INTERNAL MEDICINE

Anti-Diabetic and Haemodialysis Treatment Are Associated with Better Verbal Memory Performance

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ABSTRACT

Aim: **The study aimed to evaluate verbal memory performance in end stage renal disease (ESRD) patients on maintenance haemodialysis (HD) and determine the relationship between the socio-demographic, clinical and biochemical characteristics of patients with verbal memory performance.**

Methods: **A cross-sectional study of 91 ESRD patients on HD from December 2012 to May 2013 was conducted in nephrology unit, Hospital Sultanah Bahiyah and 3 private dialysis centres in Alor Setar, Kedah during the study period. Verbal memory performance and depression were assessed using the Malay version of the Auditory Verbal Learning Test (MVAVLT) and the Beck Depression Inventory (BDI) respectively during the first hour of HD procedures.**

Results: **Older age, male gender and none/primary education were independently associated with worse verbal memory performance. In contrast, longer duration of HD and anti-diabetic treatment were associated with better verbal memory performance. Other factors, including depression, were not significantly associated with verbal memory performance.**

Conclusion: **Anti-diabetic and HD treatment are associated with better cognitive function. Hence, this study suggests the importance of good diabetic control and regular maintenance HD to prevent cognitive impairment in ESRD patients.**

KEY WORDS

end stage renal disease (ESRD), haemodialysis (HD), verbal memory, recognition

INTRODUCTION

It is well-documented that persons with end stage renal disease (ESRD) undergoing hemodialysis (HD) are at considerably higher risk for cognitive impairment that includes memory disorders, difficulty in planning activities, changes in attention, decreased information processing speed, motor disability, or speech deficits[1]. The etiology of cognitive impairment is multifactorial. The chronic and debilitating nature of chronic kidney disease (CKD) along with its exhaustive routine treatments may be responsible for these alterations[2]. Stroke symptoms are common among patients with ESRD and strongly associated with impairments in cognition[3]. Traditional vascular risk factors include hypertension, diabetes mellitus (DM), hypercholesterolemia, cardiovascular disease, and smoking. In fact, metabolic syndrome may emerge earlier in the disease course[4]. Other nontraditional vascular risk factors that have been associated with cognitive impairment include hyperhomocysteinemia, hemostatic abnormalities, hypercoagulability, inflammation, oxidative stress and anemia[5,6].

Additionally, patients undergoing HD procedure are exposed to unique risk factors and several possible mechanisms for cognitive impairment and/or structural brain abnormalities had been investigated. Magnetic resonance imaging (MRI) studies had demonstrated significant correlation of frontal lobe atrophy with the total number of dialysis-related hypotension episodes[7], significantly higher microbleeds in HD patients compared to the control group[8] and presence of cerebral oedema in the patients following dialysis[9], which may present as acute neurologic symptoms known as dialysis disequilibrium syndrome in severe cases[10]. In addition to commonly found risk factors, such as older age, atherosclerosis, hypertension, and cerebral amyloid angiopathy[11], ESRD patients on HD frequently receive systemic anticoagulation during the dialysis procedure further increasing the risk of microbleeds. Chronic gaseous microembolization originating either from air bubbles in the hemodialysis tubes and filter or from the formation of new air bubbles as a result of pressure gradients and turbulent flow in the dialysis tubing or access is known to occur in hemodialysis patients[12]. Intradialytic hypertension is a less-recognized cardiovascular complication of HD[13] which may progress to hypertensive encephalopathy resulting in cerebral hypoperfusion.

Notwithstanding the disease processes underlying the ESRD, the HD procedure itself may cause further cognitive impairment in ESRD patients via repeated hypotensive episodes, rapid changes in blood pressure, microemboli, brain edema and cerebral microbleeds[14]. There is absence of high-quality data to support these assertions and thus additional research in this area is warranted. The objective of this study was to evaluate socio-demographic, clinical and biochemical factors associated with verbal memory performance in ESRD patients on maintenance HD. Specifically, the study would like to determine whether duration of HD would be associated with reduced verbal memory performance. Psychiatric illness and CKD put heavy social burden on caregivers in developed countries[15,16]. Identification of risk factors for cognitive impairment would help to reduce the already heavy burdened caregivers of regular HD patients.

