# INVASIVE MOLD INFECTIONS IN PEDIATRIC HEMATOLOGICAL MALIGNANCIES

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## INTRODUCTION

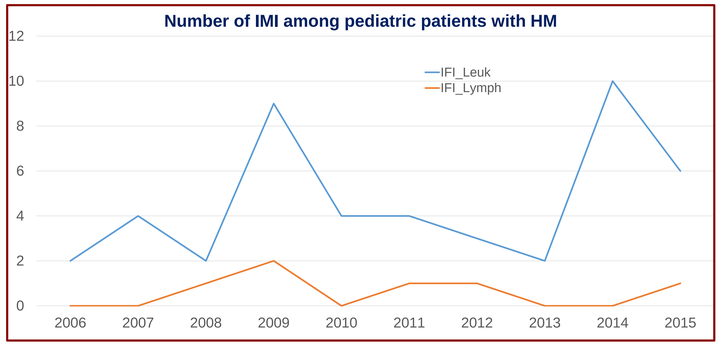
- Invasive Mold infections (IMI) are the leading cause mortality in children with hematological malignancies (HM).
- Most studies of IMI are focused on adults and few have addressed IMI specifically in immunocompromised children.
- Our study aimed to understand the epidemiology, risk factors and outcome of IMI in pediatrics patients with HM, in order to understand the spectrum of IMI and their outcomes in an era where newer antifungals and biomarkers are being used in children.

## METHODS

- We performed a retrospective chart review to evaluate epidemiology and outcomes of IMI in pediatric patients with HM from 2006-2015.
- We included patients only with a diagnosis of leukemia or lymphoma. We excluded patients with HSCT.
- We used the criteria by the EORTC/MSG Consensus Group to define IMI and only included those with proven and probable infections.

## RESULTS

- Fifty three patients were found to have either proven or probable IMI
- The cumulative incidence of IMI in patients with leukemia was 5.2%, with the majority occurring in patients with AML
- The cumulative incidence of IMI in patients with lymphoma was 2.7%.
- The incidence in patients with a new diagnosis of leukemia (not relapsed) was 4.4% compared to1.8% in lymphoma
- Nine of 47 (19%) patients with leukemia who had IMI were relapsed or refractory.




## RESULTS

### Baseline Characteristics of Pediatric HM Patients with IMI

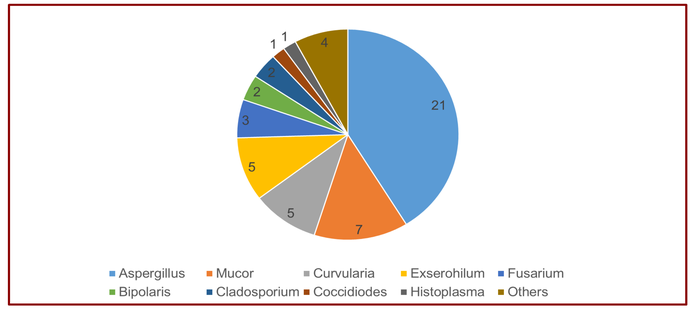
| | |
|---|---|
| Age at cancer diagnosis (years), median (range) | 8.4 (0-21) |
| Time of IMI diagnosis after cancer diagnosis (days), median (range) | 101 (10-3077) |
| HM diagnosis | N (%) |
| ALL | 38 (71.7%) |
| AML | 9 (17.0%) |
| Lymphoma | 6 (11.3%) |
| Relapsed/Refractory at time of fungal infection | 13 (24.5%) |
| Gender | |
| Male | 31 (58.5%) |
| Female | 22 (41.5%) |
| Race/Ethnicity | |
| Hispanic | 33 (62.3%) |
| Non-Hispanic White | 13 (24.5%) |
| Non-Hispanic Black | 3 (5.7%) |
| Asian | 4 (7.5%) |
| Type of fungal infection | |
| Proven combined yeast and mold | 7 (13.2%) |
| Proven 1 Mold | 34 (64.2%) |
| Proven >1 Mold | 6 (11.3%) |
| Probable | 6 (11.3%) |
| Skin lesions | 10 (18.9%) |
| Fever | 43 (81.1%) |
| Preceding hyperglycemia | 17 (32.1%) |
| Preceding neutropenia | 43 (81.1%) |
| Steroid use | 27 (50.9%) |
| Immunosuppressant use | 51 (96.2%) |
| Concurrent infection | 27 (51.9%) |
| Prior antifungal prophylaxis | 14 (26.9%) |

### Clinical Course in Patients with IMI

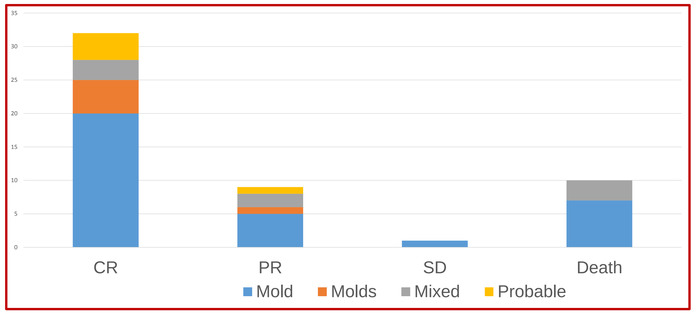
| | |
|---|---|
| Patient acuity | |
| In critical care unit prior to diagnosis | 9 (17.0%) |
| Required transfer to critical care unit | 18 (34.0%) |
| Did not require critical care | 26 (49.0%) |
| Antifungal therapy | |
| Single agent | 15 (28.3%) |
| 2 agents | 29 (54.7%) |
| >2 agents | 9 (17.0%) |
| Duration of antifungal therapy | |
| <= 6 weeks | 13 (24.5%) |
| > 6 weeks | 40 (75.5%) |
| Organs affected | |
| Lungs | 34 (64.2%) |
| Sinuses | 22 (41.5%) |
| Disseminated (≥2 organs) | 18 (34.0%) |

## RESULTS

### Distribution of fungal organisms




### Clinical Response and Outcome of IMI at 3 months




- There was no difference in risk factors or outcome when IMI from *Aspergillus* was compared to IMI from non-*Aspergillus* species.
- Non-relapsed patients were more likely to have a complete response (CR) or partial response (PR) at the end of 12 weeks compared to relapsed patients (88% vs. 55%, p=0.03).

## DISCUSSION

- Hispanic patients were over-represented in our pediatric HM population with IMI (40% Hispanic in new leukemia/lymphoma) which raises the question of the role of ethnicity in IMI
- Patients in relapse were more likely to have a poor outcome with IMI than those who were not-relapsed possibly because of more aggressive and prolonged immunosuppression. Hence the role of routine antifungal prophylaxis with a mold-active agent especially in this population needs to be addressed.

## CONCLUSIONS

- To our knowledge, this is the largest single center study of IMI in children in the United States.
- The routine use of anti-mold agents in patients with relapsed leukemia and the role of ethnicity in the development of IMI need to be further investigated.