



Clinical features, management and outcomes of peritoneal dialysis patients during Delta and Omicron waves of COVID-19 infections

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Abstract

Introduction There were discrete outbreaks of SARS-CoV-2 infection in 2021 (Delta wave) and 2022 (Omicron wave) in Singapore, which affected patients receiving peritoneal dialysis (PD).

Methods This study included all PD patients with COVID-19 infection from a single center between October 2021 and March 2022. The clinical presentation, management and outcomes of patients during the Delta and Omicron outbreaks were compared.

Results A total of 44 PD patients developed SARS-CoV-2 infection (23 during the Delta wave and 21 during the Omicron wave): median age 66 (60.5–68.5) years, male (63.6%), Chinese ethnic (77.3%), diabetes mellitus (56.8%), and cardiovascular disease (45.5%). Approximately, 93.2% received two doses of the mRNA COVID-19 vaccine. Cough (81.8%) and fever (54.5%) were common presenting symptoms. Chest radiography showed ground glass opacity in 23.5% of patients, consolidation in 55.6%, and bilateral lung involvement in 33.3%. Eleven patients (25.6%) received antiviral therapy (Remdesivir), 7 (16.3%) received steroid, and 4 (9.3%) received monoclonal antibodies. Patients infected during the Delta wave were more likely to be hospitalized (73.9 vs 14.3%; $p < 0.001$) and receive antiviral therapy (39.1 vs 10.0%; $p = 0.03$) than those during the Omicron wave. The overall mortality rate was 11.4%, with significantly higher mortality during the Delta wave than during the Omicron wave (21.7 vs 0%; $p = 0.03$).

Conclusions The mortality rate was high among infected PD patients during Delta wave of COVID-19 infection. However, during the Omicron wave, most infected patients were treated in the community with favorable outcomes.

Keywords SARS-CoV-2 · COVID-19 · Peritoneal dialysis · Delta · Omicron · Clinical features · Outcomes

Introduction

Dialysis patients have a higher risk of contracting SARS-CoV-2 infection and developing fatal complications by virtue of their immune-deficient state [1]. Several studies have reported the outcomes of COVID-19 infection among

patients receiving hemodialysis (HD) and kidney transplants [1–3], but there has been a paucity of studies evaluating clinical outcomes among peritoneal dialysis (PD) patients [4–6].

A previous case series of 11 PD patients infected with SARS-CoV-2 in the United States reported that 3 patients required mechanical ventilation and 2 died [4]. None of these patients was vaccinated as the COVID-19 vaccine was not available during that time. Since the COVID-19 vaccine was licensed to use at the end of 2020, several studies have examined the immunogenic response to the vaccine among patients receiving dialysis [7–14]. However, the protection conferred by the presence of immunogenicity against infection remains unknown. The present study reported the clinical presentations, laboratory and radiological findings, management, and outcomes of PD patients who mostly received 2 doses of mRNA COVID-19 vaccine, but infected with

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SARS-CoV-2 during Delta and Omicron waves of COVID-19 infection in Singapore.

Methods

This study included all PD patients who developed COVID-19 infection from a single center (Singapore General Hospital) in Singapore between October 2021 and March 2022. There were surge in number of infected PD patients in the last quarter of 2021 (Delta wave) and again in early quarter of 2022 (Omicron wave). The study was approved by Singhealth Centralized Institutional Review Board (CIRB), with the reference number of 2021/2823.

Data collected for the case series included demographic characteristics (such as age, gender, race), comorbid conditions (including the presence of diabetes mellitus and cardiovascular disease [composite of ischemic heart disease, cerebrovascular disease, and peripheral vascular disease]), body mass index, initial kidney replacement therapy, PD duration, PD modality (Automated PD [APD] versus Continuous Ambulatory PD [CAPD]), presenting symptoms for COVID-19 infection (presence of fever, cough, sore throat, running nose, dyspnea), vaccination status, laboratory tests (C-reactive protein, ferritin level, lactate dehydrogenase levels, hemoglobin, total white cell count, neutrophil and lymphocyte counts, serum albumin level, alanine aminotransferase [ALT], aspartate aminotransferase [AST] levels, SARS-CoV-2 IgG levels), and chest X-ray (CXR) findings (presence of ground glass/opacity, consolidation or bilateral lung involvement, and pulmonary congestion). In addition, the data regarding treatment for COVID-19 infection (antiviral therapy, corticosteroid, and monoclonal antibody therapy), need for oxygen therapy, the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) score, clinical outcomes, and admission status (hospital admission versus home recovery) were collected. All data were collected from the hospital's electronic medical records.

