

ORIGINAL ARTICLE

Changing microbiology and outcomes of PD-associated peritonitis over four decades

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ABSTRACT

Background. Peritoneal dialysis (PD)-associated peritonitis remains a major complication affecting patient outcomes and modality survival. This study aims to evaluate temporal trends in pathogen distribution and antibiotic susceptibility over four decades as well as clinical outcomes in PD-associated peritonitis.

Methods. We retrospectively analyzed 832 peritonitis cultures of PD patients across four decades from 1979 to 2024 treated at Robert Bosch Hospital, Stuttgart (Germany). For longitudinal comparison of pathogen distribution and antibiotic susceptibility, the study period was divided into four time periods: P1 (1979–1992), P2 (1993–2003), P3 (2004–2014), and P4 (2015–2024). Clinical response and outcomes were assessed in P4.

Results. Gram-positive bacteria was the most frequent causative organisms (56%), followed by Gram-negative bacteria (30%) and culture-negative peritonitis (CNP, 13%). Gram-negative peritonitis increased significantly in P4 compared to P1–P3, while coagulase-negative staphylococci (CNS) declined from 31% in P1 to 14% in P4 ($P = .0446$). Vancomycin susceptibility among Gram-positive organisms remained high, whereas ceftazolin susceptibility changed over time. In P4, the overall cure rate was 63%, with the highest in gram-positive (72%) and lowest in polymicrobial peritonitis (43%).

Received: 15.7.2025; accepted: 5.12.2025

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Regarding clinical outcomes, transition to permanent hemodialysis (HD) was significantly more frequent in Gram-negative than Gram-positive peritonitis (27% vs. 12%; $P = .03$). Both catheter removal and transition to permanent HD occurred significantly more often in polymicrobial peritonitis (54% and 40%) compared with Gram-positive (24% and 12%; $P = .001$ and $P = .0008$) and CNP (30% and 17%; $P = .01$ and $P = .04$). Regarding individual pathogens, *Staphylococcus aureus* (MSSA) was associated with a significantly higher catheter removal rate compared to other Gram-positive organisms.

Conclusion. Our findings show temporal changes of microbiological spectrum of PD-associated peritonitis over four decades. Polymicrobial and Gram-negative peritonitis were associated with poorer outcomes, emphasizing the need for ongoing microbiological surveillance and antibiotic stewardship to optimize PD care.

Keywords: clinical response, long-term observation, microbiological pattern, peritoneal dialysis, peritonitis

KEY LEARNING POINTS

What was known:

- Microbiological patterns in PD-associated peritonitis (PDaP) vary over time and influence empirical strategies.
- Gram-positive organisms have traditionally been the most common causative agents of PDaP, though a gradual increase in Gram-negative infections has been reported.
- Clinical outcomes vary depending on peritonitis and pathogen type.

This study adds:

- This is the longest observational period of microbiological patterns in PDaP to date. It emphasizes the need for ongoing local microbiological surveillance to adjust empiric antibiotic therapy based on susceptibility patterns.
- A detailed description of the laboratory response and outcomes in relation to the microbial spectrum.
- Polymicrobial, Gram-negative, and MSSA peritonitis are associated with poorer clinical response.

Potential impact:

- A regular review of local antibiograms and implementation of antibiotic stewardship programs may enhance treatment success through timely adaptation of empiric antibiotic therapy.
- Early identification of high-risk pathogens should prompt tailored antibiotic intervention.

INTRODUCTION

Peritoneal dialysis associated peritonitis (PDaP) remains a common and significant complication in patients undergoing peritoneal dialysis (PD). PDaP is associated with a high risk of treatment failure, as well as an increased morbidity and mortality risk with an episode dependent association [1]. It is important to initiate an early and effective antibiotic regimen to adequately treat PDaP and improve patient outcomes. This empiric antibiotic regimen needs to cover Gram-positive and Gram-negative organisms before microbiological identification allows for targeted adjustment. Owing to varying regional antimicrobial resistance patterns, the International Society for Peritoneal Dialysis (ISPD) recommends center-specific antibiotic therapy [2]. A previous retrospective study conducted at our regional reference center from 1979 to 2014 analyzed data on the causative pathogens and their antibiotic susceptibility, leading to an adaptation of the local antibiotic regimen [3]. Given the increasing significance of antibiotic resistance and the rising number of PD patients, we analyzed data on the microbiological profile and antibiotic susceptibility of PDaP in PD patients over a 45-year period from 1979 to 2024.

Although Gram-positive organisms remain the most common cause of PDaP, Gram-negative pathogens are increasingly reported and often associated with poorer clinical outcomes [4]. Especially some Gram-negative pathogens such as *Pseudomonas* species but also Gram-positive pathogens such as *Staphylococcus aureus* seem to be particularly virulent [5, 6]. Moreover, polymicrobial peritonitis seems to have higher rates of catheter re-

moval, and an increased likelihood of transition to permanent HD compared with monomicrobial infections [7, 8]. We additionally analyzed the clinical response and outcome of Gram-positive, Gram-negative, culture-negative peritonitis (CNP), and polymicrobial peritonitis as well as the clinical response of certain high-risk pathogens to antibiotic therapy.

MATERIALS AND METHODS

Study design

We analyzed all peritonitis cultures of hospitalized PD patients treated between 1979 and 2024 at the Robert Bosch Hospital, Stuttgart (Germany). As stated by the ISPD PDaP was defined by an effluent white blood cell count (WBCC) of $>100/\mu\text{l}$ with at least 50% polymorphonuclear cells and presence of abdominal pain or cloudy dialysis effluent [9].

