Peritoneal Dialysis-related Peritonitis: Microbiological Profile and Outcome

Periton Diyalizi İlişkili Peritonit: Mikrobiyolojik Etkenler ve Klinik Sonlanım

Arzu Özdemir, Sibel Yücel Koçak
University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Nephrology, Istanbul, Turkey

Objectives: Peritonitis is a major complication of peritoneal dialysis (PD) and leads to significant mortality and technical failure. Understanding local peritonitis rates and microbiologic profiles is important for the prevention and appropriate management of PD-related peritonitis. We investigated the incidence rate, causative agents, and outcomes of PD-related peritonitis episodes.

Methods: This retrospective study enrolled all patients who were receiving PD and had been treated for PD-related peritonitis between February 2005 and November 2021 in our PD unit. Data of the patients included demographic characteristics, causes of primary renal disease, microbiology, and outcomes (resolution, catheter loss, and death) of peritonitis episodes.

Results: During the study period, 143 PD-related peritonitis episodes were identified in 69 patients. The peritonitis rate was 0.56 episodes per patient-year. Overall, 62.9% of the episodes were due to Gram-positive organisms, 32.1% were due to Gram-negative organisms, 3.4% were culture negative and 1.3% were candida. Coagulase-negative staphylococci were isolated in half of the Gram-positive episodes. Acinetobacter and Pseudomonas were the most frequently observed microorganisms among Gram-negative episodes. Overall, 81.1% of cases improved completely with medical treatment. The PD catheter was removed in 27 (18.8%) patients, and two patients died from sepsis. Gram-negative organisms resulted in a significantly higher rate of catheter removals and a lower rate of resolution than Gram-positive organisms (p<0.001).

Conclusion: Reducing the incidence of PD-related peritonitis could be possible by knowledge of prevalent microbial agents in each center, adjusting empirical treatment accordingly, and taking the necessary measures to prevent peritonitis attacks.

Keywords: Peritoneal dialysis, peritonitis, microbiology, outcome

Address for Correspondence: Arzu Özdemir, University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Nephrology, Istanbul, Turkey
Phone: +90 532 695 79 62 E-mail: arzukayalar@yahoo.com ORCID ID: orcid.org/0000-0001-7651-7282

Cite as: Özdemir A, Yücel Koçak S. Peritoneal Dialysis-related Peritonitis: Microbiological Profile and Outcome. Med J Bakırköy 2022;18:25-30

Received: 09.12.2021
Accepted: 19.01.2022

©Copyright 2022 by Medical Journal of Bakırköy published by Galenos Yayınevi.
INTRODUCTION

Peritoneal dialysis (PD) is one of two principal modalities of renal replacement therapy and an alternative to hemodialysis. Despite the advances in technology and antibiotic therapy, PD-related infections, including peritonitis, tunnel infections, and exit-site infections, remain common and serious complications of PD (1). Peritonitis is associated with significant morbidity, structural and functional alterations of the peritoneal membrane, transient loss of ultrafiltration, eventually permanent membrane damage, catheter loss, transfer to hemodialysis, and occasionally death (2-5). Therefore, knowledge of the causative agent, course, and predisposing factors of peritonitis is important for the appropriate management and prevention of PD-related peritonitis. We determined the incidence rate, microbiological characteristics, and outcomes of PD-related peritonitis.

METHODS

This single-center study was conducted through retrospective examination of all patients who were treated for PD-related peritonitis in our PD unit between February 2005 and December 2021. Standard Tenckhoff catheter was placed in all patients with PD. All episodes of PD-related peritonitis were reviewed. Peritonitis was diagnosed if at least two of the following criteria were present: (a) Presence of symptoms and signs related to peritonitis, i.e. a cloudy peritoneal effluent or abdominal pain, (b) peritoneal effluent white blood cell count higher than 100/μL, with at least 50% polymorphonuclear cells, and (c) positive culture of peritoneal effluent. The exclusion criteria was incomplete clinical data. Empirical antibiotic therapy was initiated after appropriate microbiological specimens have been obtained. First, all episodes were treated with ciprofloxacin and intraperitoneal vancomycin, based on the center-specific treatment protocol, unless the patient had features of systemic sepsis. Antibiotic therapy was adjusted as soon as the culture results were obtained. The duration of antibiotic therapy was 14-21 days based on the causative organism.

