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ORIGINAL ARTICLE

Decreased incidence of peritoneal dialysis-associated peritonitis in young children

Peong Gang Park [1,2] Yo Han Ahn,[1,3,4] Hee Gyung Kang[1,3,4] and Il-Soo Ha[1,3]

[1]Department of Pediatrics, Seoul National University Children's Hospital, [3]Department of Pediatrics, Seoul National University College of Medicine, [4]Kidney Research Institute, Seoul National University Medical Research Center, Seoul and [2]Department of Pediatrics, Ajou University School of Medicine, Suwon, Republic of Korea

Aim: Peritonitis is the most common complication of peritoneal dialysis (PD). This study aimed to investigate changes in the incidence, risk factors, microbiology, and clinical outcomes of PD-associated peritonitis in the past decades.

Methods: This was a retrospective study that included children who initiated chronic PD at our institution between 2000 and 2017. The patients were divided into two groups according to the year of initiation: those who initiated PD between 2000 and 2008 and those who initiated PD between 2009 and 2017. The incidence and characteristics of peritonitis were compared between the groups.

Results: A total of 184 patients with a median age of 10.2 years were included in this study. Of the patients, 92 experienced 210 episodes of peritonitis. The incidence rate of peritonitis decreased from 0.35 to 0.21 episodes/patient year during the study period ($P = 0.001$). During the 2000–2008 period, the 2-year peritonitis-free survival rate was significantly lower for patients under 2 years of age than for the other age groups ($P = 0.004$), whereas this was not observed during the 2009–2017 period. The multivariable Cox proportional hazard model showed that the <2 years age group had a significantly higher risk of developing peritonitis in the 2000–2008 period. However, this was not evident in the 2009–2017 period.

Conclusions: The incidence of PD-associated peritonitis decreased, particularly in children under 2 years of age. Thus, younger age may not be a risk factor for PD-associated peritonitis.

Key words: incidence; peritoneal dialysis; peritonitis; retrospective study.

What is already known on this topic

1 Peritonitis is a well-recognised complication in patients undergoing peritoneal dialysis (PD), particularly affecting paediatric populations.
2 Various factors, including patient age and microorganisms, have been associated with the risk and outcomes of PD-associated peritonitis.

What this paper adds

1 There has been a significant decrease in the incidence rate of PD-associated peritonitis in children in Korea, particularly noted in those under 2 years of age, during the period from 2000 to 2017.
2 The study suggests that younger age may not be a significant risk factor for PD-associated peritonitis in the recent decade.

Peritoneal dialysis (PD) is a preferred dialysis modality of kidney replacement therapy for children with kidney failure (KF) due to its ease of implementation and better preservation of residual kidney function; generally in South Korea, PD is commonly used as a modality of dialysis in children and adolescents.[1,2] Although PD has several benefits, it is associated with various complications. PD-associated peritonitis is the most common complication observed in children receiving PD, occurring more frequently in children than in adults.[3,4] In 2007, the International Pediatric Peritonitis Registry reported 548 episodes of PD-related peritonitis in 392 children from 44 centres, whereas in 2011, the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) reported a peritonitis rate of 0.64 episodes/patient year.[5,6] Recent studies have reported a relatively lower peritonitis rate, as low as 0.30 episodes/patient year in the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data from 2016 to 2020.[7] However, peritonitis remains the most significant complication for children receiving chronic PD.[8] In South Korea, many studies have examined the incidence and outcomes of PD-associated peritonitis and reported peritonitis incidence rates of 0.28–0.43 episodes/patient year in 57–110 children before 2012.[9–11]

Correspondence: Dr Yo Han Ahn, Department of Pediatrics, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea. Fax: +82 2 2072 0633; email: yhahn@snu.ac.kr

