ABSTRACT

Background: The number of elderly patients undergoing hemodialysis is rising. There are several studies already that show the high prevalence of cognitive impairment in the elderly hemodialysis population and that (CKD) itself can be an independent risk factor for cognitive impairment.

Objective: To describe Mini-Mental Status Examination profile of elderly Filipino hemodialysis patients, age 60 years old and above.

Methods: Thirty-one hemodialysis patients, aged 60 years old and above were recruited from 4 different outpatient dialysis centers. All underwent a questionnaire-based interview and were evaluated using the Mini-Mental Status Examination (MMSE). All data were processed and summarized using descriptive statistics. Pearson correlation was computed.

Results: Out of the study cohort, 32.2% had MMSE scores <24, suggestive of possible dementia while 45.2% had scores from 24-26, suggestive of mild cognitive impairment. Age, previous stroke, hypothyroidism and atrial fibrillation were negatively correlated with the MMSE score (i.e. predisposes to cognitive impairment) while serum albumin and use of phosphate binders were positively correlated with MMSE scores (i.e. decreased predisposition to cognitive impairment).

Conclusion: Cognitive impairment is prevalent among the elderly hemodialysis patients in the outpatient setting, as shown by the MMSE scores obtained. A number of variables have been shown to have correlations with cognitive impairment. Larger studies are needed to further elucidate these relationships and define the true prevalence of cognitive impairment in this special group.

INTRODUCTION

The absolute number of elderly patients, starting hemodialysis continues to increase internationally; it averages an annual increase of 9.8% in the initiation of hemodialysis for the 80- and 90-year-old population.

One of the most dreaded geriatric syndromes is cognitive impairment and this becomes particularly prevalent as one ages. The prevalence of cognitive impairment in patients with end-stage renal disease is almost twice that of the general population. Most studies documents this at 1-6%. As early as the 1970s, deficits in several cognitive performance examinations were already noted in hemodialysis patients.

Baseline cognitive function was poorer and the decline in cognitive function was greater in patients with lower estimated glomerular filtration rate. Odds ratio was estimated at 1.91 for patients with eGFR of <45 ml/min at baseline. There is also a significant graded risk for cognitive impairment associated with the severity of the CKD. Age in this case adds greater risk on patients with cognitive impairment. Even adjusting for all the laboratory and baseline comorbidities of patients, the odds ratio of cognitive impairment on follow-up is still as high as 2.43. As such, chronic kidney disease might be an independent risk factor for cognitive impairment.

Even in CKD patients who are not yet on hemodialysis and had scored more than 24 in the Mini-Mental Status Exam (suggesting the lack of dementia), there are detectable changes in the electroencephalogram. Assessment of cognitive event-related potentials, specifically the prolongation of the P3 wave latency, has been shown to be the earliest sign of cognitive impairment in metabolic encephalopathies. It was significantly prolonged in patients with CKD stage 4-5 (undialyzed). It was also positively correlated with serum creatinine, blood urea nitrogen and serum uric acid. On the other hand, it is negatively correlated with haemoglobin and glomerular filtration rate. However, in this situation, creatinine and urea only serve as markers for the presence of other neurotoxic substances in
patients with stage 4-5 chronic kidney disease. Using a modified MMSE, CKD was associated with poorer baseline scores, and is associated with development of cognitive impairment at follow-up and with advancing disease.9

There are notable changes in the brain of patients with chronic kidney disease, even in “stroke-free” patients. In particular, magnetic resonance imaging (MRI) reveals white matter hyperintensities, which are partly explained by vascular dysfunction.21 These same findings are clinically correlated with hypertension, diabetes, cardiac disease and total homocysteine. It was not mentioned however if white matter hyperintensity is also correlated with cognitive impairment. However, it may again provide another pathway or serve as an imaging marker for the evolution of cognitive impairment in chronic kidney disease patients.

Dementia was associated with an increased risk of death (relative risk 1.48, 95%CI 1.32-1.66) and hemodialysis withdrawal (RR 2.01 95%CI 1.57-2.57).7 In other studies, the presence of dementia increases the chances of withdrawal from dialysis even more (RR 3.7 95%CI 1.1-12.7).5 The presence of cognitive impairment will therefore add to the cost and eventual burden of care for the patient. The decision regarding treatment, or possible withdrawal from treatment, will be affected.

