Original Article

Characteristics and Clinical Outcomes of COVID-19 in ESRD Patients Undergoing Hemodialysis in Ngudi Waluyo Wlingi General Hospital in 2020-2022

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ABSTRACT

Background: The coronavirus disease (COVID-19) pandemic is a major threat to global health care. Comorbidities, including end-stage renal disease (ESRD), are related to an increased risk of severe infection and mortality.

Objective: To assess determinants related to the clinical outcomes of COVID-19 in ESRD patients undergoing hemodialysis in Ngudi Waluyo Wlingi General Hospital in 2020-2022.

Methods: This study included ESRD patients undergoing maintenance hemodialysis who were hospitalized at Ngudi Waluyo Wlingi General Hospital due to COVID-19 from May 2020 to February 2022. Clinical characteristics were investigated in relation to the severity and survival status.

Results: A total of 26 patients (46.15% male) with a mean age of 52.27±13.65 years met the inclusion criteria. Of these, 42.3% had a mild infection, 23% had a moderate infection, 30.77% had a severe infection, and 3.8% had a critical infection. The mortality rate was 23.08%, with a mean length of stay of 15.19±7 days. Age, oxygen saturation, respiratory rate upon admission, lymphocyte and neutrophil levels, and neutrophil-to-lymphocyte ratio were significantly associated with COVID-19 severity. Length of stay was statistically influenced by respiratory rate upon admission. The mortality rate was correlated with the dialysis vintage, levels of hemoglobin, leukocytes, platelets, neutrophils, neutrophil-to-lymphocyte ratio, serum urea, serum creatinine, eGFR, and length of stay.

Conclusion: COVID-19 in ESRD patients undergoing hemodialysis were more likely to have a poor prognosis. Identifying determinants is crucial for reducing morbidity and mortality.

Keywords: Chronic Kidney Disease, COVID-19, Hemodialysis, Renal Insufficiency, Renal Dialysis.

Introduction

Coronavirus disease (COVID-19), caused by the novel beta-coronavirus SARS-CoV-2, was initially identified on December 31, 2019, in Wuhan, China. Following its declaration as a global pandemic in March 2020, it has presented a major threat to global health care.[1] As of June 7, 2024, there have been 775,522,404 confirmed cases and 7,049,617 deaths reported across 232 countries.[2]

Comorbidities, such as chronic kidney disease (CKD), are associated with an increased risk of complications and mortality. The prevalence of COVID-19 among CKD patients fluctuated between 0.4 and 49.0% in 2022.[3] In

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Indonesia, it was predicted that the number of CKD patients with COVID-19 would reach 52.200 cases.[4] Individuals with CKD who are infected with COVID-19 experience a mortality rate that is 14 to 16 times higher than that of individuals without comorbidities.[5] They produce more pro-inflammatory cytokines and oxidative stress as part of the inflammatory response to infections.[1,6]

COVID-19 in patients undergoing routine hemodialysis is associated with elevated rates of hospitalization, intensive care unit (ICU) admissions, and mortality.[3] About 35.3% of dialysis patients developed COVID-19, and 50.2% of them required hospitalization.[7] Routine hemodialysis patients face a hospitalization risk for COVID-19 that is 3 to 4 times higher than that of patients receiving peritoneal dialysis.[8] Between 6.1% and 35.7% of dialysis patients with COVID-19 experienced respiratory distress, with a mortality rate of 14%.[9] These individuals possess a compromised immune response, and face increased social interactions due to regular hospital visits, making them more susceptible to COVID-19.[5,10]

Despite significant improvement in the prognosis of COVID-19 due to vaccinations and advancements in treatment, outcomes in routine hemodialysis patients remain unclear, particularly in Indonesia. This study aims to identify the determinants related to clinical outcomes of COVID-19 in ESRD patients undergoing hemodialysis at Ngudi Waluyo Wlingi General Hospital between 2020-2022.

Methods

Design and participants

This retrospective study focused on hemodialysis patients who were treated for COVID-19 at Ngudi Waluyo Wlingi General Hospital from May 2020 to February 2022. The study population included patients aged ≥15 years with positive RT-PCR and high serum renal function who were hospitalized between May 2020 and February 2022. Inclusion criteria consisted of a diagnosis of ESRD and adherence to a regular hemodialysis schedule. In our hospital, the standard hemodialysis regimen was biweekly sessions lasting 5 hours each. The exclusion criteria were incomplete medical records. Data was retrieved from medical records, including clinical and laboratory data. The patients were grouped according to the severity of COVID-19 and survival status.

