

## ORIGINAL ARTICLE

## Trichosporon–Blood Stream Infection

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**Aim:** *Trichosporon* species are the major emerging opportunistic pathogen in immunocompromised patients. Its diverse refractoriness to conventional antifungal drugs and association with high mortality rate is worrisome. The present study aims to determine the risk factors, treatment outcome and antifungal susceptibility pattern of *Trichosporon* species in blood stream infections.

**Material and Methods:** All patients with blood culture positive for *Trichosporon* species from January 2012 to August 2016 at PD Hinduja National Hospital and research centre were evaluated retrospectively. Species identification and antifungal susceptibility by broth microdilution method for various drugs was determined using Vitek2 compact automated system.

**Results:** 12 patients were found to have *Trichosporon* blood stream infection. 9 isolates that were speciated all were *T. asahii*. All patients had central venous catheter and received prior antibiotics. Overall mortality rate was 50%.

**Conclusion:** Higher mortality was associated with central venous catheter and voriconazole should be used as drug of choice for treatment. Identification of *Trichosporon* species along with its sensitivity and proper treatment of patients is of utmost importance.

**Introduction**

*Trichosporon* species are known to be inhabitants of soil and may colonize human skin, upper respiratory tract and gastrointestinal tract.<sup>1</sup> Over the past few decades, *Trichosporon* species have emerged as an important opportunistic pathogen especially in immunocompromised patients.<sup>2</sup>

Previously, all pathogenic members of the genus *Trichosporon* were referred as a single species, *T. beigelii*.<sup>3</sup> Biochemical and morphologic differences within the genus had led to new nomenclature of *T. beigelii* into 9 distinct species, amongst them *Trichosporon asahii* is the most common cause of disseminated disease.<sup>4</sup> Phenotypic identification of *Trichosporon* species usually gives very inconsistent results, so molecular methods are required for accurate identification, but they are still expensive and not suitable for most laboratories.<sup>5,6</sup>

In the past, amphotericin B was recommended for treatment but response was poor and failure rate

was high. Even MICs of echinocandins are very high and multiple incidences of breakthrough infections have been reported. *Trichosporon* species are usually susceptible to azoles thus, treatment should be done using one of these azoles.<sup>7,8</sup>

Considering the diverse refractoriness to conventional antifungal drugs and association with high mortality rate, present retrospective study was conducted to determine the risk factors, treatment outcome and antifungal susceptibility pattern of *Trichosporon* species in blood stream infections.

**Material and Methods**

All patients with blood culture positive for *Trichosporon* species from January 2012 to August 2016 at PD Hinduja National Hospital and research centre were evaluated retrospectively.

Medical records of all patients were reviewed. According to the consensus statement of the Invasive Fungal Infections Cooperative Group of the European Organization for Research and Treatment of Cancer and the Mycoses Study Group of the National Institute of Allergy and Infectious Diseases, patients that met the criteria for proven invasive fungal infections were taken.<sup>9</sup> Risk factors, treatment regimens and outcome of each patient were recorded.

*Trichosporon* species were identified by phenotypic method. An automated Vitek2 compact system was used to identify them upto species level and for antifungal susceptibility testing. MICs of amphotericin B (AMB), 5 flucytosine, fluconazole (FLU), itraconazole (ITR) and voriconazole (VOR) were determined using broth microdilution method for antifungal susceptibility testing of yeasts described in the Clinical Laboratory and Standards Institute (CLSI) M27-S4, Volume 32.<sup>10</sup> *Candida albicans* ATCC 14053, *Candida parapsilosis* ATCC 22019, and *Candida krusei* ATCC 6258 were used as quality-control strains.

**Results**

Total 12 patients were found to have *Trichosporon* blood stream infection. 9 were *T. asahii* and 3 were not speciated. All of these isolates were primarily grown on Sabouraud's Dextrose Agar that showed dry, wrinkled cream coloured colonies (Figure 1). Lactophenol Cotton Blue (LCB) mount showed septate hyphae with arthroconidia formation along with lateral blastoconidia (Figure 2). These isolates were further confirmed by positive urease test (Figure 3). Clinical and microbiological data of 12 patients are summarized in Table 1. All 12 patients had central venous catheter

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Received: 15.09.2016; Revised: 26.12.2017; Accepted: 20.07.2018

and received prior antibiotics. Amongst them, 8(66%) patients were admitted in ICU and 6(50%) patients had CKD and were on maintenance hemodialysis. Overall mortality rate was 50%. The MIC values of *Trichosporon* isolates are shown in Table 2.

## Discussion

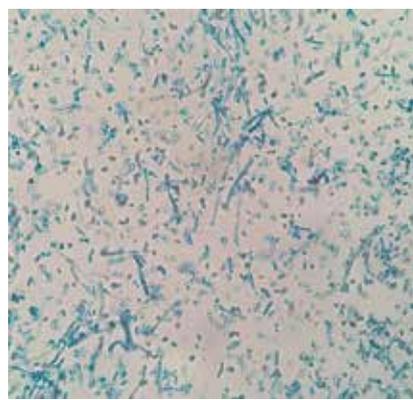
Most common risk factors for *Trichosporon* spp. are acute leukaemia, neutropenia, on chemotherapy or high doses of corticosteroids, solid tumors, transplants, peritoneal dialysis and human immunodeficiency virus.<sup>2</sup> Apart from host factors, previous or current use of antibiotics and use of central venous



**Fig. 1:** Dry, wrinkled colonies of *Trichosporon* species on Sabouraud's Dextrose Agar

catheter (CVC) are also predisposing factors for trichosporonosis.<sup>11,11</sup> In the present study, out of 12, 6(50%) were on maintenance hemodialysis due to chronic kidney disease and all (100%) the patients had central venous catheters.