With the above in mind, this study was undertaken to describe the cognitive profile of a small cohort of elderly Filipino hemodialysis patients.

OBJECTIVES

General

To describe Mini-Mental Status Examination profile of elderly Filipino hemodialysis patients, age 60 years old and above.

Specific

1. To determine the baseline demographic, medical history, chronic kidney disease and dialysis history and pertinent medication history of recruited elderly Filipino hemodialysis patients.

2. To evaluate the cognition of the recruited patients using the Mini-Mental Status Examination (MMSE).

3. To summarize/tabulate the gathered data.

4. To calculate for any correlations between the obtained MMSE scores and the various variables obtained.

MATERIALS AND METHODS

Patients

Patients 60 years old and above with chronic kidney disease of any etiology and undergoing outpatient hemodialysis of any frequency and duration were recruited from 4 private hemodialysis centers (3 in Metro Manila, 1 in Isabela). Identified patients were recruited on “as-they-come” basis in order to recruit as many patients as possible. An Informed Consent Form was provided and all patients included gave their informed consent to participate in the study (Appendix A). Excluded from the study are those with severe visual and hearing impairment, with an acute illness, currently confined and undergoing in-patient hemodialysis, had a cardiopulmonary arrest within the last 3 months, those with a previous psychiatric condition, those who had an intradialytic hypotension or arrhythmia resulting in acute confusion and those who did not give consent for the study.

Data Gathering

Patients responded to an interview-based questionnaire and other data gathered were obtained from their relatives/watchers or from their medical records. Ideally, the patients should be interviewed 24 hours after their last hemodialysis session minimize confounding effects of the hemodialysis session itself. However, due to logistic restrictions, patients were interviewed after the 1st 2 hours of their hemodialysis session, as was done in several studies. The following data were obtained: age, sex, ethnicity, educational level, comorbidities (hypertension, angina/ischemic heart disease, previous myocardial infarction, hypercholesterolemia, hypertriglyceridemia, atrial fibrillation, heart failure, previous stroke, previous cardiopulmonary arrest, diabetes mellitus, hyper-/hypothyroidism, liver cirrhosis, CNS infections and head trauma), alcohol intake, smoking, CKD etiology, interval between diagnosis of CKD and initiation of hemodialysis, time on hemodialysis, KT/V, use of aluminium-containing phosphate binders, symptoms of restless legs syndrome, laboratory results within 1 month of the interview (haemoglobin, serum creatinine, BUN, serum albumin, serum calcium, serum phosphorus, LDL, HDL, total cholesterol, use of benzodiazepines for sleeplessness, use of antihistamines for pruritus or sleeplessness and antihypertensive used (Appendix B).
Cognitive Testing

The investigators administered the Folstein Mini-Mental Status Examination to screen for cognitive impairment among the patients. To maintain sensitivity and specificity, the investigators followed the recommended script, timing and scoring of responses as specified for the MMSE. General domains tested in the MMSE are orientation, registration, attention and calculation, recall and language. Scores of 27-30 are generally considered normal, 24-26 as mild cognitive impairment and those less than 24 as possible dementia.

Statistical Analysis

SPSS 16.0 for Windows (SPSS Inc.) was used for statistical analysis. Descriptive statistics were done to summarize the data obtained. Pearson’s correlation coefficient between MMSE and the other variables was computed to check for any correlations.

RESULTS

A total of 31 patients were recruited for this study from December 2008-January 2009.

Table I summarizes the data regarding demographics, medical history and laboratory values. More than half of the number of patients are less than 70 years old, male. Tagalog regionalization and have an educational level up to high school only.