In this study, COVID-19 was confirmed through positive RT-PCR results from nasopharyngeal swabs. The hematology test was conducted using a hematology analyzer. Serum potassium level was measured with an ion-selective electrode. Serum urea was evaluated using Berthelot methods, while serum creatinine was assessed using Jaffe methods. The estimated glomerular filtration rate (eGFR) was determined using the CKD-EPI 2021 formula. CKD was classified into five stages based on the Kidney Disease: Improving Global Outcomes guideline. CKD stage 5 (eGFR <15 ml/min) or ESRD is further divided into dialysis-dependent and dialysis-independent.[3] In this study, all participants were diagnosed with CKD stage 5 and undergoing hemodialysis. Dialysis vintage was defined as the period between the date of hemodialysis initiation and hospitalization, measured by "month."[11]

Data collection

In this study, patients were divided into a group of patients with ≤12 months of dialysis and a group of patients with >12 months of dialysis. The severity of COVID-19 was classified according to the Indonesian COVID-19 Treatment Guideline into the following categories: asymptomatic (no symptoms), mild (symptomatic without evidence of viral pneumonia or hypoxia), moderate (signs of pneumonia without evidence of severe pneumonia), severe (signs of pneumonia with increased respiratory rate >30x/minute, or peripheral oxygen saturation <93% on room air, or severe respiratory distress) and critical infection (sepsis, septic shock, acute respiratory distress syndrome, or conditions requiring mechanical ventilation or vasopressors).[5]

Statistical analysis

Variables were assessed using the Saphiro-Wilk test to determine normality. The Mann-Whitney method (for categorical independent variables) and Spearman method (for numeric independent variables) were used to analyze factors that influence the severity of COVID-19 and length of hospital stay. Meanwhile, the survival status analysis used the Chi-square method (for categorical independent variables) and lambda correlation test (for numeric independent variables). Data analysis was performed using IBM SPSS 25.0, considering a *p-value* of <0.05 as a significance value. This study obtained ethical permission from the Health Research Ethics Committee of Ngudi Waluyo Wlingi General Hospital.

Results

From May 2020 to February 2022, 26 patients met the inclusion criteria, with a mean age of 52.27±13.65 years. A total of 12 (46.15%) patients were male. The majority of patients (46.15%) had unknown comorbidity in addition to CKD, and 38.46% had only one comorbidity, with hypertension identified as the most prevalent (34.62%), followed by type 2 diabetes mellitus (15.38%). The mean dialysis vintage was 22.15±15.80 months, with a maximum of 47 months and a minimum of 1 month. The average length of stay (LOS) was 15.19±7.4 days.

Risk factors of COVID-19 severity in patients with ESRD undergoing hemodialysis

Based on the severity of COVID-19, 11 (42.3%) individuals had a mild infection, 6 (23%) had a moderate infection, 8 (30.77%) had a severe infection, and 1 (3.8%) had a critical infection (Table 1). Patients with critical infection had older age (p=0.027, r=0.450) and exhibited reduced oxygen saturation (SpO2) (p<0.001,r=-0.657), increased respiratory rate (RR) (p=0.031,r=0.425), reduced lymphocyte levels (p=0.049,r=-0.389), and increased neutrophils (p=0.017,r=0.462) and neutrophil-to-lymphocyte ratio (NLR) (p=0.032,r=0.421).

Table 1. Characteristics of the participants stratified by COVID-19 severity

Characteristic	COVID-19 severity				Total	*p*-value
	Mild	Moderate	Severe	Critical		
	(*n*=11)	(*n*=6)	(*n*=8)	(*n*=1)	(*n*=26)	
Age (mean, in years±SD)	46.81±13.49	48.5±8.57	61.63±13.62	60±0	52.27±13.65	0.027
<60 years, *n*(%)	9(81.81)	6(100)	3(37.5)	-	18(69.23)	
≥60 years, *n*(%)	2(18.18)	-	5(62.5)	1(100)	8(30.77)	
Sex, male, *n*(%)	6(54.54)	2(33.33)	3(37.5)	1(100)	12(46.15)	0.722
Comorbidities, *n*(%)						0.902
0	5(45.45)	2(33.33)	5(62.5)	-	12(46.15)	
1	5(45.45)	2(33.33)	2(25)	1(100)	10 (38.46)	
>1	1(9.09)	2(33.33)	1(12.5)	-	4(15.38)	
Hypertension	4(36.36)	3(50)	1(12.5)	1(100)	9(34.62)	
Type 2 Diabetes mellitus	3(15)	2(33.33)	1(12.5)	-	4(15.38)	
Dialysis vintage (mean, in months±SD)	18.72±16.4	19.5±17.58	28.13±14.69	28±0	22.15±15.80	0.199
≤12 months, *n*(%)	4(36.36)	2(33.33)	1(12.5)	-	7(26.92)	
>12 months, *n*(%)	7(63.63)	4(66.67)	7(87.5)	1(100)	19(73.08)	
SpO2 (mean, in %±SD)	97.72±1.61	96.34±1.86	85±10.85	96±0	93±8.02	<0.001
RR (mean, in x/min±SD)	21±1.84	23±2.10	25±5.86	24±0	22.81±3.86	0.031
Laboratory, mean±SD						
Hemoglobin (g/dl)	7.54±1.98	8.45±1.81	8.81±1.69	6.1±0	8.09±1.87	0.214
Leukocyte (10^3/μL)	6.85 ±2.58	9.41 ± 3.34	8.04 ± 2.30	8.58±0	7.88 ±2.72	0.162
Platelets (10^3/μL)	312.72±134.95	304.17±164.57	271.13±81.50	491±0	304.81±127.82	0.985
Neutrophil (%)	65.54±7.37	78.43±11	77.09±11.66	82.9±0	72.74±11.17	0.017
Lymphocyte (%)	21.61±8.38	14.93±7.89	15.01±7.72	9.3±0	17.57±8.42	0.049
NLR	3.66±1.91	7.77±6.09	7.33±5.36	8.89±0	5.94±4.58	0.032
Serum potassium (mmol/L)	4.61±0.90	4.40±1.13	4.30±0.65	4.76±0	4.47±0.85	0.311
Serum urea(mg/dl)	145.18±45.39	173.5±41.75	116.5±55.65	435±0	154.041±75.98	0.143
Serum creatinine (mg/dl)	10.29±3.58	10.19±2.22	8.10±3.83	18.85±0	9.92±3.81	0.315
eGFR (mL/min/1.73 m^2)	7.66±3.68	6.84±1.62	13.41±14.97	2.88±0	9.06±8.85	0.986

