

MINI-MENTAL STATUS EXAMINATION PROFILE OF THE ELDERLY FILIPINO HEMODIALYSIS PATIENT

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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;^{13,1} it averages an annual increase of 9.8% in the initiation of hemodialysis for the 80- and 90-year-old population.¹⁰

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.^{4,6,8,16,17,18,19,20} Most studies documents this at 1-6%.⁷ As early as the 1970s, deficits in several cognitive performance examinations were already noted in hemodialysis patients.²

Baseline cognitive function was poorer and the decline in cognitive function was greater in patients with lower estimated glomerular filtration rate.⁹ 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.⁹ 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.¹¹ 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

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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 to 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.³ 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

Parameter	N	%	mean ± SD
Age	31	100	66.48±6.0
60-64 years old	13	41.9	
65-69 years old	9	29.0	
70-74 years old	6	19.4	
75-79 years old	2	6.5	
80 years old and above	1	3.2	
Sex			
Male	18	58.9	
Females	13	41.1	
Regionalization			
Tagalog	18	58.1	
Ilocano	7	22.6	
Bisaya	2	6.5	
Kapampangan	2	6.5	
Bicolano	1	3.2	
Ilonggo	1	3.2	
Educational level			
<6 years (e.g. elementary level)	2	6.5	
6-10 years (elementary graduate to high school level)	15	48.4	
College level	8	25.8	
College graduate	4	12.9	
Postgraduate	2	6.5	

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

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

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

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

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

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

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

Parameter	N	%
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.

In the orientation component, 67.6% got scores of 9-10. The remaining patients have varying degrees of disorientation. All patients have no problem with memorizing 3 items initially. About 51.6% of patients have difficulty doing serial subtraction or reverse spelling, getting only 3 out of 5 items. Only 45.2% of the patients were able to recall the previously mentioned 3 items in the registration component. Two patients were not able to identify either a watch or a pen. Eleven patients were able to repeat the test phrase "No ifs, ands or buts" within 3 attempts. About 54.8% of the patients were able to do all the steps correctly in the 3-step command. Twenty four patients were able to do a written command and write a sentence. About 71% of the patients were able to copy the given figure.

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

Parameter	N	%	Mean ± SD
MMSE	31	100	23.45 ± 5.19
<24	10	32.2	
24-26	14	45.2	
27 and above	4	22.6	
MMSE Item Analysis			
Orientation	31		8.29 ± 2.09
9-10	21	67.6	
7-8	5	16.2	
6 and lower	5	16.2	

(Table VI continue next page)

(Table VI continuation . . .)

Registration	31		3.00
3	31	100	
0-2	0	0	
Attention and calculation	31		3.10 ± 1.76
5	10	32.3	
4	5	16.1	
3 or lower	16	51.6	
Recall	31		2.10 ± 1.04
3	14	45.2	
2	10	32.3	
0-1	7	22.5	
Pen and watch	31		1.94 ± 0.25
2	29	93.5	
0-1	2	6.5	
“No ifs, ands or buts”	31		0.36 ± 0.49
Able to repeat	11	35.5	
3-step command	31		2.39 ± 0.76
All 3 steps done correctly	17	54.8	
2 steps done correctly	9	29.0	
1 or no step done correctly	5	16.1	
Do the command	31		0.77 ± 0.43
Able to do command	24	77.4	
Write a sentence	31		0.77 ± 0.43
Writes acceptable sentence	24	77.4	
Copy figure	31		0.71 ± 0.46
Able to copy figure closely	22	71.0	

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.

Table VII. Pearson Correlation Coefficients of Different Parameters Tested in Relation to the Mini-Mental Status Examination of Hemodialysis Patients, 60 Years Old and Above

Parameter	N	Pearson Correlation	Sig. (2-tailed)
Age	31	-0.559**	0.001
Sex	31	-.104	0.577
Education	31	0.132	0.478
Hypertension	31	***	
Diabetes mellitus	31	-0.174	0.349
Atrial fibrillation	31	-0.481**	0.006

(Table VII continue next column)

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Ischemic heart disease/angina	31	0.155	0.406
Heart failure	31	-0.034	0.856
Previous myocardial infarction	31	0.023	0.904
Previous stroke	31	-0.413*	0.021
Hypothyroidism	31	-0.481**	0.006
Hypercholesterolemia	31	0.004	0.983
Head trauma	31	0.198	0.285
Alcohol intake	31	-0.166	0.372
Smoking	31	0.124	0.508
Interval between CKD diagnosis and initiation of HD	31	-0.187	0.314
Months on hemodialysis	31	-0.027	0.885
Hemodialysis frequency	31	0.219	0.237
KT/V during a completed HD session within 30 days	23	-0.258	0.235
Use of aluminium-based phosphate binders	31	0.358*	0.048
Symptoms of restless legs syndrome	31	-0.156	0.401
Hemoglobin	30	-0.047	0.806
Serum creatinine	30	-0.121	0.525
BUN	28	0.139	0.481
Serum albumin	26	0.406*	0.040
Serum calcium	22	-0.023	0.920
Serum phosphorus	26	0.109	0.596
Use of benzodiazepines for sleeplessness	31	-0.347	0.056
Use of antihistamines for sleeplessness or pruritus	31	-0.048	0.799
Calcium channel blockers as antihypertensive	31	-0.149	0.425
Beta blockers as antihypertensive	31	-0.149	0.425
Beta blockers as antihypertensive	31	0.066	0.726
ARBs as antihypertensive	31	0.176	0.343
ACEi as antihypertensive	31	-0.088	0.639
Clonidine as antihypertensive	31	-0.252	0.172

