ORIGINAL ARTICLE

Demographic characteristics and outcomes of continuous ambulatory peritoneal dialysis related peritonitis in Miri General Hospital, Malaysia

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ABSTRACT

Introduction: Sarawak has a population that is geographically and characteristically widely varied. In this study we aimed to determine the demographic characteristics of our patient population who undergo continuous ambulatory peritoneal dialysis (CAPD) and to study the incidence, the microbiology and the outcome of CAPD peritonitis.

Methods: A retrospective record review of all CAPD patients on follow-up at the Miri Hospital, Sarawak, Malaysia from 2014 until 2017 was done.

Results and Discussion: During the 4-year period, the overall peritonitis rate was 0.184 episodes per patient-year. Gram-positive and gram-negative bacteria each constituted one-third of the peritonitis; fungi (2.6%), Mycobacterium tuberculosis (MTB) (5.3%), polymicrobial (2.6%) and sterile culture (26.3%). The most commonly isolated gram-positive bacteria were coagulase-negative *Staphylococcus*. Our peritonitis rate is comparable to that of other centres i.e., Japan 0.195 and Indonesia 0.25. In comparison, countries like India (0.41), Korea (0.40) and Singapore (0.59) had relatively higher rate of PD-associated peritonitis. Two tuberculosis peritonitis patients died. The rate of catheter removal was approximately 20%. Gram-negative bacteria and MTB have a higher risk of catheter loss. About one-fifth used rainwater to clean their CAPD exit site. Out of this group, 33% did not boil the rainwater prior to usage.

Conclusion: Patient's characteristics and microbial susceptibility vary in different places of practice. The high rates of culture-negative peritonitis and high mortality risks associated with TB peritonitis warrant special attention. In patients with refractory peritonitis, early catheter removal is warranted in order to reduce mortality and minimize damage to peritoneal membrane.

KEY WORDS:
Peritoneal dialysis; Peritonitis; microbiology

INTRODUCTION

Peritoneal dialysis (PD), one of the dialysis modalities, is of paramount importance for patients with end-stage renal disease. Approximately one-fifth of PD mortality is attributable to peritonitis–a frequently found complication of PD.[1-4] Peritonitis is a major contributing cause for conversion from PD to haemodialysis due to peritoneal membrane failure.[4]

Bacteria is the major culprit for the vast majority of peritonitis cases. The outcome of PD peritonitis depends on the types of causative organism.[1] Sarawak, the largest state in Malaysia, has population who are widely varied geographical and in characteristics. Currently only one study has reported the microbiology infection and outcomes of PD-related peritonitis in Sarawak.[5] However, the study data was limited to the area of Kuching located at the Southwestern part of Sarawak. The microbiological fauna may differ based on the local epidemiology trends. Therefore, we aimed to determine the demographic characteristics of our local patient population who are receiving continuous ambulatory peritoneal dialysis (CAPD) as well as to study the incidence, the microbiological infections and the outcome of CAPD peritonitis in Miri General Hospital (MGH), Sarawak.

MATERIALS AND METHODS

This was a retrospective record review of all CAPD patients on follow-up at the Nephrology Unit, MGH, Sarawak between January 2014 and December 2017. The Nephrology Unit was established in mid-2013. For all CAPD patients in our centre, similar protocols were adopted from the Nephrology Unit of the Sarawak General Hospital, Kuching, in terms of catheter placement, routine pre-operative screening for *Staphylococcus aureus* nasal carriage, CAPD connection methods, patient training programs, as well as the exit site care.

Demographic data collected included age at time of CAPD commencement, gender, age, ethnicity, body mass index, living area, education level, monthly income and causes of the end-stage renal disease (ESRD). Clinical data pertaining to peritonitis collected comprised causative organisms, date

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of peritonitis, antimicrobial treatment, date of catheter removal and/or death.