Demographic and clinical characteristics for all patients, including age, sex, the underlying cause of end-stage renal disease (ESRD), PD modality (continuous ambulatory PD or automated PD), duration of PD, episodes, etiology, and outcomes (resolution, catheter removal, and death) of peritonitis, and presence of concomitant tunnel or exit site infection were recorded. The resolution was defined as the disappearance of signs and symptoms within 96 h after the beginning of antibiotic therapy and a negative peritoneal fluid culture at least 28 days after treatment completion. Death related to peritonitis was defined as the death of the patient with active peritonitis or admitted with peritonitis or death within 30 days of a peritonitis episode. Catheter removal was indicated for refractory or relapsing peritonitis and peritonitis of fungal etiology. Peritonitis rate was calculated as the number of peritonitis episodes per number of patients-years at risk. The time at risk of peritonitis was counted from the first day of training till the occurrence of peritonitis.

This study was approved by the University of Health Sciences Turkey, Hamidiye Clinical Research Ethics Committee (decision no: 5/53, date: 05.02.2021) and adhered to the principles of the Declaration of Helsinki. Patient consent was not obtained due to the retrospective design of the study.

Statistical Analysis

Study results were expressed as numbers and percentages for categorical variables, and means ± standard deviations or data ranges for continuous variables. Variables were compared using the chi-square test. P-values of ≤0.05 were thought to be significant. Data were analyzed using SPSS Statistics version 24 for Windows (IBM, New York, U.S.).

RESULTS

During the study period, 69 (27.9%) of 247 chronic patients with PD developed 143 episodes of PD-related peritonitis over 3,028 patient months, with an overall peritonitis rate of 0.56 episodes/patient year. The demographic data of the patients with PD-related peritonitis are shown in Table 1. Thirty five (50.8%) were female, and 49 (71%) received continuous ambulatory PD. ESRD was most commonly caused by hypertension (40.5%) and diabetic nephropathy (27.5%).

Among the patients with PD-related peritonitis, 35 (50.7%) experienced one episode, 14 (20.2%) had two and the rest of the patients (28.9%) had ≥3 episodes. None of the patients had polymicrobial peritonitis. The distribution of organisms is shown in Figure 1. Gram-positive organisms were identified in 90 (62.9%) of peritonitis episodes. Among Gram-positive organisms, coagulase-negative staphylococci (CNS) was the most common Gram-positive species, accounting for 30.7% of total episodes and 48.8% of Gram-positive episodes. Gram-negative organisms were isolated in 32.1% of episodes. Among Gram-negative organisms, Acinetobacter and Pseudomonas contributed equally, followed by Escherichia coli and enterobacter. Fungal infections were observed in 1.3% of episodes and...
culture-negative peritonitis was seen in 3.4% of episodes. Organism-specific outcomes are shown in Table 2. Overall, Gram-positive infections were characterized by greater resolution with therapy and lesser need for catheter removal than Gram-negative organisms (88.8% vs 58.7%, and 10% vs 39%, p≤0.001, respectively). Among Gram-positive organisms, methicillin-resistant *Staphylococcus aureus* (MRSA) resulted in the highest catheter removal rate (23.8%). *Klebsiella* infections had the worst outcome with a 75% catheter removal rate and 25% of mortality. Fungal infections almost always resulted in catheter removal. The overall catheter removal rate was 18.8%. Two episodes resulted in death, which is caused by MRSA and *Klebsiella*.

**DISCUSSION**

This study describes the microbiological profiles and outcomes of PD-related peritonitis. Our data showed that Gram-positive organisms are the main etiological agents of peritonitis. Moreover, the results demonstrated that gram-negative organisms are associated with a lower resolution rate and a higher need for catheter removal, and candida infections always resulted in catheter loss.

There is a substantial variation in the incidence of PD-related peritonitis reported by different centers and countries, ranging from 0.06 to 1.66 episodes/patient-year (6). This probably result from different practices in the use of prophylactic antibiotics, in the training of PD staff, and varieties in guidelines (7). In our center, the overall incidence rate of PD-related peritonitis was 0.56 per patient-year at risk, which is higher than the International Society of Peritoneal Dialysis (ISPD) limit of 0.5 episodes per patient-year (8).

