

RESEARCH ARTICLE



Omicron variant infection worsen the prognosis of haemodialysis (HD) patients

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ABSTRACT

Background: Haemodialysis (HD) patients are predisposed to physical ailments, and their occurrence of coronavirus disease 2019 (COVID-19) could potentially lead to a more unfavourable prognosis. However, the impact of SARS-CoV-2 (Omicron variant) infection on the prognosis of HD patients remains unclear. This study aimed to explore the impact of Omicron variant infection on the prognosis of HD patients.

Methods: Eligible participants were patients undergoing maintenance HD treatment during a large-scale outbreak of COVID-19 (Omicron variant) in Shanghai, China, from April 7 to May 30, 2022. According to SARS-CoV-2 infection status of participants, the HD patients were divided into two groups: a COVID-19 group and a non-COVID-19 group. The primary outcome assessed was in-hospital mortality, and secondary outcomes encompassed the incidence of severe cases, admission to intensive care, length of hospital stay, and blood indices. Statistical analysis was conducted by comparative analysis and multiple logistic regression.

Results: This study recruited 588 HD patients, including 199 cases in the COVID-19 group and 389 in the non-COVID-19 group. In the COVID-19 group, the mortality rate was 8.45% (17/199), whereas in the non-COVID-19 group, the rate was 3.34% (13/389) ($p < 0.05$). Compared with the non-COVID-19 group, the COVID-19 group had a risk ratio (RR) with 95% confidence interval (CI) of 2.56 (1.27–5.15) for mortality, and the absolute risk difference (ARD) with 95% CI of 5.20% (1.34%–9.06%). Multiple logistic regression confirmed Omicron variant as a risk factor for mortality among HD patients. Additionally, the COVID-19 group had a higher proportion of severe cases, intensive care admission, hypocalcaemia and hyperphosphatemia and longer hospitalization duration, compared to the non-COVID-19 group ($p < 0.05$).

Conclusions: Omicron variant infection was associated with increased mortality risk in HD patients, and Omicron infection worsen the prognosis of HD patients. Enhancing immune protection against SARS-CoV-2 is crucial for HD patients during the ongoing COVID-19 pandemic.

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Introduction

Coronavirus disease 2019 (COVID-19), a novel respiratory infectious disease, affects the general population irrespective of age. However, older adults and individuals with underlying diseases have higher hospitalization rates for COVID-19 and a greater likelihood of

severe illness [1–4]. Haemodialysis (HD) serves as a common therapy for end-stage renal disease (ESRD) [5,6]. However, HD patients are particularly susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during their medical treatment amid the COVID-19 epidemic [7]. To date, five

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SARS-CoV-2 variants of concern (VOCs) have been identified by the World Health Organization (WHO), including the (1) Alpha variant, (2) Beta variant, (3) Gamma variant, (4) Delta variant, and (5) Omicron variant [8–10]. Previous studies have revealed that the Omicron variant demonstrates lower virulence and reduced rates of hospitalization and severe illness compared to other VOCs. However, the impact of SARS-CoV-2 (Omicron variant) infection on the prognosis of HD patients remains unclear.

Between March 2022 and June 2022, a large-scale epidemic caused by the Omicron BA.2.2 variant occurred in Shanghai, leading to an approximate cumulative infection count of 600,000 individuals [3,11,12]. The Lingang District Hospital of Shanghai Sixth People's Hospital was designated by the government department for the treatment of COVID-19 cases. Additionally, this hospital was also commissioned to treat a majority of HD patients in the Shanghai area. The fact that this hospital provided services for the coexistence of HD and COVID-19 patients was the basis for this retrospective cohort study. The objective of this study was to investigate the impact of COVID-19 (Omicron variant) infection on the prognosis of HD patients.

Materials and methods

Selection of patients

This study was designed as a retrospective cohort study. In this study, patients undergoing maintenance HD treatment in the two district hospitals of Shanghai Sixth People's Hospital during were considered eligible for inclusion. Included patients were admitted during the large-scale outbreak of COVID-19 (Omicron variant) in Shanghai, China from April 7 to May 30, 2022. The inclusion criteria comprised: (1) patients aged 18 years or older and (2) patients who had received HD treatment for a duration exceeding 3 months. The exclusion criteria encompassed: (1) repeated registration or significant data loss; (2) advanced malignant tumours; and (3) temporary HD treatment for acute renal injury. This study was approved by the Ethics Committee of Shanghai Sixth People's Hospital [Approval No: 2022-052 - (1)]. Informed consent is waived due to the retrospective nature of the study and the use of anonymized data.

Baseline data

The collected data included information on sex, age, duration of dialysis, vascular access, diseases classification, history of tuberculosis, SARS-CoV-2 infection, SARS-CoV-2

vaccination, and human immunodeficiency virus (HIV) infection, nucleic acid cycle threshold (CT) values by reverse transcription polymerase chain reaction (RT-PCR), and dexamethasone use, and the time to viral clearance in COVID-19 positive patients were obtained from through clinical consultation and medical records. The patients themselves answered questions regarding the history of SARS-CoV-2 vaccination and infection. Hierarchical variables were categorized as follows: (1) age [≥ 65 years vs. < 65 years]; (2) sex [male vs. female]; (3) Omicron variant infection [yes vs. no]; (4) diabetes [yes vs. no]; (5) dialysis duration [≥ 48 months vs. < 48 months]; (6) vascular access [central venous catheter (CVC) vs. internal fistula]; (7) nucleic acid CT values [≥ 21 vs. < 21]; and (8) time to viral clearance [≥ 11 days vs. < 11 days]. COVID-19 nucleic acid tests were conducted using fluorescence quantitative RT-PCR with an ABI7500 amplification instrument (Applied Biosystems, USA). Two investigators independently collected and crosschecked the data.

