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Cognitive Impairment and Its Associated Factors in Patients Undergoing Hemodialysis: A Cross Sectional Study

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ABSTRACT

Background: Hemodialysis is a treatment for end-stage renal disease (ESRD) that is an underlying factor of cognitive impairment in patients**.**

Objectives: This study was conducted to evaluate the prevalence of cognitive impairment and its associated factors in patients undergoing hemodialysis using Montreal Cognitive Assessment (MoCA).

Materials and Methods: This cross-sectional study was carried out in 2016 in the dialysis unit of an academic hospital in the north of Iran. A total of two hundreds and twenty-four patients with chronic renal failure and ESRD presenting to for hemodialysis were included. All the patients were evaluated by the MoCA and the cut-off point was set at ≤25 for confirming cognitive impairment. The data obtained were analyzed in SPSS-18 using the Chi-square test, Mann-Whitney's U-test, Fisher's exact test, the independent t-test and the binomial logistic regression.

Results: From the total of 224 patients examined, 93 (41.52%) had developed cognitive impairment. The variables of age, stroke, education and diabetes were entered into the logistic regression model to analyze the associated risk factors, but only age and a history of stroke showed a significant relationship with this impairment; that is, the possibility of cognitive impairment increases with increasing age and a history of stroke can increase its risk six-fold.

Conclusion: Cognitive impairment was a relatively frequent complication of hemodialysis in this study which was performed in the north of Iran. Aging and a history of stroke are risk factors of cognitive impairment in patients with chronic kidney failure undergoing hemodialysis treatment.

Keywords: Cognitive Dysfunction; Renal Dialysis; Kidney Failure

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Introduction

Chronic Kidney Disease (CKD) is a major health problem across the world that is increasing in prevalence and incidence (1). In a study conducted in Iran in 1997, the prevalence of CKD was reported as 19.8% (CI=1.82-20.6) and the disease was proposed as a threat to the future health of the community in Iran. According to the Statistical Center of Iran (for Special Diseases) and the Kidney Foundation of Iran, the prevalence of CKD grew about 12% between 2006 and 2011 in this country (2). The number of CKD patients also increased dramatically in Guilan Province between 1997 and 2002 (3). The number of patients with end-stage renal disease (ESRD) increased between 2000 and 2006 and an estimated 70% of ESRD patients are expected to live in developing countries by 2030 (4).

Currently, more than half of kidney patients are treated with hemodialysis (4). Hemodialysis is a treatment for ESRD patients that not only removes waste from the blood, but also adds certain vital substances to it (5). New measures such as hemodialysis save patients from premature death; however, they also expose them to a range of physical, psychological, economic and social problems (4). Renal failure and hemodialysis have numerous complications, such as atherosclerosis, lipid metabolism disorder, congestive heart failure, anemia, stroke, heart attack and peripheral vascular failure, which disable the patient or cause his death. Reduced blood pressure during dialysis is the most common complication that may lead to brain damage (2).

Cognitive impairment occurs following different medical condition including metabolic, hematologic, rhomatologic and cerebrovascular and the other disorders (6-8).

Cognitive impairment is a brain problem developed in people with ESRD following hemodialysis (9,10). This cognitive impairment is referred to as dialysis encephalopathy dementia and develops progressively in patients who have been on dialysis for at least three years. Initial symptoms include slurred speech disorder and stuttering, and personality disorder, seizures and dementia are later added and death also becomes a threat after six months (5).

Different statistics have been reported for the prevalence of cognitive impairment in patients with ESRD following hemodialysis, ranging from 20% to 47% (11-16). Many factors have been found to contribute to cognitive impairment in patients with ESRD undergoing hemodialysis, including salt retention, hypotension, hemodynamic instability during dialysis, anemia and different hemodialysis protocols. According to some reports, however, the exact role of the factors associated with cognitive impairment is still a matter for debate (13). In the past, the presence of aluminum in dialysate composition was introduced as a factor contributing to dialysis dementia that was proved by examining brain autopsy specimens; today, the prevalence of dialysis dementia has been reduced given that aluminum has been removed from dialysate composition (17).

