Clinical and Microbiological Spectrum of Invasive Trichosporonosis at a Tertiary Care Institute: A Retrospective Observational Study

ABSTRACT
Introduction: Invasive trichosporonosis was considered rare in the past decades, but it has emerged as an opportunistic pathogen causing invasive infections in immunocompromised patients. It can colonise various parts of the body, and it is important to differentiate between colonisation and infection. Moreover, knowledge of the epidemiology and risk factors associated with the disease is limited. Its inherent resistance to echinocandins poses a therapeutic challenge in treating patients. If not treated appropriately, it may lead to disseminated infections.

Aim: To understand the clinical and microbiological spectrum of infections caused by Trichosporon spp.

Materials and Methods: This retrospective observational study was conducted in the Department of Microbiology at Nizam’s Institute of Medical Sciences, Hyderabad, Telangana, India for a period of one year from January 2019 to December 2019. The study analysed demographic data such as age, sex, risk factors, clinical features, microbiological diagnosis, treatment, and patient outcomes related to invasive trichosporonosis from the case records. The final sample size was 14 cases. Samples were processed for both aerobic and fungal cultures. The samples were inoculated into Chromogenic agar plates (bioMeriux), 5% sheep blood agar plates (bioMeriux), and Sabouraud dextrose agar. The plates were incubated at 37°C for 48 hours. Culture identification was performed using the Vitek® 2 compact system with the yeast panel YST, and antifungal susceptibility was determined by Broth Microdilution (BMD). Descriptive statistics were used for analysis, and categorical data were described as frequencies with percentages. The data was entered into a Microsoft Excel sheet and analysed using Statistical Packages for the Social Sciences (SPSS) Version 20.0.

Results: During the study period, there were 14 cases of invasive trichosporonosis. The predominant age group was 60-70 years. Risk factors included the administration of broad-spectrum antibiotics in 13 (92.8%) of patients, followed by prolonged Intensive Care Unit (ICU) stay in 8 (57.1%) of the patients. Trichosporon spp. were isolated from urine in 10 (71.4%) cases, blood in 2 (14.2%) cases, and tissue in 2 (14.2%) cases. Trichosporon asahii was the predominant species isolated in 12 (85.7%) patients. All isolates were sensitive to voriconazole and amphotericin B. Mortality was reported in 5 (35.7%) of the patients.

Conclusion: In present study, Trichosporon spp. was predominantly isolated from urine in the majority of patients. The pathogen was isolated from patients with various risk factors. Hence, proper identification of the pathogen, understanding its clinical significance, and determining antifungal susceptibility would aid in the appropriate management of patients.

INTRODUCTION

Trichosporon species, belonging to basidiomycetes yeast, are widely found in nature in places with warm and tropical climates. There are various species of Trichosporon, among which Trichosporon asahii is the most common cause of infection. Trichosporon spp. is occasionally part of the gastrointestinal and oral cavity microbiota and can transiently colonise the respiratory tract and skin [1]. The spectrum of disease ranges from superficial infection in immunocompetent patients to systemic/disseminated infections in immunocompromised patients. Risk factors associated with trichosporonosis include prolonged use of multiple, broad-spectrum antimicrobials, prolonged hospitalisation, Intensive Care Unit (ICU) stay, neutropenia, chemotherapy, prophylactic/empirical antifungal therapy, and catheterisation [2]. As Trichosporon spp. may be part of the normal flora of human skin and perineal area, it can colonise the catheter and enter the bloodstream, causing infection [3]. It forms a biofilm that helps it evade host immune responses and the action of antifungal drugs [4].

During the past few decades, it has emerged as an opportunistic pathogen causing invasive infections in immunocompromised patients [5]. Trichosporon Fungemia (TF) is the main type of opportunistic infection, accounting for around 74.7% of infections [6], but it can also affect most organs of the human body. There are various challenges associated with trichosporonosis, such as its clinical significance, diagnosis, and management. In urine cultures, Trichosporon might be a coloniser or a pathogen causing UTI [7]. Trichosporon spp. can also colonise the perigenital region in the normal population at a rate of 11.15% [9]. These infections pose a challenge for clinicians, as there are no clear and specific guidelines for the clinical interpretation of Trichosporon spp. recovery in urine, and it is important to differentiate between colonisation and infection [9,10]. Trichosporon spp. is often misdiagnosed and treated as candida infections. Due to its inherent resistance to echinocandins, treatment becomes difficult in these patients [11]. Hence, proper identification and Antifungal Susceptibility Testing (AFST) of the pathogen are crucial in the treatment of patients.