Exposure ascertainment

We have been monitoring all HD patients who met our inclusion criteria since April 7, 2022. HD patients were divided into two groups based on the presence or absence of concomitant SARS-CoV-2 infection: the COVID-19 group and non-COVID-19 group. Each HD patients underwent a daily SARS-CoV-2 nucleic acid test. Diagnosis of SARS-CoV-2 infection in all patients followed the standardized protocol for epidemic prevention and control established by local governments. A CT value of 35 in nucleic acid amplification tests served as the threshold for PCR positivity. Individuals with a CT value of 35 or above are considered to have a negative test result, while those below are considered positive. Those who tested positive were grouped into the COVID-19 group immediately, while those with consistent negative test results during our study period were grouped in the non-COVID-19 group.

Outcome ascertainment

Based on the SARS-CoV-2 infection status of HD patients, we followed up the HD patients and collected their clinical features and prognosis from medical records. The primary outcome of this study was all-cause mortality, defined as death from any cause during the observation period. Secondary outcomes included the incidence of COVID-19 severe cases, admission to intensive care, duration of hospital stay, and blood indices such as haemoglobin, blood calcium, blood phosphorus and serum albumin levels. A patient meeting any of the following criteria is classified as a severe case: (1) difficulty in

breathing, with a respiratory rate exceeding 30 times/min; (2) with a respiratory rate exceeding 93% when inhaling air; (3) arterial blood oxygen partial pressure (PaO₂) to fraction of inspired oxygen (FiO₂) ratio less than 300 mmHg (1 mmHg = 0.133 kPa); (4) progressive deterioration of clinical symptoms within 24–48 h, as indicated by pulmonary imaging; and (5) patients exhibiting significant advancement of internal lesions exceeding 50%. Blood indices were measured by technicians in the hospital laboratory using specific methods. The haemoglobin test was conducted using the sodium lauryl sulphate haemoglobin method with a Sysmex XN-2800 automatic blood analyser (Sysmex, Japan). Serum albumin levels were determined using the bromocresol green method. Serum calcium levels were determined by the toluidine blue method. Serum phosphorus levels were assessed using the phosphomolybdate method. All techniques were performed using the Beckman AU5811 automatic biochemical analyser (Beckman, USA). Standard operating procedures were followed during testing, and laboratory personnel were unaware of the study details. Blood samples were collected within 8 h of admission.

Statistical analysis

Continuous data with a normal distribution are presented as the means \pm standard deviations (SDs). The Student's *t*-test was used to determine differences between groups. Non-normally distributed data are reported as the medians with interquartile ranges (IQRs). The Mann–Whitney U-test was used to compare the differences between groups. Data are expressed as *N* (%). The chi-square test was used for comparative analysis between groups. Multiple logistic regression models were used to identify mortality risk factors among HD patients. The mean difference (MD) was employed to evaluate the effect of continuous variables between groups. Proportional data differences between groups were estimated using the risk ratio (RR) or/and absolute risk difference (ARD). As blood calcium and phosphorus are important prognostic indicators for patients, this study statistically analysed the incidence of abnormal for both. A significance level of $p < 0.05$ was considered statistically significant. STATA 15.1 (StataCorp, USA) and GraphPad Prism 8.3.0 (LLC, USA) were used for statistical analysis.

Results

General information

The general characteristics of the HD patients included in this study are shown in Table 1. A total of

588 HD patients were included, consisting of 385 males (64.81%) and 209 females (35.19%). The age range of the patients was 24 to 92 years, with a median age of 65 years (IQR: 54.0–72.0 years). Among them, there were 389 cases in the non-COVID-19 group and 199 in the COVID-19 group. The COVID-19 HD patient group had a median time of 11 days (IQR: 9–14 days) for SARS-CoV-2 nucleic acid conversion to become negative. None of the patients in either group had a history of tuberculosis, SARS-CoV-2 infection, SARS-CoV-2 vaccination or HIV infection. There were no significant differences in age, dialysis duration, diseases classification, or vascular access approach between the two groups ($p > 0.05$). However, a significant difference was observed in terms of sex ($p < 0.05$) (Table 1).

Table 1. Demographic and clinical characteristics of haemodialysis patients.

