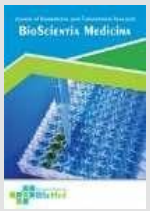
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

The Difference of Survival Rate COVID-19 in Patients with Initiated Hemodialysis and Regularly Hemodialysis

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ARTICLE INFO

Keywords:
COVID-19
Initiated hemodialysis
Regularly hemodialysis
Survival rate

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v7i10.877

A B S T R A C T

Background: Since December 2019, a novel coronavirus called SARSCoV-2 (severe acute respiratory syndrome coronavirus) has caused an international outbreak of respiratory illness described as COVID-19. This study aimed to describe the difference in the survival rate of COVID-19 induced AKI with hemodialysis and COVID-19 in patients with CKD on hemodialysis in Dr. M Djamil General Hospitals. Also, in this review, we provide a comprehensive overview of data on the factors that may be affected by COVID-19 survival rates in patients with COVID-19 induced AKI with hemodialysis and COVID-19 in patients with CKD on hemodialysis. This study was conducted to analyze the survival of COVID-19 with initiated or regular HD patients in Dr. M. Djamil General Hospital, Padang, Indonesia. **Methods:** This study was conducted from January 2021 to July 2021 in Dr. M. Djamil General Hospital, Padang, West Sumatera, Indonesia. Data for this study was collected through medical records of patients admitted for COVID-19 with CKD in hemodialysis and acute renal failure induced by COVID-19 to show the demographics, comorbidities, and survival rates of the patients who underwent hemodialysis. **Results:** Factors associated with survival in COVID-19 with hemodialysis were COVID-19 severity and abnormal potassium serum level (Table 3). Moderate COVID-19 patients tend to survive than severe COVID-19 patients (OR 60; 95% CI 16.034 – 224.525). There was no significant difference in survival between initiated and regular HD (p = 0.829). **Conclusion:** There is no difference in clinical outcome from patients with COVID-19 who initiated hemodialysis or regularly HD to the survival rates.

1. Introduction

The coronavirus disease 2019 (COVID-19) is an emerging infectious disease that was first reported in December 2019 in Wuhan, China.[1] A recently published study that utilized autopsy specimens from 26 patients who died of COVID-19 in China demonstrated that there is evidence of the invasion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into kidney tissue, along with significant acute tubular injury and endothelial damage, as well as glomerular and vascular changes indicative of underlying diabetic or hypertensive disease.[2] Moreover, Chung et al., 2021 found that the incidence of COVID-19 may be higher in people

receiving maintenance dialysis than in those with CKD not requiring kidney replacement therapy or those who are kidney or pancreas/kidney transplant recipients. In Indonesia, CKD is a known comorbidity of severe COVID-19, and AKI is a common complication of severe COVID-19, both creating a challenge for physicians to predict the survival outcomes of COVID-19 patients.[3]

2. Methods

This study was conducted from January 2021 until July 2021 in Dr. M. Djamil General Hospital, Padang, West Sumatera, Indonesia. Data for this study was collected through medical records of patients admitted for COVID-19 with CKD on HD and acute renal failure-induced COVID-19 to show demographics, clinical features, and survival rate of COVID-19 who underwent hemodialysis treatment. COVID-19 was diagnosed with a positive result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) based on reverse transcriptase polymerase chain reaction (RT-PCR) testing of a nasopharyngeal swab. Patients without known kidney disease with initiated HD were included in the initiated HD group. Patients with a known diagnosis of CKD and regular HD were included as regular HD. Peritoneal dialysis patients were not included in the study. Patients who were <18 years of age, pregnant, lacked hospital discharge information or survival data, and hospitalized for reasons other than COVID-19 were excluded from the study.

Moderate COVID-19 patients with clinical signs of pneumonia (fever, cough, shortness of breath) without signs of severe pneumonia and oxygenation status is SpO_2 93 - 95% with air room. Severe COVID-19 with clinical signs of pneumonia (fever, cough, shortness of breath) plus one respiratory rate > 30 breaths/minute, severe respiratory distress with Oxygenation status of SpO_2 < 93% in room air. All collected data is through medical records from the hospital system. Demographic information, symptoms from start to hospital SARS-CoV-2. We divided the severity of patients with hemodialysis initiation caused by AKI and CKD on regular hemodialysis. But in this study, we only report the severity moderate and severe because we are the referral hospital in Sumatra Barat. The follow-up period begins on the day of admission and ends on the day of discharge or death. It was recorded as the length of stay at the hospital. The outcome was the hospital mortality among the initially or regularly HD group.