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As PD-associated peritonitis remains a major cause of morbidity in children receiving PD, efforts have been made to lower its incidence, including the development of adequate prevention and treatment guidelines. In 2022, the International Society of PD developed consensus guidelines.[12] The guidelines recommend periodic reevaluation of peritonitis characteristics. However, few long-term studies have been conducted to investigate changes in peritonitis characteristics, despite the frequently reported cross-sectional studies on peritonitis incidence.[5,13,14] In North America, the Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease (SCOPE) collaborative, which aims to enhance patient outcomes by standardising care practices, evaluated changes in peritonitis occurrence over time. Their efforts, focusing on implementing care bundles for catheter insertion, training and follow-up, demonstrated a decline in the incidence rates of peritonitis from 0.79 episodes/patient year in the 1992–1996 period to 0.46 episodes/patient year in the 2011–2014 period.[15,16] However, despite reports from Australia and the International Pediatric Peritoneal Dialysis Network (IPPN) Registry aimed at understanding the characteristics and long-term outcomes of peritonitis in children undergoing PD, comprehensive long-term studies across different regions or centres remain limited, possibly due to the insufficient number of cases available for analysis.[14,17]

This study aimed to evaluate the incidence, risk factors, microbiology, clinical outcomes and trends of peritonitis over time in Korean children. Considering that our institution is the largest children's dialysis centre in South Korea, with about 10 children initiating PD annually, we anticipate that this study would provide informative results in terms of sequential changes in peritonitis characteristics.

Materials and Methods

Study design, data collection and definitions

This was a retrospective study reviewing the electronic medical records of children who initiated chronic PD between 1 January 2000 and 31 December 2017, at our institution. The inclusion criteria included patients who were under the age of 18 years at the initiation of PD and who received PD for a minimum duration of 3 months. If the children underwent more than two courses of PD involving other kidney replacement therapy modalities, such as kidney transplantation or haemodialysis, for a period exceeding 2 months between PD courses, only the first PD course was evaluated. The children were followed-up until the cessation of PD, death, or 30 June 2023, whichever came first.

At our centre, all paediatric patients received a double-cuff PD catheter insertion. PD was initiated at least 2 weeks after catheter insertion to minimise the risk of dialysate leak and exit site infection. Dialysis nurses and paediatric nephrologists educated patients and their caregivers on the prevention and early detection of peritonitis, both before and after the initiation of PD (Fig. S1).

Data were collected, including age, sex, cause of KF (glomerulonephritis, congenital anomalies of the kidney and urinary tract and other specified or unspecified causes), year of PD initiation, dominant PD modality (continuous ambulatory PD or automated PD (APD)), PD duration, ostomy status and information about catheter insertion surgery, such as catheter type (straight or coiled), usage of laparoscopy and concomitant omentectomy. In addition, peritoneal fluid analysis data were collected, including cell count and culture results, peritonitis symptoms and outcomes such as catheter removal.

According to the 2022 International Society of Peritoneal Dialysis guidelines,[12] PD-related peritonitis was defined as the presence of two of the following three criteria: (i) abdominal pain and/or cloudy dialysis effluent, (ii) peritoneal fluid containing 100 or more white blood cells per mm^3 with at least 50% polymorphonuclear cells and (iii) positive culture results of dialysis effluent. Relapsing peritonitis was defined when peritonitis recurs with the same organism or with sterile episode within 4 weeks after completion of antibiotic treatment. Recurrent peritonitis was defined when peritonitis recurs with different organism within 4 weeks after completion of antibiotic treatment.

Outcomes and statistical analysis

The incidence of peritonitis was calculated as episodes/patient year and stratified by age (subdivided by <2 years of age, 2 to <6 years, 6 to <13 years and ≥13 years of age), cause of KF, year of PD initiation and dominant PD modality. The year of PD initiation was divided into two periods: 2000–2008 and 2009–2017. All peritonitis episodes were analysed to determine microbiological findings (gram-positive, gram-negative, fungal, coinfection with gram-positive and gram-negative organisms and culture-negative results) and complications, such as relapsing peritonitis, recurrent peritonitis and catheter removal.