	COVID-19 group (<i>N</i> = 199)	Non-COVID-19 group (<i>N</i> = 389)	<i>P</i>
Age (Years; Median, IQR)	65 (55.0–73.0)	65 (54.0–72.0)	0.5712
Sex (<i>N</i> , %)			
Male	116 (58.29)	264 (67.87)	0.0273
Female	83 (41.71)	125 (32.13)	
Vascular access approach (<i>N</i> , %)			
Internal fistula	161 (80.90)	330 (84.83)	0.2726
CVC	38 (19.10)	59 (15.17)	
Dialysis duration (months, IQR)	48 (20–96)	49 (22–96)	0.7312
Diseases classification (<i>N</i> , %)			
Diabetic nephropathy	59 (29.65)	131 (33.68)	0.3231
Hypertensive nephropathy	29 (14.57)	53 (13.62)	0.7535
Chronic nephritis	60 (30.15)	118 (30.34)	0.9635
Polycystic kidney	16 (8.04)	33 (8.48)	0.8541
Others	35 (17.59)	54 (13.88)	0.2354
History of SARS-CoV-2 vaccination (<i>N</i> , %)	0 (0)	0 (0)	–
History of SARS-CoV-2 infection (<i>N</i> , %) [§]	0 (0)	0 (0)	–
History of tuberculosis (<i>N</i> , %)	0 (0)	0 (0)	–
HIV infection (<i>N</i> , %)	0 (0)	0 (0)	–
Nucleic acid testing			
CT (ORF) median (IQR)	21.5 (18.8–24.5)	–	–
CT (N gene) median (IQR)	20.4 (17.0–24.1)	–	–
*Nucleic acid conversion days (Median, IQR)	11 (9–14) [#]		

CT: cycle threshold.

*The time to negative nucleic acid conversion.

[#]The 90% quantile range is 7 to 18 days. CVC: central venous catheter.

[§]All HD patients received regular nucleic acid testing and the results were negative.

Main outcome

Among the 199 patients with COVID-19, there were 17 deaths (8.45%), while among the 389 patients without a history of COVID-19, there were 13 deaths (3.34%). There was a significant difference in mortality rates between the two groups ($p < 0.05$). The COVID-19 group had a higher risk of mortality compared with non-COVID-19 patients, with a risk ratio (RR) of 2.56 (1.27–5.15), $p < 0.05$, and an absolute risk difference (ARD) of 5.20% (1.34%–9.06%), $p < 0.05$ (Table 2).

The median age at death among HD patients in this study was 72 years (95% CI: 65.4–78.1), with a median dialysis duration of 52 months (IQR: 24–93). There was no significant difference in the age at death or dialysis duration between the COVID-19 HD patient group and the non-COVID-19 HD patient group ($p > 0.05$) (Figure 1).

The use of dexamethasone in HD patients did not have a significant impact on mortality [RR: 1.39 (95% CI: 0.54–3.59); $p = 0.4922$].

Table 2. Comparison of mortality among haemodialysis patients.

	COVID-19 (<i>n</i> = 199)	Non-COVID-19 (<i>n</i> = 389)	<i>P</i>
Age (Mean, SD)	63.09 (14.35)	62.84 (12.84)	0.0669
Sex (<i>N</i> , %)			<0.0001
Male	112 (58.9)	264 (67.9)	
Female	78 (41.1)	125 (32.1)	
Comparison of mortality			
<i>N</i> (%)	17 (8.54)	13 (3.34)	0.0088
RR (95% CI)	2.56 (1.27–5.15)		0.0088
ARD (95% CI)	5.20% (1.34%–9.06%)		0.0083

PSM: propensity score matching.

RR: risk ratio.

ARD: absolute risk difference.

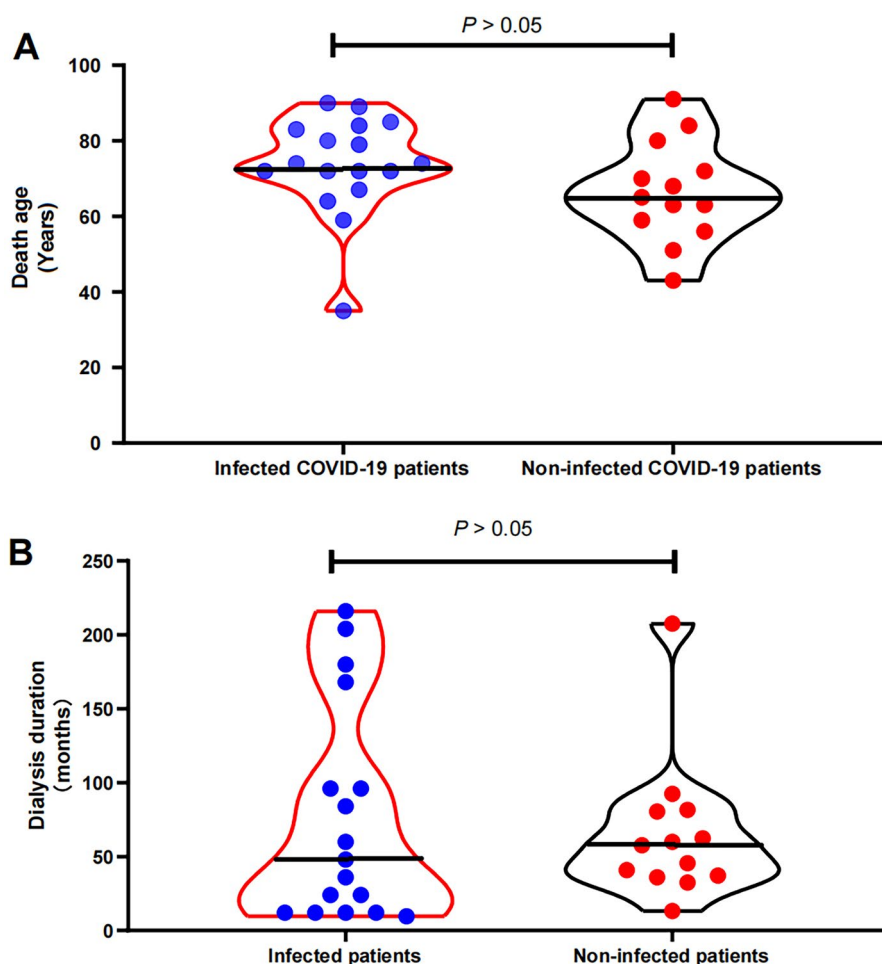


Figure 1. Comparison of the age at death and dialysis duration between the COVID-19 haemodialysis patients and non-COVID-19 haemodialysis patients.

