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# Cognitive Impairment in Dialysis and Non-Dialysis Patients Suffering from Chronic Renal Failure and Comparing Them with a Control Group

Mohammad Reza Tamadon,[1] Ali Reza Adibimehr,[2] and Raheb Ghorbani[3,*]

[1]Internal Medicine Department, Semnan University of Medical Sciences, Semnan, Iran
[2]General Practitioner, Semnan University of Medical Sciences, Semnan, Iran
[3]Social Determinants of Health Research Center,Semnan University of Medical Sciences, Semnan, Iran

[*]*Corresponding author*: Raheb Ghorbani, Social Determinants of Health Research Center,Semnan University of Medical Sciences, Semnan, Iran. Tel: +98-2333654367, Fax: +98-2333654209, E-mail: r_ghorbani@semums.ac.ir

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## Abstract

**Background:** Chronic renal failure and its end-stage disease are one of the most important causes of death and disability, and its prevalence is increasing in the world. This disease can cause many complications in the patients with end- stage renal disease.
**Objectives:** The present study aimed at comparing cognitive impairment in patients with end- stage renal disease (ESRD) and chronic renal failure (CRF) with a control group.
**Methods:** In this cross-sectional study, 85 ESRD, dialysis dependent patients, 200 CRF patients, non-dialysis dependent, as well as 180 patients with high blood pressure or diabetes as control group who referred to Kowsar hospital during 2015 and 2016 were studied. The Persian version of the mini mental status examination (MMSE) questionnaire was used to collect data. It was completed by one of the skilled and trained nurses.
**Results:** The results revealed that 28.2% of ESRD, 1% of CRF patients, and 0.6% of control group patients had severe cognitive impairment. Cognitive health score in ESRD group was lower than that in CRF ($P < 0.001$) and control group ($P < 0.001$). In addition, cognitive health score of CRF patients was lower than that in the control group ($P = 0.005$). ESRD patients had significantly higher impairment in time and place orientation, calculation, recall, language, and repetition compared to control and CRF groups ($P < 0.001$), but there were no significant differences between control and CRF groups. With respect to complex commands, the control group had a significantly lower impairment, but the other 2 groups were not significantly different in this regard. The three experimental groups were not significantly different in per-test stage.
**Conclusions:** ESRD patients have severe cognitive impairment compared to CRF patients. Therefore, it is recommended that these patients be examined cognitively and proper rehabilitation programs be considered for them.

*Keywords:* Chronic Renal Failure, End- Stage Renal Disease, Cognitive Impairment

## 1. Background

Chronic renal failure (CRF) includes a series of damaging pathophysiological processes, resulting in a progressive decline in glomerular filtration and impairment in normal kidney function. Chronic renal failure refers to a process in which the number of nephrons declines persistently and irreversibly; this is in accordance with 3 to 5 stages of chronic kidney disease (1).

End- stage renal disease (ESRD) represents the fifth stage of chronic renal disease in which accumulation of toxins, fluids, and electrolytes that are naturally excreted by the kidneys cause uremic syndrome and if these substances are not excreted by dialysis or a kidney transplant, the patient will die (2). CRF and ESRD are one of the major causes of death and disability worldwide (3). The prevalence of this disease in the world is increasing, and the average global growth of the disease in recent years has been 8% per year (4).

In Iran, the growth rate of this disease is higher than the global average and it is about 12%. The incidence and prevalence of ESRD disease in Iran in 2000 were 238 and 49.9 per million people, respectively. However, the prevalence and incidence of this disease increased to 357 and 63.8 million people, respectively in 2006 (5). According to renal patients and kidney transplantation research center in Iran, in 2007, about 29 000 patients with ESRD were treated that among them, 15 000 patients were trans-

planted and 14 000 were treated by hemodialysis (6).

This disease negatively affects various organs of the body; for instance, it causes neurological impairment such as cognitive impairment. Cognitive impairment is common in these patients and it often cannot be diagnosed. The prevalence of cognitive impairment in patients with ESRD is 2 to 7 times more than that in the general population (7), and potentially 80% of ESRD patients suffer from some cognitive impairment (8, 9). It seems that cognitive impairment began several years prior to the progress of chronic renal failure due to ESRD, and it has had a direct correlation with the severity and level of decline in renal function (9-13).