Continuous variables were presented as median with interquartile range (IQR), and categorical variables were expressed as frequencies and percentages. The characteristics of patient demographics and peritonitis were compared using the Chi-squared or Mann–Whitney *U* tests as appropriate. The time to peritonitis from catheter insertion was assessed using Kaplan–Meier survival analysis, and sequential changes were evaluated according to the era of PD initiation. In addition, the risk factors for the peritonitis-free survival period in each time period were analysed using a multivariable Cox proportional hazard model. This model was adjusted for variables such as age group, omentectomy, catheter type and PD modality. Statistical analysis was performed using R-project version 4.2.1. A P value of <0.05 was considered statistically significant.

Results

Patient characteristics and sequential changes

A total of 191 patients initiated PD during the study period at our institution. Among them, 184 patients (107 males and 77 females) who were under the age of 18 years at the initiation of PD and who received PD for more than 3 months were included in this study. The median age at the initiation of PD was 10.2 years (IQR: 4.8–13.8), and the median duration of receiving PD was 40.9 months (IQR: 23.5–63.3). Table 1 shows the sequential changes in patient characteristics. The proportion of patients using APD significantly increased from 53.6% in the 2000–2008 period to 86.2% in the 2009–2017 period. No patients underwent laparoscopic PD catheter insertion in the 2000–2008 period.

Table 1 Baseline characteristics of the patients

Characteristics	2000–2008 ($n = 97$)	2009–2017 ($n = 87$)	*P* value	All patients ($n = 184$)
Male sex	54 (55.7)	53 (60.9)	0.568	107 (58.2)
Age, years	9.5 (5.5–13.1)	10.6 (3.0–14.3)	0.603	10.2 (4.8–13.8)
Age group			0.086	
<2 years	13 (13.4)	15 (17.2)		28 (15.2)
2 to <5 years	15 (15.5)	15 (17.2)		30 (16.3)
6 to <13 years	44 (45.4)	24 (27.6)		68 (37.0)
≥13 years	25 (25.8)	33 (37.9)		58 (31.5)
Duration of PD, months	44.1 (25.1–64.3)	37.7 (19.6–59.5)	0.214	40.9 (23.5–63.3)
Cause of KF			0.156	
CAKUT	20 (20.6)	20 (23.0)		40 (21.7)
Glomerulonephritis	46 (47.4)	50 (57.5)		96 (52.2)
Others	31 (32.0)	17 (19.5)		48 (26.1)
Automated PD	52 (53.6)	75 (86.2)	<0.001	127 (69.0)
Coiled PD catheter ($n = 183$)†	16 (16.5)	23 (26.7)	0.131	39 (21.3)
Laparoscopic catheter insertion ($n = 163$)†	0 (0.0)	66 (80.5)	<0.001	66 (40.5)
Concomitant omentectomy at the time of catheter insertion ($n = 162$)†	43 (53.8)	57 (69.5)	0.057	100 (61.7)
Ostomy present	3 (3.1%)	2 (2.3%)	>0.999	5 (2.7%)
Peritonitis occurred at least once during study period	58 (59.8)	34 (39.1)	0.008	92 (50.0)

† Due to the lack of operation records, data were missing for types of PD catheters in 1 patient, usage of laparoscopy in 21 patients and concomitant omentectomy in 22 patients. Values are presented as numbers (%) or median (interquartile range). CAKUT, congenital anomalies in kidney and urinary tract; KF, kidney failure; PD, peritoneal dialysis.

However, it was the predominant surgical technique in the 2009–2017 period (80.5%).

Incidence of peritonitis

Of the 184 patients, 92 experienced 210 episodes of peritonitis. The overall incidence rate was 0.28 episodes/patient year (95% confidence interval, 0.25–0.33), and the median time from the initiation of PD to the first peritonitis episode was 9.9 months (IQR: 3.5–24.7 months). The incidence rate of peritonitis decreased from 0.35 episodes/patient year in the 2000–2008 period to 0.21 episodes/patient year in the 2009–2017 period ($P = 0.001$). When stratified by age, the incidence rate of peritonitis was the lowest in patients aged 2 to >5 years (0.19 episodes/patient year) and the highest in patients under 2 years of age (0.39 episodes/patient year). In addition, no significant difference in the incidence rate was observed between the two dominant PD modalities (Table 2).

