Original Article

Risk Factors for The First Episode of Peritonitis in Continuous Ambulatory Peritoneal Dialysis Patients in Pranangklao Hospital

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Background: Continuous ambulatory peritoneal dialysis (CAPD) is a renal replacement therapy for end stage renal disease patients. Peritonitis is a common complication in CAPD patients leading cause of technical failure and patient mortality. Investigating the risk for the first episode of peritonitis could help to prevent and improve CAPD outcomes.

Objective: To investigate the risk factors for the first episode of peritonitis in CAPD patients in Pranangklao Hospital.

Materials and Methods: A single-center, retrospective descriptive study was conducted to evaluate patients undergoing peritoneal dialysis (PD). All incident CAPD patients between October 1, 2011 and March 1, 2021 were recruited. Baseline demographic, and clinical and laboratory data were collected from medical records.

Results: In a cumulative 10,916.9 patient-months follow-up of the 411 CAPD patients, 227 were male and 184 were female. One hundred eighty-eight (45.7%) patients presented the first episode of peritonitis. The mean age of peritonitis free group and first peritonitis group was 58.2 years and 56.7 years, respectively. The mean duration from starting CAPD to the first episode of peritonitis was 19.4 months. The average peritonitis rate was 0.26 episodes per year, or one episode per 46.84 patient-months. There were no significant differences in clinical characteristics and laboratory data between these two groups, except there were more diabetes mellitus in the infectious peritonitis group at 72.6% versus 62.8% (p=0.03). Coagulase-negative *Staphylococcus* was the most common organism causing peritonitis. The multivariate logistic regression showed that diabetes mellitus (OR 1.59, 95% CI 1.03 to 2.46, p=0.04) was the risk factors associated with peritonitis.

Conclusion: Diabetes mellitus was the risk factor associated with the first episode of peritonitis. Therefore, special supervision should be provided to this group of patients by optimally controlling the diabetic conditions.

Keywords: Continuous ambulatory peritoneal dialysis; First peritonitis episode; Risk factors

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The number of patients with chronic kidney disease (CKD) has been increasing worldwide. In Thailand, 11.6 million (17.5%) people currently have CKD, 5.7 million (8.6%) have advanced CKD (stages 3 to 5), and over 0.1 million require dialysis[1]. Every year, more than 20,000 people with end-stage renal disease need treatment with hemodialysis (HD) or peritoneal dialysis (PD)[2].

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In 2008, the Thai government developed and implemented a strategy to offer universal health coverage (UHC) for renal replacement therapy using a 'PD-First' policy as the primary treatment option for end stage renal disease, based on the observation that PD was cheaper and equally effective compared with HD[3]. After launching of the 'PD-First' policy, continuous ambulatory peritoneal dialysis (CAPD) is the most popular method of PD in Thailand. This method is a patient-based therapy because the patients must run the treatment by themselves.

Peritonitis is one of the most common complications of CAPD. Peritonitis is harmful to the peritoneum. Long-term PD causes structural changes in the peritoneal membrane, leading to peritoneal fibrosis[4], and peritonitis accelerates this process[5]. The intensity of peritoneal inflammation and the frequency of infection has an impact on the peritoneal function. Multiple or recurrent episodes could cause membrane permeability changes and ultrafiltration

declines with time on PD, which finally leads to technical failure, mortality, and excess health care costs in patients treated with PD[6-9]. Previous studies have shown that lower serum albumin[8,10], higher body mass index (BMI)[8], lower hematocrit level[10], and diabetes kidney disease[8,11] are associated with peritonitis. However, there were fewer studies about the risk factors associated with the first episode of peritonitis in Thai PD patients. Therefore, the objective of the present study was to evaluate the risk factors for the first episode of peritonitis in CAPD patients in Pranangklao Hospital to decrease the risk factors associated with the development of the first episode of peritonitis.

Materials and Methods

Patient population

The present study was a single-center retrospective descriptive study that included all incident CAPD patients followed up in the PD center. The author reviewed charts of the CAPD patients treated at Pranangklao Hospital between October 2011 and March 2021.

