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Fungal peritonitis in peritoneal dialysis: a 5 years retrospective review in Northeast Thailand

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ABSTRACT

Introduction: Peritoneal dialysis (PD) is a widely used renal replacement therapy for end-stage renal disease patients, offering various advantages. However, fungal peritonitis, a rare but life-threatening complication, remains less understood than bacterial peritonitis.

Material and methods: This retrospective single-center study included all cases of fungal peritonitis in PD patients at Sakon Nakhon hospital, Northeast Thailand, from October 2017 to September 2022. Data on demographics, co-morbidities, prior antibiotic uses, laboratory values, microbiological features, treatments, and outcomes were collected.

Results: The study involved 32 PD patients with fungal peritonitis. Patients were on average 59.0 ± 11.29 years old, with a majority of females (68.8%). Diabetes (62.5%) was the leading cause of chronic kidney disease. Common co-morbidities included hypertension (75.0%) and diabetes (62.5%). Laboratory values showed variations, including elevated serum creatinine, urea levels, and low hemoglobin. Abdominal pain (81.3%) and clouding of dialysate (68.8%) were typical symptoms at presentation. Sepsis was present in 18.8% of patients. Candida species were the most common causative agents, with 100% receiving Amphotericin-B and 87.5% receiving Fluconazole for treatment. Most patients underwent catheter removal (93.8%). In terms of outcomes, 37.5% resumed PD, 43.8% transitioned to permanent hemodialysis, and the overall mortality rate was 15.6%.

Conclusions: This study provides valuable insights into fungal peritonitis in PD patients, underlining the significance of regional considerations in clinical management. The findings underscore the need for standardized guidelines for diagnosis and treatment, accounting for local variations in causative agents and outcomes.

Keywords: fungal peritonitis, peritoneal dialysis, end stage renal disease

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Introduction

Peritoneal dialysis (PD) is a widely used renal replacement therapy for patients with end-stage renal disease (ESRD). It offers several advantages, including the ability for patients to perform the procedure at home, flexibility in treatment schedules, and cost-effectiveness when compared to hemodialysis. However, peritoneal dialysis is not without its challenges, and one of the significant complications is peritonitis, which can be caused by bacteria or fungi. While bacterial peritonitis has been extensively studied and is well-documented, fungal peritonitis remains a less understood and under-explored complication of peritoneal dialysis.

Fungal peritonitis in peritoneal dialysis patients is a rare but severe complication with potentially life-threatening consequences. Fungal infections, particularly Candida and non-Candida species, can cause peritonitis when they breach the integrity of the peritoneal membrane, leading to inflammation and infection within the peritoneal cavity. The clinical presentation of fungal peritonitis can be subtle and often mimics bacterial peritonitis, making timely diagnosis and appropriate treatment essential. The incidence and characteristics

of fungal peritonitis in peritoneal dialysis patients may vary across different geographic regions and healthcare settings. It is crucial to understand the epidemiology, risk factors, clinical manifestations, treatment outcomes, and the causative fungal species associated with fungal peritonitis in specific regions to develop effective strategies for prevention and management.

As such, the present study aims to conduct a retrospective review of fungal peritonitis cases in patients undergoing peritoneal dialysis. The findings of this study will contribute valuable insights into the prevalence, characteristics, and outcomes of fungal peritonitis in a specific regional context. This information can inform healthcare providers, policy makers, and researchers in this area and beyond, helping to optimize prevention and management strategies for this potentially life-threatening complication of peritoneal dialysis.

Material and methods

Fungal peritonitis was defined by the presence of a positive yeast culture with one of the two subsequent: peritoneal effluent leucocyte count > 100 cells/mm^3 or clinical symptoms of peritonitis (abdominal pain, cloudy dialysate, fever). Death was considered secondary to the FP when both events occurred during the same hospitalization in a patient with active peritonitis or its related complications at the time of death. Permanent transfer to hemodialysis (HD) was defined in any patient for whom no transfer back to PD that was organized within the twelve months after the FP or at the end of the study period. Resumption of PD was defined by the placement of a new PD catheter and its successful use after a FP episode. A patient with more than one episode of FP during the study period was considered as two distinct FP events in the analysis of baseline characteristics and outcomes.

