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Predictors and outcomes of fungal peritonitis in peritoneal dialysis patients

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Fungal peritonitis is a serious complication of peritoneal dialysis but previous reports on this have been limited to small, single-center studies. Using all Australian peritoneal dialysis patients, we measured predictors, treatments, and outcomes of this condition by logistic regression and multilevel, multivariate Poisson regression. This encompassed 66 centers over a 4-year period that included 162 episodes of fungal peritonitis (4.5% of all peritonitis episodes) that occurred in 158 individuals. *Candida albicans* (25%) and other *Candida* species (44%) were the most common fungi isolated. Fungal peritonitis was independently predicted by indigenous race and prior treatment of bacterial peritonitis. Peritonitis episodes occurring after 7 and 60 days of treatment for previous bacterial peritonitis decreases in the probability of fungal peritonitis 23 and 6%, respectively. Compared with other organisms, fungal peritonitis was associated with significantly higher rates of hospitalization, catheter removal, transfer to permanent hemodialysis, and death. The risks of repeat fungal peritonitis and death were lowest with catheter removal combined with antifungal therapy when compared to either intervention alone. Our study shows that fungal peritonitis is a serious complication of peritoneal dialysis and should be strongly suspected in the context of recent antibiotic treatment for bacterial peritonitis.

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Fungal peritonitis is a serious complication of peritoneal dialysis (PD). It is reported to be caused by yeast (*Candida* species) in at least 75% of cases, account for between 1% and 15% of all PD-associated peritonitis episodes, respond variably to treatment and result in high rates of both technique failure ($\geqslant$40%) and death (5–53%).[1–4] The 2005 update of the International Society of PD (ISPD) Guidelines for Management of PD-related Infections recommends immediate catheter removal after fungi are identified by microscopy or culture, followed by continuation of antifungal therapy for an additional 10 days.[5] However, these recommendations are based on the limited observations involving relatively small case series (5–70 cases) from the 1980s and 1990s involving single centers (often where PD expertise is concentrated).[1–4,6–15] Moreover, there has not been a comprehensive examination of different therapeutic approaches to fungal peritonitis within each of these centers.

The aim of this study was to examine the frequency, predictors, treatment and clinical outcomes of fungal peritonitis in all Australian PD patients involving 66 PD centers.

RESULTS

Population characteristics

A total of 4675 patients received PD in Australia during the study period (1 October 2003 to 31 December 2006). They were followed for 6002 patient-years. One hundred and sixty-two episodes of fungal peritonitis occurred in 158 individuals. Fungi accounted for 4.5% of all peritonitis episodes. The rates of all peritonitis and fungal peritonitis were 0.60 and 0.03 episodes per patient-year of treatment, respectively. The organisms isolated in cases of fungal peritonitis included *Candida albicans* ($n=41$), other *Candida* species ($n=72$), and other fungi ($n=52$). In two cases, *C. albicans* was isolated together with another *Candida* species. Additional non-fungal organisms were isolated in 35 (22%) episodes of fungal peritonitis, including coagulase-negative staphylococci ($n=10$), *S. aureus* ($n=5$), streptococci ($n=3$), enterococci ($n=5$), other Gram-positive organisms ($n=1$), *Pseudomonas* ($n=2$), *Acinetobacter* ($n=2$), *Escherichia coli* ($n=5$),

Klebsiella ($n=6$), *Enterobacter* ($n=5$), other Gram-negative organisms ($n=4$), and anaerobic bacteria ($n=1$).

Predictors of fungal peritonitis

The characteristics of patients who did and did not experience fungal peritonitis are shown in Table 1. On univariate analysis, patients who experienced fungal peritonitis during the study period were more likely to be Aboriginal and Torres Strait Islander peoples, living in Western Australia or Northern Territory, and tended to be less likely to have missing baseline peritoneal equilibration test data than those individuals who did not experience fungal peritonitis.