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Table 1. Verbal memory performance according to characteristics of subject (n = 91)

	Total learning (A1-A5) Mean (SD), P-value	Delayed free recall (A7) Mean (SD), P-value	Recognition Mean (SD), P-value
All subjects	43.37 (10.75)	10.04 (3.41)	15.0[c] (1.0)[d]
Age			
< 45	47.31 (10.57)	11.39 (3.21)	14.56 (1.18)
≥ 45	40.80 (10.15)	9.16 (3.27)	14.02 (1.98)
	P = 0.005[a]	P = 0.002[a]	P = 0.145[a]
Gender			
Male	41.64 (10.26)	9.65 (3.43)	14.04 (2.05)
Female	46.03 (11.07)	10.64 (3.33)	14.53 (1.00)
	P = 0.056[a]	P = 0.179[a]	P = 0.184[a]
Ethnic			
Malay	43.24 (10.67)	10.03 (3.41)	14.21 (1.75)
Non-Malay	47.33 (16.65)	10.67 (4.51)	14.67 (0.58)
	P = 0.813[a]	P = 0.909[a]	P = 0.818[a]
Marital status			
Single	46.18 (11.75)	11.14 (3.39)	14.41 (1.40)
Married	43.03 (9.92)	9.84 (3.41)	14.23 (1.88)
	38.25 (13.10)	8.63 (2.88)	13.75 (1.28)
	P = 0.185[b]	P = 0.144[b]	P = 0.655[b]
Divorced/widower			
Education			
None/primary	33.32 (8.15)	7.58 (2.36)	13.21 (2.46)
Secondary	44.95 (9.92)	10.36 (3.32)	14.44 (1.53)
Tertiary	49.53 (10.15)	11.76 (3.33)	14.71 (0.59)
	P < 0.001[b]	P < 0.001[b]	P = 0.011[b]
Employment			
Employed	46.41 (11.27)	10.84 (3.99)	14.32 (2.19)
Unemployed	41.30 (9.95)	9.50 (2.85)	14.17 (1.33)
	P = 0.025[a]	P = 0.065[a]	P = 0.670[a]
Smoking hx			
Smoker	43.53 (7.64)	10.18 (3.09)	14.53 (0.72)
Non-smoker	43.34 (11.38)	10.01 (3.49)	14.16 (1.87)
	P = 0.948[a]	P = 0.860[a]	P = 0.430[a]
Anaemia			
Yes	44.00 (9.25)	9.94 (3.05)	14.44 (0.98)
No	43.03 (11.54)	10.10 (3.61)	14.12 (2.01)
	0.948[a]	0.828[a]	0.401[a]
Hypertension			
Yes	43.86 (10.76)	10.30 (3.41)	14.34 (1.54)
No	40.17 (10.54)	8.33 (2.93)	13.50 (2.58)
	0.270[a]	0.061[a]	0.115[a]
D/Mellitus			
Yes	38.65 (8.85)	8.45 (3.34)	13.84 (2.44)
No	45.82 (10.89)	10.87 (3.14)	14.43 (1.17)
	0.002[a]	0.001[a]	0.119[a]
Depression			
Yes	41.71 (6.80)	9.36 (2.81)	15.00c (1.00)[d]
No	43.82 (10.89)	10.21 (3.54)	15.00c (1.00)[d]
	0.007[a]	0.162[a]	0.836[a]

[a]Independent t test, [b]One way anova, [c]Median, [d]Interquartile range

METHODOLOGY

Subject

The study was approved by the Research & Ethics Committee, Universiti Sains Malaysia and Ministry of Health Malaysia. A cross sectional study over a period of a six-month was conducted at Nephrology Unit, Hospital Sultanah Bahiyah and 3 private dialysis centres in Kedah, Northern Peninsula of Malaysia. All ESRD patients age 18-65 on maintenance HD for at least 3 months were identified. Patients who were unable to complete the rating scale due to hearing, language and visual impairments or acutely ill with acute renal failure were excluded. Written informed consent was obtained from all patients after a full explanation of the procedures of the study. Ninety one patients with were recruited by the end of the study period.