We conducted a retrospective single-center descriptive analysis that included all episodes of FP among all 672 PD patients monitored at Sakon Nakhon hospital in Northeast Thailand between October 2017 and September 2022. Outcomes were kept till September 2023. From medical records and PD clinic charts, information on the patients' demographics, co-morbidities, and prior antibiotic usage was gathered. Medical record reviews were also used to acquire laboratory information, peritonitis microbiological features, treatments, and outcomes.

The continuous variables were presented as the mean ± standard deviation. Categorical variables were presented as percentages or proportion. For the univariate analysis, we compared two groups for continuous variables using the Student's t-test when normally distributed, and the Mann-Whitney test when not. The Pearson χ^2 test was applied for analysis of nominal variables. Binary logistic regression analysis was performed to predict risk factors of in-hospital mortality. Odds ratio and the 95% confidence interval for each notable risk factor in the model was derived. All tests were two-tailed and $p < 0.05$ was considered significantly. Data was analyzed using Statistics Kingdom® (2017, Australia).

Results

The 5-year incidence of peritonitis was 22.7, 23.3, 22.6, 20.8 and 20.0 episodes per patient-year respectively. The study included a total of 32 peritoneal dialysis patients with fungal peritonitis among 562 peritonitis cases therefore made up 5.7% of all total events. The average age of the patients was 59.0 ± 11.29 years, with a higher representation of females (68.8%). The leading causes of chronic kidney disease was diabetes (62.5%). The majority of patients had co-morbidities, including hypertension (75.0%) and diabetes (62.5%). The average duration of PD was 2.7 ± 2.33 years. A significant proportion of patients had received antibiotics or experienced prior peritonitis in three months before fungal peritonitis onset, 56.3% and 50% respectively (Table 1).

Laboratory values at presentation (Table 2) showed a wide range of values, including serum creatinine, blood urea level, and electrolyte levels. Hemoglobin levels were notably reduced (average 8.9 ± 2.08 g/dL). Dialysate white cell counts were elevated (average 3,047.8 ± 5,652.83/mm^3).

Common symptoms at presentation included abdominal pain (81.3%) and clouding of dialysate (68.8%). Sepsis was present in 18.8% of patients. Candida species were the most common causative agents, with Candida non-albicans and Candida albicans being predominant. All patients received Amphotericin-B, and 87.5% received Fluconazole for treatment. Catheter removal was performed in the majority of cases (93.8%). Resumption of PD occurred in 37.5% of patients, while others transitioned to permanent hemodialysis (43.8%). The study observed a mortality rate of 15.6% (Table 3).

The study compared risk factors between survivor and non-survivor group. Sepsis at presentation and cardiovascular disease were statistically significant risk factors for non-survival group ($p = 0.01$). Other factors, such as gender, age, hypertension, diabetes, and laboratory parameters, were not statistically significant predictors of survival (Table 4).

Table 1. Demographic characteristics of patients

Characteristic	Number of cases (%)
Age (years)	59.0 ± 11.29
Gender	
Male	10 (31.3)
Female	22 (68.8)
Etiology of chronic kidney disease	
Diabetes	20 (62.5)
Hypertension	7 (21.9)
Urinary tract stone	4 (12.5)
Glomerular disease	1 (3.1)
Co-morbidity	
Hypertension	24 (75.0)
Diabetes	20 (62.5)
Cardiovascular disease	6 (18.8)
Immuno-insufficiency	1 (3.1)
Duration of PD [years]	2.7 ± 2.33
Prior antibiotics < 3 months	18 (56.3)
Prior peritonitis < 3 months	16 (50.0)

Table 2. Laboratory parameters of patients

Laboratory parameters	Mean present values
Serum creatinine [mg/dL]	9.9 ± 4.61
Blood urea level [mg/dL]	44.6 ± 29.31
Serum Na^+ [mEq/L]	132.2 ± 4.97
Serum K^+ [mEq/L]	3.5 ± 0.71
HCO_3 level [mmol/L]	23.9 ± 5.25
Hemoglobin level [g/dL]	8.9 ± 2.08
White cell count [/mm^3]	9,270.3 ± 4846.76
Neutrophil [/mm^3]	76.4 ± 12.52
Dialysate white cell	3,047.8 ± 5,652.83
Serum calcium [mg/dL]	8.3 ± 1.04
Serum phosphorus [mg/dL]	5.3 ± 10.26
Serum albumin [g/dL]	2.4 ± 0.72

Risk factors for prediction of mortality, sepsis at presentation and cardiovascular disease were identified as significant risk factors for predicting mortality, OR 18.75, 95% CI 1.88–186.43, p = 0.012 and OR 12.00, 95% CI 1.39–103.48, p = 0.024 respectively. While other factors, including gender, age, comorbidities, laboratory parameters, and previous antibiotic or peritonitis episodes, did not significantly predict mortality (Table 5).