The hierarchical multivariate poisson model showed that fungal peritonitis incidence was significantly and independently predicted by Aboriginal/Torres Strait Islander racial origin (adjusted incidence rate ratio (IRR) 1.94, 95%

Table 1 | Characteristics of all Australian PD patients who did or did not experience fungal peritonitis at any stage during the period 2003–2006

Characteristic	Fungal peritonitis (*n*=158)	No fungal peritonitis (*n*=4517)	*P*-value
Age (years)	62.7 ± 16.5	61.5 ± 16.7	0.4
Women	73 (46%)	2053 (45%)	0.9
Racial origin			0.001
Caucasian	109 (69%)	3471 (77%)	
Aboriginal/Torres Strait Islander	27 (17%)	361 (8%)	
Maori/Pacific Islander	5 (3%)	76 (2%)	
Asian	13 (8%)	428 (9%)	
Other	4 (3%)	180 (4%)	
BMI (kg/m^2)	26.0 ± 5.0	26.0 ± 6.1	1.0
eGFR at dialysis start (ml/min per 1.73 m^2)	6.7 ± 6.4	7.1 ± 4.4	0.4
Late referral	43 (27%)	1068 (24%)	0.6
ESRF cause			0.4
Chronic glomerulonephritis	44 (28%)	1279 (28%)	
Diabetic nephropathy	52 (33%)	1267 (28%)	
Renovascular disease	22 (14%)	617 (14%)	
Polycystic kidneys	3 (2%)	253 (6%)	
Reflux nephropathy	8 (5%)	189 (4%)	
Other	21 (13%)	624 (14%)	
Unknown	8 (5%)	288 (6%)	
Current smoker	26 (16%)	754 (17%)	0.16
Chronic lung disease	19 (12%)	580 (13%)	0.8
Coronary artery disease	66 (42%)	1601 (35%)	0.3
Peripheral vascular disease	32 (20%)	1014 (22%)	0.8
Cerebrovascular disease	22 (14%)	586 (13%)	0.9
Diabetes mellitus	63 (40%)	1675 (37%)	0.5
HIV positive	0 (0%)	6 (0.1%)	0.6
Previous failed kidney transplant	6 (4%)	206 (5%)	0.8
Peritoneal transport status			0.10
High	17 (11%)	454 (10%)	
High average	63 (40%)	1648 (36%)	
Low average	41 (26%)	1037 (23%)	
Low	10 (6%)	188 (4%)	
Unknown/not specified	27 (17%)	1190 (26%)	
Center size (no. PD patients)			0.9
Small ($\leqslant$10)	2 (1%)	53 (1%)	
Small–medium (11–38)	13 (8%)	308 (7%)	
Medium–large (39–98)	35 (22%)	993 (22%)	
Large ($\geqslant$99)	108 (68%)	3163 (70%)	
State			<0.001
New South Wales	54 (34%)	1778 (39%)	
Northern Territory	13 (8%)	72 (2%)	
Queensland	26 (16%)	929 (21%)	
South Australia	5 (3%)	290 (6%)	
Tasmania	0 (0%)	77 (2%)	
Victoria	34 (22%)	926 (21%)	
Western Australia	26 (16%)	445 (10%)	

BMI, body mass index; eGFR, epidermal growth factor receptor; ESRF, end-stage renal failure; PD, peritoneal dialysis.

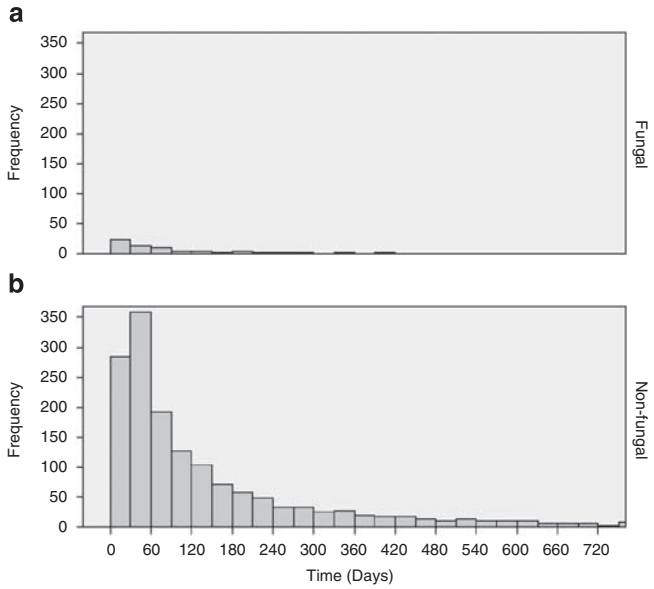

Figure 1 | Occurrence of fungal and non-fungal peritonitis following previous peritonitis. Histograms demonstrating the temporal occurrence of (**a**) fungal peritonitis and (**b**) non-fungal peritonitis in relation to an earlier episode of treated non-fungal peritonitis in Australian peritoneal dialysis patients who had experienced more than one episode of peritonitis during the study period.

