ORIGINAL ARTICLE

Incidence and Factors Associated with Peritoneal Dialysis-Related Peritonitis in Children

Mukrawee Yooyen, MD[1], Chantida Subun, MD[1], Konggrapun Srisuwan, MD[1]

[1] Division of Nephrology, Department of Pediatrics, Faculty of Medicine, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Bangkok, Thailand

Background: Since the peritoneal dialysis (PD)-first policy in Thailand, the number of end-stage renal disease (ESRD) patients receiving PD has increased significantly. Although the overall intraperitoneal infection rate has been decreased in recent years, it remains the leading cause of death and requiring a change in renal replacement therapy methods.

Objective: To study the incidence rate and factors associated with PD-related peritonitis in children at the authors' center by retrospective study.

Materials and Methods: Patients aged 18 years or younger from the onset of chronic PD were included in the present study. Medical records were reviewed between October 2008 and October 2020 and data were collected on peritonitis rates, baseline clinical characteristics, cause of ESRD, laboratory investigation, catheter type, antibiotic before catheter insertion, timing for starting continuous ambulatory peritoneal dialysis (CAPD), residual renal function, and immunosuppressive drug usage.

Results: The present study included 68 patients. The incidence of peritonitis rate was 0.3 episode/patient year. The most common symptoms were fever, abdominal pain, and cloudy effluent. The most common pathogen was gram-positive. Culture-negative accounted for 24%. Factors associated with peritonitis in univariate analysis were single-cuff catheter type (IRR 2.982, 95% CI 1.29 to 6.895, p=0.011), serum potassium less than 3.5 mEq/dL (IRR 1.827, 95% CI 1.065 to 3.133, p=0.029), lower serum albumin (IRR 0.543, 95% CI 0.447 to 0.924, p=0.017), lower serum phosphorus (IRR 0.817, 95% CI 0.686 to 0.973, p=0.023), lower blood urea nitrogen (BUN) (IRR 0.986, 95% CI 0.976 to 0.996, p=0.007), and lower serum creatinine (IRR 0.940, 95% CI 0.885 to 0.998, p=0.042).

Conclusion: The present study demonstrated a significant association between single-cuff catheter type, hypokalemia, lower serum albumin, hypophosphatemia, lower BUN, and lower serum creatinine and peritonitis, even though they did not show statistical significance in multivariate analysis. Controlling the associated factors, following standard guidelines may reduce the rate of peritonitis.

Keywords: Peritoneal dialysis (PD); Peritoneal dialysis-related peritonitis; End-stage renal disease (ESRD); Pediatric

Received 8 June 2023 | Revised 3 April 2024 | Accepted 10 April 2024

J Med Assoc Thai 2024;107(5):343-8

Website: http://www.jmatonline.com

Chronic kidney disease is a significant public health problem in Thailand. Peritoneal dialysis (PD) has comparable survival rates to hemodialysis and is more commonly used in pediatric patients because it can be performed at home without risk of vascular complications[1]. In addition, continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD) patients grow up with less restricted diet and hydration intake and can attend school normally. The Thai government has recognized the importance of these issues, and on October 30, 2008, a resolution was passed to approve the expansion of renal replacement services for end-stage kidney disease patients in the universal health insurance system by providing continuous PD to all end-stage kidney disease patients (PD-first policy), resulting in a better quality of life for patients. Consequently, the number of chronic kidney disease patients receiving CAPD has increased significantly. However, peritoneal infections have always been a serious complication and the leading cause of technique failure, morbidity, mortality, and increased health-care costs.

Before the PD-first policy in Thailand was implemented, a study of Nakwan et al. in pediatric patients with acute PD between 1994 and 2003 found that the rate of peritonitis was 3.2 episodes/patient year and the common pathogens were gram-negative organisms[2]. A study of Wisanuyotin et al.

Correspondence to:

Yooyen M.

Division of Nephrology, Department of Pediatrics, Faculty of Medicine, Phramongkutklao Hospital, Bangkok 10400, Thailand.

