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CLINICAL STUDY

Peritoneal dialysis peritonitis due to *Neisseria*: clinicopathological features of 10 patients with a review of the literature

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ABSTRACT

Background: Peritoneal dialysis-associated peritonitis (PDAP) frequently arises as a complication in patients undergoing peritoneal dialysis. However, the understanding of the role of *Neisseria*, a gram-negative coccus, in PDAP is limited.

Methods: This study retrospectively analyzed data for patients with *Neisseria*-associated PDAP who were treated at our center from January 2010 to June 2022. These patients were classified into the *Neisseria* group (Group N) and matched 1:2 by sex, age, dialysis duration, and residual kidney Kt/V with a coagulase-negative staphylococci group (Group CNS) and a *Staphylococcus aureus* group (Group S) as controls. Statistical analysis was conducted *via* SPSS 25.0 and was supplemented with a review of the relevant literature, to investigate clinical features, pathways of infection, and patient outcomes.

Results: This study included 10 cases of *Neisseria*-associated PDAP, comprising 6 male and 4 female patients. The patients had an average age of 58.10 ± 14.52 years, and the average duration of peritoneal dialysis was 72.00 ± 46.99 months. Among these patients, 3 had first-time infections, while 7 had a prior history of PDAP. After treatment, 9 patients achieved medical cure, and 1 patient was transferred to hemodialysis (HD). Baseline comparisons across the 3 groups indicated notable differences in body temperature upon admission, which were statistically significant ($p < 0.05$), with patients in Group S having higher body temperatures compared to Group N and Group CNS. Compared with Group N, Group S presented a markedly elevated high-sensitivity C-reactive protein (hs-CRP) level, decreased serum albumin levels, reduced serum potassium levels, whereas Group CNS presented a significantly lower neutrophil percentage (N%) than did Group N ($p < 0.05$). Although survival analysis did not reveal statistically significant differences due to the limited sample size, Kaplan–Meier curves indicated a trend toward lower cure rates and slightly worse long-term outcomes in Group S than in Group N and Group CNS, with the latter 2 groups showing similar results.

Conclusion: *Neisseria*-associated PDAP generally has favorable outcomes, similar to those of CNS-related PDAP and better than those of S-related PDAP. Hypoalbuminemia, hypokalemia and elevated hs-CRP are key risk factors affecting outcomes, emphasizing the need to address them during treatment.

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1. Introduction

Peritoneal dialysis (PD) is an effective treatment option for patients with end-stage renal disease. However, peritoneal dialysis-associated peritonitis (PDAP) is a significant complication that can lead to the discontinuation of PD or even death [1–3]. The genus *Neisseria* is classified as a β-proteobacteria, within the Neisseriales order and the Neisseriaceae family. It consists of 23 species and subspecies, most of which are gram-negative cocci. Common species include *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Neisseria sicca*, *Neisseria subflava*, *Neisseria flavescens*, *Neisseria mucosa*, and *Neisseria elongata*. Among them, *Neisseria meningitidis* and *Neisseria gonorrhoeae* are the two most common pathogenic strains. Other *Neisseria* subspecies are typically normal flora in the human respiratory tract [4] and are generally nonpathogenic under normal conditions but can become opportunistic pathogens when the host's immune system is compromised.

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Currently, there are clinical reports of meningitis [5], urethritis [6], conjunctivitis [7], and endocarditis [8] caused by *Neisseria* species, but reports of *Neisseria*-induced PDAP are rare [9–28]. This study aimed to investigate the clinical characteristics, pathogenic mechanisms, infection routes, and prognoses of *Neisseria*-associated PDAP by reviewing cases treated in our hospital.

2. Materials and methods

2.1. Study participants

Data were retrospectively gathered from patients with PDAP who were undergoing continuous ambulatory peritoneal dialysis (CAPD) and were treated at Hangzhou Traditional Chinese Medicine Hospital in Zhejiang Province, China, from January 2010 to June 2022. The inclusion criteria were as follows: (1) age ≥ 18 years; (2) met the diagnostic criteria for PDAP set by the International Society for Peritoneal Dialysis (ISPD) [29], satisfying 2 of the following 3 criteria: the presence of clinical symptoms of peritonitis, such as abdominal pain and/or cloudy dialysis effluent; peritoneal dialysis effluent with a dwell time exceeding 2 h and showing a white blood cell (WBC) count greater than 100/μL (or 0.1 × 10^9/L) with polymorphonuclear cells (PMNs) accounting for more than 50%; and a positive pathogen culture from peritoneal dialysis fluid. The exclusion criteria were as follows: (1) age < 18 years; (2) insufficient clinical data; (3) peritoneal dialysis duration < 1 month; (4) no culture or negative culture of peritoneal dialysis fluid; and (5) concurrent malignancies. Meeting any of the above criteria would lead to exclusion. Patients who met the criteria for *Neisseria*-associated PDAP were included in Group N. Patients with coagulase-negative staphylococci (CNS) and *Staphylococcus aureus* (S) PDAP were matched 1:2 with Group N patients on the basis of sex, age, dialysis duration, and residual kidney Kt/V and were included in Groups CNS and S, respectively. The process is shown in Figure 1.

