DOI: https://doi.org/10.53555/nnmhs.v9i7.1765

Publication URL: https://nnpub.org/index.php/MHS/article/view/1765

### PERITONEAL DIALYSIS-ASSOCIATED PERITONITIS: A SYSTEMATIC REVIEW

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#### Abstract

**Background:** Peritoneal dialysis is infectious and non-infectious. Peritoneal dialysis causes catheter exit, tube tunnel, and peritonitis. Noninfectious consequences of peritoneal dialysis include catheter malfunction, external leakage, abdominal wall anomalies, scrotal edoema, pleural-peritoneal fistulas, failed ultrafiltration, and encapsulated sclerosis. PD complications include peritonitis. The International Society for Peritoneal Dialysis (ISPD) offers specific recommendations on PD-associated peritonitis prevention and treatment, however clinical practise differs greatly amongst dialysis units.

Aim: This article examines the link between peritoneal dialysis and peritonitis and presents its findings.

**Methods:** By evaluating the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 standards, this study demonstrated that it met all of the requirements. This enabled the researchers to ensure that the study was as up to date as feasible. Publications published between 2000 and 2023 were included in the search strategy, which included a variety of electronic reference databases (including Pubmed and SagePub). We did not consider review papers, duplicate publications, or half completed articles.

**Result:** In the PubMed database, the results of our search brought up 133 articles, whereas the results of our search on SagePub brought up 69 articles. The results of the search conducted for the last year of 2000 yielded a total of 20 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 21 papers, six of which came from PubMed and three of which came from SagePub. We included nine research that met the criteria.

**Conclusion:** Gram-positive bacteria are the most common cause of Parkinson's disease-associated peritonitis. Despite the high frequency of PD-associated peritonitis, it has a high cure rate.

Keyword: Chronic Kidney Disease (CKD); Infection; Peritoneal Dialysis; Peritonitis

#### **INTRODUCTION**

Chronic kidney disease, or CKD, is an umbrella word for a decline in kidney function of any severity, including mild, moderate, and severe chronic kidney impairment. CKD is a public health problem all over the world. Renal failure is becoming more common and more common in many countries. This is a bad thing because it can lead to bad results and expensive costs.<sup>1</sup> Indonesian chronic renal failure patients grow about 10% year. Indonesia has no epidemiological chronic renal disease studies. According to Indonesian nephrology centres, chronic renal disease affects 100–150 people per million.<sup>2</sup>

According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), one out of every ten people in the United States has CKD at some point in their lives.<sup>3</sup> It is very important for people with CKD to get an early evaluation and treatment of the root cause and/or secondary prevention. This step can slow or even stop the disease from getting worse. Patients with CKD who need medical help right away should focus on delaying or stopping the disease from getting worse, figuring out what's wrong and treating it, and making plans for long-term renal replacement treatment.<sup>4-6</sup> There are two distinct types of dialysis that may be performed on a patient undergoing treatment for kidney disease: hemodialysis and peritoneal dialysis. Every method of renal replacement therapy comes with its own set of advantages and disadvantages. The choice of dialysis modality is determined by a number of different aspects, including the patient's ability to handle large amounts of fluid, the presence of comorbid disorders, the patient's socio-economic level, the dialysis centre, the patient's home circumstances, and the surgical procedure that is utilised by the clinician. Availability and convenience are two other aspects to consider.<sup>7</sup>

Peritoneal dialysis (PD) filters blood internally using the belly lining to treat kidney failure. Medical practitioners call this peritoneum lining. Patients can receive home dialysis with PD. Patients have similar outcomes to those on HD dialysis, and the system spends less. Educating patients and implementing a PD-first strategy in all dialysis patients can improve patient experience and mortality rates while saving money on the rising cost of ESRD therapy.<sup>8,9</sup> Peritoneal dialysis has infectious and non-infectious problems. Peritonitis, catheter exit, and tube tunnel infections are related with peritoneal dialysis.<sup>10,11</sup>

Peritoneal dialysis can cause noninfectious complications include catheter malfunction, external leakage, abdominal wall anomalies, scrotal edoema, pleuralperitoneal fistulas, failed ultrafiltration, and encapsulated peritoneal sclerosis.<sup>10,11</sup> Peritonitis is a frequent and serious peritoneal dialysis complication (PD). The International Society for Peritoneal Dialysis (ISPD) has published detailed recommendations on the prevention and treatment of PD-associated peritonitis, but clinical practice varies significantly between dialysis units.<sup>12</sup> This article examines the link between peritoneal dialysis and peritonitis and presents its findings.