The present results showed that Gram-positive peritonitis rates exceed Gram-negative rates, similar to the previous studies in which Gram-positive bacteria accounted for approximately two-thirds of the peritonitis episodes (9-11).
Among gram-positive peritonitis, CNS was the most common organism isolated in the current study, in line with the literature (12-14). Moreover, Pseudomonas and Acinetobacter were the most commonly isolated organisms among Gram-negative peritonitis episodes in our study, in contrast with previous studies in which Escherichia coli was the most common causative agent (13,15,16). Interestingly, 6 patients developed Acinetobacter infection at the same time in our facility and PD catheter was removed in all of them. Acinetobacter is rarely reported in association with PD-related peritonitis but it results in serious infection and increases the possibility of drop-out or mortality. In a multicenter study conducted in Australia (17), 253 (2.3%) of 11,122 peritonitis episodes were developed due to Acinetobacter species. One hundred thirty one (74%) out of 176 patients who developed a single episode of Acinetobacter peritonitis recovered completely with antibiotic therapy. In contrast to our results, Htay et al. (17) reported that the rates of withdrawal of PD catheter and conversion to hemodialysis were lower with Acinetobacter peritonitis than with Pseudomonas peritonitis. Acinetobacter can be isolated from skin, respiratory tract, and aqueous sources including river waters, humidifiers, and water baths used to warm peritoneal dialysate before administration. The most common causes of Acinetobacter peritonitis in patients with PD are a break in exchange sterility, and exit site infection/tunnel infection. None of the participants in our cohort had exit site infection or tunnel infection. We suggested that the development of Acinetobacter peritonitis results from the hygiene breaks and contaminated medical equipment. Appropriate measures, such as education of patients, healthcare providers, and caregivers on good hygiene were taken. Additionally, healthcare providers paid attention to infection control practices, including rigorous cleaning of the shared medical equipment and patient rooms to reduce the spread of Acinetobacter.

The culture negativity was 3.6% in our study, which is lower than the recommended range by ISPD (8) that should not be more than 20%. Culture negativity may be a result of technical problems with the dialysate cultures, recent antibiotic use, and infection by fastidious organisms. In our center, PD staff takes PD fluid samples for culture in all patients with suspected peritonitis in adherence to international recommendations on diagnostic methods.

Severe and prolonged peritonitis episodes are a major cause of patients discontinuing PD and switching to hemodialysis. Therefore, early and appropriate treatment of peritonitis is important for rapid resolution of inflammation.

### Table 2. Microbiology and outcome of peritonitis episodes

| Organism                        | Episode (n=143) | Resolution (n=112) | Catheter removal (n=29) | Death (n=2) |
|---------------------------------|-----------------|--------------------|------------------------|-------------|
| Gram-positive                   | 90 (62.9)       | 80 (88.8)          | 9 (10)                 | 1 (1.1)     |
| Coagulase-negative staphylococci| 44 (30)         | 40 (91)            | 4 (9)                  | -           |
| *Staphylococcus aureus* excluding MRSA | 3 (2)          | -                  | -                      | -           |
| MRSA                            | 22 (15.3)       | 16 (72.7)          | 5 (22.7)               | 1 (4.5)     |
| *Streptococcus viridans*        | 19 (13.2)       | -                  | -                      | -           |
| *Enterococcus*                  | 1 (0.6)         | -                  | -                      | -           |
| Diphtheroids (Corynebacterium)  | 1 (0.6)         | -                  | -                      | -           |
| Gram-negative                   | 46 (32.1)       | 27 (58.7)          | 18 (39.1)              | 1 (2.1)     |
| *Escherichia coli*              | 8 (5.5)         | 7 (87.5)           | 1 (12.5)               | -           |
| *Pseudomonas*                   | 10 (6.9)        | 7 (0)              | 3 (30)                 | -           |
| *Klebsiella*                    | 4 (2.7)         | -                  | 3 (75)                 | 1 (25)      |
| *Enterobacter*                  | 8 (5.5)         | 6 (75)             | 2 (25)                 | -           |
| *Serratia*                      | 5 (3.4)         | 2 (40)             | 3 (60)                 | -           |
| *Acinetobacter*                 | 10 (6.9)        | 4 (40)             | 6 (60)                 | -           |
| *Pantoea agglomerans*           | 1 (0.6)         | -                  | -                      | -           |
| Fungal (candida)                | 2 (1.3)         | -                  | 2 (100)                | -           |
| Culture-negative                | 5 (3.4)         | 5 (100)            | -                      | -           |

