Original Contribution/Clinical Investigation

Cognitive Impairment among Egyptian Older Adults on Hemodialysis

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ABSTRACT

Background: Older patients are now the rule rather than the exception in hemodialysis (HD). Cognitive impairment is common among persons with end stage renal disease (ESRD) and is associated with poor outcomes.

Aim: To assess the prevalence of cognitive impairment among older adults on HD and the association of different patients' demographics and characteristics with cognitive impairment.

Materials and methods: A cross section study was conducted to assess the cognitive functions of elderly subjects on HD. 94 subjects, 60 years old and above, were included. All subjects were subjected to: 1- comprehensive geriatric assessment. 2- Laboratory investigations including: hemoglobin, serum creatinine, serum urea, serum potassium, serum sodium and serum albumin. Kt/V as a marker of dialysis adequacy was calculated.

Results: The study revealed that 26 (27.7%) patients had normal cognitive function, 32 (43%) had mild cognitive impairment, 21 (23%) had mild dementia, 8 (8.5%) had moderate dementia and 7 (7.4%) had severe dementia. Older age, low education level and longer duration of dialysis history were found to have significant associations with cognitive impairment, [P: < 0.001, 0.002, and 0.012 respectively]. While hemoglobin, serum albumin, serum creatinine, serum urea, serum potassium and Kt/V showed no significant association with cognitive impairment, Serum sodium and dry weight dialysis showed significant difference between patients with normal cognitive function and patients with cognitive impairment, [P <0.001 both].

Conclusion: Cognitive impairment is prevalent in Egyptian older adults on HD and more prevalent and severe in those with older age, low education, lower level of serum sodium, longer duration of dialysis history and higher dry weight.

Key words: Cognitive impairment, Egypt, Hemodialysis

Introduction

Older patients are now the rule rather than the exception on hemodialysis (HD). According to the United States Renal Data System (USRDS) data from 2006, nearly one half of incident dialysis patients in the United States are senior citizens, with the median age at dialysis initiation at 64.4 years old. Furthermore, the elderly are the fastest-growing group of incident dialysis patients, meaning that this median age will continue to increase. Nearly all of these elderly patients employ HD, with only 3 to 5% using peritoneal dialysis (PD). (1)

Cognitive impairment is common among persons with end stage renal disease (ESRD) and is associated with poor outcomes, (2) but its underlying mechanisms remain poorly understood. As a result, few evidence-based strategies exist for treating this serious morbidity. Uncontrolled studies have reported improvements in cognitive function after kidney transplantation and more recently, after conversion from conventional to nocturnal hemodialysis, suggesting that modifiable factors associated with ESRD and/or its treatment may be implicated in the pathogenesis of this disorder. (3)

Many studies found that cognitive impairment was prevalent in older adults with CKD on HD as one reported that 37 percent of patients had severe cognitive impairment. (4) And another study found that 38 percent had severe impairment in executive function and 33 percent severe memory impairment. (5)

Several ESRD- and dialysis-associated factors such as retention of uremic solutes, hypertension, hemodynamic instability during dialysis, and anemia may be favorably modified by more frequent hemodialysis schedules. Several of these conditions have also been implicated in the pathogenesis of cognitive impairment. For example, in the National Cooperative Dialysis Study, higher levels of urea clearance were correlated with better cognitive performance. (6) In addition, cardiovascular and hemodynamic factors (hypertension, and at the other extreme, intra dialysis hypotension) may lead to stroke or cerebral ischemia and contribute to cognitive impairment in patients with ESRD. (7)

The etiology of cognitive impairment among HD patients is thought to be multifactorial, and includes factors such as cerebrovascular lesion, (7) hypotension, (8) abnormalities of serological data, (9) social history, (10) and e GFR level; (11) as, each 10 mL/min/1.73 m2 decrement in e GFR was found to correspond to an approximately 15 to 25 percent increase in the risk of cognitive dysfunction among individual cognitive domains. (12) In addition, the high prevalence of cardiovascular risk factors might overshadow the roles of aging and non-vascular factors in the development of cognitive impairment. (13)

Dementia is associated with an increased risk of multiple adverse outcomes. Prevalent dementia in hemodialysis patients increases the risk of hospitalization. Dementia also increases costs of care; in 2002 approximately $19,100 more Medicare dollars were spent over one year on hemodialysis patients with dementia compared to those without. (14) Among hemodialysis patients, dementia was associated with a 1.48 fold increased risk of death over one year. (10)

In this study we assessed the prevalence of cognitive impairment among older adults on HD and association between cognitive impairment and different demographics and characteristics of these patients.

