International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Quality of Life, Cognitive Functions and Residual Kidney Function in Chronic Kidney Disease

Tamer Mohamed Goda, Sherif Ahmed Ragae *, Ibrahim Mohamed Salem, Mabrouk Ibrahim Ismail, Mohamed Abdelaziz Gendia

Internal Medicine Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

***Corresponding Author:** Sherif Ahmed Ragae

Email: drshiko7@gmail.com,

Abstract:

Residual kidney function (RKF) may provide many benefits to patients on permanent renal replacement therapy that are reflected in better control of biochemical parameters. In hemodialysis patients, quality of life (QOL) and cognitive function are often impaired.

Keywords: Quality of life, cognitive functions, residual kidney function, CKD.

Introduction:

Health-related quality of life (HRQOL) is a multidimensional index to calculate wellbeing. It is related to the physical, emotional, mental, and social functioning of people or cases. Dialysis patients have compromised HRQOL when compared with the general population and have decrements comparable to cases with other chronic diseases including cancer and heart failure **(1).**

HRQOL might be influenced by a lot of factors, such as clinical manifestations, adverse effects of medications, nutritional condition, hospitalization, and certain biochemical factors involving Kt/V, calcium-phosphorus (Ca × P) product, parathyroid hormone (PTH) levels, anemia, and serum albumin level. HRQOL might enhance over time as cases grow accustomed to the HD therapy, however, parameters including recurrent hospital admission, adverse effects and related medications, as well as RKF loss might induce HRQOL worsening **(1).**

Considering the worldwide growing prevalence of CKD and increasing importance of HRQoL in chronic diseases, improving our knowledge about HRQoL and its predictors in CKD patients is important. Assessment of HRQoL early in disease course will help to identify high risk patients in whom modifying these factors may help them lead an active and healthy life **(2)**. Inadequate HD badly affects quality of life and improving adequacy refines many components of quality of life **(3)**.

Health-related quality of life (QOL) assumes an increasing importance as a marker of treatment quality in many chronic diseases **(4)**. Its evaluation allows the quantification of the diseases consequences according to the patient's subjective perception and enables adjustment of medical decisions to their physical, emotional and social needs **(2)**. It also improves the adhesion to the therapeutic plan, the quality of the health care provided and the patient survival **(5)**.

The quality of life of CKD patients is a frequently overlooked yet critical consideration when evaluating their overall medical care **(6)**. The importance of measuring HRQOL has been underscored by studies indicating an association between various HRQOL measures and mortality and hospitalization rates in dialysis patients **(7)**. These studies have raised the question of whether addressing HRQOL problems in dialysis patients and patients with CKD can improve medical outcomes. Given the well documented, high mortality and hospitalization rate in

CKD patients, understanding the HRQOL issues of CKD patients would seem to be an important area to explore **(8)**.

Cognitive impairment among chronic kidney diseases

Cognitive impairment (CI) is described as recently appearing deficits in two or more regions of cognitive functions, such as memory deficits, executive functioning, attention or speed of data processing, or languag. Cognitive impairment and dementia are more prevalent in ESKD patients who receive hemodialysis compared with age matching the general population. Patients with CI are at higher risk of hospitalization, mortality, and a poorer quality of life. Furthermore, CI in patients with ESKD may reduce their abilities to adhere to complex medical or dietary regimens and to fully participate in medical decisions **(9).**

Cognition impairment (CI) in patients with CKD has become a major concern. It is well established that CI may positively correlate with the degree of decline in residual renal function, even in early CKD. A decrease in multiple cognitive functions, including processing, memory, and executive function, has been shown in CKD patients. Moreover, magnetic resonance imaging techniques showed that hippocampus atrophy, cortical atrophy, and white matter lesions are frequent in CKD patients, and are likely to lead to cognitive disturbance **(10).**

CI was independently associated with mortality in elderly hemodialysis (HD) patients. However, it should be noted that the prevalence of CI in patients with CKD is variable. It has been reported that a 23–28% prevalence of CI in stage 3–4 CKD patients, nearly 87% in patients with HD, and 50% in patients with peritoneal dialysis (PD) . The prevalence of CI in CKD patients varies widely around the world, reaching 58% in the USA, 49.9% in Asia, 30.3% in Europe, and 35% in Africa. However, quantitative studies on the current epidemiology of CI in patients with CKD are few **(11).**