This study adhered to the Declaration of Helsinki and received approval from the Institutional Review Board of Hangzhou Traditional Chinese Medicine Hospital, which is affiliated with Zhejiang Chinese Medical University (Approval No. 2021KY052). Given the retrospective nature of the research, the requirement for informed consent was waived (Approval No. 2021KY052).

2.2. Research methods

2.2.1. Treatment regimen

In accordance with the latest guidelines at the time [29–32], each peritonitis patient received early initiation of empirical antibiotic therapy either intraperitoneally or systemically after sufficient biological samples were collected. The empirical treatment for PDAP should target both gram-positive and gram-negative bacteria. The recommended empirical antibiotic regimen includes a first-generation cephalosporin or vancomycin targeting gram-positive bacteria combined with a third-generation cephalosporin or aminoglycoside targeting gram-negative bacteria. Alternatively, cefepime may be used as a monotherapeutic option. Furthermore, the choice of treatment often considers common pathogens in the local area and is adjusted according to drug sensitivity results and clinical effectiveness. Previous research [33] indicates that gram-positive bacteria are one of the most common gut pathogens at our center. In addition to the recommended treatment regimens, levofloxacin can also be used empirically at our center. For the treatment of comorbidities such as renal anemia, renal osteodystrophy, and renal hypertension, appropriate medications were selected according to the KDIGO/ISPD guidelines. Active management of underlying conditions such as diabetes and cardiovascular diseases was implemented. In accordance with ISPD guidelines, exit site care was provided to patients in all groups, and routine prophylactic antifungal treatment was given to PD patients who received antibiotic therapy for more than 3 days. The distribution of years across the groups was relatively balanced,

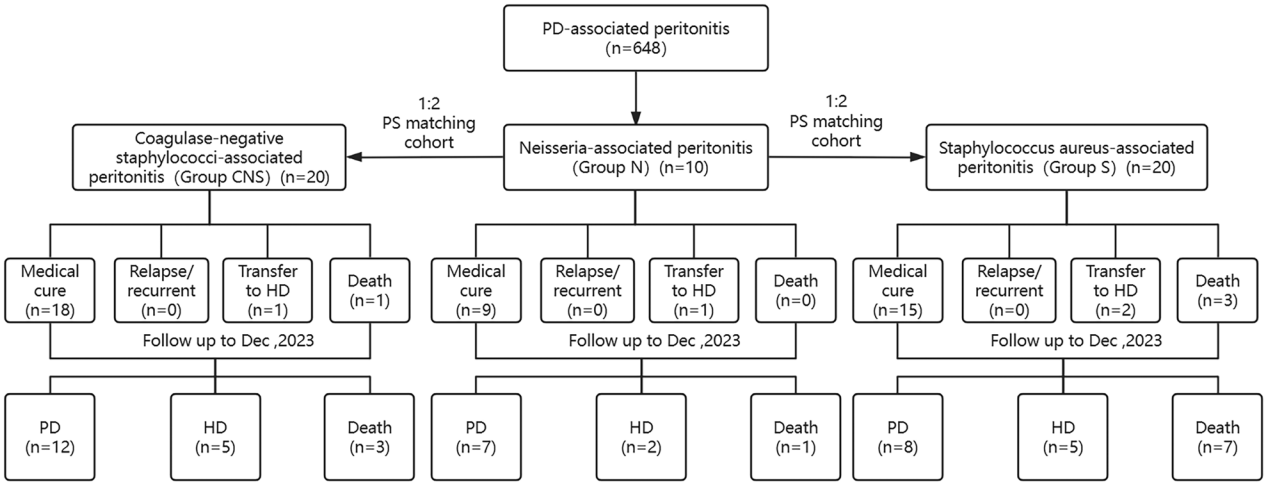

Figure 1. Technical roadmap for patients with *neisseria*, coagulase-negative staphylococci, and *Staphylococcus Aureus* peritoneal dialysis-related peritonitis.

ensuring that there were no significant differences in the treatment regimens between them.