*Correlation is significant at the 0.05 level (2-tailed) – shaded area

**Correlation is significant at the 0.01 level (2-tailed) – shaded area

***Cannot be computed because at least one of the variables is constant.

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,^{7,8,16,17,18,20} 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.¹²

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.^{7,17}

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.⁷ Other studies also support this correlation with albumin levels.²² Previous stroke is negatively correlated with MMSE score and again it is consistent with an OR of 5.15 for cerebrovascular disease.^{4,7} 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.¹⁴ Other studies have shown improvement of anemia will improve cognitive function up to some degree; as to whether this improvement is due to increase in haemoglobin or erythrocyte volume or due to the effects of erythropoietin remain to be tested.¹²

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.¹² The equilibrated KT/V in this study had not computed correlation, in contrast to other studies wherein it is positively correlated with cognitive impairment.¹⁶

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.^{9,11} 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.⁷ 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.¹⁶ 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,¹⁵ 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.¹¹

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.

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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-uuliyarin (cognitive impairment) at mga kundisyong posibleng nagdudulot nito sa mga pasyenteng edad 60 at pataas na naghe-hemodialysis. Ang pagkakaroon ng problema sa memorya o pag-uuliyarin 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 eksamination sa laboratoryo. Walang gamut na ibinibigay sa inyo at wala po tayong inaasahan na mga *side effect* sa gagawin nating pagsusuri.

Ang paglahok nyo sa pananaliksik na ito ay voluntary, o kusang-loob lamang. Hindi po ito makakaapekto sa inyong kasalukuyang pagtanggap ng mga serbisyong medical. Pakibasa lamang po ang mga susunod na detalye para sa inyong kaalaman bago po kayo magdesisyon sa inyong paglahok sa aming pananaliksik. Marami pong salamat.

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 benepisyong gagawing MMSE?

- Madaliang madiskubre kung may mga sintomas ng mga problema sa memorya

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 komplikasyon 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 komplikasyon 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 walang ibang makakaalam ng inyong mga pribadong sensitibong impormasyon sa mga dokumentong ilalathala sa mga siyentipikong babasahin (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 mga nasabing paglalathala ngunit hindi ito maikokonekta sa inyong pangalan at pagkatao.

CONSENT

Ako si (Pangalan ng Pasyente) _____, na nakatira sa (Address ng Pasyente) _____, pagkatapos basahin ang mga panimulang impormasyon at pagkatapos ipaliwanag sa akin ng mananaliksik ang mga detalye ng pag-aaral na ito, ay nagsasabing:

PUMAPAYAG AKO na sumali sa pananaliksik na ito.
PUMAPAYAG AKO na makapanayam tungkol sa mga heneral na impormasyon.
PUMAPAYAG AKO na sumailalim sa Mini Mental Status Examination.
PUMAPAYAG AKO na suriin ang aking mga *medical records*.
NAIINTINDIHAN KO na walang komplikasyon akong mararanasan sa aking pagsali.
NAIINTINDIHAN KO na ang lahat ng impormasyong medical na madiskubre ditto ay maaaring gamitin sa anumang paglalathala ng pag-aaral na ito.
NAIINTINDIHAN 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.
NAIINTINDIHAN KO na kusang loob akong sumali sa pananaliksik na ito ng walang inaasahang benepisyong material o pinansyal.

Pirma ng Pasyente: _____
Petsa: _____
Buong Pangalan: _____

Pirma ng Saksi/Kamag-Anak: _____

Petsa: _____

Buong Pangalan: _____

Pagkumpirma ng mananaliksik sa pahintulor:

Kinukumpirma ko na wala ng ibang tanong ang pasyente at kusang loob niyang binigay ang pahintulot sa pagsali niya sa pananaliksik na ito.

Pangalan at Pirma ng Mananaliksik: _____

Petsa: _____

**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 stopped
 <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 U M

Recall:

Paper Table Apple

Language:

Pen/Pencil Watch

Repeat "NO IFS, ANDS OR BUTS"

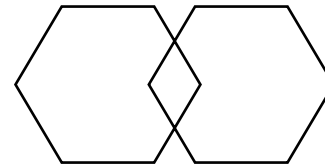
3-step command: Take the paper in (non-dominant hand)
 Fold the paper in half once.
 Give it to the examiner

Do the following:

CLOSE YOUR EYES.
IPIKIT ANG MGA MATA.

Write a sentence:

Copy the Figure:



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