The study aimed to compare the outcomes of infected PD patients during Delta and Omicron waves of COVID-19 infection, and also examine the clinical features, laboratory, radiological findings and management of PD patients infected with COVID-19 infection.

The data were presented as frequency (percentage) or median and interquartile range. Descriptive statistical analysis was performed for clinical presentation, laboratory, and radiological findings. Comparisons of outcomes of patients between the Delta and Omicron waves were analyzed using Fisher's Exact tests for categorical data and the Wilcoxon–Mann–Whitney test for continuous data, as appropriate. Data were analyzed using Stata version 14.0 (Stata

Corp LP, College Station, TX, USA). *p* values of <0.05 were considered statistically significant.

Results

The study included all PD patients who developed COVID-19 infection from a center during the study period. A total of 44 (7.9%) out of 560 PD patients from our center developed SARS-CoV-2 infection. Of these, 23 patients developed infection between October and December 2021 (Delta wave) and 21 patients developed infection between January and March 2022 (Omicron wave). The median age was 66 years (60.5–8.5), the majority of patients were Chinese ethnic (77.3%), and the median PD duration was 2.4 (0.9–3.8) years (Table 1). The main etiology of kidney failure was diabetic kidney disease (54.6%). The majority of patients (81.8%) were receiving Automated PD therapy. There were no significant differences in the baseline characteristics of the two groups of patients (Table 1). Twenty patients (45.5%) were hospitalized for COVID-19 infection and the median length of stay in the hospital was 8 (5–11) days.

Clinical symptoms, laboratory and radiological findings of hospitalized patients

Clinical presentation symptoms for COVID-19 infection for hospitalized infected PD patients are presented in Fig. 1. The most common presenting symptom of was cough (81.8%) and fever (54.5%). Laboratory findings upon presentation of COVID-19 infection are presented in Supplemental Table 1. The median ferritin level was extremely high at 1906 (752–2785) U/L, and the other inflammatory marker, C-reactive protein level was also high, while serum albumin level was low. The radiological findings of consolidation, ground glass or opacity, and bilateral lung involvement were observed in 55.6, 23.5, and 33.3%, respectively (Supplemental Fig. 1). There was a wide variation in levels of IgG antibodies to SARS-CoV-2 (RBD) (<50 to >40,000 Au/mL) in infected PD patients (supplemental Table 1). Two patients had non-protective (negative) anti-SARS-CoV-2 antibody titer results (<50 Au/mL).