Table I. Summary of Demographic Data of Interviewed Hemodialysis Patients, 60 Years Old and Above

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>%</th>
<th>mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-64 years old</td>
<td>13</td>
<td>41.9</td>
<td></td>
</tr>
<tr>
<td>65-69 years old</td>
<td>9</td>
<td>29.0</td>
<td></td>
</tr>
<tr>
<td>70-74 years old</td>
<td>6</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>75-79 years old</td>
<td>2</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>80 years old and above</td>
<td>1</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18</td>
<td>58.9</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>13</td>
<td>41.1</td>
<td></td>
</tr>
<tr>
<td>Regionalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tagalog</td>
<td>18</td>
<td>58.1</td>
<td></td>
</tr>
<tr>
<td>Ilocano</td>
<td>7</td>
<td>22.6</td>
<td></td>
</tr>
<tr>
<td>Bisaya</td>
<td>2</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Kapampangan</td>
<td>2</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Bicolano</td>
<td>1</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Ilonggo</td>
<td>1</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 years (e.g. elementary level)</td>
<td>2</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>6-10 years (elementary graduate to high school level)</td>
<td>15</td>
<td>48.4</td>
<td></td>
</tr>
<tr>
<td>College level</td>
<td>8</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>4</td>
<td>12.9</td>
<td></td>
</tr>
<tr>
<td>Postgraduate</td>
<td>2</td>
<td>6.5</td>
<td></td>
</tr>
</tbody>
</table>

Table II summarizes pertinent previous medical history. Most patients are hypertensive, hypercholesterolemic, diabetic and have ischemic heart disease. More than half are either former occasional or regular drinkers, although all of them have stopped drinking alcohol. Less than half are smokers.

Table II. Pertinent Comorbid Conditions Noted in Interviewed Hemodialysis Patients, 60 Years Old and Above

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>31</td>
<td>100.0</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>17</td>
<td>54.8</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15</td>
<td>48.4</td>
</tr>
<tr>
<td>Ischemic heart disease/angina</td>
<td>15</td>
<td>48.4</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>Heart failure</td>
<td>4</td>
<td>12.9</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>4</td>
<td>12.9</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>Head trauma</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>CNS infection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Previous CP arrest</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>11</td>
<td>35.5</td>
</tr>
<tr>
<td>Former occasional (1-2 beers or 1 shot hard liquor per month)</td>
<td>5</td>
<td>16.1</td>
</tr>
<tr>
<td>Former regular (more than 1-2 beers or 1 shot hard liquor per month)</td>
<td>15</td>
<td>48.4</td>
</tr>
<tr>
<td>Currently drinking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>18</td>
<td>58.1</td>
</tr>
<tr>
<td>&lt;10 pack years</td>
<td>5</td>
<td>16.1</td>
</tr>
<tr>
<td>10-30 pack years</td>
<td>3</td>
<td>9.7</td>
</tr>
<tr>
<td>&gt;30 pack years</td>
<td>5</td>
<td>16.1</td>
</tr>
</tbody>
</table>

Table III shows pertinent data regarding their chronic kidney disease and hemodialysis history. Majority of patients included in the study have diabetic nephropathy, started hemodialysis either within a month or after 6 months of diagnosis of CKD, have been on hemodialysis for more than a year and dialyzed 2x a week. Most patients have a KT/V of at least 1.2 for the last measured dialysis session. About a third of the patients have used aluminium-based phosphate binders. Almost half of the patients complain of “restless legs syndrome.”
Table III. Pertinent Chronic Kidney Disease History in Interviewed Hemodialysis Patients, 60 Years Old and Above

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM nephropathy</td>
<td>16</td>
<td>51.6</td>
</tr>
<tr>
<td>Hypertensive nephrosclerosis</td>
<td>10</td>
<td>32.3</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>3</td>
<td>9.7</td>
</tr>
<tr>
<td>Gouty nephropathy</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>Interval between CKD diagnosis and initiation of HD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 1 month</td>
<td>12</td>
<td>38.7</td>
</tr>
<tr>
<td>1-6 months</td>
<td>7</td>
<td>22.6</td>
</tr>
<tr>
<td>&gt;6 months</td>
<td>12</td>
<td>38.7</td>
</tr>
<tr>
<td>Months on hemodialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 months</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>6-12 months</td>
<td>7</td>
<td>22.6</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>16</td>
<td>51.6</td>
</tr>
<tr>
<td>Hemodialysis frequency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2x/week</td>
<td>26</td>
<td>83.9</td>
</tr>
<tr>
<td>3x/week</td>
<td>5</td>
<td>16.1</td>
</tr>
<tr>
<td>KT/V during a completed HD session within 30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1.2</td>
<td>3</td>
<td>9.7</td>
</tr>
<tr>
<td>1.2 and higher</td>
<td>20</td>
<td>64.5</td>
</tr>
<tr>
<td>Use of aluminium-based phosphate binders</td>
<td>10</td>
<td>32.3</td>
</tr>
<tr>
<td>Symptoms of restless legs syndrome</td>
<td>14</td>
<td>45.2</td>
</tr>
</tbody>
</table>

