton blue mount from colony of *Curvularia lunata* showing the three septed conidia.

STATISTICAL ANALYSIS

The data were entered in excel spreadsheet and analysed using SPSS 28.0 version. The p-values were calculated with Chi-square test, wherever applicable.

RESULTS

After careful analysis of the data, 24 cases of IFI were observed, out of the 78 patients, included in the study. This corresponds to an IFI prevalence of 30.77%. Patients with probable IFI accounted for 15 (62.5%) whereas, those with proven IFI constituted 8 (33.3%) and those with possible IFI 1 (4.2%) of IFI affected population. It was seen that highest number of proven IFI was seen in 4 (16.67%) of the patients belonging to age group 12-21 years and highest probable IFI in 4 (16.67%) of the patients of age group 22-31 years [Table/Fig-4].

Age group (years)	Proven IFI	Probable IFI	Possible IFI	Total no. of patients N=24
2-11	2 (8.33%)	1 (4.16%)	0	3 (12.5%)
12-21	4 (16.67%)	2 (8.33%)	0	6 (25%)
22-31	2 (8.33%)	4 (16.66%)	0	6 (25%)
32-41	0	3 (12.50%)	0	3 (12.5%)
42-51	0	3 (12.50%)	0	3 (12.5%)
52-61	0	2 (8.33%)	1 (4.2%)	3 (12.5%)
Total	8 (33.3%)	15 (62.5%)	1 (4.2%)	24 (100%)

[Table/Fig-4]: Distribution of population according to age and presence of invasive fungal infections (N=24).
Chi-square value=15.6; p-value=0.11

Out of the 78 study subjects, 49 (62.82%) were males and 29 (37.18%) were females. Among the 24 IFI cases, proven IFI was seen in 8.33% females and 25% males. Probable IFI was present in 25% females and 37.5% males. No possible IFI was present in female while 4.2% males had possible IFI [Table/Fig-5].

Gender	Invasive fungal infections			Total no. of patients (N)
	Proven IFI	Probable IFI	Possible IFI	
Female	2 (8.33%)	6 (25%)	0	8 (33.3%)
Male	6 (25%)	9 (37.5%)	1 (4.2%)	16 (66.7%)

[Table/Fig-5]: Distribution of population according to gender and prevalence of invasive fungal infections (N=24).
Chi-square value=1.05; p-value=0.59

Two different types of acute haematological malignancies were considered in the recruited group. Out of the 78 patients, 47 had ALL, 31 had AML. The prevalence of IFI was found to be higher in (15 out of 31) AML patients (48.4%) as compared to the 9 out of 47 ALL patients (19.47%) (p-value=0.006) [Table/Fig-6a]. Among AML patients 4 (16.66%) had proven IFI, 10 (41.66%) had probable IFI and 1 (4.16%) had possible IFI. In ALL patients 4 (16.66%) had proven IFI and 5 (20.83%) had probable IFI and no cases of possible IFI [Table/Fig-6b] (p-value 0.87).

Type of malignancy	With IFI	Without IFI	Total
ALL	9	38	47
AML	15	16	31
Total	24 (30.77%)	54 (69.23%)	78 (100%)

[Table/Fig-6a]: Invasive fungal infection among different types of acute haematogical malignancies.
Chi-square value=7.49, p-value=0.006

Type of malignancy	Proven IFI	Probable IFI	Possible IFI	Total number of IFI (N=24)
ALL	4 (16.66%)	5 (20.83%)	0	9 (37.5%)
AML	4 (16.66%)	10 (41.66%)	1 (4.16%)	15 (62.5%)
Total	8 (10.5%)	15 (62.5%)	1 (4.16%)	24 (99.99%)

[Table/Fig-6b]: Distribution of IFI cases in EORTC/MSG groups.
Chi-square value=1.244; p-value=0.87

Majority 49 (36.73%) of the patients who had undergone induction therapy developed IFI. Induction chemotherapy was found out to be a significant risk factor for the development of IFI (0.01). Neutropenia was a risk factor for IFI (p=0.04) and considering the duration of neutropenic state incidence of IFI was found in 11.76% patients having neutropenia for <10 days, 23.07% patients with 10-21 days of neutropenia and 59.09% patients with >21 days of neutropenia [Table/Fig-7].