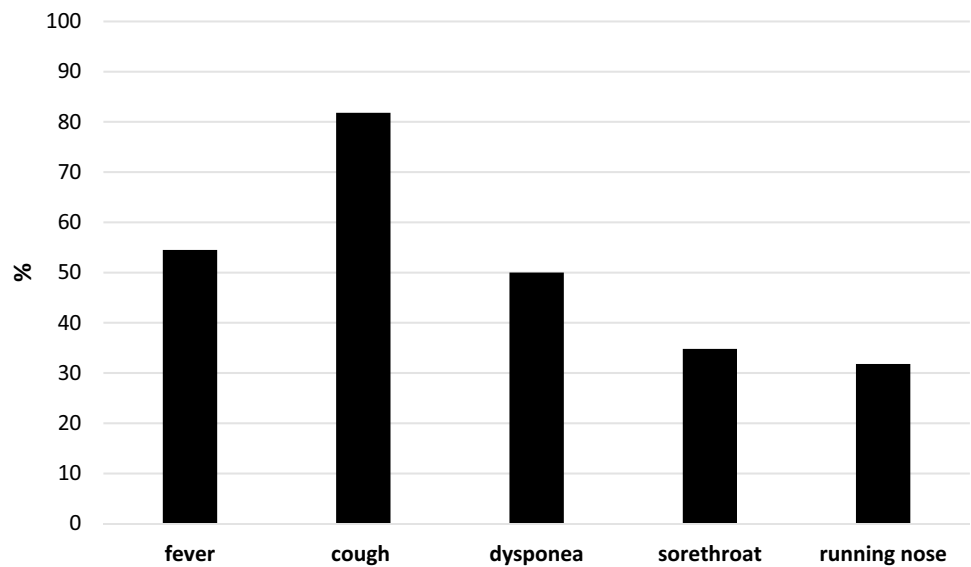
Treatment for COVID-19 infection

More infected PD patients were admitted to the hospital for monitoring and treatment during the Delta wave than the Omicron wave of COVID-19 infection. Given the virulence of the Delta strain, all infected PD patients, regardless of age or immunization status, were advised to be admitted for close monitoring and treatment during the Delta strain outbreak. However, during the Omicron wave, only high-risk PD patients were advised to admit for observation and

Table 1 Demographic and baseline characteristics of PD patients with COVID-19 infection

Variables	All patients (<i>n</i> =44)	Delta wave (<i>n</i> =23)	Omicron wave (<i>n</i> =21)	<i>p</i> value
Age (years)	66 (60.5–68.5)	67 (56.0–72.0)	66 (61.0–68.0)	0.75
Sex (male)	28 (63.6)	14 (60.9)	14 (66.7)	0.76
Race				1.0
Chinese	34 (77.3)	18 (78.3)	16 (76.2)	
Malay	8 (18.2)	4 (17.4)	4 (19.1)	
Indian	2 (4.5)	1 (4.3)	1 (4.7)	
Body mass index (kg/m ²)	23 (21.0–26.8)	23.6 (21.0–28.6)	22.8 (20.9–26.5)	0.68
Comorbid conditions				
Diabetes mellitus	25 (56.8)	12 (52.2)	13 (61.9)	0.56
Cardiovascular disease	20 (45.5)	12 (52.2)	8 (38.1)	0.38
Etiology of kidney failure				0.09
Diabetes kidney disease	24 (54.6)	12 (52.2)	12 (57.1)	
Hypertensive kidney disease	5 (11.4)	4 (17.4)	1 (4.8)	
Chronic glomerulonephritis	9 (20.5)	2 (8.7)	7 (33.3)	
Polycystic kidney disease	3 (6.8)	3 (13.0)	0 (0)	
Others	3 (6.8)	2 (8.7)	1 (4.8)	
PD vintage (years)	2.4 (0.9–3.8)	2.5 (0.9–4.3)	2.3 (0.9–3.3)	0.41
Initial PD modality (APD)	36 (81.8)	18 (78.3)	18 (85.7)	0.70
Vaccination status				0.49
Received 2 doses	41 (93.1)	20 (87.0)	21 (100)	
Received 1 dose	2 (4.6)	2 (8.7)	0 (0)	
Unvaccinated	1 (2.3)	1 (4.4)	0 (0)	