#### **METHODS**

The basis for the formulation of the guidelines that regulated the conduct of this systematic review was the Preferred Reporting Items for Systematic Review and MetaAnalysis (PRISMA) 2020 checklist. This systematic review was created to examine articles on "peritoneal dialysis"; and "peritonitis". These are the topics covered by the study under consideration. The following conditions must be fulfilled for your work to be considered: 1) Articles must be available online in their entirety; 2) Articles must be written in English; and 3) Articles must have been published after 2017, but before this systematic review was conducted. Textual contributions of the following type will under no circumstances be accepted: 1) Editorial letters, 2) submissions without a DOI, and 3) article reviews and similar submissions.

The search for papers to be included in the systematic review began on July 14<sup>th</sup>, 2022 using the PubMed and SagePub databases with the search terms on "peritoneal dialysis"; and "peritonitis". Where (("peritoneal dialysis"[MeSH Terms] OR ("peritoneal"[All Fields] AND "dialysis"[All Fields]) OR "peritoneal dialysis"[All Fields]) AND ("peritoneally"[All Fields] OR "peritoneum"[MeSH Terms] OR "peritoneum"[All Fields] OR "peritoneal"[All Fields] OR "peritonitis"[All Fields] OR "peritonitis"] or "peritonitis"[All Fields]) AND (2017:2022[pdat]) is used as search keywords. After conducting a literature analysis and looking at the titles and abstracts of previously published research, the author of the study revised the criteria for what should be included and what should be excluded from the study. Throughout the process of developing the systematic review, we took into consideration only research studies that met each and every one of our criteria. It is possible to collect the following information on each study: title, author, publication date, study origin location, research study design, and research variables.

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To determine which studies should be taken into account, the writers carried out their own independent assessments on a selection of the research that was contained in the titles and abstracts of the papers. The full texts of the studies that satisfy the requirements for inclusion in the systematic review will next be analysed to see which pieces of research would be applicable to the aims of the review. This will be done so that the review can be as thorough as possible.

### RESULT

In the PubMed database, the results of our search brought up 133 articles, whereas the results of our search on SagePub brought up 69 articles. The results of the search conducted for the last year of 2000 yielded a total of 20 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 21 papers, six of which came from PubMed and three of which came from SagePub. We included nine research that met the criteria.

Ljungman, et al  $(2023)^{13}$  showed 33% (223/671) patients had a first peritonitis episode. Univariable Cox proportional hazard regression indicated a substantial connection between time-updated PD bags connected per 24 h (PD bags/24 h) and time to first peritonitis episode (hazzard risk [HR] = 1.35; 95% confidence interval [CI] = 1.171.57), even after including PD modalities. Multivariable Cox regression showed that age (HR = 1.16 per 10 years; 95% CI = 1.05-1.28), PD bags/24 h, serum albumin <35 versus >35 g/L, and body weight per 10 kg independently predicted time to first peritonitis episode.

Pavlina, et al  $(2021)^{14}$  showed peritonitis occurred at a rate of 0.47 incidents per patient year. Gram-positive bacteria were the most common causal pathogens (53.5%). Infection was cured in 84.9% of peritonitis episodes, catheter removal in 11.3% of episodes, and mortality occurred in 3.8% of peritonitis episodes. A Kaplan-Meier analysis and log-rank test indicated that the group with peritonitis lived substantially longer than the group without peritonitis. When compared to the peritonitis-free group, the peritonitis group had a 67% lower risk of patient death (hazard ratio [HR] = 0.33, 95% CI = 0.190.57, P < 0.01).<sup>14</sup>