Table IV shows selected laboratory results obtained within 1 month of the interview. Patients are generally anemic and below the recommended haemoglobin levels for hemodialysis patients. Creatinine and blood urea nitrogen (BUN) levels are typical for hemodialysis patients, although BUN is marked elevated. Albumin levels are for the most part within acceptable limits. Serum calcium is likewise acceptable while phosphorus levels are elevated. Only 3 patients have measured LDL and HDL levels. This may be due to the fact that these labs are not included in the usual monthly periodic assessment package of the partner diagnostic center.

Table IV. Selected Laboratory Parameters in Interviewed Hemodialysis Patients, 60 Years Old and Above

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>30</td>
<td>9.99 ± 1.95</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>30</td>
<td>7.64 ± 2.94</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>28</td>
<td>57.33 ± 15.50</td>
</tr>
<tr>
<td>Serum albumin (mg/dl)</td>
<td>26</td>
<td>3.89 ± 0.50</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)</td>
<td>22</td>
<td>9.50 ± 1.34</td>
</tr>
<tr>
<td>Serum phosphorus (mg/dl)</td>
<td>26</td>
<td>5.78 ± 1.87</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>3</td>
<td>82.78 ± 30.56</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>3</td>
<td>54.87 ± 9.99</td>
</tr>
</tbody>
</table>

Table V summarizes some of the medications used by the interviewed patients. Of particular focus is the use of medications with neuropsychological properties like benzodiazepines and antihistamines. Antihypertensive used are also summarized below.

Table V. Summary of Selected Medications Used By Interviewed Hemodialysis Patients, 60 Years Old and Above

| Use of benzodiazepines for sleeplessness | 6 | 19.4|
| Use of antihistamines for sleeplessness or pruritus | 6 | 22.6|
| Antihypertensive used                  |   |   |
| Calcium channel blockers              | 25| 80.6|
| Beta blockers                        | 13| 41.9|
| ARBs                                | 12| 38.7|
| Clonidine                           |  9|  29.0|
| ACEI                                |  1|  3.2|

Table VI summarizes the MMSE scores obtained by the patients included in the study. The table also summarizes the details of the score per domain tested. The language domain is further broken down to its component tasks. Mean MMSE score noted is 23.45 with 45.2% of the recruited patients having scores ranging from 24-26 (suggesting possible mild cognitive impairment). About 32.2% of the patients have scores <24, suggesting possible dementia.

Table VI. Summary of Mini-Mental State Examination Results in Interviewed Hemodialysis Patients, 60 Years Old and Above

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>31</td>
<td>23.45 ± 5.19</td>
</tr>
<tr>
<td>&lt;24</td>
<td>10</td>
<td>32.2</td>
</tr>
<tr>
<td>24-26</td>
<td>14</td>
<td>45.2</td>
</tr>
<tr>
<td>27 and above</td>
<td>4</td>
<td>22.6</td>
</tr>
<tr>
<td>Orientation</td>
<td>31</td>
<td>8.29 ± 2.09</td>
</tr>
<tr>
<td>9-10</td>
<td>21</td>
<td>67.6</td>
</tr>
<tr>
<td>7-8</td>
<td>5</td>
<td>16.2</td>
</tr>
<tr>
<td>6 and lower</td>
<td>5</td>
<td>16.2</td>
</tr>
</tbody>
</table>

(Table VI continue next page)
Table VII summarizes the obtained Pearson Correlation Coefficients calculated from available data of the different variables in relation to the Mini-Mental Status Examination. Variables were excluded from the analysis if data was available for less than 50% of the recruited patients. As can be seen from the table, there is a significant positive correlation between the MMSE score, aluminium-based phosphate binders and serum albumin levels. Significant negative correlation was noted between MMSE, atrial fibrillation, previous stroke and hypothyroidism. Correlation was not computed for the hypertension variable since all of the patients are hypertensive.