Results were divided into two parts: In the first part, we compared the causative organisms and their antibiotic susceptibility across time. A quantitative analysis of the most prevalent pathogens was performed, and a comparison of the relative numbers and their antibiotic resistance profile was made with previous data from 1979 to 2014 already published by Kitterer et al. [3]. There were three different time periods defined by Kitterer et al.: period 1 (P1) from 1979 to 1992, period 2 (P2) from 1993 to 2003, and period 3 (P3) from 2004 to 2014 [3]. We defined our data as period 4 (P4) from 2015 to 2024. We not only compared individual pathogen species, but pathogen groups with clinical relevance, including SPICE

bacteria (*Serratia* spp., *Pseudomonas* spp., *Proteus* spp., *Citrobacter* spp., *Enterobacter* spp.). These organisms exhibit intrinsic resistance to aminopenicillins (e.g. ampicillin, amoxicillin) due to chromosomally encoded beta-lactamase activity and may develop resistance to third-generation cephalosporins (e.g. ceftriaxone, cefotaxime, ceftazidime) via inducible AmpC beta-lactamases, potentially leading to treatment failure.

In the second part, clinical response and outcomes were analyzed in P4 (clinical response data was only available in patients hospitalized from 2015 onward due to a change in the hospital information system). To allow for a more accurate assessment of outcomes, the analysis was based on peritonitis episodes rather than individual culture results, as some episodes involved polymicrobial peritonitis. A total of 235 peritonitis episodes (284 cultures) with diagnosed PDaP between 2015 and 2024 were available for analysis.

In the ISPD peritonitis guideline a good response to antibiotic therapy is defined by a decrease in effluent WBCC by at least 50% in 72 hours [9]. According to the guideline we used effluent WBCC on days 0, 3, and 5 as well as C-reactive protein (CRP) levels and blood leucocyte count on days 0, 3, and 5 to measure clinical response.

We further analyzed clinical outcomes following the ISPD guideline including cure rate (complete resolution of peritonitis together with none of the following complications: relapse/recurrent peritonitis, catheter removal, transfer to hemodialysis for ≥ 30 days or death), the need for peritonitis-associated catheter removal with temporary or permanent transfer to HD, peritonitis-associated death (death occurring within 30 days of peritonitis onset or death during hospitalization due to peritonitis) as well as the occurrence of relapse (peritonitis episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism) or refractory peritonitis (peritonitis episode with persistently cloudy bags or persistent dialysis effluent leukocyte count $>0.1 \times 10^9/l$ after 5 days of appropriate antibiotic therapy) [9].

Data collection

The data were extracted from the hospital information system and the digital archive. Only routine parameters were recorded. Collected parameters included sex, date of birth, height, weight, abdominal pain, fever, length of hospital stay, effluent WBCC, CRP, procalcitonin (PCT), lactate, blood WBCC, pathogen isolated from effluent culture, antimicrobial susceptibility testing (antibiogram), initiated antibiotic therapy, modification of antibiotic therapy, the use of immunosuppressive medication, and the presence of diabetes mellitus (DM). It was also evaluated if the patients were treated with continuous ambulatory peritoneal dialysis (CAPD), or automated PD (APD), the need for catheter removal, recurrent peritonitis, or death associated with peritonitis.

As the dataset was limited to entries from the in-house system, external antibiograms and microbiological findings from other sources could not be included in the analysis.

Empiric therapy and prophylactic strategy during study periods

From 1979 to 2014, empiric therapy for PDaP at the RBK consisted of cefazolin and gentamicin. Following the results of the previous study by Kitterer et al. in 2014, the empiric regimen was revised to vancomycin and gentamicin [3]. After an internal analysis of the antibiotic susceptibility data in 2022 the empiric an-

tibiotic regimen was further modified to vancomycin and ceftazidime. Patients with nasal colonization by MSSA received prophylactic treatment with intranasal mupirocin. In addition, all patients received a single-dose perioperative antibiotic prophylaxis prior to PD catheter insertion.

Ethics

The ethical commission of the University of Tuebingen (Germany) approved this study (Ethical approval/Registration Number 755/2024B02). The study was conducted retrospectively without written or verbal consent from participants due to the extended study period and the retrospective, anonymized nature of the analysis.

Statistical analysis

For group comparisons of baseline characteristics, categorical variables were analyzed using the Fisher's exact and chi-square tests, and of continuous variables using the t- and Mann-Whitney tests, respectively, for normally and non-normally distributed variables. Analysis was performed using the statistical software package Prism (version 10.4.1, GraphPad Software Inc, San Diego, CA, USA). $P < .05$ was considered significant.

RESULTS

Change of microbiological spectrum over four decades

In total, 832 peritonitis cultures from 1979 to 2024 were analyzed. Gram-positive bacteria were the most frequent causative organisms, accounting for 56% of peritonitis episodes. Gram-negative bacteria were identified in 30% and CNP in 13% of peritonitis cultures (Table 1 and Fig. 1). While a slight but non-significant increase in Gram-negative infections was observed from P1 to P3, a significant rise was noted in P4 compared with all previous periods (Fig. 1). In addition, the proportion of CNP was higher in P4 compared with P1.

Spectrum of Gram-positive bacteria

From P1 to P4 staphylococci—especially coagulase-negative staphylococci (CNS)—were the most frequently detected pathogen, accounting for 41% ($n = 190$) of Gram-positive cultures.

The incidence of CNS decreased significantly from 31% in P1 to 14% in P4 ($P = .0446$) (Fig. 2a).

The only methicillin-resistant *Staphylococcus aureus* (MRSA) detected was in P3. Methicillin-resistant *Staphylococcus epidermidis* (MRSE) increased in P3 (16%) compared to P1 (5%) and P2 (6%) but decreased again in P4 (5%) ($P = .002$). In P2 vancomycin-resistant enterococcus appeared with 13% of all enterococci in P2, 19% in P3, and 16% in P4, without significant difference in number of cases between time periods.

Spectrum of Gram-negative bacteria

Escherichia coli (*E. coli*) was the most common Gram-negative bacteria (37%; $n = 93$) and the relative numbers of *E. coli* increased over time, although not significantly. *Klebsiella* spp. and *Pseudomonas* spp. were also common Gram-negative bacteria with stable numbers over time.

In P4, there were 29 cultures caused by SPICE bacteria, accounting for 10% of all PDaP cultures. There was no significant

Table 1: Distribution of organisms over time.