confidence interval (CI) 1.15–3.28). There were also trends toward a lower incidence in patients with a diagnosis of polycystic kidney disease compared with other causes of ESKD (IRR 0.36, 95% CI 0.11–1.18, $P = 0.09$) and with a higher estimated glomerular filtration rate (eGFR) at the time of commencement of dialysis (IRR for highest quartile 0.64, 95% CI 0.38–1.06, $P = 0.09$). The development of fungal peritonitis was not associated with age, gender, body mass index, chronic lung disease, coronary artery disease, current smoking at renal replacement therapy start, peripheral vascular disease, cerebrovascular disease, diabetes mellitus, or late referral within 3 months of needing to start dialysis.

Effect of previous peritonitis episodes and antifungal prophylaxis

A history of previous peritonitis was equally likely for any given episode of fungal peritonitis episode as for a non-fungal peritonitis episode (43 vs 45%, respectively, $P = 0.3$). However, the time elapsed between an earlier peritonitis episode and the subsequent one was shorter for fungal peritonitis (median period 53 days, interquartile range (IQR) 20–131 days) than for non-fungal peritonitis (median 79 days, IQR 36–186 days, $P = 0.002$), such that the probability of an episode of peritonitis being caused by a fungus progressively increased as the time elapsed since an earlier peritonitis episode decreased (Figure 1). Specifically, if a peritonitis episode occurred within 7, 15, 30, or 60 days of completion of treatment for an earlier peritonitis episode, the respective probabilities of the current peritonitis episode being caused by a fungus were 23, 13, 7, and 6%. The corresponding odds ratios for fungal peritonitis were 7.00 (95% CI 2.51–19.6), 3.75 (95% CI 1.93–7.26), 2.16 (95% CI 1.30–3.60), and 1.68 (95% CI 1.04–2.73). No difference was observed in the time elapsed between an earlier peritonitis episode and subsequent fungal peritonitis due to *Candida* species (median 53 days, IQR 14–121.5 days) versus other fungal organisms (median 53 days, IQR 21–159 days, $P = 0.6$). Moreover, the occurrence of culture-negative peritonitis before a fungal peritonitis episode was not significantly different from the occurrence of culture-negative peritonitis in the total population (16 vs 12%, respectively, $P = 0.4$).

Only 260 (7%) patients were co-prescribed antifungal prophylaxis during any given peritonitis episode. In patients experiencing more than one peritonitis episode, the occurrence of fungal peritonitis was comparable between those who did and did not receive antifungal prophylaxis during earlier peritonitis episodes (4 vs 5%, respectively, $P = 0.8$).

Treatment of fungal peritonitis

The vast majority of patients with fungal peritonitis were initially treated with either intraperitoneal vancomycin or cephazolin in combination with gentamicin as empiric therapy (Table 2). Antifungal chemotherapy was administered in the initial empiric regimen in 33 (20%) episodes. Ultimately, 105 (65%) fungal peritonitis episodes were treated with antifungal agents, either alone (11 or 7%) or in conjunction with catheter removal (94 or 58%). Forty-eight (30%) fungal peritonitis episodes were treated with catheter removal alone, whereas 9 (6%) patients died before receiving either antifungal agents or catheter removal. The most commonly administered antifungal regimen in the initial, second, or third antimicrobial treatment courses was fluconazole monotherapy (90%), followed by amphotericin B monotherapy (20%), fluconazole and flucytosine (3%), amphotericin and fluconazole (2%), and ketaconazole (1%). Of the 13 episodes of fungal peritonitis initially treated with amphotericin monotherapy, treatment was changed to fluconazole monotherapy in four (31%) cases. Of the 91 episodes of fungal peritonitis initially treated with fluconazole monotherapy, treatment was changed to amphotericin monotherapy in seven (8%) cases, combination of amphotericin and fluconazole in two (2%) cases, and combination of fluconazole and flucytosine in three (3%) cases. Overall, the median total antifungal course duration was 15 days (Table 3). Heparin was administered to dialysate in 35 (22%) episodes of fungal peritonitis. Streptokinase was instilled in the PD catheter in one (1%) episode of fungal peritonitis. The approach to treatment of fungal infections did not appreciably vary between Australian states.

