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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, I²: 87%, $P < .01$), which was 2.1 times higher than controls (95%CI: 1.8-2.5, I²: 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 FIs.

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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 adventitia. 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.

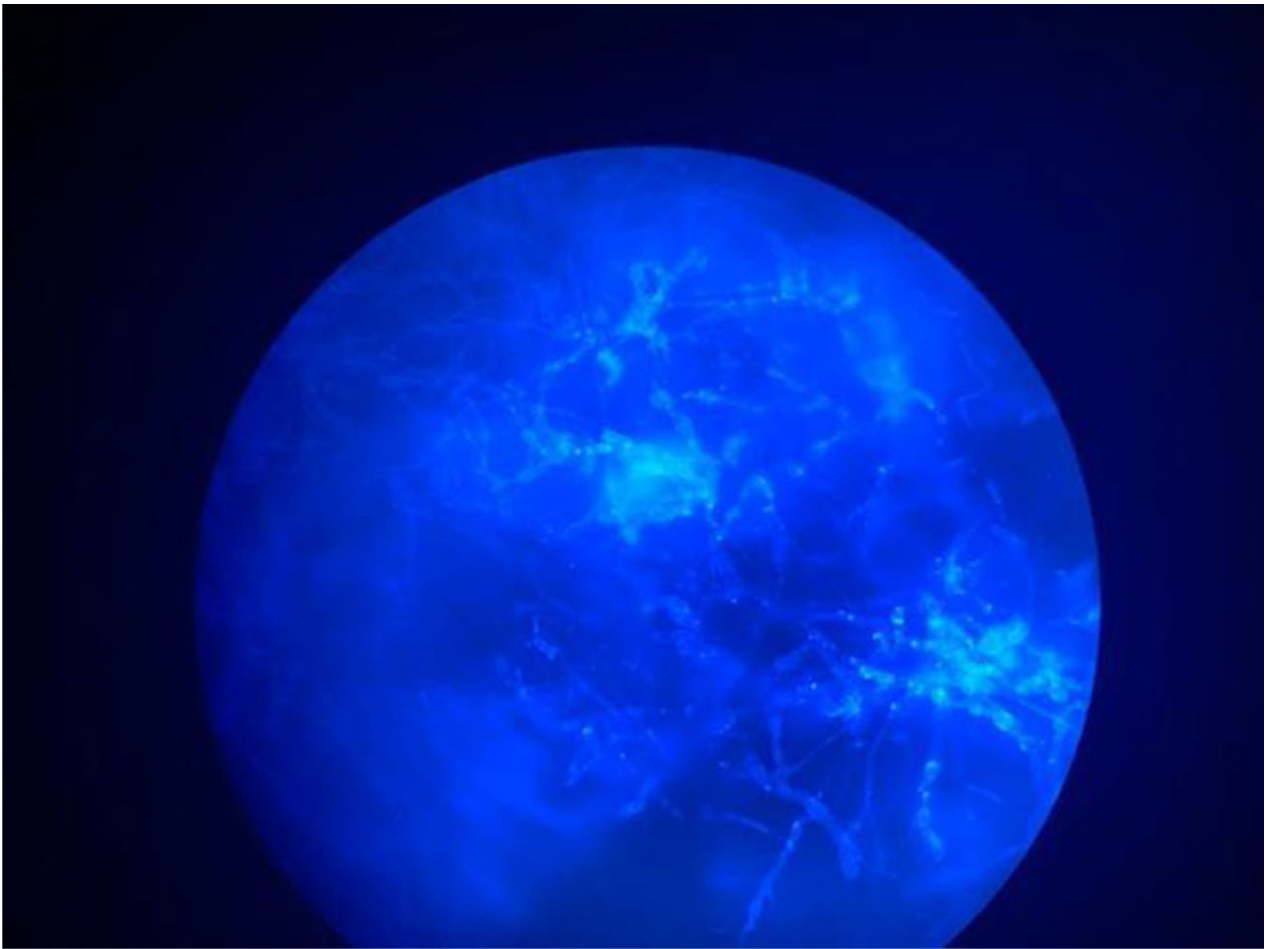
Results: A total of 12 patients with *Fusarium* infections were encountered during this period. The mean age was 49. In all, 5 were females and 7 were males, and 5 patients had diabetes as a risk factor. Other risk factors included were chemotherapy for multiple myeloma (1) and lymphoma (1), polytrauma (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. oxysporium* 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.





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Jorge lobo's disease in brazil: a new recognized reservoir?

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Lobomycosis (lacaziosis) is a chronic subcutaneous disease caused by the uncultivated fungus *Lacazia loboi*. The disease was first described in 1931 by Jorge Lobo in Brazil and has been reported in South and Central America. Lobomycosis is a rare disease that affects certain geographic regions, mainly in countries of low socioeconomic status, but its prevalence among indigenous people in Brazil is exceptionally high. The state of Maranhão is located in the northeast region of the country and there are rare clinical reports of imported cases of the disease in our region. This is the first published series of autochthonous cases of lacaziosis in Maranhão.

