Jurnal Profesi Medika : Jurnal Kedokteran dan Kesehatan
DOI: https://doi.org/ 10.33533/jpm.v18i1.7830
Vol 18 No 1 (2024) ISSN 0216-3438 (print); ISSN 2621-1122 (online)

ARTICLE

IMPACT OF AGE INITIATION AND DURATION OF HEMODIALYSIS ON IMPAIRED COGNITIVE FUNCTION EXPERIENCED BY CHRONIC KIDNEY DISEASE (CKD) PATIENTS

Rini Nindela[1*], Sigit Nur Prastowo[2], Eka Febri Zulissetiana[3], Selly Marisdina[1], Siti Sarahdeaz Fazzaura Putri[2]

[1]Departemen Ilmu Penyakit Syaraf, Fakultas Kedokteran, Universitas Sriwijaya, Palembang, Indonesia
[2]Fakultas Kedokteran, Universitas Sriwijaya, Palembang, Indonesia
[3]Departemen Fisiologi, Fakultas Kedokteran, Universitas Sriwijaya, Palembang, Indonesia

*Correspondence email : rini_nindela@unsri.ac.id

ABSTRACT

Chronic kidney disease (CKD) increases with age in Indonesia. Cognitive impairment is one of the CKD consequences that can lead to mortality. Furthermore, end-stage CKD treatments like hemodialysis raise the risk of cognitive impairment consequences. About 10%-40% of CKD patients lose cognitive function. This study investigates hemodialysis patients' cognitive impairment risk factors. We conducted this study at Mohammad Hoesin Hospital Palembang in October-November 2022. Patients were given the Montreal Cognitive Assessment-Indonesian version (MoCA-Ina) to assess global and domain-specific cognitive function, including visuospatial/executive, naming, attention, language, abstraction, delayed recall, and orientation. The data were tested with Chi-square or Fisher exact. In CKD patients, age, education, and hemodialysis initiation age affect global cognitive function. Cognitive domains investigation showed that age, sex, and age at hemodialysis initiation affected executive/visuospatial function and attentional function, respectively. Several demographic and hemodialysis variables are linked to cognitive impairment in patients. These at-risk populations need education and cognitive screening to prevent and identify cognitive deterioration.

Keywords: Chronic kidney disease (CKD); Cognitive function; Hemodialysis

АБСТРАКТ

Хроническая болезнь почек (ХБП) увеличивается с возрастом в Индонезии. Когнитивные нарушения - одно из последствий ХПЗ, которое может привести к смертности. Кроме того, лечение ХПН в конечной стадии, например гемодиализ, повышает риск развития последствий когнитивных нарушений. Около 10-40 % пациентов с ХПН теряют когнитивные функции. В данном исследовании изучаются факторы риска развития когнитивных нарушений у пациентов, находящихся на гемодиализе. Мы провели это исследование в больнице Mohammad Hoesin Hospital Palembang в октябре-ноябре 2022 года. Пациентам был предложен Монреальский когнитивный опросник индонезийской версии (MoCA-Ina) для оценки глобальных и специфических когнитивных функций, включая визуально-пространственные/исполнительные, называние, внимание, язык, абстрагирование, отсроченное вспоминание и ориентацию. Данные проверялись с помощью критерия Хи-квадрат или точного критерия Фишера. У пациентов с ЦП возраст, образование и возраст начала гемодиализа влияют на глобальные когнитивные функции. Исследование когнитивных областей показало, что возраст, пол и возраст начала гемодиализа влияют на исполнительную/визуально-пространственную функцию и функцию внимания, соответственно. Несколько демографических и гемодиализных переменных связаны с когнитивными нарушениями у пациентов. Эти группы риска нуждаются в просвещении и когнитивном скрининге для профилактики и выявления когнитивных нарушений.