Time period	Total	P1 ^a (1979–1992)	P2 ^a (1993–2003)	P3 ^a (2004–2014)	P4(2015–2024)
Total cultures, n	832	132	140	276	284
		n (%)	n (%)	n, (%)	n (%)
Culture-negative	108 (13)	12 (9)	15 (11)	34 (12)	47 (17)
Gram-positive	462 (56)	87 (66)	81 (58)	168 (61)	126 (44)
MSSA	76 (9)	23 (17)	11 (8)	15 (5)	27 (10)
MRSA	2 (1)	0 (0)	0 (0)	2 (1)	0 (0)
CNS	190 (23)	41 (31)	35 (25)	73 (26)	41 (14)
MRSE	75 (9)	6 (5)	9 (6)	45 (16)	15 (5)
Enterococcus spp.	50 (6)	5 (4)	8 (6)	16 (6)	21 (7)
Streptococcus spp.	109 (13)	13 (10)	23 (16)	40 (15)	33 (12)
Others	35 (4)	5 (4)	4 (3)	22 (8)	4 (1)
Gram-negative	249 (30)	31 (24)	39 (28)	71 (26)	108 (38)
Pseudomonas spp.	36 (4)	7 (5)	8 (6)	10 (4)	11 (4)
Escherichia coli	93 (11)	12 (9)	11 (8)	31 (11)	39 (14)
Klebsiella spp.	29 (4)	3 (2)	2 (1)	9 (3)	15 (5)
Acinetobacter spp.	15 (2)	2 (2)	4 (3)	3 (1)	6 (2)
Enterobacter spp.	14 (2)	3 (2)	1 (1)	3 (1)	7 (3)
Citrobacter spp.	9 (1)	1 (1)	4 (3)	2 (1)	2 (1)
Serratia spp.	12 (1)	1 (1)	2 (1)	4 (1)	5 (2)
Bacteroides spp.	9 (1)	1 (1)	1 (1)	0 (0)	7 (3)
Others	32 (4)	1 (1)	6(4)	9 (3)	16 (6)
Fungi	12 (1)	2 (2)	4 (3)	3 (1)	3 (1)
Candida spp.	12 (1)	2 (2)	4 (3)	3 (1)	3(1)
Mycobacteria	1 (0)	0 (0)	1 (1)	0 (0)	0 (0)

^adata from Kitterer et al.

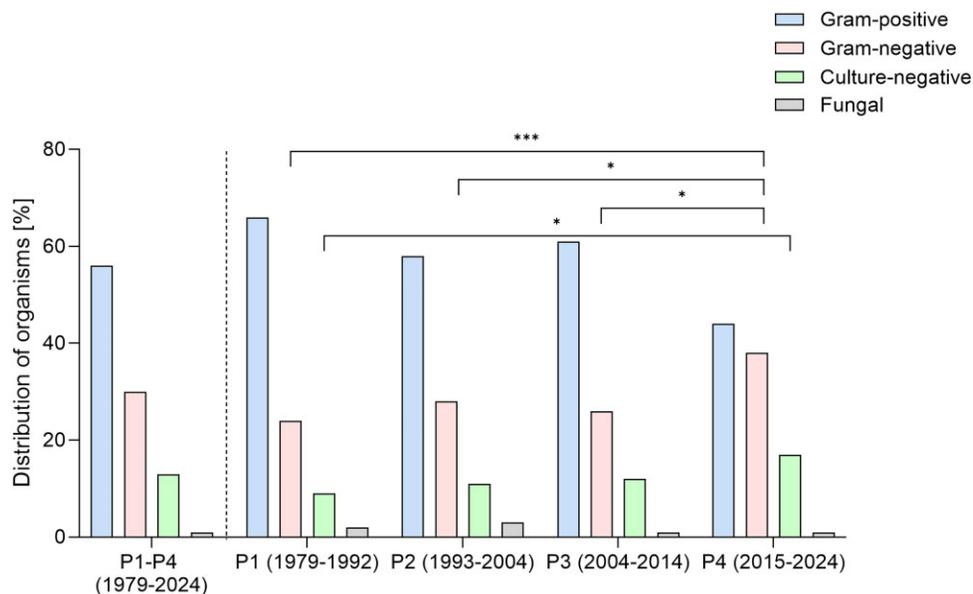


Figure 1: Distribution of organisms during the four different time episodes. Statistical differences were determined by Fisher's exact test, * $P < .05$; *** $< .001$.

difference in the prevalence of SPICE bacteria between the time periods [In P1 10% ($n = 12$), in P2 13% ($n = 16$), and in P3 8% ($n = 19$)] (Fig. 2b).

In vitro susceptibility rates to empiric initial intraperitoneal therapies

The ISPD guideline recommends an empirical Gram-positive coverage with first-generation cephalosporin or vancomycin

and an empirical Gram-negative coverage with a third-generation cephalosporin or aminoglycoside until a pathogen is identified [9].

Reviewing the susceptibility rates for vancomycin in P1 showed that 100% of tested Gram-positive organisms were susceptible to vancomycin, which was consistent in P2 (99%), P3 (98%), and P4 (96%).

The susceptibility to cefazolin reduced over the time periods (P1 93%, P2 75%, P3 58%). In P4 no organisms were directly tested for susceptibility to cefazolin. Instead, organisms susceptible to