Previous studies showed that voriconazole and posaconazole were the best *in vitro* antifungal drugs. However, MICs were higher for Amphotericin B.<sup>5,12</sup> Even echinocandins are not recommended as they have little or no activity against *Trichosporon* spp.<sup>13</sup>



**Fig. 2:** Lactophenol cotton blue mount showing arthroconidia and blastoconidia

Breakthrough *Trichosporon* infections have been reported in patients treated with echinocandins.<sup>14,15</sup> ESCMID guidelines recommends voriconazole as the preferred agent because it displays good *in vitro* activity.<sup>16</sup> In the present study, according to the MIC values observed, voriconazole should be used as treatment of choice. But, literature showed that despite appropriate treatment with antifungals, outcome was always poor and failure rate was very high.<sup>17</sup> In the present study too, mortality rate was 50%.

The Infectious Diseases Society of America (IDSA) guidelines recommends



**Fig. 3:** Positive urease test with control

**Table 1:** Clinical and microbiological data of patients that grew *Trichosporon* spp. from blood culture

Age/sex	current diagnosis	ICU stay	CVC/HD catheter	Bacteremia	<i>Trichosporon</i> .spp	Antifungal drug given	Catheter removal	Outcome
69/M	Liver cirrhosis, DM	Yes	Yes	-	T. spp	Fluconazole, Anidulafungin, Voriconazole	Yes	Expired
54/F	CKD, on MHD	Yes	Yes	S. maltophilia, P. aeruginosa	T. spp	Voriconazole	Yes	Discharged
34/M	Chronic pancreatitis	Yes	Yes	E. agglomerans	T. asahii	Fluconazole	yes	Expired
54/F	CKD, on MHD	No	Yes	-	T. spp	Not received	Not done	Discharged
67/F	CKD, on MHD, ESRD	Yes	Yes	S. maltophilia	T. asahii	Voriconazole, Fluconazole	yes	Expired
63/F	CKD, on MHD	No	Yes	E. coli	T. asahii	Not received	Yes	Discharged
76/M	CKD, on MHD	No	Yes	Gram positive cocci	T. asahii	Fluconazole	Not done	Discharged
12/F	Osteosarcoma with chickenpox	Yes	Yes	-	T. asahii	Not received	Not done	Expired
85/M	DM, TB meningitis, Lt. pyelonephritis	Yes	Yes	P. aeruginosa	T. asahii	Voriconazole	Yes	Expired
91/F	CKD, not on MHD, TKR, Fracture humerus	No	Yes	-	T. asahii	Fluconazole	Yes	Discharged
64/M	Fracture supracondylar humerus	Yes	Yes	Enterobacter, Klebsiella	T. asahii	Fluconazole, Anidulafungin, Caspofungin	Not done	Expired
66/M	Myelodysplastic syndrome	Yes	Yes	CONS	T. asahii	Fluconazole, Voriconazole	Yes	Discharged

**Table 2:** Antifungal susceptibility pattern of *Trichosporon* species by microbroth dilution method

MICs*	pt 1	pt 2**	pt 3	pt 4**	pt 5	pt 6**	pt 7	pt 8**	pt 9	pt 10	pt 11	Pt 12
5FC	≤ 4	-	< 4	-	< 4	-	8	-	16	< 1	2	≤ 1
AMB	≤ 0.5	-	< 5	-	< 5	-	≥ 16	-	< 5	0.5	1	0.5
FLU	1	-	32	-	2	-	≥ 64	-	16	2	4	4
ITR	≤ 0.125	-	0.25	-	0.25	-	-	-	0.5	-	-	-
VOR	-	-	-	-	-	-	≥ 8	-	-	< 0.12	< 0.12	≤ 0.12

\*Minimum Inhibitory Concentration of 5FC- 5 Flucytosine, AMB-Amphotericin B, FLU-Fluconazole, ITR-Itraconazole, VOR-Voriconazole; \*\*Antifungal susceptibility testing not done.

that, CVC should be removed in all patients with a CRBSI caused by *Candida* species.<sup>18</sup> Raad *et al*<sup>19</sup> (2004) and Nucci *et al*<sup>20</sup> (2005) also reported that CVC should be removed in all patients with *Trichosporon* CRBSI. In the present study, severity of primary condition and delay in initiation of appropriate antifungal treatment for *Trichosporon* species lead to higher mortality rate. Hence, the best therapeutic approach to optimize clinical outcome is using triazoles therapy and removal of central venous lines.

*Trichosporon* species are well known for its refractoriness to conventional antifungal drugs. Because of limited data available on *in vitro* and *in vivo* activities of antifungal drugs and no MIC interpretative criteria for *Trichosporon* species, treatment of trichosporonosis remains a challenge.

The present study has a limitation that the sample size was very less and antifungal susceptibility testing of all isolates was not done. So, a larger study is needed to better understand the epidemiology of *Trichosporon* species.

### Conclusion

*Trichosporon* species is an emerging fungal infection which can be easily misidentified as *Candida*. But dry wrinkled colonies, LCB mount showing arthroconidia & blastoconidia and positive urease test help in its identification. In our study, the major

risk factors for trichosporonosis were use central venous catheters and multiple antibiotics. Hence, strict infection control measures should be followed while handling patients with invasive medical devices. Higher mortality rate was observed because of its refractoriness to conventional antifungal drugs. Voriconazole should be used as drug of choice for treatment.

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