

Increased Mortality with Comorbid Hypertension and Diabetes Mellitus in Hemodialysis Patients with COVID-19

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ABSTRACT

Objective. The purpose of this study was to identify an association between two of the most common comorbidities of hemodialysis patients affected by COVID-19, namely hypertension and diabetes mellitus, and mortality.

Methods. This research was an analytical study with a case control approach. The subjects of this study were patients undergoing hemodialysis with comorbid hypertension and diabetes mellitus who were confirmed positive for COVID-19. They were divided into two groups; the case group consisted of patients who died, and the control group consisted of patients who were living. The total number of respondents was 50. The data were taken from the status medical records of patients in two hospitals in North Jakarta.

Results. There was a significant relationship between comorbid hypertension and diabetes mellitus with mortality in hemodialysis patients with COVID-19 ($p = 0.014$). Hemodialysis patients affected by COVID-19 with comorbid hypertension have a risk of dying that is 0.172 (odds ratio, OR) times greater than hemodialysis patients with comorbid diabetes mellitus.

Conclusions. Patients with confirmed COVID-19 with dialysis-requiring chronic kidney failure and other comorbid diseases have a risk of heightened disease severity and even death. Therefore, comorbidities must be controlled in these patients.

Keywords: COVID-19, comorbid, diabetes mellitus, hemodialysis, hypertension

INTRODUCTION

The Indonesian government reported that as of October 19, 2021, there were 4,236,287 (903 new) confirmed cases of COVID-19 and 143,049 (50 new) deaths and 4,076,541 recovered cases from 510 districts in 34 provinces.¹ Up to June 3, 2020, comorbid diseases in confirmed COVID-19 patients in Indonesia consist of hypertension (52.1%) followed by diabetes mellitus (33.6%), cardiovascular disease (20.9%), COPD (15.1%), respiratory tract disease – others (9%), kidney disease (4.9%), asthma (3.1%), cancer (2.3%), tuberculosis (1.8%), liver disorders and immune diseases (1.2%).²

Elderly patients with confirmed COVID-19 with cardiovascular disease and diabetes mellitus have an increased risk of severe disease, even death.³ There is also an increased risk of COVID-19 infection and its complications among chronic kidney disease patients undergoing hemodialysis. These patients tend to be older, and are often in-and-out of the hospital for treatment. This is why chronic kidney disease patients tend to be more exposed to COVID-19 compared to other populations.⁴



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The results of Yang et al.'s study studied 39 patients with chronic kidney disease were exposed to COVID-19 and found that 15 of them were on dialysis with comorbid hypertension (80%), cardiovascular disease (20%), and diabetes mellitus (13.3%). Yang et al. also a higher mortality rate among patients on dialysis (66.7%) compared with those who were not (50%).⁵ Through ERACODA data (European Renal Association COVID-19 Database), Hilbrands et al. (2020) found that among 768 patients undergoing any dialysis therapy, 96% of hemodialysis patients and 4% of peritoneal dialysis patients were exposed to COVID-19. Dialysis patients with COVID-19 were elderly and were likely to have comorbid hypertension (82%), diabetes mellitus (42%), and cardiovascular disease (30%). Hilbrands et al. added that 25% of dialysis patients who died after 28 days of treatment had comorbid hypertension (77%), diabetes mellitus (48%), and cardiovascular disease (32%).⁶ In contrast, Jung et al. (2020) found the most common comorbid disease was diabetes mellitus (50%) among 14 chronic kidney disease patients with COVID-19 who underwent hemodialysis in South Korea. Among these, 14.3% of patients died, with comorbid hypertension and hypoxemia cited as the primary causes.⁷ Although the main cause of mortality is respiratory failure, cardiac ischemic disease contributes as a concomitant cause of death.⁸

Based on the description above, chronic kidney disease patients with comorbidities undergoing hemodialysis were susceptible to COVID-19 infection, with hypertension being the most common comorbidity, followed by diabetes mellitus. Deaths were caused by respiratory failure and ischemic heart disease.

METHODS

This was a case control study, which is an analytic study that analyzes a causal relationship using reverse logic, namely determining the disease (outcome) first and then identifying the cause (risk factor). In this study, the independent variable was the comorbidity of diabetes mellitus and hypertension, and the dependent variable was the death of confirmed COVID-19 positive hemodialysis patients. The population in this study were hemodialysis patients infected with COVID-19 with comorbid diabetes mellitus or hypertension in two hospitals in the North Jakarta area who were registered from March 2020 to March 2021, and underwent routine hemodialysis for at least the last three months before being diagnosed with COVID-19. The sampling method used in this research was total sampling with a total of 50 respondents.

They were divided into two groups, namely the case group were living patients, and the control group were patients who died. The data were taken from the patients' medical record. The data was then de-identified and converted

into quantitative data in the form of code. In this study, researchers used SPSS Statistics 21 to process the data. This research has passed the ethical test by the Jakarta Veterans National Development University Health Research Ethics Commission with letter number: 335/VI/2021/KEPK.

RESULTS

This study recorded at the respondent's age, duration of hemodialysis, gender, comorbidity, and mortality in hemodialysis patients exposed to COVID-19 (Tables 1-3).