Assessment

The Malay Version of Auditory Verbal Learning Test (MVAVLT) is a validated Malay version of the Rey Auditory Verbal Learning Test, developed to suit the Malaysian population. It has good validity (factor analysis 0.66 to 0.98), test-retest reliability (Pearson correlation 0.24 to 0.84) and sensitive in discriminating between normal and schizophrenia patient[17]. The researcher read a list of words (List A comprised of 15 concrete nouns), and participants were asked to recall as many of the words as they could, in any order (immediate free recall: A1). This procedure was repeated four times (A2-A5), so that there were five trials total. Total learning (A1-A5) reflects the acquisition phase in the memory information processing operations. Following the list-learning procedure in A1 to A5, participants heard a second list of words (List B comprised of another 15 concrete nouns) and subsequently tried to name as many of these words as possible (immediate free recall: B). Then, the participants were asked to name as many words as possible from the first list again (post-interference free recall: A6). Following a delay of approximately 20 min during which participants engaged in other assessment (e.g., interview for socio-demographic, clinical and other rating scales), they were asked to recall words from the first list that was read to them (delayed free recall: A7). Participants were not expecting this free recall condition, as they were not told that there would be further tests with the word lists. Following this, a recognition task was given, in which participants had to respond yes or no as to whether a word, interspersed among semantically or phonetically related words in a third list that comprised of 30 words, had been on the list A (recognition).

The Beck Depression Inventory (BDI) was designed to assess the severity of depression[18]. The BDI is a 21-item self-report rating inventory measuring characteristic symptoms of depression. The 21 items are answered on a four-point Likert scale in which 0 represents the absence of a problem and 3 represents an extreme problem, with a possible total score ranging 0 to 63 (normal score 0-10; mild depression 11-20 ; moderate depression 21-30 ,severe depression 31-40 and very severe depression 41-63). Both MVAVLT and BDI were administered within the first hour of HD to ensure good cooperation of the participants and standardization of the timing of assessment. Socio-demographic and clinical data was ascertained through the participants interview and medical records.

Statistical analysis

All data will be collected and analyzed using SPSS Version 20. The continuous variables were expressed as mean and standard deviation. Median and inter-quartile range were used when they were not normally distributed. Independent t-test or ANOVA were used to compare the mean between the normally distributed clinical data between groups of patients on haemodialysis. *P*-value of less than 0.05 was taken as significant at 95% confidence interval for all variables. The associations between characteristics of subjects with verbal memory performance (total learning A1-A5 scores of MVAVLT) were analyzed using single linear regression (SLR) analysis to measure the strength of the relationship and control the potential confounding factors. Variables with P-value of less than 0.25 were further analyzed using multiple linear regression (MLR).

RESULTS

A total of 91 patients (55 males, 36 females) with median age 45.5 (IQR = 12.1) were recruited. Majority of the subjects were Malay (95.6%), married (67%), unemployed (59.3%) and educated up to secondary level (60.4%). The mean (SD) for total learning (A1-A5), post-interference free recall (A6) and delayed free recall (A7) were 43.37 (10.75), 10.3 (3.39) and 10.04 (3.41), respectively. Subjects age < 45 years, received tertiary education, employed, not having diabetes

Table 2. Simple linear regression analysis to determine factors associated with total learning (A1-A5) in ESRD patients on maintenance HD

