

Background. Histoplasmosis is considered uncommon in India, and the diagnosis usually depends on invasive tissue sampling. The histoplasma urinary antigen assay is a non-invasive test that has been recently introduced in India.

Methods. This was a single-centre retrospective study done from January 2013 till February 2018. Case records of patients with proven (confirmed by demonstrating intra-cellular yeast like organisms on histopathology or culture) and probable (presence of antigenuria—done by IMMY Alpha Histoplasma enzyme immunoassay) histoplasmosis were analysed.

Results. A total of 37 patients (18 proven and 19 probable) with mean age of 51.59 ± 11.17 years were studied. Diabetes was the most common co-morbidity (15 patients) followed by HIV (6), whereas no co-morbidity was found in 10 patients. Adrenals (29%), lungs (27%), lymph nodes (27%), and skin and oral mucosa (24.3%) were the most common organs involved (Figure 1). Anti-tubercular therapy based on granulomatous inflammation was given to 10 patients prior to the diagnosis. Raised GGTP and ALP (54%) and hyperglobulinemia (40%) were the common laboratory features. Most patients (83.7%) came from endemic areas (North-Eastern states, West Bengal, and Bangladesh) whereas all six cases from non-endemic areas were classified as probable (Figure 2). All-cause mortality rate was 10.8%, with 27 cases (72.9%) showing improvement at a median follow-up of 6 months. Comparison of proven and probable cases revealed that the following features were significantly higher in the probable group: female sex ($P = 0.001$), coming from nonendemic areas ($P = 0.009$), requiring in-patient care ($P = 0.001$), leucocytosis ($P = 0.043$), absence of skin and oral mucosal findings ($P = 0.002$), simultaneous alternate diagnosis ($P = 0.039$), and death ($P = 0.039$).

Conclusion. This study emphasises that histoplasmosis is an under recognised entity in India. Histoplasma antigenuria does help in making the diagnosis easily and needs to be more extensively utilized by clinicians. However, it can yield false-positive results in patients belonging to nonendemic areas and lacking typical clinical features of histoplasmosis. Further studies are needed to determine the utility of the antigen test in Indian settings.

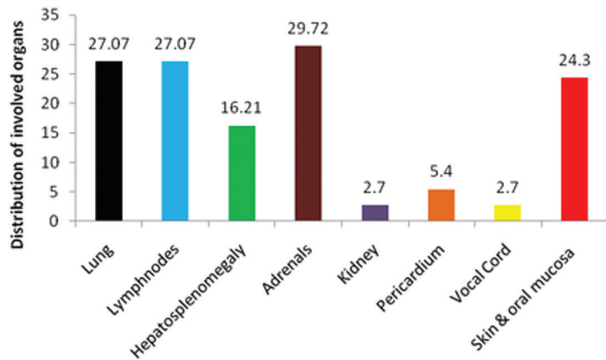


Figure 1. Distribution of involved organs.

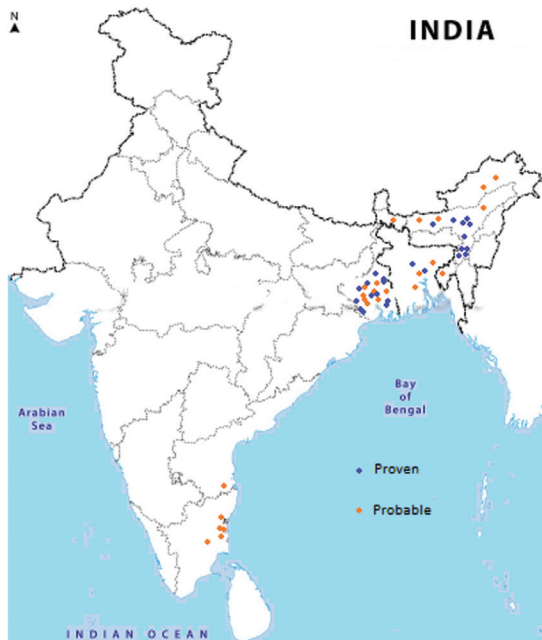


Figure 2. Distribution of cases in the study across Indian states.