Phone & Fax: +66-83-5849666

Email: mukwee.yy@gmail.com

How to cite this article:

Yooyen M, Subun C, Srisuwan K. Incidence and Factors Associated with Peritoneal Dialysis-Related Peritonitis in Children. J Med Assoc Thai 2024; 107:343-8.

DOI: 10.35755/jmedassocthai.2024.5.13986

in pediatrics with chronic PD between 1994 and 2007 found that the rate of peritonitis was 1.4 episodes/patient year, with gram-positive organisms being the most common pathogen[3]. Since the PD-first policy was implemented, the peritonitis rate has not increased as a study of Wisanuyotin et al. in pediatrics with chronic PD between 2007 and 2016 showed that the rate of peritonitis was 0.6 episodes/patient year[4]. The results were consistent with the study of Perl et al. done between 2014 and 2016, which showed that the rate of peritonitis infection in Thailand was 0.4 episode/patient year[5]. Although recently, the overall peritonitis rate is within the targeted range, it remains a major cause of death and requires changing the method of renal replacement therapy[6]. Therefore, the present research aimed to study the incidence of PD-related peritonitis and factors associated with peritonitis as a guide for future prevention measures.

Materials and Methods

The present study included 68 CAPD patients, 18 years of age or younger, who received PD therapy in the authors' hospital between October 2008 and October 2020. The patients who had incomplete medical records and relapsed peritonitis were excluded. The authors collected data on baseline patients' characteristics, peritonitis rates, factor associated peritonitis, organisms that cause peritonitis, and drug resistance. The mean of the laboratory results for patients who did not experience peritonitis and the last results prior to the occurrence of peritonitis were utilized to calculate the laboratory results. Peritonitis was defined by at least two or more of the following criteria, clinical features indicative of peritonitis such as abdominal pain, cloudy effluent, white blood cell counts more than 100 cells/mm^3 and polymorphonuclear cells greater than 50% in the dialysate after at least two hours of dwell time, and positive dialysis effluent culture. Sample size for estimation of incidence was calculated using the formula:

$$n = \frac{Z_\alpha^2 P(1-P)}{d^2}$$

Z_α was 1.96, α was 0.05, P was incidence of peritonitis 56.4%[4], and d was standard error 10%. The calculated sample size was 95 patients. The single-center retrospective study was approved by the Independent Ethics Committee of Phramongkutklao Hospital (no. R076h/64_Exp).

Statistical analysis

Data were analyzed using Stata/MP, version 12 (StataCorp LP, College Station, TX, USA). Demographic data were displayed as descriptive statistics. Numbers and percentages were used to express categorical data. The mean and standard deviations were used to measure quantitative data. The same set of demographic information was utilized for re-infected patients. Associated factors of PD-related peritonitis were determined by univariate analysis and presented as crude and adjusted incident rate ratios (IRR) with 95% confidence interval (CI). Multivariate analysis was conducted on variables with probability values 0.25 based on univariate analysis. To determine factors associated with peritonitis, Poisson regression with a p-value of less than 0.05 was considered statistically significant.

Table 1. Baseline clinical characteristics of CAPD patients

	n (%)
Sex	
Male	33 (48.5)
Female	35 (51.5)
Reimbursement scheme	
Universal coverage scheme	62 (91.2)
Government/state enterprises	5 (7.4)
Self-support	1 (5.1)
Catheter type	
Single cuff	7 (10.3)
Double cuff	56 (82.3)
No data	5 (7.4)
Connectology	
ANDY-disc	33 (48.5)
Ultrabag	33 (48.5)
No data	2 (3.0)
Topical antibiotic at exit site	
2% Mupirocin	56 (82.3)
2% Fucidic acid	4 (5.9)
Gentamicin	2 (2.9)
No antibiotics	1 (1.5)
No data	5 (7.4)

Results

The present study included 68 patients with CAPD and 82 episodes of catheter insertion that included 65 CAPD and 3 APD. The mean duration of follow-up was two years per patient. Baseline characteristics are shown in Table 1 and the etiology of ESRD are shown in Table 2.

