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The Association of Serum Albumin Level with Cognition and Daily Function in Patients Undergoing Hemodialysis

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Abstract

Background: Due to the high prevalence of cognitive disorders in end-stage renal disease (ESRD) patients undergoing hemodialysis and its negative effects on the quality of life of dialysis patients, recognizing the factors affecting cognitive disorders in essential. We investigated the relationship of cognitive condition and functional status of elderly patients undergoing hemodialysis with serum albumin levels.

Methods: The present study was performed on 80 patients aged higher than 60 years who suffering regular hemodialysis due to ESRD. The Barthel Index was used to assess basic daily activities. To assessgeneral cognitive function, the Mini–Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) tests were used.

Results: Our study indicated cognitive disorder in 57% of subjects. The mean level of serum albumin level in the groups with and without cognitive disorders was 3.91±1.74 mg/dl and 4.32± 1.83 mg/dl respectively indicating lower albumin level in the groups suffering cognitive abnormality (P<0.001). Our study also showed an adverse association between serum albumin level and functional status as independence to others in daily activities. We showed higher rate of cognitive impairment in those with underlying congestive heart failure (P=0.018) and also in diabetic and hypertensive ones (P=0.002).

Conclusion: In hemodialysis patients, duration of dialysis along with low serum albumin affect patients' cognition and daily function.

Keywords: Serum Albumin Level, Montreal Cognitive Assessment, Mini–Mental State Examination, Hemodialysis

Introduction

Studies have shown that the rate of cognitive impairment in chronic kidney disease (CKD) patients, especially those who suffering end-stage renal disease (ESRD), is much higher than in healthy elderly people (1-3). Although the underlying mechanisms of cognitive impairment in hemodialysis patients are unknown, the researchers found a link between CKD and cognitive impairment, in which uremic toxins accumulate in the body following decreased renal function, causing excessive phosphorylation of Tau Protein from through the path of Silent Information regulator 1 which ultimately leads to a decrease in cognitive function in the patient, especially in the areas of general cognitive ability, abstract reasoning and verbal memory (4,5). The studies have also shown that cerebral ischemia due to hemodynamic and cardiovascular abnormalities

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are another major cause of cognitive impairment in elderly hemodialysis patients (6). Moreover, studies have shown that even in the general population, hypoproteinemia is associated with an increased risk of cognitive impairment and dementia (7).Inflammation is an effective factor in cognitive function that plays an important factor in the development of mild cognitive impairment. Serum albumin itself is a marker of inflammation and it can be thus suggested a close link between reducing serum albumin level and increasing the likelihood of cognitive disorders (8). Hypoalbuminemia is common in hemodialysis patients. An important cause of decreased serum albumin is protein loss during dialysis (9). Alteration of albumin homeostasis in ESRD patients due to inflammatory reactions directly affects the prognosis of patients and especially their functional level (10). It has been found that people with hypoalbuminuria are 15% more likely to develop dementia than normal people (11).

Due to the high prevalence of cognitive disorders in ESRD patients undergoing hemodialysis and the its negative effects on the quality of life of dialysis patients, recognizing the factors affecting cognitive disorders and its timely diagnosis and treatment in dialysis wards is becoming more and more necessary. Thus, the aim of this study was to investigate the relationship of cognitive condition and functional status of elderly patients undergoing hemodialysis with serum albumin levels.

Materials and Methods

The present study was performed on 80 patients aged higher than 60 years who suffering regular hemodialysis due to ESRD at Firousabadi hospital between 2019 and 2020. Patients with debilitating neurological and orthopedic diseases and patients with definitive dementia were excluded from the study. Demographic information including age, gender, body mass index, primary kidney disease, education, history of alcohol and smoking, medications, living situation (single, nursing home, and etc.) as well as serum levels of serum albumin were collected from the hospital recorded files. The duration of dialysis was also collected.