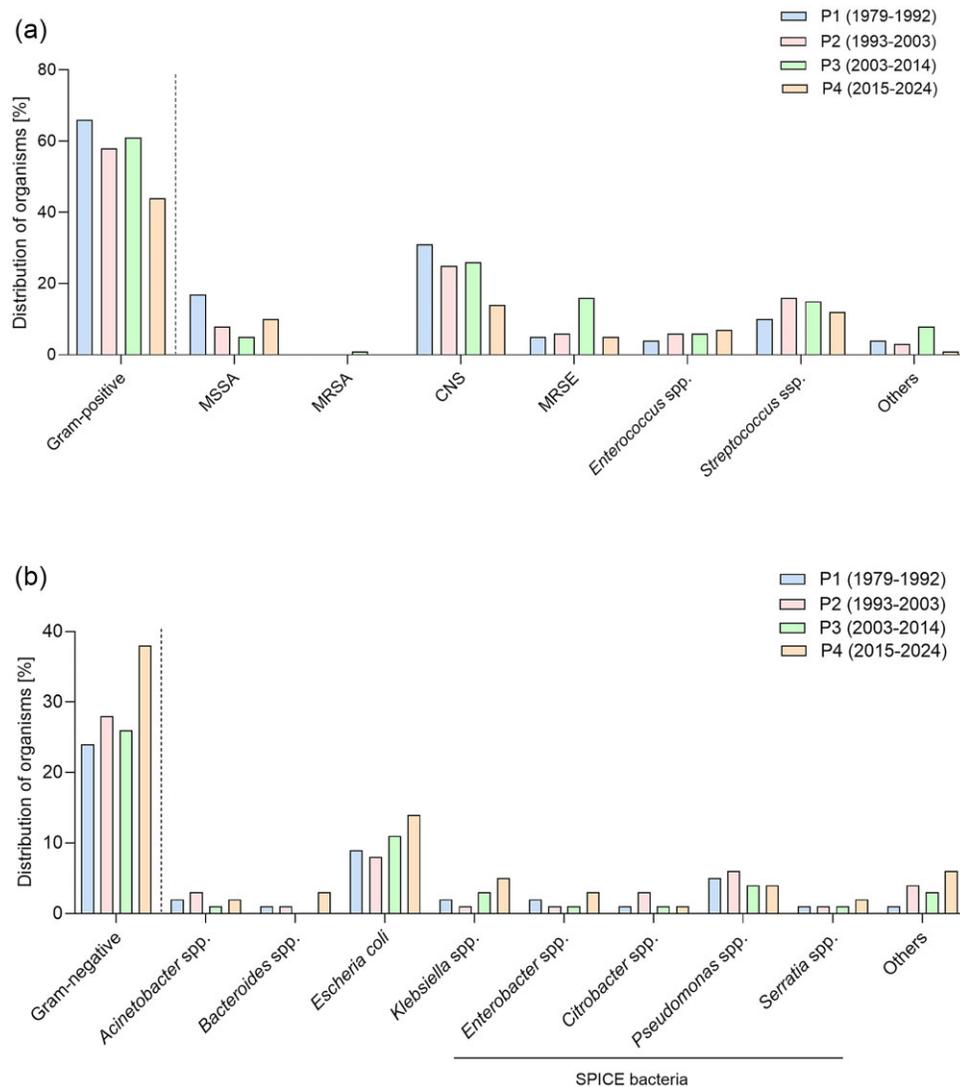


Figure 2: Etiologic spectrum of Gram-positive (a) and Gram-negative (b) bacteria over time. Distribution of organisms in period 1 (1979–1992), period 2 (1993–2003), period 3 (2004–2014), and period 4 (2015–2023).

penicillin/oxacillin and with cefoxitin screening suggestive of susceptibility were interpreted as ceftazolin susceptible. This applied to 78% of the tested Gram-positive organisms. Across all time periods the susceptibility to vancomycin was significantly higher than to ceftazolin ($P < .0001$).

The *in vitro* susceptibility for Gram-negative organisms to gentamicin in P1 was 94%, in P2 82%, P3 90%, and in P4 91%. In P1 only 3 Gram-negative organisms were tested for ceftazidime, all of them susceptible (100%). In P2 84%, in P3 93%, and in P4 95% of tested Gram-negative organisms were susceptible. There was no significant difference in the susceptibility of Gram-negative organisms to gentamicin vs. ceftazidime.

The two heatmaps (Fig. 3a and b) illustrate the antibiotic resistance rates (%) of the most common pathogens across the four time periods (P1–P4).

Clinical response and outcomes P4

For the analysis of clinical response and outcomes, a total of 235 peritonitis episodes from the most recent study period (P4,

2015–2024) were included (Table 2). Comparisons were made between CNP, Gram-positive, Gram-negative, and polymicrobial peritonitis.

Polymicrobial peritonitis was observed in 15% ($n = 35$) of cases. Of those 29% were Gram-negative, 17% Gram-positive, and 51% mixed Gram-positive and Gram-negative. Furthermore 40% ($n = 93$) were Gram-positive, 25% ($n = 59$) were Gram-negative, and 20% ($n = 46$) were CNP.

Baseline results and study population

The median age of patients was 61 years (IQR 49–73) and 43% were female. DM was present in 26% of patients, and 9% were receiving immunosuppressive therapy (Prednisolone 5–10 mg/d, Tacrolimus 0.5–1 mg/d, Azathioprine 100 mg/d or Mycophenolate mofetil 250 mg/d). The median duration on PD before the onset of peritonitis was 34 months (IQR 16.0–60.3). Most patients (92%) were treated with CAPD, 6% with APD and 2% were treated with CAPD and APD (Table 3).

(a)	MSSA				MRSE				Enterococcus spp.				Streptococcus spp.			
	P1 n=23	P2 n=11	P3 n=15	P4 n=23	P1 n=6	P2 n=9	P3 n=45	P4 n=15	P1 n=5	P2 n=8	P3 n=16	P4 n=20	P1 n=13	P2 n=23	P3 n=40	P4 n=32
Ampicillin	48%	64%	53%	NT	100%	100%	100%	NT	0%	37%	31%	20%	8%	5%	7%	0%
Amp/Sulb	NT	10%	0%	NT	NT	100%	100%	NT	NT	NT	NT	NT	NT	0%	0%	0%
Oxacillin	NT	NT	NT	0%	NT	NT	NT	100%	NT	NT	NT	NT	NT	NT	NT	NT
Cefazolin	0%	9%	0%	NT	100%	100%	100%	NT	NT	NT	NT	NT	8%	NT	NT	NT
Ceftriaxon	NT	50%	NT	NT	NT	100%	NT	NT	NT	NT	NT	NT	NT	0%	0%	0%
Moxifloxacin	NT	NT	0%	0%	NT	NT	87%	100%	NT	NT	60%	34%	NT	NT	11%	0%
Levofloxacin	NT	0%	0%	0%	NT	87%	88%	67%	NT	17%	60%	20%	NT	67%	18%	0%
Doxycycline	30%	9%	0%	0%	0%	22%	16%	8%	60%	0%	42%	56%	15%	52%	37%	25%
Gentamicin	30%	9%	0%	0%	33%	33%	44%	58%	20%	37%	47%	25%	46%	75%	56%	NT
Vancomycin	0%	0%	0%	0%	0%	0%	0%	0%	NT	12%	19%	16%	NT	0%	0%	8%
Linezolid	NT	0%	0%	0%	NT	0%	0%	0%	NT	0%	0%	5%	NT	0%	0%	8%
Imipinem	0%	9%	0%	NT	NT	100%	100%	NT	NT	37%	27%	25%	0%	0%	0%	0%