Hospitalization duration in days (mean,±SD)	15.09±6.55	15±8.15	16.25±8.94	9±0	15.19±7.40	0.557
Death, *n*(%)	2(18.18)	1(16.67)	2(25)	1(100)	6(23.08)	0.303

eGFR, estimated glomerulus filtration rate; HHD, hypertensive heart disease; NLR, neutrophil-leukocyte ratio; RR, respiratory rate; SpO2, peripheral oxygen saturation.

Risk factors of length of hospital stay of COVID-19 in patients with ESRD undergoing hemodialysis

Length of stay (LOS) was significantly affected by respiratory rate upon admission (p=0.012, r=-0.484). The analysis of determinants related to LOS is provided in Table 2.

Table 2. Correlation of risk factors of length of hospital stay

Variable	*r*	*p*-value
Age	-0.018	0.932
Sex	-	0.327
Comorbidities	0.006	0.978
Dialysis vintage	-0.013	0.948
SpO2 on the admission	0.054	0.792
RR on the admission	-0.484	0.012
Laboratory		
Hemoglobin	-0.024	0.908
Leukocyte	0.097	0.638
Platelets	-0.028	0.892
Neutrophil	-0.211	0.300
Lymphocyte	0.167	0.414
NLR	-0.093	0.653
Serum potassium	0.057	0.786
Serum urea	0.122	0.561
Serum creatinine	0.292	0.157
eGFR	0.025	0.905

Risk factors of mortality of COVID-19 in ESRD patients undergoing hemodialysis

The characteristics of patients according to survival status are summarized in Table 3. A total of 6 (23.07%) patients died. The number of deaths in each infection group was as follows: mild (2 deaths, 18.18%), moderate (1 deaths, 16.67%), severe (2 deaths, 25%), and critical infection (1 deaths, 100%). Factors such as dialysis vintage (p=0.041), levels of hemoglobin (p=0.009), leukocytes (p=0.009), platelets (p=0.009), neutrophils (p=0.009), NLR (p=0.009), serum urea (p=0.019), serum creatinine (p=0.008), eGFR (p=0.002), and length of hospitalization (p=0.02) were significantly associated with the mortality rate. The causes of death were mostly uremic encephalopathy, disseminated intravascular coagulation, acute respiratory distress syndrome, and septic shock.

Table 3. Characteristics of the participants stratified by survival status

Characteristic	Survival status			*p*-value
	Non-survivor	Survivor	Total	
	(*n*=6)	(*n*=20)	(*n*=26)	
Age (mean, in years±SD)	54.67±13.88	51.55±13.86	52.27±13.65	0.245
<60 years, *n*(%)	3(50)	15(75)	18(69.23)	
≥60 years, *n*(%)	3(50)	5(25)	8(30.77)	
Sex, male, *n*(%)	3(50)	9(45)	12(46.15)	0.829
Comorbidities, *n*(%)				0.958
0	3(50)	9(45)	12(46.15)	
1	2(33.33)	8(40)	10 (38.46)	
>1	1(16.67)	3(15)	4(15.38)	
Hypertension	2(33.33)	7(35)	9(34.62)	
Type 2 Diabetes mellitus	2(33.33)	2(10)	4(15.38)	
Dialysis vintage (mean, in months±SD)	31.67±10.98	19.3±16.11	22.15±15.80	0.041
≤12 months, *n*(%)	-	7(35)	7(26.92)	
>12 months, *n*(%)	6(100)	13(65)	19(73.08)	
SpO2 on the admission (mean, in %±SD)	92.67±6.62	93.10±8.55	93±8.02	0.475
RR on the admission (mean, in x/min±SD)	28.83±3.25	22.5±4.05	22.81±3.86	0.066