The diagnosis of PD peritonitis was made when at least two of the following were present: (1) clinical features consistent with peritonitis, i.e. abdominal pain and/ or cloudy dialysis effluent; (2) dialysis effluent white cell count more than 100/μL or 50% polymorphonuclear; and (3) positive dialysis effluent culture. These criteria were recommended by International Society for Peritoneal Dialysis (ISPD).[6] Patients who were transferred care to other hospitals were excluded in this study. Peritonitis which occurred out of the study period was excluded. An episode of peritonitis within four weeks after the treatment of a previous episode was considered a relapse and was not classified as a new infection. A peritonitis episode which occurred within seven days after catheter placement was also excluded in this study. Refractory peritonitis was defined as peritonitis that did not respond to second-line antimicrobial treatment and resulted in catheter removal. The culture of PD fluid was traced from the microbiology department of MGH. The causative organisms were divided into gram-positive, gram-negative, fungal, mycobacterium, polymicrobial and culture-negative.

Outcomes of peritonitis were categorised as initial cure, catheter loss due to non-resolution of peritonitis as well as patient death. Initial cure was defined as resolution of peritonitis with antimicrobial therapy. Patient death was included when all other possible causes of mortality had been ruled out.

The time at risk for peritonitis was counted from the first day of CAPD training until the occurrence of peritonitis. Peritonitis rate was calculated by totalling all episodes of peritonitis that occurred throughout the entire time at risk for all patients in the program during the study period. This total was divided by the time at risk in years. Peritonitis rate was expressed as episodes per patient-year.

Normally distributed numerical data were expressed as mean ± standard deviation (SD). Ordinal or categorical data were expressed as frequency and percent. Differences in the proportion of causative organisms were analysed according to each calendar year. The relationship between peritonitis rate and patient's factors was analysed using Mann-Whitney test as the sample size for each group was small and the data was skewed. The association between catheter loss and gram positive/ gram negative causative organisms was analysed using Fisher's exact test. Statistical significance was determined as p value less than 0.05.

RESULTS

Study patient characteristics

Thirty-eight episodes of peritonitis were detected among 57 CAPD patients during the four-year study period. Thirteen patients had a single episode, nine patients had two episodes, one patient had three episodes, and one patient had four episodes of peritonitis. Six patients (10.5%) were carriers of *Staphylococcus aureus*, detected via routine nasal swab, and eradication therapy was given prior to catheter insertion. Thirty-three patients (57.9%) were on the Baxter system, while the remaining were on the Fresenius system. The baseline characteristics of patients are shown in Table I.

Table I: Baseline characteristics of patients

	Total
Patients (n)	57
Gender, n (%)	
Male	26 (45.6)
Female	31 (54.4)
Age (years) (±SD)	45.5 (±15.1)
Ethnicity, n (%)	16 (28.1)
Chinese	15 (26.3)
Malay	16 (28.1)
Iban	3 (5.3)
Lumbawang	7 (12.3)
Others	
Body mass index (kg/m^2) (±SD)	24.6 (±4.2)
Living area, n (%)	
Miri urban	30 (52.6)
Miri suburban	18 (31.6)
Bintulu	2 (3.5)
Lawas	2 (3.5)
Limbang	3 (5.3)
Marudi	3 (5.3)
Education level, n (%)	
Illiterate	5 (8.8)
Primary	7 (12.3)
Secondary	34 (59.6)
Tertiary	11 (19.3)
Monthly income (RM), n (%)	
Less than 1000	23 (40.4)
1000 – 3000	28 (49.1)
3000 – 5000	6 (10.5)
Above 5000	None
Underlying disease, n (%)	
Diabetes mellitus	14 (24.6)
Hypertension	21 (36.8)
Glomerulonephritis	9 (15.8)
Obstructive nephropathy	2 (3.5)
Polycystic kidney	2 (3.5)
Systemic lupus erythematosus	2 (3.5)
Unknown	7 (12.3)

SD – Standard Deviation

Peritonitis and the causative organisms

The overall peritonitis rate was 0.184 episodes per patient-year (Table II). Each gram-positive and gram-negative bacterium constituted about one-third (31.6%) of the peritonitis, respectively. The remaining cases were caused by fungi (2.6%), *Mycobacterium tuberculosis* (5.3%), polymicrobial (2.6%) and sterile culture (26.3%). The most commonly isolated gram-positive bacteria leading to CAPD peritonitis was coagulase-negative *Staphylococcus* (CoNS). *Escherichia coli (E. coli)* was the most common gram-negative organism at our centre. The microbiological infection in peritonitis is shown in Table III.