Table 3. Presentation, causative agent, treatment and outcome

Characteristic	Number of cases (%)
Symptom at presentation	
Fever	10 (31.3)
Abdominal pain	26 (81.3)
Clouding dialysate	22 (68.8)
Sepsis at presentation	6 (18.8)
Causative agent	
Candida non-albicans	16 (50.0)
Candida albicans	13 (40.6)
Fusarium solani	2 (6.3)
Cryptococcus neoformans	1 (3.1)
Antibiotic treatment	
Amphotericin-B	32 (100.0)
Fluconazole	28 (87.5)
Duration of treatment (days)	20.5 ± 9.69
Catheter removal	30 (93.8)
Time interval between the onset of peritonitis and catheter removal (days)	9.4 ± 4.37
Staying on PD	1 (3.1)
Resumption of PD	12 (37.5)
Permanent HD	14 (43.8)
Death	5 (15.6)

Discussion

This study reported fungal peritonitis cases with an average age of 59.0 ± 11.29 years, which is in line with similar studies that have found fungal peritonitis to be more common in older PD patients [1–3]. The predominance of females in the study population aligned with previous research, suggesting a higher prevalence of female PD patients, possibly due to longer life expectancy [4, 5]. The leading causes of chronic kidney disease (CKD) in this study were diabetes and hypertension, consistent with known risk factors for CKD [6]. Moreover, cardiovascular disease was identified as a significant comorbidity, which is a known predictor of adverse outcomes in PD patients [7, 8]. The average duration of ongoing PD was 2.7 ± 2.33 years, which could influence the risk of developing fungal peritonitis. Long-term PD might lead to catheter-related complications, such as exit-site infections, tunnel infections, and catheter cuff extrusion, which could serve as potential entry points for fungal pathogens [9]. Prior antibiotics (56.3%) could alter the peritoneal microbiota and promote the

Table 4. Comparison of risk factors between survivor and non-survivor group

Risk factor	Survivor (n = 27) (%)	Non-survivor (n = 5) (%)	p-value
Male gender	9 (33.3)	1 (20.0)	0.55
Age ≥ 60 years	15 (55.6)	2 (40.0)	0.52
Sepsis at presentation	3 (11.1)	3 (60.0)	0.01*
Hypertension	21 (77.8)	3 (60.0)	0.78
Diabetes	16 (59.3)	4 (80.0)	0.38
Cardiovascular disease	3 (11.1)	3 (60.0)	0.01*
Prior antibiotics use < 3 months	15 (55.6)	3 (60.0)	0.85
Prior peritonitis < 3 months	14 (51.9)	2 (40.0)	0.63
Hematocrit < 24%	6 (22.2)	3 (60.0)	0.08
Albumin < 3 g/L	21 (77.8)	3 (60.0)	0.89
Effluent white cell > 3,000 /mm^3	7(25.9)	1(20.0)	0.78
No catheter removal	1 (3.7)	1 (20.0)	0.17
Catheter removal > 5 days	21 (77.8)	2 (40.0)	0.08

*statistical significance (p < 0.05)

Table 5. Risk factors for prediction of mortality

Factor	Odds ratio	95% Confidential Interval	p-value
Male gender	0.50	0.05–5.15	0.560
Age ≥ 60 years	0.17	0.02–1.75	0.137
Sepsis at presentation	18.75	1.89–186.43	0.012*
Co-morbidity			
Diabetes	2.75	0.27–28.04	0.393
Hypertension	0.43	0.06–3.19	0.408
Cardiovascular disease	12.00	1.39–103.48	0.024*
Laboratory			
Serum albumin < 3 g/dL	0.43	0.06–3.19	0.408
Hemoglobin < 8 g/dL	3.83	0.48–30.70	0.206
Dialysate white cell > 3,000/mm^3	0.71	0.07–7.52	0.779
Previous antibiotic < 3 months	1.20	0.17–8.38	0.854
Previous peritonitis < 3 months	0.53	0.08–3.73	0.526
Catheter removal > 5 days	0.23	0.03–1.70	0.151

*statistical significance (p < 0.05)

overgrowth of fungal organisms, particularly Candida species. Exposure to broad-spectrum antibiotics could disrupt the balance of microorganisms in the peritoneal cavity and create an environment conducive to fungal colonization [10]. Previous episodes of peritonitis (50%), whether bacterial or fungal, might increase the risk of recurrent fungal peritonitis. The peritoneal membrane could undergo structural changes and become more susceptible to infection after previous peritonitis episodes. Additionally, patients with a history of peritonitis might have alterations in their immune responses, making them more vulnerable to subsequent infections.