(b)	Pseudomonas spp.				Klebsiella spp.				Escherichia coli				Other gram-neg. organisms			
	P1 n=7	P2 n=8	P3 n=10	P4 n=11	P1 n=3	P2 n=2	P3 n=9	P4 n=15	P1 n=12	P2 n=11	P3 n=31	P4 n=38	P1 n=7	P2 n=13	P3 n=15	P4 n=44
Ampicillin	43%	NT	0%	NT	100%	100%	100%	100%	33%	55%	54%	30%	86%	92%	73%	89%
Amp/Sulb	NT	NT	0%	NT	NT	50%	22%	14%	NT	33%	20%	25%	NT	91%	43%	53%
Cefotaxim	43%	100%	NT	NT	0%	0%	22%	9%	0%	0%	11%	0%	0%	NT	9%	12%
Ceftazidim	0%	25%	0%	0%	NT	0%	22%	7%	0%	0%	6%	3%	NT	0%	7%	10%
Cefepime	NT	50%	0%	12%	NT	0%	25%	NT	NT	0%	3%	NT	NT	NT	8%	0%
Ofloxacin	NT	NT	NT	NT	NT	0%	NT	NT	NT	0%	NT	NT	NT	0%	NT	NT
Ciprofloxacin	NT	0%	20%	12%	NT	0%	11%	27%	0%	25%	13%	14%	NT	NT	43%	12%
Levofloxacin	NT	0%	20%	50%	NT	0%	11%	8%	NT	37%	16%	20%	NT	0%	43%	6%
Gentamicin	14%	0%	10%	15%	0%	50%	11%	10%	0%	18%	3%	22%	0%	17%	29%	7%
Imipinem	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	8%	0%	0%
TMX-SMX	43%	100%	67%	NT	0%	0%	0%	NT	17%	36%	16%	14%	17%	33%	23%	20%

Figure 3: Important Gram-positive (a) and Gram-negative (b) organisms causing PDaP and their in vitro resistance rates over four decades. All variables are expressed as resistance percentage rates, all variables are expressed as percentages. Period 1 (1979–1992), period 2 (1993–2003), period 3 (2004–2014), and period 4 (2015–2024). NT, not tested; Amp/Sulb, ampicillin/sulbactam; TMX/SMX, trimethoprim/sulfamethoxazole. The detailed case numbers can be found in the [Supplementary data \(Table S1 and S2\)](#).

Table 2: Peritonitis episodes in P4 (2015–2024).

Time period	P4 (2015–2024)
Total peritonitis episodes, n	235
CNP, n (%)	46 (20)
Gram-positive peritonitis, n (%)	93 (40)
Gram-negative peritonitis, n (%)	59 (25)
Polymicrobial peritonitis, n (%)	35 (15)
Mixed (Gram-positive, Gram-negative), n (%)	18 (8)
Mixed (Gram-negative, fungi), n (%)	1 (0)
Polymicrobial Gram-negative, n (%)	10 (4)
Polymicrobial Gram-positive, n (%)	6 (3)
Fungi, n (%)	2 (1)

Clinical response

Clinical response was measured using blood CRP and WBCC, as well as effluent WBCC. Polymicrobial and Gram-negative peritonitis showed significantly higher CRP levels than Gram-positive peritonitis on days 0, 3, and 5 (Fig. 4a–c).

Regarding the effluent WBCC, polymicrobial peritonitis demonstrated significantly higher WBCC on days 0 and 3 compared with Gram-positive, Gram-negative, and CNP. By day 5, this difference persisted only between polymicrobial peritonitis and CNP. Blood WBCC only showed a significant difference on day 5 between Gram-positive and Gram-negative peritonitis. The hospital stay of patients with polymicrobial peritonitis was 14 days (IQR 8–22), compared with 11 days (5.0–17.7) for CNP, 9 days

Table 3: Baseline characteristics of the study population in P4 (2015–2024).

Episodes, n = 235	n (%) / median (IQR)
Age (years)	61 (49–73)
Female gender	100 (43)
BMI (kg/m ²)	27 (23.0–30.4)
NA	9 (4)
T2DM	62 (26)
Immunosuppressive medication	21 (9)
NA	7 (3)
PD-modality	
CAPD	216 (92)
APD	14 (6)
Both	5 (2)
Time on PD until peritonitis (months)	34 (16.0–60.3)

Abbreviations: BMI, body mass index, T2DM, Type 2 DM.

[4–23] for Gram-negative, and 7 days (4.0–13.5) for Gram-positive peritonitis.

Clinical response of specific pathogens

Methicillin-sensitive *Staphylococcus aureus* (MSSA)

While Gram-positive infections showed the lowest catheter removal rate at 24%, episodes caused by MSSA were associated