Although there are case reports and reviews on invasive trichosporonosis, there are few studies from South India regarding the clinical-microbiological spectrum of trichosporonosis [3,4,12]. In the present study, rare species like Trichosporon dohaense have been isolated, and the sites from which they were isolated were also...
not frequently reported in previous literature. Hence, the present study would provide overall knowledge on the clinical features, risk factors, microbiological spectrum, and management of patients with *Trichosporon* spp. isolated from various samples.

**MATERIALS AND METHODS**

The present study was a retrospective observational study conducted at Nizam’s Institute of Medical Sciences, Hyderabad for a period of one year from January 2019 to December 2019. The final sample size was 14 cases. As this was a time-bound study, records available for the required isolate in the study duration, only those cases where taken into consideration in the study. As this was a retrospective study of samples routinely sent to the department, and history was collected for reporting of isolates as a routine, no Institutional Ethics Committee (IEC) approval was obtained.

**Inclusion criteria:** All patients with clinically significant isolation of *Trichosporon* spp. from various samples during that period were included in the study.

**Exclusion criteria:** Other patients who did not satisfy the above criteria were excluded.

**Study Procedure**

In present retrospective study, the details regarding demographic data such as age, sex, risk factors, clinical features, microbiological diagnosis, treatment, and outcome of patients with invasive trichosporonosis were analysed from the case records.

The risk factors mentioned previously in the literature were considered in this study [2]. Samples were processed for aerobic and fungal cultures. The samples were inoculated onto Chromogenic agar plates (bioMerieux), 5% sheep blood agar plates (bioMerieux), and Sabouraud dextrose agar. The plates were incubated at 37°C for 48 hours. Identification of the cultures was done using the Vitek® 2 Compact system with the yeast panel YST (bioMerieux). AFST was performed using BMD according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) [13]. As no clinical breakpoints for *Trichosporon* spp. have been established by CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST), the following breakpoints were used: the isolate was considered susceptible if the MIC value was 2-8 μg/mL for Fluconazole, ≤1 μg/mL for Amphotericin B, as suggested by Wolf DR et al., and ≤1 μg/mL for Voriconazole, as suggested by Pfaffer MA et al., [14,15]. The isolates were sent to the National Culture Collection of Pathogenic Fungi (NCCPF), Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, for confirmation of identification by MALDI-TOF.

**STATISTICAL ANALYSIS**

Descriptive statistics were used for analysis. Categorical data were described as frequencies with percentages. The data were entered into a Microsoft Excel sheet and analysed using SPSS version 20.0.

**RESULTS**

There were 14 cases of trichosporonosis during the study period.

The predominant age group was 60-70 years [Table/Fig-1]. The number of males were 12, and the number of females were two, resulting in a male-to-female ratio of 6:1. The range of hospitalisation was from 6-34 days, with a median of 10.5 days. The predominant risk factor was the administration of broad-spectrum antibiotics in 13 out of 14 cases (92.8%) patients [Table/Fig-2]. The clinical presentation of the patient at admission is presented in [Table/Fig-3].

*Trichosporon* spp. was isolated from the urine in 10 patients (71.4%). Among these patients, seven out of 10 (70%) had Catheter-Associated Urinary Tract Infections (CA-UTI), and three out of 10 (30%) had pyelonephritis. Other samples included blood in two out of of 14 patients (14.2%) and tissue in two out of 14 patients (14.2%). Of the two patients with TF, the patient with ALL had a central line present and received empiric antifungal therapy for 20 days. *Trichosporon asahii* [Table/Fig-4] was the predominant species isolated in 12 patients (85.7%). Other *Trichosporon* spp. include *Trichosporon inkin* and *Trichosporon dohaense* [Table/Fig-5]. All the isolates were sensitive to voriconazole and amphotericin B. Of 14 isolates, 9 (64.2%) were sensitive to fluconazole, as shown in [Table/Fig-6].