#### Table 1. The litelature include in this study

Author Size	Origin	Method	Sample	Result
Ljungman, 2023 <sup>13</sup>	Denmark	RCT	671 patients	According to the findings of this study of patients with incident PD, a higher body weight, a lower albumin level, a higher age, and a greater number of PD bags connected per 24 hours are individually linked with a shorter amount of time before the onset of the first peritonitis episode.
Pavlina, 2021 <sup>14</sup>	North Macedonia	Retrospective study	159 patients	0.47 patients per year developed peritonitis. Grampositive bacteria (53.5%) caused most infections. 84.9% of peritonitis episodes were treated, 11.3% were catheterized, and 3.8% were fatal. Kaplan-Meier and logrank tests showed that peritonitis patients lived longer than those without it. The peritonitis group had 67% reduced patient mortality than the peritonitis-free group.
Xu, 2020 <sup>15</sup>	China	RCT	150 patients	Oral instruction did not reduce initial non-enteric peritonitis, but method inspection did. First non- enteric peritonitis was substantially greater in the usual care group (0.07/patient-year) than in the method inspection group (0.02/ patientyear; $P <$ 0.01) but comparable with the oral education group (0.06/patient-year). Haemodialysis and all-cause mortality were similar between groups.
Hu, 2018 <sup>16</sup>	China	Single-center cohort study	218 patients	Enterococcus peritonitis rose from 15.1% to 27.3%. Cardiovascular disease, under 55 yo, non- independent operator, low potassium, and high calcium-phosphate product were linked with peritonitis. Time to 1st episode adversely correlated with peritonitis rate (r=-0.291, P=0.001). Time to 1st episode was not associated with patient survival (P=0.151). High peritonitis
Htay, 2017 <sup>17</sup>	Australia	Retrospective study	9,362 patients	patients had lower technique survival ( $P < 0.001$ ). Technique failure was less likely in centers with more peritoneal dialysis patients (>29%; adjusted hazard ratio, 0.83; 95% confidence interval, 0.73 to 0.94) and more likely in smaller centers (16 new patients per year; adjusted hazard ratio, 1.10; 95% confidence interval, 1.00-1.21) and centers with fewer patients achieving target baseline serum phosphate levels (40%; adjusted hazard ratio, 1.15; 95% confidence interval, 1.004,00 death-censored method failure, center target phosphate was not substantially linked.
<b>Zelenitsky,</b> <b>2017</b> <sup>18</sup>	Canada	Retrospective study	539 patients	44% of peritonitis cases involved <i>staphylococci</i> 58% versus 24% of monomicrobial PDRP infections were gramnegative. 2005–2014 showed stable antibiotic resistance. 57% of <i>staphylococci</i> were methicillin-resistant. MRSA caused 11% of <i>S. aureus</i> peritonitis, up from 2% in 1991-1998. Ciprofloxacin-resistant <i>Escherichia coli</i> rose from 3% to 24% between 2005 and 2014.

Xu, et al (2020) showed the technique inspection group showed a lower risk of first non-enteric peritonitis than the usual care group, while the oral education group did not show a significant benefit. The incidence of first non-enteric peritonitis in the usual care group (0.07/patient-year) was significantly higher than that in the technique inspection group (0.02/patient-year; P < 0.01) but was comparable with that in the oral education group (0.06/patient-year). Transfer to haemodialysis and all-cause mortality were not significantly different between the groups.<sup>15</sup>

Hu, *et al*<sup>16</sup> study showed occurrence of enterococcus peritonitis increased from 15.1% of the first to 27.3% of the later episodes. Multivariate logistic regression showed that the presence of cardiovascular disease, age  $\leq$ 55, non-independent operator, lower values of potassium and higher values of calcium-phosphate product were associated with peritonitis. Spearman analyses indicated that the time to the 1st episode was negatively related to the peritonitis rate (r=-0.291, P=0.001). Time-dependent Cox regression showed no association between the time to the 1st episode and patient survival (P=0.151). Patients with a high peritonitis rate (HPR) demonstrated worse technique survival (P < 0.001).

Htay, et al  $(2017)^{17}$  showed technique failure was less likely in centers with more peritoneal dialysis patients (>29%; adjusted hazard ratio [aHR] = 0.83; 95% CI = 0.730.94) and more likely in smaller centers (16 new patients/year; aHR = 1.10; 95% CI = 1.00-1.21) and centers with fewer patients achieving target baseline serum phosphate levels. Centre target phosphate did not affect death-censored technique failure. Infection, social causes, mechanical causes, and death were linked to centre size, proportion of PD patients, phosphate goal accomplishment, automated PD exposure, icodextrin use, and antifungals. Patient- and center-specific variables reduced method failure by 28% and 53%, respectively.

Zelenitsky, et al (2017) showed 85% of the patients, new episodes of peritonitis were related with a single organism, and staphylococci were implicated in 44% of those instances. Polymicrobial PDRP had 58% gram-negative organisms, while monomicrobial infections were 24%. Antimicrobial resistance barely changed between 2005 and 2014. *Staphylococcus epidermidis* was 57% methicillin-resistant, compared to 20% of other coagulase-negative staphylococci. *Methicillin-resistant Staphylococcus aureus* (MRSA) caused 11% of *S. aureus* peritonitis, although our 1991–1998 PDRP research showed 2%. Between 2005 and 2014, 24% of *Escherichia coli* bacteria were ciprofloxacin-resistant, up from 3% in our earlier studies.<sup>18</sup>