Fifty-four episodes of peritonitis, excluding relapsing peritonitis, occurred in 160 patient-years, resulting in a rate of 0.3 episode/patient year. The

Table 2. Cause of end-stage renal disease

Cause of ESRD	n (%)
Glomerular cause	22 (32.3)
SLE with lupus nephritis	4 (5.9)
IgA nephropathy	4 (5.9)
Congenital nephrotic syndrome	3 (4.4)
Anti-GBM disease	2 (2.9)
IgM nephropathy	2 (2.9)
ANCA vasculitis	2 (2.9)
Focal segmental glomerulosclerosis	1 (1.4)
Atypical HUS	1 (1.4)
Chronic glomerulonephritis	1 (1.4)
IgA vasculitis nephritis	1 (1.4)
APSGN	1 (1.4)
Non-glomerular cause	33 (48.5)
Renal hypoplasia	22 (32.3)
Posterior urethral valve	3 (4.4)
MCDK	2 (2.9)
ARPKD	2 (2.9)
Prune belly syndrome	1 (1.4)
Primary hyperoxaluria	1 (1.4)
Nephronophthisis	1 (1.4)
Unknown cause	13 (19.1)

ANCA=antineutrophil cytoplasmic antibodies; Anti-GBM=anti-glomerular basement membrane; APSGN=acute poststreptococcal glomerulonephritis; ARPKD=autosomal recessive polycystic kidney disease; HUS=hemolytic uremic syndrome; MCDK=multicystic dysplastic kidney; SLE=systemic lupus erythematosus

Table 3. Causative organisms of peritonitis

Organisms	n (%)
Gram-positive organisms	21 (38.9)
Coagulase negative *Staphylococcus*	10 (18.5)
Staphylococcus aureus	5 (9.3)
MRCONS	3 (5.5)
Streptococcus viridans	1 (1.8)
Micrococcus spp.	1 (1.8)
Corynebacterium spp.	1 (1.8)
Gram-negative organisms	17 (31.5)
Pseudomonas aeruginosa	6 (11.1)
Acinetobactor baumanii	5 (9.2)
Klebsiella pneumoniae	2 (3.7)
Enterobacter cloacae	2 (3.7)
Escherichia coli	1 (1.8)
Citrobacter spp.	1 (1.8)
Fungus	2 (3.7)
Candida albicans	2 (3.7)
Mycobacterium tuberculosis	1 (1.9)
Negative culture	13 (24.00)

MRCONS=methicillin-resistant coagulase negative *Staphylococcus*

most common symptoms were fever, abdominal pain, and cloudy effluent. All patients received antibiotic prophylaxis prior to catheter insertion. At the exit site, 98.4% of patients received a daily topical antibiotic.

The results of culture are shown in Table 3. The most common pathogen were gram-positive organisms at 38.9%. The most common gram-positive pathogen was coagulase-negative *Staphylococcus* at 47.6%, followed by *Staphylococcus aureus* at 23.8%, all of which were methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant coagulase-negative *Staphylococcus* (MRCONS) at 14.3%. Methicillin-resistant *S. aureus* (MRSA) infection was not found in the present study. The second most common culture was gram-negative at 31.5%, with the most common being *Pseudomonas aeruinosa*, *Acinetobactor baumanii*, *Klebsiella pneomoniae*, and *Enterobacter cloacae* at 35.3%, 29.4%, 11.7%, and 11.7%, respectively. Extended spectrum beta-lactamase (ESBL)-producing strains accounted for 20%. Culture-negative accounted for 24%. Fungus and tuberculosis (TB) peritonitis were found in 3.7% and 1.9% of the cases, respectively.

PD catheters were removed from all patients with fungal peritonitis. As previously reported in the PDOPPS[8], fungal peritonitis was a significant risk factor for PD catheter removal, hemodialysis transfer, and death when compared to gram-positive peritonitis.