Continuous variables were expressed using the proper medians and ranges or means and standard deviations. The summaries of categorical variables were the counts and percentages within each category. Categorical variables were subjected to the Chi-square test. The odds ratio (OR) and 95% confidence interval (CI) were utilized as indicators of relative risk. Adjusted odds ratios (AOR) were calculated using multivariate logistic regression to ascertain the impact of important parameters. The survival was evaluated using the Kaplan-Meier curve and Cox regression model. Statistical significance was set at $p < 0.05$. The SPSS 26.0 was utilized to complete all of these statistical calculations (SPSS Inc, Chicago, USA).

3. Results

A total of 90 patients were involved in this study. The demographics and clinical characteristics of the study subjects are shown in Table 1. The proportion of selecting severe cases was 55 (61.1%). The average age was 58 (12.334) years old. 35 (38.9%) patients survived, and 55 (61.1%) were dead after a long stay of 13 (5.440) days.

The level of hemoglobin, leucocyte, thrombocyte, ureum, sodium, pH, pCO_2, SO_2, pT, apTT, and globulin serum was significantly different between pre and post-hemodialysis in initiated HD patients ($p<0.05$). However, no significant difference was observed in terms of creatinine, potassium, chloride, pO_2, HCO_3^-, D-Dimmer, albumin, AST, and ALT serum (Table. 2).

Table 1. Characteristics of samples.

Variables	Mean (SD)	n (%)
Gender		
Male		57 (63.3)
Female		33 (36.7)
Age	58.2 (12.334)	
COVID-19 severity		
Moderate		35 (38.9)
Severe		55 (61.1)
Length of stay	12.58 (5.440)	
Outcome		
Survive		35 (38.9)
Death		55 (61.1)
Anemia		
Yes		50 (55.6)
No		40 (44.4)
Leucocytosis		
Yes		50 (55.6)
No		40 (44.4)
Thrombocytopenia		
Yes		12 (13.3)
No		78 (86.7)
Ureum > 200		
Yes		39 (43.3)
No		51 (56.7)
Creatinine > 3		
Yes		65 (72.7)
No		25 (27.8)
Abnormal sodium		
Yes		47 (52.2)
No		43 (47.8)
Abnormal potassium Yes		27 (30)
No		63 (70)
Hypercoagulable state		
Yes		71 (78.9)
No		19 (21.1)
Metabolic acidosis		
Yes		13 (14.4)
No		77 (85.6)
Liver dysfunction		
Yes		50 (55.6)
No		40 (44.4)
Hypoalbuminemia		
Yes		42 (46.7)
No		48 (53.3)
Hypoxemia		
Yes		37 (41.1)
No		53 (58.9)
Hemodialysis status		
Regularly		45 (50)
Initiation		45 (50)

Table 2. Laboratory parameters initiated hemodialysis patients.

Variable	At initiation	Post Hemodialysis	P value
Hb (g/dl)	11.8 (6.0 – 16.8)	10.3 (4.1 – 14.4)	<0.001
Leucocyte (/mm^3)	13020 (3010 – 30760)	18660 (6800 – 47820)	<0.001
Thrombocyte (/mm^3)	225000 (69000 – 455000)	135000 (42000 – 516000)	0.001
Ureum (mg/dl)	124 (19 – 259)	182 (41 – 419)	0.008
Creatinine (mg/dl)	3.0 (0.6 – 17.3)	3.6 (0.7 – 14.0)	0.824
Na (mmol/l)	135 (122 – 153)	136 (128 – 162)	0.021
K (mmol/l)	4.2 (2.6 – 9.7)	4.4 (2.4 – 8.8)	0.083
Cl (mmol/l)	104 (93 – 118)	104 (90 – 135)	0.222
pH	7.380 (7.013 – 7.560)	7.315 (6.859 – 7.560)	0.020
pCO_2 (mmHg)	30.6 (16.0 – 100.0)	40.6 (24.2 – 128.5)	0.002
pO_2 (mmHg)	64.0 (29.6 – 183.0)	60.9 (20.1 – 308.6)	0.135
HCO_3 (mmol/l)	20.3 (6.9 – 37.6)	20.1 (7.1 – 42.9)	0.874
SO_2 (%)	91.4 (43.0 – 100.0)	89.2 (42.8 – 99.8)	0.032
pT (second)	11.0 (10.0 – 34.0)	13.0 (9.9 – 69.2)	<0.001
apTT (second)	29.4 (19.6 – 105.3)	34.7 (21.3 – 180.0)	<0.001
D-Dimmer (ng/ml)	2612 (200 – 10000)	2426 (111 – 10000)	0.434
Albumin (g/dl)	3.0 (1.6 – 3.9)	2.9 (2.1 – 3.6)	0.549
Globulin (g/dl)	3.3 (1.6 – 4.8)	2.8 (1.7 – 4.2)	0.006
AST (u/l)	42 (11 – 2057)	43 (19 – 2444)	0.527
ALT (u/l)	32 (8 – 1753)	42 (8 – 2537)	0.487