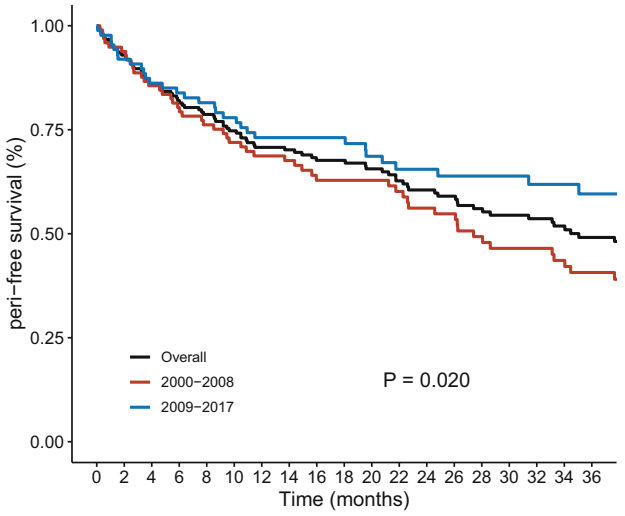
Peritonitis-free survival

The overall peritonitis-free survival rates were 82.0% at 6 months, 70.8% at 1 year and 60.5% at 2 years. Figure 1 shows Kaplan–Meier curves stratified by age and year of PD initiation. The peritonitis-free survival rate significantly differed based on the year of PD initiation ($P = 0.020$). However, no significant difference was observed among the age groups ($P = 0.381$). Subgroup analysis was performed, and Kaplan–Meier curves stratified by age for patients who initiated PD in the 2000–2008 and 2009–2017 periods were presented (Fig. 2; Table S1). Interestingly, patients under 2 years of age at the initiation of PD showed the most drastic change in the peritonitis-free survival rate over time. The 2-year peritonitis-free survival rates for patients under 2 years of age were 26.9% in the 2000–2008 period and 93.3% in the 2009–2017 period. In the

Table 2 Incidence of peritonitis

	No. of episodes	Total duration of PD (months)	Incidence (95% CI)
All patients	211	739	0.29 (0.25–0.33)
Age			
<2 years	37	96	0.39 (0.28–0.54)
2 to <6 years	14	73	0.19 (0.11–0.33)
6 to <13 years	64	238	0.27 (0.21–0.34)
≥13 years	96	332	0.29 (0.24–0.35)
Cause of KF			
CAKUT	47	167	0.28 (0.21–0.38)
Glomerulonephritis	114	406	0.28 (0.23–0.34)
Others	50	166	0.3 (0.23–0.4)
Year of initiation			
2000–2008	141	398	0.35 (0.3–0.42)
2009–2017	70	341	0.21 (0.16–0.26)
Dominant PD modality			
CAPD	70	238	0.29 (0.23–0.37)
APD	141	501	0.28 (0.24–0.33)

APD, automated PD; CAKUT, congenital anomalies in kidney and urinary tract; CAPD, continuous ambulatory PD; CI, confidence interval; KF, kidney failure; PD, peritoneal dialysis.