In a study conducted on cardiovascular health and cognitive impairment, it was found that the risk of dementia in patients with CRF increases (10). Although the principle of creation of cognitive impairment in renal failure has been almost accepted by the scientific communities, the level of cognitive impairment in different stages of renal failure including the end- stage is not clear. Because previous studies have compared ESRD patients and healthy people, this study was conducted.

## 2. Objectives

The present study aimed at comparing cognitive impairment in patients with ESRD, CRF, and patients with at least high blood pressure or diabetes diseases.

## 3. Methods

In this cross-sectional study, all patients with ESRD, dialysis dependent patients who met the inclusion criteria of the study (n = 85), 200 CRF patients, non-dialysis dependent, and 180 patients with at least one of the high blood pressure or diabetes (as the control group) admitted to Kowsar hospital during 2015 and 2016 were studied.

The questionnaire was completed by one of the trained and experienced nurses in the hemodialysis ward of Kowsar hospital. Accordingly, the questions were explained for patients and their answers were recorded. Those patients, who were not prepared during questioning, were coordinated to complete the questionnaire later.

Inclusion criteria were as follow: having a serious problem, lack of underlying cognitive disease, and passing at least 6 months from dialysis in dialysis patients group. Patients using nutritional supplements such as vitamins and minerals were excluded. Mini mental status examination (MMSE) questionnaire, which is one of the most common means of measuring the overall cognitive impairment and has been standardized to many languages, was used to collect the data. The questionnaire was validated in Persian by Froghan et al. and its internal consistency was acceptable (Cronbach's Alpha coefficient = 0. 78) (14).

The questionnaire had 30 questions, and each had 1 score, and the total score of the questionnaire was 30. Those patients with the scores of 27 to 30 are considered healthy, scores 22 to 26 were considered as having mild cognitive impairment, and those with scores of less than 22 were considered as having severe cognitive impairment (15). Questions were divided into 8 areas of cognitive function as follow: orientation to time (5 questions); orientation to place (5 questions); registration (3 questions); recall (3 questions); attention and calculation (5 questions); language (2 questions); repetition (1 question); and complex commands (6 questions) (13, 16).

This study was approved by the research ethics committee of Semnan University of Medical Sciences. All stages of the project were fully explained to the participants before entering the study and all patients announced their consent to participate in the study.

### 3.1. Data Analysis

Statistical analysis was performed by Kolmogorov-Smirnov, chi-square, ANOVA, Kruskal-Wallis, and Mann-Whitney tests using SPSS16.0. A P value less than 0.05 was considered statistically significant.

## 4. Results

The mean ± SD of the age of ESRD patients was 61.4 ± 14.2 years, it was 60.1 ± 13.4 years in CRF patients, and 60.1 ± 10.8 years in patients of the control group; no significant difference was found among the 3 groups with respect to age (P = 0.752). It was found that 51.8% of the ESRD patients, 55% of the CRF patients, and 53.3% of the patients in the control group were male. Gender distribution was matched in the 3 groups (P = 0.872). In addition, 83.5% of ESRD patients, 84% of CRF patients, and 90% of the patients in the control group had one underlying disease. The 3 groups were matched for underlying disease (P = 0.162) (Table 1). Mean ± SD of the duration of dialysis for ESRD patients was 2.83 ± 2.1 years (1 to 8 years). Duration of dialysis was less than one year in 35.3 % of the patients, it was 1 to 4 years in 40% of the patients, and more than 4 years in 24.8% of the patients.

