



COVID-19 vaccination in peritoneal dialysis patients

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Abstract

Background COVID-19 vaccine is recommended in Peritoneal dialysis (PD) patients, but a paucity of data is available regarding vaccine-related adverse effects among PD patients.

Method A cross-sectional study was conducted in a single center between October and November 2021. PD patients were provided with the online survey link to participate in the study.

Results A total of 107 PD patients responded to the survey (55%: male, 79%: Chinese, 40%: > 65 years old). Of these, 95% received the COVID-19 vaccine (77% received two doses and 22% received three doses). Most participants (91%) received Pfizer vaccine. The main source of vaccine information was from the government (48%). The most common reason to receive and refuse vaccines were the perception of the seriousness of COVID-19 infection (63%) and concern about vaccine safety (60%), respectively. After the first dose, 25% of patients developed one or more vaccine-related adverse effects. Common local adverse effect was pain at the injection site (21%), and systemic adverse effects were muscle pain (15%), fatigue (13%). Similar adverse effects were observed with subsequent doses. None of them required hospitalization for vaccine-related adverse effects. Female patients had a higher risk of developing adverse effects than male patients after the first dose (odds ratio: 3.37; 95% confidence interval: 1.25 – 9.08). No such difference was observed in the subsequent dose. Age, race, employment status and history of drug allergy were not associated with the risk of adverse effects.

Conclusions The COVID-19 vaccine was well-tolerated by most PD patients, but few experienced non-severe adverse effects. All PD patients should be vaccinated against SAR-COV-2 infection.

Keywords COVID-19 · SAR-COV-2 · Vaccine · Adverse effects · End-stage kidney disease · Peritoneal dialysis

Introduction

COVID-19 infection in kidney failure patients receiving dialysis has been reported to have high morbidity and mortality. [1, 2] Hospitalization of dialysis patients for COVID-19 infection not only utilizes hospital isolation beds, and dialysis facilities but also increases the workload of inpatient dialysis nurses. Therefore, prevention of COVID-19

infection by applying strategies to minimize the risk of infection among kidney failure patients receiving dialysis [3–6] is of paramount importance to reduce morbidity, mortality, and healthcare cost.

Peritoneal dialysis (PD) patients are vulnerable to COVID-19 infection due to their immunocompromised state and are at increased risk of developing serious complications if they contract the virus. In a case series of 11 PD patients with COVID-19 infection, 3 required mechanical ventilation, and 2 died. [7] Therefore, in addition to the practice of preventive strategies for COVID-19 infection, such as wearing a face mask, social distancing, and hand hygiene, immunization against severe acute respiratory syndrome coronavirus 2 (SAR-COV-2) is recommended to mitigate the risk of infection and its associated complications in PD patients. The safety of the SAR-COV-2 vaccine has been tested in the general population and kidney failure patients, [8–11] particularly in hemodialysis patients, however, there is a

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paucity of studies available on the adverse effects of SAR-COV-2 vaccine among PD patients. There was a previous report of adverse effects of the COVID-19 vaccine among 32 PD patients, [12] however, the study was limited by small sample size. The present cross-sectional study, using online self-administered survey questionnaires, aimed to provide information on the local and systemic adverse effects of the COVID-19 vaccine experienced by PD patients, factors associated with adverse effects, source of vaccine information for PD patients, and reasons for delay or rejection of the vaccine.

Materials and methods

This was a single-center, cross-sectional study conducted between the period of October 2021 to November 2021. The study included PD patients who were followed up at Singapore General Hospital (SGH). The study has obtained approval from the local Ethics Committee, Singapore Health Service (SingHealth) Centralized Review Institutional Board (CRIB), reference number 2021/2563.

The study included anonymized data from patients, and the survey was conducted using the secured online survey platform; form.sg platform. PD patients who were followed up in the center were provided with a survey link or barcode to assess the survey. The survey questions were available in English Language only. Data collected for the survey included age, gender, race, marital status, employment status, education status, first modality of kidney replacement therapy (KRT), modality of PD, duration of PD, and self-care or assisted PD. The other data collected in the study included a source of information regarding the vaccine. COVID-19 vaccination record, types of vaccine, reasons for or against the COVID-19 vaccine, adverse effects of vaccine (local and systemic effects) for each dose of vaccine, hospitalization for vaccine-related adverse effects, history of COVID-19 infection, history of immunization with influenza vaccine, and history of drug allergy. Survey questions related to adverse effects, source of vaccine information, and reasons for or against the vaccine, were presented as multiple-choice questions, and participants were allowed to choose more than one answers that applied to them, and also a free text for them to include additional response.