Laboratory, mean±SD				
Hemoglobin (g/dl)	8±1.73	8.11±1.96	8.09±1.87	0.009
Leukocyte (10^3/µL)	6.76±0.97	8.21±3	7.88 ±2.72	0.009
Platelets (10^3/µL)	309.67±107.42	303.35±135.84	304.81±127.82	0.009
Neutrophil (%)	76.68±11.01	71.56±11.22	72.74±11.17	0.009
Lymphocyte (%)	15.97±8.14	18.05±8.65	17.57±8.42	0.115
NLR	6.27±3.73	5.84±4.89	5.94±4.58	0.009
Serum potassium (mmol/L)	5.26±0.84	4.24±0.72	4.47±0.85	0.114
Serum urea (mg/dl)	213.67±115.27	136.15±51.39	154.041±75.98	0.019
Serum creatinine (mg/dl)	10.41±4.78	9.78±3.61	9.92±3.81	0.008
eGFR (mL/min/1.73 m²)	7.70±4.50	9.46±9.84	9.06±8.85	0.002
Hospitalization duration in days (mean,±SD)	16.5±13.32	14.80±4.96	15.19±7.40	0.020

eGFR, estimated glomerulus filtration rate; HHD, hypertensive heart disease; NLR, neutrophil-leukocyte ratio; RR, respiratory rate; SpO2, peripheral oxygen saturation.

Discussion

Patients with CKD undergoing hemodialysis are more susceptible to infections due to various comorbidities, advanced age, and reduced immune function.[9] This is related to accelerated immune aging characterized by reduced CD8+ and CD4+ T cells, as well as B lymphocytes. Hemodialysis can also lead to increased neutrophil apoptosis and the release of myeloperoxidase. Uremic toxins and non-self-antigens from hemodialysis materials contribute to chronic inflammation.[12] Furthermore, regular hospital visits further increase the risk of transmission.[8]

Dialysis patients have vitamin D and erythropoietin deficiencies that exacerbate pro-inflammatory effects while diminishing anti-inflammatory responses.[9] COVID-19 causes hyperinflammation, leading to increased production of cytokines, chemokines, inflammatory monocytes, and macrophages.[12] Angiotensin-converting enzyme 2, the COVID-19 target organ, is expressed in proximal tubule cells. This allows the virus to invade cells and disrupt fluid, acid-base, and electrolyte balance, further damaging the kidneys.[6,13] This contributes to a "cytokine storm" and further renal vascularization impairment.

A retrospective study in Indonesia found that the average age of CKD patients with COVID-19 was between 46 and 55 years.[14] The elderly were reported to have a worse infection and higher incidence of death.[1,15] A study documented that the 28-day mortality rate among dialysis patients aged 75 years or older could reach as high as 31.4%.[3] Several other studies have also indicated that the average age of those who died was older.[16,17] This is attributed to immune system degeneration in the elderly, which is characterized by a reduction in cellular quantity, immune receptors, and B lymphocyte differentiation.[18] This is consistent with our study findings, which showed that age correlated with the severity of COVID-19 but not with the survival status and length of stay.

Male patients are associated with a higher risk of death, possibly due to their role as breadwinners, which often entails greater social activity and, consequently, increased social contact.[6,7,15,19] Moreover, the protective effects of sex hormones and the X chromosome may influence the immune response.[6] Smoking and alcohol consumption, which are more prevalent among men, could also increase susceptibility. A retrospective study in Indonesia found that male patients had an increased risk of COVID-19.[14,20] In contrast, similar to our study's findings, a cohort study found no association between sex,

disease severity, length of stay, and survival status.[17,21]

ESRD patients with comorbidities tend to experience more severe COVID-19 symptoms and have a higher risk of death.[1,3,22,23] Chronic diseases can impair the immune system, making individuals more vulnerable to infections like COVID-19, leading to worse outcomes. The presence of comorbidities increases the likelihood of being admitted to ICU due to severe infection.[18] In Indonesia, hypertension and diabetes mellitus are the most common comorbidities in CKD with COVID-19.[14] Several studies and meta-analyses showed that cardiovascular disease, hypertension, and diabetes were linked to higher mortality rates and greater severity of COVID-19. Another meta-analysis reported that individuals with diabetes mellitus, cardiovascular disease, cancer, and hypertension face a higher risk of death from COVID-10 compared to those without these conditions.[3] Among comorbidities, diabetes mellitus with complications and severe liver disease were identified as the highest risk factors for hospitalization. Other conditions, such as dementia and coronary artery disease, were associated with higher mortality.[24] Patients with hemoglobin disorders are reported to have the longest hospital stay, followed by those with severe obesity and diabetes. Those with multiple comorbidities tend to have longer stays in the ICU and hospital admission compared with those with just one comorbidity.[25] In this study, the majority of the participants had unknown comorbidities. However, despite the presence of comorbidities, there was no statistically significant association between these comorbidities and the severity, mortality, or length of hospital stay due to COVID-19 infection.