The present research included 68 patients and 82 catheter insertion events. In 82 catheter insertion occurrences, 100 events, all peritonitis and non-peritonitis events, occurred. By univariate analysis, factors associated with peritonitis were single-cuff catheter type (p=0.011, 95% CI 1.29 to 6.895), serum potassium less than 3.5 mEq/dL (p=0.029, 95% CI 1.065 to 3.133), lower serum albumin (p=0.017, 95% CI 0.447 to 0.924), lower serum phosphorus (p=0.023, 95% CI 0.686 to 0.973), lower blood urea nitrogen (BUN) (p=0.007, 95% CI 0.976 to 0.996), and lower serum creatinine (p=0.042, 95% CI 0.885 to 0.998) (Table 4). Additionally, the cause of ESRD had no association with peritonitis in the present study. None of the factors had a statistically significant correlation in multivariate analysis.

At the end of the present study, approximately 40% of the patients had kidney transplants, 10% had switched to hemodialysis, and the majority of the causes were volume overload. In the present study, nine patients died. The causes of death were infection and volume overload, and three patients had no medical record of the cause of death.

Table 4. Factors associated with peritoneal-dialysis-related peritonitis in children

	Non-peritonitis	Peritonitis	Crude IRR	p-value	95% CI
n=82					
Sex; n (%)				0.657	0.602 to 2.240
• Male	22 (52.4)	20 (47.6)	1.161		
• Female	24 (60.0)	16 (40.0)	1.000		
Immunosuppressive drug; n (%)				0.053	0.991 to 4.771
• Yes	4 (33.3)	8 (66.7)	2.174		
• No	42 (60.0)	28 (40.0)	1.000		
Catheter type; n (%)				0.011	1.290 to 6.895
• Single cuff	0 (0.0)	7 (100)	2.982		
• Double cuff	45 (64.3)	25 (35.7)	1.000		
Connectology; n (%)				0.242	0.755 to 3.047
• ANDY-disc	27 (69.2)	12 (30.8)	1.000		
• Ultrabag	18 (43.9)	23 (56.1)	1.516		
Antibiotic prophylaxis before catheter insertion; n (%)					
• Yes	41 (60.3)	27 (39.7)			
• No	0 (0.0)	0 (0.0)			
Age at catheter insertion; mean±SD	10.31±4.22	7.39±5.37	0.953	0.186	0.888 to 1.023
Time to initiate peritoneal dialysis after catheter insertion; n (%)	0.659	0.503 to 2.968			
• Less than 14 days	35 (57.4)	26 (42.6)	1.222		
• More than 14 days	11 (64.7)	6 (35.3)	1.000		
Performed CAPD; n (%)				0.117	0.838 to 4.918
• By themselves	17 (73.9)	6 (26.1)	1.000		
• By parents	27 (50.0)	27 (50.0)	2.031		
Cause of ESRD; n (%)				0.667	0.565 to 2.436
• Non-glomerular cause	23 (56.1)	18 (43.9)			
• Glomerular cause	15 (55.6)	12 (44.4)	1.174		
n=100					
Residual urine volume; mean±SD	568.64±395.53	362.2±355.68	0.999	0.096	0.998 to 1.000
BMI (kg/m^2); mean±SD	17.02±3.96	17.78±5.22	1.005	0.853	0.955 to 1.057
Hemoglobin (g/dL); mean±SD	9.5±1.91	10.4±1.8	1.083	0.256	0.943 to 1.244
Serum sodium (mEq/L); mean±SD	137.57±3.4	139.04±4.14	1.016	0.717	0.934 to 1.105
Serum calcium (mEq/L); mean±SD	8.16±1.83	8.37±1.09	1.010	0.918	0.832 to 1.227
Serum phosphate (mg/dL); mean±SD	6.47±2.72	5.28±1.31	0.817	0.023	0.686 to 0.973
Serum intact PTH (pg/ml); mean±SD	714.98±757.86	530.18±507.03	1.000	0.644	0.999 to 1.000
Serum potassium (mEq/L); n (%)				0.029	1.065 to 3.133
• <3.5	6 (20.7)	23 (79.3)	1.827		
• ≥3.5	32 (50.8)	31 (49.2)	1.000		
Serum albumin (g/dL); mean±SD	3.58±0.98	3.4±0.63	0.543	0.017	0.447 to 0.924
Serum BUN (mg/dL); mean±SD	86.56±39.29	59.93±25.13	0.986	0.007	0.976 to 0.996
Serum creatinine (mg/dL); mean±SD	9.37±5.31	8.11±4.37	0.940	0.042	0.885 to 0.998