Seven patients (50%) were discharged and treated with voriconazole for a period of 14 days, with advice to follow-up. Mortality due to

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**S. No.** | **Age (n years)** | **n (patients)**
--- | --- | ---
1 | 0-10 | 0
2 | 11-20 | 0
3 | 21-30 | 2
4 | 31-40 | 0
5 | 41-50 | 3
6 | 51-60 | 2
7 | 61-70 | 4
8 | 71-80 | 3

**Table/Fig-1:** Age group of patients.

**S. No.** | **Risk factor** | **n% (patients)**
--- | --- | ---
1 | Prolonged broad antibiotic therapy | 13 (92.8) Range: 6-30 days
2 | Prolonged ICU stay | 8 (57.1) Range: 7-30 days Median: 10 days
3 | Central venous catheter | 8 (57.1) Range: 1-25 days Median: 10-12 days
4 | Urinary catheter | 6 (42.8) Fluconazole-5 Fluconazole-casposfungin-1 Range: 3-18 days
5 | Previous antifungal therapy | 5 (35.7)
6 | Diabetes | 2 (14.2)
7 | Chemotherapy | 2 (14.2)
9 | Corticosteroids | 2 (14.2)
10 | Neutropenia | 1 (7.1)

**Table/Fig-2:** Risk factors associated with trichosporonosis (N=14).

**S. no.** | **Clinical condition** | **n (patients)** | **Percentage** | **Specimen isolated**
--- | --- | --- | --- | ---
1 | Traumatic | 4 | 28.5 | Urine
2 | Fracture of the femur with urosepsis and acute kidney injury | 1 | | Urine
3 | Crush injury | 1 | | Tissue
4 | Frontotemporal parietal craniotomy with sepsis | 2 | | Urine
5 | Bilateral loin pain-Bilateral pyelonephritis | 3 | 21.4 | Urine
6 | Chronic kidney disease with haemodialysis and recurrent UTI | 2 | 14.2 | Urine
7 | Haematological malignancy | 2 | 14.2 | Urine
8 | APML | 1 | | Urine
9 | ALL | 1 | | Blood
10 | Bilateral pneumonia | 1 | 7.1 | Urine
11 | Acute febrile illness | 1 | 7.1 | Blood
12 | Rétroviral disease with bedsore | 1 | 7.1 | Tissue

**Table/Fig-3:** Clinical presentation of patients at the time of admission (N=14).

APML: Acute promyelocytic leukaemia; ALL: Acute lymphoblastic leukaemia.
underlying disease was reported in 5 (35.7%) patients. Among the five patients, two died before the culture report was available, and three patients died after 1-6 days of treatment. Two (14.2%) patients left against medical advice before receiving the culture report. This information is presented in Table/Fig-7.

**DISCUSSION**

The first case of invasive trichosporonosis was described by Watson KC and Kallichurum S in 1970 [16]. Since then, several cases of trichosporonosis have been reported worldwide. It is the second most common agent causing disseminated yeast infections in cases of haematological malignancies, with high mortality [17]. In a medical centre in Taiwan [2], out of the 19 patients with invasive trichosporonosis, 14 (74%) had bloodstream infections, 3 (16%) had pulmonary infections, 1 (5%) had a central nervous system infection, and 1 (5%) had a soft-tissue infection. In the present study, 10 (71.4%) had UTIs, 2 (14.2%) had bloodstream infections, and 2 (14.2%) had soft tissue infections.

In the study from Taiwan, it was found that 95% of patients had received antibiotic therapy within 1 month of hospital admission, 90% had central catheters, 58% had malignancy, and 47% were admitted to the intensive care unit [2]. A review of Trichosporon infections found that 68.9% of patients had received antimicrobial therapy and were in intensive care units [18]. In a large review from 1975-2014, 52.8% of patients with fungemia had a central line [19]. In the present study, 13 (92.8%) received broad-spectrum antibiotics, 6 (42.8%) were on previous antifungal therapy, 8 (57.1%) were in the ICU, 7 (50%) had urinary catheters, 2 (14.2%) each were on chemotherapy and corticosteroids, and one (7.1%) patient had neutropenia. The hospitalisation period ranged from 6 to 34 days, with a median of 10.5 days. Although 8 (57.1%) patients had a central line, only 1 patient had TF.

Co-morbidities such as anaemia and hypoalbuninaemia [20], diabetes [2], haematological malignancy [17,19,21], retroviral diseases, peritoneal dialysis, and solid tumours [1,12] may lead to infection with *T. asahii*. Disruption of the skin and mucous membranes may also lead to *Trichosporon* infections in patients with chronic illnesses [5,12]. In the present study, 5 (35.7%) patients were diabetic, 2 (14.2%) patients had haematological malignancies, 2 (14.2%) patients were on haemodialysis, and 1 (7.1%) had a retroviral disease.