**DISCUSSION**

At present, this study is the first attempt to describe the cognitive profile of Filipino elderly hemodialysis patients using the Mini-Mental Status Examination. Even in the general population, the prevalence of dementia is vastly underestimated and often relegated to the effects of aging. Physicians often ignore its presence in their patients, or not assess due to the multiplicity of other comorbidities. Most doctors are also not familiar with the evaluation of cognitive function of patient, especially during bedside rounds.

Cognitive impairment is a prevalent condition in this study cohort. About a third presented with
an MMSE score consistent with possible dementia and almost half have a score consistent with mild cognitive impairment. The results are similar to the previously noted studies on cognitive impairment in dialysis patients, although the fact that this study focused on the elderly cohort greatly overestimates the resulting percentage.

The effect of timing of the MMSE could not be evaluated as all patients were examined 2 hours into the dialysis. This is because examination 2 hours into the dialysis is the most logistically feasible timing for the investigators. Ideally, evaluation 24 hours after the last hemodialysis is the optimal time for examination.

Age is a well-defined independent risk factor for cognitive impairment. The computed Pearson correlation is consistent with the adjusted OR for dementia of 1.94 for patients 60-74 years old and 4.40 for those 75 years old and older.

Serum albumin levels are positively correlated with MMSE scores which is again consistent with the odds ratio for dementia of 2.06 for patients with hypoalbuminemia. Other studies also support this correlation with albumin levels. Previous stroke is negatively correlated with MMSE score and again it is consistent with an OR of 5.15 for cerebrovascular disease. The negative correlation between atrial fibrillation and MMSE might be related to the positive correlation of atrial fibrillation with strokes. Hypothyroidism is one of the known secondary causes of reversible cognitive impairment.

No correlation with cognitive impairment and anemia was noted for this cohort, in contrast to that noted by Kurella in 2006 wherein a haemoglobin of <10 g/dl has an odds ratio of 1.24 for dementia. This lack of correlation persists even after transforming the results of this cohort, using a cut-off of 10 g/dl of haemoglobin as the definition of anemia. It is worthy to mention that anemia can predispose to cognitive impairment in other studies involving the elderly. Although the fact that this study focused on the elderly cohort greatly overestimates the resulting percentage.

The lack of correlation between BUN and creatinine and cognitive impairment may be attributable to the low sample size or attenuation of other variables. Sarcopenia is a common geriatric syndrome in the elderly and the resultant lower muscle mass results in relatively lower creatinine levels for the stage of chronic kidney disease. The lack of correlation with regards to the CKD-related variables like dialysis vintage (i.e. length of time on hemodialysis) may again be related to the small sample size. However, vintage has been mentioned as a possible risk factor for cognitive impairment as mentioned in reviews. The equilibrated KT/V in this study had not computed correlation, in contrast to other studies wherein it is positively correlated with cognitive impairment.

A somewhat surprising result is the positive correlation between previous use of aluminium-containing phosphate binders and MMSE score. Aluminum toxicity predisposes to cognitive impairment and is one substance being implicated in the development of Alzheimer’s disease. One way to interpret this is that the intermittent intake of aluminium to lower phosphorus either attenuates the effects of other risk factors that lead to cognitive impairment, e.g. by lowering phosphorus levels, or this might just be a sampling bias.

Almost half of the study cohort had a MMSE score of 24-26. This is significant in that this is the population that is at high risk for further cognitive deterioration and consequent development of dementia. These will be the patients that will have significant cognitive impairment in the future, assuming that regular dialysis and control of their other medical conditions prolong their lives significantly.

The lack of significant association between cognitive impairment and the other variables tested was similar to other studies. However, the study cohort is small and not adequately powered, so any correlations may be underestimated at this point. For example, with regard to hypercholesterolemia or hypertension, there may be other risk factors at play through which these variables will affect cognition. Time dependency may also come into play with most of these factors. About 60% of the cohort is less than 70 years old and as such, may not have been exposed to the combination of CKD and other risk factors long enough to manifest cognitive impairment at this time. There may also be inherent genetic differences that modify any existing association. The influence of cholesterol for example is affected by the genotype of the apolipoprotein itself, particularly ApoE4, which was not tested in these patients. The use of benzodiazepines and clonidine, has a trend towards a negative correlation with MMSE scores, although not significant after mathematical assessment. These two medications are often implicated agents in delirium.
LIMITATIONS AND RECOMMENDATIONS

Only a small cohort was recruited for this study and the true prevalence of cognitive impairment may be overestimated.