Ключевые слова: Хроническая болезнь почек (ХБП); Когнитивная функция; Гемодиализ

Submitted: 30 April 2024 ; Received in revised form: 13 May 2024 ; Accepted: 11 June 2024 Available online: 15 June 2024
Published regularly: June 2024

INTRODUCTION

The definition of chronic kidney disease (*CKD*) according to *Kidney Disease: Improving Global Outcomes* (KDIGO) 2012 is an abnormality in the structure of kidney function that lasts more than 3 months with various implications for health.[1] In CKD patients there is kidney damage or a continuous decrease in *the glomerular filtration rate* (GFR) or glomerular filtration rate (GFR) below 60 mL/minute/1.73 m^2.[2] The prevalence of CKD ranges from 10% to 14% of the world's general population[3] and most are in CKD stages 3–5.[4] The incidence of CKD varies greatly between countries. In England, the prevalence of *End Stage Kidney Disease* (ESKD) is 962 per million population.[5] In Indonesia, the results of Riskesdas 2013 showed that 0.2% of the population aged ≥15 years were diagnosed with chronic kidney failure and the prevalence increased with age, where the number of patients aged 35–44 years increased significantly compared to the number of patients aged 25–34 years.[6] Thus, CKD is still a global health problem today.

CKD patients are at risk of experiencing various complications and even death, especially those in the final stages. Several complications that can occur in advanced and end-stage CKD patients include anemia, renal osteodystrophy, hyperkalemia, protein malnutrition, metabolic acidosis, and a decline in cognitive function.[3] Therefore, end-stage CKD patients must immediately receive kidney replacement therapy including kidney transplantation, peritoneal dialysis, and hemodialysis. Hemodialysis is a therapy that is often given to CKD patients.[7] In hemodialysis, there is a process of passive diffusion of dissolved particles and water through the blood into the dialysate fluid compartment through a semipermeable membrane in the dialysis machine. Next, the dialysis machine will pump the blood through the filter and return the blood to the body.[8]

Decreased cognitive function is a complication that often occurs in CKD patients with an incidence rate of around 10–40%.[3,7] Cognitive function is the ability of the nervous system to process sensory data which is then converted, processed, stored, and used in connections between neurons to enable a person to identify and understand sensory input.[9] Factors that contribute to impaired cognitive function in CKD patients according to several studies include high cardiovascular risk factors, anemia, neuropathological changes in the brain, and side effects of hemodialysis.[10] Several studies on CKD patients show impaired cognitive function in patients undergoing hemodialysis. As many as 70% of the 336 respondents undergoing hemodialysis therapy experienced cognitive impairment as reported in Murray's research.[11] Likewise, in the research of Aliruddin *et al.* as many as 90% of patients undergoing hemodialysis suffer from impaired cognitive function.[12]

Several studies have also tried to examine various aspects of hemodialysis that influence cognitive function disorders in CKD patients. In Alirudin's research, as many as 66% of CKD patients who experienced impaired cognitive function had undergone hemodialysis for more than 2 years.[12] Herman *et al*. also reported a relationship between the duration of hemodialysis in CKD patients and impaired cognitive function.[10] In contrast, research conducted by Wahyuni *et al.* showed that there was no relationship between the duration of hemodialysis and cognitive function.[13] The differences in these results encouraged the authors to further examine the factors that influence impaired cognitive function in CKD patients undergoing hemodialysis considering that decreased cognitive function in CKD patients has an impact on reducing the patient's quality of life and increasing the risk of death.[14]

MATERIAL AND METHOD

The subjects of this research were all CKD patients who routinely underwent hemodialysis at the Hemodialysis Unit of RSUP Dr. Mohammad Hoesin Palembang from 1 October 2022 to 30 November 2022. The minimum sample size in this study was 60

 DOI: https://doi.org/ 10.33533/jpm.v18i1.7830 Vol 18 No 1 (2024)

subjects based on the Lemeshow formula. The inclusion criteria in this study were :

1. Patients diagnosed with CKD and undergoing hemodialysis therapy;
2. being able to read and write; and
3. being willing to be a research subject.

This study excluded hemodialysis patients in an unstable condition. This study used a complete sampling strategy. The variables investigated in this study are age, gender, education level, comorbidities, length of hemodialysis, and age at initiation of hemodialysis therapy. These data were gathered through interviews. Cognitive function was measured using the Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina). All variables were then evaluated univariately and bivariately with the Chi-square or Fisher Exact test, as appropriate for each test. Data is processed with Statistical Product & Service Solution version 21.

RESULT

The subjects of this research were 65 patients with almost the same ratio of men and women [33 (50.8%) and 32 (49.2%) patients, respectively). The oldest subject was 79 years old and the youngest was 25 years old with a median age of 48 years. It was found that 24 (36.9%) subjects had completed high school education, followed by 18 (27.7%) college graduates, 15 (23.1%) elementary school graduates, and 8 (12.3%) junior high school graduates.