With the high prevalence of cognitive impairment, the need for its timely diagnosis and treatment has become more striking than ever in kidney patients, especially in those undergoing dialysis (18). Learning of the exact prevalence of this impairment and determining its associated factors can offer a more comprehensive perspective on the prevention and treatment strategies that should be adopted and can ultimately help improve quality of life and life expectancy in these patients. Regional statistics are limited on this disease, especially in the case of patients undergoing dialysis in northern Iran (15). Given the recommendations of previous studies to further examine cognitive impairment in patients with ESRD undergoing hemodialysis (16), and also given the need to identify the underlying factors causing this disorder, the present study was designed. Its objective was to examine the prevalence of cognitive impairment and its associated factors in hemodialysis patients in the north of Iran. Interestingly it used the relatively-new Montreal Cognitive Assessment (MoCA), which has a higher sensitivity compared to previously-used tools such as the Mini Mental Status Exam (MMSE) (19).

Materials and Methods

This cross-sectional study was conducted in 2016 on two hundreds and twenty-four patients with ESRD presenting to the Dialysis Unit of a teaching hospital affiliated to Guilan University of Medical Sciences for hemodialysis. The participants were selected through convenience sampling. They signed informed consent forms before beginning their hemodialysis session. The required sample size was calculated as 224 based on the sample size equation for estimating the ratio of a trait in a community (20) and considering P=30% as per previous studies (13,14) and with a confidence interval of 95% and a precision of 0.06. The inclusion criteria consisted of being diagnosed with ESRD based on the medical records and at least a three-month history of dialysis. The exclusion criteria consisted of absolute illiteracy, not consenting to participation in the study, the use of brain suppressants such as opioids and sedative hypnotics, having anxiety and severe depression based on the medical history and the use of anti-anxiety medications and antidepressants and mental disability (15,19).

The subjects were randomly selected in 2015 according to the inclusion and exclusion criteria and sampling continued until the calculated sample size was reached. During sampling, 48 randomly-selected patients were excluded or were not entered because four of them had not completed their informed consent form, two were mentally disabled, five had severe anxiety and depression according to their medical records, nine took sedative hypnotics or opioids, 11 were absolutely illiterate and 17 had started hemodialysis less than three months ago.

A researcher-made questionnaire was used to collect the patients' demographic details, including gender, age, education and BMI. Their clinical information was extracted from the medical records included the duration of hemodialysis, underlying diseases and etc. The Montreal Cognitive Assessment (MoCA) translated into Persian and validated for use in Iran by Nasreddine *et al.* (21) was used to check for cases of cognitive impairment (22,23).

The MoCA has a high sensitivity in the diagnosis of mild cognitive impairment (90%) and Alzheimer's disease (100%). The single-sheet screening tool has a Cronbach's alpha reliability of 92% and gives the respondents a maximum score of 30 and takes less than 15 minutes to complete and has a cut-off point of 26. This test evaluates seven cognitive domains, including attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations and orientation. Those who receive a score of ≥26 are considered normal (23), and a score is added to the total score obtained for those with less than 12 years of education (22,23). Previous studies conducted on this subject in Iran or in other countries have often used the MMSE to assess cognitive impairment (12,15,16); however, since the MMSE is not highly capable of making an early diagnosis of mild cognitive impairment compared to the MoCA (19,24) and also has a low specificity of 53% (22), the researchers set out to use the newer MoCA, which has been developed mainly to resolve the defects in the MMSE and which has a higher sensitivity (19).

The data obtained were analyzed in SPSS-18. At first by Kolmogorov-Smirnov test the normality of variable distribution was examined. The independent t-test and Mann-Whitney's U-test were selected based on the normality of variable distribution for the continuous quantitative variables. The Chi-square test and Fisher's exact test were used for the qualitative variables, and the binomial logistic regression analysis for determining the factors contributing to cognitive impairment. The level of statistical significance was set at $p \leq 0.05$.