The average age among patients was 49 years old with the youngest being 29 years and the oldest being 71 years. The average length of hemodialysis was 35 months (3 years), with the longest value being 106 months or 8.8 years. Most patients were male and the most common comorbidity were hypertension ($n = 37$) and diabetes mellitus ($n = 13$). The mortality rate of all hemodialysis patients exposed to COVID-19 was 32% or 16 patients.

Table 3 shows that there was a significant relationship between the comorbid disease and mortality in hemodialysis patients with confirmed COVID-19 ($p = 0.014$). An odds ratio of 0.172 means that hemodialysis patients affected by COVID-19 with comorbid hypertension have a risk of dying 0.172 times greater than hemodialysis patients with comorbid diabetes mellitus.

Table 1. Characteristics of Hemodialysis Patients with Confirmed COVID-19 Based on Age and Duration of Hemodialysis ($n = 50$)

Variable	Mean	Standard Deviation	Min - Max	95% CI
Age (years)	49.32	11.58	29 - 71	46.02 - 52.61
Hemodialysis duration (months)	35.32	26.26	3 - 106	27.85 - 42.78

Table 2. Characteristics of Hemodialysis Patients with Confirmed COVID-19 by Sex, Comorbidities, and Mortality ($n = 50$)

Variable	n	%
Sex		
Female	23	46
Male	27	54
Total	50	100
Comorbidity		
Hypertension	37	74
Diabetes Mellitus	13	26
Total	50	100
Mortality		
Alive	34	68
Dead	16	32
Total	50	100

Table 3. Relationship of Hypertension and Diabetes Mellitus with Mortality in Hemodialysis Patients with Confirmed COVID-19 (n = 50)

Variable	Mortality				Total	p-value	OR
	Dead	%	Alive	%			
Comorbidity							
Hypertension	8	16%	29	58%	37 (74%)	0.014*	0.172 (0.044 –0.675)
Diabetes Mellitus	8	16%	5	10%	13 (26%)		
Total	16	32%	34	68%	50 (100%)		

*p-value was significant (<0.05)

DISCUSSION

Hemodialysis patients are highly susceptible to COVID-19 infection because routine hemodialysis activities are carried out in hospitals, entailing substantial interaction with other patients or health workers.

Hypertension and diabetes mellitus were the most common comorbid diseases among patients with dialysis-requiring chronic kidney disease who have contracted COVID-19, as corroborated by other studies. Xiong reports that among their population, 95.4% had at least one comorbidity, with cardiovascular disease (including hypertension) being the most common (68.7%), followed by diabetes (22.9%). Other co-morbidities included chronic obstructive pulmonary disease (3.8%), hepatitis B virus infection (8.4%), hepatitis C virus infection (2.3%), and cancer (1.5%).⁹ Stefan, et al., also reported an 81% incidence of comorbid hypertension, 51% for coronary heart disease, 35% for diabetes mellitus, 8% for COPD, 27% for atrial fibrillation, and 5% for cancer.¹⁰ For Sipahi's study of 23 patients, the incidences are 100% for hypertension, 52.2% for cardiovascular disease, 47.8% for diabetes, and 13% for chronic obstructive pulmonary disease.¹¹

In addition, hypertension is 58% of confirmed COVID-19 patients requiring ICU treatment and is associated with the highest mortality rate (48%).¹²

This COVID-19 disease is caused by infection by the SARS-CoV-2 virus. SARS-CoV-2 is a virus that expresses affinity for ACE2 (angiotensin-converting enzyme 2) receptors. Cardiac cells have a high number of ACE2 receptors on their surface. These cells are more susceptible to viral entry with a high COVID-19 viral load, causing more severe disease. Additionally, this receptor is upregulated in conditions with over-activation of the renin-angiotensin system such as ischemic heart disease, hypertension and congestive heart failure.^{13,12} Once the SARS-CoV-2 binds to the ACE2 receptor, the receptor can no longer facilitate the breakdown of angiotensin II which is a potent vasoconstrictor.¹⁴

Hyperglycemia in diabetes mellitus can cause an upsurge in pro-inflammatory cytokines, especially interleukin IL-1, IL-6 and tumor necrosis factor (TNF)- α .¹⁵ Diabetes mellitus was significantly associated with the risk of death from COVID-19 with a pooled odds ratio of 1.90 (95% CI: 1.37–2.64; $p < 0.01$) with low heterogeneity ($I^2 = 32\%$).¹⁶ Similarly, reports indicate that diabetes mellitus is an independent factor contributing to the severity of complications experienced by COVID-19 patients.^{17,18} This is an indication that diabetic patients infected with COVID-19 have a tendency to experience severe complications and death, just like the previous coronavirus disease.

CONCLUSION

In this COVID-19 pandemic, hemodialysis patients, especially those with comorbid hypertension and diabetes, the two most common comorbidities among patients in Indonesia, are highly susceptible to infection, complications, and death. The highest mortality rates of dialysis-requiring chronic kidney disease patients with COVID-19 were associated with comorbid hypertension, diabetes mellitus, and heart disease.

We recommend to expand the research sample to include other comorbidities. This research is limited by the lack of supporting laboratory data that can further describe the patient's condition.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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