Increased dialysis vintage is associated with impaired cardiovascular functional capacity. A cross-sectional study showed that individuals with dialysis vintage >12 months developed a lower oxygen uptake at peak exercise compared to those with dialysis vintage ≤12 months.[26] Moreover, higher dialysis vintage was also associated with a higher prevalence of unpleasant symptoms, lower hemoglobin levels, iron stores, and dialysis adequacy levels.[11] It was also identified as an independent predictor of a poor serological response.[27] In this study, we found that higher dialysis vintage was associated with a higher rate of mortality.

Severe respiratory impairment is indicated by decreased SpO2 and increased RR.[28] An observational study found that more patients with CKD required oxygen support than those without CKD (55.9% vs 31.8%). Moreover, in patients undergoing routine hemodialysis with COVID-19, a SpO2 level below 95% was linked to ICU admission and had a mortality rate 16.6 times higher than those with higher oxygen saturation levels.[15,19,21] These studies align with our results, which showed that SpO2 was statistically related to the severity of COVID-19. Additionally, the RR was statistically associated with both COVID-19 severity and LOS.

Patients with CKD typically have lower hemoglobin levels compared to individuals with normal eGFR due to reduced kidney function.[22] Moreover, COVID-19 can lead to hemolysis, which further decreases hemoglobin levels.[29] A multicenter study found that CKD patients with COVID-19 had a higher incidence of anemia compared to those without CKD.[30,31] A cross-sectional study in Indonesia found that patients who survived COVID-19 had higher levels of hemoglobin, platelets, and albumin.[20] We also found that hemoglobin levels were statistically related to survival status.

COVID-19 patients often exhibit elevated levels of leukocytes, neutrophils, and NLR, while their lymphocyte counts are typically decreased.[21] Moreover, uremia negatively impacts lymphocyte production and impairs neutrophil functions.[24] In routine hemodialysis patients with COVID-19, lower lymphocyte counts, higher levels of pro-inflammatory cytokines, and activated monocytes have been observed. Lymphopenia may result from a decrease in CD4+ T, CD8+ T, and B lymphocytes.[12] In the non-survivor group, patients exhibited lower lymphocyte counts alongside higher leukocyte counts and NLR, suggesting a correlation

between these immune markers and poor outcomes.[15,17,32] A cross-sectional study in Bali found that 87.2% of hemodialysis patients with COVID-19 had elevated NLR levels, which were associated with higher D-Dimer values.[4] A study in Malang also reported higher neutrophil counts and NLR in ESRD patients. An NLR value of 1 or more was associated with a 1.3 times higher mortality rate compared to an NLR value below 1.[33] These findings align with our study, which also found a statistical association between neutrophils, lymphocytes, and NLR levels with the severity of COVID-19. Moreover, leukocytes, neutrophils, and NLR levels were associated with the survival status in this population.

Thrombocytopenia is often associated with COVID-19 infection, with younger patients generally exhibiting higher platelet counts.[21] The "cytokine storm" in COVID-19 can lead to hypercoagulability, which contributes to thrombocytopenia.[29] Damage to lung tissue caused by COVID-19 triggers platelet activation and thrombus formation, leading to increased platelet consumption. A significant association between platelet counts and survival status was also found in this study.

Hyperkalemia is associated with unfavorable outcomes in ESRD patients undergoing hemodialysis with COVID-19, especially when there are delays in receiving dialysis sessions.[28] However, consistent with our findings, several studies have indicated no significant relationship between potassium levels and the severity, LOS, or mortality of COVID-19.[1,28]

Some studies, including in Indonesia, found that non-survivors of COVID-19 tend to have elevated levels of urea and creatine.[20,21,34] In this study, serum urea and creatinine levels were statistically linked to survival status. Moreover, estimated GFR at admission was linked to 28-day mortality in ESRD patients undergoing hemodialysis and COVID-19.[2] A study found that individuals with an eGFR between 30-50mL/min/1.73 m^2 had an increasing 60-day mortality risk prior to admission.[24] Another study reported that non-survivors had lower eGFR values compared to survivors. In our study, eGFR was found to be related to disease mortality.

The prognosis for COVID-19 in ESRD patients undergoing hemodialysis is worse than in the general population. Around 64.4% of these patients require hospitalization due to the severity of the disease.[6,28] CKD patients, especially those with ESRD, are at a 2-3 times greater risk of severe COVID-19.[3,10,24] Several factors, such as critical infection, advanced age, elevated ferritin levels, high aspartate aminotransferase levels, and low platelet count, are related to an increased risk of death.[29] However, our study did not find a significant correlation between disease severity and mortality.