Subjects and Methods

Study setting and sample:

- A cross section study was conducted to assess the cognitive functions in elderly subjects on HD. 94 elderly subjects 60 years old and above (Both males: n=39, and females: n= 55) were recruited from Ain Shams University hospitals.

Exclusion criteria:

- The study did not include subjects with stroke, delirium, alcoholism or drug abuse, psychiatric disease, thyroid disease and auditory or visual impairment were excluded as these conditions are known to affect cognitive functions. Also subjects with chronic liver disease and Chronic Obstructive Pulmonary Disease (COPD) were excluded.

Data collection:

All subjects were subjected to:

A. Informed oral consent.
B. Comprehensive geriatric assessment, including
1. Medical history and physical examination.
2. The Mini-Mental Status Examination MMSE was applied to all the participants to assess their cognitive function. (15)

All subjects were screened for presence of dementia by using the Arabic version of MMSE. (16)

The MMSE was selected because it is the best studied instrument for screening for dementia. (17)

The MMSE comprises 30 questions with 10 devoted to orientation (five regarding time and five regarding place). Three items requiring registration of new information (repeating three words). Five questions addressed attention and calculation. Mental control questions requiring patient to make five serial subtractions of 7 from 100 or spell word backward); three recall items (remembering the three registration items), eight items assessing language skills (two naming items, repeating phrase, following a three-step command, reading and following a written command and writing a sentence), and one construction question (copying a figure consisting of two overlapping pentagons) were used.

According to the MMSE, the subjects were classified into two groups:

Group 1 (controls): cognitively intact: MMSE = 30
Group 2 (cases): cognitively impaired: MMSE < 30

And according to the severity of cognitive impairment, participants in group 2 were further classified into 4 subgroups:

Group a: mild cognitive impairment: MMSE: 26 - 29.
Group b: early dementia: MMSE: 21 - 25.
Group c: moderate dementia: MMSE: 11 - 20.
Group d: severe dementia: MMSE: 0 - 10.

Results

<< Table 1: Patient's demographics and characteristics

Age:	
Min	60
Max	80
Mean & SD	67.26 ± 4.95
Sex:	
Male	39 (41.5%)
Female	55(58.5%)
Education:	
Illiterate	17 (18.1%)
Less than High school education	40 (42.6%)
High school education and more	37(39.3%)
Dialysis duration (year):	
Min	1
Max	11
Mean & SD	4 ± 2.75
Total score of MMSE:	
Min	6
Max	30
Mean & SD	25 ± 6
History of diabetes mellitus (DM):	
Absent	37 (39.4%)
Present	57 (60.6%)
History of hypertension:	
Present	12 (12.8%)
Absent	82 (87.2%)
History of heart Disease:	
Present	25 (26.6%)
Absent	69 (73.4%)
Hemoglobin(g\dl):	
Min	7.7
Max	13.3
Mean & SD	10.75 ± 1.36
Serum albumin(g\dl):	
Min	2.4
Max	4.2
Mean & SD	3.5 ± 0.39
Serum Potassium (mmol\L):	
Min	3.5
Max	6.8
Mean & SD	4.9 ± 0.72
Serum sodium (mmol\L):	
Min	123
Max	146
Mean & SD	136.05 ± 5.86
Serum creatinine (mg\dl):	
Min	3.4
Max	18.4
Mean & SD	10.1 ± 2.8
Serum urea (mg\dl):	
Min	34
Max	93
Mean & SD	63.2 ± 11.92
Dialysis adequacy (*Kt/V*):	
Min	0.64
Max	1.98
Mean & SD	1.23 ± 0.29
Dry weight (Kg):	
Min	56
Max	126
Mean & SD	80.75 ± 18.07

C. Laboratory Investigations including:

- Hemoglobin (g\dl)
- Serum creatinine (mg\dl)
- Serum urea (mg\dl)
- Serum potassium (mmol\L)
- Serum sodium (mmol\L)
- Serum albumin (g\dl)
- Serum blood urea nitrogen (mg/dl) pre-dialysis and post-dialysis

D. Dialysis adequacy:
Kt/V as a marker of dialysis adequacy
Kt/V is a number used to quantify hemodialysis treatment adequacy.