The baseline characteristics of all patients were collected, including demographic data such as age, gender, education level, region where patients live urban or rural, comorbidities such as diabetes mellitus, hypertension, heart disease, and cerebrovascular disease, biochemical data such as serum creatinine (mg/dL), hemoglobin levels (g/dL), potassium (mEq/L), calcium (mg/dL), phosphate (mg/dL), serum albumin levels (g/dL), intact parathyroid hormone (pg/mL), and microbiological characteristics of the first episode of peritonitis.

Definition of peritonitis and the first episode of peritonitis

Recorded episodes of peritonitis met at least two of the following three criteria from the 2010 International Society for Peritoneal Dialysis (ISPD) guideline recommendations[12], 1) symptoms of peritoneal inflammation such as abdominal pain, 2) an effluent white blood cell count exceeding 100/mL after a dwell time of at least two hours, with at least 50% polymorphonuclear neutrophilic cells, and 3) presence of organisms on Gram stain or subsequent culturing of PD fluid.

The first episode of peritonitis was defined as the first case in which cloudy peritoneal fluid was observed, with a leukocyte count equal to or greater than 100 cells/mm^3, and with 50% polymorphonuclear cells.

Table 1. Baseline clinical characteristics of CAPD patients

Baseline clinical characteristics	n (%)
Sex	
Male	227 (55.2)
Female	184 (44.8)
Age (years); mean±SD	57.5±13.8
Comorbid diseases	
Hypertension	409 (99.5)
Diabetes mellitus	280 (68.1)
Heart disease	78 (19.0)
Gout	30 (7.3)
Cerebrovascular disease	15 (3.6)
Cirrhosis	10 (2.4)
COPD	4 (1.0)

COPD=chronic obstructive pulmonary disease; SD=standard deviation

Statistical analysis

All analyses were performed using the SPSS Statistics software, version 17.0 (SPSS Inc., Chicago, IL, USA). Variables normally distributed were expressed as mean ± standard deviation (SD) and the group comparisons were assessed by independent sample t-test. Variables not normally distributed were expressed as median (min, max) and the group comparisons were assessed by chi-square test. Values of p-value less than 0.05 were considered statistically significant. The multivariate logistic regression model was performed to select significant risk factors for peritonitis, such as older age, gender, education level, diabetes mellitus, serum hemoglobin, potassium, and albumin levels, which was in accordance with previous studies[8,10,11].

Ethical approval

The present study was approved by Ethics Committee of the Pranangklao Hospital, Nonthaburi, Thailand (EC 24/2564).

Results

Four hundred eleven CAPD patients were enrolled. There were 188 patients with infectious peritonitis and 223 patients who had been never infected. The baseline clinical characteristics are shown in Table 1. The mean age was 57.5±13.8 years and 55.2% were male. Most patients had hypertension. Other comorbid diseases included diabetes mellitus and heart disease. The comparisons of demographics and physical examination findings between the two groups are shown in Table 2. There were no significant

Table 2. The comparisons of demographics and physical examination findings between the patients with infectious peritonitis and the patients with no infectious peritonitis

Baseline clinical characteristics	Peritonitis free group; n (%)	First peritonitis group; n (%)	p-value
Patients	223 (54.3)	188 (45.7)	
Sex: male	127 (57.0)	100 (53.2)	0.45
Age (years); mean±SD	58.2±12.6	56.7±15.2	0.26
SBP (mmHg); mean±SD	141±23	140±24	0.70
DBP (mmHg); mean±SD	79±15	80±16	0.90
Urine (mL); mean±SD	502±485	535±445	0.49
Performed CAPD by caregivers	146 (65.5)	116 (61.7)	0.43
Region where patients live			0.24
Urban	64 (28.7)	64 (34.0)	
Rural	159 (71.3)	124 (66.0)	
Education level			
Uneducated	12 (5.4)	19 (10.1)	0.07
Primary school	137 (61.4)	116 (61.7)	0.66
Junior high school	31 (13.9)	17 (9.1)	0.13
Senior high school	17 (7.6)	10 (5.3)	0.35
Technical college	14 (6.3)	13 (6.9)	0.80
Bachelor's degree	12 (5.4)	13 (6.9)	0.52
Comorbid diseases			
Diabetes mellitus	162 (72.6)	118 (62.8)	0.03
Hypertension	222 (99.6)	187 (99.5)	0.36
Heart disease	38 (17.0)	40 (21.3)	0.28
Gout	16 (7.2)	14 (7.4)	0.92
Cerebrovascular disease	10 (4.5)	5 (2.7)	0.33
Cirrhosis	6 (2.7)	4 (2.1)	0.76
COPD	2 (0.9)	2 (1.1)	1.00