2.2.2. Prognostic assessment

Clinical prognosis assessment was conducted according to the ISPD guideline standards [29–32], which include both short-term outcomes and long-term prognosis. Short-term outcomes include medical cure, relapse/recurrent peritonitis, transfer to hemodialysis (HD) or death. Medical cure: complete resolution of peritonitis together with NONE of the following complications: relapse/recurrent peritonitis, catheter removal, transfer to hemodialysis for 30 days or death. Relapse/recurrent peritonitis: Relapsing: peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism or one sterile (culture negative) episode (i.e. specific organism followed by the same organism, culture negative followed by a specific organism or specific organism followed by culture negative). Recurrent: peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism. Transfer to hemodialysis (HD): during treatment, the patient required catheter removal and transitioned to temporary HD due to peritonitis, or was switched to permanent HD after catheter removal. Peritonitis-associated death: death occurring within 30 days of peritonitis onset or death during hospitalization due to peritonitis. Long-term prognosis, including continuation of PD, conversion to HD, or death, was evaluated through follow-up, with the final follow-up conducted in December 2023.

2.3. Data collection

Clinical data from all cases were extracted from the computerized medical records in the hospital's information system. The collected data included age, sex, duration of peritoneal dialysis, body temperature (T), heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), history of peritonitis, clinical symptoms, risk factors for PDAP, treatment medications, short-term outcomes and long-term prognosis. The laboratory indicators included inflammation-related markers such as procalcitonin, high-sensitivity C-reactive protein (hs-CRP), white blood cell (WBC) count in the peritoneal effluent on the third day posttreatment, blood WBC, percentage of neutrophils (N%), absolute neutrophil count (ANC), hemoglobin, and platelet count; biochemical indicators such as serum uric acid, serum albumin, high-density lipoprotein (HDL), lactate dehydrogenase, alkaline phosphatase, potassium, calcium, sodium, magnesium, phosphorus, and serum ferritin; coagulation function indicators such as activated partial thromboplastin time (APTT) and D-dimer; and peritoneal effluent culture results.

2.4. Statistical methods

Statistical analysis was conducted using SPSS software version 25.0. Patients diagnosed with *Neisseria*-associated PDAP were included in Group N. Based on sex, age, dialysis duration, and residual kidney Kt/V, 1:2 matching was performed to create Group CNS and Group S as cohort control groups. Quantitative data were analyzed as follows: normally distributed data are reported as means ± standard deviations, with comparisons between groups conducted *via* multivariate analysis of variance (ANOVA). For data not normally distributed, the results are presented as medians and interquartile ranges (IQRs), and intergroup differences were assessed *via* nonparametric rank-sum tests. Chi-square tests and Fisher's exact tests were applied to qualitative data. Survival curves were constructed *via* the Kaplan–Meier approach, with statistical significance determined *via* the log-rank test.

3. Results

3.1. General information

From January 2010 to June 2022, our center treated 376 PDAP patients who experienced 648 episodes of peritonitis, resulting in a peritonitis rate of 0.11 episodes per patient year [34]. The distribution of causative organisms was as follows: gram-positive bacteria were responsible for 315 episodes (48.6%), gram-negative bacteria for 152 episodes (23.5%), and polymicrobial infections for 48 episodes (7.4%). Fungi were identified in 31 episodes (4.8%), while tuberculosis accounted for 2 episodes (0.3%). Additionally, negative culture results were found in 110 episodes (17.0%). Ten episodes (1.5%) with *Neisseria*-associated PDAP were ultimately included in the study: 6 males (60%) and 4 females (40%) aged 38–81 years. Three patients (30%) had first-time infections, whereas the remaining 7 patients (70%) had a history of PDAP. The education levels were as follows: 1 had a college diploma, 5 had a middle school education, 3 had a primary school education, and 1 was illiterate. The primary underlying diseases included chronic glomerulonephritis ($n=7$), diabetic nephropathy ($n=1$), antineutrophil cytoplasmic antibody-associated vasculitis ($n=1$), and uric acid nephropathy ($n=1$). The patients had comorbidities such as hypertension ($n=8$), a personal history of cerebral hemorrhage ($n=3$), coronary heart disease ($n=2$), and diabetes ($n=2$). The main symptoms reported were abdominal pain ($n=8$) and cloudy dialysis effluent ($n=8$), followed by fever ($n=4$), diarrhea ($n=3$), and nausea and vomiting ($n=3$). The possible causes of infection included 4 cases due to contamination from improper handling (2 of which involved patients biting open the dialysis bag), 2 cases due to gastrointestinal infections, and 4 cases with unknown causes. With respect to pathogen detection, among the 10 *Neisseria* strains identified, 3 cases were *Neisseria cinerea*, 3 cases were *Neisseria elongata*, 2 cases were *Neisseria sicca*, 1 case was *Neisseria flavescens*, and 1 case was *Neisseria mucosa*. The details are presented in Table 1.