In our study, LOS in the hospital was linked to disease mortality. A study reported that hemodialysis patients with COVID-19 had an average hospitalization of 18.5 days and a mortality rate of 44.9%.[35] Another study reported an average hospital stay of 19.2±12 days, with a mortality rate of 15%.[15] Dialysis patients face a higher risk of hospitalization and mortality compared to individuals not on dialysis. They often present with atypical symptoms, experience rapid changes in mental status, and are more likely to be admitted to the ICU at an earlier stage of the disease.[32] Approximately 17.6% of hemodialysis patients with COVID-19 required intensive care, with contributing factors including advanced age, nosocomial pneumonia, gastrointestinal bleeding, arrhythmia, and SpO2 levels below 95% at admission.[35] However, it was reported that patients receiving maintenance hemodialysis had a 15-day longer survival rate than those receiving emergency hemodialysis.[4]

The mortality rate for COVID-19 in ESRD patients undergoing hemodialysis is 24%, which is higher compared to individuals without CKD.[6,28,30] A retrospective study in Indonesia showed a mortality rate of 23.6% among this

population.[20] CKD patients on dialysis face a 1.41-fold higher risk of 28-day mortality, while those who are not on dialysis have 1.25-fold increased risks compared to individuals without CKD. The primary causes of death in these patients were respiratory failure, kidney failure, and septic shock.[32] In our study, several factors, such as dialysis vintage, levels of hemoglobin, leukocytes, platelet counts, neutrophils, NLR, serum urea, serum creatinine, eGFR, and length of hospitalization, were significantly associated with the mortality rate.

SARS-CoV-2 variants significantly influence the transmission, severity, and mortality of COVID-19. In Indonesia, some variants of concern have been identified. Alpha variant (B.1.1.7) is associated with a higher transmission rate, an increased secondary attack rate, more frequent hospitalization, and reduced neutralizing activity in monoclonal antibody-based therapies with a similar risk of reinfection. Beta variant (B.1.351) also leads to higher transmission and hospitalization rates, along with diminished neutralizing activity.[36] Delta variant (B.1.617.2) is linked to even higher transmission rates, ICU admission, and mortality, characterized by higher viral load for longer periods, and a shorter latent period. The Omicron variant (B.1.1.529) has the highest transmission rate but is associated with higher survival and reinfection rates. Its clinical symptoms tend to be milder compared to other variants.[37] In this study, genome sequencing of COVID-19 was not performed due to limited resources.

This study emphasizes that patients with ESRD undergoing hemodialysis need special care and attention when dealing with COVID-19, as they are at higher risk for severe outcomes. Screening for COVID-19-related signs and symptoms is essential for early diagnosis of the infection, allowing for timely intervention. These patients should be closely monitored to minimize the risk of morbidity and mortality.

Conclusion

Several risk factors influence clinical outcomes in ESRD patients undergoing hemodialysis with COVID-19. Age, oxygen saturation, respiratory rate upon admission, lymphocyte and neutrophil levels, and neutrophil-to-lymphocyte ratio were significantly associated with COVID-19 severity. Length of stay was statistically influenced by respiratory rate upon admission. The mortality rate was correlated with dialysis vintage, hemoglobin, leukocytes, platelets, neutrophils, neutrophil-to-lymphocyte ratio, serum urea, serum creatinine, eGFR levels, and length of stay.

Limitations of the Study

This study has several limitations. First, there was no information on how COVID-19 progressed over time, making it impossible to track the natural history of the disease. Second, the data were not adjusted for confounding factors. Additionally, SARS-CoV-2 variants and immunization status were not collected during the hospitalization. Moreover, this study was conducted with a small sample size from a single center. Further investigation with a larger sample size across multicenter is recommended to yield more reliable and comprehensive results.

Declarations

Ethics approval and consent to participate

This study received approval from the Ethics Committee of Ngudi Waluyo General Hospital.

Competing interests

There are no conflicts of interest in writing this article. This article is written neutrally with actual results.

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None.

Author's Contribution

Idea/concept: FHW. Design: AZI. Control/supervision: FHW. Data collection/ processing: AZI, SM. Analysis/interpretation: AZI. Literature review: FHW, AZI. Writing the article: AZI. Critical review: AZI. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

