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# Systemic candidiasis by *Candida kefyr*: Case series from Pakistan

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## Abstract

Fungal diseases in humans cause high mortality and morbidity, especially in immunocompromised patients. *Candida kefyr* has rapidly emerged as an invasive pathogen affecting immunocompromised individuals, particularly patients with indwelling central lines, mechanical ventilation, more extended hospital stays, and on hematological malignancies. We present two cases of *C. kefyr* infections reported from our hospital. This case series highlights the emergence of novel opportunistic fungi, which clinicians and laboratorians need not ignore.

**Keywords:** Systemic candidiasis, *Candida kefyr*, immunocompromised

## Introduction

### Background

The emergence of resistant fungal infections has been a critical healthcare concern. These have resulted in increased morbidity and mortality, especially in immunocompromised patients.**[1]** *Candida spp.,* although described as asymptomatic commensal, has now evolved as the primary pathogen causing life-threatening invasive infections.**[2]** It is regarded as a "disease of diseased" in immunocompromised patients.**[3]**

*Candida albicans* account for > 50 % of candidemia/ invasive candidiasis cases. Since the last few decades, other Candida species, including *C. kefyr, C. auris, C. haemulonii* complex members, *C. glabrata, C. guilliermondii, C. krusei, C. lusitaniae, C. rugosa* are frequently being reported from nosocomial infections with high mortality rates. **[4-7]** The extensive use of immunosuppressive therapies and broad-spectrum antifungal prophylaxis resulted in this transition. The emergence of inherent or acquired resistance to major antifungal agents is alarming.**[8]**

*Candida kefyr* (*Kluyveromyces marxianus*), previously isolated from dairy products, has also been reported from clinical samples and the hands of healthcare workers.**[9]** *C. kefyr* has rapidly emerged as an invasive pathogen affecting immunocompromised individuals, particularly patients with indwelling central lines, mechanical ventilation, more extended hospital stay, and on hematological malignancies.**[10]** Moreover, recent studies have reported reduced sensitivity of *C. kefyr* to Amphotericin B, which has raised concern in the healthcare community.**[11]** The epidemiology of *C. kefyr* needs to be better understood due to the lack of data available, particularly from our part of the world. This study reports, for the first time, the emergence of *C. kefyr* strains infecting human patients in Pakistan.

## Case Reports

### Patient No. 1:

A 77-year-old female reported complaints of shortness of breath, wheezing, and productive cough with a copious amount of whitish sputum in the emergency department. She was a known case of COPD with a history of pulmonary tuberculosis 6 years back, for which she completed ATT and was on LTOT for the past 4 yrs. She was conscious and oriented on examination, with a pulse rate of 112/min, blood pressure 130/80mmHg, and oxygen saturation of 97%. Chest auscultation revealed bilateral Ronchi and coarse crepitation in all lung fields. No significant finding was found on the X-ray chest, and the MRI brain reported no intra/extra-axial lesion or hematoma.

Laboratory findings were unremarkable except for the sputum C/S sent to the microbiology department, which revealed pure heavy growth of lactose fermenting *Candida spp*. Primary identification was made on MacConkey agar which yielded large, rough pink colonies, whereas growth on SDA at 25oC lost smooth, shiny off-white colonies of *Candida spp*. The isolated strain was identified phenotypically by standard mycological procedures such as Gram stain. The sample was sent to NRL at NIH Islamabad for confirmation up to species level and antifungal susceptibility. Isolate was confirmed by MALDI-TOF mass spectrometry (bioMerieux, France) as *C. kefyr*. Antifungal susceptibility was tested using VITEK 2

(bioMerieux, France). The isolate was found sensitive to Amphotericin B, Voriconazole, and Flucytosine. The patient was started on Itraconazole and Hydrocortisone and was advised chest physiotherapy. The patient improved with therapy and was shifted to the chest ward and later discharged.

