Evaluation of attention and memory function in hemodialysis patients; a study based on hemodialysis duration

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\textbf{ABSTRACT}

\textbf{Introduction:}
End-stage renal disease (ESRD) is one of the health problems in today’s world. Neuropsychological problems are more common in hemodialysis (HD) patients than in healthy individuals.

\textbf{Objectives:}
The aim of this study was to investigate the effect of long-term HD on memory function of these patients.

\textbf{Patients and Methods:}
Our study, included 80 HD patients of whom 39 were under 6 months of HD and 41 patients as another group which had a history of HD more than 6 months.

\textbf{Results:}
The population had a mean age of 51.60 years old (27.5% female). The scores of patients who have been hemodialyzed for a long-time (median time of HD was up to 4 years) had lower score in forward digit (FD), backward digit score test (BD), letter digit modality task (LDMT), letter symbol digit modality task (LSDMT) (5.49; 3.61; 21.12; 17.66) than the HD patients who underwent HD for a shorter term, with the median time of 3 to 5 months (7.38; 4.79; 39.77; 43.38) ($P<0.001$).

\textbf{Conclusion:}
The present study demonstrated that end-stage HD patients who were under HD for a long time had significantly lower scores in the memory and attention tests. However, additional researches are needed in this area.

\textbf{Implication for health policy/practice/research/medical education:}
ESRD patients who were under HD for a long time had significantly lower scores in the memory and attention tests.

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\textbf{Introduction}
In the last decades, by the advancement in renal replacement therapies, the survival of patients with kidney disease has significantly improved (1). Developments in medical technology and betterment in public health have brought about a progressive enhancement in the population undergoing hemodialysis (HD) (2), which increase the diagnosis of various types of psychological disorders in patients undergoing dialysis. One of the neuropsychological problems is cognitive impairment.

Cognitive impairment has more serious consequences such as hospitalization and reduced life expectancy. The consequences are even more severe in HD patients and may prevent the presence of treatment and also have some limitation for dialysis patients (3). Furthermore, studies show that patients undergoing dialysis for long-time have persistent cognitive impairment (4,5). Several studies have shown that HD patients have significant impairment on cognitive functions (6-8). Among various domains of cognition, memory and attention reported to be frequently affected (9,10). The impairment in memory and attention in patients with kidney disease may be related to disturbed brain function secondary to uremic toxins, and psychological distress (11-13).

Alzheimer’s disease as a mental and behavior disorder declines memory and attention (14). Dementia is a chronic medical condition presenting with the progressive decline in memory and limiting daily functions (15). Brain and kidneys are controlled by the cardiovascular system and are both affected by factors like high blood pressure. Therefore, it is normal that changes in one organ also reflect changes in other organs. Davey et al revealed that the prevalence of cognitive impairment in kidney patients is more than other people (16). Patients suffering from kidney impairment are at a higher risk for dementia (17,18). Although the literature is limited regarding the

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influence of HD on the risk of dementia, evidence suggests that the prevalence of cognitive impairment is relatively high in patients undergoing HD (6).

Several studies generally investigated cognitive functions in these patients (18-20). However, in the present study, attention and memory, as one of the most important symptoms of cognitive decline and Alzheimer’s disease have been studied. Additionally, the questionnaire applied in this study highlighted the areas of memory and attention in Iranian population.

**Objectives**
This study aimed to investigate the risk of decreasing cognitive function including attention and memory in relation to the duration of dialysis in HD patients.

**Patients and Methods**

**Population selection**
Of 98 HD patients aged 40 to 70, only 80 people responded to enter the research. It should be noted that patients with myocardial infarction, stroke, cerebral surgery, epilepsy and depression were excluded from the study. Data were collected from Ali-e-Ebne-Abitaleb and Khatamol-Anbia hospitals, in Zahedan, South-East of Iran.

**Instruments**
The Persian paper and pencil cognitive assessment package (PCAP), from the sections of forward digit, backward digit, letter-number sequence, letter-digit sequence and symbol digit modality task were used to gather information on socio-demographic data, attention and memory information. The instrument was administered by trained health in language (Dr. Hamed Ekhtiari) best understood by participants. The study was conducted over a 12-month period (March 2016 and April 2017).

**Measurements**
At first, two groups of HD patients from the mentioned hospital were selected. Patients were divided into two groups; (1) patients who were under HD less than 6 months and (2) patients who were under HD over 6 months.