Outcomes of fungal peritonitis

Fungal peritonitis episodes frequently resulted in hospitalization (98%), catheter removal (88%), permanent hemodialysis transfer (74%), and death (9%) (Table 3). Compared with non-fungal peritonitis, fungal peritonitis was associated with significantly greater frequencies of occurrence of these

Table 2 | Antimicrobial agents prescribed in initial, second, and third antibiotic regimens for fungal peritonitis episodes in Australian peritoneal dialysis patients 2003–2006

Antibiotic	First regimen (*n*=162)	Second regimen (*n*=108)	Third regimen (*n*=39)
Amphotericin	4 (2%)	12 (11%)	5 (13%)
Fluconazole	28 (17%)	50 (46%)	17 (44%)
Flucytosine	0 (0%)	1 (1%)	2 (5%)
Ketoconazole	1 (1%)	0 (0%)	0 (0%)
Cephazolin	49 (30%)	8 (7%)	3 (8%)
Vancomycin	76 (47%)	18 (17%)	7 (18%)
Gentamicin	84 (52%)	9 (8%)	4 (10%)
Other aminoglycoside	2 (1%)	0 (0%)	0 (0%)
Other cephalosporin	39 (24%)	16 (15%)	5 (13%)
Ciprofloxacin	6 (4%)	5 (5%)	4 (10%)
β-Lactam	8 (5%)	8 (7%)	2 (5%)
Teicoplanin	1 (1%)	0 (0%)	0 (0%)
Imipenem	1 (1%)	0 (0%)	0 (%)
Rifampicin	1 (1%)	0 (0%)	0 (0%)
Metronidazole	4 (2%)	7 (6%)	4 (10%)
Other	7 (4%)	14 (13%)	7 (18%)

Results represent number of episodes treated with antibiotic (% of total treated with first-, second-, or third-line regimen). Note that values within each column add to more than 100% because of the use of combination antimicrobial regimens.

Table 3 | Treatment characteristics and clinical outcomes of peritoneal dialysis-associated peritonitis because of fungi or other organisms in Australia 2003–2006

Outcome	Fungal peritonitis (*n*=162 episodes)	Non-fungal peritonitis (*n*=3432 episodes)	*P*-value
Treatment			
Change to second antibiotic regimen	108 (67%)	1902 (55%)	0.006
Time to second antibiotic regimen	3 [1–6]	3 [2–5]	0.8
Change to third antibiotic regimen	39 (24%)	458 (13%)	<0.001
Time to third antibiotic regimen	6 [3.75–15.5]	6 [4–10]	0.5
Total antibiotic treatment duration	15 [5–26]	14 [8–19]	0.4
Hospitalisation			
Number (%)	159 (98%)	2345 (68%)	<0.001
Duration (days)	10 [5–24.5]	6 [3–11]	<0.001
Catheter removal			
Number (%)	142 (88%)	633 (18%)	<0.001
Time to occurrence (days)	5 [2–9]	7 [4–14]	<0.001
Temporary hemodialysis			
Number (%)	20 (12%)	132 (4%)	<0.001
Time to occurrence (days)	4 [2–11]	6 [3–12]	0.5
Duration (days)	90 [61–152]	65.5 [21.75–99.25]	0.017
Permanent hemodialysis			
Number (%)	120 (74%)	515 (15%)	<0.001
Time to occurrence	6 [3–10]	7 [4–13.5]	0.003
Death			
Number (%)	14 (9%)	68 (2%)	<0.001
Time to death	14 [5–26]	11 [3–22.5]	0.8

Results are expressed as number (%) or median days [interquartile range].

outcomes, as well as a longer duration of hospitalization and shorter time to catheter removal (Table 3). The frequencies of hospitalization, catheter removal, permanent hemodialysis transfer, and death were comparable between peritonitis episodes in which a fungus only was isolated or those in which multiple organisms (including a fungus) were isolated (98 vs 100%, 87 vs 89%, 71 vs 81%, and 8 vs 9%, respectively).