	b[a] (CI 95%)	t stat	*P*-value
Socio-Demographic Factors			
Age	-0.352 (-0.52,-0.19)	-4.301	0.001
Gender (male vs. female)	4.391 (-0.12, 8.90)	1.935	0.056
Ethnicity	-3.009 (-13.97,7.95)	-5.450	0.587
Malay	2.047 (-4.24,8.33)	0.647	0.519
Chinese	-0.216 (-7.32,-0.66)	-0.035	0.972
Indian/Others	-5.109 (-9.56,-0.66)	-0.236	0.814
Employment			
Marital Status			
Single	3.149 (-2.12,8.42)	1.188	0.238
Married	-0.517 (-2.91,1.87)	-0.430	0.669
Divorced/Widower	-1.594 (-4.25,1.06)	-1.193	0.236
Education			
None/primary	-12.71 (-17.56,-7.87)	-5.211	0.001
Secondary	1.987 (-0.28,4.25)	1.744	0.085
Tertiary	2.52 (0.67,4.37)	2.711	0.008
Smoking			
Past	0.192(-5.58,5.97)	0.066	0.948
Current	-0.159 (-2.49,2.18)	-0.135	0.893
Never	0.102 (-1.87,2.07)	0.103	0.919
Clinical Factors			
No of Hospitalization (months)	-0.668 (-1.19,0.85)	-0.328	0.744
Duration of illness (months)	0.050 (0.01,0.91)	2.438	0.015
Duration of haemodialysis (months)	0.060 (0.03,0.10)	2.827	0.006
Systolic (mmHg)	-0.007 (-0.12,0.10)	-0.126	0.400
Diastolic(mmHg)	0.085 (-0.05,0.22)	1.267	0.209
Interdialytic weight gain (kg)	0.702 (-1.15,2.55)	0.756	0.452
Depressive symptoms (BDI score)	-0.087 (-0.38, 0.21)	-0.034	0.588
Medical History			
Anaemia	-0.967 (-5.68,3.74)	-0.408	0.685
Hypertension	-3.694 (-10.3,2.91)	-1.111	0.270
Diabetes mellitus	7.17 (2.67,11.67)	3.165	0.002
Hypercholestrolaemia	-1.455 (-5.99,3.08)	-0.637	0.526
Stroke	0.378 (-21.21.21.97)	0.035	0.972
Heart Disease	-5.689 (-27.25,15.87)	-0.524	0.601
Medications			
Antihypertensive	0.082 (-5.09,5.26)	0.031	0.975
Anticholesterol	3.745 (-0.72,8.20)	1.666	0.099
Antidiabetic	7.048 (1.92,12.18)	2.729	0.008
Heamoglobin agents	-1.212 (-7.12,4.69)	-0.408	0.685
Calcium agents	-0.095 (-8.54,8.35)	-0.022	0.982
Antidiuretic	1.952 (-2.59,6.49)	0.853	0.396
Antiplatelet	2.446 (-4.19,9.07)	0.733	0.466
Biochemical Factors			
Sr Creatinine (mmol/L)	-0.006 (-0.02,0.01)	-1.072	0.287
Blood Urea (mmol/L)	-0.121 (-0.64,0.39)	-0.465	0.644
Sodium (mmol/L)	0.975 (-0.03,1.98)	1.931	0.057
Phosphate (mmol/L)	-0.975 (-3.83,1.88)	0.681	0.498
Haemoglobin (g/dL)	-0.833 (-2.11,0.44)	-1.303	0.196
Fasting Blood Sugar (mmol/L)	-0.004 (-0.44,0.43)	-0.021	0.984
Fasting Lipid Profile (mmol/L)	-0.619 (-3.26,2.02)	-0.466	0.642
Sr Albumin (g/dL)	-0.272 (-0.63,0.08)	-1.506	0.136
Potassium (mmol/L)	0.603 (-3.18,4.39)	0.317	0.752

[a]Crude regression coefficient

Table 3. Multiple linear regression analysis to determine factors associated with total learning (A1-A5) in ESRD patients on maintenance HD

	b[a] (95% CI)	*P*-value
Age	-0.255 (-0.43, -0.08)	0.005
Gender (male)	-4.403 (0.54, 8.27)	0.026
None/primary education	-10.665 (-15.44, -5.89)	< 0.001
Duration of HD	0.052 (0.01, 0.09)	0.009
Antidiabetic	6.406 (2.00, 10.81)	0.005
Sr creatinine	-0.008 (-0.02, 0.01)	0.037
Depressive symptoms	-0.077 (-0.38, 0.23)	0.614

[a]Adjusted regression coefficient, Coefficient of determination (R2) = 0.411

Table 4. Comparison of verbal memory performance in other studies using MVAVLT

Subjects (n)	Age	Total learning	Delayed free recall	Recognition
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Healthy controls (n = 15)[17]	38.2 (9.5)	53.2 (7.7)	11.1 (2.5)	14.3 (0.9)
Postmenopausal women on EPT (n = 39)[20]	55.3 (3.1)	44.4 (1.3)	9.9 (0.4)	13.6 (0.3)
ESRD on maintenance HD (n = 91)	45.5[a] (12.1[b])	43.37 (10.75)	10.04 (3.41)	15.0[a] (1.0[b])
Smoking schizophrenia patients (n = 30) [21]	35.5 (8.0)	42.7 (11.0)	9.4 (2.5)	14.0 (2.0)
Schizophrenia patients (n = 114)[22]	34.6 (10.2)	35.6 (9.8)	7.4 (2.7)	12.6 (2.6)

[a]Median, [b]Interquartile range,

mellitus and depression, scored significantly higher total learning ($P < 0.05$) compared to their counterparts. Additionally, 3 of the characteristics (i.e., age, education and absence of diabetes mellitus) were significantly associated with better delayed free recall (A7). However, none of the characteristics were significantly associated with recognition, as shown in table 1.