Firstly, a Beck’s Depression Inventory test was conducted to determine whether patients had depression, and to ensure that, attention and memory function is not the result of symptoms of depression in patients. Attention and memory function were tested 24 hours after the last HD using forward digit, backward digit, letter-number sequence, letter-digit sequence and symbol digit modality tests from PCAP.

**Ethical issues**
The study was conducted in accordance with the principles of Declaration of Helsinki, 1996 version and its later amendments and also Good Clinical Practice standards. Each subject signed consent form before they were admitted into the study. Ethics approval was also received from Zahadan University of Medical Sciences and ethics committee (# IR.ZAUMS.REC.1395.361). Also, during the study, patients would be excluded from research if they did not consent to continue their research. The results of this study were presented to the patients.

**Data analysis**
The data were analyzed by SPSS version 20 (SPSS Inc., Chicago IL, USA). Standard descriptive statistics were applied to examine baseline demographic characteristics and cognitive values. Descriptive statistics were reported as mean ± standard deviation (SD) for continuous variables and as frequencies and proportions for categorical variables. Independent sample *t*-test was used to compare the groups and to show relation regression had been used.

**Results**
The data were available for 80 individuals. Table 1 shows the demographic and clinical characteristics of study participants. The 63.8% of patients were ≥55 years of age. The 72.5% of patients were male. Most of patients had under middle school degree 36 (45%), 20 (25%) patients had an academic degree (associate, bachelor, master and Ph.D. degree). The HD duration in 39 (48.7%) patients was under 6 month and 41 (51.3%) in patients over 6 months.

The variables (forward digit, backward digit, letter-number sequence, letter digit sequence modality test and Letter symbol digit modality task) used to evaluate memory and attention in HD patients are demonstrated in Table 2.

Forward digit score in patients who were under HD for less than 6 months was higher (7.35±1.35) compared to patients who had been under HD for more than 6 months.

### Table 1. Demographic and clinical characteristic among studied population

<table>
<thead>
<tr>
<th>Variables</th>
<th>No.</th>
<th>%</th>
<th>Means SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6 Months</td>
<td>39</td>
<td>48.7</td>
<td></td>
</tr>
<tr>
<td>&lt;6 Months</td>
<td>41</td>
<td>51.3</td>
<td>49.77±9.15</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>58</td>
<td>72.5</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>27.5</td>
<td>53.34±8.08</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under middle school</td>
<td>36</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>High school diploma</td>
<td>24</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Associate’s degree</td>
<td>2</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>16</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Masters or PHD</td>
<td>2</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6 Months</td>
<td>39</td>
<td>48.8</td>
<td>1.51± 0.503</td>
</tr>
<tr>
<td>&lt;6 Months</td>
<td>40</td>
<td>51.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: HD, hemodialysis.
to patients who were under HD for more than 6 months (5.49±0.92) (P<0.001). Additionally, backward digit mean score in less than 6 months patients was higher (4.75±1.27) than patients who had been under long-term HD (3.61±1.44). Letter-digit sequence in patients under HD of less than 6 months was higher (39.77±14.71) than patients that under HD of more than 6 months. Similarly, in symbol digit modality task less than 6 months patients scores were higher (43.38±18.02) compared to patients with up to 6 months of HD (17.66±6.73).

The result of regression test presented in Table 3 shows that the relationship between the duration of HD as independent variable with forward digit (FD), and letter symbol digit modality task (LSDMT) significantly inverse. As the HD time increases, FD and LSDMT decrease. However, in other variables [letter digit modality task (LDMT) and backward digit score test (BD)] there was no significant relationship.

### Discussion

In this cross-sectional investigation, we showed that cognitive function in particular memory and attention are lower in patients that underwent HD for a longer duration. Our results suggest that decline in attention and memory may be common in this population (8,21,22). We showed, long-term HD is associated with worse function of memory and attention tests. According to the study by Gholamzadeh et al, 7.85% of Iranian people were identified with cognitive impairment. However, the prevalence of Alzheimer’s disease was 2.3% (23). Reduction of attention and memory in HD patients may cause some limitations to attend in their dialysis schedules, give medications, fluid and dietary limitations and eventually lead to raised costs for dialysis unit care and hospitalization (20). Especially these items (memory and attention as the important factors of cognition) may influence their judgments and decisions (4).