Table 1. Demographic and Clinical Characteristics of Research Subjects

Subject's characteristics	Cognitive Impairment n (%)	Normal Cognition n (%)	Total (%)	p-value
Age				
<40 years old	3 (4,6%)	14 (21,5%)	17 (26,2%)	
40–50 years old	17 (26,2%)	4 (6,2%)	21 (32,3%)	**0.000***
>50 years old	25 (38,5%)	2 (3,1%)	27 (41,5%)	
Gender				
Male	19 (29,2%)	14 (21,5%)	33 (50,8%)	0,059**
Female	26 (40,0%)	6 (9,2%)	32 (49,2%)	
Level of education				
Elementary school graduates	13 (20,0%)	2 (3,1%)	15 (23,1%)	
Junior high school graduates	8 (12,3%)	0 (0,0%)	8 (12,3%)	**0,032***
Senior high school graduates	13 (20,0%)	11 (16,9%)	24 (36,9%)	
University graduates	11 (16,9%)	7 (10,8%)	18 (27,7%)	
Comorbidities* **				
Hypertension				
• Yes	34 (52,3%)	18 (27,7%)	52 (80,0%)	0,314**
• No	11 (16,9%)	2 (3,1%)	13 (20%)	
Diabetes mellitus				
• Yes	13 (20,0%)	4 (6,2%)	17 (26,1%)	0,551**
• No	32 (49,2%)	16 (24,6%)	48 (73,8%)	
Cardiovascular disease				
• Yes	1 (1,5%)	1 (1,5%)	2 (3,0%)	0,673*
• No	44 (67,7%)	19 (29,2%)	63 (96,9%)	
Systemic Lupus Erythematosus				
• Yes	1 (1,5%)	1 (1,5%)	2 (3,0%)	0,524**
• No	44 (67,7%)	19 (29,2%)	63 (96,9%)	
Duration of hemodialysis				
<12 months	20 (30,8%)	11 (16,9%)	31 (47,7%)	
12-24 months	5 (7,7%)	3 (4,6%)	8 (12,3%)	0,544*
>24 months	20 (30,8%)	6 (9,2%)	26 (40,0%)	
Frequency of hemodialysis				
Once a week	1 (1,5%)	0 (0,0%)	1 (1,5%)	1,000**
Twice a week	44 (67,7%)	20 (30,8%)	64 (98,5%)	
Age at hemodialysis initation				
<40 years old	9 (13,8%)	14 (21,5%)	23 (35,4%)	
40–50 years old	13 (20,0%)	5 (7,7%)	18 (27,7%)	**0,000***
>50 years old	23 (35,4%)	1 (1,5%)	24 (36,9%)	

**chi-square test, **fisher-exact test*

***some patients had >1 comorbidities

The majority (45 subjects or 69.2%) of hemodialysis patients in this study experienced a decline in cognitive function. Subjects who experienced disorders were more likely to be found in the group of patients aged >50 years (25 out of 45 subjects or 56%)

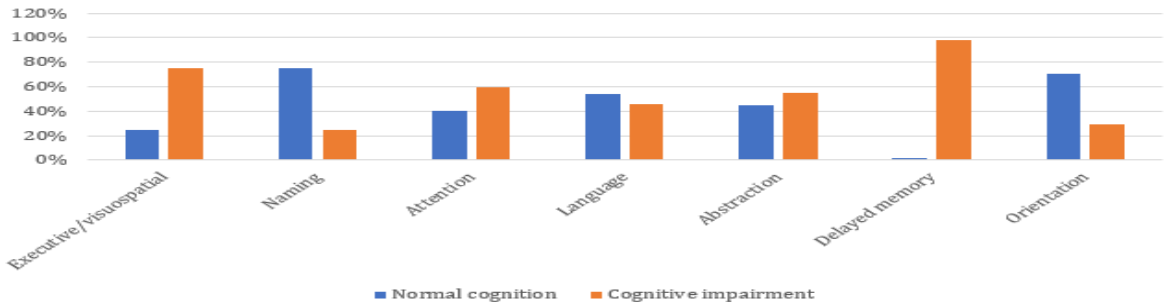
 DOI : https://doi.org/ 10.33533/jpm.v18i1.7830 Vol 18 No 1 (2024)

and females (26 out of 45 subjects or 58%). Based on education level, the number of subjects who completed elementary school and completed high school were the ones who most often experienced cognitive impairment (13 out of 45 subjects or 29% each). The most common comorbidity suffered by research subjects is hypertension (80,0%).