References

1. Cai R, Zhang J, Zhu Y, Liu L, Liu Y, He Q. Mortality in chronic kidney disease patients with COVID-19: a systematic review and meta-analysis. Int Urol Nephrol. 2021;53(8):1623–9. doi:10.1007/s11255-020-02740-3
2. WHO. Number of COVID-19 cases reported to WHO (cumulative total) [Internet]. World Health Organization. 2024. Available from: https://data.who.int/dashboards/covid19/cases?n=o
3. Jdiaa SS, Mansour R, El Alayli A, Gautam A, Thomas P, Mustafa RA. COVID–19 and chronic kidney disease: an updated overview of reviews. J Nephrol. 2022;35(1):69–85. doi:10.1007/s40620-021-01206-8
4. Hyodo T, Hirawa N, Kuragano T, Takemoto Y, Pham B V, Nguyen HM. The status of dialysis patients in Asian countries under COVID-19 disaster as of December 2019–June 2022: Vietnam, Indonesia, and Mongolia. Ren Replace Ther. 2024;10(1):1–12. doi:10.1186/s41100-024-00572-w
5. Perhimpunan Dokter Paru Indonesia (PDPI), Perhimpunan Dokter Spesialis Kardiovaskular Indonesia (PERKI), Perhimpunan Dokter Spesialis Penyakit Dalam Indonesia (PAPDI), Perhimpunan Dokter Anestesiologi dan Terapi Intensif Indonesia (PERDATIN), Ikatan Dokter Anak Indonesia (IDAI). Pedoman tatalaksana COVID-19. 4th ed. Jakarta; 2022.
6. Li P, Guan Y, Zhou S, Wang E, Sun P, Fei G, et al. Mortality and risk factors for COVID-19 in hemodialysis patients: A systematic review and meta-analysis. Sci Prog. 2022;105(3):003685042211108. doi:10.1177/00368504221110858
7. Ahmed N, Khderat AH, Sarsour A, Taher A, Hammoudi A, Hamdan Z, et al. The vulnerability of maintenance dialysis patients with COVID-19: mortality and risk factors from a developing country. Ann Med. 2022;54(1):1511–9. doi:10.1080/07853890.2022.2075914
8. Brogan M, Ross MJ. COVID-19 and Kidney Disease. Annu Rev Med. 2023;74(1):1–13. doi:10.1146/annurev-med-042420-104753
9. Zhang X, Chen Q, Xu G. Clinical manifestations of COVID-19 infection in dialysis patients and protective effect of COVID-19 vaccine. Inflamm Res. 2023;72(5):989–1000. doi:10.1007/s00011-023-01723-1
10. Bhinder OS, Swarnim S, Mantan M, Dabas A, Ahlawat RS. Chronic Kidney Disease and COVID-19: Outcomes of hospitalised adults from a tertiary care centre in North India. Med J Armed Forces India. 2023;79(Suppl 1):S68–74. doi:10.1016/j.mjafi.2021.12.004
11. Zhu L, Li XL, Shi R, Wang DG. Dialysis vintage is associated with a high prevalence and severity of unpleasant symptoms in patients on hemodialysis. Ren Fail. 2023;45(1):2201361. doi:10.1080/0886022x.2023.2201361
12. González-Cuadrado C, Caro-Espada PJ, Chivite-Lacaba M, Utrero-Rico A, Lozano-Yuste C, Gutierrez-Solis E, et al. Hemodialysis-associated immune dysregulation in SARS-CoV-2-infected end-stage renal disease patients. Int J Mol Sci. 2023;24(2):1712. doi:10.3390/ijms24021712
13. Liu YF, Zhang Z, Pan XL, Xing GL, Zhang Y, Liu ZS, et al. The chronic kidney disease and acute kidney injury involvement in COVID-19 pandemic: A systematic review and meta-analysis. PLoS One. 2021;16(1):e0244779. doi:10.1371/journal.pone.0244779
14. Pranandhira RAW, Rahman EY, Khatimah H. Karakteristik pasien

chronic kidney disease yang dilakukan hemodialisis di RSUD Ulin Banjarmasin selama pandemi COVID-19. Homeostasis. 2023;6(1):69–78. doi:10.20527/ht.v6i1.8790