3.2. Comparison of baseline characteristics and laboratory indicators between groups

An analysis of the baseline data, which refers to the condition of the patients at the time of presentation with PDAP,

Table 1. Clinicopathological data of cases in our series ($n = 10$).

No	Sex and age	Dialysis duration (m)	Pathogenic bacteria	Education level	Primary disease or comorbidity	Symptoms	Suspected infection factors	Treatment	
								Empirical medication	Eventual antimicrobial(s)
1	M:49	72	N.cinerea	Middle school	Chronic glomerulonephritis	Abdominal pain	Unknown	Levofloxacin (i.p.) + Vancomycin (i.p.) + Levofloxacin (i.v.)	Cefodizime(i.p.)
2	M:57	120	N.mucosa	Middle school	Uric-acid nephropathy, hypertension, personal history of cerebral hemorrhage	Abdominal pain, turbid PD effluent, diarrhea	Bite open the PD fluid package with teeth	Cefazolin sodium (i.p.) + Piperacillin/ Tazobactam (i.v.)	Meropenem(i.v.)
3	M:73	132	N.elongata	Primary school	Chronic glomerulonephritis, hypertension, coronary heart disease	Abdominal pain, turbid PD effluent	Unknown	Amikacin (i.p.) + Cefazolin sodium (i.p.) + Vancomycin (i.v.)	Amikacin (i.p.) + Vancomycin (i.v.)
4	F:59	36	N.sicca	Illiteracy	Chronic glomerulonephritis, hypertension, personal history of cerebral hemorrhage	Abdominal pain, turbid PD effluent, diarrhea, nausea, vomiting	Gastrointestinal infection	Amikacin (i.p.) + Vancomycin (i.p.) + Piperacillin/ Tazobactam (i.v.)	Amikacin (i.p.) + Piperacillin/ Tazobactam (i.v.)
5	F:81	60	N.flavescens	Junior college	Chronic glomerulonephritis, hypertension	Turbid PD effluent, diarrhea, fever	Unknown	Levofloxacin (i.p.) + Piperacillin/ Tazobactam (i.v.)	Meropenem (i.v.) + Vancomycin (i.v.)
6	M:49	48	N.cinerea	Middle school	Diabetic nephropathy, hypertension, personal history of cerebral hemorrhage	Abdominal pain, turbid PD effluent, fever	Improper PD procedure	Amikacin (i.p.) + Piperacillin/ Tazobactam (i.v.) + Vancomycin (i.v.)	Piperacillin/ Tazobactam (i.v.) + Vancomycin (i.v.)
7	F:41	36	N.elongata	Middle school	Chronic glomerulonephritis, hypertension	Abdominal pain, diarrhea	Gastrointestinal infection	Amikacin (i.p.) + Piperacillin/ Sulbactam (i.v.) + Vancomycin (i.v.)	Amikacin (i.p.) + Piperacillin/ Sulbactam (i.v.)
8	M:75	24	N.sicca	Primary school	Chronic glomerulonephritis, hypertension, diabetes, coronary heart disease	Turbid PD effluent, abdominal distension, panting	Bite the PD catheter connection with teeth	Levofloxacin (i.p.)	Meropenem (i.p.)
9	F:59	156	N.elongata	Primary school	Chronic glomerulonephritis, hypertension	Abdominal pain, turbid PD effluent, fever, nausea, vomiting	Unknown	Levofloxacin (i.p.) + Meropenem (i.v.)	Levofloxacin (i.p.) + Piperacillin/ Tazobactam (i.v.)
10	M:38	36	N.cinerea	Middle school	IgA nephropathy, hypertension, chronic hepatitis b	Abdominal pain, turbid PD effluent, diarrhea, nausea, vomiting	Improper PD procedure	Amikacin (i.p.) + Cefazolin sodium (i.p.) + Cefazolin sodium (i.v.)	Amikacin (i.p.) + Cefazolin sodium (i.p.) + Cefazolin sodium (i.v.)

revealed that, excluding the matched variables of sex, age, dialysis duration, and residual kidney Kt/V, there were no statistically significant differences in prior infection history ($p > 0.05$). However, there were statistically significant differences in T stage ($p < 0.01$). Compared to Group N, patients in Group S had higher body temperatures, as detailed in Table 2.

In terms of laboratory biochemical indicators, compared with Group N, Group S presented a markedly elevated high-sensitivity C-reactive protein (hs-CRP) level, decreased serum albumin levels, reduced serum potassium levels, whereas Group CNS presented a significantly lower neutrophil percentage (N%) than did Group N ($p < 0.05$), as detailed in Table 3.