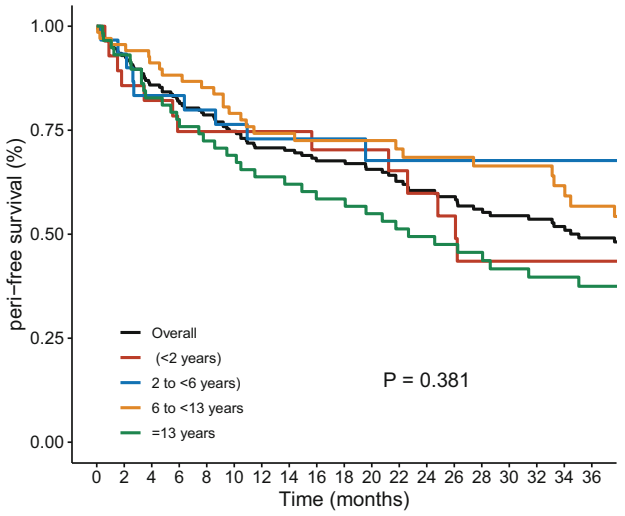
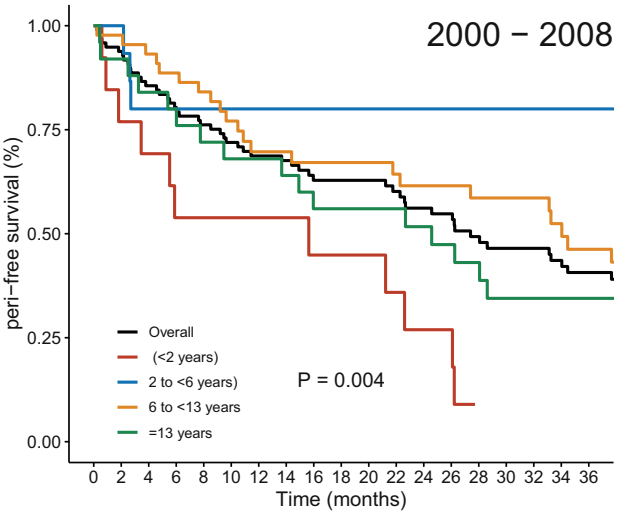


Fig. 1 Peritonitis-free survival stratified by (a) year of initiation and (b) and age groups.



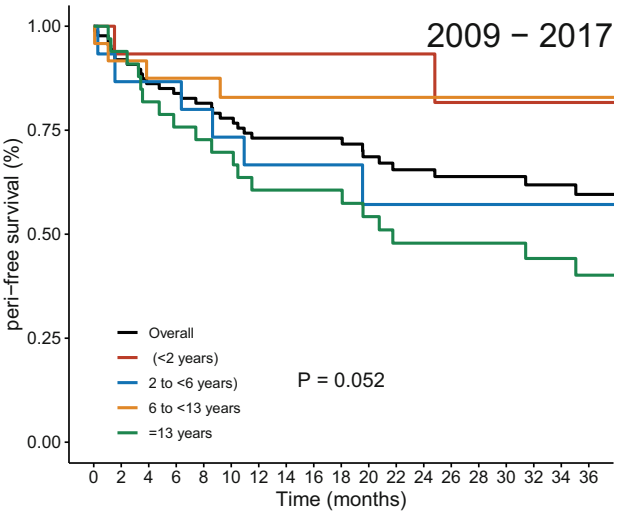


Fig. 2 Peritonitis-free survival stratified by age in (a) the 2000–2008 period and (b) the 2009–2017 period.

2000–2008 period, the 2-year peritonitis-free survival rate was significantly lower for patients under 2 years of age than for other age groups ($P = 0.004$). In the 2009–2017 period, the 2-year peritonitis-free survival rate for patients under 2 years of age was higher than for other age groups. However, no statistically significant difference was observed. The multivariable Cox proportional hazard model showed that patients under 2 years of age had a significantly higher risk of developing peritonitis than the ≥13 years of age group in the 2000–2008 period (adjusted hazard ratio 3.05 (95% confidence interval 1.23–7.53), $P = 0.016$). However, this was not evident in the 2009–2017 period (Table 3). Peritonitis-free survival did not significantly differ based on catheter type, omentectomy status, laparoscopy, or dominant PD modality in our cohort (Fig. S2).