**Patient No. 2:**

A 62-year-old female presented in the emergency department complaining of oliguria, hematuria, and fever (100oF) for 3 days. She had an acute confusional state and loss of memory. She had a history of CCF with EF < 45 %, DM with left foot amputation, and multiple hospital visits due to recurrent UTIs. Lower limb Doppler suggested monophasic flow in the right dorsal pedis. A plain CT scan brain revealed chronic lacunar infarcts in the right centrum semiovale, left the periventricular region, and pons, with white matter microangiopathic ischemic changes. Laboratory findings revealed deranged RFTs with CrCl <120mg/dl. Urine R/E showed numerous pus cells and red blood cells. Urine culture was inoculated on CLED, and after 48 hrs of incubation at 37oC, there was pure growth of lactose fermenting smooth, shiny colonies confirmed on Gram stain to be *Candida spp*. The sample was sent to National Reference Laboratory at NIH Islamabad for confirmation up to species level and antifungal susceptibility. Isolate was confirmed by MALDI-TOFmass spectrometry (Biomerieux, France) as *C. kefyr*. Antifungal susceptibility was tested using Vitek 2. The isolate was found sensitive to Amphotericin B, Voriconazole, and Flucytosine. The patient was put on IV Voriconazole, but due to underlying debilitating illnesses, the patient could not survive.

## Discussion

Non-albicans *Candida spp.,* previously considered non-pathogenic, are now being considered responsible for debilitating infections in immunocompromised patients. In this case series, the two patients infected with *C. kefyr* had underlying chronic illnesses and prolonged drug therapies that affected their immune systems. The first patient had pulmonary tuberculosis, whereas the second had DM and CCF, which increased the risk of fungal infections. Both the *C. kefyr* isolates from our hospital were susceptible to Amphotericin B, Voriconazole, and Flucytosine. Other studies, however, reported some resistance to Amphotericin B. **[12,13]**

*C. kefyr* is increasingly being isolated from patients with neutropenic leukemia. **[14]** Recently, *C. kefyr* was described as a pathogen causing invasive fungal enteritis in a patient with an underlying hematological disease following bone marrow transplantation.10 Sendid et al. reported a twofold detection rate of *C. kefyr* isolates from adult patients in onomatology wards compared to patients in other wards (4.8 % vs. 1.9 %).**[15]**

## Conclusion

Among non-albicans *Candida spp., C. kefyr* has emerged as a significant pathogen in nosocomial infections. This study reports the emergence of *C. kefyr* strains from Pakistan for the first time. It is highly recommended that its isolation from the clinical specimens should no longer be ignored or considered a contaminant. An early diagnosis and prompt treatment may improve the morbidity and mortality rates.

## List of Abbreviations

COPD - chronic obstructive pulmonary disease
ATT - anti-tuberculosis therapy
LTOT - long-term oxygen therapy
MRI – Magnetic resonance imaging
C/S – Culture and sensitivity
SDA - Sabouraud-dextrose agar
NRL - National Reference Laboratory
NIH - National Institute of Health
MALDI-TOF – Matrix Assisted Laser Desorption Ionization – Time Of Flight
CCF - Congestive cardiac failure
EF – Ejection fraction
DM - diabetes mellitus
UTI - Urinary tract infection
CT – Computed tomography
CrCl – Creatinine clearance
RFT - Renal function test
R/E – Routine examination
CLED - Cysteine lactose electrolyte deficient agar
IV – Intravenous

## Declarations

**Ethics approval:** Approval to conduct this study was acquired from Ethical Review Committee, Fauji Foundation Hospital, Rawalpindi.

**Consent for publication:** Not applicable.

**Availability of data and materials:** Not applicable.

**Competing interest:** None to declare.

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**Author's contribution:** SS wrote the manuscript and made substantial contribution to the concept and design of the article, AA provided advanced laboratory diagnostic techniques for the identification of isolates, HA and SI contributed in analysis and interpretation of data, MWA and SAA revised the manuscript critically and approved the version to be published.

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