3.3. Treatment and outcomes

All 10 patients received empirical antibiotic therapy upon admission. The top 5 commonly used antibiotics were vancomycin (20.7%), piperacillin-tazobactam (17.2%), amikacin (17.2%), levofloxacin (13.8%), and meropenem (13.8%), as detailed in Table 1. With respect to clinical treatment

outcomes, 9 patients achieved medical cure, and 1 patient was transferred to HD. The disease remission rate in Group N was 90%, similar to that in Group CNS (90%) and higher than that in Group S (75%), but there was no statistically significant difference between the groups ($p = 0.531$), as detailed in Table 4.

With respect to long-term outcome, all patients were followed up until December 2023, with follow-up durations ranging from 1 month to 107 months. In Group N, 20% of patients transitioned to hemodialysis in the long term, which was slightly lower than that in Group CNS (25%) and Group S (25%), but the differences among the 3 groups were not statistically significant. The mortality rate in Group N was 10%, which is similar to that in Group CNS (15%) and lower than that in Group S (35%), but there was no significant difference among the 3 groups ($p = 0.185$) (Table 4). Kaplan–Meier analysis revealed no significant difference in cumulative survival rates among the 3 groups (log-rank $\chi 2 = 2.396$, $p = 0.302$) (Figure 2). Owing to the limited number of cases, no significant difference was found in the analysis of the 3 groups. However, the figure suggests that Group S has a lower cure rate and slightly worse long-term prognosis than did Groups N and CNS, which had similar outcomes.

Table 2. Comparison of general data of 3 groups of patients.

	Group N	Group CNS	Group S	*P*-value
Sex (male/female)	6/4	12/8	12/8	1.00
Age (years)	58.10 ± 14.52	58.40 ± 13.76	54.15 ± 12.97	0.80
Dialysis duration (months)	72.00 ± 46.99	72.60 ± 52.59	68.40 ± 50.03	0.96
Residual kidney Kt/V	0.00 (0.00, 0.05)	0.00 (0.00,0.08)	0.00 (0.00, 0.04)	0.99
First infection (*n*)	3	13	9	0.17
Comorbid with diabetes (*n*)	2	5	3	0.90
T (℃)	37.23 ± 0.86**	37.12 ± 0.53***	37.90 ± 0.92***	<0.01

Notes: Group *N* represents *Neisseria*-associated peritoneal dialysis-related peritonitis, Group CNS represents coagulase-negative staphylococci-associated peritoneal dialysis-related peritonitis, and Group S represents *Staphylococcus aureus*-associated peritoneal dialysis-related peritonitis. *indicates *P*-value < 0.05 between the Group N and the Group CNS, **indicates *P*-value < 0.05 between the Group N and the Group S, ***indicates *P*-value < 0.05 between the Group CNS and the Group S.

4. Discussion

PDAP is the leading complication associated with PD. Although the widespread use of mupirocin has reduced the proportion of cases in which gram-positive cocci are the primary pathogens, they still remain the leading cause of PDAP [35,36]. In clinical practice, the most frequently encountered pathogenic cocci are *Staphylococcus aureus* and coagulase-negative staphylococci, including *Staphylococcus epidermidis*, *Staphylococcus capitis*, and *Staphylococcus hemolyticus*. Several studies have shown that compared to other gram-positive bacterial infections, *Staphylococcus aureus* infections lead to higher rates of failure to achieve medical cure and all-cause mortality [37–40], whereas coagulase-negative staphylococci generally have better outcomes, a conclusion supported by numerous studies [41,42]. Among gram-negative bacteria, *Escherichia coli* is commonly reported [43], while reports of gram-negative cocci are rare, leaving our understanding of this bacterial group relatively limited. *Neisseria* species, commonly known as diplococci, are gram-negative cocci. All the species within this genus are aerobic, nonmotile, and oxidase positive. In addition to *Neisseria meningitidis* and *Neisseria gonorrhoeae*, most *Neisseria* species do not possess typical virulence factors such as pili, opacity-associated proteins, or H8 antigens. As a result, they generally only cause infections when the host immune system is compromised [44]. However, few case reports have highlighted the pathogenic potential of these traditionally nonpathogenic *Neisseria* species. Through a literature search and review, we identified a total of 20 case

Table 3. Comparison of physical and chemical indexes among the 3 groups.