Data are expressed as numbers and percentages. MRSA: Methicillin-resistant *Staphylococcus aureus*
preservation of peritoneal membrane function, and patient survival. Our study showed an overall primary cure rate of 81.1%. The catheter was removed in 18.8%, a rate that was similar to previous reports in which the catheter removal rate ranged between 9.8 and 20.4% (12-14,16,18). The closeness of catheter removal rate to the highest level in literature might be explained by a higher rate of Gram-negative peritonitis attacks in our data (32.1%) as numerous studies have reported that Gram-negative peritonitis was associated with a higher rate of antimicrobial resistance, catheter loss, shift of PD to hemodialysis, and death (13,19,20). CNS was accounted for almost half of all Gram-negative peritonitis attacks. Approximately, 9% of catheters were removed for CNS peritonitis supporting the continued use of empiric vancomycin for Gram-positive cover to control peritonitis attacks. As known, morbidity, and mortality are higher in patients with fungal peritonitis (21). The number of patients with fungal peritonitis in the current study was small but both were switched to hemodialysis.

Peritonitis is rarely associated with a mortal outcome but it is a contributing factor for mortality in 16% of patients with PD related peritonitis (22,23). Two patients died due to *Klebsiella* and MRSA peritonitis septicemia in our cohort. As we found that the peritonitis rate was higher than the recommended range, we must determine the root cause of each episode, adjust empirical treatments accordingly and take the necessary measures to prevent the peritonitis attacks. Given the most common cause of PD-related peritonitis is Gram-positive microorganism, which is a normal flora of the skin, patient re-education about sterility rules and fluid exchange procedures may prevent peritonitis attacks. Further actions, including developing a home visit protocol to observe patients’ home environment are also important in achieving good PD outcomes.

This study has several limitations. First, it has all problems associated with retrospective studies. Second, data of patients with PD without peritonitis were not collected. Therefore, the risk factors associated with peritonitis were not determined. Finally, some results cannot be extrapolated to other centers as the study was conducted at a single center.

**CONCLUSION**

This study offers insights into the etiology and outcomes of PD-related peritonitis. The incidence of peritonitis was higher than recommended range by ISPD in our population. Gram-positive organisms are the main causative agents of peritonitis and Gram-negative organisms are associated with a lower resolution rate and higher need for catheter removal. Determination of the etiology of each attack, and prevention of next episodes by directing intervention against any reversible risk factors are essential for preserving peritoneal membrane function and patient survival.

**Acknowledgments**: I am grateful to Elber Uzunoğlu, and Arzu Öztürk for expert support in the data collection process.

**ETHICS**

**Ethics Committee Approval**: This study was approved by the University of Health Sciences Turkey, Hamidiye Clinical Research Ethics Committee (decision no: 5/53, date: 05.02.2021) and adhered to the principles of the Declaration of Helsinki.

**Informed Consent**: Informed consent was not obtained due to the retrospective design of the study.

**Authorship Contributions**

Concept: A.Ö., Design: S.Y.K., Data Collection or Processing: A.Ö., S.Y.K., Analysis or Interpretation: S.Y.K., Literature Search: A.Ö., Writing: A.Ö.

**Conflict of Interest**: The authors declare that they have no conflict of interest.

**Financial Disclosure**: The authors declared that this study received no financial support.

**REFERENCES**

1. Mujais S. Microbiology and outcomes of peritonitis in North America. Kidney Int Suppl 2006;S55-62.
2. Brown MC, Simpson K, Kerssens JJ, Mactier RA; Scottish Renal Registry. Peritoneal dialysis-associated peritonitis rates and outcomes in a national cohort are not improving in the post-millennium (2000-2007). Perit Dial Int 2011;31:639-50.
3. Boudville N, Kemp A, Clayton P, Lim W, Badve SV, Hawley CM, et al. Recent peritonitis associates with mortality among patients treated with peritoneal dialysis. J Am Soc Nephrol 2012;23:1398-405.
4. Hsieh YP, Chang CC, Wen YK, Chiu PF, Yang Y. Predictors of peritonitis and the impact of peritonitis on clinical outcomes of continuous ambulatory peritoneal dialysis patients in Taiwan—10 years’ experience in a single center. Perit Dial Int 2014;34:85-94.
5. Hsieh YP, Chang CC, Wang SC, Wen YK, Chiu PF, Yang Y. Predictors for and impact of high peritonitis rate in Taiwanese continuous ambulatory peritoneal dialysis patients. Int Urol Nephrol 2015;47:183-9.
6. Piraino B, Bernardini J, Brown E, Figueiredo A, Johnson DW, Lye WC, et al. ISPD position statement on reducing the risks of peritoneal dialysis-related infections. Perit Dial Int 2011;31:614-30.
7. Mehrotra R, Devuyst O, Davies SJ, Johnson DW. The Current State of Peritoneal Dialysis. J Am Soc Nephrol 2016;27:3238-52.
8. Li PK, Szeto CC, Piraino B, de Arteaga J, Fan S, Figueiredo AE, et al. ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment. Perit Dial Int 2016;36:481-508.
9. Zelenitsky SA, Howarth J, Lagacé-Wiens P, Sathianathan C, Ariano R, Davis C, et al. Microbiological Trends and Antimicrobial
Resistance in Peritoneal Dialysis-Related Peritonitis, 2005 to 2014. Perit Dial Int 2017;37:170-6.