Although the Mini-Mental Status Examination is adequately sensitive to detect the presence of cognitive impairment, it is not sufficiently specific to describe all of the aspects of a person’s cognitive function. It is also open to false negative results, especially in patients with a high premorbid educational attainment. Also, adjustment for educational background was not done, in fulfillment of the previously defined method of scoring the MMSE. Future studies may therefore include the use of more extensive instruments or evaluation scales in assessing cognitive function. As delirium, both acute and chronic, is a distinct possibility in these patients, and can affect the MMSE in a similar fashion, concurrent use of a diagnostic modality like EEG can help in further distinguishing the etiology of the cognitive impairment. The EEG may also help detect cognitive impairment in patients with acceptable MMSE scores.

Ideally, the patients should be evaluated 24 hours after the last hemodialysis session to minimize the effects of the dialysis process itself on the evaluation of cognition. This can be a tedious process that requires extensive manpower and other logistic resources.

The investigators did not assess for the presence of mood disorders, especially depression, which can significantly affect the MMSE score, a phenomenon called pseudodementia. This may also be included in future studies.

The study is inadequately powered to predict any causality among the tested variables in this study. It would be helpful if all of the laboratory parameters were available in all patients. Also other laboratory parameters like plasma homocysteine and C-reactive protein were not considered in the evaluation since these labs are not routinely extracted in monthly patient assessments. The patients are currently included in a larger ongoing study that will attempt to predict possible causality between the variables and cognitive impairment.

Despite the small size of our cohort, the investigators recommend routine screening of cognitive impairment in elderly hemodialysis patients. The detection of cognitive impairment will help facilitate proper treatment and rehabilitation of these patients. It will also aid in decision making regarding future management of the patient, especially regarding issues of withdrawal of treatment and the formulation of advance directives. The information gathered in future larger studies will help in revising the recommendations for treatment with hemodialysis and hopefully aid in the discovery of better dialysis regimens or modalities.

CONCLUSION

Cognitive impairment is a prevalent condition among elderly patients, more so in the elderly outpatient hemodialysis patient, as shown by the MMSE scores obtained. The results have similarities to bigger studies done internationally. Several variables, like age, previous history of stroke and albumin levels have a positive correlation with cognitive impairment, similar to that found in other studies. The positive correlation of aluminum-based phosphate binders and MMSE scores should be interpreted with caution since aluminium exposure is an identified risk factor for cognitive impairment. It might just be an effect of sampling bias. Further studies are needed, involving larger cohorts of patients to define the actual prevalence of cognitive impairment and identify its risk factors in the outpatient hemodialysis patients.

ACKNOWLEDGEMENT

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REFERENCES


APPENDIX A
INFORMED CONSENT USED DURING RECRUITMENT

INFORMED CONSENT FORM
IDENTIFICATION OF COGNITIVE IMPAIRMENT AND ITS POSSIBLE RISK FACTORS AMONG ELDERLY HEMODIALYSIS PATIENTS

Panimula:

Kayo po ay malugod na inaanyayahan na lumahok sa isang pananaliksik tungkol sa problema sa memorya or pag-uuliyanin (cognitive impairment) at mga kundisyong posibleng nagdulot nito sa mga pasyenteng edad 60 at pataas na naghe-hemodialysis. Ang pagkakaroon ng problema sa memorya o pag-uuliyanin ay tumataas habang nagkaka-edad. Marami ring ibang mga kundisyong pwedeng magdulot ng problema sa memorya tulad ng ibang mga sakit at mga kemikal. Ang kumbinasyon ng sakit sa bato, pag-hemodialysis, problema sa memorya at iba pang mga sakit ay maraming implikasyon sa pasyente, pamilya at sa lipunan. Layunin ng pananaliksik na ito ay upang lalong mapaganda ang kalidad ng panggagamot at pag-aalaga sa mga pasyenteng tulad ninyo.

Kung sakaling kayo po ay pumayag na lumahok sa pananaliksik na ito, ang inyong memorya ay susuriin sa pamamagitan ng MINI-MENTAL STATUS EXAMINATION (MMSE), isang questionnaire na binubuo ng ilang mga katanungan upang malaman kung may problema sa memorya ang isang pasyente. Ang MMSE ay simpleng gawin, at hindi kinakailangan gawan ng kahit anong examination sa laboratoryo. Walang gamut na ibinibigay sa inyo at wala po tayong inaasahan na mga side effect sa gagawin nating pagsusuri.