BMI=body mass index; BUN=blood urea nitrogen; CAPD=continuous ambulatory peritoneal dialysis; CI=confidence interval; ESRD=end-stage renal disease; IRR=incident rate ratio; PTH=parathyroid hormone; SD=standard deviation

n=100, events of peritonitis and non-peritonitis in 82 catheter insertions; n=82, catheter insertion events

Discussion

CAPD is the most commonly used dialysis modality in children with ESRD who are unable to receive a kidney transplant because it can be performed at home without requiring a hospital visit[9]. Between October 2008 and February 2022, the government established CAPD as the first modality to operate without contraindication. The most common complication in CAPD patients is peritonitis. Peritonitis has been shown to have

a significant impact on peritoneal function and morbidity in a previous study[6]. In the present study, the incidence of peritonitis in 68 ESRD patients was 0.3 episodes/patient year, which was within the ISPD guideline 2016 recommendation[7]. The reason that the present study had lower peritonitis rate than the previous study in Thailand is because the patients were treated according to the standard guidelines, most patients had two cuff catheters, antibiotic prophylaxis was given to all patients before catheter insertion, and all patients did the flush before fill technique. There was CAPD clinic where pediatric dialysis nursing staff retrained children and/or parents on the CAPD technique every month or two, and after a peritonitis episode[10]. The present staff performed home visits with a multidisciplinary team. In addition, since a longer CAPD duration is more associated with peritonitis, kidney transplantation was performed shortly after the initiation of CAPD[4,11]. Previous research had found that single-cuff catheters did not cause more peritonitis than double-cuff catheters[12], but the present study found that the single-cuff catheter type was significantly associated with peritonitis. This could be due to the fact that the majority of patients in the single-cuff group were under the age of one year who were at risk of peritonitis[13]. Other variables associated with peritonitis included serum potassium less than 3.5 mEq/L and lower serum albumin, similar to the prior studies of Liawnoraset in CAPD patients between 2008 and 2010. The three-year study found that the factors related to intraperitoneal infection were age over 60, hypokalemia, and hypoalbuminemia[14]. Ozturk et al. study[15] showed that serum albumin deficiency had also been linked to an increased risk of peritonitis. Furthermore, hypoalbuminemia was also associated with malnutrition according to the 2008 Kidney Disease Outcomes Initiative (KDOQI) recommendation[16] on serum albumin to assess nutritional status. Furthermore, the previous studies have found that malnutrition was a significant risk factor for peritonitis. In addition, lower serum phosphorus, BUN, and creatinine levels were significantly related to peritonitis in the present study.

In the present study, the immunosuppressive drug was not related to peritonitis because the majority of the patients received a low-dose immunosuppressive drug, whereas, prior studies have shown that higher infection rates were associated with the intensity of immunosuppression[17]. The higher-than-recommended rate of culture-negative peritonitis in the present study may have been attributable to the administration of antibiotics prior to specimen collection for culture, as well as improper specimen collection. The limitations are single center study, small sample size, and retrospective review, so there might have been incomplete data in the record and there were not enough patients for multivariate analysis to be significant.

Conclusion

Results of the present study demonstrated a significant association between single-cuff catheter type, hypokalemia, lower serum albumin, lower serum phosphate, lower BUN, lower serum creatinine, and peritonitis in univariate analysis, even though they did not show statistical significance in multivariate analysis. Although the rate of peritonitis in the present study was not higher than the ISPD recommendation, controlling the associated factor, following standard guidelines may reduce the rate of peritonitis.

What is already known on this topic?

Although recently, the overall peritonitis rate in Thailand is within the targeted range, it remains a major cause of death and requires changing the method of renal replacement therapy.

What does this study add?

This study revealed the incidence of peritonitis is 0.3 episode/patient year. By univariate analysis, factors associated with peritonitis were single-cuff catheter type, serum potassium less than 3.5 mg/dL, lower serum albumin, lower serum phosphorus, lower BUN, and lower serum creatinine.