Variable	Normal range	Group N	Group CNS	Group S	*P*-value
Procalcitonin (ng/mL)	0.00–0.25	2.75 (0.41, 9.01)	0.85 (0.29, 1.67)***	9.29 (2.53, 17.83)***	<0.01
Hs-CRP (mg/L)	0.00–3.00	92.34 ± 63.32**	86.64 ± 59.03***	154.47 ± 69.62** ***	**<0.01**
Blood WBC (10^9/L)	3.50–9.50	9.23 ± 3.64	7.12 ± 2.77***	12.26 ± 4.58***	<0.01
Absolute Neutrophyl Count (10^9/L)	1.80–6.30	8.06 ± 1.09	5.42 ± 2.59***	10.42 ± 4.91***	<0.01
***N* (%)**	40.0–75.0	89.85 (82.32, 92.65)*	73.50 (67.58, 80.80)*	84.75 (75.20, 91.65)	**<0.01**
Hemoglobin (g/L)	130–175	97.50 (86.25, 107.25)	87.00 (77.50, 101.75)	85.50 (75.50, 94.25)	0.40
Platelet count (10^9/L)	125–350	167.00 (129.00, 194.25)	176.50 (149.00, 222.75)	183.00 (146.25, 205.00)	0.69
Uric acid (μmol/L)	119–416	330.10 ± 84.83	314.10 ± 92.51	365.55 ± 78.73	0.17
Serum albumin (g/L)	40.0–55.0	30.44 ± 5.29**	27.77 ± 4.96	26.27 ± 4.97**	0.11
Lactate dehydrogenase (U/L)	120–250	173.50 (142.25, 223.00)	163.00 (154.00, 213.50)	204.00 (170.00, 264.00)	0.14
Alkaline phosphatase (U/L)	45–125	83.00 (57.00, 99.00)	90.00 (73.25, 181.50)	82.00 (60.75, 104.00)	0.47
Potassium (mmol/L)	3.50–5.30	3.74 ± 0.73**	3.83 ± 0.67***	3.29 ± 0.45** ***	**0.02**
Calcium (mmol/L)	2.02–2.70	2.35 (2.32, 2.48)	2.26 (2.12, 2.40)	2.16 (1.97, 2.34)	0.08
Sodium (mmol/L)	137.0–147.0	137.95 (135.65, 138.88)	137.40 (133.62, 139.62)	136.75 (133.50, 138.25)	0.63
Magnesium (mmol/L)	0.60–1.14	0.76 ± 0.18	0.69 ± 0.14	0.63 ± 0.08	0.05
Phosphorus (mmol/L)	0.80–1.60	1.25 ± 0.36	1.26 ± 0.52	1.47 ± 0.49	0.32
Parathyroid hormone (pg/mL)	7.00–53.00	224.15 (79.28, 349.18)	143.25 (71.50, 350.95)	257.70 (171.25, 363.48)	0.47
Dialysate WBC count at day 3 (10^6/L)		160.00 (45.75, 531.75)	103.00 (22.50, 258.25)	450.00 (64.25, 1060.00)	0.07
Serum ferritin (ng/mL)	21.8–274.6	121.50 (71.00, 158.80)	217.80 (137.00, 394.30)	188.30 (144.20, 379.30)	0.08

Notes: *indicates *p*-value < 0.05 between the Group N and the Group CNS, **indicates *p*-value < 0.05 between the Group N and the Group S, ***indicates *p*-value < 0.05 between the Group CNS and the Group S.

reports of *Neisseria*-related PDAP patients from around the world. At our single center alone, there have been 10 cases of *Neisseria* infection, suggesting that our center has an advantage when it comes to analyzing its characteristics. Moreover, comparing and analyzing data from our center alongside previous case reports may be beneficial for exploring the clinical characteristics and outcomes of *Neisseria*-related PDAP.

Based on data from a meta-analysis of all available relevant literature to date, we identified 20 cases, consisting of 13 males and 7 females. The mean age of the patients was 40.00 ± 3.72 years, with a peritoneal dialysis duration of 15.50 (3.00, 42.00) months. Among these patients, 16 patients achieved a clinical cure, 2 required catheter removal, and 1 had the catheter reinserted 2 weeks after removal. Compared with the meta-analysis data, our center's patients were older (58.10 ± 14.52 years) and had a longer duration of peritoneal dialysis, averaging 72.0 ± 46.99 months. The older age at onset may be related to factors such as the overall age distribution of PD patients at our center. Additionally, the longer dialysis duration in our *Neisseria*-infected patients than in other reports may suggest that, as peritoneal function declines, patients are more susceptible to opportunistic infections. This warrants further investigation into the correlation between dialysis duration and *Neisseria* infection in future studies.

The mechanism by which *Neisseria* bacteria enter the peritoneal cavity of patients is still unclear. The relevant literature mentions a total of 6 cases of transmission routes, 4 of which are considered to be contamination by respiratory tract-colonized pathogens, and 2 cases have a personal history of pet ownership. In this study, 2 cases involved improper procedures in which patients used their teeth to tear open the peritoneal dialysis fluid opening, which may have caused displacement and infection by *Neisseria* colonizing the oral and nasal mucosa, suggesting that contamination by upper respiratory tract commensal bacteria remains the most likely transmission source. Additionally, this study included 2 patients with intestinal infections, showing that as the duration of dialysis increased, the role of intestinal bacterial translocation in pathogenesis became more evident.