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397. Long-Term Mortality of HIV Patients Following Cryptococcal Infection

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Background. Prevalence of cryptococcosis in HIV-positive patients in the developed world has decreased considerably in the modern antiretroviral (ART) era. While early mortality of cryptococcal infection is lower than in non-HIV-infected patients, late mortality in HIV+ patients has not been previously evaluated. Here, we describe the presentation and outcomes of HIV+ patients with cryptococcosis.

Methods. We conducted a retrospective cohort study of patients with HIV infection and cryptococcosis from January 2002 to June 2017 at our institution. Data included demographics, clinical features, diagnostics, and outcomes. Death date was obtained from the hospital system's Medical Informatics database and the Social Security Death Index.

Results. We reviewed 105 HIV+ patients with cryptococcosis. At time of analysis: 55 were living (52.4%), 17 died within 90 days of cryptococcal diagnosis (early mortality, 16.2%), and 33 died after 90 days (late mortality, 31.4%) (Figure 1). Late mortality patients were more likely to have known HIV+ status at the time of cryptococcal diagnosis (97% than living (70.9%) or early mortality (70.6%) ($P = 0.03$); less likely to be ART adherent (15.2% than living (43.6%) or early mortality (35.3%) ($P = 0.02$); less likely to have private insurance (6.1% than living (34.5%) or early mortality (17.6%) ($P = 0.007$); and more likely to have Medicaid (51.5% than living (29.1%) or early mortality (17.6%) ($P = 0.03$). Presenting symptoms and diagnostics were similar between groups. Prevalence of substance abuse (48.6%) and psychiatric history (31.4%) were high in all groups but not significantly different.

Conclusion. Despite improvements in ART, HIV+ patients have high mortality following cryptococcal infection which persists beyond their initial hospitalization. Identifying patients at higher risk for mortality is critical for successful treatment and outcomes. In our study, nonadherence to ART was associated with a higher risk of dying. Follow-up studies of late mortality in other opportunistic infections would be beneficial.

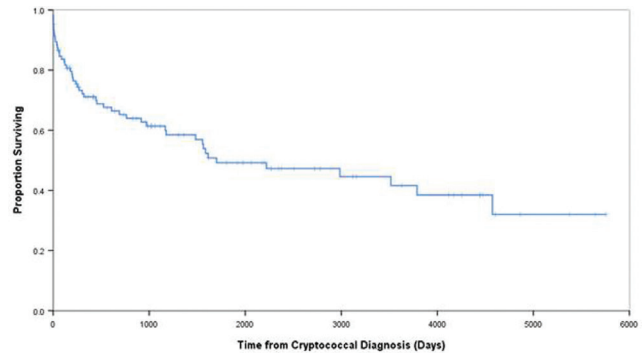


Figure 1. Kaplan-Meier curve of 105 patients with HIV and cryptococcosis. Overall mortality of 47.6% at 5,000 days with 17 patients dying in first 90 days (16.2%) and 33 patients dying after 90 days (31.4%).

Disclosures. All authors: No reported disclosures.

398. Review of Mucormycosis Cases at the University of Colorado Hospital From 2012 to 2018 and Evaluation of Risk Factors and Appropriateness of Antifungal Prophylaxis

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Background. Healthcare associated outbreaks of mucormycosis have been described in the literature. In 2017, the University of Colorado Hospital (UCH) had an increased number of cases of mucormycosis. The objective of this study was to evaluate possible risk factors and weather patterns associated with cases of mucormycosis diagnosed at UCH from 2012 to 2018 in order determine whether the current antifungal prophylaxis used at UCH should be modified.

Methods. A retrospective cohort was conducted involving patients >18 years old who were admitted to UCH between 2012 and 2018 and were diagnosed with proven or probable mucormycosis as defined by the European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG) criteria. Medical records were reviewed, and data were collected on risk factors, antifungal prophylaxis, and mortality outcome. Weather data were collected from the National Centers for Environmental Information (NCEI).