SBP=systolic blood pressure; DBP=diastolic blood pressure; COPD=chronic obstructive pulmonary disease; SD=standard deviation

Table 3. Baseline laboratory biochemistry data

Biochemistry findings	Peritonitis free group (n=223); mean±SD	First peritonitis group (n=188); mean±SD	p-value
Creatinine (mg/dL)	9.4±3.9	9.4±4.0	1.00
Hemoglobin (g/dL)	10.5±1.9	10.5±2.0	0.73
Glucose (mg/dL)	132.6±65.5	133.5±74.0	0.90
Potassium (mEq/L)	3.7±0.7	3.7±0.8	0.97
Calcium (mg/dL)	9.4±0.9	9.4±0.9	0.81
Phosphorus (mg/dL)	4.5±1.7	4.5±1.8	0.81
Albumin (g/dL)	3.2±0.6	3.2±0.6	0.17
LDL-C (mg/dL)	117.7±41.9	119.3±37.9	0.69
Parathyroid hormone (pg/mL)	329.0±277.5	347.6±285.7	0.51

LDL-C=low-density lipoprotein cholesterol; SD=standard deviation

Table 4. Causative organisms of the first episode of peritonitis

Causative organisms	Peritonitis episodes; n (%)
Culture negative	75 (39.9)
Gram positive organisms	
Coagulase-negative *Staphylococcus*	26 (13.8)
Enterococcus spp.	18 (9.6)
Staphylococcus aureus	7 (3.7)
Streptococcus spp.	6 (3.2)
Corynebacterium spp.	2 (1.1)
Bacillus spp.	1 (0.5)
Gram negative organisms	
Esherichia coli	19 (10.1)
Klebsiella spp.	14 (7.4)
Acinetobacter spp.	5 (2.7)
Enterobacter spp.	5 (2.7)
Pseudomonas aeruginosa	3 (1.6)
Other gram negative	2 (1.1)
Fungus	5 (2.7)

differences between these two groups, except there were more diabetes mellitus in the group of infectious peritonitis at 72.6% versus 62.8% (p=0.03). Most of the patients required a caregiver to perform the CAPD exchange. The mean duration from starting CAPD to the first episode of peritonitis was 19.4 months.

The biochemistry findings are demonstrated in Table 3. There were no significant differences between these two groups.

The causative organisms of the first episode of peritonitis are shown in Table 4. Of the 188 patients, 60 (31.9%) were due to gram-positive organisms, 48 (25.5%) gram-negative organisms, and five (2.7%) due to fungi. Among the gram-positive organisms, the most frequent was coagulase-negative *Staphylococcus* (13.8%), followed by *Enterococcus* spp. (9.6%), *Staphylococcus aureus* (3.7%) and *Streptococcus* spp. (3.2%). Among the gram-negative organisms, *Esherichia coli* was the main gram-negative bacteria causing 10.1% of the cases, followed by *Klebsiella* spp. (7.4%), *Acinetobacter* spp. (2.7%), *Enterobacter* spp. (2.7%), and other gram-negative organisms (1.1%). Negative culture was observed in 75 (39.9%).