The pathophysiology of cognitive decline in CKD patients is complex. Various clinical factors could contribute to CI in CKD, including traditional risk factors (e.g., older age, education level, diabetes, and dyslipidemia) and other specific factors (e.g., dialysis modality, anemia, vitamin D). It is imperative that the risk factors and prompt treatment of CI in the CKD population should be emphasized **(11).**

Thus far, studies regarding the prevalence of CI in CKD patients are limited and with inconsistent conclusions. Our study aimed to estimate the overall prevalence of CI in CKD patients not on dialysis, and receiving dialysis or kidney transplantation. Furthermore, the specific risk factors for CI were also explored **(11).**

Cognitive impairment and hemodialysis

Significant changes in the circulatory system during hemodialysis cause impairment of tissue blood supply, including the central nervous system. The reason for this is the loss of water, both in the ultrafiltration process and from migration to tissues from blood vessels. This leads to a decrease in blood volume, an increase in its density and viscosity, and a resistance increase **(12).**

Cognitive impairment and systemic cardiovascular risk factors: Many studies have found that Pulse Wave Velocity (PWV) and Ankle-Brachial Index (ABI) are important factors associated with cognitive impairment in dialysis patients. These parameters have been validated as tools for assessing arterial health as measured by arterial stiffness. The first scientific study found that having a high PWV or a low ABI is associated with poor cognitive function in HD patients **(13).**

Other studies support the link between PWV and cognitive impairment in hemodialysis patients. Orthostatic pressure reduction is another cardiovascular factor linked to cognitive performance. According to the findings of the study, an excessive reduction in orthostatic pressure in HD patients causes memory impairment **(14).**

Another factor to consider is left ventricular function. CKD increases the risk of developing left ventricular hypertrophy at a young age. In the early stages of HD, 70% - 80% of patients have left ventricular hypertrophy. Furthermore, chronic hemodialysis reduces cerebral blood flow, which may exacerbate the effects of low left ventricular function (LVEF). According to research, a mildly reduced LVEF correlates with cognitive impairment **(14)**.

Cognitive impairment and nervous system: It has been proposed that hemodialysis causes brain damage associated with recurrent hemodynamic changes, specifically a decrease in cerebral intradialytic perfusion. Dialysis factors such as ultrafiltration volume or intradialytic hypotension could be one cause of this phenomenon **(15)**.

Cognitive impairment and markers related to the inflammatory process and cell damage: Inflammatory cytokines play an important role in the pathogenesis of hemodialysis-related side effects associated with brain diseases and it has been found that IL-6 and TNF- levels increased significantly in HD patients **(16)**.

The next marker under consideration is fibroblast growth factor-23 (FGF-23), whose level is elevated in HD patients and is linked to left ventricular hypertrophy and increased mortality. In another study, elevated levels of FGF23 were linked to memory deterioration as measured by composite memory scores. This suggests that in HD patients, this marker may contribute to CI **(12)**.

Quality of life, cognitive functions and residual kidney function IN CKD PATHIENTs

RKF is the remaining kidney function in cases receiving renal replacement therapy (RRT) for renal failure. Higher RKF is associated with better outcomes such as improved survival by maintaining fluid and metabolic homeostasis, mitigating mineral abnormalities, optimizing uremic toxin clearance, and sustaining higher production of endogenous vitamin D and erythropoietin. RKF is recognized as an important factor influencing morbidity, mortality, and quality of life in chronic dialysis patients**(17)**.

- **Quality of Life and Residual Renal Function**

A publication by Mitema and Jaar has investigated a variety of validated tools which are readily available to assess HD patients QOL. They have recommended using each tool in an individualized manner to address specific patient needs and recommended including the preservation of the RRF. These authors also reported from patients with self-reported urine output at baseline of at least 250 ml/day were reporting better social functioning, vitality, cognitive functioning and quality of life over a year **(18).**

Poulsen et al. surveyed 82 HD patients using the Kidney Disease Quality of Life Short Form Version 1.3 (KDQOL-SFTM) at the start of treatment, at six and 12 months. The study concluded that health related quality of life (HRQOL) is largely impacted in patients receiving HD treatment. Although the patient can become used to the HD and this could lead to an improved HRQOL. However, other debilitating factors such as multiple side effects of HD, frequent hospitalisation, diabetes and the decline in RRF after 12 months can eventually lead to a further decrease in HRQOL **(19).**

Decreasing glomerular filtration rate (GFR) was measured by collecting urine for 24 hours at baseline, 6 and 12 months in this study. A decreasing GFR in patients with CKD also lowers HRQOL, was concluded by these authors. Other studies have found a marked correlation between decreased urine volume and a decreased quality of life. The lower HRQOL is associated with increased restrictions in diet, fluids, and the duration of dialysis sessions as the RRF declines **(20).**

Preservation of residual renal function seems to be important for HRQOL. In newly started HD patients, HRQOL showed little change after 12 months. HRQOL was negatively affected by comorbidity, especially diabetes, hospital admissions, female gender, and age **(19)**.

