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RESEARCH ARTICLE **OPEN ACCESS**

THE CORRELATION BETWEEN THE NUMBER OF VASCULAR RISK FACTORS AND THE ONSET OF HEMODIALYSIS WITH COGNITIVE IMPAIREMENT IN CHRONIC KIDNEY DISEASE (CKD) PATIENTS

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ABSTRACT

Background: Cognitive impairment is a common disorder in patients with chronic kidney disease (CKD). At least, 50% of CKD patients experience impaired cognitive function caused by ischemia associated with impaired vascular function. In addition, significant changes during the dialysis process such as loss of water and ultrafiltration will disrupt the blood supply to the brain and exacerbate ischemia that underlies the incidence of impaired cognitive function.
Objective: This study aims to analyze the correlation between number of vascular risk factors and onset of dialysis with cognitive impairment in CKD patients
Methods: This research is an analytic observational study. The sample in this study was taken from chronic kidney disease patients undergoing hemodialysis treatment during February-July 2023. The sampling technique used purposive sampling. Patients who met the inclusion and exclusion criteria were interviewed and examined for cognitive function using the MOCA-INA. The statistical analysis used was Spearman's rho (non-parametric) with a 95% confidence level and $p < 0.05$.
Results: The results of correlation test using Spearman Rho showed patients undergoing hemodialysis for more than 5 years had a correlation with impaired cognitive function, P=0.02. Cognitive domains that are most affected sequentially are memory/delayed recall, visuospatial, abstraction, language, attention and naming. While the number of vascular risk factors did not have a correlation with cognitive impairment with P=1.38.
Conclusion: CKD patients undergoing hemodialysis for more than 5 years have a correlation with impaired cognitive function, with the most affected cognitive domains sequentially are memory or delayed recall, visuospatial, abstraction, language, attention and naming. However, the number of vascular risk factors has no correlation with cognitive impairment.

Keywords: chronic kidney disease, cognitive impairement, onset of hemodialysis

Introduction

Chronic renal failure (CKD) is defined as a glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2 for more than 3 months or kidney damage resulting from structural or functional abnormalities other than decreased GFR, which is characterized by albuminuria; accumulation of urinary sediment, electrolyte disturbances, and other abnormalities or impairement detected by histology or imaging. End Stage Renal Disease (ESRD) occurs due to loss of kidney function with a GFR of less than 15 mL/minute requiring hemodialysis or kidney transplantation.[1–3] Cognitive impairment and deficits in one or more brain functions such as memory, executive function, and sensory processing are common in patients with CKD, with a prevalence that depends on the stage of CKD[4]. Murray et al studied 374 patients with chronic renal failure, found that 50% of them had moderate cognitive impairment and 37% had severe cognitive impairment.[5–7] Cognitive impairment begins early in the course of CKD and worsens as kidney function worsens. In the final stage of CKD, which requires hemodialysis, 85% of patients experience memory impairment, impaired executive

function, or language deficits. Because many CKD patients suffer from impaired cognitive function, CKD is considered as a risk factor for mild cognitive impairment and dementia.[4]

Several risk factors that have been studied recently show that age, female gender, educational status, diabetes mellitus, hypertension, and cardiovascular disease are risk factors for impaired cognitive function in CKD patients.[4,8–10] Various mechanisms play a role in the process of impaired cognitive function in patients with CKD, including vascular lesions and impaired cerebral blood flow autoregulation, neuroinflammation, urea neurotoxins and renal neurotrophins. Low GFR is believed to be an independent risk factor for cognitive impairment.[1,5] Impaired cognitive function increases by 15-25% for every 10 ml/min decrease in GFR per 1.73 m2. This shows that patients with CKD have at least two times the risk of impaired cognitive function compared to those who do not suffer from CKD. If the GFR decreases to <30 ml/minute per 1.73 m2, this risk will increase up to four times. This is equivalent to 6-7 years of aging in cognitive function compared to the general population.[3,5,6] In addition, ischemic condition in the subcortical microvascular also underlie the process of cognitive function disorders in CKD patients.[7–9]