The HD procedure may straightly bring to reduction of attention and memory by inducing cerebral ischemia. The acute intravascular volume loss and fluid shifts that happen throughout dialysis make cerebral edema and decline intracerebral blood pressure, blood speed, and cerebral perfusion (24,25). It is possible that cerebrovascular disease and underlying micro-vascular pathology (7), or mixed vascular cognitive impairment and Alzheimer’s disease appear to be more common in HD patients than Alzheimer’s disease alone (26).

Previous studies showed that long-term HD is linked to cognitive impairments (27). The strengths of our study include the prospective design in a large sample of HD patients, who do not have any cardiac and depression problems as a risk factor for declining attention and memory. We also applied an especial test, which assessed particularly, memory and attention for the Iranian population. The forward digit and backward digit tests measured auditory memory and attention in patients. Auditory memory enables efficiently attention and encoding and maintenance of relevant information in memory, at the expense of irrelevant information (28). By reducing attention and auditory memory, the ability to organize healthcare and patients’ lives will be affected. The letter-number digit sequence measures the visual memory of HD patients. In these tests, time has an important role in acquiring a score. In other words, patients had to take the test in a designated time and therefore had to pay attention and memorize tasks in a limited time and manage their stress in this situation. Given an increased risk of stress among individuals on renal dialysis, it is expected that performing these tasks is harder (29). The most significant difference in evaluations of attention and memory is related to letter symbol digit modality task. This trend could be the result of the complexity of this test and needs more attention and visual memory. In fact, in this test patients should match unfamiliar sign with the numbers and this makes the test harder for them (30). Based on regression-model, our results demonstrate associations between duration of HD with memory and attention.

### Table 2. Variables which evaluated memory and attention in hemodialysis patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>HD Duration</th>
<th>Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;6 Months</td>
<td>&gt;6 Months</td>
<td></td>
</tr>
<tr>
<td>FD</td>
<td>7.38±1.35</td>
<td>5.49±0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BD</td>
<td>4.79±1.26</td>
<td>3.61±1.44</td>
<td>&lt;0.14</td>
</tr>
<tr>
<td>LDMT</td>
<td>39.77±14.71</td>
<td>21.12±7.14</td>
<td>&lt;0.016</td>
</tr>
<tr>
<td>LSDMT</td>
<td>43.38±18.02</td>
<td>17.66±6.73</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Abbreviations: FD, forward digit; BD, backward digit; LDMT, letter digit sequence modality task; LSDMT, Letter symbol digit modality task.

### Table 3. Regression analysis of HD duration with attention and memory in HD patients

<table>
<thead>
<tr>
<th>Model (HD time)</th>
<th>F</th>
<th>t</th>
<th>Adjusted R2</th>
<th>Beta</th>
<th>R2</th>
<th>P value</th>
<th>Dependent variables</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>27.35</td>
<td>-4.515</td>
<td>0.572</td>
<td>-0.422</td>
<td>0.593</td>
<td>0.000</td>
<td>FDST</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-1.372</td>
<td></td>
<td>-0.113</td>
<td></td>
<td>0.174</td>
<td>BDST</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-3.125</td>
<td></td>
<td>-0.419</td>
<td></td>
<td>0.003</td>
<td>LSDMT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-.179</td>
<td></td>
<td>-0.026</td>
<td></td>
<td>0.858</td>
<td>LDMT</td>
</tr>
</tbody>
</table>
Conclusion
We relied on neuropsychological assessment alone to define memory and attention status. Despite this limitation, our findings suggest a reduction of auditory and visual memory in HD patients. Extended insight among clinicians on the effects of cognitive impairment on daily function; quality of life; and medication, fluid, and dietary compliance is needed. Additionally, more studies are needed to illuminate the pathways that are involved in cognitive impairment in patients with kidney disease. In clinical practice, cognitive testing is regularly performed in order to detect cognitive impairment in patients undergoing dialysis.

Limitations of the study
Our investigation is restricted by its cross-sectional design and therefore, the causal associations could not be established. Hence, we suggest longitudinal studies in a larger population. The strength of this investigation lies in the homogeneity of the Baloochi and Zaboli population in the South-East of Iran.

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Authors’ contribution
NMB, AA and BS conceived the idea of this publication. AA and BS performed the data collection. BS, AAM and NMB contributed to the literature review, data analysis, and review of the article for final publication.

Conflicts of interest
The authors declare that there is no conflict of interest.

Ethical considerations
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References

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