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Cirrhosis and fungal infections-a cocktail for catastrophe: a systematic review and meta-analysis with machine learning

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Objectives: We evaluated the magnitude and factors contributing to poor outcomes among cirrhosis patients with fungal infections (FIs).

Methods: We searched PubMed, Embase, Ovid, and WOS and included articles reporting mortality in cirrhosis with FIs. We pooled the point and relative-risk (RR) estimates of mortality on random-effects meta-analysis and explored their heterogeneity (I2) on subgroups, meta-regression, and machine learning (ML). We assessed the study quality through New-Castle-Ottawa-Scale and estimate-asymmetry through Eggers regression (CRD42019142782).

Results: Of 4345, 34 studies (2134 patients) were included (good/fair/poor quality: 12/21/1). Pooled mortality of FIs was 64.1% (95%CI: 55.4-72.0, 12: 87%, $P < .01$), which was 2.1 times higher than controls (95%CI: 1.8-2.5, 12:89%, $P < .01$). Higher CTP (MD: +0.52, 95%CI: 0.27-0.77), MELD (MD: +2.75, 95% CI: 1.21-4.28), organ failures, and increased hospital stay (30 vs. 19 days) was reported among cases with FIs. Patients with ACLF (76.6%, RR: 2.3), and ICU-admission (70.4%, RR: 1.6) had the highest mortality. The risk was maximum for pulmonary-FIs (79.4%, RR: 1.8), followed by peritoneal-FIs (68.3%, RR: 1.7) and fungemia (55%, RR: 1.7). The mortality was higher in FIs than bacterial (RR: 1.7) or no-infections (RR: 2.9). Estimate-asymmetry was evident ($P < .05$). Up to 8 clusters and 5 outlier studies were identified on ML, and the estimate-heterogeneity was eliminated on excluding such studies.

Conclusions: A substantially worse prognosis, poorer than bacterial infections in cirrhosis patients with FIs indicates an unmet need for improving fungal diagnostics and therapeutics in this population. ACLF and ICU admission should be included in host criteria for defining IFIs.

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***Scedosporium* spp. and *Lomentospora prolificans*, fungal agents with unexpected vascular tropism**

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Objectives: Invasive scedosporiosis and lomentosporiosis are deadly fungal infections due to *Scedosporium* spp. and *Lomentospora prolificans*. The Scedosporiosis/lomentosporiosis Observational Study (S.O.S.) highlighted for the first time a frequent vascular involvement in these infections including aortitis and peripheral arteritis (PA). We here describe the clinical, microbiological, radiological and anatomopathological characteristics of these vascular infections.

Methods: We retrospectively reviewed cases of arteritis (with the exception of central nervous system arteritis) from the S.O.S. cohort and from the literature.

Results: Seven cases of vascular infections were identified from the S.O.S. cohort representing 24% (7/29) of the disseminated scedosporiosis/lomentosporiosis. Four cases had both aortitis and PA, 2 patients were diagnosed with PA and one patient with aortitis. A total of 9 aortitis and 4 PA cases were identified from the literature. All 20 cases were proven scedosporiosis/lomentosporiosis. The main species was *S. apiospermum* [60% of cases (12/20)] followed by *L. prolificans* [35% of cases (7/20)]. One infection was caused by both species. An underlying immunosuppression was present in 70% of the cases (14/20, with 10 cases of solid organ transplantation and 3 cases of hematologic malignancies). The main risk factor in immunocompetent patients was a previous cutaneous trauma (4/6). Interestingly, vascular involvement was identified at diagnosis of the scedosporiosis/lomentosporiosis in only half of the cases. Aortitis was mainly abdominal (8/13). Various PA localizations were reported with frequent iliac or femoral involvement (4/10). Arteritis was the only localization in only 10% (2/20) of the scedosporiosis/lomentosporiosis, other sites involved being mainly osteoarticular (10/20), and pulmonary (9/20) followed by central nervous system (5/20), cutaneous localizations (4/20), and endocarditis (4/20). Of note, three-quarters of the cases were disseminated. Aneurysmal lesion was the most frequent imaging aspect (8/11 of aortitis and 6/10 of PA) which was complicated by a rupture in half of the aortitis (4/8) and only one PA (1/6). Vascular wall thickening (2/11 of aortitis and 1/10 of PA) and perivascular abscess (1/11 and 1/10, respectively) were more rarely described. Hypermetabolism was constant on PET-CT scan when performed (6/6). When available (11/20), pathological analysis showed an invasion of the artery wall by fungal hyphae (10/11), particularly in the media and the adventice. A total of 3-months of mortality related to infection was 44% (8/18), rising to 71% (5/7) in case of fungemia.

Conclusion: The vascular tropism of *Scedosporium* spp. and *L. prolificans* underlies the necessity of vascular imaging in the management of these infections, especially in case of dissemination seeking in particular aneurysmal lesions of the abdominal aorta and iliofemoral arteries.

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Clinical profile of *fusarium* infections: case series from a tertiary care hospital

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Objective: To study the clinical profile of patients with *Fusarium* infections diagnosed at our tertiary care center during the study period from February 2017 to March 2022.

Methods: We conducted a retrospective case study wherein all consecutive patients with *Fusarium* infections between February 2017 to March 2022 were accessed. The diagnosis was categorized based on either fungal culture alone or fungal culture with histopathology findings.

Results: A total of 12 patients with *Fusarium* infections were encountered during this period. The mean age was 49. In all, 5 were females and 7 were males, and 5 patients had diabetes as a risk factor. Other risk factors included were chemotherapy for multiple myeloma (1) and lymphoma (1), polytrauma (1), and surgery after pituitary macroadenoma. A total of 8 (66.7%) patients were on antifungal prophylaxis at the time of diagnosis.

A total of 6 (50%) had localized infections whereas, remainder 6 (50%) had disseminated infection, and 25% presented with onychomycosis. Seven patients were diagnosed based on fungal culture and five were diagnosed based on histopathology findings collaborated with a fungal culture. There was one patient with *Fusarium* blood stream infection, who expired within 2 weeks of hospitalization.

A total of 10 patients had *F. solani* whereas, 2 had *F. oxysporum* isolated in fungal cultures. In all, 42% of patients in the study had high Beta- D-Glucan (BDG) and 67% of the patients underwent source control of the involved region. A total of 9 patients (75%) received voriconazole as antifungal treatment and 3 patients received Amphotericin B. Four patients expired, three were lost to follow up and five did not develop relapse on follow-up.

Conclusion: *Fusarium* is an opportunistic human pathogen severely affecting immunocompromised patients, especially patients with hematological malignancies, prolonged neutropenia, and post-hematopoietic stem cell transplantation. Our study records a notable number of *Fusarium* infections among diabetics and onychomycosis was a common presentation. A high index of suspicion is of utmost importance in patients with risk factors and serum BDG may help in suspicion of invasive *Fusarium* infections. The 33% mortality in our study stresses the need for early diagnosis and treatment.