In a review from 1975-2014, 185 cases of TF were reported [19]. There have been numerous reports of TF in the literature [17,21], and the largest series of 115 cases was reported from Taiwan [22]. In the present study, 2 (14.2%) patients had fungemia. One patient was a case of acute lymphocytic leukaemia with febrile neutropenia on immunosuppression and empirical antifungal therapy for 20 days. The other patient was a case of acute febrile illness. The incidence of urinary infection by *T.asahii* has increased in recent years in hospitals, particularly in patients with urinary obstruction, prolonged bladder catheterisation, and broad-spectrum antibiotics [7,10]. In some cases, it may lead to renal damage and worsen renal dysfunction [10].

In a study from Brazil, it was found that 6% of urine cultures from severely ill patients in the ICU showed the growth of *Trichosporon* spp. [23]. There have been reports of urinary trichosporonosis in renal transplant patients [9] and patients with urinary catheters [7,10]. Another study from Chennai, India, reported two cases of complicated UTI caused by *Trichosporon loubieri* after catheterisation [3]. In the present study, *Trichosporon* spp. was isolated from urine in 10 (71.4%) patients. Three patients were diagnosed with pyelonephritis, and seven patients had catheter-related UTIs. The duration of hospitalisation ranged from 6 to 34 days.

*Trichosporon* was isolated from pus in a case of mastoiditis [24] and tissue in a case of skin ulcer [25]. In the present study, it was isolated from tissue in two cases. *T.asahii* is the most common species of *Trichosporon* isolated from various samples. In a study from Brazil, *T.asahii* was the predominant species isolated in 76.6% of cases [8]. In the present study, 12 (85.7%) of the isolates were *T.asahii*. *T.inkin* has rarely been reported as a cause of deep fungal infections, but it can also cause severe illness in patients with predisposing factors. It can even lead to disseminated infection in immunocompromised patients [26]. In a study from Brazil, approximately 10.7% of perigenital skin in asymptomatic males was colonised with *T.inkin* [8]. In the present study, *T.inkin* was isolated from the urine of a patient with pyelonephritis.

*T.dohaense* is a rare species that causes human infections. It was first isolated in 2009 in Qatar, accounting for 11.1% of clinical isolates of *Trichosporon* from immunosuppressed patients with onychomycosis, catheter-related infection, and tinea pedis [27]. It has also been isolated from the blood cultures of two patients from China [28]. In the present study, one isolate of *T.dohaense* was obtained from the tissue of a patient with a crush injury.

Triazoles appear to have better activity against *Trichosporon* spp. compared to amphotericin B [9,29], and patients treated with azoles have shown longer survival rates [30]. In-vitro resistance to amphotericin B has been observed in several *Trichosporon* species, making it unsuitable for invasive infections. Voriconazole is the preferred agent due to its effective in-vitro and in-vivo activity against most *Trichosporon* spp. [31]. In the present study, patients who were discharged received voriconazole treatment for a period of 14 days, with follow-up advised.
Echinocandins have limited or no activity against Trichosporon spp. and are not recommended for the treatment of trichosporonosis. Additionally, prophylactic use of echinocandins may lead to breakthrough trichosporonosis [32]. In the present study, six patients received prophylactic antifungal therapy.

In a review of 203 cases, the all-cause mortality rate for Trichosporon infections caused by Trichosporon spp. was found to be 44.3% [18]. In the present study, the overall mortality rate was 35.7%. The present study provides an overview of various cases of trichosporonosis, including those involving urine, blood, and tissue samples. Species identification was confirmed using MALDI-TOF, and a rare species, T.dohaense, was isolated. The highlighted risk factors associated with invasive trichosporonosis are similar to other fungal infections. However, the treatment for Trichosporon differs from other yeast infections, such as Candida. Therefore, identification and AFST of the isolate are important for effective management of these infections.

Limitation(s)
The study was of a relatively short duration and included a limited number of patients who had significant isolation of Trichosporon spp. from various samples during that period. Conducting multicenter studies with larger sample sizes would provide a better understanding of the infection.

CONCLUSION(S)
Urinary Tract Infection (UTI), particularly Catheter Associated Urinary Tract Infection (CA-UTI), was the most common clinical presentation of trichosporonosis in the present study. Prolonged broad-spectrum antibiotic therapy was identified as the most common risk factor. The growth of Trichosporon spp. from various samples cannot be disregarded and should be interpreted with caution, as the organism can also exist as a coloniser in different body sites. Therefore, a high index of clinical and microbiological suspicion is required for the optimal diagnosis and treatment of Trichosporon infections.

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REFERENCES