Since there are no specific tools to assess the functional status of hemodialysis patients, the Barthel Index was used to assess basic daily activities such as eating, moving, shaving and personal hygiene, going to the bathroom, bathing, mobility, climbing stairs, dressing, and urine and fecal control status were used to assess patients' functional status. The Barthel Index is scored between 0 (complete dependence) and 100 (complete independence) and the higher the score, the greater the independence in daily activities. In this regard, a score of 60 is the boundary between dependence and minimum independence, between 60 and 84 indicates partial independence, between 85 and 94 indicates moderate independence, and 95 to 100 indicates complete independence. The translation of the Barthel index into Persian had a reliability coefficient of 0.994, repeatability coefficient of 0.989 and credibility coefficient of 0.998.

To assessgeneral cognitive function, the Mini–Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) tests wereused. The MMSE inventory assesses the following domains: attention and focus, executive function (intermittent pursuit), language (verbal psychology and naming), navigation, computing, conceptual thinking, memory (instant reminders and delayed reminders) and visual perception instead of perceptual vision skills. Each correct answer is awarded 1 point. In total, the maximum score is 30 points, a score less than 9 indicates severe cognitive impairment, a score of 10 to 20 indicators of moderate cognitive impairment and more than 21 indicators of mild cognitive impairment and 25 and above is normal.The MoCA also evaluated the following cognitive abilities: Orientation, Short-term

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memory/delayed recall, Executive function/visuospatial ability, Language abilities, Abstraction, Animal naming, Attention and Clock-drawing test. Scores on the MoCA range from zero to 30, with a score of 26 and higher generally considered normal. As indicated by Seyedian et al, F-MMSE has acceptable validity and a cut-off point of22 can reliably differentiate patients with dementia from healthy subjects.Badrkhahan et al also indicated MoCA a sensitive tool for the detection of mild cognitive impairment and dementia among Persian population.

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t test or Mann-Whitney test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using chi-square test. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

Results

A total of 80 patients were interviewed by census method. The mean age of study participants was 67.97±7.12 years. 55% of participants were male and 45% were female. Overall, 47% of the participants had their spouses alive while 53% of them had lost their spouses. Also, 87.5% of the participants were literate and the rest were illiterate and about 93% of them lived in their own homes. The baseline characteristics of study participants are shown in Table 1.

Table 1: Baseline characteristics of study population

Mean age, year	67.97±7.12
Gender	
Male	44 (55.0)
Female	36 (45.0)
Body mass index, kg/m^2	25.97±1.98
Duration od dialysis, year	5.38±4.21
Hours of dialysis, per day	3.48±0.22
Serum hemoglobin level, g/dL	12.35±1.02
Serum hemoglobin level, mg/dL	4.05±0.32
Causes for renal disease	
Diabetes mellitus	44 (55.0)
Hypertension	12 (15.0)
Congestive heart failure	9 (11.3)
Others	15 (18.7)
History of smoking	6 (7.5)
Functional status	
Complete dependence	74 (92.5)
Partial dependence	4 (5.0)
Complete dependence	2 92.5)
Past medical history	
Diabetes mellitus	21 (28.5)
Hypertension	10 (12.5)
Diabetes mellitus+ Hypertension	10 (12.5)

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The mean serum albumin level was found to be 4.05±0.32 mg/dl ranged 2.80 ± 4.60 mg/dl. The mean cognition score according to the MMSE and MOCA inventories was 21.60±1.34 (ranged 21 to 24) and 25.53±2.16 (ranged 19 to 29) respectively indicating cognitive disorder in 57% of subjects (men 28.75% versus women 26.25%, p = 0.371). Regarding functional status, 92.5% were completely independent, 5.0% were partially dependent and 2.5% were functionally dependent to others. There was no difference in men and women in the status of functional status (Figure 1) (p = 0.276).