Results. Twenty-five cases of proven or probable mucormycosis were identified. On average patients had at least two risk factors associated with mucormycosis. The most common risk factors included diabetes mellitus (DM) (13 patients), hematologic

malignancy or hematopoietic stem cell transplant (HSCT) (11 patients), use of immunosuppressing medications (11 patients), and invasive procedures. (9 patients). At the time of diagnosis, only six patients were on an antifungal with mold activity. Eight patients died during hospitalization. The distribution of cases over time was compared with weather data for Colorado. A cluster of cases occurred in 2013 (6 cases) and in 2017 (8 cases). A majority of cases were diagnosed during the summer and fall months with July being the month with the most number of cases. There were higher levels of precipitation that occurred prior to or during the cluster of cases.

Conclusion. Cases of mucormycosis at UCH were associated with DM, hematologic malignancy/HSCT, use of immunosuppressive therapy, and invasive procedures. The increase of cases seen 2013 and 2017 occurred in the summer and fall months after higher levels of precipitation were observed in Colorado. Providers at UCH may consider modifying antifungal prophylaxis to include mold coverage in patients with >2 risk factors for mucormycosis who are admitted during the summer and fall.

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399. Multi-centre Observational Study on Epidemiology, Treatment, and Outcome of Mucormycosis in India

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Background. Though the rise in number of mucormycosis cases has been reported globally, the rise in India is alarming especially in uncontrolled diabetics. However, multiple gaps exist in the understanding of the disease in this country.

Methods. To describe the epidemiology, diagnosis, treatment practices, and outcome of mucormycosis in India. A single-arm prospective observational study was conducted in the network of 17 tertiary care centres across India during April 2016 through September 2017. All consecutive proven mucormycosis patients were enrolled in this study. Clinical data including risk factors, investigations, and treatment were collected. All isolates and histopathological specimens were sent to Mycology Reference Laboratory at Chandigarh for final identification (phenotypic and sequencing) and drug susceptibility testing.

Results. A total of 474 cases were enrolled between the study period. Rhino-orbito-cerebral mucormycosis was common (42.7%) presentation with 22.8% patients had brain involvement, followed by pulmonary (14.6%), cutaneous (11.8%), isolated renal (3.9%), and intra-abdominal (2.8%) mucormycosis. The underlying disease or predisposing factors were noted in 79.7% cases (84.9% diabetes mellitus, 12.9% steroids, 10.3% trauma or history of surgery, 9.7% malignancy, and 9.2% transplant). The most common agents isolated were *Rhizopus* species (75.9%, *R. arrhizus* [74.3%] and *R. homothallicus* [6.7%]) followed by *Apophysomyces variabilis* (7.4%), *Mucor* species (6%), and *Lichtheimia corymbifera* (4%). The patients were managed by medical therapy in 82.8%, surgery in 56.8% while 51.7% received combined medical and surgical management. Amphotericin B (96.8%) either lipid formulations (65.7%) or conventional form (39.1%) was the common antifungal used. The mortality of patients was 30.4%; of which, 80.3% patients died within 6 weeks of their diagnosis. 24.3% patients left hospital against medical advice while 50.1% survived.

Conclusion. Rhino-orbital-cerebral mucormycosis in uncontrolled diabetics is common presentation in India. *R. arrhizus* followed by *A. variabilis* are common species isolated from those patients. Survival was noted only in half of the patients despite increased awareness and diagnosis.

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400. The Frequency and Clinical Characteristics of Positive Galactomannan Assay Results in Patients With Mucormycosis

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Background. Discrepancies between histomorphologic finding and indirect test results such as galactomannan (GM) assay make diagnosis of invasive fungal infection difficult. We investigated the frequency and clinical characteristics of positive GM assay results in patients with mucormycosis.