Table 5 demonstrates a binary logistic regression model for the analysis the risk factors associated with the first episode of peritonitis. The result showed that diabetes mellitus (OR 1.59, 95% CI 1.03 to 2.46, p=0.04) was the risk factor associated with

Tables 5. Risk factors for the first episode of peritonitis

Risk factors	Odd ratio	95% CI	p-value
Age >60 years	1.01	0.67 to 1.54	0.95
Sex: male	1.12	0.75 to 1.68	0.58
Education level: ≤ primary school	0.79	0.51 to 1.23	0.30
Diabetes mellitus	1.59	1.03 to 2.46	0.04
Hemoglobin <10.0 g/dL	0.89	0.59 to 1.34	0.58
Potassium <3.5 mEq/L	0.84	0.56 to 1.26	0.40
Albumin <3.5 g/dL	1.18	0.78 to 1.78	0.44

CI=confidence interval

peritonitis. Other variables such as old age, lower serum hemoglobin, and potassium and albumin levels were not significantly associated with peritonitis.

Discussion

Peritonitis is the major complication and the main cause of PD failure. The previous studies had demonstrated the risk factors for peritonitis in CAPD patients included hypoalbuminemia[13,14], hypokalaemia[15], anemia[10], and diabetes mellitus[15], while the present study shows that diabetes mellitus is a strong risk factor for first peritonitis episode in CAPD patients. Diabetic patients are compromised hosts and experienced many complications. The effect of diabetes with hyperglycemia including neutrophil chemotaxis is the adherence to vascular endothelium, phagocytosis, intracellular bactericidal activity, opsonization, and cellmediated immunity impairment[16,17]. Furthermore, diabetic patients mistake the process of PD as potentially contributing to visual disorder and peripheral neuropathy[13,18,19]. Joshi et al found that glucose load impaired the peritoneal defense system[20]. The presence of diabetes mellitus may affect the incidence of PD-associated peritonitis via several mechanisms. The present study did not find that fasting blood sugar levels were associated with peritonitis. This may be because the patients had not been tested for hemoglobin A1c. Therefore, it cannot be concluded that the patients had good glucose control in both the infected and non-infected groups. In addition, the present study did not find that serum albumin and potassium levels were associated with the first episode of peritonitis because the hospital's treatment process realized the importance of serum albumin and potassium levels from the starting of PD. Therefore, the patients in the present study had normal serum albumin and potassium levels.

The previous studies had reported that elderly, male gender, and lower education level were associated with peritonitis[21-23]. However, the present study did not find any significant association.

In the present study, the median time to the first episode of peritonitis was 19.4 months. Coagulase-negative *Staphylococcus* was the most common causative organism of peritonitis, and the frequency of gram-positive bacterial peritonitis is higher than gram negative bacteria were similar to a previous study[24]. It could be related to incorrect operation of the peritoneal fluid exchange. The incidence of culture negative peritonitis is higher than the recommendation of ISPD guideline 2010[12], which is less than 20% versus 39.9% in Pranangklao Hospital. The explanation for the present study result might be that some patients had already received the antibiotic from local community hospitals prior to admission at the present study center or technical problems during dialysate culture.

There are several limitations to the present study. First, several factors that may have some impacts on peritonitis such as nutritional assessment scoring, assessment of physical or mental handicap, the details of the assistants, as well as nasal and skin colonization were not included in the present study. Second, the present study was a single center retrospective study, and the sample size was small. Further studies, such as multi-center and prospective studies are necessary.

Conclusion

Diabetes mellitus is the risk factor of peritonitis. Therefore, improvement of glycemic control would decrease the incidence of peritonitis in CAPD patients.

What is already known on this topic?

Peritonitis is a major cause of morbidity, technique failure, mortality, and excess health care costs in patients treated with peritoneal dialysis. Previous studies have shown that lower serum albumin, higher BMI, lower hematocrit level, and diabetic kidney disease are associated with peritonitis. However, there were few studies about the risk factors associated with the first episode of peritonitis in Thai PD patients.

What this study adds?

This study demonstrated the risk factors for the first episode of peritonitis in CAPD patients. Diabetes mellitus was the risk factor associated with peritonitis. Lower serum hemoglobin, potassium and albumin levels were not significantly associated with peritonitis.

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Conflicts of interest

The author declares no conflict of interest.

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