A: Comparison of the age at death between the two groups; B: Comparison of the dialysis duration between the two groups.

The *P* values were obtained by the Mann–Whitney U-test, representing the differences of age at death and the dialysis duration in the two groups.

Table 2 illustrated that the COVID-19 group had a higher risk of mortality compared to the non-COVID-19 group, with a risk ratio (RR) of 2.50 (95% CI: 1.21–5.17), $p < 0.05$. The ARD with 95% CI was 5.17% (0.7%–9.64%), $p < 0.05$.

Logistic regression demonstrated that SARS-CoV-2 infection, patient age, dialysis duration and time to negative conversion of RT-PCR were independent risk factors influencing the mortality of HD patients ($p < 0.05$). However, a diabetes history, sex, viral nucleic acid load with a CT value of 21 or higher, and vascular access approach did not show statistically significant associations ($p > 0.05$) (Table 3).

Secondary outcomes

Compared to non-COVID-19 patients, COVID-19 patients showed a significant increase in (1) the incidence rate of severe cases [RR: 2.75 (95% CI: 1.97–3.83), ARD: 21.08% (95% CI: 13.78%–28.38%); $p < 0.05$], the rate of intensive care admission [RR, 2.55 (95% CI: 1.52–4.27), ARD: 9.16% (95% CI: 3.67%–14.66%); $p < 0.05$], and (2) a longer duration of hospital stay [MD (days): 9.0 (95% CI: 8.6–9.4)]. (Table 4).

In comparison to non-COVID-19 patients, COVID-19 patients showed a significant decrease in (1) haemoglobin levels (g/L) [MD, –3.30 (95% CI: –6.51 to –0.09)], calcium levels [MD, –0.05 (95% CI: –0.09 to –0.01)] and phosphorus levels (mmol/L) [MD, –0.48 (95% CI: 0.42 to 0.54)], while (2) the change in albumin levels (g/L) was not statistically significant [MD: –0.64 (95% CI: –0.16, 1.44)]. (Table 5).

The rate of abnormal serum calcium levels in the COVID-19 group was significantly higher than that in the non-COVID-19 group ($p < 0.05$), indicating the presence of low calcium levels (Supplementary Material Table 1). Additionally, the COVID-19 group had a higher rate of abnormal serum phosphorus level ($p < 0.05$), indicating the presence of notable hyperphosphatemia (Supplementary Material Table 2).

Discussion

The COVID-19 epidemic poses an increased risk of adverse outcomes for HD patients due to their heavy burden of comorbidities [13,14]. For instance, in Poland, between January 1, 2020, and January 31, 2020, the fatality rate among HD patients with COVID-19 was reported to be 30.4% [15], which highlights an alarmingly high mortality rate associated with the early stages of the COVID-19 pandemic. In a report from Paris in 2020, it was found that 27.3% of HD patients with COVID-19 died, while 58.5% were discharged from the hospital, including only two patients (13.3%) who had been admitted to the intensive care unit [16]. Similarly, a retrospective cohort study conducted in Brazil among 741 HD patients with COVID-19 between February 2020 and December 2020, revealed that there were 139 deaths (18.8%), with 66% occurring in the first 15 days of the disease [17]. A meta-analysis report between January 2020 and March 2022 [18] that HD patients infected with SARS-CoV-2 had a very high mortality rate (24% [95% CI: 19%–28%]).

Table 3. Associations between risk factors and mortality among haemodialysis patients by multiple logistic regression analysis.

Factors	Univariate		Multivariate	
	OR (95% CI)	P	Adjusted OR (95% CI)	P
Omicron variant infection				
Yes vs. no	2.70 (1.29–5.65)	0.0084	2.64 (1.25–5.58)	0.0109
Age				
≥65 years vs. <65 years	2.33 (1.08–5.03)	0.0311	2.34 (1.08–5.07)	0.0312
Sex				
Female vs. male	1.06 (0.48–2.34)	0.8854	0.97 (0.43–2.19)	0.9415
Diabetes				
Yes vs. no	1.42 (0.65–2.99)	0.3791	1.50 (0.68–3.31)	0.3151
Dialysis duration				
≥48 months vs. <48 months	1.12 (1.04–1.21)	0.0027	1.15 (1.06–1.25)	0.0008
Vascular access approach				
CVC vs. internal fistula	2.89 (1.25–6.68)	0.0131	2.24 (0.93–5.40)	0.0722
*Nucleic acid quantification				
CT values (ORF)				
≥21 vs. <21	2.54 (0.39–9.62)	0.3259	2.65 (0.40–16.54)	0.3259
CT values (N gene)				
≥21 vs. <21	1.90 (0.29–12.45)	0.5033	2.06 (0.31–13.69)	0.4545
*Days to viral clearance				
≥11 days vs. <11 days	6.01 (2.33–15.50)	0.0002	5.78 (2.15–15.54)	0.0005

CVC: central venous catheter.

CT: cycle threshold.

OR: odds ratio.