The primary outcome was vaccine-related adverse effects experienced by PD patients. Secondary outcomes were sources of information for the vaccine, reasons to receive or decline the vaccine, and factors associated with the development of adverse effects of the vaccine. Data were presented as frequency (percentage) for the primary outcome and some secondary outcomes. Factors associated with vaccine adverse effects for first and second doses of vaccine were analyzed using logistic regression. Variables examined

included age group (> 65 versus ≤ 65 years), gender, race (Chinese versus non-Chinese), employment status (full/part-time versus not employed/retired), presence of drug allergy, types of vaccine (Pfizer versus Moderna), and history of receiving influenza vaccine. Variables with a $p < 0.2$ in univariate analysis were included in the final analysis. $P < 0.05$ were considered statistically significant. Data were analyzed with Stata (version 14.0 Stata Corp LP).

Results

A total of 107 PD patients responded to the survey for the COVID-19 vaccine between October and November 2021. Of these, 102 (95%) patients reported receiving vaccines: 23 patients (22%) received 3 doses, 78 patients (77%) received 2 doses and 1 patient (1%) received 1 dose of COVID-19 vaccine (Supplemental Table 1). The majority of patients (91%) received the mRNA (Pfizer) vaccine and few received Moderna (8%) or Sinovac (1%) vaccines. The demographic data of the study participants are presented in Table 1; 50% were male, 79% Chinese ethnic, and most of them performed PD therapy themselves. Four patients developed vaccine breakthrough infection and all recovered at home without requiring hospitalization.

Local and systemic adverse effects

No severe adverse effects were observed with the SAR-COV-2 vaccine in PD patients. After the first dose of COVID-19 vaccines, 75% did not suffer any adverse effects of the vaccine, whilst 25% reported having one or more local and systemic adverse effects of the vaccine (Figs. 1 and 2). The common local adverse effect was pain at the injection site (20.6%), and the common systemic adverse effects were muscle pain (14.7%) and fatigue (12.7%). Most patients (72%) did not experience any local or systemic adverse effects, whilst 29 patients (28%) experienced one or more local or systemic adverse effects after the second dose of the vaccine. The common local and systemic effects were similar to those after the first dose such as pain at the injection site (21.6%), fatigue (18.6%), muscle pain (14.7%), and fever (14.7%), respectively (Figs. 1 and 2). Among 23 PD patients who received the third dose, 10 patients reported having at least one local or systemic adverse effect with the vaccine. The common adverse effects were similar including pain at injection, fatigue, muscle pain, or fever (Figs. 1 and 2). Among all PD patients who received the vaccine, none of them required hospitalization for vaccine-related adverse effects. Individuals who did not develop adverse effects with the first dose were significantly less likely to experience adverse effects with subsequent doses of the vaccine. Approximately 86% of patients who had no adverse

Table 1 Demographic data of study participants

Variables	Values (n = 107)
Age (years)	
21 – 45	15 (14.0)
46 – 65	47 (43.9)
66 – 75	32 (29.9)
> 75	13 (12.2)
Sex (male)	53 (49.5)
Race	
Chinese	84 (78.5)
Malay	13 (12.1)
Indian	8 (7.5)
Others	2 (1.9)
Marital status	
Married	62 (57.9)
Single	19 (17.7)
Widowed	13 (12.2)
Divorced/Separated	13 (12.2)
Employment status	
Full time	32 (29.9)
Part-time	16 (15.0)
Not employed/retired	59 (55.1)
Education status	
Did not complete primary school	20 (18.7)
Secondary or high school	42 (39.2)
Professional certificate	25 (23.4)
Undergraduate/Bachelor's degree	15 (14.0)
Post graduate degree (master/PhD)	5 (4.7)
First KRT	
PD	85 (79.4)
HD	19 (17.8)
Kidney transplant	3 (2.8)
PD modality	
Automated PD	87 (81.3)
Duration on PD	
0 – 1 year	33 (30.8)
> 1 – 3 years	44 (41.1)
> 3 – 6 years	20 (18.7)
> 6 years	10 (9.3)
PD therapy performed by	
Self-care	70 (65.4)
Family	28 (26.2)
Helper	9 (8.4)

KRT kidney replacement therapy; PD peritoneal dialysis; APD Automated PD

effects with the first dose did not experience any adverse effects with the second dose of the vaccine. Similarly, 80% of patients experiencing adverse effects with the third dose of vaccine had previous adverse effects with the second dose of vaccine.