The level of hemoglobin, leucocyte, thrombocyte, creatinine, sodium, chloride, pH, pCO_2, pT, apTT, albumin, and globulin serum were significantly different between pre and post-hemodialysis in regular HD patients ($p<0.05$). However, no significant difference was observed in terms of potassium, pO_2, $HCO3^-$, SO_2, D-Dimmer, AST, and ALT serum (Table. 3).

Table 3. Laboratory parameters of regular hemodialysis patients.

Variable	At initiation	Post hemodialysis	P-value
Hb (g/dl)	8.2 (6.1 – 11.9)	9.5 (4.1 – 14.9)	<0.001
Leucocyte (/mm^3)	10260 (3010 – 87750)	19110 (1650 – 305000)	<0.001
Thrombocyte (/mm^3)	213000 (13000 – 682000)	146000 (11000 – 404000)	0.007
Ureum (mg/dl)	246 (45 – 378)	199 (102 – 419)	0.080
Creatinine (mg/dl)	4.9 (2.3 – 17.3)	4.0 (2.5 – 14.0)	0.013
Na (mmol/l)	136 (118 – 153)	141 (129 – 160)	<0.001
K (mmol/l)	3.7 (3.0 – 6.7)	4.3 (2.6 – 7.3)	0.163
Cl (mmol/l)	104 (90 – 117)	107 (90 – 127)	0.028
pH	7.460 (7.013 – 7.546)	7.317 (6.873 – 7.560)	0.004
pCO_2 (mmHg)	33.3 (20.9 – 70.6)	41.0 (25.6 – 163.8)	0.002
pO_2 (mmHg)	64.0 (30.8 – 192.0)	62.0 (18.7 – 148.0)	0.157
HCO_3 (mmol/l)	25.2 (9.1 – 40.7)	23.8 (8.9 – 42.9)	0.894
SO_2 (%)	90.3 (43.0 – 99.8)	91.0 (18.7 – 99.0)	0.148
PT (second)	11.2 (9.3 – 117.0)	11.9 (10.3 – 39.8)	0.021
APTT (second)	28.4 (11.3 – 78.4)	30.4 (17.5 – 180.0)	0.020
D-Dimmer (ng/ml)	1789 (159 – 10000)	3172 (625 – 10000)	0.616
Albumin (g/dl)	3.0 (1.6 – 3.9)	2.9 (1.8 – 3.4)	0.034
Globulin (g/dl)	3.1 (1.7 – 4.4)	2.3 (1.2 – 4.9)	<0.001
AST (u/l)	48 (11 – 2057)	47 (11 – 3705)	0.302
ALT (u/l)	38 (7 – 1753)	41 (10 – 1136)	0.236

Factors associated with survival in COVID-19 with hemodialysis were COVID-19 severity and abnormal potassium serum level (Table 4). Moderate COVID-19 patients tend to survive than severe COVID-19 patients (OR 60; 95% CI 16.034 – 224.525). There was no significant difference in survival between initiated and regular HD ($p = 0.829$).

Table 4. Factor associated with survival in COVID-19 with hemodialysis patients.