Maaring lumahok sa pananaliksik na ito kung ikaw ay:

- Pasyenteng edad 60 taong gulang at pataas, at kahit anong kasarian, at katayuan sa buhay.
- May permanenteng pinsala sa bato (kahit ano ang sanhi at tagal ng sakit) at nangangailangan ng panghabambuhay at regular hemodialysis (kahit anong “schedule” at dalas ng “session”) bilang outpatient.
- Pumirma sa Informed Consent at pumapayag na makapanayam, sumailalim sa Mini-Mental Status Examination at masuri ang medical records.

Hindi maaring lumahok sa pananaliksik na ito kung:

- Ayaw pumirma sa Informed Consent, ayaw pumapayag na makapanayam, ayaw sumailalim sa Mini-Mental Status Examination at ayaw masuri ang medical records.
- in-patient o kasalukuyang naka-“confine” sa ospital
- grabeng pagkabingi at pagkabulag
- cardiopulmonary arrest sa loob ng 3 buwan
Kung pumayag kang lumahok, ang mga sumusunod ang gagawin:

- Kayo ay susuriin gamit ang MMSE 1 oras pagkatapos mag-umpisa ng inyong hemodialysis session o 1 oras pagkatapos matapos ng hemodialysis (tatagal ito ng 10-15 minutes)
- Isang maiksing panayam tungkol sa heneral na impormasyon
- Pagsusuri ng mga impormasyon sa inyong medical records.

Ano ang mga benepisyo sa gagawing MMSE?

- Madaliang madidiskubre kung may mga sintomas ng mga problema sa memory

Ano ang hindi nyo makukuha sa pagsali sa pananaliksik na ito?

- Walang benepisyong pinansyal na maibibigay ang mga mananaliksik para sa inyong paglahok; ang inyong pagsali ay kusang-loob ninyong ginawa para sa ikabubuti ng ating kaalaman.

May mga kumplikasyon ba na mangyayari sa akin o problema sa “privacy” sa aking pagsali?

- Dahil ang MMSE ay isang questionnaire at walang anumang gagawing ibang mga laboratoryo sa mga sasali, walang kumplikasyon na mangyayari.
- Sinisigurado namin ang “privacy” ng inyong pagkatao at mga impormasyon na malalaman namin sa pananaliksik na ito. Hindi makikita ang inyong pangalan at lahat ng mga pribadong sensitibong impormasyon sa mga dokumentong ilalathala sa mga siyentipikong babasahan (scientific journals), pagtitipon (scientific meetings/conferences/symposia) at iba pang tipo ng mga paglalathala.
- Ang mga impormasyong medikal na aming pag-aaralan at susuriin at makikita sa aking pagsali ay ang lahat ng mga impormasyon na madidiskubre ditto ang mga personal na impormasyon sa aking pagkatao at mga pagkatao at susuriin.
- Ang mga kumplikasyon na mangyayari o problema sa “privacy” ay hindi makikita sa aking pagsali.

CONSENT

Ako si (Pangalan ng Pasyente) _______________________________, na nakatira sa (Address ng Pasyente) ________________________________________, pagkatapos basahin ang mga panimulang impormasyon at susuriin ang aking pagsali. Pumasabing:

PUMAPAYAG AKO na sumali sa pananaliksik na ito.
PUMAPAYAG AKO na makapanayam tungkol sa mga heneral na impormasyon.
PUMAPAYAG AKO na suriin ang aking mga medical records.
NAILINTIDIHAN KO na walang kumplikasyon akong mararanasan sa aking pagsali.
NAILINTIDIHAN KO na ang lahat ng impormasyon medical na madidiskubre ditto ay maaaring gamitin sa anumang paglalathala sa mga pag-aaral na ito.
NAILINTIDIHAN KO na sinisiguro ng mga mananaliksik na mabibigyan ako ng kaukulang privacy at hindi magagamit ang aking pangalan at anumang personal na impormasyon sa mga paglalathala ng pag-aaral na ito.
NAILINTIDIHAN KO na kusang loob akong sumali sa pananaliksik na ito ng walang inaasahang benepisyong material o pinansyal.