*The analysis data included only COVID-19 patients.

Table 4. Effect of omicron variant infection on incidence of disease severity, intensive care admission and length of hospital stay of haemodialysis patients.

	COVID-19 group (N=199)	Non-COVID-19 group (N=389)	Effect size (95% CI)	P
Incidence of severe cases (N, %)	66 (33.17)	47 (12.08)	RR: 2.75 (1.97 to 3.83) ARD: 21.08% (13.78% to 28.38%)	<0.0001 <0.0001
Intensive care admission (N, %)	30 (15.08)	23 (5.91)	RR: 2.55 (1.52 to 4.27) ARD: 9.16% (3.67% to 14.66%)	0.0004 0.0011
Length of hospital stay (days, Mean±SD)	16.0±3.0	7.0±2.5	MD: 9.0 (8.6 to 9.4)	<0.0001

RR: risk ratio.

ARD: absolute risk difference.

MD: mean difference.

Table 5. Effect of omicron variant infection on blood indices of haemodialysis patients.

	COVID-19 group (Mean±SD, N)	Non-COVID-19 group (Mean±SD, N)	MD (95% CI)	P
Haemoglobin (g/L)	100.51±21.52 (199)	103.81±16.89 (376)	-3.30 (-6.51 to -0.09)	<0.0001
Calcium (mmol/L)	2.22±0.23 (196)	2.27±0.21 (373)	-0.05 (-0.09 to -0.01)	0.0093
Phosphorus (mmol/L)	2.37±0.37 (197)	1.89±0.34 (373)	0.48 (0.42 to 0.54)	<0.0001
Albumin (g/L)	36.86±5.51 (199)	37.5±4.04 (373)	-0.64 (-1.43 to 0.15)	0.0833

MD: mean difference.

The above studies showed that the mortality rate for HD patients with COVID-19 is significantly higher than that of the general population following COVID-19. The abnormally high mortality rate of HD patients after SARS-CoV-2 infection may be related to low vaccination rates among HD patients, electrolyte disorders, and a higher prevalence of cardiovascular and cerebrovascular complications [15,19,20]. Notably, mortality rates among HD patients in different studies may vary due to factors such as viral variants and patient characteristics.

Unlike previous studies examining the impact of COVID-19 infection on HD patients without the Omicron variant, our retrospective cohort study investigated the influence of Omicron variant infection on HD patients during the same period. Our research revealed that 17 of 199 HD patients with COVID-19 died, with a mortality rate of 8.45%; 13 of the 389 HD

patients without COVID-19 died, with a mortality rate of 3.34%. The mortality risk for infected patients was 2.5 times higher than that for uninfected patients. While our results demonstrate a significant reduction in mortality rates among HD patients attributed to the Omicron variant compared to some previous studies [16,17,21], the presence of survivorship bias within our study could potentially underestimate the impact of Omicron variant infection among HD patients. This is because those who die early have less opportunity to become infected. Therefore, the true mortality rate due to Omicron virus infection in the HD patients may be higher than the mortality rate reported in this study.

Our findings showed that the majority of deceased HD patients were aged over 65 years and had dialysis durations exceeding 3 years. Notably, there were no significant differences in age or dialysis duration between COVID-19 and non-COVID-19 patients, indicating a balanced distribution within the two groups, which enhance the credibility of our research findings.

Furthermore, we performed a logistic regression analysis to identify the risk factors for mortality among HD patients. The findings revealed that Omicron variant infection, a time to viral clearance exceeding 11 days, age above 65 years, and a dialysis duration > 41 months were identified as adverse risk factors for mortality among HD patients. However, factors such as sex, dexamethasone use, diabetes, time to viral clearance and vascular access approach did not have a significant impact on mortality. Additionally, our study observed that the median time to viral clearance among HD patients was 11 days, with an IQR of 9–14 days. Compared to the general population, the time to viral clearance among HD patients was extended [22–24]. Our findings suggest that a prolonged duration of nucleic acid positivity is associated with increased mortality risk in HD patients. This further supports the notion that the Omicron variant poses substantial harm to patients undergoing HD.

Based on our findings, compared with non-COVID-19 patients, COVID-19 patients showed a significant increase in the incidence of severe cases, intensive care admission and length-of-hospital stay. These results further confirmed that HD patients with SARS-CoV-2 infection are more susceptible to experiencing adverse outcomes.

This study revealed that the haemoglobin levels of HD patients with COVID-19 were lower than those of non-infected patients, which may be related to dysregulated haematopoiesis in patients after being infected with SARS-CoV-2 [25,26]. The incidence of anaemia among patients with COVID-19 is 77% [16], which is much higher than that in the general population.

In terms of calcium and phosphorus metabolism and nutrition, compared with the non-COVID-19 group, the normal calcium and phosphorus rates of COVID-19 group were significantly lower; this indicates that more patients had low calcium and high phosphorus levels. The previous studies suggest that the abnormal levels of serum albumin [27–30], serum phosphorus [28,31] and serum calcium [32,33] can affect the prognosis of HD patients. However, the specific mechanism requires further study. Since COVID-19 patients are prone to abnormal calcium levels and phosphorus metabolism, blood biochemical indices should be used to monitor and maintain electrolyte balance in HD patients with COVID-19. There was no difference in the serum albumin levels between HD patients with and without COVID-19, indicating that patients' protein intake and absorption were not significantly affected by the infection.