- **K** - dialyzer clearance of urea
- **t** - dialysis time
- **V** - volume of distribution of urea, approximately equal to patient's total body water

In the context of hemodialysis, Kt/V is a pseudo-dimensionless number; it is dependent on the pre- and post-dialysis concentration. It is not the product of K and t divided by V, as would be the case in a true dimensionless number. (18)

It was developed by Frank Gotch and John Sargent as a way of measuring the dose of dialysis when they analyzed the data from the National Cooperative Dialysis Study. (19) In hemodialysis the US National Kidney Foundation Kt/V target is ? 1.3, so that one can be sure that the delivered dose is at least 1.2 (20)

Calculation of Kt/V needs serum blood urea nitrogen (mg/dl) pre-dialysis and post-dialysis, weight of the patient pre-dialysis and post-dialysis, treatment time (minute) and frequency of treatments/week. With these parameters Kt/V is calculated by using an online calculator:
http://www.davita.com/ktvcalculator/

Statistical Methods:
All data were entered into the 21st version of SPSS (Statistical Package of Social Science) and analyzed using frequency and descriptive statistics to analyze the study population. Frequency and percentage was calculated for all qualitative variables. Description of all data in the form of mean (M) and standard deviation (SD) was done for all quantitative variables. Comparison of qualitative variables was done using Chi-square test; it is a test that determines the extent that a single observed series of proportions differs from a theoretical or expected distribution of proportions, or the extent that two or more series of proportions or frequencies differ from one another based on the chi-square distribution.

Comparison between quantitative variables was done using ANOVA (analysis of variance) to compare between more than two groups.

The level of significance for Chi-square test and ANOVA was taken at P value < 0.05 is significant, otherwise it is non-significant.

Results

The study was conducted on 94 older patients on regular haemodialysis. Table 1 shows the demographics and characteristics of the older adults: The mean age of the sample was 67.26 ± 4.95 (range: 60 - 80). The sample included 39 (41.5%) males and 55 (58.5%) females. Among the 94 older subjects; 17 (18.1%) were illiterate, 40 (42.6%) had less than high school education and 37 (39.3%) had high school education or more. The mean dialysis duration in years was 4 ± 2.75 (range: 1 - 11). The mean of Total score of MMSE was 25 ± 6 (rang 30-6). 37 (39.4%) subjects had no history of DM and 57 (60.6%) had history of DM. 25 (26.6%) subjects had history of heart disease and 69 (73.4%) did not. 12(12.8%) subjects had history of HTN and 82 (87.2%) had no HTN. The mean hemoglobin level was 10.75 ± 1.36 (range 7.7 - 13.3). The mean level of serum albumin was 3.5 ± 0.39 (range 2.4 - 4.2). The mean level of serum potassium was 4.9 ± 0.72 (range 3.5 - 6.8). The mean level of serum sodium was 136.05 ± 5.86 (range 123 - 146). The mean level of serum creatinine was 10.1 ± 2.8 (range 3.4 - 18.4). The mean level of serum urea was 63.2 ± 11.92 (range 34 - 93). The mean value of dialysis adequacy (Kt/V) was 1.23 ± 0.29 (range 0.64 - 1.98). The mean value of dry body weight (Kg) 80.75 ± 18.07 (range 56 - 126).

Figure 1:

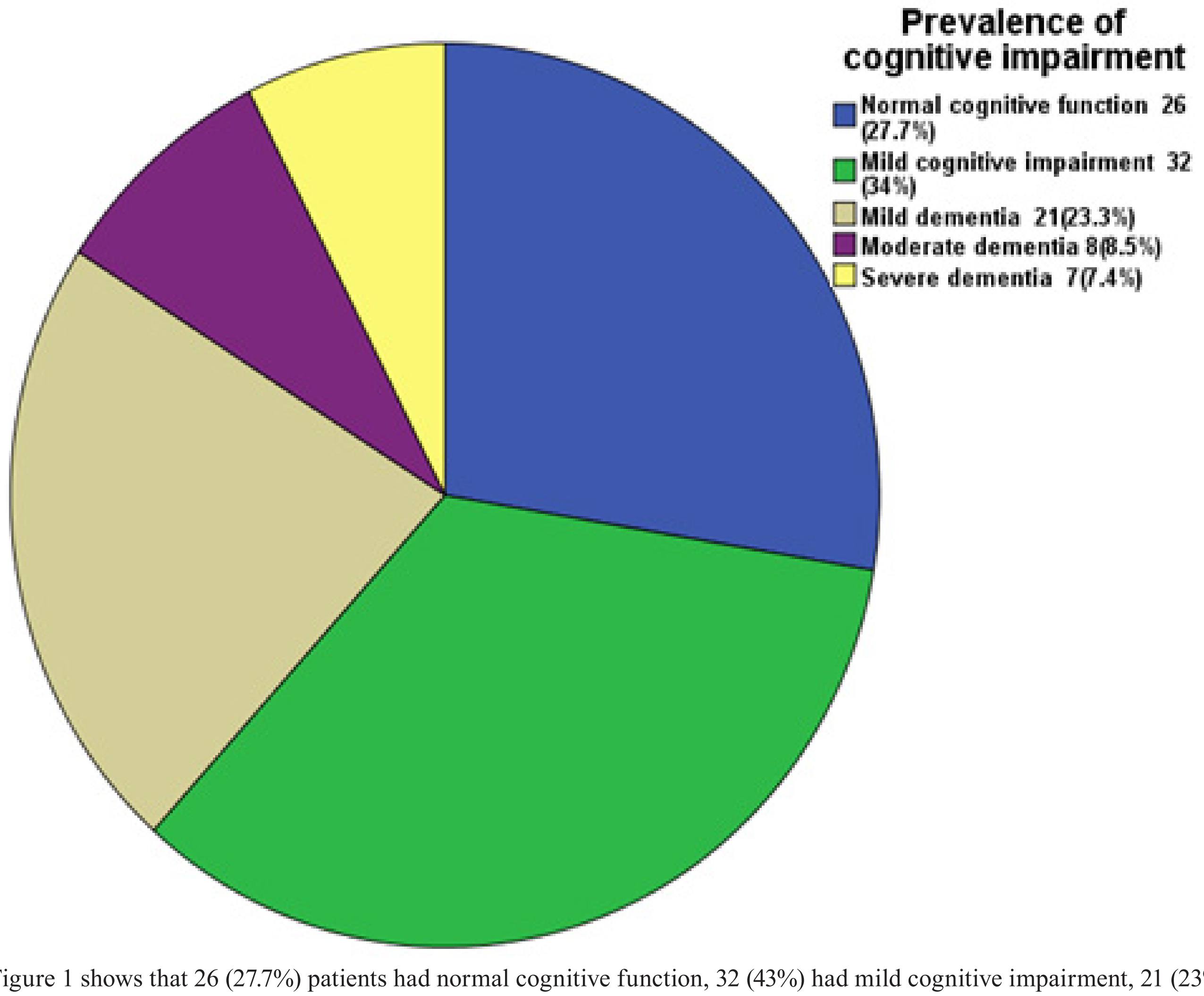

Figure 1 shows that 26 (27.7%) patients had normal cognitive function, 32 (43%) had mild cognitive impairment, 21 (23%) had mild dementia, 8 (8.5%) had moderate dementia and 7 (7.4%) had severe dementia.

Table 2 (next page) shows the association of patients' demographics and characteristics with cognitive function; the mean age of the patients with normal cognitive function was 67.1 ± 3.16, while for patients with severe dementia was 73.85 ± 3.33, [P:<0.001]. Sex did not show a significant difference between patients with normal cognitive function and patients with cognitive impairment [P: 0.35]. Also history of DM, HTN heart disease did not show significant association with cognitive function [P: 0.21, P: 0.87, P: 0.82 respectively]. The education level and the duration of dialysis history showed significant differences between patients with normal cognitive function and patients with cognitive impairment, [P: 0.002, P: 0.012 respectively]. While hemoglobin level, serum albumin, serum creatinine, serum urea and serum potassium showed no significant difference between patients with normal cognitive function and patients with cognitive impairment, [P: 0.099, P: 0.17, P: 0.18, P: 0.08, P: 0.35 respectively]. Serum sodium showed significant difference between patients with normal cognitive function and patients with cognitive impairment, [P:< 0.001]. And also Dry weight dialysis showed significant difference between patients with normal cognitive function and patients with cognitive impairment, [P :< 0.001], while dialysis adequacy (Kt/v) showed no significant difference between patients with normal cognitive function and patients with cognitive impairment, [P: 0.79].