The subgroup analyses were performed to examine risk factors associated with adverse effects of the vaccine. Age, race, employment status, and history of drug allergy or history of receiving influenza vaccine were not significantly associated with the development of adverse effects of the COVID-19 vaccine (Table 2). However, gender (female) was significantly associated with a higher risk of developing local or systemic adverse effects (odds ratio: 3.37; 95% confidence interval (CI) 1.25 – 9.08; $p=0.02$) with first dose COVID-19 vaccine (Table 3). The association between gender and adverse effects was not observed in the second dose of the vaccine.

Information for COVID-19 vaccine

Sources of information for the COVID-19 vaccine were explored during the survey and 107 participants completed the survey, indicating that the common sources of information for the COVID-19 vaccine were government (48%), followed by family members (36%), and media (television or newspaper) (32%) (Fig. 3).

Reasons for receiving or refusal or delay in receiving COVID-19 vaccine

Reasons for receiving the vaccine were examined among participants ($n=102$) who received at least one dose of the vaccine. The common reasons to receive the vaccine were perception of the seriousness of COVID-19 infection (63%), followed by a recommendation by the government (46%), and recommendation by doctors (36%) (Fig. 4). Reasons for refusal or delay in receiving the vaccine were explored among participants ($n=5$) who have not received the vaccine during the study, the main reason for vaccine hesitancy was concern about the safety of the vaccine (60%).

Discussion

The study demonstrated that the majority of PD patients did not experience any adverse effects of COVID-19 vaccination. The common local adverse effect of the vaccine was pain at the injection site, and common systemic adverse effects were muscle pain, fatigue, or fever. None of them required hospitalization for vaccine-related adverse effects. The female gender was associated with a higher risk of developing adverse effects than the male gender after the first dose of the vaccine but such association was not observed in the subsequent dose. Most patients reported that the main source of vaccine information was the government. The main reason for receiving the vaccine for PD patients was the perception of the seriousness of COVID-19 infection

Fig. 1 Local adverse effects reported by study participants after COVID-19 vaccination