Pirma ng Pasyente: _________________________________
Petsa: _________________________________________
Buong Pangalan: _________________________________
APPENDIX B
SAMPLE QUESTIONNAIRE USED TO EVALUATE RECRUITED PATIENTS

QUESTIONNAIRE
IDENTIFICATION OF COGNITIVE IMPAIRMENT AND ITS POSSIBLE RISK FACTORS
AMONG ELDERLY HEMODIALYSIS PATIENTS

Code: __________________________
Name of Patient: __________________________
Address: __________________________
Contact No.: __________________________
Informant other than the Patient: __________________________
Contact No. of Informant: __________________________
Date and Time of Evaluation: __________________________
Relationship of Evaluation to Hemodialysis Session: ☐ 2 hours into HD ☐ 1 hour after HD termination

Demography:
Age: ________ ☐ 60-64 yo ☐ 65-69 yo ☐ 70-74 yo ☐ 75-79 yo ☐ 80 yo and up
Sex: ☐ Male ☐ Female
Ethnicity: ☐ Tagalog ☐ Ilocano ☐ Muslim
☐ Bisaya ☐ Ilonggo ☐ Mixed with Caucasian
☐ Waray ☐ Bicolano ☐ Mixed with Chinese
Education: ☐ no formal education
☐ <6 years (e.g. elementary level)
☐ 6-10 years (e.g. elementary graduate – high school level)
☐ College level
☐ College graduate
☐ Postgraduate/masteral/doctoral

Previous Medical History:
Co-morbidities: ☐ Hypertension ☐ Stable Angina ☐ Previous MI ☐ hypercholesterolemia
☐ Diabetes Mellitus ☐ Heart Failure ☐ Previous Stroke ☐ hypertriglyceridemia
☐ Atrial Fibrillation ☐ previous CP arrest ☐ Liver Cirrhosis ☐ Head Trauma
☐ CNS infections ☐ hyperthyroidism ☐ hypothyroidism

Alcohol Intake: ☐ Never
☐ Former occasional (1-2 beers or 1 shot of hard liquor per month or less)
Former regular (more than 1-2 beers or 1 shot of hard liquor per month)
Currently drinking

Smoking:
- never
- 10-30 pack years
- <10 pack years
- >30 pack years

ESRD History:
Etiology of ESRD:
- hypertensive
- DM nephropathy
- PCKD
- CGN
- obstructive uropathy
- vasculitic (e.g. SLE)
- CPN
- NSAID nephropathy
- others ________

Interval between CKD diagnosis and initiation of hemodialysis:
- Less than 1 month
- 1-6 months
- >6 months

Months on hemodialysis:
- 0-6 months
- 6-12 months
- >12 months

eKt/V within the last 30 days:
- <1.2
- 1.2 and higher

use of aluminum-based phosphate binders:
- yes
- no

symptoms of restless legs syndrome:
- yes
- no

Laboratories:
Hemoglobin:
- <12.0
- 12.0 and above

Serum creatinine:

BUN:

Serum albumin:

Serum calcium:

Serum phosphorus:

LDL:

HDL:

Total cholesterol:

Medications:
Use of benzodiazepines for sleeplessness:
- yes
- no

Use of antihistamines for sleeplessness or pruritus:
- yes
- no

Antihypertensive used:
- Calcium channel blockers
- ARBs
- clonidine
- Beta blockers
- ACEi
- others: ________________

Mini-Mental Status Examination:
Handedness:
- left
- right

Orientation:
- Year:
- Date:
- Month:
- Day:
- Season:
- Country:
- Province:
- Town:
- Center:
- Floor

Registration:
- Paper
- Table
- Apple

Attention and Calculation:
- 93
- 86
- 79
- 72
- 65 or
- D
- L
- R
- O
- W or
- O
- D
- N
- D
- M

Recall:
- Paper
- Table
- Apple

Language:
- Pen/Pencil
- Watch
Repeat “NO IFS, ANDS OR BUTS”

3-step command: Take the paper in (non-dominant hand)
Fold the paper in half once.
Give it to the examiner

Do the following:
CLOSE YOUR EYES.
IPIKIT ANG MGA MATA.

Write a sentence:  

Copy the Figure:


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