The results indicated that Group N had a slightly higher cure rate than Group S. The trend in the Kaplan–Meier curve suggested a potentially better long-term prognosis, even though statistical significance was not achieved because of the limited sample size. There was also no difference in short-term outcomes and long-term prognosis between Group N and Group CNS. Based on a large-sample retrospective study [34] previously conducted at our center involving the same cohort of patients, we found that elevated hs-CRP, hypoalbuminemia, and hypokalemia are risk factors for

Table 4. Comparison of outcomes and prognosis among the 3 groups.

	Group N	Group CNS	Group S	*P*-value
Short-term outcomes				
Medical cure (*n*)	9	18	15	0.531
Relapse/recurrent peritonitis (*n*)	0	0	0	1.000
Transfer to HD (*n*)	1	1	2	1.000
Peritonitis-associated death (*n*)	0	1	3	0.513
Long-term prognosis				
PD (*n*)	7	12	8	0.235
HD (*n*)	2	5	5	1.000
Death (*n*)	1	3	7	0.185

Notes: Prompt: Long-term prognosis refers to the observation of the long-term prognosis of patients, including the continuation of peritoneal dialysis treatment(PD), withdrawal from peritoneal dialysis to hemodialysis(HD), and death. The time limit is December 2023.

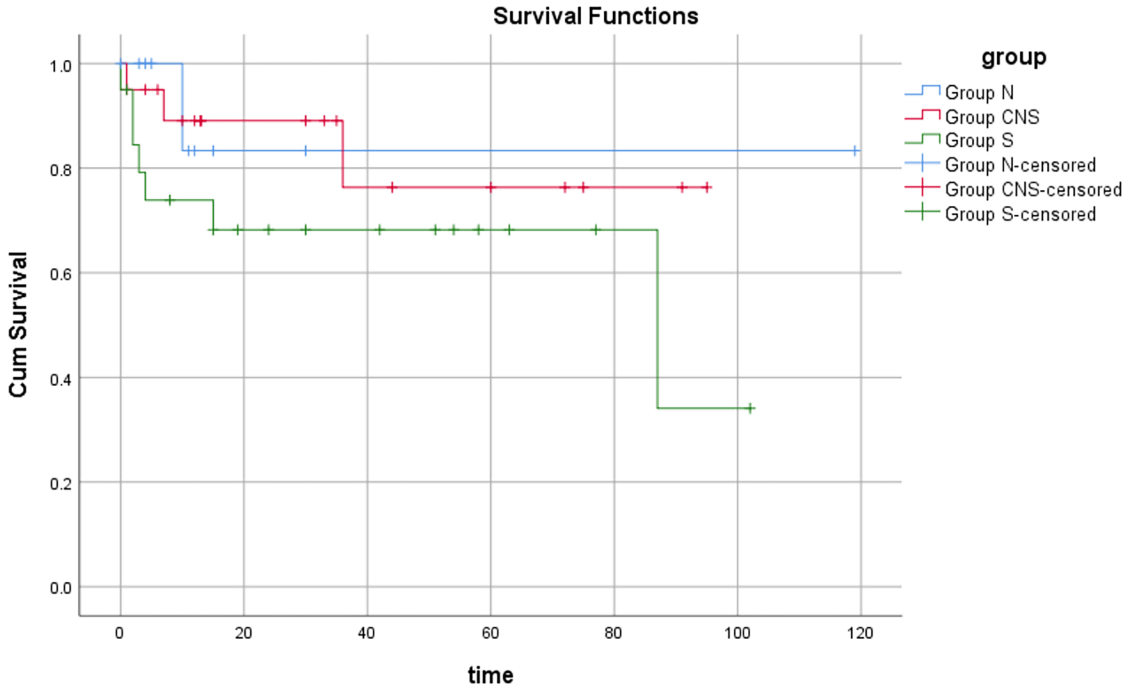

Figure 2. Kaplan–Meier survival analysis in 3 groups.