47.7% of the study's participants had only received hemodialysis for less than a year. Most individuals (98.5%) had hemodialysis twice a week. 36.9% of research participants began therapy when they were older than 50 years old. Table 1 displays the subjects' cognitive functions and the distribution of their features. The incidence of reduced cognitive function was observed to be correlated ($p<0.05$) with age, education level, and age at initiating hemodialysis in this study.

Cognitive function distribution of research individuals is shown in graph 1. Most individuals (98.5%) had delayed memory issues. 75.4% of respondents had executive/visuospatial impairment, the second most. Attendance and abstraction were also hampered in 60% and 55.4% of participants. Many subjects retained normal naming, language, and orienting functions. The age and length of hemodialysis had a significant effect on attention function with p-values of 0.005 and 0.020, respectively. Age, gender, and age at hemodialysis initiation also affected executive/visuospatial function (p-values of 0.000, 0.026, and 0.000).

Graph 1. Subject's distribution based on impaired cognitive domain



DISCUSSION

Chronic kidney disease and cognitive impairment are linked through several mechanisms. A number of conditions in CKD include anemia, increased levels of pro-inflammatory cytokines, oxidative stress, and changes in lipid and homocysteine metabolism. CKD patients also generally have vascular risk factors which are also risk factors for developing dementia, including Alzheimer's dementia.[15]

Half of the hemodialysis patients who had cognitive impairment in this study were >50 years old. This data is in line with Yaffe's study in Zammit which found that as many as 40.8% of advanced CKD patients aged over 55 years experienced cognitive impairment.[16] Another study by Murray also stated that cognitive impairment was experienced by around 70% of patients undergoing hemodialysis aged 55 years and over.[11] In line with these two studies, Alirudin also found that 72.2% of hemodialysis patients who were over 50 years old experienced cognitive impairment.[12]

This study's statistical tests demonstrate that age is strongly associated with a reduction in global cognitive performance and in attention and executive/visuospatial function. Age has been shown to affect cognition. Research on brain aging suggests that brain damage begins at 50 and worsens after 70.[11] Elderly people with CKD and declining kidney function are associated with decreased cognitive function when compared with the general elderly population.[16]

A slightly higher percentage of female research subjects had cognitive impairment. Further research of this study indicated that gender impaired executive/visuospatial function. Laksmidewi found that 69.6% of female CKD patients had a MoCA-Ina score below 26 (cognitive impairment).[17] Studies in

 DOI : https://doi.org/ 10.33533/jpm.v18i1.7830 Vol 18 No 1 (2024)

the general population also report that *mild cognitive impairment* /MCI and dementia are more common in women, with proportions of 50.4% and 57% respectively.[18] A thorough review found no difference in cognitive function loss between men and women with normal aging. Endocrine shifts like menopause may cause cognitive impairment in women. Iwata says women with CKD are more prone to pro-inflammatory cytokines, oxidative stress, and cardiovascular disease, which can cause cognitive impairment.[18]

In this study, the subjects most likely to experience cognitive impairment came from elementary school and high school graduates, followed by college graduates and finally junior high school graduates. In line with these results, Alirudin reported that almost half (47.2%) of hemodialysis patients and experiencing decreased cognitive function had a high school education. Statistically, this study found that the level of education was related to the cognitive function of hemodialysis patients. This result is also in line with previous studies which found that education level was related to general cognitive function. Education is a protective factor for cognitive function through a reserve *mechanism*. Education can trigger the development of brain and cognitive reserves through the addition of dendritic branching.[19] Studies show that highly educated people have a much larger brain capacity with more synapses compared to less educated people.[20]