Table II: Peritonitis rate per patient-month

	2014	2015	2016	2017
Cumulative episodes	2	5	14	17
Cumulative patient-months	88.1	408.9	938.1	1491.2
Peritonitis episode per patient-month	0.023	0.012	0.015	0.011
Peritonitis episode per patient-year	0.272	0.147	0.179	0.137

Table III: Causative organisms of peritonitis episodes

Microbiology	Number isolated in 2014	Number isolated in 2015	Number isolated in 2016	Number isolated in 2017	Total number isolated (n=38)	Percentage of total episode
Gram-positive organism	1	3	5	3	12	31.6
Staphylococcus aureus	0	0	1	1	1	2.6
Coagulase-negative Staphylococcus (CoNS)	1	3	2	1	7	18.4
Streptococcus sp.	0	0	1	0	1	2.6
Other gram-positive organisms						
Gram-negative organism	0	2	3	7	12	31.6
Escherichia coli (E. coli)	0	1	2	2	5	13.2
Klebsiella sp.	0	1	0	1	2	5.3
Enterobacter sp.	0	0	1	0	1	2.6
Citrobacter sp.	0	0	0	2	2	5.3
Corynebacterium sp.	0	0	0	2	2	5.3
Fungi	0	0	0	1	1	2.6
Mycobacterium tuberculosis	0	0	0	2	2	5.3
Polymicrobial	0	0	0	1	1	2.6
Culture-negative	0	1	4	5	10	26.3
Total	1	6	12	19	38	100.0

Table IV: Comparing peritonitis rate between different factors

	Factors	n	Rate Median (IQR)	z statistic [a]	p-value [a]
Peritonitis episode per patient-month	Education level				
	Illiterate/ Primary	12	0.067 (0.119)[b]	- 3.31	0.001
	Secondary/ Tertiary	45	0.000 (0.006)[b]		
	Monthly income (RM)				
	Less than 1000	23	0.045 (0.091)[b]	- 3.37	0.001
	Above 1000	34	0.000 (0.006)[b]		
	Living area				
	Urban	39	0.000 (0.043)[b]	-1.55	0.121
	Suburban	18	0.027 (0.071)[b]		
	Water sources				
	Government-supplied	45	0.000 (0.027)[b]	- 3.641	<0.001
	Rainwater				
	Cooked	8	0.049 (0.081)[b]	- 0.679	0.497
	Uncooked	4	0.070 (0.093)[b]		

[a] Mann-Whitney test
[b] Skew to the right

Table V: Peritonitis-related catheter loss in various causative organisms

	Catheter loss		Total
	Yes	No	
Gram-positive	1 (8.3%)	11 (91.7%)	12
Gram-negative	3 (25.0%)	9 (75.0%)	12
Tuberculosis	2 (100.0%)	0 (0.0%)	2
Fungal	0 (0.0%)	1 (100.0%)	1
Polymicrobial	1 (100.0%)	0 (0.0%)	1
Culture-negative	0 (0.0%)	10 (100.0%)	10
Total	7 (18.4%)	31 (81.6%)	38

Peritonitis and patient factors

The medians of peritonitis rate were significantly different between different education level and income groups (Table IV). This demonstrated that CAPD patients with better education level and monthly income had lower rate of peritonitis. There was no statistically significant difference in terms of peritonitis rate between urban and suburban groups of patients (Table IV). In addition, there was a significant difference between sources of cleaning water and the peritonitis rate (Table IV). When sub-analysis was done between boiled and un-boiled rainwater sources, the medians of peritonitis rate were not significantly different (Table IV).

Peritonitis outcome

Two deaths were reported during the period of study. Both cases were attributable to tuberculosis (TB) peritonitis. The PD catheter was removed in about one-fifth (18.4%) of peritonitis episodes due to unsatisfactory response to antimicrobial treatment. There was no statistically significant association between catheter loss and gram-positive/ gram-negative peritonitis episodes (p-value = 0.590; Fisher's exact test)