Variable	Survive		Statistical indices		OR (95% CI)
	Yes n (%)	No n (%)	x^2	p	
Gender			0.945	0.331	0.649 (0.270-1.556)
Male	20 (35.1)	37 (64.9)			
Female	15 (45.5)	18 (54.5)			
COVID-19 severity			52.840	<0.001	
Moderate	30 (85.7)	5 (14.3)			60 (16.034-224.525)
Severe	5 (9.1)	50 (90.9)			
Anemia			1.237	0.226	
Yes	22 (44)	28 (56)			1.632 (0.687-3.879)
No	13 (32.5)	27 (67.5)			
Leucocytosis			2.246	0.134	
Yes	16 (32)	34 (68)			0.520 (0.220-1.228)
No	19 (47.5)	21 (52.5)			
Thrombocytopenia			1.124	0.829	
Yes	3 (25)	9 (75)			0.479 (0.120-1.909)
No	32 (41)	46 (59)			
Ureum >200			0.05	0.942	
Yes	15 (38.5)	24 (61.5)			0.969 (0.412-2.279)
No	20 (39.2)	31 (60.8)			
Creatinine >3			3.229	0.072	
Yes	29 (44.6)	36 (55.4)			2.551 (0.902-7.217)
No	6 (24)	19 (76)			
Abnormal sodium			0.556	0.456	
Yes	20 (42.6)	27 (57.4)			1.383 (0.589-3.245)
No	15 (34.9)	28 (65.1)			
Abnormal potassium			4.508	0.034	
Yes	15 (55.6)	12 (44.4)			2.688 (1.065-6.785)
No	20 (31.7)	43 (68.3)			
Metabolic acidosis			0.001	0.973	
Yes	5 (38.5)	8 (61.5)			0.979 (0.293-3.276)
No	30 (39)	47 (61			
Hypercoagulable state			3.661	0.056	
Yes	24 (33.8)	47 (66.2)			0.371 (0.132-1.045)
No	11 (57.9)	8 (42.1)			
Liver dysfunction			1.131	0.287	
Yes	17 (34)	33 (66)			0.630 (0.268-1.480)
No	18 (45)	22 (55)			
Hypoalbuminemia			1.336	0.246	
Yes	19 (45.2)	23 (54.8)			1.652 (0.703-3.881)
No	16 (33.3)	32 (66.7)			
Hypoxemia			3.720	0.054	
Yes	10 (27)	27 (73)			0.415 (0.168-1.024)
No	25 (47.2)	28 (52.8)			
Hemodialysis status			0.047	0.829	
Regularly	18 (40)	27 (60)			1.098 (0.470-2.564)
Initiation	17 (37.8)	28 (62.2)			

Multivariate logistic regression to determine the predictors of survival of COVID-19 with hemodialysis patients revealed that COVID-19 severity was the only predictor. Patients with moderate COVID-19 had higher survivability than severe COVID-19 (OR 73.310; 95% CI 15.002 – 377.549, p < 0.001) (Table 5).

Table 5. Predictors of survival in COVID-19 with hemodialysis patients.

Variable	OR (95% CI)	P-value
Moderate COVID-19	75.310 (15.002-377.549)	<0.001
Anemia	0.540 (0.108-2.706	0.454
Leucocytosis	0.369 (0.080-1.709)	0.202
Creatinine > 3	5.037 (0.764-33.231	0.093
Abnormal potassium	3.713 (0.642-21.480)	0.143
Hypercoagulable state	1.808 (0.235-13.926	0.570
Hypoalbuminemia	1.034 (0.235-13.926)	0.965
Hypoxemia	0.318 (0.069-1.469)	0.142

To identify the factors that affect the survival progression of samples, COVID-19 severity was included in the analysis by using the Kaplan-Meier curve and Cox regression model. The overall time to death of samples was 15.668 (0.896) days. Figure 1 showed that moderate COVID-19 had a longer time to death, with a time to event being 21.756 (1.098) days, than severe COVID-19, with a time to event being 12.899 (0.829) days (p <0.001).

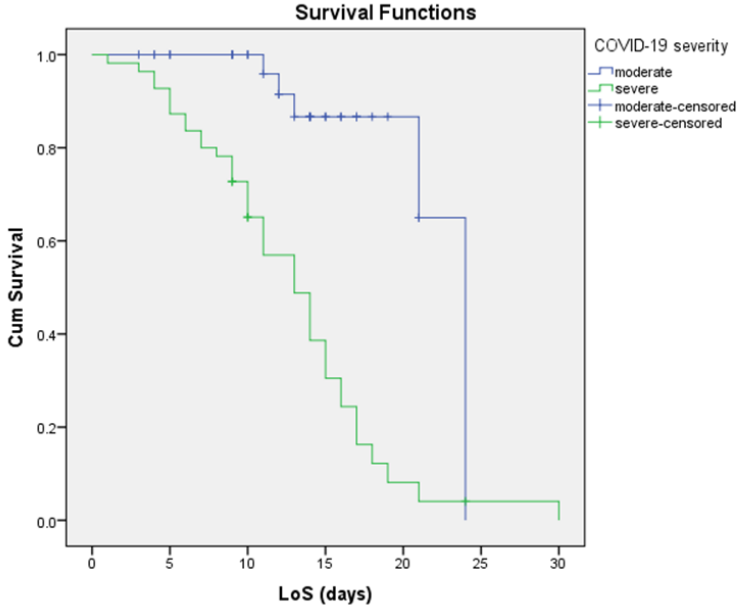

Figure 1. Survival Analysis using the Kaplan-Meier curve and Cox regression model.