Most of the research subjects who experienced cognitive impairment had comorbidities such as hypertension and diabetes mellitus. This data follows the results of Laksmidewi's research where 65.2% of CKD patients with cognitive impairment also had hypertension.[17] These two diseases have indeed been proven to be risk factors for decreased cognitive function not only in the CKD patient population but also in the general population. In people with hypertension, changes in the walls of blood vessels will then cause hypoperfusion, ischemia, and cerebral hypoxia. This condition will ultimately cause the accumulation of *amyloid precursor protein* /APP and amyloid-beta and also trigger the expression of presenilin which is the pathophysiological basis for dementia.[19] In people with diabetes mellitus, insulin levels affect the metabolism of amyloid-beta and tau proteins which form neuritic plaques and *neurofibrillary tangles*, which is also the basic mechanism of dementia.[19] Cognitive decline is also likely to happen in patients with cardiovascular disease because both have similar risk factors as well as direct consequences of heart disease on the brain, defined as the heart-brain axis.[20] In addition, cognitive impairment also falls within the clinical spectrum of neuropsychiatric-systemic lupus erythematosus (NP-SLE). Many factors have been associated with cognitive dysfunction in NP-SLE including depression status, longer disease duration, regular glucocorticoid use, the presence of anti-neuronal and anti-phospholipid antibodies, structural brain alterations, traditional cardiovascular risk factors, physical inactivity, and vitamin D deficiency.[21]

The study found that cognitive impairment was most prevalent in groups that had received hemodialysis for <12 months and >24 months. Similarly, Lestari found that individuals undergoing hemodialysis for >24 months and <12 months had 39.2% and 37.1% impaired cognitive performance, respectively.[22] Alirudin also reported that cognitive impairment mostly came from the group of CKD patients who had undergone hemodialysis for >24 months, as much as 66.7%.[12] On the other hand, most patients with normal cognitive function came from the group who had only undergone hemodialysis for <12 months. Similar results were also reported by Zahroh where hemodialysis patients with normal cognitive function mainly came from the group with hemodialysis duration <12 months (80%).[23]

Hemodialysis length did not affect global cognitive function, although it did lower attentional function statistically. The effects of chronic hemodialysis on cognitive deterioration are unknown. Murray and Joseph observed that hemodialysis decreased brain function.[11,24] There is a fluid shift and

 DOI : https://doi.org/ 10.33533/jpm.v18i1.7830 Vol 18 No 1 (2024)

acute intravascular volume loss during the hemodialysis process which then causes edema and decreased perfusion due to decreased pressure and cerebral blood flow velocity. Cerebral edema and hypoperfusion cause damage to subcortical structures which ultimately causes impaired cognitive function.[11] However, changes in brain structure may have occurred early in the course of CKD because imaging-based studies show that there is degeneration and lesions in brain white matter in as many as 70% of CKD patients who have not required hemodialysis.

This study links executive/visuospatial cognitive impairment to hemodialysis initiation age. Patients who started hemodialysis after 50 had a higher rate of cognitive loss (35.4% versus 1.5% with normal cognition). In contrast, individuals who began hemodialysis at age <40 had a lower proportion of normal cognition (13.8%) compared to cognitive decline (21.5%). This result may be due to the initial condition of cognitive function in patients who started hemodialysis at a younger age being better than patients who started it at an older age. Apart from that, generally, the decline in cognitive function begins at 50 years, where the process of brain degeneration begins and continues with increasing age.[22]

This study found that hemodialysis patients had the greatest delayed memory, followed by executive/visuospatial and attention. In hemodialysis patients, delayed memory (27.5%), executive/visuospatial (22%), and attention (19.3%) reduced, according to Alirudin.[12] Grams stated that cognitive dysfunction in CKD patients ranges in severity from *mild cognitive impairment* (MCI) to severe (dementia) and involves a decline in several cognitive domains, such as memory, attention, language, visuospatial skills, and executive function.[25] In another Bugnicourt study, CKD patients had higher cognitive impairment in all domains.26 This study did not explore other factors that may affect cognitive performance, such as inheritance, head trauma, physical exercise, and others. Patient unwillingness to participate due to weariness from long hemodialysis treatments, unstable hemodynamic conditions, and lengthy MoCA-Ina tests (10–15 minutes) caused uneven sample features. This study is limited by several restrictions.

CONCLUSION

A large majority of hemodialysis patients exhibited cognitive impairment in this study. Age, gender, length of therapy, and age at hemodialysis initiation affect cognitive performance in CKD patients. Regular cognitive function tests for hemodialysis patients help identify impairment early and start treatment faster. Patients should also learn how to maintain cognitive function through physical activity appropriate to their needs, social involvement, and mental-strengthening activities like chess and crossword puzzles.

ACKNOWLEDGMENT

The researchers are thankful to contributing parties because this research may not be completed without their assistance. First and foremost, the researchers praise God the Almighty, Allah SWT.

DECLARATIONS

Conflict of interest. The authors declare no conflict of interest.

Additional information. No additional information is available for this paper.