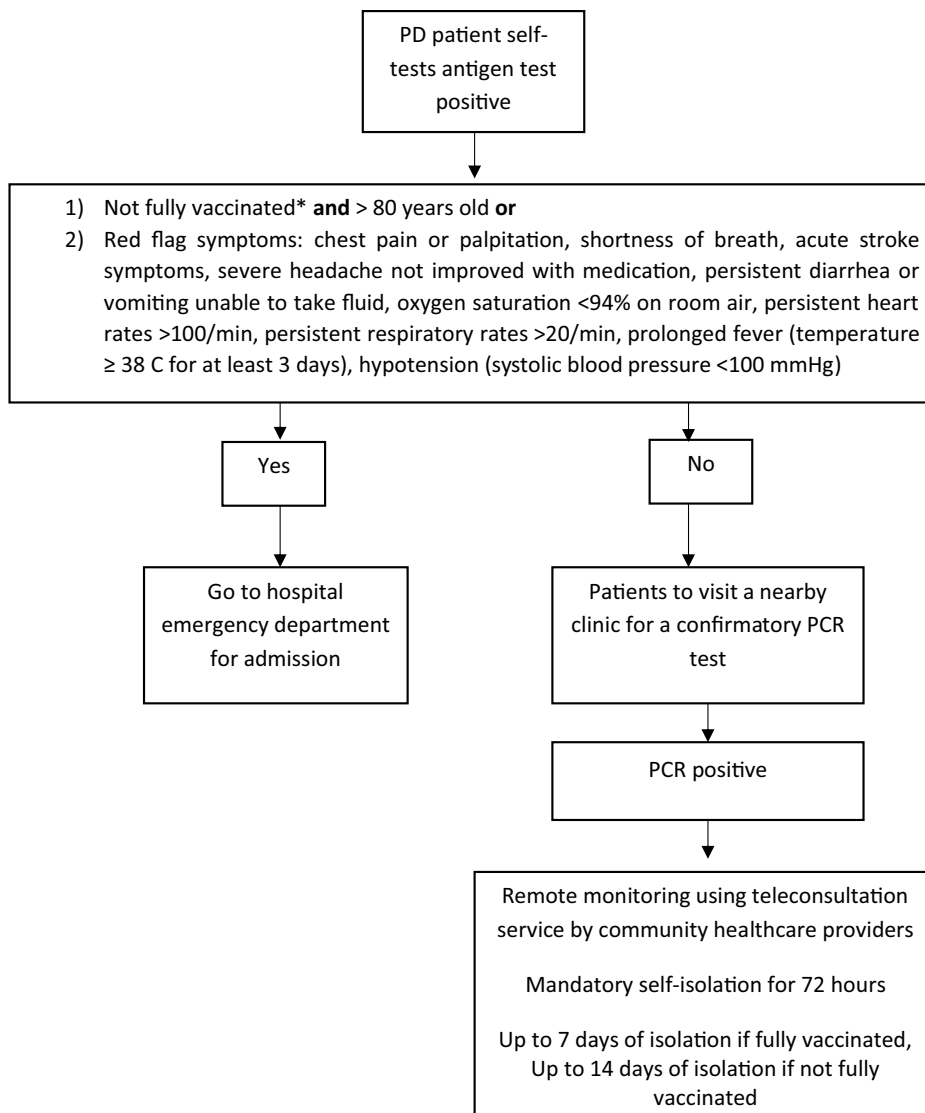
PD peritoneal dialysis. APD automated PD

Fig. 1 Clinical presentation of hospitalized peritoneal dialysis patients with COVID-19 infection

management, according to Ministry of Health (MOH) Advisory (Fig. 2). Infected PD patients who recovered at home were monitored remotely using teleconsultation services by the designated community healthcare providers.

During hospitalization, patients were co-managed by infectious disease specialists and nephrologists. Seven patients (15.9%) received oxygen therapy (Table 2). More patients received antiviral therapy (Remdesivir) during the

Fig. 2 Workflow for peritoneal dialysis patients who had a positive COVID-19 antigen test during the Omicron wave of infection



*Fully vaccinated status is defined as individuals within 270 days of the second dose of vaccination

Table 2 Comparisons of management and outcomes between infected peritoneal dialysis patients during Delta and Omicron waves of COVID-19 infection

Variables	All patients (n=44)	Delta wave (n=23)	Omicron wave (n=21)	p value
Hospitalization	20 (45.5)	17 (73.9)	3 (14.3)	<0.001
Antiviral therapy	11 (25.6)	9 (39.1)	2 (10)	0.03
Steroid therapy	7 (16.3)	6 (26.1)	1 (5)	0.06
m Ab therapy	4 (9.3)	4 (17.4)	0 (0)	0.07
Oxygen therapy	7 (15.9)	6 (26.1)	1 (4.8)	0.06
Mortality	5 (11.4)	5 (21.7)	0 (0)	0.03

mAb anti-SARS-CoV-2 monoclonal antibodies

Delta wave than during the Omicron wave (39.1 versus 10.0%). Similarly, infected patients during the Delta wave were more likely to receive steroid (Dexamethasone) or monoclonal antibodies (mAbs) therapy than those during the Omicron wave.