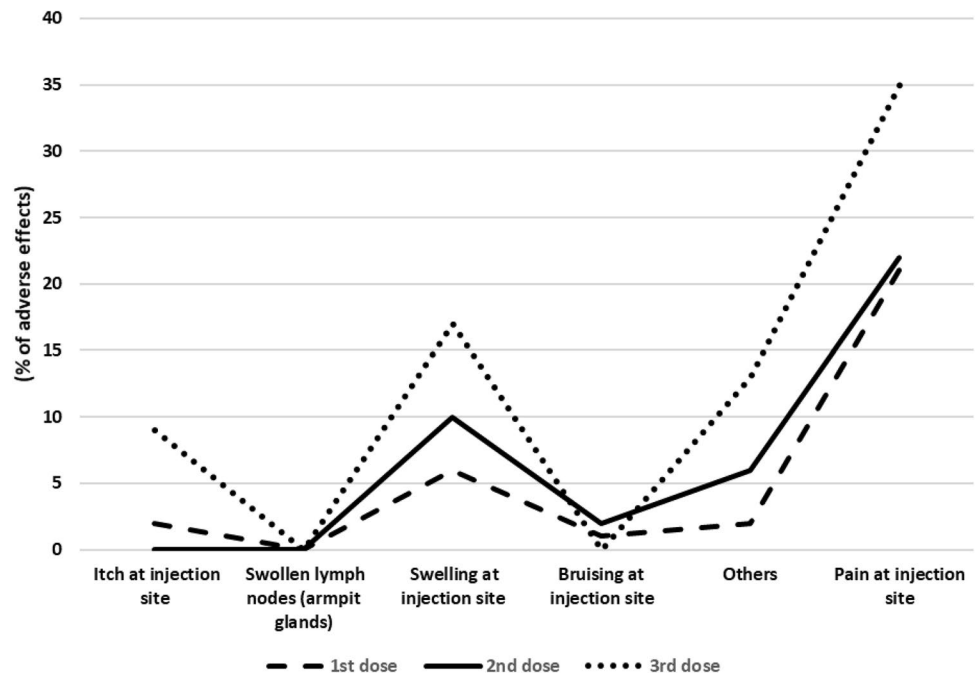
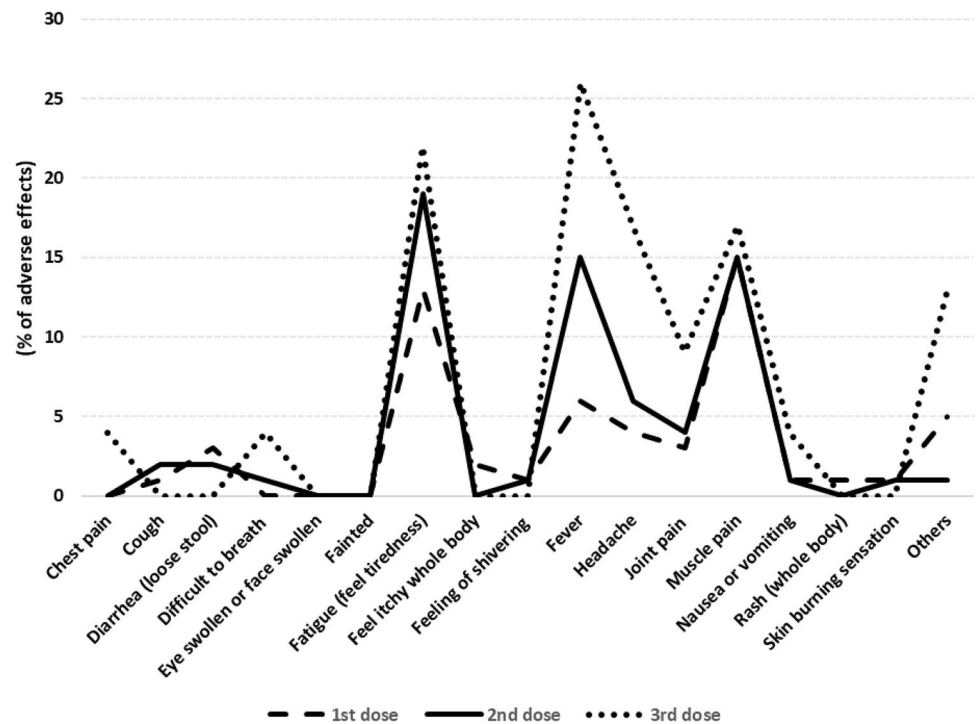


Fig. 2 Systemic adverse effects reported by the study participants after COVID-19 vaccination



and the main reason for vaccine hesitancy was a concern for the safety of the vaccine.

In a previous study, it has been reported that physician recommendations influenced vaccine uptake among dialysis patients. [13] In the present study, approximately one-third of participants indicated that physicians' recommendations encouraged them to receive the vaccine. Given that PD patients are usually followed up by physicians at PD clinic,

the vaccination status should be included as a part of the routine checklist for the PD program.

Most participants in the study received the mRNA (Pfizer) vaccine, which has 95% vaccine efficacy. [11] In the present study, 4 PD patients developed vaccine breakthrough COVID-19 infection but none of them required hospitalization and recovered at home. Vaccination has been shown to minimize the severity of infection in the

Table 2 Univariate logistic regression of risk of developing adverse effects with COVID-19 vaccination