Variables	Total no. of patients (n)	No. of patients with IFI (%)
Type of chemotherapy	78	24 (23.07)
Induction/Reinduction	49	18 (36.73)
Consolidation	22	6 (27.3)
Maintenance	27	0
Total neutrophil count*	**78**	**24 (23.07)**
≥500/mm^3	37	5 (13.5)
<500/mm^3 (neutropenia)	41	19 (46.3)
Duration of neutropenia (in days)	**78**	**24 (23.07)**
≤10	17	2 (11.76)
>10-<21	39	9 (23.07)
>21	22	13 (59.09)

[Table/Fig-7]: Distribution of patients according to phase of treatment, level and duration of neutropenia.
Chi-square value=1.24; p-value=0.80

24 samples showed fungal growth after culture. Of 15 AML patients, 10 invasive Candidiasis (66.7%) was the most common type followed by Aspergillosis 5 out of 15 (33.33%). In ALL patients, invasive candidiasis constituted 4 out of 9 (44.44%) followed by dematiaceous mycosis, 3 out of 9 (33.33%) followed by Aspergillosis 2 out of 9 (22.22%). As a whole, Candidiasis were identified in 14 (58.33%), Aspergillosis in 7 (29.17%) and dematiaceous mycosis in 3 (12.5%) patients. Candidiasis and Aspergillosis cases were identified in majority of AML cases whereas dematiaceous fungi were seen mainly in ALL cases [Table/Fig-8].

Mycological characteristics	Type of haematological malignancy		Grand total
	ALL	AML	
Candida species	**4 (28.6%)**	**10 (71.4%)**	**14 (100%)**
Candida kruzei	1 (20%)	4 (80%)	5 (100%)
Candida tropicalis	2 (40%)	3 (60%)	5 (100%)
Candida glabrata	1 (33.3%	2 (66.7%)	3 (100%)
Cndida lucitanae	0	1 (100%)	1 (100%)
Aspergillus species	**2 (28.6%)**	**5 (71.4%)**	**7 (100%)**
Aspergillus fumigatus	1 (33.3%)	2 (66.7%)	3 (100%)
Aspergillus tereus	0	1 (100%)	1 (100%)
Aspergillus flavus	1 (33.3%)	2 (66.7%)	3 (100%)
Dematiaceous fungi	**3 (100%)**	**0**	**3 (100%)**
Alternaria spp.	1 (100%)	0	1 (100%)
Curvularia spp.	2 (100%)	0	2 (100%)
Grand total	**9 (37.5%)**	**15 (62.5%)**	**24 (100%)**

[Table/Fig-8]: Distribution of fungal pathogens in two cell lines of acute haematological malignancies (N=24).
p-value not calculated

Lung was the commonest site of true fungi involvement accounting for 10 (41.67%) of the IFIs. Invasive aspergillosis and non albicans candidiasis caused pulmonary infections. The other site of involvement was bloodstream, constituting 11 (45.83%) of the IFIs. All bloodstream infections were due to non *albicans Candida* species. One (4.16%) *Alternaria* spp was isolated from bone marrow and maxillary sinus tissue sample of one patient and *Curvularia* spp. was isolated from urine of 2 (8.33%) ALL affected paediatric patients [Table/Fig-9]. The prevalence of IFI in patients with antifungal prophylaxis was lower (9.09%) than those who did not receive any antifungal prophylaxis (46.66%). However, this difference (p-value=0.004) was statistically significant [Table/Fig-10].

Site of lesion	Number (n=24)	Percentage %
Lungs	10	41.66
Blood stream	11	45.83
Maxillary sinus and bone marrow	1	4.16
Urine	2	8.33
Total	24	99.99

[Table/Fig-9]: Distribution of study population as per site of involvement.
p-value not calculated

Antifungals prophylaxis received	No. of patients	IFI cases	Percentage
Yes	33	3	9.09%
No	45	21	46.66%

[Table/Fig-10]: Distribution of study population according to antifungal prophylaxis and development of invasive fungal infections (n=78).
z score=4. p-value=0.004

DISCUSSION

In the above study, the prevalence of IFI among patients with acute haematological malignancies was found to be 30.77%. This result was in agreement with previous studies showing an increased prevalence of IFI in patients with acute leukaemia affecting 11-30% in such population [1,8,14]. Immunosuppression is seen in patients with acute leukaemia either due to disease itself or due to treatment and thus, risk of IFIs develops. The humid and warm conditions in West Bengal substantially explains this finding as similar studies yielded identical result [12-15]. Wasylyshyn A et al., [15] showed a prevalence of IFI as 28% with proven IFI 13%, probable IFI 21% and possible IFI 66%. The prevalence of IFI was found to be higher (16.66%) among the age groups 12-41 years as compared to those at extremes of ages in present study. This was in similar with another study which have stated that the risk of IFI was higher in those <40 years. In the study by Lien MY et al., mentioned the median age of patients was 51 (range 19-76) [16]. Other studies state that patients >65 years of age were at increased risk [7,8,12,14,17,18]. However, present study sample population did not include a significant proportion of representative from that age group. So, it could not be commented. In present study, the prevalence of IFI was higher in men as compared to women although the difference was not statistically significant (p-value=0.59). In the study by Neofytos D et al., females were found to be at significant risk for developing IFIs p-value <0.006 [19]. This finding was unlike from the study by Hammond SP et al., getting 17.4% prevalence in male and 8.75% in females [14]. Zhang R et al., and Lien MY et al., also found males to be at significant risk for developing IFI [12,16].