It has been found that HD patients with maintained RKF had better QOL and cognitive function. The duration of HD and the age of the patients were found to be related to RKF and PCS in this study. RKF was associated with the cognitive performance of hemodialysis patients **(21)**.

Clinical trials have shown residual kidney function (RKF) to be an important and favorable prognostic indicator of reduced morbidity, mortality, and higher quality of life in both PD and HD **(22)**.

Kong, Davies and Mount conducted a literature review to explore the relationship between RRF and the outcomes for patients on HD treatment. The study found that the preservation of RRF, even at very low levels, contributes to increased quality of life and patient survival **(23).**

- **Cognitive function and residual kidney function**

Cognitive impairment is a highly relevant clinical factor for disease progression in HD patients, possibly also affecting daily life activities, thereby impeding adherence to therapeutic regimes and compromising the quality of life. It was evident that cognitive impairment is more prevalent in individuals with CKD than in the general population **(21)**.

As regards cognitive function domains according to RKF status, visuospatial, executive, attention, language, delayed recall and total score of MoCA were significantly higher in the RKF group compared to the non-RKF group. Also, there was a statistically significant positive correla- tion between the measured RKF and visuospatial, executive, attention, delayed recall and the total MoCA score. Moreover, the measured RKF were proved to be one of the predictors of the total MoCA score by multivariate linear regression analysis **(21)**.

Chronic kidney disease–associated pruritus (itching) (CKD-aP) affects up to 70% of dialysis patients, and ~40% report being at least moderately bothered by pruritus. The presence of CKD-aP in dialysis patients is associated with poor sleep, depression, interference with people's work, overall lower quality of life and increased risk of death. Higher residual eGFR and lower serum phosphate level, but not the dialysis dose, were related with lower burden of CKD-aP in dialysis patients **(24)**.

Lower levels of kidney function are associated with an increased prevalence of cognitive impairment **(25)**. The prevalence of impairment appears to increase early in the course of kidney disease; therefore, screening for impairment should be considered in all adults with CKD **(26)**.

References:

1. Chen, S. S., Al Mawed, S. & Unruh, M. 2016. Health-Related Quality of Life in End-Stage Renal Disease Patients: How Often Should We Ask and What Do We Do with the Answer? Blood Purif, 41, 218-24.
2. Aggarwal, H., Jain, D., Pawar, S. & Yadav, R. 2016. Health-related quality of life in different stages of chronic kidney disease. *QJM: An International Journal of Medicine,* 109, 711-6.
3. Hasan, L. M., Shaheen, D. A., El Kannishy, G. A., Sayed-Ahmed, N. A. & Abd El Wahab, A. M. 2021. Is health-related quality of life associated with adequacy of hemodialysis in chronic kidney disease patients? *BMC Nephrol,* 22, 1-12.
4. Ojelabi, A. O., Graham, Y., Haighton, C. & Ling, J. 2017. A systematic review of the application of wilson and cleary health-related quality of life model in chronic diseases. *Health Qual Life Outcomes,* 15, 1-15.
5. Varghese, S. A. 2018. Social support: An important factor for treatment adherence and health-related quality of life of patients with end-stage renal disease. *J Soc Serv Res,* 44, 1-18.