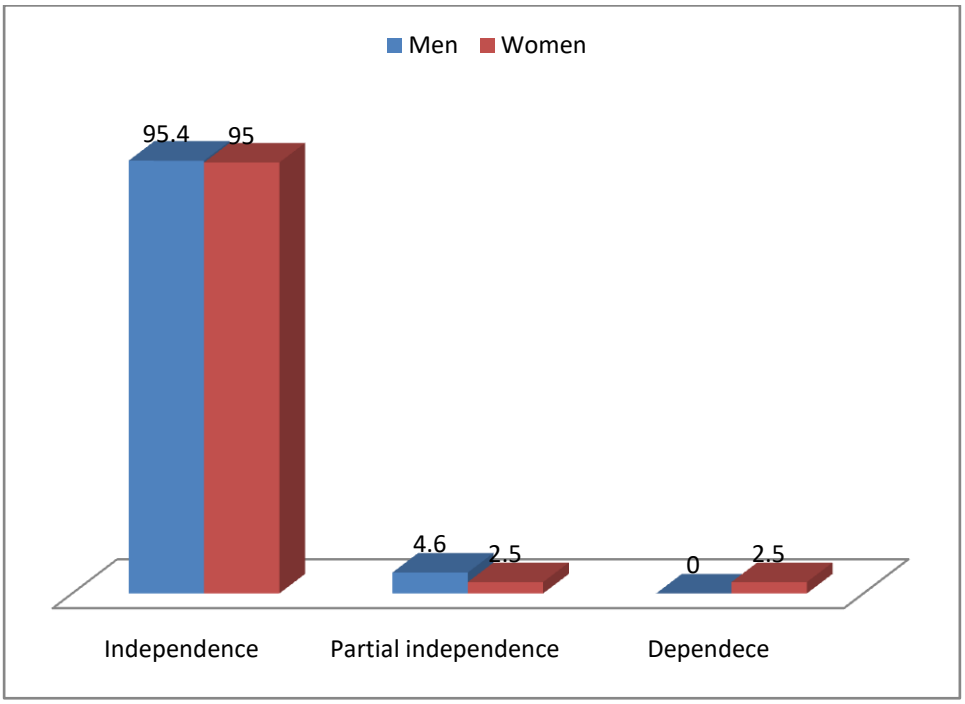

Figure 1: Functional status in men and women undergoing hemodialysis

The mean level of serum albumin level in the groups with and without cognitive disorders was 3.91±1.74 mg/dl and 4.32± 1.83 mg/dl respectively indicating lower albumin level in the groups suffering cognitive abnormality (p<0.001). We revealed also a significant difference in the levels of serum albumin level across the groups with complete and partial independence functionally (p=0.040) as well as between those with partial independence and dependence (p=0.015) indicating a close link between hypoalbuminemia and overall lowering the level of functional status (p=0.009). Although the functional ability of the patients was adversely associated with the duration of dialysis (p=0.014), the function level of patients did not influenced by hours of dialysis (p=0.992). Regarding the relationship between cognitive impairment and underlying comorbidites as the cause of renal failure, we showed higher rate of cognitive impairment in those with underlying congestive heart failure (p=0.018) and also in diabetic and hypertensive ones (p=0.002). The results also showed that the number of patients with cognitive impairment among patients taking insulin was significantly lower than healthy individuals (p=0.039), but among patients who took insulin with other drugs, the number of patients with cognitive disorders was significantly higher (p=0.013). The results of Chi-square test also showed that the relationship between patients' functional level and the cause of ESRD was significant (p<0.001). Also in this study, based on the results of independent t-test, a significant relationship was found

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between age and the incidence of cognitive disorders, so that with increasing age, the probability of developing cognitive disorders significantly increased ($p<0.001$).

Discussion

Cognitive and functional disorders are among the most common symptoms in elderly patients that have been associated with various outcomes. Various studies have shown that functional disorders precede cognitive disorders such as dementia, so early detection of functional disorders is essential to prevent more severe disorders such as dementia (12).As in previous studies (13-16), in this study we hypothesized that patients with CKD were more likely to develop cognitive impairment. In order for these patients to survive and improve their performance, it is essential to improve their cognitive status so that they can recall complex stages of treatment, such as controlling their diet and taking regular medications. If dialysis patients lose their ability to manage and control, they are closer to death (17,21). However, few studies have so far addressed the role of cognitive health in improving the treatment of dialysis patients.