Cognitive impairment is also common in chronic kidney disease and in patients on dialysis. Patients undergoing hemodialysis have worse cognitive function than the general population on tests of global cognition, attention and orientation, concepts and reasoning, motor construction and performance, executive function, language, and memory. This phenomenon is due to significant changes in the circulatory system during the dialysis process. One of them is the loss of water, both in the process of ultrafiltration and from migration to the tissues from the blood vessels which causes a decrease in blood volume and an increase in its density and viscosity, as well as an increase in peripheral resistance which causes a disruption in the blood supply of tissues, including the central nervous system.[10,11] Radiological study by Mizumasa et al. also showed that the hypotension experienced during hemodialysis affected the extent of the lesion in the frontal lobe white matter. The extent of these lesions will then increase the risk of frontal lobe atrophy.[12]

Methods

This research has passed the ethical review of the Health Research Ethics Committee at RS Islam Jakarta Cempaka Putih through Letter Number of 009/EC/KEP/05/2023. This research was conducted with a quantitative observational analytic approach. This research was conducted in the hemodialysis unit of the Jakarta Islamic Hospital Cempaka Putih. The sample in this study was taken from chronic kidney disease patients undergoing hemodialysis treatment during February-July 2023. The sampling technique used was purposive sampling, by selecting subjects who met the inclusion and exclusion criteria as follows:

Inclusion Criteria

1) Patients with chronic kidney disease undergoing hemodialysis at the RS Islam Jakarta Cempaka Putih
2) 30-60 years old
3) The patient is fully awake and cooperative
4) Hgb > 8 g/dL
5) Sodium > 125 mEq/L
6) Blood sugar level >60 and <400 mg/dL

Exclusion Criteria

1) Have a history of stroke as evidenced by the results of a head CT scan
2) Have an intracranial lesion as evidenced by imaging studies
3) Having a neurological deficit based on neurological examination

The minimum sample size is calculated using the open-epi application with a design effect for cluster survey (DEEF) power of 0.75. Based on the calculation of the number of samples, with the prevalence of CKD in Indonesia based on the 2018 Riskesdas of 3.8%[17], a minimum sample of 43 is obtainedPatients who met the inclusion and exclusion criteria were interviewed to meet the characteristics of the research data, number of vascular risk factors, and the onset since the first time they underwent hemodialysis. The onset of hemodialysis was divided into two groups with a cut off of 5 years: less than 5 years and more than 5 years. The patient then underwent a MOCA-INA examination with a normal value of ≥ 26 and an abnormal value (impaired cognitive function) of <26.

Statistical analysis using Spearman Rho (95% confidence level and p <0.05) was then performed to see the relationship between the onset of hemodialysis with impaired cognitive function.

Results

During April 2023, there were 168 patients diagnosed with chronic kidney failure and undergoing hemodialysis. Of the 168 patients, we sampled 45 patients who met the inclusion and exclusion criteria with the following basic characteristics (table 1).

Table 1. Characteristics of Sample Data

Variables	Frequency	%
Gender		
Male	25	57%
Female	19	43%
Age		
30-50 years old	20	45%
>50 years old	24	55%
Onset of CKD		
<1 year	10	23%
1-5 years	24	55%
6-10 years	7	16%
Level of education		
Elementary School	1	2%
Junior High School	12	30%
Senior High School	20	43%
Bachelor	12	25%
MOCAINA Examination Results		
Normal	23	50%
MCI	20	45%
Cognitive Impairement	2	5%

Number of Vascular Risk Factors		
≤ 1	25	64%
>1	18	36%

Table 1 shows that most of the kidney disease patients undergoing hemodialysis were aged fifty years and over (51%) and most of them had suffered from chronic kidney failure for around 1-5 years (51%). Most of the patients who underwent hemodialysis and participated in this study had more than 9 years of education (high school and undergraduate), where the length of education was also an influential factor and was considered in the MOCA-INA examination. 51% of patients had normal MOCA-INA examination results, while 44% had Mild Cognitive Impairment, and a small proportion had Cognitive Impairment (4%). Approximately 44% of patients have more than one vascular risk factor. The results of the correlation analysis between the onset hemodialysis and impaired cognitive function using the Spearman Rho test are shown in table 2.