REFERENCES

1. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco ALM, De Jong PE, et al. Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International Supplements [Internet]. 2013 Jan 1 [cited 2022 Jun 30];3(1):1–150. Available from: https://jhu.pure.elsevier.com/en/publications/kidney-disease-improving-global-outcomes-kdigo-ckd-work-group-kdi-4
2. Shafi T, Coresh J. Chronic Kidney Disease: Definition, Epidemiology, Cost, and

Outcomes. In: Chronic Kidney Disease, Dialysis, and Transplantation: A Companion to Brenner and Rector's The Kidney [Internet]. Fourth Eddie. Elsevier Inc.; 2018. p. 2-22.e3. Available from: https://doi.org/10.1016/B978-0-323-52978-5.00001-X
3. Vaidya SR, Aeddula NR. Chronic Renal Failure. The Scientific Basis of Urology, Second Edition [Internet]. 2021 Oct 29 [cited 2022 Jul 1];257–64. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535404/
4. Mitch WE. Chronic Kidney Disease. In: Goldman-Cecil Medicine [Internet]. Twentieth. Elsevier Inc.; 2022. p. 799-804.e2. Available from: https://doi.org/10.1016/B978-0-323-53266-2.00121-1
5. Noble R, Taal MW. Epidemiology and causes of chronic kidney disease. Medicine (United Kingdom) [Internet]. 2019;47(9):562–6. Available from: https://doi.org/10.1016/j.mpmed.2019.06.010
6. Indonesian Ministry of Health. Information on the situation of chronic kidney disease. Chronic Kidney Disease Situation. 2017;1–10.
7. Ikzier TA, Burgner AM, Concepcion BP. Chronic Kidney Disease - ClinicalKey. In: Wing EJ, Schiffman FJ, editors. Cecil Essentials of Medicine Tenth Edition [Internet]. Tenth. Elsevier Health Sciences; 2021 [cited 2022 Jul 6]. p. 334–41. Available from: https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323722711000306?scrollTo=%23hl000451
8. Webster AC, Nagler EV, Morton RL, Masson P. Chronic Kidney Disease. Lancet (London, England) [Internet]. 2017 Mar 25 [cited 2022 Jul 28];389(10075):1238–52. Available from: https://pubmed.ncbi.nlm.nih.gov/27887750/
9. Pramadita AP, Wati AP, Muhartomo H, Kognitif F, Romberg T. Relationship between cognitive function and postural balance disorders in the elderly. Diponegoro Medical Journal (Diponegoro Medical Journal). 2019;8(2):626–41. Available from: https://ejournal3.undip.ac.id/index.php/medico/article/download/23782/21618
10. Herman I. The relationship between duration of hemodialysis and cognitive function in patients with chronic kidney disease undergoing hemodialysis at RSUD Abdul Moeloek Bandar Lampung. Thesis, Faculty of Medicine, University of Lampung, Bandar Lampung. 2016;7:47–53. Available from: http://digilib.unila.ac.id/21745/4/SKRIPSI%20FULL%20tanpa%20bab%20pembahasan.pdf
11. Murray AM. Cognitive Impairment in the Aging Dialysis and Chronic Kidney Disease Populations: an Occult Burden. Advances in chronic kidney disease [Internet]. 2008 Apr [cited 2022 Jul 2];15(2):123. Available from: https://pubmed.ncbi.nlm.nih.gov/18334236/
12. Alirudin C, Hendellyn A, Sumada IK, Yuliani D, Sunaka IW. Profile of Cognitive Function Disorders in Hemodialysis Patients at Wangaya Regional General Hospital. 2020;3:400.
13. Wahyuni A, Kartika IR, Asrul IF. Correlation of Hemodialysis Time with Cognitive Function. Real in Nursing Journal. 2019;2(1):1. Available from: https://ojs.fdk.ac.id/index.php/Nursing/article/view/328
14. Oktaviana N, Verawati J, Putra D, Helpin H, Onangego O. Relationship between Hemodialysis Frequency and Stress Level in Chronic Kidney Failure Patients Undergoing Hemodialysis at Royal Prima Hospital Medan 2019. PANNMED Scientific Journal (Pharmacist, Analyst, Nurse, Nutrition, Midwifery, Environment, Dentist). 2019;13(3):182–9. DOI: https://doi.org/10.36911/pannmed.v13i3.588
15. Zammit AR, Katz MJ, Bitzer M, Lipton RB. Cognitive impairment and dementia in older adults with chronic kidney disease: A review. Alzheimer's disease and associated disorders [Internet]. 2016 [cited 2022 Nov 21];30(4):357. Available from: https://ncbi.nlm.nih.gov/pmc/articles/PMC5123843/
16. Yaffe K, Ackerson L, Tamura MK, Le Blanc P, Kusek JW, Sehgal AR, et al. Chronic kidney disease and cognitive function in older

adults: Findings from the chronic renal insufficiency cohort cognitive study. Journal of the American Geriatrics Society. 2010;58(2). Available from: https://pubmed.ncbi.nlm.nih.gov/20374407/