In general, 28.2% of ESRD patients, 1% of CRF patients, and 0.6% of control group patients had severe cognitive impairment (Table 2). Cognitive health scores of the 3 groups were significantly different (P < 0.001), and the cognitive health score of ESRD patients was lower than that in CRF patients (P < 0.001) and control group (P < 0.001) patients. In addition, the score of the control group was

**Table 1.** Distribution of Age, Gender and Underlying Disease in Three Groups

| Characteristics | Group Name | | | | | | P Value |
|---|---|---|---|---|---|---|---|
| | ESRD Patients | | CRF Patients | | Control | | |
| | n | % | n | % | n | % | |
| **Age (year)** | | | | | | | - |
| < 50 | 19 | 22.4 | 39 | 19.5 | 24 | 13.3 | |
| 50 - 59 | 11 | 12.9 | 54 | 27.0 | 62 | 34.4 | |
| 60 - 69 | 25 | 29.4 | 60 | 30.0 | 55 | 30.6 | |
| ≥ 70 | 30 | 35.3 | 47 | 23.5 | 39 | 21.7 | |
| **Gender** | | | | | | | 0.872 |
| Male | 44 | 51.8 | 110 | 55.0 | 96 | 53.3 | |
| Female | 41 | 48.2 | 90 | 45.0 | 84 | 46.7 | |
| **Underlying disease** | | | | | | | 0.162 |
| None | 14 | 16.5 | 32 | 16.0 | 18 | 10.0 | |
| Diabetes | 54 | 63.5 | 109 | 54.5 | 110 | 61.1 | |
| Hypertension | 11 | 12.9 | 37 | 18.5 | 25 | 13.9 | |
| Diabetes + Hypertension | 6 | 7.1 | 22 | 11.0 | 27 | 15.0 | |

Abbreviations: CRF, chronic renal failure (non-dialysis dependent); ESRD, end stage renal disease (dialysis dependent).

significantly higher than that of the CRF group (P = 0.005) (Table 3). There was a significant difference among the 3 groups in their scores with respect to orientation of time, orientation of place, attention and calculation, recall, language, and repetition, (P < 0.001). Moreover, ESRD patients had lower cognitive status than CRF (P < 0.001) and control group (P < 0.001) patients, but the scores of CRF and control groups were not significantly different (Table 3). Scores of the 3 groups were significantly different in complex commands (P = 0.004), and score of the control group was significantly higher than that of the CRF group (P = 0.001). However, the scores of ESRD patients and the control group patients (P = 0.060), as well as ESRD and CRF (P = 0.507) patients, were not significantly different (Table 3). Scores of the 3 groups were not significantly different in registration (P = 0.654) (Table 3).

## 5. Discussion

The findings of this study revealed that 62.3% of ESRD patients, 28% of CRF patients, and 21.2% of control patients had some degree of cognitive impairment. A significant correlation was found between dialysis and cognitive impairment level, and it was found that hemodialysis patients had more severe cognitive impairment.

Bossola et al. (2011) conducted a study on 80 hemodialysis patients and 160 elderly patients whose cognitive scores were measured at baseline and one year after the study using the MMSE. They found that one-year reduction in MMSE score was higher in hemodialysis patients and the higher percentage of hemodialysis patients changed from normal status to mild, moderate, and severe status (P < 0.001). They did not find another factor associated with reduced scores in hemodialysis patients and they concluded that reduced hemoglobin and cardiovascular comorbidities may affect this reduction (17).

Dahbour et al. (2009) measured MMSE scores in hemodialysis patients and the control group patients, and they found that scores before dialysis and 2 to 4 weeks later were significantly lower in hemodialysis patients compared to the control group, but the scores before and after dialysis were not significantly different in the dialysis patients (18).

Eslami Amirabadi et al. (2014) in their study on 189 patients suffering from renal failure in Tehran reported that cognitive impairment was common in these patients (It was seen in 47% of the cases) (19). Salehi et al. (2014) study results indicated the prevalence of mental disorders in hemodialysis patients (20). In a study conducted by Kalirao et al. (2011) on peritoneal dialysis patients, similar to hemodialysis patients, they found that two-thirds of patients had moderate to severe impairment. They recommended that these patients be evaluated before and after dialysis (21). In a study conducted by Pereira et al. (2007)

**Table 2.** Severity of Cognitive Impairment Distribution in Three Groups

| Severity of Cognitive Impairment | Group Name | | | | | |
|---|---|---|---|---|---|---|
| | ESRD Patients | | CRF Patients | | Control | |
| | n | % | n | % | n | % |
| **Severe (< 22)** | 24 | 28.2 | 2 | 1.0 | 1 | 0.6 |
| **Mild (22 - 26)** | 29 | 34.1 | 54 | 27.0 | 37 | 20.6 |
| **Normal (27 - 30)** | 32 | 37.6 | 144 | 72.0 | 142 | 78.9 |
| **Total** | 85 | 100 | 200 | 100 | 180 | 100 |

Abbreviations: CRF, chronic renal failure (non-dialysis dependent); ESRD, end stage renal disease (dialysis dependent).