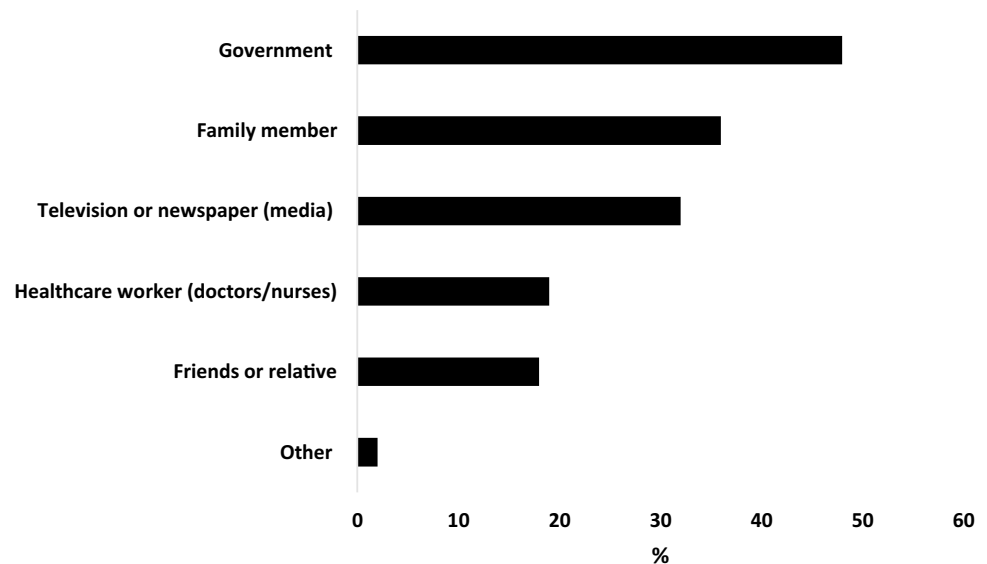
Variables	First dose			Second dose		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Age group (> 65 years)	0.49	0.18–1.31	0.16	0.46	0.18–1.18	0.11
Gender (female)	3.43	1.28–9.16	0.01	1.98	0.82–4.78	0.13
Race (Chinese)	1.60	0.49–5.3	0.44	1.46	0.48–4.40	0.51
Employment vs unemployed	1.18	0.48–2.92	0.72	0.63	0.27–1.51	0.30
Drug allergy	0.87	0.33–2.28	0.78	0.81	0.32–2.04	0.66
Influenza vaccinated	0.76	0.29–1.96	0.57	0.82	0.33–2.05	0.57
Type of vaccine (Pfizer vs Moderna)	2.47	0.29–21.13	0.41	1.25	0.24–6.57	0.80

CI confidence interval; *OR* Odds ratio

Table 3 Multivariate logistic regression of risk of developing adverse effects with COVID-19 vaccination

Variables	First dose			Second dose		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Age group (> 65 years)	0.51	0.18–1.39	0.19	0.47	0.18–1.22	0.12
Gender (female)	3.37	1.25–9.08	0.02	1.93	0.79–4.71	0.15

CI confidence interval; *OR* Odds ratio

Fig. 3 Sources of information for COVID-19 vaccine

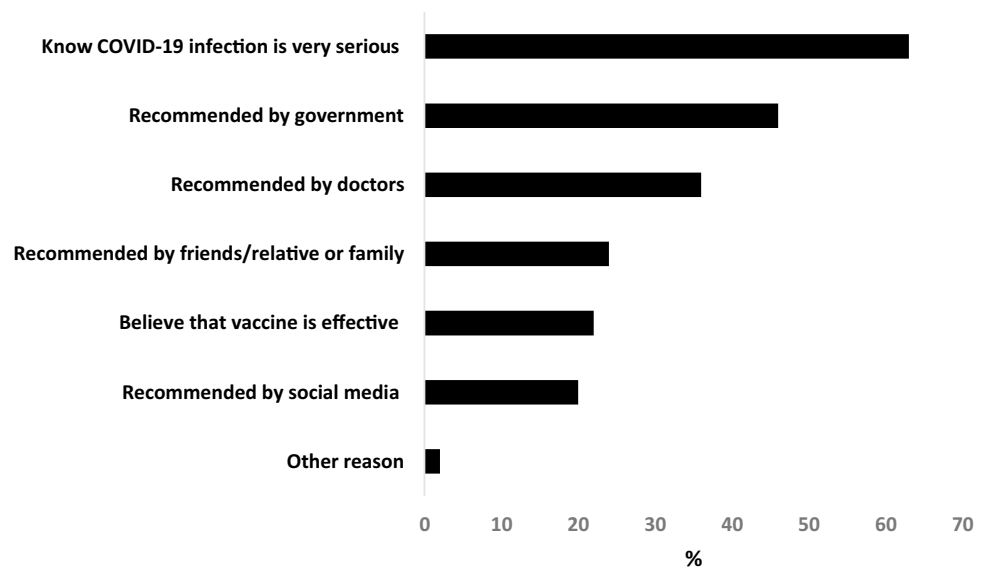
general population. [14, 15] In a previous study of influenza vaccine in PD patients, vaccinated individuals were significantly associated with reduced morbidities and mortality. [16] Association between vaccination and outcomes of COVID-19 infection among PD patients should be examined in future studies.