The MVAVLT total learning (A1-A5) was regressed onto each of socio-demographic, clinical and biochemical variables by using SLR analysis, as presented in table 2. Six variables had $P < 0.05$: age; education; duration of illness; duration of HD; diabetes mellitus and receiving anti-diabetic treatment. In order to allow for more important variables to be included in this analysis, all factors with $P < 0.25$ were further analyzed using MLR. Forward multiple linear regression method applied model assumptions are fulfilled. There were no interactions amongst independent variables and no multi-colinearity detected. A total of 5 factors were significant and independently associated with verbal memory performance, as shown in table 3. Older age, male gender and none/primary education were associated with worse verbal memory performance. In contrast, longer duration of HD and anti-diabetic treatment were associated with better verbal memory performance. Serum creatinine ($P = 0.037$) was considered not significant because the 95% confidence interval include zero[19]. Other factors such depressive symptoms and biochemical parameters were not significantly associated with verbal memory performance.

DISCUSSION

ESRD patients on maintenance HD showed impairment of verbal

memory performance which includes measures of immediate memory, delayed recall and recognition. The first author had conducted studies on verbal memory performance in different patient populations using the same rating scale, as summarized in table 4. Overall, verbal memory performance of the ESRD subjects was better compared to schizophrenia patients even though schizophrenia patients were on average 10 years younger. However, this study subjects performed worse compared to postmenopausal women on estrogen-progestin therapy (EPT) or healthy controls. This was despite the postmenopausal women were on average 10 years older. Nevertheless, the above comparison across different studies does not allow the conclusion that these differences are significant since the study settings were different and many potential confounders were not controlled.

The findings that older age, male gender and none/primary education were independently associated with worse verbal learning performance were generally consistent with other studies. The finding that anti-diabetic treatment was independently associated with better verbal memory performance is consistent with a prospective study of 119 patients with CKD stage 3-5 (including dialysis) and 54 control patients without dialysis but with similar vascular risk profile[23]. Linear regression showed that only 3 factors namely: age, HbA1c, and fibrinogen predicted cognitive performance. Other factors such as overt vascular diseases (i.e., coronary artery disease, stroke, and peripheral artery disease), subclinical arteriosclerosis markers (namely carotid intima-media thickness and ankle-brachial index), other vascular risk factors (namely systolic blood pressure, dyslipidemia, smoking, and body-mass index), and mood disturbances (namely depression and anxiety) were not significant. These results suggest that disturbed glucose control and inflammation contribute to cognitive impairment in CKD. Advanced glycation end products (AGE) have recently been considered to be metabolic mediators of diabetes, cardiovascular disease and renal disease. In a recent study[24], circulating RAGE is associated with reduced eGFR in non-diabetic healthy subjects suggesting the important role in modifying renal disease and other vascular risk factors.

HD patients reveal considerable changes of cognitive performance across the treatment. HD improves attention and memory performance, which subsequently deteriorate in between HD sessions[25,26]. However, only a minority of patients exhibit significant individual cognitive fluctuations, predominantly showing deterioration after dialysis in attention and executive functions[27]. In conclusion, longer duration of HD was independently associated with better verbal memory performance. It suggests HD has an overall long term beneficial effect on cognitive function even though various mechanisms had been suggested to cause cognitive impairment. Other factors including depressive symptoms, which affect almost one-fifth of ESRD patients on HD[28], were not significantly associated with cognitive impairment.

The limitation of this study was that the cognitive assessment was performed during the first hour of HD procedure. Although, this was chosen mainly to standardize, facilitate the assessment process and ensure good cooperation from the patients, the best cognitive function probably was not achieved until after the completion of the procedure. The first hour of HD represents the period of rapid physiological and biochemical change in patients undergoing HD. Future study should perform multiple assessments and involved a larger sample.