In this study, the prevalence of cognitive disorders in the study population was 45%, which is much higher than the normal population (29%).Recent studies have reported a prevalence of cognitive impairment in ESRD patients undergoing hemodialysis of up to 60%, which is 2.5 times that of the general population (6).In studies conducted so far in line with our study, it has been proven that compared to healthy elderly people, the rate of cognitive impairment in people with CKD, especially ESRD, is much higher. Although the underlying mechanisms of cognitive impairment in hemodialysis patients are unknown, the researchers found a link between CKD and cognitive impairment, in which uremic toxins accumulate in the body following decreased renal function, causing excessive phosphorylation of Tau Protein through the path of Silent Information regulator 1 (18), which ultimately leads to a decrease in cognitive function.

In the present study, the relationship between albumin level and cognitive function of patients was significant.The results of the study of Amirabadi et al. (13) reported that there was no significant difference between albumin level and cognitive function of patients, which is inconsistent with the findings of the present study, which can be attributed to differences in cognitive function level measurement tools in the two studies.Other studies have reported abnormalities in capillaries, the body's smallest arteries, in patients with cognitive impairment that cause dementia in the brain.Similarly, vascular involvement has been seen in all patients with albuminuria, and other studies have shown that vascular involvement and albuminuria go hand in hand to cause cognitive impairment in the elderly on hemodialysis.It has been observed that people with albuminuria are 15% more likely to develop dementia than normal people, which is in line with the results of our study (11).

In the present study, no significant relationship was reported between the duration of dialysis and the incidence of cognitive disorders in patients that the study of Amirabadi et al also confirms our findings (13).The reason for this finding can be attributed to the early diagnosis and treatment of renal failure, which has led to a reduction in brain tissue exposure to uremic toxins and its complications.Therefore, it can be inferred that hemodialysis treatment is not in itself a risk factor for cognitive impairment.However, more studies are needed to draw more accurate conclusions in this regard. The researchers also concluded that during the period of hemodialysis there is no significant relationship with cognitive impairment in these patients (16).

In this study, only a significant association was observed between congestive heart failure and HTN associated with diabetes mellitus in cognitive impairment.The study of Amirabadi et al (13) showed that patients with diabetes mellitus have a significantly increased risk of cognitive

impairment, which is inconsistent with the findings of our study.Another study used the Wechsler test to determine the functional status of hemodialysis patients stated that type 2 diabetes is associated with decreased cognitive function, especially with reduced verbal memory, information processing speed, and executive functions (19), which is inconsistent with the findings of our study, which can be attributed to the difference in functional health measurement tools in the mentioned studies with the present study was mentioned. In addition, the results of this study showed that using insulin reduces the level of cognitive disorders. Studies have shown that disruption of insulin signaling is involved in Alzheimer's disease. Diabetes and Alzheimer's disease are common in increasing oxidative stress, including advanced glycation terminal products (AGEs).Diabetic patients are at a higher risk of developing Alzheimer's disease due to the accumulation of AGEs in the neurofibrillary tangles and amyloid plaque in the brain (20).
Regarding the level of function in ESRD patients in the present study, there was a significant difference between the level of ALB and independent and semi-independent function, which is consistent with studies that have reported that alb affects performance and cognitive levels. But there was no significant difference between independent function and dependent functional level and on the other hand there was a significant relationship between patients with dependent functional level and independent functional level and duration of dialysis that was in line with studies reported that the duration of dialysis inversely affects the functional level of dialysis patients and that patients with longer dialysis periods are more functionally dependent.The DOPPS study showed that functional status was independently associated with mortality in dialysis patients, a finding that was true for age and other related factors even after adjustment. Mental and physical health conditions are often interrelated, and studies have reported that increased mortality in hemodialysis patients has been associated with mental and physical health status of patients.One study reported that CKD patients often have peripheral artery disease and diabetic neuropathy, so it is possible that gait speed assessment alone may not be sufficient and other cognitive domains may need to be assessed simultaneously.

Conclusion

The results of this study showed that the level of cognitive and functional health of patients over 60 years undergoing hemodialysis is associated with a history of ESRD. Factors such as duration of dialysis and serum albumin deficiency affect patients' cognition and function, and therefore, cognitive and functional screening should be performed in these patients to prevent exacerbation of symptoms.

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