In the present survey, only 5% of participants have not received a vaccine, which was largely due to concern about vaccine safety. A previous survey of beliefs and attitudes towards the COVID-19 vaccine among maintenance dialysis patients (mainly HD patients) reported a similar reason for vaccine hesitancy. [17, 18] Therefore, the study on the safety profile of vaccines on patients receiving dialysis

would potentially encourage vaccine uptake among dialysis patients. Unfortunately, there was a paucity of data on the adverse effects of the SARS-CoV-2 vaccine among the PD population.

A previous large randomized control trial (RCT) on the efficacy and safety of the COVID-19 vaccine in the general population ($n = 43,448$) reported that the adverse effects of the vaccine were 27%. [11] Similarly, in the present study, the adverse effects of the vaccine were 25% and 27% after the first and second dose of the vaccine, respectively. Only a few patients have received the third dose during the time of the survey and therefore, caution should be exercised in the interpretation of the proportion of patients who developed

Fig. 4 Sources of information for COVID-19 vaccine



adverse effects with the third dose. A previous RCT of safety and efficacy of the vaccine in 30,420 individuals reported that pain at the injection site was the most common local adverse effect of the vaccine. [8] A previous small study of COVID-19 vaccine tolerability in 28 PD patients reported having mild adverse effects, such as pain at the injection site (36%). [12] Similarly, in the present study, the main local side effect of the vaccine was pain at the injection site.

A study of COVID-19 vaccine safety among solid organ transplant recipients also reported female individuals had a higher risk of developing systemic adverse effects than male individuals. [19] Similarly, the present study also demonstrated that the female gender was associated with a higher risk of developing adverse effects after the first dose of the vaccine. The reason for such association is unclear, but gender was no longer associated with vaccine adverse effects in the subsequent doses of the vaccine.

To date, this is one of few studies of SARS-COV-2 vaccine adverse effects on the PD population. The study also explored the source of information for vaccines and the reasons for PD patients receive or reject vaccination. However, the study suffers from several limitations including a single-center study, cross-sectional study design, and using the online survey platform, which might potentially exclude those patients who were not equipped with technology to use the online survey. In addition, the survey was conducted in the English language only, therefore, excluding those patients who are illiterate or have a language barrier. Moreover, there is a possibility of recall bias and selection bias due to the study design. Moreover, the majority of patients received a particular type of vaccine (Pfizer), therefore, findings from the study may not be generalizable to other

types of vaccines. Nonetheless, with a paucity of available data on the adverse effects of vaccines experienced by PD patients, the findings from the present study would potentially encourage more PD patients to receive the vaccine.

In summary, the SARS-COV-2 vaccine was generally safe for PD patients and a minority of them developed mild local and systemic adverse effects, which were commonly observed with other viral or influenza vaccines. None of them required admission for vaccine-related adverse effects. Most PD patients received vaccines because of the perception of the severity of COVID-19 infection, and also vaccine was recommended by the government and doctors. Among patients who have not received the vaccine, vaccine safety was the main concern. The government was the main source of information about the vaccine. Only 5% of patients developed vaccine breakthrough infection and they recovered without requiring hospitalization. This finding may need to be confirmed in a future large study. Finally, the findings generated from the study would help address the vaccine hesitancy among PD patients.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11255-022-03302-5>.

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Availability of data and material Not applicable.

Code availability Not applicable.

Declarations

Conflicts 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. The other authors have nothing to disclose.

Ethical approval Centralised Institutional Review Board (CIRB) was consulted for approval. The study was approved by CIRB given that the study involved the collection of anonymized data from study participants (CIRB reference number 2021/2563).

Consent for publication The consent was waived as only anonymized data were used.

Consent to participate The consent was waived as only anonymized data were collected.