Peritonitis characteristics

Of the 211 episodes of peritonitis, 109 episodes (51.7%) were caused by gram-positive organisms, whereas 21 (10.0%) were classified as sterile episodes. No change in the proportion of gram-positive and -negative organisms as causative pathogens was observed throughout the study period (Table S2). Methicillin-resistant organisms were found in 30% (6 out of 20) of *S. aureus* episodes and 49% (22 out of 45) of coagulase-negative Staphylococcus episodes. Relapsing peritonitis occurred in 26 episodes (12.3%), and recurrent peritonitis occurred in 16 episodes (7.6%). Catheter removal was necessary for 20 (9.5%) patients due to fungal peritonitis ($n = 6$), relapsing peritonitis ($n = 6$), refractory peritonitis ($n = 6$) and exit site infection ($n = 2$). No significant differences in the complications were observed between the two periods.

Discussion

This study showed that the incidence of peritonitis declined gradually in recent years. Interestingly, this decline was most significant in young children under 2 years of age. Contrary to previous

Table 3 Cox proportional hazard ratio of developing peritonitis

	The 2000–2008 period			The 2009–2017 period		
	aHR	95% CI	*P* value	aHR	95% CI	*P* value
Age group						
<2 years	3.05	1.23–7.53	0.016	0.28	0.06–1.37	0.116
2 to <6 years	0.31	0.07–1.44	0.136	0.79	0.27–2.31	0.669
6 to <13 years	1.15	0.55–2.41	0.703	0.44	0.15–1.28	0.131
≥13 years	Reference			Reference		
Omentectomy	0.65	0.36–1.16	0.143	1.07	0.49–2.33	0.863
Coiled catheter	1.45	0.67–3.13	0.341	0.98	0.41–2.39	0.973
APD	0.88	0.49–1.58	0.677	0.75	0.27–2.06	0.576

aHR, adjusted hazard ratio; APD, automated PD; CI, confidence interval; PD, peritoneal dialysis.

studies, this finding suggests that younger age may not be associated with a higher risk of infectious complications in paediatric patients on PD. To the best of our knowledge, this is the first study to present comprehensive findings regarding the decline in the trends of peritonitis incidence in East Asia.

The cause of improvement in peritonitis over time may be multifactorial. The enhancement of training and follow-up practices may be one of the most important factors. In addition, the widespread use of APD in recent years may have contributed to this improvement. In South Korea, the use of APD has dramatically increased since the Korean Ministry of Health and Welfare provided insurance benefits to patients with KF in 2008. Although a consensus has not been reached on this matter, many international and Korean studies favour APD over continuous ambulatory PD in terms of peritonitis.[6,9] However, this study did not find a significant difference in the peritonitis-free survival rates between the two modalities. Moreover, laparoscopic catheter insertion or omentectomy has recently become more common. Previous studies on adult patients have shown no significant difference in peritonitis rates between laparoscopy and laparotomy.[18] However, laparoscopy may be beneficial for children due to the smaller surgical incisions, although one recently published study found no significant difference between two methods.[19] Our data also did not demonstrate significant differences in development of peritonitis based on surgical techniques for PD catheter insertion. Perioperative care could influence the occurrence of peritonitis; throughout the study period, we consistently administered preoperative antibiotics and allowed time for wound healing in all children to minimise exit site infections. However, considering the small cohort size, further international collaborative studies are needed to validate these results.