Acknowledgement

The present study was supported by Faculty of Medicine, Phramongkutklao Hospital and Phramongkutklao College of Medicine, Thailand. The authors would like to thank Supak Ukritchon for the assistance in statistical analyses.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Raina R, Joshi H, Chakraborty R, Sethi SK. Challenges of long-term vascular access in pediatric hemodialysis: Recommendations for practitioners. Hemodial Int 2021;25:3-11.
2. Nakwan N, Dissaneewate P, Lim A, Vachvanichsanong P. Peritoneal dialysis-related peritonitis in southern

Thailand. Int J Artif Organs 2008;31:49-54.
3. Wisanuyotin S, Lertchanaruengrith P, Jiravuttipong A. Peritonitis in children receiving continuous ambulatory peritoneal dialysis in northeast Thailand. J Med Assoc Thai 2011;94:789-93.
4. Wisanuyotin S, Bannalai P, Panombaulert S. Incidence of peritonitis and associated factors in children receiving continuous ambulatory peritoneal dialysis: A retrospectve survey in a hospital in Northeastern Thailand (2007-2016). Southeast Asian J Trop Med Public Health 2020;51:270-9.
5. Perl J, Fuller DS, Bieber BA, Boudville N, Kanjanabuch T, Ito Y, et al. Peritoneal dialysis-related infection rates and outcomes: Results from the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS). Am J Kidney Dis 2020;76:42-53.
6. Chadha V, Schaefer FS, Warady BA. Dialysis-associated peritonitis in children. Pediatr Nephrol 2010;25:425-40.
7. 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.
8. Al Sahlawi M, Zhao J, McCullough K, Fuller DS, Boudville N, Ito Y, et al. Variation in peritoneal dialysis-related peritonitis outcomes in the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS). Am J Kidney Dis 2022;79:45-55.e1.
9. Wang H, Wang X, Dou H, Li C, Cui M, Gu C, et al. Risk factors for peritoneal dialysis–associated peritonitis. Eur J Inflamm 2018;16:2058739218772243.
10. Auron A, Simon S, Andrews W, Jones L, Johnson S, Musharaf G, et al. Prevention of peritonitis in children receiving peritoneal dialysis. Pediatr Nephrol 2007;22:578-85.
11. Zhai Y, Zhou Q, Fang X, Shen X, Chen J, Zhang J, et al. Reduction in peritonitis rates: 18-year results from the most active pediatric peritoneal dialysis center in China. Pediatr Nephrol 2022;37:2437-48.
12. Nessim SJ, Bargman JM, Jassal SV. Relationship between double-cuff versus single-cuff peritoneal dialysis catheters and risk of peritonitis. Nephrol Dial Transplant 2010;25:2310-4.
13. Keswani M, Redpath Mahon AC, Richardson T, Rodean J, Couloures O, Martin A, et al. Risk factors for early onset peritonitis: the SCOPE collaborative. Pediatr Nephrol 2019;34:1387-94.
14. Liawnoraset W. Prevalence and factors affecting peritonitis in CAPD patients in Maharat Nakhon Ratchasima Hospital under universal coverage scheme during 2008-2010: a three-year experience. J Med Assoc Thai 2011;94 Suppl 4:S19-24.
15. Ozturk S, Soyluk O, Karakaya D, Yazici H, Caliskan YK, Yildiz A, et al. Is decline in serum albumin an ominous sign for subsequent peritonitis in peritoneal dialysis patients? Adv Perit Dial 2009;25:172-7.
16. National Kidney Foundation. KDOQI Work Group. KDOQI clinical practice guideline for nutrition in children with CKD: 2008 update. Executive summary. Am J Kidney Dis 2009;53(3 Suppl 2):S11-104.
17. Andrews PA, Warr KJ, Hicks JA, Cameron JS. Impaired outcome of continuous ambulatory peritoneal dialysis in immunosuppressed patients. Nephrol Dial Transplant 1996;11:1104-8.