4. Discussions

COVID–19 has affected millions of people worldwide. Many chronic medical diseases were reported as risk factors for increased mortality and severity of COVID–19, such as diabetes, hypertension, chronic obstructive pulmonary disease, malignancies, and CKD. Many clinicians suggest that CKD and AKI are well-known risk factors for mortality in COVID-19 patients, but most previous studies on the association between CKD or AKI and clinical outcomes of COVID-19 patients, were performed using limited cohorts, such as studies involving patients from a single center or those utilizing multicenter data from regional hospitals.[4]

Pecly et al, 2021 found that CKD under conservative treatment or maintenance dialysis is associated with more adverse clinical outcomes, more severe disease, higher mortality, and poorer prognosis in patients with COVID-19 infection. Similar to the study from Jdiaa, et al. 2021 also demonstrated an increased risk of mortality and hospitalization in patients with CKD and COVID–19. However the extent to which CKD increases the likelihood of the rate of infection and other poor outcomes is not currently well

understood, and the results are inconsistent among studies. In this study, we found the correlation between CKD and Hemodialysis in COVID-19 severity is the only factor that affects outcome.[5]

Moreover, AKI is a common complication among patients hospitalized for a wide range of diagnoses. The etiology of AKI in COVID-19 cases has not been fully elucidated. The close temporal relationship between AKI and respiratory failure occurrence is somewhat suggestive of ischemic acute tubular necrosis. Arrestier, et al. 2022 concluded that acute kidney injury is a serious feature in critically ill hospitalized patients with COVID-19. It is more common in patients with comorbidities such as hypertension and diabetes, in addition to the development of AKI, which is associated with increased severity of illness, prolonged duration of hospitalization, and increased mortality.[6,7]

Aparicio, et al. 2021 in Mexico also found that in COVID-19 patients, the risk factors for mortality were obesity, the requirement of vasoactive drugs on admission, and AKI. Mortality was more frequent in patients with AKI stages 2–3.[8] In this study, we found the correlation of potassium level and severity as factors that affect the outcome of survival rates of COVID-19-induced AKI. Patients with more severe cases of COVID-19 may be at greater risk for developing AKI. According to the Kidney Disease Improving Global Outcomes definition of AKI. Twenty-four patients (39%) out of 61 patients died, and the most common cause of death was sepsis, cytokine storm with respiratory failure, heart failure, and AKI.[9]

From the laboratory parameters, patients with initial Hemodialysis have elevated leucocytes, Ur, Na, PCO_2, pT, and apTT, as well as a lowering of Hb, thrombocyte, pH, SO_2, and globulin. The characteristic of these parameters is the same with patients with regular HD. We found elevated Hb, Leucocyte, Na, and pCO_2 with decreased thrombocytes, creatine, pH, HCO_3-, albumin, and globulin. However, Wang et al. 2020, found Hemodialysis in COVID-19 lowers Hb, absolute neutrophil count, and higher globulin. It shows that coronavirus may suppress cellular immune function in vivo by depleting immune cells and after hemodialysis they found the lowering of neutrophil that indicator successful pass the exacerbation, that difference in this study. We predict the outcomes of the patient in our hospital is because the severity, and the delayed for hemodialysis of the patients, and the dialysis that we used in our hospital is not compatible to clear the cytokine and inflammatory mediators in patients with COVID-19. Cantaluppi et al. 2019, extracorporeal blood purification is a treatment that is used primarily in patients with renal failure, but it also can remove inflammatory mediators from the plasma of septic patients. COVID-19 also makes cytokine effect the so-called “cytokine storm” that can potentially be removed with hemofiltration that we are not using in this hospital.[10,11] In this study, we found no significant statistic that shows the difference in outcome between AKI induced by COVID-19 with initiated HD and CKD on HD with COVID-19. Only the severity of COVID-19 can influence the outcome of survival rates. The limitation of this study is we are too focused on laboratory parameters and still lack reporting factors that can influence the survival rates.

5. Conclusion

There is no difference in clinical outcome between patients with COVID-19 who initiated hemodialysis or regular HD to the survival rates. The study can’t predict the outcomes of mortality patients COVID-19 by the rule statute of kidney impairment alone because it is a systemic infection. Overall, the results still need to be explored because renal failure can still lead to severe COVID-19, worsening the outcomes.

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