The study revealed significant laboratory abnormalities. These findings reflected the compromised kidney function and anemia frequently observed in PD patients, despite all patients receiving erythropoiesis stimulating agents. Low serum albumin concentration was important to note that inflammation and

malnutrition both reduce the concentration of albumin by suppressing the synthesis rate, while inflammation alone was associated with a greater fractional catabolic rate and increased shift of albumin out of the vascular compartment [11]. Abdominal pain and fever were the predominant symptoms, consistent with previous reports of clinical presentation in fungal peritonitis [12, 13]. Candida species were the most common causative agents, which was consistent with the global trend of Candida as the leading fungal pathogen in PD-related peritonitis [14, 15]. However, it was worth noting that the proportion of Candida non-albicans (50.0%) in this study was relatively high, emphasizing the diversity of fungal causative agents in different regions [16, 17].

The study reported that all patients received Amphotericin-B and catheters were removed 93.8%, which were standard treatments for fungal peritonitis in PD. The cornerstone of treatment for fungal peritonitis is antifungal therapy. Amphotericin-B is the preferred antifungal agent and is typically administered intravenously and intraperitoneally [18]. It has broad-spectrum activity against various fungal species, including Candida. Fluconazole is another antifungal option that may be used in combination with Amphotericin-B or as a sole agent, especially when the causative pathogen is susceptible to this drug. Removing the PD catheter is important to prevent reinfection and improve treatment outcomes. In some situations, if the patient's clinical condition improves rapidly with appropriate antifungal therapy, the catheter may be salvaged. However, this is less common, and close monitoring is necessary. In a study by Chang et al. (2011), catheter removal within 5 days was associated with a lower risk of recurrence and treatment failure in fungal peritonitis cases [19]. The study highlighted the importance of early catheter removal to improve clinical outcomes. In contrast, in two studies which the duration of catheter removal was not a significant predictor of mortality in patients with fungal peritonitis [20, 21].

The overall mortality rate of 15.6% was in line with previous studies that have reported mortality rates ranging from 10% to 35% [22, 23]. This highlighted the severity of fungal peritonitis and the challenges in achieving favorable outcomes. A study by Szeto et al. (2008) found that sepsis at presentation was associated with a higher mortality rate in patients with recurrent fungal peritonitis [24]. This aligns with the present study's findings and underscores the importance of recognizing and managing sepsis in fungal peritonitis. The impact of cardiovascular disease on mortality in fungal peritonitis has been highlighted in various studies [25, 26]. In a position statement by Piraino et al. (2011), cardiovascular disease was mentioned as a comorbidity that could lead to adverse outcomes in peritoneal dialysis-related infections, including fungal peritonitis [27]. Studies on peritoneal dialysis-related infections have often pointed to the significance of laboratory parameters. For instance, in a study by Davenport (2009), elevated inflammatory markers, including low serum albumin, were associated with a higher risk of peritonitis-related complications [28]. The role of dialysate white cell counts in predicting outcomes in peritonitis had been explored in some studies [29, 30]. Increased white cell counts had been linked to peritoneal membrane dysfunction and worse clinical outcomes in peritonitis.

Limitation

Because the surveyed hospital was a small tertiary hospital in a rural area. Therefore, there is no potential to separate the species of Candida non-albicans fungi. While research comparing peritonitis between bacterial and fungal in peritoneal dialysis related peritonitis is very interesting. This may require further study.

Conclusions

The results of this study emphasize the need for heightened vigilance in the management of PD patients, particularly those with cardiovascular comorbidities. Early recognition of fungal peritonitis, aggressive treatment with appropriate antifungal agents, and consideration of catheter removal are crucial in improving survival rates. Additionally, ongoing monitoring of laboratory parameters, including anemia and electrolyte imbalances, can aid in early detection and management of complications.

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