Results

The results obtained from the cognitive assessment showed that 93 patients (41.52%) had cognitive impairment and 131 patients (58.48%) had normal cognition. Table 1 presents the mean and standard deviation of the MoCA and its seven sub-domains for the 224 patients examined.

According to table 1, the highest mean score was obtained in the orientation domain and the lowest in the conceptual thinking and memory domains. The total MoCA score obtained in the study was 20.76±9.22.

Table 1. The mean score of the MoCA and its seven sub-domains in the patients undergoing hemodialysis (n=224)

Cognitive domains	M±SD	range
Visuospatial/executive	1.12±1.64	0-5
Naming	1.80±1.06	0-3
Attention, Memory	2.33±1.88	0-6
Language	1.48±1.28	0-3
Abstraction	0.82±0.83	0-2
Delayed recall	1.31±0.64	0-5
Orientation	4.78±1.57	0-6
MoCA Total Score	20.76±9.22	0-30

Based on the Kolmogorov-Smirnov test, the mean age had a normal distribution but the mean BMI and duration of dialysis had non-normal distributions. The independent t-test and Mann-Whitney's U-test were used to determine the difference between the groups with and without cognitive impairment. Table 2 presents the inter-group differences observed.

Table 2. The mean age, BMI and duration of dialysis in patients undergoing hemodialysis with and without cognitive impairment

Variables	Cognitive impairment	n	M±SD	*p-value*
Age (in years)	Yes	93	63.40±15.15	0.0001
	No	131	54.58±16.41	
BMI	Yes	93	26.26±2.61	0.616
	No	131	26.16±2.70	
dialysis duration (in month)	Yes	93	15.62±11.88	0.724
	No	131	14.79±10.93	

As shown in table 2, the independent t-test revealed a significantly higher mean age in the group of patients with cognitive impairment compared to the other group ($p<0.0001$); Mann-Whitney's U-test, however, showed no significant differences between the group with and the group without cognitive impairment in terms of BMI and the duration of dialysis ($p=0.616$ and $p=0.724$, respectively). Table 3 presents the frequency of gender, education, dialysis sessions and underlying diseases by cognitive status.

Table 3. The frequency of gender, education, dialysis sessions and underlying diseases in patients undergoing hemodialysis with and without cognitive impairment

Variables		Cognitive impairment				*p-value*
		Yes		No		
		n	%	n	%	
Gender	Male	56	41.5	79	58.5	1
	Female	37	41.6	52	58.4	
Education	Low literacy	44	61.1	28	38.9	0.0001
	Under diploma	39	38.2	63	61.8	
	High school diploma	7	24.1	22	75.9	
	collegiate	3	14.3	18	85.7	
Dialysis episode (in week)	1 time	2	50.0	2	50.0	0.486
	2 time	21	51.2	20	48.8	
	3 time	67	38.7	106	61.3	
	emergency	3	50.0	3	50.0	
Underlying disease	Yes	62	48.8	65	51.2	0.014
	No	31	32.0	66	68.0	

As shown by Fisher's exact test in table 3, *p*=1.000 for the groups of patients with and without cognitive impairment in terms of gender distribution; however, the same test showed a significant difference between the two groups in terms of underlying diseases (*p*=0.014); that is, the patients with cognitive impairment more commonly suffered from underlying diseases (48.8% vs. 32%). The Chi-square test also showed that the two groups differed significantly in terms of the frequency distribution of education (*p*<0.0001); in other words, the frequency of lower levels of education was higher in the group with cognitive impairment. Nonetheless, no differences were observed between the two groups in terms of the frequency of dialysis sessions (*p*=0.486). Table 4 presents the patients' clinical data by cognitive status.