Nine (6%) patients died before receiving treatment with either antifungal therapy or catheter removal. The risk of death was higher with antifungal treatment alone (18%) than with either catheter removal alone (6%) or catheter removal plus antifungal treatment (7%), although the differences did not reach statistical significance due to the relatively small numbers of deaths in each group (2, 3, and 7, respectively). The risk of a subsequent repeat fungal peritonitis episode was

Table 4 | Effect of timing of catheter removal on subsequent clinical outcomes in 142 patients with fungal peritonitis requiring catheter removal

Characteristic	Number of days from peritonitis onset to catheter removal		*P*-value
	≤5 Days (*n*=64)	>5 Days (*n*=78)	
Permanent hemodialysis transfer	67 (86%)	53 (83%)	0.6
Death	6 (8%)	4 (6%)	0.8

significantly lower with combined catheter removal and antifungal therapy (0%) than with antifungal treatment alone (9%) or catheter removal alone (6%, $P=0.03$). In patients who had their catheters removed, the probabilities of returning to PD following an interim period of hemodialysis were comparable for fungal peritonitis episodes, which were or were not treated with concomitant antifungal therapy (15 vs 17%, $P=0.8$). Tenckhoff catheter removal occurred in 142 (88%) cases of fungal peritonitis after a median period of 5 days. In those patients who had their catheters removed, the outcomes for early (within 5 days) versus late (>5 days) removal were comparable with respect to permanent hemodialysis transfer (83 vs 86%, $P=0.6$) and death (6 vs 8%, $P=0.8$) (Table 4).

DISCUSSION

This study, involving 162 cases of PD-associated fungal peritonitis across 66 different PD centers, represents the largest examination to date of the frequency, predictors, treatment and clinical outcomes of this important condition. Fungal peritonitis accounted for 4.5% of all PD-related peritonitis episodes and was mostly (68%) caused by *Candida* species. Importantly, other micro-organisms in addition to fungi were isolated in 22% of cases. Fungal peritonitis was predicted by Aboriginal and Torres Strait Islander racial origin and recent completion of antibiotic treatment for bacterial peritonitis. Compared with other types of PD-associated peritonitis, fungal peritonitis was associated with significantly higher rates of hospitalization (98 vs 68%), catheter removal (88 vs 18%), permanent hemodialysis transfer (74 vs 15%), and death (9 vs 2%). In the context of polymicrobial peritonitis, the presence of fungus was the principal determinant of clinical outcome. Catheter removal in combination with antifungal therapy resulted in the best overall outcome with the lowest rates of repeat fungal peritonitis episodes and death compared with either therapeutic intervention on its own. However, no difference in outcome was observed between those episodes treated with earlier (within 5 days) rather than later catheter removal.

The clinical outcomes of fungal peritonitis in Australia were generally comparable with those of a number of single-center experiences. Wang *et al.*[14] reported on 70 episodes of fungal peritonitis at a single center in Hong Kong between 1989 and 1998. Similar to the findings of our study, they observed that fungal peritonitis accounted for 5.8% of all peritonitis episodes with 70% of all fungal peritonitis caused by *Candida* species. However, compared with our study, they reported lower rates of catheter removal (83 vs 88%) and permanent hemodialysis transfer (14.5 vs 74%), but higher mortality (44 vs 9%). The higher incidence of death from fungal peritonitis in the Hong Kong experience may have been attributable to a higher proportion of rare non-*Candida* fungal organisms, lower rate of catheter removal, longer time to median catheter removal (7 days vs 5 days), and lower rate of permanent hemodialysis transfer. The low rate of hemodialysis transfer probably reflected the predominant usage of PD as renal replacement therapy in this country. Leaving the PD catheter *in situ* was significantly associated with increased mortality. Similarly, in a recent single-center experience from India[16] of 43 episodes of fungal peritonitis between January 1998 and February 2008, catheter removal occurred in only 58% of cases, with the 1 month mortality rate being 60%. The subsequent multivariate analysis demonstrated that the only two significant, independent predictors of death were a serum albumin concentration less than 30 g/l and the PD catheter remaining *in situ*.

More comparable outcomes to those of our paper were reported in a series of 18 PD-associated fungal peritonitis episodes in the UK population between December 1999 and September 2003.[17] These fungal peritonitis cases represented 6% of all peritonitis episodes during this period and *Candida* species were the infecting organism in 83% of cases. Catheter removal occurred in 83% of cases, mostly between 2 and 13 days following diagnosis. Mortality in this population was 11% attributed to fungal peritonitis and 6% because of withdrawal from dialysis from other causes. All surviving patients were permanently transferred to hemodialysis.