Methods. Patients who met the modified criteria for proven or probable mucormycosis and had serum and/or bronchoalveolar lavage (BAL) fluid GM assay result were enrolled at a tertiary hospital from July 2009 to October 2017. Proven mucormycosis was defined as histologic evidence of tissue invasion of hyphae with positive mucormycosis immunohistochemistry (IHC) test result and the recovery of agents of mucormycosis (*Rhizopus* spp., *Cunninghamella* spp., *Apophysomyces* spp., *Saksenaia* spp., *Absidia* spp., *Mucor* spp.) by culture from sterile specimens. Probable mucormycosis was defined as histologic evidence of tissue invasion of hyphae with positive mucormycosis IHC test result with or without recovery of agents of mucormycosis by culture from nonsterile specimens.

Results. Among 50 patients of proven or probable mucormycosis, 20 (40%) patients were positive for serum and/or BAL fluid GM assay results; 13 of 20 (65.0%) were positive in serum, nine of 12 (75.0%) were positive in BAL fluid, and two of 12 (16.7%) were positive in both. There were more patients with gastrointestinal infections (4 of 20 [20%] vs. 0 of 30 [0%], $P = 0.021$) and diagnosed as histomorphologically aspergillosis (6 of 20 [30%] vs. 1 of 30 [3%], $P = 0.012$) in GM positive group than GM negative group.

Conclusion. These results suggest that positive GM assay results are not uncommon in mucormycosis. GM assay results from the patients with mucormycosis appear to be related with gastrointestinal infections and histomorphologic diagnosis of aspergillosis. Further studies are needed on the mechanism of positive GM results in patients with mucormycosis and possible coinfection with other fungi such as *Aspergillus* species in these patients.

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401. Pneumocystis jirovecii Pneumonia in Renal Transplant Recipients After a 6-Month Trimethoprim-Sulfamethoxazole Prophylaxis: A Case-Control Study

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Background. *Pneumocystis jirovecii* pneumonia (PCP) is an important cause of morbidity and mortality in kidney transplant recipients (KTRs). Chemoprophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) is recommended about 6–12 months after solid-organ transplantation. However, PCP occasionally occurs after the recommended prophylaxis periods. The aim of this study was to investigate the incidence and risk factors for PCP in KTRs with 6-month TMP-SMX prophylaxis.

Methods. We performed a case-control study of adult patients diagnosed with PCP from 1999 to 2015 in a tertiary care hospital. All patients received 6-month PCP prophylaxis with TMP-SMX after kidney transplantation (KT). If there were rejection episodes, PCP prophylaxis was provided for additional 3 months. During the study period, CMV viremia was not indication of PCP prophylaxis because of the concern of the nephrotoxicity of TMP-SMX. We defined the classification of early or late-onset PCP as one year after transplantation.

Results. Among 3,941 kidney or pancreas-kidney transplant recipients, 67 (1.7%) patients developed PCP after the discontinuation of TMP-SMX prophylaxis. Among them, patients who was transferred from other hospitals ($n = 14$) and pancreas-kidney transplant recipients ($n = 6$) were excluded. Finally, 47 of KT PCP and 94 control patients were included. Of the 47 patients with PCP, 24 (51%) revealed early PCP while the remaining 23 (49%) exhibited late PCP. Duration of PCP prophylaxis was similar between case and control (median 6 months, respectively). In multivariate analysis, rejection (OR, 3.9; 95% CI, 1.4–11.1) and cytomegalovirus infection (OR, 2.4; 95% CI, 1.0–5.8) were independently associated with the development PCP after TMP-SMX prophylaxis. Rejection or CMV viremia were observed in 70% of patients with PCP patients. Time to development of PCP after rejection (median 6 months; IQR 5–19 months) was slightly shorter than that after CMV viremia (median 9 months; IQR 5–12 months), although this difference did not reach any statistical significance ($P = 0.18$).

Conclusion. Rejection and CMV viremia appear to be risk factors for the development of PCP after completing early transplantation period chemoprophylaxis. Our data suggest that at least 6- to 9-month chemoprophylaxis for PCP may be needed for KTRs with rejection or CMV viremia.

Disclosures. All authors: No reported disclosures.

402. Breakthrough Pneumocystis jirovecii Pneumonia Among Cancer Patients: Opportunity for Antimicrobial Stewardship?

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