This study showed a novel finding that patients under 2 years of age group showed a significant decline in the rate of peritonitis compared with ≥13 years of age group. This finding is inconsistent with the findings of previous studies that showed an inverse relationship between age and the rate of peritonitis in children.[5,8] Moreover, during the 2009–2017 period, patients under 2 years of age showed the highest rate of peritonitis-free survival. In 2012, the International Society for Peritoneal Dialysis (ISPD) guidelines highlighted the importance of a PD teaching programme conducted by experienced PD nurses, including detailed prophylaxis and exit care.[20] Our centre has developed a formalised teaching programme for children and their caregivers in accordance with the ISPD guidelines (Fig. S1). Extensive caregiver education may be particularly beneficial for younger children, as patients under 2 years of age have limited interactions with people other than their primary caregivers at school or daycare centres. As per the ISPD guidelines, the appropriate implementation of prophylactic measures can reduce the development of peritonitis. In addition, the care of paediatric PD patients in our centre has been operated by a multidisciplinary team composed of paediatric nephrologists, dialysis nurses, paediatric surgeons, pharmacists and nutritionists. Over time, this team has gained valuable experience in managing younger children undergoing PD, and they have developed a protocolized management approach over the decades. This approach is inspired by initiatives such as the SCOPE collaborative, which has demonstrated significant improvements in patient outcomes through collaborative quality improvement initiatives and highlighted the benefits of a protocolized approach in paediatric dialysis care.[15,16] Furthermore, evidence from broader medical literature supports the benefits of protocolized care in enhancing patient outcomes, ensuring consistency in treatment and facilitating continuous quality improvement.[21] Moreover, APD may have a more apparent positive impact on younger children due to fewer connections and favourable outcomes of performing flush procedures. Laparoscopic surgery with small surgical incisions might also offer advantages for younger children.[22] The placement of gastrostomy in children is considered an additional risk factor for PD-related peritonitis.[20] In South Korea, cultural reasons cause caregivers to be reluctant about gastrostomy. As a result, the rate of gastrostomy in infants is significantly lower compared to other countries and recommendations; only five infants underwent gastrostomy in our study.[19,23] While this may have had an adverse impact on nutrition, it may have contributed to reducing the prevalence of peritonitis. However, establishing conclusive evidence is challenging because no prior studies have assessed changes in the trend of peritonitis with respect to age groups.

Compared with younger children, ≥13 years of age group have demonstrated the lowest rate of peritonitis-free survival in recent

years. Furthermore, adolescents' poor adherence may result in elevated morbidity rates and an increased risk of complications. This resembles the common nonadherence observed in adolescents with chronic diseases. For instance, a nationwide analysis of kidney-transplanted adolescents identified significant nonadherence during the transition phase, impacting graft outcomes. Similarly, adolescents with type 1 diabetes encounter adherence challenges that affect disease management, underscoring the necessity for strategies to enhance adherence.[24,25]

Many previous studies have evaluated peritonitis-free survival rates in children in recent years. The most recent annual report of the NAPRTCS revealed an overall peritonitis-free survival rate of 49% at 2 years, while a study using ANZDATA data reported a 2-year peritonitis-free survival rate of 36%.[6,14] However, no direct comparisons were made with similar regions because no similar studies have conducted survival analysis in Eastern Asia. The incidence rates of PD-associated peritonitis in children vary from region to region.[26] The incidence rate of PD-associated peritonitis in Eastern Asia has been reported to be lower than that in other regions, with a rate as low as 0.19 episodes/patient year, as reported from Japan.[27] Nevertheless, peritonitis remains the most common complication and the primary cause of PD failure. Thus, it is important to collect regional epidemiological data to better plan for treatment and prevention options for peritonitis.[8]

This study has a limitation. This was a single-centre retrospective medical chart review study. Thus, it was difficult to collect important data, including patient adherence, adherence and the status of exit site care. These missing data might affect our overall understanding of peritonitis cases. Moreover, one of the interesting findings that reports decreased incidence of peritonitis, particularly in patients <2 years of age, was done on only 28 patients; this finding should be interpreted with caution given our small sample size. Consequently, these limitations present challenges in assessing and drawing definitive conclusions on the incidence and risk factors for PD-related peritonitis in children, highlighting the need for further research. Nevertheless, this study has important strengths as we collected data over a long period and showed changes in peritonitis characteristics, which were scarcely reported in children.

In conclusion, the incidence of peritonitis significantly decreased, mainly in young children, whereas the incidence has not changed significantly in adolescents. Further large-scale studies investigating peritonitis characteristics, including the incidence rate in relation to patients' ages, microbiology and outcomes, are needed to establish adequate centre- and region-based guidelines for proper treatment and prevention of peritonitis.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Data S1: Supporting Information.