Recent antibiotic treatment for peritonitis (or any other indication) has consistently been identified as an important risk factor for fungal peritonitis.[2,7,8] In a report of six cases of fungal peritonitis observed between 1980 and 1992 in an Italian center, Amici *et al.*[7] observed that all six patients had suffered at least one episode of treated bacterial peritonitis in the 2 months before the fungal infection appeared. The authors subsequently analyzed 22 published reports of fungal peritonitis and identified that the major predisposing factors were earlier antibiotic therapy and bacterial peritonitis. Similarly, Michel *et al.*[2] found that 16 of 20 patients experienced bacterial peritonitis during the month before they developed fungal peritonitis. In our study, a history of earlier treated peritonitis was more than twice as likely with fungal peritonitis compared with non-fungal peritonitis, and became even more likely if the elapsed time between episodes was short. Specifically, 6% of peritonitis episodes occurring within 2 months of a previous non-fungal peritonitis event were confirmed to be fungal peritonitis. However, if the peritonitis occurred within 7 days of completing treatment for previous peritonitis, approximately one-quarter of such events were fungal. Clinicians should therefore be highly

suspicious of fungal peritonitis in patients presenting with signs and symptoms of peritonitis soon after treatment for PD-associated peritonitis and, under such circumstances, strongly consider empiric antifungal therapy. It is also important to note that 57% of cases of fungal peritonitis in our study had no earlier history of antibiotic treatment for bacterial peritonitis.

When fungus is identified by microscopy or culture, the ISPD guidelines recommend immediate catheter removal and continuation of antifungal agents for an additional 10 days. Although these recommendations are based on the reports of several single-center studies,[1,2,12,14,15,18] other single-center case series have advocated for catheter removal alone (followed by antifungal therapy if the clinical response is poor)[3] or antifungal therapy alone (followed by catheter removal if the clinical response is poor).[7,8,11] In our large multicentre study, the risk of death was higher with antifungal treatment alone (18%) than with either catheter removal alone (6%) or catheter removal plus antifungal treatment (7%). Moreover, the risk of a subsequent repeat fungal peritonitis episode was significantly lower with combined catheter removal and antifungal therapy (0%) than with antifungal treatment alone (9%) or catheter removal alone (6%, $P = 0.03$). These findings support the current ISPD recommendations,[5] although we were unable to demonstrate a clinical benefit for immediate or early (within 5 days) catheter removal, as opposed to later removal, provided antifungal therapy had been instituted.

Another noteworthy finding of our study was the relatively low (7%) use of antifungal prophylaxis during treatment for bacterial peritonitis in Australia. A previous randomized controlled trial of oral nystatin 500,000 U q.i.d. whenever antibiotics were prescribed resulted in a significant reduction of the risk of superimposed fungal peritonitis (397 patients, 1168 patient-months, relative risk 0.10, 95% CI 0.03–0.31).[19,20] Consequently, the ISPD Guidelines recommend that fungal prophylaxis during antibiotic therapy may prevent some cases of *Candida* peritonitis in programs that have high rates of fungal peritonitis.[5] The occurrence of fungal peritonitis in our study was comparable between those who did and did not receive antifungal prophylaxis during earlier peritonitis episodes (4 vs 5%, respectively, $P = 0.8$). However, these results may have been limited by selection bias and type 2 statistical error due to limited sample size. Further randomized controlled trials to address the efficacy of oral nystatin prophylaxis are warranted.

In addition to recent antibiotic therapy for bacterial peritonitis, our study also identified Aboriginal/Torres Strait Islander racial origin as an independent risk factor for fungal peritonitis. We have previously demonstrated that indigenous racial origin is associated with a higher risk of peritonitis in general, which is independent of the increased risks of diabetes mellitus, obesity, and other co-morbidities in this group.[21] Socioeconomic factors, such as housing conditions, and remoteness of living are likely to be important contributors to the increased risk of fungal peritonitis in this study, as environmental exposures have been found to predispose to *Candida* peritoneal infections.[22,23] Unfortunately, social disadvantage and remoteness could not be evaluated in this study because of the limited data collected by the ANZDATA Registry. Nevertheless, as hospitals serve areas with differing socioeconomic status, there will have been some accounting for this effect by the hierarchical nature of the poisson analysis. Previous studies have identified a strong association between socioeconomic disadvantage and end-stage kidney disease among indigenous Australians.[24] On the basis of the residential postcodes, we have previously demonstrated that Aboriginal PD patients were more likely to reside in non-metropolitan than metropolitan areas, but we were unable to adequately evaluate how remoteness (compared with urban and peri-urban residences) influenced fungal peritonitis risk in indigenous patients.[21] It is likely, however, that the high rates of fungal infection observed in Western Australia (6%) and Northern Territory (15%) compared with other Australian states (0–3.5%) reflected a high proportion of indigenous PD patients (Western Australia 22% vs Northern Territory 77% vs other states 5%), often living in disadvantaged circumstances in remote and rural locations.[25]