References

- Weinhandl ED, Wetmore JB, Peng Y, Liu J, Gilbertson DT, Johansen KL (2021) Initial effects of COVID-19 on patients with ESKD. *J Am Soc Nephrol* 32(6):1444–1453
- Robinson BM, Guedes M, Alghonaim M, Cases A, Dasgupta I, Gan L et al (2021) Worldwide early impact of COVID-19 on dialysis patients and staff and lessons learned: a DOPPS roundtable discussion. *Kidney Med* 3(4):619–634
- Ikizler TA, Klinger AS (2020) Minimizing the risk of COVID-19 among patients on dialysis. *Nat Rev Nephrol* 16(6):311–313
- Htay H, Wong PMPK, Choo RER, Dawood US, Foo MWY, Jayaballa M et al (2020) Strategies for management of peritoneal dialysis patients in Singapore during COVID-19 pandemic. *Ann Acad Med Singapore* 49(12):1025–1028
- Strategies regarding COVID-19 in PD patients - International Society for Peritoneal Dialysis [Internet]. [cited 2022 Feb 19]. Available from: <https://isspd.org/strategies-covid19/>
- Alfano G, Fontana F, Ferrari A, Guaraldi G, Mussini C, Magistroni R et al (2020) Peritoneal dialysis in the time of coronavirus disease 2019. *Clin Kidney J* 13(3):265–268
- Sachdeva M, Uppal NN, Hirsch JS, Ng JH, Malieckal D, Fishbane S et al (2020) COVID-19 in hospitalized patients on chronic peritoneal dialysis: a case series. *Am J Nephrol* 51(8):669–674
- Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R et al (2021) Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 384(5):403–416
- Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R et al (2021) Safety of the BNT162b2 mRNA covid-19 vaccine in a nationwide setting. *N Engl J Med*. <https://doi.org/10.1056/nejmoa2110475>
- Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P et al (2021) Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID symptom study app in the UK: a prospective observational study. *Lancet Infect Dis* 21(7):939
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S et al (2020) Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 383(27):2603–2615. <https://doi.org/10.1056/nejmoa2034577>
- Haase M, Lesny P, Haase-Fielitz A, Anderson M, Cloherty G, Stec M et al (2021) Immunogenicity and tolerability of COVID-19 vaccination in peritoneal dialysis patients—a prospective observational cohort study. *Semin Dial*. <https://doi.org/10.1111/sdi.13043>
- Wallace H, Mount PF (2021) COVID-19 beliefs and vaccination uptake in dialysis patients: lessons from an anonymous patient survey. *Intern Med*. <https://doi.org/10.1111/imj.15636>
- Naito T, Suzuki M, Kanazawa A, Takahashi H, Fujibayashi K, Yokokawa H et al (2020) Pneumococcal vaccination reduces in-hospital mortality, length of stay and medical expenditure in hospitalized elderly patients. *J Infect Chemother* 26(7):715–721
- Mykietiuik A, Carratalà J, Domínguez A, Manzur A, Fernández-Sabé N, Dorca J et al (2006) Effect of prior pneumococcal vaccination on clinical outcome of hospitalized adults with community-acquired pneumococcal pneumonia. *Eur J Clin Microbiol Infect Dis* 25(7):457–462
- Wang IK, Lin CL, Lin PC, Chang SN, Chou CY, Yen TH et al (2016) Seasonal influenza vaccination is associated with reduced morbidity and mortality in peritoneal dialysis patients. *Nephrol Dial Transplant* 31(2):269–274
- Blanchi S, Torreggiani M, Chatrenet A, Fois A, Mazé B, Njandjo L et al (2021) COVID-19 Vaccine Hesitancy in Patients on Dialysis in Italy and France. *Kidney Int Reports* 6(11):2763–2774
- Garcia P, Montez-Rath ME, Moore H, Flotte J, Fults C, Block MS et al (2021) SARS-CoV-2 vaccine acceptability in patients on hemodialysis: a nationwide survey. *J Am Soc Nephrol* 32(7):1575–1581
- Ou MT, Boyarsky BJ, Motter JD, Greenberg RS, Teles AT, Ruddy JA et al (2021) Safety and reactogenicity of 2 Doses of SARS-CoV-2 vaccination in solid organ transplant recipients. *Transplantation* 105(10):2170

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