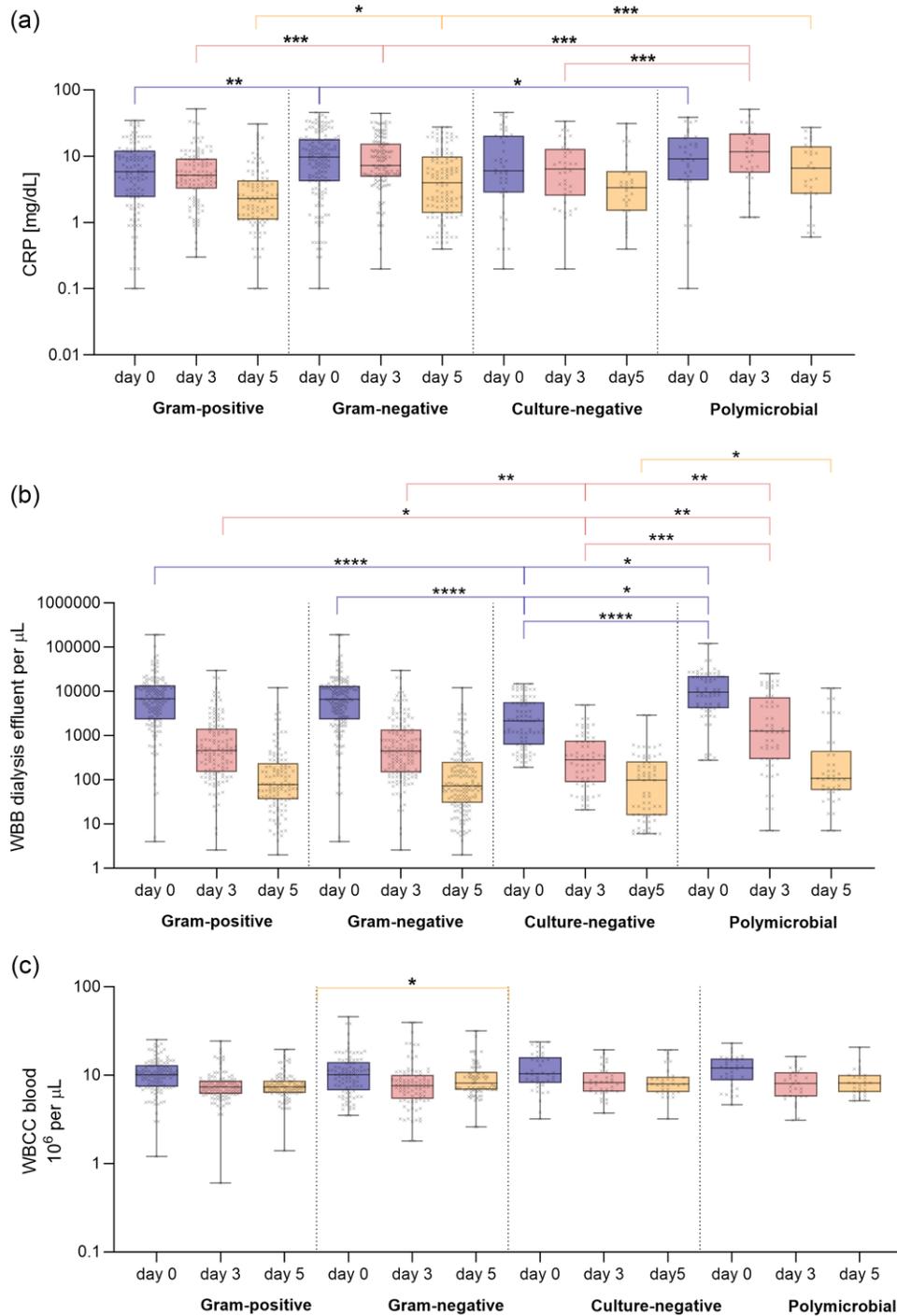


Figure 4: Clinical response Gram-positive, Gram-negative, culture-negative, and polymicrobial PDAp. (a) CRP levels, (b) WBCC dialysis effluent, and (c) WBCC blood on day 0, 3, and 5 after diagnosis of PDAp. Box, Median, IQR; Whiskers, min-max; Statistical differences were determined by the Mann-Whitney test, * <0.05 ; ** <0.01 ; *** <0.001 ; **** <0.0001 .

with a significantly higher removal rate of 52% ($P < .05$) compared to other Gram-positive peritonitis. They also showed significantly higher effluent WBCC on days 3 and 5 ($P < .05$).

Pseudomonas spp.

The need for catheter removal in *Pseudomonas* spp.-associated peritonitis was higher (50%) compared to other Gram-negative

peritonitis (34%), although not significantly. Although patients with *Pseudomonas* spp.-associated peritonitis showed a significantly higher effluent WBCC at initiation of therapy (day 0), no significant differences were found on day 5.

SPICE bacteria

Catheter removal was required in 36% of episodes with SPICE bacteria, which was the same in peritonitis caused by other

Table 4: Clinical outcome of peritonitis episodes in P4 (2015–2024).

Clinical outcome n (%)	Total n = 235	Gram-positive n = 59	Gram-negative n = 35	Polymicrobial n = 93	Culture-negative n = 46	Fungal n = 2
Cure	147 (63)	67 (72)	34 (58)	15 (43)	31 (67)	0 (0)
Recurrent	2 (1)	1 (1)	1 (2)	0 (0)	0 (0)	0 (0)
Relapse	2 (1)	0 (0)	1 (2)	1 (3)	0 (0)	0 (0)
Peritonitis-associated death	6 (3)	3 (3)	1 (2)	0 (0)	2 (4)	0 (0)
NA	2 (1)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
Catheter removal	76 (32)	22 (24)	21 (36)	19 (54)	14 (30)	0 (0)
Temporary transfer to HD	20 (9)	10 (11)	5 (9)	3 (9)	2 (4)	0 (0)
Permanent transfer to HD	51 (22)	11 (12)	16 (27)	14 (40)	8 (17)	2 (100)
Peritonitis-associated death	5 (2)	1 (1)	0 (0)	2 (6)	2 (4)	0 (0)

Gram-negative bacteria. There was no difference in clinical response compared to other Gram-negative bacteria.

E. coli

Among all Gram-negative bacteria, *E. coli* was the most common cause of PDaP. There were no differences in clinical response or catheter removal rate between *E. coli* and other Gram-negative bacteria.

MRSE

There was no difference in the clinical response or catheter removal rate between MRSE and other Gram-positive bacteria.

Enterobacter spp.

None of the *Enterobacter* peritonitis episodes required catheter removal. There was no difference in clinical response compared to other Gram-negative bacteria.

Clinical outcomes

Clinical outcomes were evaluated according to the definitions of ISPD guidelines and are shown in Table 4. All patients were hospitalized because of PDaP.

The overall cure rate was 63%, with the highest rate observed in Gram-positive peritonitis (72%), which was significantly higher compared to all other peritonitis episodes ($P = .03$). CNP showed a cure rate of 67%, followed by Gram-negative episodes (58%), whereas polymicrobial peritonitis demonstrated the lowest cure rate (43%), which was significantly lower than that of Gram-positive peritonitis ($P = .003$) and CNP ($P = .04$).