This study identified confounding factors between the COVID-19 and non-COVID-19 groups. Multiple regression models were used to balance and adjust for covariates, thereby enhancing the reliability of the findings. Importantly, there were no missing data for the main outcome measure. For the secondary outcomes, the percentage of missing data were less than 5% of the total dataset. This indicates a minimal likelihood of information bias resulting from data withdrawal or missing information.

This study provides strong evidence supporting the association between SARS-CoV-2 infection and increased mortality rates among HD patients. Nevertheless, this study has some limitations, such as the fact that baseline data may have ignored potential secondary confounding factors and the lack of repeated and long-term follow-up.

Surprisingly, none of the HD patients included in this study received SARS-CoV-2 vaccination. Vaccination hesitancy is prevalent in China, particularly among older individuals. Previous research has highlighted that this hesitancy can stem from various factors, such as contraindications, frailty, and insufficient knowledge regarding COVID-19 vaccines. However, COVID-19 vaccination among HD patients is associated with a lower incidence of infection, as well as reduced severity of illness and mortality during the COVID-19 pandemic [34–38]. Therefore, implementing a comprehensive SARS-CoV-2 vaccination program is necessary for HD patients.

Since HD patients are more likely to be infected with SARS-CoV-2, which poses a serious threat to the survival of HD patients. Therefore, it is imperative to prioritize immune protection measures for HD patients in order to prevent SARS-CoV-2 infection during the COVID-19 pandemic. However, lymphocyte counts are significant for the prediction of short-term mortality in

HD patients with COVID-19 and HD patients with lung involvement have poorer survival rates [39]. Considering that the survival of HD patients is inevitably influenced by many factors; in the future, further research on prognostic factors affecting HD patients would be great significance in improving clinical management and treatment strategies for this population.

Collectively, this study uniquely focuses on the impact of the Omicron variant on unvaccinated HD patients, providing comprehensive real-world data and confirming its significant health threat.

Conclusion

The COVID-19 epidemic poses an increased risk of adverse outcomes for HD patients due to their heavy burden of comorbidities. Although the mortality of HD patients caused by the Omicron variant has been significantly reduced compared to other SARS-CoV-2 variants, Omicron variant infection still had detrimental effects on the prognosis and was associated with increased mortality rate of HD patients. Therefore, it is imperative to prioritize and promote COVID-19 vaccination for HD patients as crucial measure for protection them against SARS-CoV-2 infection during the COVID-19 epidemic.

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Ethics statement

This study was approved by the Ethics Committee of Shanghai Sixth People's Hospital [Approval No: 2022-052 - (1)].

Consent for publication

Not applicable.

Author contributions

CTZ, TFC, JYY, MSC and SGY contributed to the design of the study; TFC, YPG, and XHS contributed to data collection; MSC, TFC, YSG and CTZ contributed to data analysis and methodology; CTZ, TFC, and YPG contributed to project supervision; CTZ, TFC, JYY, MSC, and SGY contributed to the original draft. CTZ, SGY, MSC, TFC, JYY, XHS, and YPG revised the manuscript and approved the final manuscript for submission.

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Data availability statement

Data available on request from the authors.