10. Kavanagh D, Prescott GJ, Mactier RA. Peritoneal dialysis-associated peritonitis in Scotland (1999-2002). Nephrol Dial Transplant 2004;19:2584-91.

11. Ma TK, Chow KM, Kwan BC, Pang WF, Leung CB, Li PK, et al. Peritonitis before Peritoneal Dialysis Training: Analysis of Causative Organisms, Clinical Outcomes, Risk Factors, and Long-Term Consequences. Clin J Am Soc Nephrol 2016;11:1219-26.

12. Ghali JR, Bannister KM, Brown FG, Rosman JB, Wiggins KJ, Johnson DW, et al. Microbiology and outcomes of peritonitis in Australian peritoneal dialysis patients. Perit Dial Int 2011;31:651-62.

13. Prasad KN, Singh K, Rizwan A, Mishra P, Tiwari D, Prasad N, et al. Microbiology and outcomes of peritonitis in northern India. Perit Dial Int 2014;34:188-94.

14. Kim DK, Yoo TH, Ryu DR, Xu ZG, Kim HJ, Choi KH, et al. Changes in causative organisms and their antimicrobial susceptibilities in CAPD peritonitis: a single center’s experience over one decade. Perit Dial Int 2004;24:424-32.

15. Han SH, Lee SC, Ahn SV, Lee JE, Choi HY, Kim BS, et al. Improving outcome of CAPD: twenty-five years’ experience in a single Korean center. Perit Dial Int 2007;27:432-40.

16. Higuchi C, Ito M, Masakane I, Sakura H. Peritonitis in peritoneal dialysis patients in Japan: a 2013 retrospective questionnaire survey of Japanese Society for Peritoneal Dialysis member institutions. Renal Replacement Therapy 2016;2:1-8.

17. Htay H, Cho Y, Pascoe EM, Hawley C, Clayton PA, Borlace M, et al. Outcomes of Acinetobacter Peritonitis in Peritoneal Dialysis Patients: A Multicenter Registry Analysis. Perit Dial Int 2018;38:257-65.

18. Lee S, Kim H, Kim KH, Hann HJ, Ahn HS, Kim SJ, et al. Technique failure in Korean incident peritoneal dialysis patients: a national population-based study. Kidney Res Clin Pract 2016;35:245-51.

19. Siva B, Hawley CM, McDonald SP, Brown FG, Rosman JB, Wiggins KJ, et al. Pseudomonas peritonitis in Australia: predictors, treatment, and outcomes in 191 cases. Clin J Am Soc Nephrol 2009;4:957-64.

20. Jarvis EM, Hawley CM, McDonald SP, Brown FG, Rosman JB, Wiggins KJ, et al. Predictors, treatment, and outcomes of non-Pseudomonas Gram-negative peritonitis. Kidney Int 2010;78:408-14.

21. Basturk T, Koc Y, Unsal A, Ahbap E, Sakaci T, Yildiz I, et al. Fungal peritonitis in peritoneal dialysis: a 10 year retrospective analysis in a single center. Eur Rev Med Pharmacol Sci 2012;16:1696-700.

22. Choi P, Nemati E, Banerjee A, Preston E, Levy J, Brown E. Peritoneal dialysis catheter removal for acute peritonitis: a retrospective analysis of factors associated with catheter removal and prolonged postoperative hospitalization. Am J Kidney Dis 2004;43:103-11.

23. Johnson DW, Dent H, Hawley CM, McDonald SP, Rosman JB, Brown FG, et al. Associations of dialysis modality and infectious mortality in incident dialysis patients in Australia and New Zealand. Am J Kidney Dis 2009;53:290-7.