Outcomes of COVID-19 infection

A total of 5 PD patients (11.4%) died from complications of SARS-CoV-2 infection (Table 2). Patients who acquired infection during the Delta wave had a significantly higher

risk of mortality than those infected during the Omicron wave (21.7 vs 0%; $p=0.03$). The median ISARIC scores for patients who survived and died were not significantly different, [9.5 (8–10.5) versus 12.5 (9–15); $p=0.22$]. Of 44 PD patients who contracted COVID-19 infection, 39 survived and remained on PD at the end of the study.

Discussion

This study reported the clinical presentation, laboratory and radiological findings, treatment, and clinical outcomes of PD patients with COVID-19 infection. In this study, 93.1% of patients received at least 2 doses of the SARS-CoV-2 vaccine. The common presenting symptoms, cough and fever, were similar to those of the general population, hemodialysis and kidney transplant patients [2, 15]. During the Delta wave of COVID-19, most infected PD patients were managed as in-patients, whereas during the Omicron wave, most PD patients were managed in out-patient settings. A higher proportion of patients required antiviral therapy during the Delta wave than those during the Omicron wave. Mortality was higher during the Delta wave than in the Omicron wave.

Despite being immunized against SARS-CoV-2 and the availability of antiviral or mAbs therapy, 5 patients (11.4%) died from complications of SARS-CoV-2 infection. A previous PD case series by Sachdeva et al. reported that 2 out of 11 PD patients (18.2%) died from COVID-19 infection [4]. Another multi-center study of 18 infected PD patients reported a mortality rate of 22.2% [6]. The lower overall mortality rate in the present study was due to having almost half of the patients infected during Omicron wave of COVID-19 infection.

The SARS-CoV-2 Delta variant is infectious [16] and was responsible for the outbreak of COVID-19 infection in Singapore in the last quarter of 2021 with daily new infection rates ranging between 2000 and 3000 cases in October 2021 [17]. In December 2021, the Omicron variant was first detected in Singapore and culminated in a subsequent outbreak of infection starting in January 2022. Despite being vaccinated, some PD patients developed vaccine breakthrough infection during the surge of COVID-19 infection. PD is a home-based therapy and is considered to have a lower risk of acquiring COVID-19 infection during a pandemic compared with in-center HD. However, during the surge in infection, a minority of PD patients acquired the infection through their household contacts despite staying at home.

In the present study, some patients developed severe complications despite being vaccinated against SARS-CoV-2. This would have been due to a lack of humoral response to vaccine or of durability of humoral response to vaccine over time. In a study of humoral responses to the SARS-CoV-2

vaccine in 32 PD patients, seroconversion was observed only in 62.5% after the first dose and 97% after the second dose of the vaccine [18]. A recently published meta-analysis by Chen et al. reported that immunogenic response after COVID-19 vaccination was significantly lower in the dialysis population compared with those not receiving dialysis. [7] A subgroup analysis showed that the immunogenic response rate was lowest with incomplete vaccination, while people receiving a booster dose of vaccine had the highest response rate [7]. The longevity of humoral response after vaccination among PD patients has not been examined previously, although a previous study of antibody titers among 10 HD patients with SARS-CoV-2 infection reported that the titers declined after 3 months of infection [19]. Given the immunodeficient state of dialysis patients and low immunogenic responses to other viral vaccines, such as the hepatitis B vaccine [20], the booster doses of vaccine have been prescribed in dialysis patients to counteract the decline of vaccine-specific antibodies levels. Similarly, the booster dose of vaccine against SARS-CoV-2 has been recommended for dialysis patients.