References

- [1] Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Effect of Sotrovimab on hospitalization or death among high-risk patients with mild to moderate COVID-19: a randomized clinical trial. *JAMA*. 2022;327(13):1236–1246. doi: [10.1001/jama.2022.2832](https://doi.org/10.1001/jama.2022.2832).
- [2] Can O, Bilek G, Sahan S. Risk factors for infection and mortality among hemodialysis patients during COVID-19 pandemic. *Int Urol Nephrol*. 2022;54(3):661–669. doi: [10.1007/s11255-021-02926-3](https://doi.org/10.1007/s11255-021-02926-3).
- [3] Chen X, Yan X, Sun K, et al. Estimation of disease burden and clinical severity of COVID-19 caused by Omicron BA.2 in Shanghai, February–June 2022. *Emerg Microbes Infect*. 2022;11(1):2800–2807. doi: [10.1080/22221751.2022.2128435](https://doi.org/10.1080/22221751.2022.2128435).
- [4] Lu G, Zhang Y, Zhang H, et al. Geriatric risk and protective factors for serious COVID-19 outcomes among older adults in Shanghai Omicron wave. *Emerg Microbes Infect*. 2022;11(1):2045–2054. doi: [10.1080/22221751.2022.2109517](https://doi.org/10.1080/22221751.2022.2109517).
- [5] Kalaycı B, Onan E, Paydaş S, et al. The effect of hemodialysis adequacy on ventricular repolarization in end-stage kidney disease. *Turk Kardiyol Dern Ars*. 2019;47(7):572–580. doi: [10.5543/tkda.2019.64359](https://doi.org/10.5543/tkda.2019.64359).
- [6] Sánchez-Alvarez E, Macía M, de Sequera Ortiz P. Management of hemodialysis patients with suspected or confirmed SARS-CoV-2 infection: perspective from the Spanish nephrology. *Kidney*. 2020;1(11):1254–1258. doi: [10.34067/KID.0002602020](https://doi.org/10.34067/KID.0002602020).
- [7] Perna AF, Capolongo G, Trepiccione F, et al. COVID-19, low-molecular-weight heparin, and hemodialysis. *Kidney Blood Press Res*. 2020;45(3):357–362. doi: [10.1159/000508460](https://doi.org/10.1159/000508460).
- [8] Zhang GF, Meng W, Chen L, et al. Neutralizing antibodies to SARS-CoV-2 variants of concern including Delta and Omicron in subjects receiving mRNA-1273, BNT162b2, and Ad26.COV2.S vaccines. *J Med Virol*. 2022;94(12):5678–5690. doi: [10.1002/jmv.28032](https://doi.org/10.1002/jmv.28032).
- [9] Cheng CC, Platen L, Christa C, et al. Improved SARS-CoV-2 neutralization of Delta and Omicron BA.1 variants of concern after fourth vaccination in hemodialysis patients. *Vaccines (Basel)*. 2022;10(8):1328. doi: [10.3390/vaccines10081328](https://doi.org/10.3390/vaccines10081328).
- [10] Jungnick S, Hobmaier B, Mautner L, et al. In vitro rapid antigen test performance with the SARS-CoV-2 variants of concern B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta). *Microorganisms*. 2021;9(9):1967. doi: [10.3390/microorganisms9091967](https://doi.org/10.3390/microorganisms9091967).
- [11] Zhang X, Zhang W, Chen S. Shanghai's life-saving efforts against the current Omicron wave of the COVID-19 pandemic. *Lancet*. 2022;399(10340):2011–2012. doi: [10.1016/S0140-6736\(22\)00838-8](https://doi.org/10.1016/S0140-6736(22)00838-8).
- [12] Ao Y, Li J, Wei Z, et al. Clinical and virological characteristics of SARS-CoV-2 Omicron BA.2.2 variant outbreaks during April to May, 2022, Shanghai, China. *J Infect*. 2022;85(5):573–607. doi: [10.1016/j.jinf.2022.07.027](https://doi.org/10.1016/j.jinf.2022.07.027).
- [13] Fisher M, Yunes M, Mokrzycki MH, et al. Chronic hemodialysis patients hospitalized with COVID-19: short-term outcomes in the Bronx, New York. *Kidney360*. 2020;1(8):755–762. doi: [10.34067/KID.0003672020](https://doi.org/10.34067/KID.0003672020).
- [14] Ay N, Danış R, Kılıç J, et al. Analysis of SARS-CoV-2 infection in hemodialysis and kidney transplant patients in a pandemic hospital. *J Infect Dev Ctries*. 2022;16(6):1016–1024. doi: [10.3855/jidc.15829](https://doi.org/10.3855/jidc.15829).
- [15] Puchalska-Reglińska E, Dębska-Ślizień A, Biedunkiewicz B, et al. Extremely high mortality rates among hemodialysis patients with COVID-19 before the era of SARS-CoV-2 vaccination: results from a large database from the North of Poland. *Pol Arch Intern Med*. 2021;131(7-8):643–648. doi: [10.20452/pamw.16028](https://doi.org/10.20452/pamw.16028).
- [16] Tortonese S, Scriabine I, Anjou L, et al. COVID-19 in patients on maintenance dialysis in the Paris region. *Kidney Int Rep*. 2020;5(9):1535–1544. doi: [10.1016/j.ekir.2020.07.016](https://doi.org/10.1016/j.ekir.2020.07.016).
- [17] Lugon JR, Neves PDMdM, Pio-Abreu A, et al. Evaluation of central venous catheter and other risk factors for mortality in chronic hemodialysis patients with COVID-19 in Brazil. *Int Urol Nephrol*. 2022;54(1):193–199. doi: [10.1007/s11255-021-02920-9](https://doi.org/10.1007/s11255-021-02920-9).
- [18] Li P, Guan Y, Zhou S, et al. Mortality and risk factors for COVID-19 in hemodialysis patients: a systematic review and meta-analysis. *Sci Prog*. 2022;105(3):368504221110858. doi: [10.1177/00368504221110858](https://doi.org/10.1177/00368504221110858).
- [19] Hsu CM, Weiner DE, Aweh G, et al. COVID-19 among US dialysis patients: risk factors and outcomes from a national dialysis provider. *Am J Kidney Dis*. 2021;77(5):748–756.e1. doi: [10.1053/j.ajkd.2021.01.003](https://doi.org/10.1053/j.ajkd.2021.01.003).
- [20] Valeri AM, Robbins-Juarez SY, Stevens JS, et al. Presentation and outcomes of patients with ESKD and COVID-19. *J Am Soc Nephrol*. 2020;31(7):1409–1415. doi: [10.1681/ASN.2020040470](https://doi.org/10.1681/ASN.2020040470).
- [21] Bruchfeld A. The COVID-19 pandemic: consequences for nephrology. *Nat Rev Nephrol*. 2021;17(2):81–82. doi: [10.1038/s41581-020-00381-4](https://doi.org/10.1038/s41581-020-00381-4).
- [22] Dorabawila V, Bassett MT, Rosenberg ES. Risk of infection and hospitalization among children and adolescents in New York after emergence of the SARS-CoV-2 Omicron variant-Reply. *JAMA*. 2022;328(14):1460–1461. doi: [10.1001/jama.2022.14484](https://doi.org/10.1001/jama.2022.14484).
- [23] Dorabawila V, Hoefer D, Bauer UE, et al. Risk of infection and hospitalization among vaccinated and unvaccinated children and adolescents in New York after the emergence of the Omicron variant. *JAMA*. 2022;327(22):2242–2244. doi: [10.1001/jama.2022.7319](https://doi.org/10.1001/jama.2022.7319).
- [24] Miller PG, Fell GG, Foy BH, et al. Clonal hematopoiesis of indeterminate potential and risk of death from COVID-19. *Blood*. 2022;140(18):1993–1997. doi: [10.1182/blood.2022018052](https://doi.org/10.1182/blood.2022018052).