The prevalence of fungal infections was found to be higher in AML (15 out of 24;62.5%) as compared to ALL (9 out of 24;37.5%) which was similar to the study by Bhatt VR et al., getting AML in 12% and ALL in 6.5% and Zhang R et al., getting AML in 11.8% and ALL in 7.1% patients [1,12]. AML has long been thought to have a higher risk of IFI than that in ALL. The recent addition of antifungal prophylaxis to induction chemotherapy has shown to significantly reduce the prevalence of IFI in AML [17]. Present study confirms the same but the prevalence of IFI was not found to be significantly lower in ALL patients in this era of antifungal prophylaxis. Neutropenia for a prolonged period (>10 days) was found to be significantly associated with invasive fungal infections [13,20-25]. Among 24 patients with IFI, 13 (59.09%) had a duration of neutropenia >21 days whereas 9 (23.07%) patients with IFI had a duration of neutropenia >10 to <21 days and 2 (11.76%) had neutropenia <10 days. Thus, a greater proportion of patients with IFI had a prolonged duration of neutropenia.

In present study, majority of the IFIs were caused by non *albicans Candida* species as compared to true fungi. A Taiwanese study by Lin GL et al., had also found invasive candidiasis (*Candida* species 59.1%) as predominant form of IFI. The increased prevalence of non *albicans Candida* species as found in present study was similar to other studies by [1,4,5,9,10,13,20], respectively. Among these, *Candida krusei* infection was predominant in AML whereas *Candida tropicalis* invasion was seen more commonly in ALL in present study. *C. glabrata* and *C. lucitanae* infection had lower incidence rate in both AML and ALL. Neither in AML nor in ALL *C. albicans* was detected as agent of IFI. Hansen BA et al., mentioned of *C. krusei* and *C. glabrata* infection contributing 80% of candidiasis [20]. Among the hyaline hyphae, *Aspergillus fumigatus*, *A. flavus* and *A. terreus* were in the list of pathogen causing pulmonary aspergillosis. In the AML patients number of cases of Aspergillosis was more than that in ALL. These fungi were isolated from induced sputum or bronchoalveolar lavage fluid. The studies have mentioned that fungus isolated from these two types of samples are to be considered as coloniser, but authors considered these as pathogen as there were radiological signs of fungal invasion in lungs. The studies by Kauffman CA and Neofytos D et al., had also found such a mycological profile in those with acute leukaemia [11,19]. *Aspergillus fumigatus* caused 60% (n=3) of the IFIs. This was similar to other studies [3,6,9,10,13,16,25] where Aspergillosis varied from 10% [10] to 81.9% [16]. The unusual finding of present

study work was the isolation of *Alternaria* and *Curvularia* species from three cases of ALL. The *Alternaria* species was isolated from bone marrow aspirate and nasal mass evacuated from maxillary sinus of a 16-year-old girl. *Curvularia lunata* was isolated from urine of two boys of less than 8 years and suffering from ALL. The other studies have mentioned dematiaceous fungi causing rhionosinusitis in patients with acute haematological malignancy [18,23]. *Alternaria* spp. was isolated from maxillary sinus as well as bone marrow aspirate of a female patient. The *Curvularia lunata* was isolated from urine of a 6-year-old boy on two consecutive occasions and from another boy of 8 years on one occasion. There was no history of rhinosinusitis in these two cases.

The blood stream was the predominant site (45.83%) of IFI followed by lung (41.66%) among the patients with leukaemia. Bhatt VR et al., reported that lung was the commonest site accounting for around 75% of IFI [1]. Similar reports have been made by Hansen BA et al., [20] and Tang JL et al., [26]. From a 16-year-old girl of ALL, *Alteraria* spp. was isolated from the bone marrow aspirate first and then from right maxilla which might be the primary site from where systemic dissemination occurred. Lastly, present study isolated *Curvularia lunata* from urine samples of two boys suffering from ALL. No study mentioned of urine samples from where dematiaceous fungi could be isolated, but present study found same fungus on two successive samples collected on different day.