The strengths of this study included its very large sample size, inclusiveness, and robust analyses. We included all patients receiving PD in Australia across 66 centers during the study period, such that a variety of centers were included with varying approaches to the treatment of peritonitis. This greatly enhanced the external validity of our findings. These strengths should be balanced against the study's limitations, which included limited depth of data collection. ANZDATA does not collect important information, such as the presence of concomitant exit site and tunnel infections, patient compliance, individual unit management protocols, post-infection surveillance programs, concurrent medications (such as glucocorticoids), laboratory values (such as C-reactive protein and dialysate white cell counts), severity of co-morbidities, antifungal dosages, or routes of antifungal administration. Even though we adjusted for a large number of patient characteristics, the possibility of residual confounding could not be excluded. In common with other Registries, ANZDATA is a voluntary Registry and there is no external audit of data accuracy, including the diagnosis of peritonitis. Consequently, the possibility of coding/classification bias cannot be excluded.

In conclusion, fungal peritonitis is a serious, not infrequent complication of PD, which is associated with a high rate of hospitalization (98%), catheter removal (88%), permanent hemodialysis transfer (74%), and death (9%). Previous treated bacterial peritonitis (especially if recent) and indigenous racial origin are major risk factors for this condition. Catheter removal in combination with antifungal therapy appears to result in the best overall outcome with the lowest rates of repeat fungal peritonitis episodes and death compared with either therapeutic intervention alone.

MATERIALS AND METHODS

Study population

The study included all Australian adult patients from the ANZDATA Registry who were receiving PD between 1 October 2003 (when detailed peritonitis data started to be collected) and 31 December 2006. The data collected included demographic data, cause of primary renal disease, co-morbidities at the start of dialysis (coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, diabetes, hypertension, and smoking status), body mass index, late referral (defined as commencement of dialysis within 3 months of referral to a nephrologists), microbiology of peritonitis episodes (up to three organisms for polymicrobial episodes), and the initial and subsequent antibiotic treatment regimens. The organism responsible for fungal peritonitis was coded as *C. albicans*, other *Candida* species, or other fungus. In cases of polymicrobial peritonitis, fungal peritonitis was recorded if a fungus was at least 1 of the isolated organisms. Center size was categorized according to quartiles: small (<11 patients), small-medium (11–38 patients), medium-large (39–98 patients), and large (>99 patients).

The outcomes examined were peritonitis relapse, repeat peritonitis, peritonitis-associated hospitalization, catheter removal, temporary or permanent transfer to hemodialysis, and patient death. Peritonitis recurrence was defined as an episode of peritonitis occurring within 4 weeks of the last antibiotic dose (or within 5 weeks if intermittent vancomycin used) for peritonitis due to the same organism. Repeat peritonitis was defined as an episode of peritonitis occurring more than 4 weeks after the last antibiotic dose (or more than 5 weeks if intermittent vancomycin used) for peritonitis due to the same organism.

Statistical analysis

Results were expressed as frequencies and percentages for categorical variables, mean ± s.d. for continuous variables, and median and IQR for nonparametric data. Differences between two groups of patients were analyzed by χ^2-test for categorical data, unpaired *t*-test for continuous parametric data, and Mann–Whitney test for continuous nonparametric data. The independent predictors of fungal peritonitis were determined by multivariate poisson regression using backward stepwise elimination.[26] First-order interaction terms between the significant covariates were examined for all analyses. To account for the structure of the data, a multi-level hierarchical model was created with a random effect for state of residence, treating unit and individual patient. Predictors of peritonitis outcomes were assessed by multivariable binary logistic regression. Data were analyzed using the software packages SPSS for Windows release 12.0 (SPSS Inc., North Sydney, Australia) and Stata/SE 10.1 (College Station, TX). *P*-values less than 0.05 were considered statistically significant.

DISCLOSURE

Professor David Johnson is a consultant for Baxter Healthcare Pty Ltd and has previously received research funds from this company. He has also received speakers' honoraria and research grants from Fresenius Medical Care. Dr Kym Bannister is a consultant for Baxter Healthcare Pty Ltd. Dr Stephen McDonald has received speaking honoraria from Fresenius Australia and Baxter Australia. All other authors declared no competing interests.

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