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Factors related to outcome of bloodstream infections due to *Candida parapsilosis* complex: A single center observation study from Central India

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Objectives: *Candida parapsilosis* infection has recently emerged as an important antifungal-resistant nosocomial pathogen having the unique ability to grow on inanimate objects and surfaces. Very limited studies from low and middle-income countries are available on the association of risk factors and antifungal susceptibility testing (AFST) of this species. The aim of this study was to analyze the predisposing conditions, outcome, and antifungal susceptibility pattern of candidemia due to *C. parapsilosis* complex.

Methods: A single-center retrospective observational study from January 2019 to December 2021 of all cases of candidemia was carried out at an 890-bedded University Hospital in central India. Data regarding demographic characteristics and clinical risk factors were collected from the patient's medical records. Antifungal susceptibility testing was performed; MIC results were interpreted according to CLSI breakpoints (M27-A3). Risk factors and outcome association at the species level were analyzed by using Fisher's exact test. Variables with a $P \leq .05$ at the descriptive analysis were analyzed by Cox regression. A P -value of $\leq .05$ was considered to represent the statistical significance and all statistical tests were two-tailed.

Results: Of 211 patients diagnosed with Candidemia during the study period, 53 (25.1%) were infected with *C. parapsilosis* which represented the second most frequently isolated yeast after *C. albicans* ($n = 98$; 46.4%). A total of 26 (49%) *C. parapsilosis* isolates were non-susceptible to fluconazole (NSF), which included resistant ($n = 20$) and susceptible dose-dependent ($n = 06$) isolates. The median patient age was 63 years. 15.3% were neonates. The majority of patients (90%) suffered from multiple comorbidities, diabetes mellitus (43%) being the commonest. A total of 55% of patients underwent surgical intervention within 30 days from the onset of candidemia. Univariate logistic regression revealed that ICU admission [odds ratio (OR) 2.45], central venous catheter use (OR 2.46), renal impairment (OR 1.687) were more common among NSF isolates than fluconazole-susceptible (FS) isolates (all $P < .05$). The overall crude mortality at 30 days was 36%; higher in patients infected with FNS isolates than FS isolates.

Conclusion: There is an increase in the absolute number of invasive infections by *C.parapsilosis* observed over the past 2 years. At this moment, the percentage of fluconazole non-susceptible *C. parapsilosis* is very high and poses a threat to infected patients and has a clinical impact in our hospital. Being able to identify and treat infections caused by this pathogen is important to prevent clinical outbreaks.

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A rare presentation of subcutaneous Entomophthoromycosis

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Entomophthoromycosis is a chronic granulomatous type of subcutaneous infection seen mainly in immunocompetent individuals. The usual focus of Conidiobolomycosis infection is as rhinotomophthoromycosis, characterized by chronic, indolent, and localized swelling of the nose, paranasal tissues, sinuses, cheeks, and upper lips and it infrequently affects the lower extremities.

We report a case of subcutaneous Conidiobolomycosis in a 21-year-old male with an alleged history of trauma to left foot by a wooden stake 6 months back. Primary treatment of the wound was done at a local hospital. A total of 4 months post-trauma he developed multiple pus discharging sinuses on the dorsal and plantar aspects of the left foot, for which local dressing was done in a nearby hospital. He presented to our hospital with non-healing multiple sinuses, with active serosanguinous discharge. He underwent wound debridement under spinal anesthesia and tissue was sent for fungal culture, histopathological examination.

Aerobic culture of the wound swab revealed moderate growth of Methicillin-resistant *Staphylococcus aureus* sensitive to clindamycin, gentamicin, and linezolid. Histopathological examination of the tissue showed a resolving abscess with granulation tissue. Direct microscopic examination of the tissue by KOH mount showed no fungal elements. It was inoculated into Sabouraud's dextrose agar with and without cycloheximide and incubated at both 25°C and 37°C. Sabouraud's dextrose agar without cycloheximide incubated at 37°C after 48 h of incubation grew cream-colored glabrous colonies adherent to surface with pale reverse. Lactophenol cotton blue preparation revealed broad, sparsely septate hyphae with primary conidia which are globose approx. 40 µm in diameter, produced singly. They have a characteristic protruding papilla on one side. The fungal isolate was identified as *Conidiobolus* species. Sequencing results are awaited for species identification and confirmation.

Serial wound dressings were done following strict infection control policies and he was started on tablet linezolid 600 mg twice daily, tablet itraconazole 400 mg twice daily for 1 week, followed by 400 mg once daily for 6 months.

Conidiobolus is a soil saprophyte, found in decaying vegetation in most warm climates in tropical countries. There has been only one published case report of subcutaneous entomophthoromycosis of the foot, in a 49-year-old female from Venezuela. To the best of our knowledge, we report the first case of subcutaneous entomophthoromycosis of the lower extremity in India and the second case in the world.

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Infant-juvenile paracoccidioidomycosis. Two Argentine endemic zones with different epidemiological and clinical aspects? What influences this situation?

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Argentina has two endemic areas of paracoccidioidomycosis (PCM). It is noteworthy that epidemiological characteristics differ in both areas, especially in frequency, and clinical aspects of infant-juvenile PCM form (I-JF). In this work, we have reviewed and analyzed 10 years of juvenile PCM form (JF) in both areas emphasizing in acute/subacute I-JF cases.