treatment failure in PDAP patients. By analyzing the baseline data of this study, we observed that compared to Group N and Group CNS, Group S had higher hs-CRP levels, lower serum albumin levels, and lower blood potassium levels. These differences may explain why the clinical outcomes in Group N are similar to those in Group CNS, but better than those in Group S. A study by N.Y. Zalunardo et al. [45] revealed that elevated CRP levels are significantly associated with poor short-term and long-term outcomes in PDAP patients. hs-CRP is a critical marker of inflammation and is widely used to assess the presence and severity of inflammation and infection. Persistently high CRP levels suggest that the infection is not effectively controlled or is recurrent, which can lead to deterioration of peritoneal function [46]. Additionally, a high CRP level is associated with an increased risk of systemic inflammatory response syndrome (SIRS) and cardiovascular complications [47]. These factors collectively contribute to the worsening of the short-term and long-term prognoses of patients. Serum albumin is an essential plasma protein that not only helps immune cells maintain normal function and activity [48] but also supports the effectiveness and stability of PD [49]. A high serum albumin level enhances the body's ability to resist infections and serve as a crucial indicator of nutritional status. Patients with hypoalbuminemia, who typically have poor nutritional status, are at a greater risk of infection and have worse prognoses [50,51]. Therefore, we conducted a factor analysis on patients with PDAP who did not achieve medical cure due to coccus infections, further clarifying the impact of high hs-CRP levels and low serum albumin concentration on outcomes, which confirmed the combined effect of these 2 factors on outcomes. Among these, serum albumin was an independent protective factor. A high hs-CRP level and low serum albumin concentration are the main reasons for the poor outcomes in Group S, whereas the relatively low hs-CRP level and higher serum albumin level in Group N may explain its relatively favorable outcomes. Moreover, the blood K levels differed among the 3 groups, with Group S showing a lower level. Studies have indicated that the severity and duration of hypokalemia are closely related to peritonitis [52]. Correcting hypokalemia in PD patients has been shown to reduce the risk of peritonitis [53]. Additionally, patients with low blood potassium levels often present low protein levels, high inflammatory marker levels, and poor nutritional status [54]. The impact of blood potassium levels on treatment and prognosis has been confirmed by others. For example, Murata et al. [55] reported that lower average blood potassium levels in 4 months preceding peritonitis were associated with a poor response to treatment.

Among the 10 patients in our center, 9 were cured, which is similar to the outcomes reported in other cases, suggesting that the overall clinical cure rate of *Neisseria* is relatively high. This could be due to the lower virulence of commensal *Neisseria* and its reduced exposure to antibiotics compared with other bacteria [56], leading to better antibiotic sensitivity in cases of *Neisseria* infections [57], which may account for the favorable treatment effects. However, one patient in our center was transferred to HD. The data suggest that this patient had the longest duration of peritoneal dialysis, a history of multiple peritonitis infections, and hypoalbuminemia, all of which are risk factors for ultimately not achieving medical cure. Although the outcomes of *Neisseria* infections is relatively good, owing to the lack of consensus, treatment is primarily based on empirical therapy. In cases of drug resistance, it is difficult to obtain pathogen susceptibility data in later stages, and empirical adjustments to treatment can lead to prolonged therapy, increased pathogen resistance, and a poor outcome.

5. Conclusion

In conclusion, this study retrospectively analyzed 10 cases of *Neisseria*-related PDAP at our center and reviewed the literature on *Neisseria*-related PDAP. We observed an increasing frequency of infections by traditionally nonpathogenic *Neisseria* species in recent years, although the underlying pathogenesis is unclear. At our center, factors such as a low education level leading to respiratory viral colonization and prolonged dialysis contributing to gut bacterial translocation may have contributed to these infections. According to case reports, although *Neisseria*-related PDAP may exhibit varying sensitivities to different drugs, overall treatment is effective, with an outcome similar to that of Group CNS and better than that of Group S. Factors such as hypoproteinemia, elevated hs-CRP, and hypokalemia may affect the outcomes of the disease, so addressing these risk factors during the course of the disease is important.

5.1. Limitations

This is a single-center, retrospective study that presents our center's treatment characteristics for *Neisseria*-related PDAP, with the aim of providing a reference for other clinicians. However, due to the small sample size and the retrospective design, the findings may not be generalizable to other populations or countries. Additionally, the lack of standardized guidelines for the diagnosis and treatment of *Neisseria*-related PDAP has led to variations in treatment approaches, which could introduce bias. Therefore, more cases need to be collected in the future to enable the formulation of more comprehensive guidelines for the prevention, diagnosis, treatment, and prognostic evaluation of *Neisseria*-related PDAP.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Hangzhou Traditional Chinese Medicine Hospital affiliated with Zhejiang Chinese Medical University (Approval No. 2021KY052). Due to the retrospective nature of the study, informed consent was waived (Approval No. 2021KY052).

Consent for publication

Not applicable.

Author contributions

YS contributed to the study design and data collection, as well as critically reviewing the manuscript. XC contributed to the statistical analysis of the data and the drafting of the initial manuscript. JN provided technical support for data analysis and contributed to the interpretation of the results. JY provided manuscript review and language editing. All authors have thoroughly examined and accepted the finalized version.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets utilized and analyzed in this study can be obtained from the corresponding author upon reasonable request.

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