Objective: To describe seven cases of *Lacazia loboi* infections in immunocompetent patients in an endemic area for other subcutaneous mycoses.

Methods: We retrospectively reviewed the medical records of all patients who developed Jorge Lobo's diseases in a new area recognized as a potential environment reservoir. An incident case was defined as a patient who developed proven lacaziosis based on the presence of topical fungal elements in the tissue on histopathology or mycologic direct exam. Epidemiological and clinical data of all cases of lacaziosis were collected using a standard clinical form.

Results: In the period from 2000 to 2021, seven patients were identified. All cases were diagnosed by histopathology and direct mycological examination of the lesions. A total of 6 out of 7 (85.7%) patients were men and the mean age was 57 years (52-70 years). The median time between onset of infection symptoms and diagnosis was >2 years in 6 patients, with 15 years of symptoms duration in patient 7. All patients reported having worked with agricultural activities before. A total of 50% of patients were diagnosed with localized lesions and the other half with disseminated lesions. Subcutaneous lesions involved the upper limbs (4/6; 66.6%), ears (2/6; 33.3%), lower limbs (1/6; 16.6%), and trunk (1/6; 16.6%). All patients exhibited nodules as a dominant pattern of skin lesion, sometimes coalescing with the tumor's appearance. Regarding treatment, a combination of itraconazole and clofazimine therapy was added to all patients. Surgical excision was possible only in 2 episodes due to the limited availability of this procedure at the site. Cure was documented in 2 cases, with no recurrence to date.

Conclusion: The present series represents the first and largest collection of case studies of lacaziosis in Maranhão state, with all cases classified as autochthonous. Lacaziosis involves mainly adult males with different occupational risks such as agricultural labor, and other workers exposed to contaminated soil and plant materials. Few data are available to support suggested therapy with itraconazole and clofazimine. Excision surgery is important for treatment due to the absence of clinical trials in the medical literature. Epidemiological surveillance studies of new cases of lacaziosis in Maranhão are important for mapping this new reservoir and developing public policies for diagnosis and treatment.

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Clonal outbreak of *Trichophyton tonsurans* causing tinea capitis among wrestlers in Beijing, China

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Objectives: *Trichophyton tonsurans*, an anthropophilic dermatophyte, mostly causes tinea capitis and tinea corporis and is often associated with outbreaks among athletes involved in combat sports, such as wrestlers and judo athletes. Here, we report an outbreak of tinea capitis caused by *Trichophyton tonsurans* among five juvenile athletes aged ten to fourteen in a wrestling team in Beijing, China.

Methods: A total of 5 wrestlers aged 10-14 years presented with alopecia, erythema, scales, and pustule on the scalp (Fig. 1a). Scrapings from the lesions were performed by direct microscopic examination using 10% potassium hydroxide (KOH) with calcofluor white and fungal culture. The fungal pathogens were identified by morphology and sequencing of the internal transcribed spacer (ITS) regions. Multilocus genotyping analysis was performed by sequencing of the five gene loci including the ITS and non-transcribed spacer (NTS) of the ribosomal RNA (rRNA) locus, alkalinephosphatase-1 (ALP1), metalloprotease-5 (MEP5), carboxypeptidases Y (CarbY), which show intraspecies diversity and can be applied to epidemiological investigations and determining the route of infection transmission. Antifungal susceptibility of terbinafine (TBF), itraconazole (ITC), fluconazole (FLC), ketoconazole (KTC), and amphotericin B (AMB) against the causative fungal isolates was determined by broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI) M38-A3 document.

Results: The five patients were diagnosed with tinea capitis because of the scalp lesions, spores, and hyphae observed by direct microscopic examination (Fig. 1b), and positive fungal culture. The causative isolates were all identified as *T. tonsurans* by macroscopic and microscopic characteristics (Fig. 2) and sequencing of ITS regions. The sequences of ITS, NTS, ALP1, MEP5, and CarbY were identical among the five isolates, revealing a single genotype. The abovementioned sequences have been deposited to Genbank. The minimum inhibitory concentrations (MICs) of TBF, ITC, FLC, KTC, and AMB against five *T. tonsurans* isolates were 0.015 µg/ml, 0.015 µg/ml, 8 µg/ml, 0.06 µg/ml, and 0.5 µg/ml, respectively.

Conclusion: We report an outbreak of tinea capitis caused by *T. tonsurans* among wrestlers in Beijing, China. Multilocus genotyping analysis revealed that all isolates consisted of a single genotype, suggesting the outbreak may be caused by a single strain of *T. tonsurans*. The isolates were all susceptible to the common antifungal drugs treating tinea capitis.