In the present study, it was found that, the prevalence of IFI was lower (9.09%) in those who had received antifungal prophylaxis than those who had not (46.6%). This difference was statistically significant (p=0.004) like the study by Zhang R et al., [12]. Randomised controlled trials with prophylactic antifungals need more research work to establish the efficacy in preventing morbidity due to IFIs.

Limitation(s)

One limitation was that the study did not use any novel bio-markers and invasive procedures for the diagnosis, which could have underestimated the prevalence of IFIs. Further prospective studies are, therefore, required to increase the external validity of present study results. A larger randomised control trial is needed to justify the efficacy of posaconazole which was the prophylactic antifungal used in present study setting. Present study did not perform the antifungal susceptibility of culture positive specimens as that facility was not available at our hospital setting which might have given a better picture of the drug resistant species in this era of antifungal prophylaxis.

CONCLUSION(S)

It is evident from the present study that AML patients suffered more from IFI than ALL ones. Invasive non albicans candidiasis complicated both types but more cases were seen in AML affected group. *Aspergillus* spp. affected lungs of both groups and dematiaceous fungi were isolated mainly from ALL affected paediatric patients. Preponderance of either yeast or mold to a particular cell line like myeloid or lymphoid was not established in present study, except dematiaceous fungus. In cases of haematological malignancies, the antifungal agents are prescribed empirically to prevent fungal infection. The susceptibility of hyphal form to antifungal agents is different from that of yeasts. So, present study result will help in selecting right group of antifungal agent.

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[ANNEXURE-1]

QUESTIONNAIRE- A study on clinicomycological profile in acute haematological malignancies in a tertiary care hospital in kolkata target respondents:

To be completed by the patient and the attending physician. REQUIREMENTS: If you give consent to participate in the study, you will be asked relevant questions to establish the EORTC/MSG criteria (2008) for proven/probable/possible invasive fungal infection (IFI) and to assess the risk factors.

PURPOSE: The information gathered through this questionnaire will be used as a part of the research into the clinicomycological profile in acute haematological malignancies in MEDICAL COLLEGE, KOLKATA. The research will offer the opportunity to participate in medical research and contribute to the advancement of medical sciences.

POTENTIAL RISKS: Practically there will be no risk for the participants.

CONFIDENTIALITY: Please note that the responses you provide are completely anonymous and confidential. The research outcome and report will not include reference to any individual. The compiler of this questionnaire has sole ownership of completed questionnaire and the questionnaire will be destroyed after the completion of research.

OTHER INFORMATION: Please note that you are free to withdraw yourself from the study at any time you choose without providing us the necessary reason. This will not hamper your future treatment procedure.

SECTION A

(Patient particulars)

1. Patient serial no.- .....
2. Age- .....
3. Gender- .....
4. Residence- .....
5. Occupation- .....
6. Any habit- .....

Section B (To be filled by the patient)

1. Presenting complaints: .....
2. Duration of suffering: .....
3. Presenting complaints suggestive of fungal infections:
    a. Any patches in the oral cavity?: .....
    b. Any alteration in taste sensation? .....
    c. Any difficulty in swallowing? .....
    d. Any nasal ulcer? .....
    e. Any chest pain/difficulty in breathing? .....
    f. Whether there is any complaints of coughing? .....
    g. Any other significant lesion? .....
    h. Was he suffering from fever during admission? .....
    i. If so, for how many days? .....
    j. Whether any medications was taken for it? .....
    k. Did the fever subside? .....

Section C (to be filled by the attending physician)

1. Total leukocyte count: .....
2. Differential count of leucocyte: .....
    a. Is neutropenia present? .....
    b. If so, for how long? .....
3. RBC count: .....
4. Hb%: .....

5. Platelet count: ……
6. Blood sugar report: ……
7. CT scan of chest: ……
8. CT scan of brain: ……..
9. Pulmonary function test: ……
10. Bronchoscopy result: ……..
11. Kidney function test: ……
12. Liver function test: ……..
13. Mycological culture report: ……..
14. Any other significant laboratory finding: ……

Section D (To be filled by the attending physician)

1. Drugs prescribed for chemotherapy: ……
2. Duration of chemotherapy: ……..
3. Whether steroids are prescribed or not: ……
4. Whether any prophylactic antifungals are prescribed or not: ……
5. If so, what? .....
6. Whether there is any history of organ dysfunction? .....
7. Usage of central venous catheter? .....……
8. Whether on total parenteral nutrition? ……
9. Whether suffering from any other significant co-morbidities? .....