Table 4. The patients' clinical data by cognitive status

Variables		Cognitive impairment				*p-value*
		Yes		No		
		n	%	n	%	
Diabetes mellitus	Yes	37	57.8	27	42.2	0.003
	No	56	35.0	104	65.0	
Stroke	Yes	9	81.8	2	18.2	0.009
	No	84	39.4	129	60.6	
Hypertension	Yes	24	39.3	37	60.7	0.761
	No	69	42.3	94	57.7	
Vasculitis	Yes	2	33.3	4	66.7	1
	No	91	41.7	127	58.3	
Hyperlipidaemia	Yes	23	37.1	39	62.9	0.451
	No	70	43.2	92	56.8	
Kidney stone	Yes	5	55.6	4	44.4	0.459
	No	88	40.9	127	59.1	
Hypothyroidism	Yes	3	25.0	9	75.0	0.367
	No	90	42.5	122	57.5	
Hyperthyroidism	Yes	4	44.4	5	55.6	1
	No	89	41.4	126	58.6	
Ischemic heart disease	Yes	9	47.4	10	52.6	0.632
	No	84	41.0	121	59.0	

As shown in table 4 and according to Fisher's exact test, the two groups differed significantly in terms of diabetes mellitus (p=0.003) and stroke (p=0.009); in other words, diabetes and a history of stroke were more frequent in the group of patients with cognitive impairment. Nonetheless, the two groups did not differ in terms of the other clinical variables (p>0.05). Table 5 shows the results of the binomial logistic regression analysis for determining the risk factors of cognitive impairment. To determine these risk factors, only those variables were entered into the logistic model that had p<0.2 in the univariate statistical analysis.

Table 5. The binomial logistic regression analysis for determining the risk factors of cognitive impairment in patients undergoing hemodialysis

Predictors	β	OR	*p-value*	95 % CI	
				Lower	Upper
Diabetes mellitus	0.605	1.832	0.067	0.958	3.502
Stroke history	1.804	6.076	0.033	1.155	31.953
Low literacy (ref)	--	--	0.881	--	--
Under diploma (1)	-0.032	0.969	0.928	0.491	1.913
High school diploma (2)	-0.328	0.721	0.464	0.300	1.731
Collegiate (3)	-0.169	0.844	0.788	0.245	2.906
Age	-0.034	1.035	0.001	1.014	1.056
Constant	-2.541	0.079	0.0001	--	--

As shown in table 5, the binomial logistic regression analysis showed that only age, stroke, education and diabetes were entered into the model, and from these variables, only stroke and age had a significant relationship with cognitive impairment in the patients undergoing hemodialysis; that is, the possibility of cognitive impairment increases with increasing age and a history of stroke can increase its risk six-fold.

Discussion

The prevalence of cognitive impairment in the hemodialysis patients presenting to Razi Hospital of Rasht in Guilan province in the north of Iran was 41.52% according to the MoCA. Previous studies conducted throughout the world and in Iran have mostly used the MMSE to assess cognitive impairment, which does not have a high sensitivity for the early detection of mild cognitive impairment and has a reported low specificity of 53%. A study conducted in Iran although it was done based on the MMSE, estimated the frequency of cognitive impairment as 47.22% which is higher than our results (15). This and similar studies cited have unanimously concluded that cognitive impairment is worryingly common in patients with renal failure. The prevalence of cognitive impairment was reported as 18.8% in Japanese patients undergoing hemodialysis (12) and as 25% in Moroccan patients by Wechsler memory test (16).

Different studies have thus reported different prevalence rates for cognitive impairment in hemodialysis patients; this disparity may be attributed to the different diagnostic methods used, the different measures used for assessing cognitive impairment and the different sample populations examined and methods of sampling used. In a study by Murray *et al.* (25) on hemodialysis patients aged over 55, severe cognitive impairment was reported as 37%.

The present study found that the possibility of cognitive impairment increases with age and that a history of stroke increases the risk of cognitive impairment six-fold. Many studies have examined whether hemodialysis is an independent factor that causes cognitive impairment or if other risk factors are also at play, and different results have been obtained. For example, Odagiri *et al.* (12) argued that hemodialysis treatment is an independent risk factor for cognitive impairment in patients with renal failure. Fadili *et al.* (16) also found that lower levels of education and anemia are risk factors for the incidence of cognitive impairment in patients undergoing hemodialysis. In a study by Eslami-Amirabadi *et al.* (15), cognitive impairment was found to be associated with age, lower levels of education and diabetes mellitus, depression and positive qualitative CRP. A review of previous studies and the noted dispersion in the assessment of factors associated with cognitive impairment suggest that a clear direction has not yet been developed for the treatment and prevention of cognitive impairment in renal failure patients or for their rehabilitation. Old age and a low level of education are common associated factors both in the present study and in previous studies.