Management of PD patients for SARS-CoV-2 infection was guided by infection disease specialists. In general, the antiviral therapy (mainly Remdesivir) was prescribed in the early course of infection for patients who required supplemental oxygen therapy or developed SARS-CoV-2 pneumonia or abnormal CXR imaging. Dexamethasone was added for those who required supplemental oxygen therapy. Monoclonal antibodies therapy was considered for those who were unvaccinated against SARS-CoV-2 infection or patients who had low anti-SARS-CoV-2 antibodies, and Janus kinase (JAK) inhibitors or interleukin-6 (IL-6) inhibitors (Tocilizumab) was considered for those who deteriorated despite being on other therapeutics. Patients on PD with COVID-19 infection were temporarily suspended from the transplant waiting list for 3 months.

During the Delta wave of infection, an increasing number of admissions of infected PD patients imposed a strain on the nursing workload in the hospital. The PD nursing team had to adapt to increasing demand in workload by temporarily converting continuous ambulatory PD (CAPD) therapy to APD therapy for all hospitalized PD patients to reduce nursing time spent on PD exchanges, and by switching from daily exit-site care with topical gentamicin cream to weekly chlorhexidine impregnated dressings for all PD in-patients who had no active exit-site infection. PD nurses had to wear full Personal Protective Equipment (PPE) when attending to the infected patients and discard the PD effluents and consumables [21, 22]. All infected patients were admitted to the isolation ward and only APD therapy was prescribed for them regardless of their usual PD modality to minimize the frequency of contact with patients. A dedicated APD machine was used for individual patients until they were discharged

from the hospital [21]. APD machines were cleaned with alcohol wipes daily and finally disinfected with Ultraviolet-C (UVC) after hospital discharge.

The outcomes of infection were associated with the strain of the infected virus, with the Omicron variant appearing less virulent than the Delta variant. Being aware of the generally favorable outcomes of infected patients during the Omicron wave, the management of the clinically stable infected PD patients shifted from mainly in-patient care to community-based out-patient care. Patients were assessed and monitored by a community healthcare team using telemedicine and were provided with a hotline to seek medical help if needed. Shifting to this care model not only avoided unnecessary admission but spared precious in-patient beds for those who needed them.

This is one of few large studies of vaccinated PD patients infected with SARS-CoV-2 during two waves of COVID-19 infection. The study described the clinical features, laboratory and radiological findings, treatment, and outcomes of vaccine breakthrough COVID-19 infection in PD patients and also discussed the practical points in managing the surge in admission for PD patients with COVID-19 infection. However, there are some limitations of this study, including its single-center retrospective study design, relatively small number of infected PD patients, and the classification of cohorts for Delta and Omicron waves was solely based on the period of outbreaks of these dominant strains rather than actual testing of all infected patients for SARS-CoV-2 strains. Nonetheless, the study provides important information on the clinical features, outcomes, and care strategies for handling of infected PD patients during the two waves of COVID-19 infection.

In conclusion, this study described the clinical features and outcomes of vaccinated PD patients infected with SARS-CoV-2 during Delta or Omicron waves of infection. The majority of such patients presented with cough or fever. The mortality rate was high among PD patients during the Delta wave of infection. However, during the Omicron wave, most patients were treated in the out-patient setting, yet had favorable outcomes. These findings should be further confirmed in the future larger studies.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11255-023-03496-2>.

Declarations

Conflict of interest Htay Htay has received consultancy fees, speaker's honoraria and travel sponsorships from Baxter Healthcare and consultancy fees and travel sponsorships from AWAK Technologies, speaker's honoraria from Fresenius Medical Care, grants from Johnson & Johnson Company, grants from Singhealth NIG, outside the submitted work and Marjorie WY Foo has received grants from National Medical Research Council for the study; consultancy fees and speaker's honoraria and travel sponsorships from Baxter Healthcare, consultancy fees

and travel sponsorships from AWAK Technologies. David Johnson has received consultancy fees, research grants, speaker's honoraria and travel sponsorships from Baxter Healthcare and Fresenius Medical Care, consultancy fees from Astra Zeneca, Bayer, and AWAK, speaker's honoraria from ONO and BI & Lilly, and travel sponsorships from Ono and Amgen. He is a current recipient of an Australian National Health and Medical Research Council Leadership Investigator Grant. The other authors have nothing to disclose.

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