From January 2012 to December 2021 data of epidemiological characteristics, clinical history and laboratory results of I-JF cases were recorded on standardized protocols and entered into a database that helped consolidate the information.

Although the more extensive area of PCM historically with the highest incidence is located in Northeast Argentina (NEA), the major number of I-JF was observed in the smaller PCM endemic area, located in the Northwest of the country (NWA).

In NWA, 32 JF were recorded including 20 cases of I-JF form in children from 1-13 years old. No outbreak was registered. Cases were equally distributed over the 10 years.

In NEA, 28 JF were recorded including 8 cases of I-JF form in children from 7-14 years old. Of these cases, 6/8 (75%) presented as an outbreak in 2012. The rest were only registered in 2018-2020.

More frequent clinical manifestation of I-JF:

NWA: 70% hepatosplenomegaly with peritonitis and ascites, 33% gastrointestinal symptoms including diarrhea. Adenomegaly (70% cervical, 15% mediastinal).

Serology (ID) non-reactive: 32%

NEA: 62% cutaneous, 37% hepatosplenomegaly, 25% osteolytic lesions, 25% pulmonary nodules, 25% pericardial effusion, 25% mucocutaneous. Adenomegaly (75% cervical, 62% mediastinal-retroperitoneal).

Serology (ID) non-reactive: 12.5%

NWA records most cases of I-JF with a constant frequency and with a lower median age. NEA seems to only occur in outbreaks.

Are striking the different epidemiological characteristics observed? Predominantly hepatosplenomegaly and intestinal forms in NWA, being with fecal material the first sample where Paracoccidioides is detected in many cases. In contrast, more diverse clinical manifestations are observed in NEA. Most cases with cutaneous/mucocutaneous lesions and the presence of pulmonary and pericardial forms characterized I-JF in this zone.

Considering serological tests are important in the PCM diagnosis and to follow up the treatment success, no-reactive tests obtained (32% in NWA, 12.5% in NEA) show a serious diagnostic problem emphasize the need to work on more sensitive tools to reduce the high mortality of this clinical form. The variable expression of gp43 among isolates of Paracoccidioides species may suggest not to use a single antigen preparation for serological tests and include autochthonous isolates.

Our group reported climatic and anthropogenic changes influencing the appearance of I-JF outbreaks in the NEA, a region where the observation of these cases was historically very rare. Probably, NWA provides a different ecological niche for Paracoccidioides, which favors its constant appearance over time. We have already started a multicenter molecular epidemiological, probably include soil studies of NWA would be important to try to better understand this situation.

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Persistent Fungemia with *Candida auris* in a patient with enterocutaneous fistula

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Objective: *Candida auris* (*C. auris*) is a major emerging threat to the healthcare sector in view of the difficulty in early identification by standard methods, multidrug resistance, and ease of spread in healthcare settings. Here, we report a case of persistent *C. auris* fungemia (>2 months) in a patient with enterocutaneous fistula.

Methods: A 57-year-old man without any comorbidities underwent surgery for diverticular perforation which was complicated by intra-abdominal abscesses, anastomotic leak, and multidrug-resistant bacteremia requiring higher antibiotics, total parenteral nutrition, and prolonged ICU stay. Patient was admitted to our center with sepsis and blood culture grew *C. auris*. Patient was managed with injection of caspofungin (in the absence of sensitivity breakpoints). Patient continued to grow *C. auris* in the blood so flucytosine was added as a part of combination antifungal therapy. On dual antifungal therapy for 28 days there was a transient clearance of fungemia. Work up for endocarditis, intrabdominal collection, and endophthalmitis were negative. But Patient was continued on total parenteral nutrition via central line in view of enterocutaneous fistula. Patient developed a recurrence of fungemia after 4 days of stopping antifungal treatment. Patient was started on injection of micafungin and voriconazole (in view of on treatment resistance to flucytosine), on which cultures turned sterile and patient improved. Plan was made to give total 6 weeks of parenteral combination antifungal therapy.

Results: *C. auris* management complexities stem from multiple factors. The above case emphasizes the urgent need for *C. auris* specific minimum inhibitory concentration breakpoints and standard guidelines for treatment. Currently, treatment is based on the Center for Disease Control's proposed breakpoints (extrapolated from other *Candida* spp.). Upfront combination antifungal treatment might be the answer till further studies.

Conclusion: Management of invasive *C. auris* infection presents a major therapeutic challenge to clinicians and a major threat to healthcare sector even after timely identification.

Candida auris	drugs	5/3/22	8/3/22	19/3/22	27/3/22	19/4/22	25/4/22	2/5/22
	Flucytosine	≤ 1	≤ 1	≤ 1	≤ 1	≤ 1	≥ 64	Sterile
	Fluconazole	32	32	32	32	32	32	
	Voriconazole	1	1	1	1	1	0.5	
	Caspofungin	0.25	0.25	0.25	0.25	0.25	0.25	
	Micafungin	0.12	0.12	0.12	0.12	0.12	0.12	
	Amphotericine B	8	≥ 16	8	8	≥ 16	≥ 16	

Table 1.
Serial MIC of antifungal drugs for *C. auris* with persistent candidemia