DISCUSSION

Sarawak General Hospital (SGH) and MGH are both located in the state of Sarawak. The former is situated at the Southwestern part, while the latter is at the North-eastern part of the state. Despite the geographical vicinity, our patients in Miri demonstrated slightly different demographic characteristics. The peritonitis rate in Miri was much lower–0.184 episodes per patient-year, as compared to what has been reported by the latest study conducted in SGH (0.40 episodes per patient-year).[5] Our peritonitis rate is comparable to that of other centres, i.e. in Japan 0.195 and Indonesia 0.25.[7,8] In comparison, countries like India (0.41), Korea (0.40), Australia (0.60) and Singapore (0.59) had relatively higher rate of PD-associated peritonitis.[1,9-11] These differences may be attributable to several factors: (a) Nephrology unit in MGH is newly established with much less patients on CAPD; (b) almost 80% of our patient population have at least secondary-to-tertiary level of education, possibly resulting in better adherence to aseptic technique during PD exchange; (c) majority of the patients (68.4%) are urban dwellers, leading to faster access to medical treatment; (d) the number of new patients on CAPD becomes fewer over the years in MGH – eleven in 2014, twenty-seven in 2015, fourteen in 2016 and four in 2017, resulting in closer patient follow-up and better care.

The current study demonstrated the microbiological profile in CAPD peritonitis in our local population. Escherichia coli remained the most common gram-negative causative organism, while coagulase-negative *Staphylococcus* was the popular gram-positive bacteria. Similar findings have been found in previous studies.[1,9,10] It is clearly shown by Table III that there was an increasing trend in gram-negative peritonitis which led to an increment in the overall peritonitis rate. This finding is in parallel with those reported by other studies.[9,12,13] In our setting, equal proportions of peritonitis were shared by gram-positive and gram-negative bacteria at the end of the 4-year follow-up.

Our culture-negative peritonitis rate was 26.3%. This was comparable with other centers.[5,10,14] In contrast, this proportion was higher than the standard set by ISPD.6 Two studies reported an average of 15 percent culture-negative rate.[15,16] This group of patients should be treated with empiric antibiotics covering both gram-positive and negative organisms. The major reasons for negative effluent cultures include recent antibiotic usage and technical issues in culturing and specimen handling.[17] Some of our patients were from suburb areas and it took them hours to days prior to reach our centre for treatment. Therefore, these patients were often commenced on antimicrobial therapy at their first visit to district hospitals.

TB peritonitis has high morbidity and mortality rate. Two of our TB peritonitis cases succumbed despite best supportive care. Clinicians should have high index of suspicion and consider TB peritonitis as one of the differential diagnosis when any patient presents with refractory or relapsing peritonitis with multiple negative cultures.[6] Most PD-related peritonitis cases resolve with antimicrobial therapy. The risk of catheter loss varies widely between centres and with individual organisms.[18] In our centre, the rate of catheter removal was approximately 20%. This is similar to the data reported by Htay et al.[19] Gram-negative bacteria and MTB have a higher risk of catheter loss.[18] Our study did not find any statistically significant association between catheter loss and individual organisms. This might be explained by the relatively small sample size. In patients with refractory peritonitis, early catheter removal is warranted in order to reduce mortality and minimise damage to peritoneal membrane.[19-20]

In our study, about one-fifth of the patients used rainwater to clean their CAPD exit site. Out of this group of patients, one-third did not boil the rainwater prior to usage. This finding was similar to the data reported by Abraham et al in which about 20% of their patients did not have access to

government-supplied water.[21] This emphasizes the importance of getting accessed to clean water sources so as to minimise the rate of peritonitis.

The strength of this study is that it includes all CAPD patients receiving care in MGH. The demographic data and outcomes described are unique to our study population. It also demonstrates the relationship between several patient factors and the rate of peritonitis. On the other hand, the retrospective design of this study is the major flaw. The sample size is small, thus resulting in skewness of the data.

CONCLUSIONS

In summary, patient's characteristics and microbial susceptibility vary in different places of practice. The high rates of culture-negative peritonitis and high mortality risks associated with TB peritonitis warrant special attention. CAPD catheter design, insertion technique, connection methods and dialysis solution are the major issues of interest and not to be neglected. Future research on risk factors of CAPD peritonitis is mandatory so as to improve the outcome of CAPD patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia with registered ID NMRR-18-1124-41315 dated 25 October 2018.

COMPETING INTERESTS

The authors declare that they have no competing interest.

FUNDING

The authors declare no financial disclosure.

AUTHORS' CONTRIBUTIONS

ASOT was responsible for the study design, data collection, data analysis and manuscript writing. CYI, SD and STY participated in data collection and contributed to data analysis. KHK was involved in the design of the study and manuscript editing. All authors read and approved the final manuscript.

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