Table 2: Relationship between Patients' characteristics and cognitive impairment:

	Normal cognitive function	Mild cognitive impairment	Mild dementia	Moderate dementia	Severe dementia	
Age	Mean SD 67.1 ± 3.16	Mean SD 67.1 ± 3.1	Mean SD 67.9 ± 4.36	Mean SD 74.25 ± 2.3	Mean SD 73.85 3.33	F 24.4 P:< 0.001
Sex Male Female	 8 18	 17 15	 7 14	 4 4	 3 4	 X: 3.8 P: 0.425
Education -Illiterate -Less than High school education -High school education and more	 0 8 18	 6 16 10	 4 9 8	 3 4 1	 4 3 0	X: 24.3 P: 0.002
Dialysis duration (year)	Mean SD 3.69 ± 2.4	Mean SD 3.0 ± 2.26	Mean SD 4.7 ± 2.7	Mean SD 5.0 ± 3.5	Mean SD 6.42 ± 3.55	F 3.42 P: 0.012
History of DM No history of DM History of DM	 13 13	 8 24	 8 13	 5 3	 3 4	X: 5.84 P: 0.21
History of HTN No history of HTN History of HTN	 22 4	 28 4	 18 3	 7 1	 7 0	X: 1.23 P: 0.87
History of Heart Disease No history of Heart disease: History of Heart disease:	 17 9	 24 8	 17 4	 6 2	 5 2	X: 1.53 P: 0.82
Hemoglobin(g\dl)	Mean SD 10.8 ± 1.26	Mean SD 10.4 ± 1.47	Mean SD 11.0 ± 1.24	Mean SD 10.3 ± 1.68	Mean SD 11.8 ± 0.9	F: 2.01 P:0.099
Serum albumin (g\dl)	Mean SD 3.4 ± 0.37	Mean SD 3.6 ± 0.31	Mean SD 3.5 ± 0.44	Mean SD 3.36 ± 0.42	Mean SD 3.3 ± 3.55	F: 3.42 P: 0.17
Serum Potassium (mmol\L)	Mean SD 4.8 ± 0.69	Mean SD 4.98 ± 0.7	Mean SD 4.9 ± 0.73	Mean SD 5.2 ± 0.82	Mean SD 4.5 ± 0.5	F: 1.6 P: 0.35
Serum sodium (mmol\L)	Mean SD 142.9 ± 1.74	Mean SD 137.2 ± 1.87	Mean SD 132 ± 2.6	Mean SD 127.7 ± 1.6	Mean SD 126.2 ±2.3	F 167.5 P<0.001
Serum creatinine (mg\dl)	Mean SD 9.1 ± 1.7	Mean SD 10.1 ± 3.18	Mean SD 11.1 ± 3.6	Mean SD 10.2 ± 3.2	Mean SD 11.3 ± 0.8	F: 1.59 P: 0.18
Serum urea (mg\dl)	Mean SD 58.1 ± 5.8	Mean SD 65.56 ± 13.65	Mean SD 63.0 ± 16.0	Mean SD 67.3 ± 5.5	Mean SD 671.5 ±3.64	F: 2.13 P: 0.08
Dialysis adequacy (Kt/V)	Mean SD 1.27 ± 0.3	Mean SD 1.18 ± 0.26	Mean SD 1.25 ± 0.28	Mean SD 1.24 ± 0.37	Mean SD 1.25 ±0.29	F: 0.42 P:0.79
Dry weight (Kg)	Mean SD 84.9 ± 10.9	Mean SD 69.3 ± 12.9	Mean SD 74.5 ± 6.28	Mean SD 105.8 ± 12.1	Mean SD 107.3 ±8.7	F: 22.8 P:<0.001

Discussion

The purpose of this study was to determine prevalence of cognitive impairment among older adults on HD and to assess the association between the prevalence and severity of cognitive impairment with different demographics and characteristics of these patients.

Despite the growing numbers of patients with ESRD and dementia, the medical literature did not truly explore the intersection of these two groups of patients. Recently, Seliger et al, 2004 [21] reported that elevated serum creatinine was associated with a higher risk for dementia in older adults who reported either good or excellent health.

In our study we found that prevalence of cognitive impairment among older adults on HD was 72.3 % (43% had mild cognitive impairment, 23% had mild dementia, 8.5% had moderate dementia and 7.4% had severe dementia).

