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# Ten-year prevalence of fungal peritonitis in the city of Nis, South Serbia

**Research Article**

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**Abstract:** Fungal peritonitis is a rare but serious complication in patients with chronic renal failure on continuous ambulatory peritoneal dialysis (CAPD). The purpose of this study was to report the prevalence of fungal peritonitis in patients on CAPD in the Clinical Center-Nis (South Serbia) in the period from 1997 until the end of 2007. Fungal species were isolated in 66 cases (4.5%) of 1471 peritoneal fluid (PF) samples that we examined. During the study period, 22 (1.5%) cases of fungal peritonitis were registered. In 19 cases, *Candida* isolates were identified, *Candida albicans (C. albicans)* being the most common species (n=15). Two cases of fungal peritonitis caused by *Aspergillus fumigatus* and 1 possible case caused by *Cladosporium cladosporioides (Cl. cladosporioides)* were also detected.

**Keywords:** *Peritoneal dialysis • Candida spp. • Cladosporium cladosporioides*



## Abbreviations

peritoneal dialysis - PD
peritoneal fluid - PF
continuous ambulatory peritoneal dialysis - CAPD
Candida albicans - C. albicans
*Cladosporium cladosporioides - Cl. cladosporioides*

## 1. Introduction

Peritonitis is a serious clinical complication in patients with terminal chronic renal failure on peritoneal dialysis (PD). Fungi are an infrequent cause of peritonitis in patients on PD: the incidence of fungal peritonitis varies from 1% to 15% [1]. Yeast, and rarely filamentous fungi [2,3], are the most frequent causes of fungal peritonitis. In our study, the intent was to report all cases in our institution, from January 1997 until and including December, 2007, where fungal species were isolated from peritoneal fluid (PF) of patients with peritonitis on PD who exhibited some clinical and diagnostic characteristics of fungal peritonitis. We also describe one possible case of peritonitis caused by *Cladosporium cladosporioides (Cl. cladosporioides)*.

Microbiological data from the Department of Microbiology and Parasitology, Medical faculty-Nis (Serbia), and medical histories of patients on continuous ambulatory peritoneal dialysis (CAPD) from the Clinic for Nephrology, Clinical Centre-Nis, were reviewed.

## 2. Material and Methods

In the eleven year period, peritoneal fluid from 1471 patients was examined using standard mycological techniques (direct microscopic examination, culture, and until the end of 2000, by the antifungal susceptibility

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test). In the last 5 years of the study, the BACTEC 9240 system (Becton Dickinson and Company, MD, USA) for microbiological investigation of peritoneal fluid was used. Species and antifungal susceptibility of yeast genus *Candida* were differentiated using the commercial Candifast test (Mycolasma, France). The CandiFast test is a commercial kit for determining antifungal susceptibility to amphotericin B (4 μg/mL), nystatine (200 IU/mL), 5-fluorocytosine (35 μg/mL), econazole (16 μg/mL), ketoconazole (16 μg/mL), miconazole (16 μg/mL) and fluconazole (16 μg/mL).

*Candida albicans* (*C. albicans*) was identified using the germ tube formation test and by growth on chromogenic media (Cromogen albicans, Parquetecnologico de Madrid, Spain). Filamentous fungi were identified on the basis of their morphological and morphometric characteristics.

## 3. Results

In 66 cases (4.5%), fungal species were isolated from patients; 22 cases of fungal peritonitis were identified, accounting for 1.5% of all microbiology reports. In all cases, clinical signs (abdominal pain accompanied by abdominal guarding, fever, and cloudy dialysate effluent) of fungal peritonitis did not differ from those of bacterial peritonitis.

In 15 patients, the cause of fungal peritonitis was *C. albicans*, and in 4 cases, non-albicans species. In 10 cases, *Candida spp.* were isolated from the catheter site (9 isolates, *C. albicans*; 1 isolate, non-albicans *Candida spp.*). During this period, 2 cases of fungal peritonitis caused by *Aspergillus fumigatus* were detected. Forty-four cultures from PF-samples were positive for fungi. They were considered contaminants, since growth of such fungi was detected in only one of the PF samples examined. The patients had bacterial peritonitis and responded well to antibacterial treatment. Such presumed contaminants were identified as *Aspergillus fumigatus* (n=33), *Aspergillus niger* (n=3), *Penicillium spp.* (n=5), *Cl. cladosoprioides* (n=2) and *Geotrichum candidum* (n=1).

All patients received antibacterial agents; however, only 2 of the patients received systemic antifungal agents within 1 month of the PD diagnosis.