15. Ghonimi TAL, Alkad MM, Abuhelaiqa EA, Othman MM, Elgaali MA, Ibrahim RAM, et al. Mortality and associated risk factors of COVID-19 infection in dialysis patients in Qatar: A nationwide cohort study. PLoS One. 2021;16(7):e0254246. doi:10.1371/journal.pone.0254246
16. Wang F, Ao G, Wang Y, Liu F, Bao M, Gao M, et al. Risk factors for mortality in hemodialysis patients with COVID-19: a systematic review and meta-analysis. Ren Fail. 2021;43(1):1394–407. doi:10.1080/0886022x.2021.1986408
17. Yilmaz G, Timur O. Factors related to mortality in hemodialysis patients with COVID-19. J Ren Inj Prev. 2023;12(4):e32005. doi:10.34172/jrip.2022.32005
18. Haq AD, Nugraha AP, Wibisana IKGA, Anggy F, Damayanti F, Syifa RRDM, et al. Faktor – faktor terkait tingkat keparahan infeksi coronavirus disease 2019 (COVID-19): sebuah kajian literatur. JIMKI. 2021;9(1):48–55. doi:10.53366/jimki.v9i1.338
19. SZE X, Fuah KW, Lim CTS, Alias AA, Fadhlina NZ, Md Shah A, et al. Pos-966 clinical outcome of Covid-19 infection and end stage kidney disease patients in a nephrology specialized ward: are we moving towards better? Kidney Int Rep. 2022;7(2):S421. doi:10.1016/j.ekir.2022.01.1006
20. Nasution MFG. Prevalence and characteristics of regular hemodialysis patients with COVID-19 at USU Hospital in 2020-2021 at the University Hospital of North Sumatra. Maj Kedokt Andalas. 2023;46(2):206–15. doi:10.25077/mka.v46.i2.p206-215.2023
21. Ziuzia-Januszewska L, Januszewski M, Sosnowska-Nowak J, Janiszewski M, Dobrzyński P, Jakimiuk AA, et al. COVID-19 severity and mortality in two pandemic waves in Poland and predictors of poor outcomes of SARS-CoV-2 infection in hospitalized young adults. Viruses. 2022;14(8):1700. doi:10.3390/v14081700
22. Gur E, Levy D, Topaz G, Naser R, Wand O, Kitay-Cohen Y, et al. Disease severity and renal outcomes of patients with chronic kidney disease infected with COVID-19. Clin Exp Nephrol. 2022;26(5):445–52. doi:10.1007/s10157-022-02180-6
23. Pecly IMD, Azevedo RB, Muxfeldt ES, Botelho BG, Albuquerque GG, Diniz PHP. COVID-19 and chronic kidney disease: a comprehensive review. J Bras Nefrol. 2021;43(3):383–99. doi:10.1590/2175-8239-jbn-2020-0203
24. Artborg A, Caldinelli A, Wijkström J, Nowak A, Fored M, Stendahl M, et al. Risk factors for COVID-19 hospitalization and mortality in patients with chronic kidney disease: a nationwide cohort study. Clin Kidney J. 2024;17(1):sfad283. doi:10.1093/ckj/sfad283
25. Al-Otaiby M, Almutairi KM, Vinluan JM, Al Seraihi A, Alonazi WB, Qahtani MH. Demographic characteristics, comorbidities, and length of stay of COVID-19 patients admitted into intensive care units in Saudi Arabia: A nationwide retrospective study. Front Med. 2022;9:893954. doi:10.3389/fmed.2022.893954
26. Arroyo E, Umukoro PE, Burney HN, Li Y, Li X, Lane KA. Initiation of dialysis is associated with impaired cardiovascular functional capacity. J Am Hear Assoc. 2022;11(14):e025656. doi:10.1161/jaha.122.025656
27. Karoui K El, Vriese AS De. COVID-19 in dialysis: clinical impact, immune response, prevention, and treatment. Kidney Int. 2022;101(5):883–94. doi:10.1016/j.kint.2022.01.022
28. Cancarevic I, Nassar M, Daoud A, Ali H, Nso N, Sanchez A, et al. Mortality rate of COVID-19 infection in end stage kidney disease patients on maintenance hemodialysis: A systematic review and meta-analysis. World J Virol. 2022;11(5):352–61. doi:10.5501/wjv.v11.i5.352
29. Turgutalp K, Ozturk S, Arici M, Eren N, Gorgulu N, Islam M, et al. Determinants of mortality in a large group of hemodialysis patients hospitalized for COVID-19. BMC Nephrol. 2021;22(1):29. doi:10.1186/s12882-021-02233-0
30. Ozturk S, Turgutalp K, Arici M, Odabas A, Altiparmak M, Aydin Z, et al. Mortality

analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey. Nephrol Dial Transpl. 2020;35(12):2083–95. doi:10.1093/ndt/gfaa271

31. Selvaskandan H, Hull KL, Adenwalla S, Ahmed S, Cusu MC, Graham-Brown M, et al. Risk factors associated with COVID-19 severity among patients on maintenance haemodialysis: a retrospective multicentre cross-sectional study in the UK. BMJ Open. 2022;12(5):e054869. doi:10.1136/bmjopen-2021-054869
32. Brogan M, Ross MJ. The impact of chronic kidney disease on outcomes of patients with COVID-19 admitted to the Intensive Care Unit. Nephron. 2022;146(1):67–71. doi:10.1159/000519530
33. Gunawan A, Rosita L, Arthamin MZ, Arifin MS, Apramadha N, Normahayu I. Does end stage renal disease increase severity of COVID-19? Udayana J Intern Med. 2023;7(1):7–10. doi:10.36216/jpd.v7i1.197
34. Kang SH, Kim SW, Kim AY, Cho KH, Park JW, Do JY. Association between chronic kidney disease or acute kidney injury and clinical outcomes in COVID-19 patients. J Korean Med Sci. 2020;35(50):e434. doi:10.3346/jkms.2020.35.e434
35. Supayah J, Wong HS, Lee FY, Chidambaram SK, Wong EFS. Pos-965 Characteristics, predictive factors and outcomes of hemodialysis patients with Covid 19 infection in the Intensive Care Unit at a State Covid Referral Centre. Kidney Int Rep. 2022;7(2):S421. doi:10.1016/j.ekir.2022.01.1005
36. Choi JY, Smith DM. SARS-CoV-2 variants of concern. Yonsei Med J. 2021;62(11):961–8. doi:10.3349/ymj.2021.62.11.961
37. Haryati H, Rahmawaty D, Isa M, Assagaf A, Nurrasyidah I, Kusumawardhani E. Clinical characteristic of different SARS-CoV-2 variants in South Kalimantan, Indonesia: A case study. Althea Med J [Internet]. 2023;10(1). Available from: https://journal.fk.unpad.ac.id/index.php/amj/article/view/2810doi:10.15850/amj.v10n1.2810