Clinical outcome and in vitro antifungal susceptibility of clinical isolates of rhino-orbital-cerebral Aspergillus associated with post COVID-19 from North India

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Objectives: This study aimed primarily to determine the etiology, characteristics, and comorbidities of patients with rhino-orbital-cerebral mycosis. Secondly, antifungal susceptibility pattern of the isolates and linkage by ITS-sequencing was also studied.

Methods: The study was conducted from May to December 2021 on all suspected cases of rhino-orbital-cerebral mycosis in post COVID-19 patients a setting that represents the demographics, current COVID-19 clinical scenarios, clinical features, comorbidities, laboratory, radiological investigations, and outcomes were collected after obtaining informed consent of the study participants. Specimen collection was done using the proposed code Mascot and diagnosis of COVID-19 was done by basis of real-time polymerase chain reaction (RT-PCR) test. KOT Mount examination, fungal cultures, and histopathological examination was performed on samples collected endoscopically or post-debridement. Mycosis was further confirmed by using in vitro susceptibility profiles for antifungal drugs by CLSI microbroth dilution method (M38-A2) was studied by HMC180™ plate (Himedia) for for A. fumigatus, A. flavus, A. terreus, A. niger, and A. parasiticus. MIC ranges and the drug concentrations required to inhibit 50% (MIC50) or 90% (MIC90) of the fungus were determined by CLSI.

Results: A total of 70 patients were diagnosed with mycosis. Rhino-orbital and rhino-orbital-cerebral forms were observed in 55.7% of cases each. Diabetes mellitus (DM) was present in 91.7% patients while 78.5% of the patients were treated with corticosteroids in past year, and 21.7% presented with active COVID-19 pneumonia. Most cases showed onset of symptoms of mycosis between 2.17 days to diagnosis of COVID-19. On imaging, it was observed in 74.3% and cranial involvement was in 55.7% of patients. Diagnosis of mycosis was established on KOH direct microscopy 68.6% cultures 47.14%, immunological 57.5%. Isolates obtained were Rhizopus arrhizus (42.4%), A. fumigatus (25.6%), A. terreus (17%), and A. parasiticus (15.1%). Overall treatment included intravenous amphotericin B along with probucillate (fluconazole, voriconazole, and terbinafine) in 84% of patients. A. fumigatus and A. terreus strains were 0.21 and 4 µg/ml and MIC50 and MIC90 results for intravenous amphotericin B, voriconazole, and terbinafine were 8 and 2, 2, and 2 and 8 µg/g respectively. Ampicillin was susceptible to amphotericin B (18%), itraconazole (15%), terbinafine (10.2%), flucytosine (8%), and voriconazole (7%) and was resistant to micafungin (4%). Micafungin and voriconazole performed 43% sensitive. Overall, mortality was 34.4%.

Conclusion: In conclusion, rhino-orbital-cerebral mycosis is a clinically challenging disease, and appropriate management of mycosis can improve survival. Rational use of medical and strict glycemic control in diabetic patients can prevent recurrence of mycosis. Use of medical methods for antifungal susceptibility testing to guide antifungal treatment may be clinically useful in cases of failure treatment.