Catheter removal was required in 32% of all episodes and occurred significantly more often in patients with polymicrobial peritonitis (54%) compared to those with Gram-positive (24%, $P = .001$) and CNP (30%, $P = .01$).

Temporary transfer to HD occurred in 9% and transition to permanent HD in 22% of all episodes. The highest rate of transition to permanent HD was observed in polymicrobial peritonitis (40%), followed by Gram-negative (27%), whereas Gram-positive (12%, $P = .0008$) and CNP (17%, $P = .04$) showed significantly lower rates. Similarly, patients with Gram-negative peritonitis required conversion to permanent HD significantly more often than those with Gram-positive peritonitis ($P = .03$). Although the rate of conversion to HD was also higher in polymicrobial compared to Gram-negative infections (40% vs. 27%), this difference did not reach statistical significance.

Peritonitis-associated mortality was 4.6%, with no statistically significant differences observed between the groups.

Catheter removal: risk factors

Patients who underwent catheter removal showed higher inflammatory markers; they exhibited significantly higher CRP levels and effluent WBCC from day 0 to 5, as well as significantly higher blood leucocyte counts on day 5 compared to patients whose catheter got retained (Fig. 5a–c).

DISCUSSION

To our knowledge, our observational study, combined with the preceding data by Kitterer et al. represents the longest observational period of pathogen profiles in PDaP to date. Furthermore, a detailed description of laboratory findings with clinical outcome parameters in relation to the microbial spectrum has not yet been shown.

Change in microbiological spectrum over four decades

In the literature, Gram-positive pathogens are the most common cause for PDaP [10, 11]. However, several studies have demonstrated a relative increase in Gram-negative organisms and decrease in Gram-positive organisms in PDaP in the past decades [12, 13]. The incidence of Gram-negative organisms causing PDaP has been described in the range of 10%–32%, with the most recent data from 2009 to 2019 showing an incidence of up to 38% [11, 14, 15].

Our findings are in line with those observations: the most common causative organisms were Gram-positive but the relative number of Gram-negative organisms in PDaP increased significantly in P4 compared to P1–3. We also observed a significant decrease in CNS in P4. This decrease and the decrease in other Gram-positive organisms might be attributed to improved prevention in Gram-positive infections (e.g. improvements in the connection system or the use of prophylactic measures such as nasal eradication of *S. aureus*). Another contributing factor could be that our study only included hospitalized patients, whereas CNS-associated peritonitis is often managed in an outpatient setting [16]. In addition, improved hygiene practices during the COVID-19 pandemic may have further contributed to the observed reduction of CNS [17, 18]. Conversely, the increase in Gram-negative pathogens might be related to selective antibiotic pressure from prophylactic use, for example during catheter insertion or exit-site care or changes in patient population with

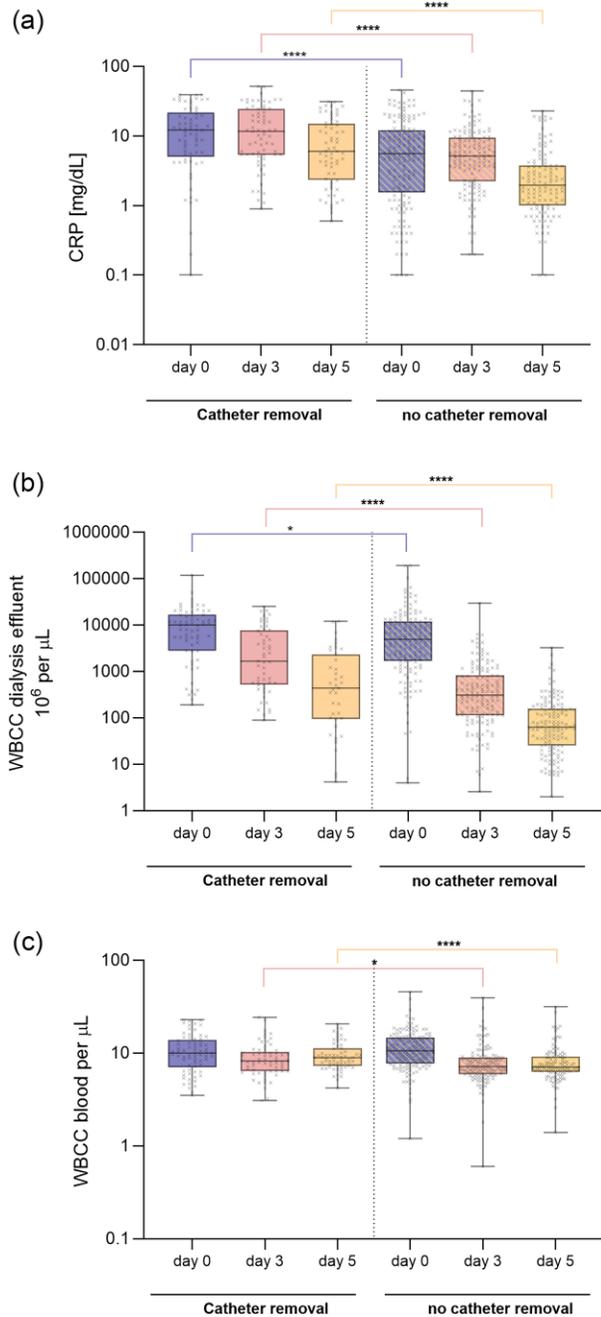


Figure 5: Risk factors for catheter removal. (a) CRP levels, (b) WBCC dialysis effluent, and (c) WBCC blood, on day 0, 3, and 5 after diagnosis of PDaP. Box, Median, IQR; Whiskers, min–max. Statistical differences were determined by the Mann-Whitney test, * <0.05 ; **** <0.0001 .

an increase in multimorbid and immunocompromised patients [2, 19, 20].