**Table 3.** Mean ± SD (Standard Deviation) Scores of Eight Areas of Cognitive Function in Three Groups

| Areas of Cognitive Function | Group Name | | | P Value |
|---|---|---|---|---|
| | ESRD Patients | CRF Patients | Control | |
| **Orientation to time** | 3.67 ± 1.61 | 4.87 ± 0.36 | 4.9 ± 0.32 | < 0.001 |
| **Orientation to place** | 6.80 ± 0.63 | 4.99 ± 0.10 | 4.98 ± 0.17 | < 0.001 |
| **Registration** | 2.86 ± 0.54 | 2.92 ± 0.28 | 2.89 ± 0.31 | 0.654 |
| **Recall** | 2.61 ± 0.62 | 3.00 ± 0.07 | 2.99 ± 0.11 | < 0.001 |
| **Attention and calculation** | 3.32 ± 1.46 | 4.75 ± 0.67 | 4.80 ± 0.55 | < 0.001 |
| **Language** | 1.84 ± 0.43 | 1.97 ± 0.22 | 1.99 ± 0.07 | < 0.001 |
| **Repetition** | 0.79 ± 0.41 | 0.98 ± 0.16 | 0.97 ± 0.17 | < 0.001 |
| **Complex commands** | 3.95 ± 1.32 | 3.80 ± 1.38 | 4.27 ± 1.30 | 0.004 |
| **Total** | 23.84 ± 5.27 | 24.26 ± 1.94 | 27.80 ± 1.81 | < 0.001 |

Abbreviations: CRF: chronic renal failure(non-dialysis dependent); ESRD: end stage renal disease (dialysis dependent).

on 25 hemodialysis patients, all scores were MMSE > 24 and the patients had no history of cerebrovascular disease. They reported that mild cognitive impairment is common in these patients (22).

In our study, the score of ESRD patients in attention, calculation, and recall was lower than that in CRF patients and the control group patients, which is in line with the study conducted by Thimmaiah et al. (2012), who observed a significant reduction of attention and recall in dialysis people (23). In the study of Thimmaiah et al. (2012), 24 hours after dialysis, impairment of attention and recall was improved. Other studies also reported memory impairments in dialysis patients (8, 21, 24).

The present study also showed more severe language and function impairment in dialysis people, which is in line with the study conducted by Murray et al. (2006), who examined patients over 55 years as well as the study conducted by Gad et al. (2012) on dialysis people (8, 24).

According to the results, cognitive impairment is common in ESRD (dialysis dependent) patients, which is not often diagnosed or considered. However, its timely prevention and treatment can improve the patient's social and individual performance. On the other hand, due to the increasing prevalence of CRF and the effects of cognitive impairment on quality of life and mortality, its prevention and early diagnosis is highly important. Therefore, it is suggested that cognitive function of these patients be examined in all periodic examinations so that it can be diagnosed early and treated properly.

One limitation of this study was that using dietary supplements was confounding and despite the exclusion of patients who took them, it was not realized fully.

### 5.1. Conclusion

This study revealed that dialysis patients have more severe cognitive impairment than non-dialysis and control group patients. As the optimal cognitive function is a vital factor in promoting and maintaining the mental health and quality of life in hemodialysis patients, it is recommended that these patients be examined periodically for their cognitive function so that proper rehabilitation programs can be considered for these patients.

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## Footnotes

**Authors' Contribution:** Mohammad Reza Tamadon: study conception, design; Ali Reza Adibimehr: design, data gathering, writing the article; Raheb Ghorbani: study conception, design, data analysis, and writing the article.

**Conflict of Interest:** No conflict of interest was declared.

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