Isolates were tested for antifungal susceptibility in the period from 1997 until the end of 2000. Isolated yeast (9 isolates) *in vitro* showed susceptibility to amphotericin B, 5-fluorocytosine, nystatine, and ketoconazole, but were resistant to econazole, miconazole and fluconazole. Due to economic constraints, we did not perform antifungal susceptibility testing in the following years.

Until the end of 2000, 5-fluorocytosine was administered; this antifungal showed high effectiveness *in vitro*, and also improved clinical symptoms and signs of fungal infections in all 9 treated patients.

Clinical data shows that fluconazole was initially empirically administered in the remaining cases after year 2000. Duration of the antifungal therapy ranged from 10 to 28 days (intravenously). Fluconazole had high effectiveness in all treated patients, except in 3 cases of peritonitis caused by *C. albicans*. In these 3 cases, candemia persisted and amphotericin B was administrated to eliminate the fungal infection. In all cases of fungal peritonitis, the peritoneal catheter was removed.

During the study period, an interesting case of peritonitis was registered and diagnosed as possible fungal peritonitis caused by *Cl. Cladosporioides*, based on clinical and laboratory data.

The 68-year–old man was on CAPD for end-stage renal failure and had commenced CAPD 2 years prior to this episode of peritonitis. During that period, there had been 2 episodes of peritonitis: one episode was confirmed by culture as being caused by *Staphylococcus epidermidis* and other by *Eschericia coli*. These bacterial infections were treated appropriately.

The third episode, with a 2-day history of abdominal pain, was accompanied by a slightly elevated temperature, nausea, and cloudy PF. On examination, the patient was found to be febrile (37.3°C) and had a tense abdomen. The catheter site was clean without signs of inflammation. A complete blood examination showed an elevated white cell count with predominant neutrophils, an albumin level of 37 g/L, a urea level of 18.1x $10^6$ mmol/L , and a creatinine level of 370 x $10^6$ μmol/L. The patient had been admitted to the hospital with presumed bacterial peritonitis, and started on a peritonitis protocol. During the patient's hospital stay, 6 samples of PD fluid were sent for microscopy and culture. No significant organisms were detected in the first samples. Fungal growth was detected in the second sample (microscopically and by culture) and was also identified in the next 3 PD fluid samples. At this point, fluconazole was started intravenously at 250 mL per day for 28 days. The catheter was removed and a central venous catheter was inserted for hemodialysis.

For microbiological analysis, peritoneal fluid was collected and processed according to the standard laboratory protocol (direct microscopic examination, culture), using a BACTEC 9240 system in addition to the protocol. The presence of conidiae was confirmed after 2 days in wet preparation from the liquid media, and after 4 days the growth of fungi was evident on primary Sabouraud agar plates that had been incubated at 30°C.

The detection time of positive growth ranged from 2–4 days using a BACTEC system. Bacteriologic analyses of all samples were negative.

The fungi were determined to be of the *Cladosporium* genus by microscopic and macroscopic morphological characteristics: they grew rapidly within 5 days to a dark green colony with suede-like surface interrupted by irregular rugae. *Cladosporium*-type sporulation is characterized by the formation of freely branching hyphae that give rise to long chains of dark-staining, elliptical conidia that often show scars or dysjunctors at the site of attachment with conidiophore or another conidia [4].

Morphometric characteristics of the conidia were obtained by television image analysis (Nikon, Japan). We identified this species as *Cl. cladosporioides* by morphological and morphometric characteristics (conidioconidia are ellipsoidal or lemon-like in shape, measuring from 3.7 to 6 µm x 1.6 to 3.2 µm). Based on our laboratory findings and resolution of symptoms and signs of peritonitis after fluconazole treatment, we hypothesized that *Cl. cladosporioides* was a possible cause of fungal peritonitis.

## 4. Discussion

Fungal peritonitis caused by molds in patients under PD is a rare clinical problem. Peritonitis caused by *Aspergillus spp*. is described in the literature [5]; however, there is insufficient data about fungal peritonitis caused by *Cl. cladosporioides,* a ubiquitous organism that is thought to be one of the most common airborne fungi frequently isolated as a contaminant. Initially, based on literature data, *Cl. cladosporioides* was known to produce pulmonary infection and keratitis [6,7]. Later, it was reported to be the cause of cutaneous phaehyphomycosis [8]. We first reported this possible infection [9]. However, our observations suggest that these species may cause problems in patients on CAPD.

## 5. Conclusion

Based on our results, and in accordance with the results of other authors, the conclusion can be drawn that the majority of serious complications of fungal peritonitis in patients on CAPD are caused by *Candida spp.* [10-14]. Despite recent reports that non-albicans *Candida* species are more common in serious fungal infections, [12,14-16], our results showed exactly the opposite: that *C. albicans* is the most common cause of fungal peritonitis.

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