In vitro susceptibility rates to empiric initial intraperitoneal therapies

Looking at the empiric initial antibiotic strategy, the ISPD guideline recommends that Gram-positive organisms be covered by a first-generation cephalosporin or vancomycin and Gram-negative organisms by a third-generation cephalosporin or an

aminoglycoside [9]. The observed changes in antibiotic susceptibility over time (e.g. the decline in cefazolin susceptibility from P1 93% to P2 75% and P3 58%, and the apparent increase in P4 79%), prompted our center to revise its antibiotic regimen in 2014, changing from cefazolin and gentamicin to vancomycin and gentamicin [3]. After another internal review of antibiotic susceptibility rates in 2022, we observed a slight difference between the susceptibility patterns of gentamicin and ceftazidime, which—although not significant—led us to modify our empiric antibiotic regimen for Gram-negative coverage to ceftazidime. This highlights the importance of regularly reviewing empiric antibiotic strategies, considering local resistance patterns that may vary considerably between centers or regions. It also emphasizes the critical role of antibiotic stewardship as the increasing prevalence of antimicrobial resistance remains a major clinical challenge.

Clinical response and outcome in P4

To assess clinical response and outcomes in our cohort of hospitalized patients, we analyzed a total of 235 peritonitis episodes in P4. Among these, 35 episodes (15%) were polymicrobial, 93 (40%) Gram-positive, 59 (25%) Gram-negative, and 45 (20%) were CNP.

The ISPD guideline recommends a target of $<15\%$ of CNP [9]. The comparatively high CNP rate observed in our cohort is also seen in other centers [21] and may be attributed to the structural characteristics of our hospital-based center, which frequently manages referred patients who have already received antibiotic treatment prior to admission, which is a risk factor for CNP [22]. These pre-treated cases were included in the analysis and may have contributed to an increased number of CNP. Nevertheless, our aim is to further educate and retrain staff on appropriate sampling procedures. This shows how continuous quality monitoring play essential roles in improving patient outcomes.

Regarding clinical response, higher CRP levels and effluent WBCC in Gram-negative and polymicrobial peritonitis compared with Gram-positive and CNP indicated a more severe inflammatory response. This is consistent with previous reports showing that peritonitis caused by Gram-negative and mixed organisms show a stronger systemic inflammatory reaction [7, 12]. Contrary to possible expectations, SPICE bacteria or *Enterobacter* peritonitis did not show a worse clinical response in our study [23, 24]. Although there are data showing that the clinical outcome and catheter removal rate of MSSA are similar to those of other Gram-positive organisms [25], most studies show a poorer clinical outcome with MSSA-associated peritonitis [5, 26]. In our study, MSSA-associated peritonitis was also linked to a poorer clinical response with persistent higher effluent WBCC and higher catheter removal rate compared to other Gram-positive peritonitis.

The overall cure rate was 63%, with reported cure rates ranging between 65% and 86% [4, 27, 28] and catheter removal was necessary in 32% of episodes, which is higher than in most outpatient-based cohorts [29, 30]. Both these findings might reflect the greater severity of infections in hospitalized patients, who are typically older, have multiple comorbidities, and present with more complex clinical conditions [31]. In addition, it is possible that more severe cases were referred to our center, which may have contributed to this observation.

Consistent with previous findings, Gram-positive peritonitis showed the highest cure rate, whereas polymicrobial and Gram-negative infections were associated with poorer outcomes [4]. Polymicrobial peritonitis, in particular, was linked to the lowest cure rate (43%), the highest rate of catheter removal (54%),

and permanent transition to hemodialysis (40%). This is consistent with earlier observations [7, 32], although there are data that suggest that it is not the polymicrobial nature of the infection itself but rather the presence of enteric pathogens that primarily drives the poorer clinical outcomes [33]. In our study, data on the enteric origin of peritonitis were unfortunately not available. However, according to the ISPD guidelines, the presence of multiple Gram-negative organisms or a mixture of Gram-positive and Gram-negative bacteria should raise suspicion of an underlying gastrointestinal source, this was the case for 80% of all polymicrobial cases [9].

The PD-associated mortality rate (death related to the peritonitis episode, occurring during hospital admission or within 30 days thereafter) was 4.6%, which is comparable to previously reported figures [34, 35].

Risk factors for catheter removal were a slower clinical response with persistently higher inflammatory markers (CRP and effluent WBCC). This aligns with previous studies: a persistent high effluent WBCC on day 5 after initiation of therapy has been shown to be an independent risk factor for catheter removal [36–38].

Limitations

Our study has several limitations. Due to the long observation period, the microbiological testing methods changed over time and certain antibiotics that were tested for susceptibility in P1 were not consistently tested in later periods, which makes a direct comparison difficult. Furthermore, the structure of our center as a hospital-based referral unit may have influenced the distribution of causative pathogens and contributed due to a selection bias with more severe cases to the higher rate of catheter removals and the comparatively lower cure rate. This may limit the direct comparability of our results with outpatient-based cohorts. Furthermore, data on simultaneous catheter-associated infections were not available.

However, our study has unique strengths: The analysis of antimicrobial susceptibility patterns spans more than four decades, representing the longest observation period of a large PD-cohort reported to date. In addition, the clinical data including detailed description of laboratory response and outcome in relation to the microbial spectrum as well as outcome data were available for a wide range of pathogens over a 10-year period.

CONCLUSIONS

This study presents one of the longest observational analyses of pathogen distribution, antimicrobial susceptibility, and clinical outcomes in PDaP. Over four decades, we observed a shift from Gram-positive to Gram-negative organisms and changing antibiotic susceptibility patterns, underscoring the importance of ongoing local surveillance and antibiotic stewardship. Gram-positive peritonitis showed the most favorable outcomes, whereas Gram-negative and polymicrobial infections were associated with poorer clinical response and higher rates of technique failure. These findings highlight the need for continuous evaluation of empiric antibiotic regimens and preventive strategies to improve outcomes in PDaP.

SUPPLEMENTARY DATA

Supplementary data are available at [Clinical Kidney Journal](#) online.

ACKNOWLEDGEMENTS

We thank our PD nursing staff for their support.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author after internal board review.

CONFLICT OF INTEREST STATEMENT

None declared.

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Received: 15.7.2025; accepted: 5.12.2025

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