#### DISCUSSION

Chronic kidney disease, also known as CKD, is an umbrella term referring to any degree of decline in kidney function, including mild, moderate, and severe chronic renal impairment. There are approximately 3,8 million people worldwide who have reached the end stage of renal disease and require dialysis to survive. It is estimated that approximately 11% of dialysis patients are treated with peritoneal dialysis. The evaluation focuses on the more pragmatic aspects of providing medical care to this population.<sup>19</sup>

Peritonitis is a common and severe complication of peritoneal dialysis (PD). In over 15% of PD patients, peritonitis is the direct cause of death or a significant contributing factor. In addition, a single episode of severe peritonitis or repeated episodes of peritonitis are the leading cause of conversion to long-term hemodialysis due to decreased peritoneal ultrafiltration capacity.<sup>17,20</sup> Guidelines on the treatment and prevention of PD-associated peritonitis have been published and updated regularly over the past three decades (ISPD) under the auspices of the International Society for Peritoneal Dialysis.<sup>21,22</sup>

Many other modifiable risk factors for PD peritonitis have been reported, but their absolute risk (e.g., cirrhosis, polycystic kidney disease, left ventricular assist device, neutropenia during chemotherapy) is unclear, and few interventions have been shown to reduce risk. In PD patients, colonoscopy and hysteroscopy can cause peritonitis. Before colonoscopy or invasive gynecologic procedures, consider prophylactic antibiotics. Intravenous ampicillin with or without aminoglycoside or metronidazole is most usually employed. Intraperitoneal prophylactic antibiotics before invasive surgeries are unproven.<sup>12</sup>

PD-associated peritonitis and catheter-related infections were treated and prevented in two sets of guidelines. 2010 includes these proposals.<sup>22</sup> PD-associated peritonitis treatment and prevention guidelines were combined in the 2016 version. 2017 guidelines addressed catheter-related infections. Their advice differs because they prioritise different topics.<sup>23</sup> Although method inspection and oral instruction reduced the incidence of non-enteric PD-related peritonitis, neither significantly reduced the risk of all-cause peritonitis compared to standard care. Despite method inspection reducing the incidence of non-enteric PD-related peritonitis.<sup>15</sup>

Exit site and catheter tunnel infections increase PD-associated peritonitis risk. Preventing peritonitis requires early identification and antibiotic therapy. Prevention relies on catheter exit site management.<sup>24</sup> Antibiotic cream or ointment should be applied to the catheter exit site daily, preferably mupirocin. Mupirocin cream or ointment applied daily to the skin around the exit site lowers *S. aureus* exit site infection and possibly peritonitis. Intranasal mupirocin reduces *S. aureus* exit site infection but not peritonitis. Catheter erosion can result from excessive topical mupirocin on polyurethane or silicone catheter surfaces. Patients need application instructions.<sup>25</sup>

Despite the high number of peritonitis patients, recurrence, relapse, and repetition were minimal. Most first-time peritonitis patients were cured. Our research found that patients with higher and lower peritonitis rates had similar survival rates, whereas HPR patients had a lower technique survival rate. 75% of patients who transitioned to permanent HD had peritonitis, and their comparatively high rate of hospital admissions suggests an unfavourable consequence. Patients who transitioned to permanent HD had more hospitalisations than those without peritonitis.<sup>16</sup>

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Figure 2. Causes of PD-associated peritonitis

S. epidermidis, E. faecalis, and E. coli induced gram-positive peritonitis, while E.

*coli* caused gram-negative. *S. epidermidis* caused most gram-positive peritonitis, while *E. coli* caused most gram-negative cases. These findings match recent studies. Since *S. epidermidis* is almost often discovered in contact contamination, patient training and retraining on aseptic technique must be improved immediately. The rise of enterococcus peritonitis and VRE is also concerning. These results suggest that gastrointestinal disorders and bacterial sensitivity patterns should be prioritised.<sup>18,26,27</sup>

Empirical antibiotics for Gram-positive and Gram-negative infections should be given to PD patients with clinical signs of peritonitis. Prefer intraperitoneal. Antifungal prophylaxis—especially oral nystatin—prevents fungal peritonitis. PD effluent Gramme stain or culture and sensitivity may change antibiotics. ISPD recommendations list antibiotic doses. Antibiotics last 2-3 weeks. Refractory, relapsing, or fungal peritonitis necessitates catheter removal and hemodialysis. Some people get PD catheters after peritonitis. Remove refractory exit site or tunnel infections. Clinical care has reduced PDassociated peritonitis worldwide, supporting its use as a first-line dialysis modality.<sup>28</sup>

### CONCLUSION

The majority of cases of PD-associated peritonitis are brought on by gram-positive bacteria. Despite the high frequency of PD-associated peritonitis, there is a good chance of recovery from the condition.

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