17. Laksmidewi AAAP, Dewi CIG, Kandarini Y. Correlation between cognitive function impairment and chronic kidney disease with a low glomerular filtration rate at Sanglah Hospital Denpasar. Open Access Macedonian Journal of Medical Sciences. 2020;8. Available from: https://oamjms.eu/index.php/mjms/article/view/4691
18. Iwata A, Iwatsubo T, Ihara R, Suzuki K, Matsuyama Y, Tomita N, et al. Effects of sex, educational background, and chronic kidney disease grading on longitudinal cognitive and functional decline in patients in the Japanese Alzheimer's Disease Neuroimaging Initiative study. Alzheimer's & Dementia: Translational Research & Clinical Interventions. 2018 Jan 1;4:765–74 Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6324255/#:~:text=In%20patients%20with%20MCI%2C%20sex,of%20amyloid%20pathology%20in%20women.
19. Silva MVF, Loures CDMG, Alves LCV, De Souza LC, Borges KBG, Carvalho MDG. Alzheimer's disease: Risk factors and potentially protective measures. Journal of Biomedical Science. 2019; 26(33): 1–11. DOI: https://doi.org10.1186/s12929-019-0524-y
20. Xu C, Tao X, Ma X, Zhao R, Cao Z. Cognitive Dysfunction after Heart Disease: A Manifestation of the Heart-Brain Axis. Oxid Med Cell Longev. 2021 Aug 18;2021:4899688. DOI: https://doi.org/10.1155/2021/4899688
21. Seet D, Allameen NA, Tay SH, Cho J, Mak A. Cognitive Dysfunction in Systemic Lupus Erythematosus: Immunopathology, Clinical Manifestations, Neuroimaging and Management. Rheumatol Ther. 2021 Jun;8(2):651-679. doi: 10.1007/s40744-021-00312-0. Epub 2021 May 15. DOI: https://doi.org/10.1007/s40744-021-00312-0
22. Lestari W, Annisa R, Buston E, Nursing J, Bengkulu Ministry of Health Jalan Indragiri Number P, Harapan P. Factors Associated with Cognitive Function of Chronic Kidney Failure Patients in the Hemodialysis Room. MNJ (Mahakam Nursing Journal) [Internet]. 2021 May 24 [cited 2022 Jul 2];2(9):386–96. Available from: http://ejournalperawat.poltekkes-kaltim.ac.id/index.php/nursing/article/view/186
23. Zahroh R, W bovi amalia. Lama Terapi Hemodialisis Dengan Fungsi Kognitif Pasien Penyakit Ginjal Kronis. Program Studi Ilmu Keperawatan dan Ners Fakultas Ilmu Kesehatan Universitas Gresik. 2019;10:11–9. DOI: https://doi.org/10.55129/jnerscommunity.v10i1.825
24. Joseph SJ, Bhandari SS, Dutta S. Cognitive Impairment and its Correlates in Chronic Kidney Disease Patients Undergoing Haemodialysis. Journal of evolution of medical and dental sciences [Internet]. 2019 Sep 9 [cited 2022 Aug 15];8(36):2818. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6800659/
25. Grams ME, McDonald SP. Epidemiology of Chronic Kidney Disease and Dialysis [Internet]. Sixth Edit. Vol. 01, Comprehensive Clinical Nephrology. Elsevier Inc.; 2019. 903-912.e1 p. Available from: https://doi.org/10.1016/B978-0-323-47909-7.00077-9
26. Bugnicourt JM, Godefroy O, Chillon JM, Choukroun G, Massy ZA. Cognitive disorders and dementia in CKD: The neglected kidney-brain axis. Vol. 24, Journal of the American Society of Nephrology. 2013. DOI: 10.1681/ASN.2012050536