- [25] Bolton KL, Koh Y, Foote MB, et al. Clonal hematopoiesis is associated with risk of severe Covid-19. *Nat Commun.* 2021;12(1):5975. doi: [10.1038/s41467-021-26138-6](https://doi.org/10.1038/s41467-021-26138-6).
- [26] Caudrelier N, Cyr P, Kokta V, et al. Extramedullary hematopoiesis secondary to COVID-19: a first case report in a newborn. *SAGE Open Med Case Rep.* 2022;10:2050313–X–221117643. X.
- [27] Hannan JL, Radwany SM, Albanese T. In-hospital mortality in patients older than 60 years with very low albumin levels. *J Pain Symptom Manage.* 2012;43(3):631–637.;doi: [10.1016/j.jpainsymman.2011.04.009](https://doi.org/10.1016/j.jpainsymman.2011.04.009).
- [28] Chen C, Zhang J, Zhou Z, et al. Impact of serum albumin level and variability on short-term cardiovascular-related and all-cause mortality in patients on maintenance hemodialysis. *Medicine (Baltimore).* 2021;100(43):e27666. doi: [10.1097/MD.00000000000027666](https://doi.org/10.1097/MD.00000000000027666).
- [29] Peng F, Sun L, Chen T, et al. Albumin-globulin ratio and mortality in patients on peritoneal dialysis: a retrospective study. *BMC Nephrol.* 2020;21(1):51. doi: [10.1186/s12882-020-1707-1](https://doi.org/10.1186/s12882-020-1707-1).
- [30] Wang X, Han Q, Wang T, et al. Serum albumin changes and mortality risk of peritoneal dialysis patients. *Int Urol Nephrol.* 2020;52(3):565–571. doi: [10.1007/s11255-020-02389-y](https://doi.org/10.1007/s11255-020-02389-y).
- [31] Zhu M, Dou L, Zhu M, et al. Variability of serum phosphorus and its association with mortality among hemodialysis patients. *Clin Nephrol.* 2018;90(2):79–86. doi: [10.5414/CN109265](https://doi.org/10.5414/CN109265).
- [32] Kitamura M, Tateishi Y, Sato S, et al. Association between serum calcium levels and prognosis, hematoma volume, and onset of cerebral hemorrhage in patients undergoing hemodialysis. *BMC Nephrol.* 2019;20(1):210. doi: [10.1186/s12882-019-1400-4](https://doi.org/10.1186/s12882-019-1400-4).
- [33] Kitamura M, Tateishi Y, Sato S, et al. Lower serum calcium and pre-onset blood pressure elevation in cerebral hemorrhage patients undergoing hemodialysis. *Clin Exp Nephrol.* 2020;24(5):465–473. doi: [10.1007/s10157-020-01846-3](https://doi.org/10.1007/s10157-020-01846-3).
- [34] Spensley KJ, Gleeson S, Martin P, et al. Comparison of vaccine effectiveness against the Omicron (B.1.1.529) variant in hemodialysis patients. *Kidney Int Rep.* 2022;7(6):1406–1409. doi: [10.1016/j.ekir.2022.04.005](https://doi.org/10.1016/j.ekir.2022.04.005).
- [35] Ashby DR, Caplin B, Corbett RW, et al. Outcome and effect of vaccination in SARS-CoV-2 Omicron infection in hemodialysis patients: a cohort study. *Nephrol Dial Transplant.* 2022;37(10):1944–1950. doi: [10.1093/ndt/gfac209](https://doi.org/10.1093/ndt/gfac209).
- [36] Tylicki L, Biedunkiewicz B, Puchalska-Reglinska E, et al. COVID-19 vaccination reduces mortality in patients on maintenance hemodialysis. *Front Med (Lausanne).* 2022;9:937167. doi: [10.3389/fmed.2022.937167](https://doi.org/10.3389/fmed.2022.937167).
- [37] Christensen PA, Olsen RJ, Long SW, et al. Signals of significantly increased vaccine breakthrough, decreased hospitalization rates, and less severe disease in patients with Coronavirus Disease 2019 Caused by the Omicron variant of Severe Acute Respiratory Syndrome Coronavirus 2 in Houston, Texas. *Am J Pathol.* 2022;192(4):642–652. doi: [10.1016/j.ajpath.2022.01.007](https://doi.org/10.1016/j.ajpath.2022.01.007).
- [38] Wing S, Thomas D, Balamchi S, et al. Effectiveness of three doses of mRNA COVID-19 Vaccines in the hemodialysis population during the Omicron period. *Clin J Am Soc Nephrol.* 2023;18(4):491–498. doi: [10.2215/CJN.0000000000000108](https://doi.org/10.2215/CJN.0000000000000108).
- [39] Bao WJ, Fu SK, Zhang H, et al. Clinical characteristics and short-term mortality of 102 hospitalized hemodialysis patients infected with SARS-CoV-2 Omicron BA.2.2.1 variant in Shanghai, China. *New Microbes New Infect.* 2022;49:101058. doi: [10.1016/j.nmni.2022.101058](https://doi.org/10.1016/j.nmni.2022.101058).