6. Shirazian, S ,.Aina, O., Park, Y., Chowdhury, N., Leger, K., Hou, L., et al. 2017a. Chronic kidney disease-associated pruritus: Impact on quality of life and current management challenges. *Int J Nephrol Renov Dis,* 7, 11-26.
7. Burlacu, A., Artene, B., Nistor, I., Buju, S., Jugrin, D., Mavrichi, I., et al. 2019. Religiosity, spirituality and quality of life of dialysis patients: A systematic review. *Int Urol Nephrol,* 51, 839-50.
8. Bakarman, M. A., Felimban, M. K., Atta, M. M. & Butt, N. S .2019 .The effect of an educational program on quality of life in patients undergoing hemodialysis in western saudi arabia. *Saudi Med J,* 40, 66-71.
9. Neumann, D., Mau, W., Wienke, A. & Girndt, M. 2018. Peritoneal dialysis is associated with better cognitive function than hemodialysis over a one-year course. *Kidney Int,* 93, 430-8.
10. Drew, D. A., Weiner, D. E. & Sarnak, M. J. 2019. Cognitive Impairment in CKD: Pathophysiology , Management, and Prevention. *Am J Kidney Dis,* 74, 782-90.
11. Zhang, J., Wu, L., Wang, P., Pan, Y., Dong, X., Jia, L., et al. 2024. Prevalence of cognitive impairment and its predictors among chronic kidney disease patients: A systematic review and meta-analysis. *PLoS One,* 19, e0304762.
12. Giuseppe, P., Fortuna, P., Chiara, G. M., Caterina, L., Ivana, C., Daniela, P., et al. 2024. Cognitive Impairment in Renal Replacement Therapy: Comparison between Methods. *Journal of Clinical Nephrology,* 8, 001-7.
13. Wu, P. H., Lin, Y. T., Wu, P. Y., Huang, J. C., Chen, S. C., Chang, J. M., et al. 2019. A Low Ankle-Brachial Index and High Brachial-Ankle Pulse Wave Velocity Are Associated with Poor Cognitive Function in Patients Undergoing Hemodialysis. *Dis Markers,* 2019, 9421352.
14. Liu, W., Wang, L., Huang, X., Yuan, C., Li, H. & Yang, J. 2019. Orthostatic blood pressure reduction as a possible explanation for memory deficits in dialysis patients. *Hypertens Res,* 42, 1049-56.
15. MacEwen, C., Sutherland, S., Daly, J., Pugh, C. & Tarassenko, L. 2017. Relationship between Hypotension and Cerebral Ischemia during Hemodialysis. *J Am Soc Nephrol,* 28, 2511-20.
16. Polinder-Bos, H. A., García, D. V., Kuipers, J., Elting, J. W. J., Aries, M. J. H., Krijnen, W. P., et al. 2018. Hemodialysis Induces an Acute Decline in Cerebral Blood Flow in Elderly Patients. *J Am Soc Nephrol,* 29, 1317-25.
17. Shafi, T. & Levey, A. S. 2018. Measurement and Estimation of Residual Kidney Function in Patients on Dialysis. *Adv Chronic Kidney Dis,* 25, 93-104.
18. Mitema, D. & Jaar, B. G. 2016. How Can We Improve the Quality of Life of Dialysis Patients? *Semin Dial,* 29, 93-102.
19. Poulsen, C. G ,.Kjaergaard, K. D., Peters, C. D., Jespersen, B. & Jensen, J. D. 2017. Quality of life development during initial hemodialysis therapy and association with loss of residual renal function. *Hemodial Int,* 21, 409-21.
20. Steinwandel, U., Kheirkhah, H. & Davies, H. 2021. Residual Renal Function - How Fast Does the Residual Urine Output Function Decline in the First Year of Haemodialysis? - A Scoping Review. *Front Nephrol,* 1, 808909.
21. Elgendy, A ,.Abdelsalam, A. I., Mansour, M. & Nassar, M. K. 2022. Can residual kidney function affect quality of life and cognitive function in hemodialysis patients? *BMC Nephrol,* 23, 263.

22. Li, T., Wilcox, C. S., Lipkowitz, M. S., Gordon-Cappitelli, J. & Dragoi, S. 2019. Rationale and Strategies for Preserving Residual Kidney Function in Dialysis Patients. *Am J Nephrol,* 50, 411-21.
23. Kong, J., Davies, M. & Mount, P. 2018. The importance of residual kidney function in haemodialysis patients. *Nephrology (Carlton),* 23, 1073-80.
24. Lengton, R., van der Willik, E. M., de Rooij, E. N. M., Meuleman, Y., Le Cessie, S., Michels, W. M., et al. 2023. Effect of residual kidney function and dialysis adequacy on chronic pruritus in dialysis patients. *Nephrol Dial Transplant,* 38, 1508-18.
25. Burns, C. M., Knopman, D. S., Tupper, D. E., Davey, C. S., Slinin, Y. M., Lakshminarayan, K., et al. 2018. Prevalence and risk of severe cognitive impairment in advanced chronic kidney disease. *J Gerontol Series A* 73, 393-9.
26. Kurella Tamura, M., Wadley, V., Yaffe, K., McClure, L. A., Howard, G., Go, R., et al. 2008. Kidney function and cognitive impairment in US adults: The reasons for geographic and racial differences in stroke (REGARDS) study. *Am J Kidney Dis,* 52, 227-34.