This result was supported by Kurella et al, 2004 [5] who studied 80 HD patients (mean age 61.2 ± 14.3 years) and found that prevalence of severe memory impairment was 33 %.

Also Tyrrell et al, 2005 [22] found that in older adult patients on HD the prevalence of cognitive impairment, based on the Mini-Mental State Examination (MMSE), was 47% of 51 HD outpatients.

This was also supported by Gen et al, 2011 [23] who found that the prevalence of cognitive impairment based on the MMSE was 18.8% in HD patients. They stated that HD patients had showed a higher prevalence of cognitive impairment in older groups (50 years and older).

Also we agreed with another study conducted by Murray et al, 2006 [4] to assess the cognitive function across multiple cognitive domains in 338 HD patients (mean age, 71.2 ± 9.5 years) and found that among older adults on HD, 13.9% were classified with mild impairment, 36.1% with moderate impairment, 37.3% with severe impairment, and 12.7% with normal cognition.

The prevalence of severe cognitive impairment in some studies was higher than our study as the authors included patients with history of cerebrovascular diseases. But in our study we excluded them and other diseases that could directly affect cognitive function e.g. alcoholism, drug abuse, psychiatric disease, thyroid disease, auditory or visual impairment, chronic liver disease and chronic obstructive pulmonary disease (COPD).

Rakowski et al, 2006 [24] and Laudanski et al, 2010 [25] reported that in patients undergoing HD, cognitive impairment brought more serious consequences, such as hospitalization and reduced life expectancy. They also added that cognitive impairment in HD patients might hinder them from complying with dialysis schedules, medications, and dietary restrictions

Also our study revealed that cognitive impairment was more prevalent and more severe in patients with older age, lower education level, longer duration of hemodialysis, lower level of serum sodium and higher dry weight.

This was supported by Gen et al, 2011 [23] who found that among HD patients, level of education was associated with MMSE score, and added that serum sodium level, dry weight and history of cerebrovascular disease tended to be associated with low MMSE score of HD patients.

Also Murray et al, 2006 [4] who assessed the cognitive function across multiple cognitive domains in 338 HD patients, found that low education was associated with severe cognitive impairment.

Sehgal et al, 1997 [26] stated that older age and lower education level were independently associated with less than 24 points achievement on MMSE test in multivariable analysis.

As regards hyponatremia, Gen Odagiri1 et al, 2011 [27] found a significant relationship [P = 0.05] between hyponatremia and the MMSE score among HD patients; they added that this relationship was also reported in a previous study by Maugeri et al. 1999 [28]

Hyponatremia depends on various factors including blood dilution by chronic fluid overload and dietary sodium restriction. [29] These factors might explain why no correlations were observed with other blood parameters, which were, to some extent, stabilized by HD.

The relationship between higher dry weight and cognitive impairment could be explained by the known relationship between obesity and cognitive impairment as reported by Gustafson et al, 2003 [30] who found an association between greater BMI at age 70 and greater risk of incident dementia in an 18-year longitudinal observational study.

Our result also showed although the mean levels of serum urea and serum creatinine were higher in patients with severe cognitive impairment than patients with normal cognitive function, this was statistically insignificant. This can be explained by the relatively small sample size.

Also the results showed that although dialysis adequacy (mean of Kt/v) was high in patients with normal cognitive function than those with cognitive impairment this was statistically insignificant. This can be explained as the dialysis adequacy (mean of Kt/v) for the whole sample (with and without cognitive impairment) was satisfactory.

This study was supported by Dahbour et al, 2009 [31] who studied and compared the predialysis (PrHDSc) and postdialysis (PoHDSc) mini mental status examination score Patients' (PrHDSc) correlated positively with PoHDSc and dialysis efficiency measured by Kt/V (r=0.58, 0.4, and 0.34, respectively). Education level correlated positively with PrHDSc r=0.41 but not PoHDSc.

Conclusion

Cognitive impairment was prevalent in Egyptian older adults on HD and more prevalent and severe in those with older age, lower education, longer history of hemodialysis duration, lower level of serum sodium and higher dry weight. So we recommended including cognitive evaluation in assessment of older adults on HD and conduction of of a larger sample size case control study to identify modifiable risk factors of cognitive impairment in older adults on HD.

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