In justifying the mechanism through which aging can make patients susceptible to cognitive impairment, it seems that aging is an independent factor that can lead to cognitive changes with the atrophic changes it brings to the brain tissue.

In line with the results of previous studies (15,16), the present findings show that a lower level of education increases the risk of cognitive impairment in hemodialysis patients. This finding can be justified by noting that a low level of education is generally associated with lower cognitive and functional reserves and may lead to a poorer lifestyle (26). The concept of cognitive reserve was first introduced by Yaakov Stern and holds that, when injured, the brain is assisted by certain compensation processes that allow the brain to escape cognitive impairment unless with a greater amount of injury; the present finding implies that a higher cognitive reserve, which is itself affected by a higher level of education, can help combat cognitive impairment (27).

In the present study, a history of stroke was one of the underlying diseases that were proposed as an effective and significant risk factor for cognitive impairment in hemodialysis patients. Previous studies have also shown that hemodialysis patients with a history of stroke are more likely to score below 24 on the MMSE (34.6%) compared to patients without a history of stroke (15.6%) (12). In support of this finding, researchers have proven over the years that patients with a history of stroke with large infarcts involving the cerebral cortex or the anterior and posterior arteries in the left hemisphere of the brain experience significant cognitive impairment in their memory functions, attention, orientation and language abilities (28). Researchers also believe that stroke can cause cognitive impairment, especially in areas of executive functioning, attention, memory and recall by the lesions it creates in the white matter (29). Researchers have also found that learning ability and verbal recall can be weakened even in patients with a mild stroke (30). Nonetheless, stroke explains only part of the cause of cognitive impairment in hemodialysis patients and cannot justify this defect entirely (12,15).

Cognitive function was not significantly related to the duration of dialysis and the number of dialysis sessions per week in the present study, which may be due to the early diagnosis and treatment of renal failure in the patients and their being monitored by the physicins, which have led to the lower exposure of their brain tissue to the toxins of uremia and its complications; this finding explains how, despite the long period of suffering from renal failure and the adequate number of dialysis sessions, the patients have survived the cognitive side-effects of this treatment. Further studies are still needed on this subject to achieve more accurate results. Odagiri *et al.* (12) found that the duration of hemodialysis has no significant relationships with cognitive impairment in renal failure patients. It can thus be concluded that hemodialysis is not a risk factor for cognitive impairment per se, and the hypothesis of “associated factors” should thus be further investigated.

One of the limitations of this study was lack of cooperation of some patients because of their poor physical and medical condition.

Conclusion

The present findings show that cognitive impairment has a significant prevalence (41.52%) in patients with renal failure undergoing hemodialysis in Guilan Province. Cognitive impairment is one of the common problems faced by patients with renal failure and those undergoing dialysis that is often left undiagnosed or neglected (17); nonetheless, the prevention and timely treatment of renal dysfunction can help improve personal and social functioning in the patients. Given the increasing prevalence of chronic renal failure and the effect of cognitive impairment on the quality of life and mortality in these patients, prevention and early diagnosis are key (3,5, 11-16). Cognitive functioning is therefore recommended to be examined in all the periodic examinations of renal failure patients so as to ensure the early diagnosis and the proper treatment of this impairment. Moreover, the exacerbating factors of cognitive impairment should also be identified in patients undergoing hemodialysis, as optimal cognitive functioning is crucial for improving and maintaining mental health and quality of life in these patients (31,32) and cognitive rehabilitation programs are highly recommended for these patients. Aging and a history of stroke were identified as independent risk factors of cognitive impairment in patients with chronic renal failure undergoing hemodialysis.

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Conflict of Interest

The authors have no conflict of interest.

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