Table 2. Correlation Between the Onset Hemodialysis and Impaired Cognitive Function

Variables		Cognitive Impairement
Onset of hemodialysis	Correlation Coefficient	0.367
	P value	0.07
Number of vascular risk factors	Correlation Coefficient	-0.161
	P value	0.148

Table 2 shows a significant relationship (P=0.02; P<0.05) between the duration of hemodialysis and impaired cognitive function. While the correlation between number of vascular risk factors with cognitive function is not significance with P value of 0.138.

Table 3. Most Influenced Cognitive Domain

Domain	Mean	Normal Value	Percentation
Memory/Delayed Recall	3,4	5	68%
Visuospatial/ Executive Function	3,6	5	72%
Abstract Thinking	1,5	2	77%
Language	2,4	3	78%
Attention	4,9	6	81%
Naming	2,7	3	90%
Orientation	5,4	6	90%

Discussion

Chronic kidney disease is a risk factor for cognitive impairment and have been proofed by many studies. Impaired cognitive function that occurs in CKD patients is caused by many factors, one of them is hemodialysis. Other study by Herman et al[13] using MMSE shows a correlation between onset of dialysis and cognitive impairment after 12 months, while other study by Rustanti using MMSE shows no correlation between onset of dialysis even after 24 months. Our study, using MOCAINA to asses cognitive impairment due to it's sensitivity to asses mild cognitive impairment. We uses a 5-year cut-off to assess the relationship between the onset since the first time undergoing hemodialysis and impaired cognitive function, which was showed that there might be a positive correlation between the onset of hemodialysis over 5 years and cognitive impairment. Means, the longer onset of first time undergoing dialysis, the higher probability to become cognitive impaired.

Cognitive impairment in dialysis patient may be related to the statement of Xie et al[4] which explains that cognitive impairment will worsen as kidney function worsens, since the patient who undergone dialysis has reached end stage renal failure. Stated that the hemodialysis process and the intense catabolic characteristics of CKD may contribute to and even accelerate brain aging so that patients undergoing hemodialysis have poorer cognitive test performance. In their study, showed that the most influential domains of impaired cognitive function were attention and calculation. Meanwhile, our research shows that the most affected cognitive domains respectively are memory/delayed recall, visuospatial, abstraction, language, attention and naming. This process was described by Olcyzk et al[14] who stated that significant changes in the circulatory system during the dialysis process would cause water loss and disruption of the brain's blood supply resulting in a decrease in white matter volume. As a result, patients undergoing hemodialysis have worse cognitive function than the general population on tests of global cognition, attention and orientation, concepts and reasoning, motor construction and performance, executive function, language, and memory.

Although vascular risk factors are closely related to impaired cognitive function in CKD patients. Our results show that more vascular risk factors are not correlated with impaired cognitive function, since almost all of our patients have a similar number of vascular risk factors, and most of these vascular risk factors have been controlled during their hospitalization. Even so, a lot of literature state that vascular risk factors have an important role in the occurrence of impaired cognitive function in CKD patients.[4,14] We realize that our study has it own limitations. Therefore, we suggest other study to assess any risk factors that might cause cognitive dysfunction in patients with chronic kidney disease. We also suggest other study to compare cognitive function before and after undergoing hemodialysis.

We realize that our study has some limitations: (1) A lot of confounding factors cannot be excluded (example: B12 and folic acid deficiency) because our facility cannot provide the laboratory test for those parameters, (2) Further studies are needed to really conclude the correlation between dialysis and cognitive impairment. For example: comparation of cognitive impairment between dialysis and dialysis patient or comparison between two different type dialysis duration (fast/slow).

Conclusion

Our study concludes that CKD patients undergoing hemodialysis for more than 5 years have a positive

correlation with impaired cognitive function, means longer the patient had undergone dialysis will probably have the higher chance to had cognitive impairment. The most affected cognitive domains sequentially are memory or delayed recall, visuospatial, abstraction, language, attention and naming. However, the number of vascular risk factors has no correlation with cognitive impairment. Further study to compare groups with and without dialysis or imaging study should be reconsidered.

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