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REFERENCES

1) Madero M, Gul A, Sarnak MJ. Cognitive function in chronic kidney disease. Sem Dial 2008; 21: 29-37.
2) Karkar A. Modalities of hemodialysis: Quality improvement. Saudi J Kidney Dis Transpl 2012; 23: 1145-61.
3) Kurella Tamura M, Meyer JB, Saxena AB, Huh JW, Wadley VG, Schiller B. Prevalence and significance of stroke symptoms among patients receiving maintenance dialysis. Neurology 2012; 79(10): 981-7.
4) Al-Bitar S, Hawoot Z, Farhood S, Salman S. Metabolic syndrome in chronic renal failure. Saudi J Kidney Dis Transpl 2012; 23: 1080-3.
5) Nasser Mel T, Shawki S, El Shahawy Y, Sany D. Assessment of cognitive dysfunction in kidney disease. Saudi J Kidney Dis Transpl 2012; 23(6): 1208-14.
6) Radić J, Ljutić D, Radić M, Kovaćić V, Sain M, Curković KD. The possible impact of dialysis modality on cognitive function in chronic dialysis patients. Neth J Med 2010; 68: 153-7.
7) Mizumasa T, HirakataH, Yoshimitsu T, Hirakata E, KuboM,Kashiwagi M, Tanaka H, Kanai H, Fujimi S, IidaM: Dialysis-related hypotension as a cause of progressive frontal lobe atrophy in chronic hemodialysis patients: a 3-year prospective study. Nephron Clin Pract 2004; 97: c23-c30.
8) Yokoyama S, Hirano H, Uomizu K, Kajiya Y, Tajitsu K, Kusumoto K: High incidence of microbleeds in hemodialysis patients detected by T2*-weighted gradient-echo magnetic resonance imaging. Neurol Med Chir (Tokyo) 2005; 45(11): 556-560 discussion 560.
9) Walters RJ, Fox NC, Crum WR, Taube D, Thomas DJ: Haemodialysis and cerebral oedema. Nephron 2001; 87: 143-147.
10) Zepeda-Orozco D, Quigley R. Dialysis disequilibrium syndrome. Pediatr Nephrol 2012; 27(12): 2205-11.
11) Poels MM, Vernooij MW, Ikram MA, Hofman A, Krestin GP, van der Lugt A, Breteler MM: Prevalence and risk factors of cerebral microbleeds: an update of the Rotterdam scan study. Stroke 2010; 41(Suppl 10): S103-S106.
12) Stegmayr B, Brännström T, Forsberg U, Jonson P, Stegmayr C, Hultdin J. Microbubbles of air may occur in the organs of hemodialysis patients. ASAIO J 2012; 58(2): 177-9.
13) Inrig JK: Intradialytic hypertension: a less-recognized cardiovascular complication of hemodialysis. Am J Kidney Dis 2010; 55(3): 580-589.
14) Madero M, Sarnak MJ. Does hemodialysis hurt the brain? Semin Dial 2011; 24(3): 266-8.
15) Toyoshima Y, Washio M, Ishibashi Y, Onizuka J, Miyabayashi I, Ara Y. Burden among Family Caregivers of the Psychiatric Patients with Visiting Nursing Services in Japan. International Medical Journal 2012; 19(2): 127-9.
16) Washio M, Yoshida H, Ura N, Togashi N, Sakauchi F, Arai Y, Mori M, Shimamoto K. Burden among family caregivers of patients on chronic hemodialysis in northern Japan. International Medical Journal 2012; 19(3): 221-223.
17) Jamaluddin R, Othman Z, Musa KI, Alwi MNM. Validation of the Malay version of auditory verbal learning test (MVAVLT) among schizophrenia patients in Hospital Universiti Sains Malaysia (HUSM), Malaysia, ASEAN J Psychiatry 2009; 10(1): 54-74.
18) Mukhtar F, Tian PSO. Exploratory and confirmatory factor validation and psychometric properties of the Beck Depression Inventory for Malays (BDI-Malay) in Malaysia. Malaysian Journal of Psychiatry 2008; 17(1): 51-64.
19) du Prel JB, Hommel G, Röhrig B, Blettner M. Confidence interval or p-value? Part 4 of a series on evaluation of scientific publications. Dtsch Arztebl Int 2009; 106(19): 335-339.
20) Shafin N, Zakaria R, Hussain NHN, Othman Z. Association of oxidative stress and memory performance in postmenopausal women receiving estrogen-progestin therapy. Menopause 2013; 20(6): 661-6.
21) Hamzah H, Abdullah WNW, Jamaluddin R, Othman Z. Verbal working memory in schizophrenia: relationship to cigarette smoking and psychopathology. Malaysian Journal of Psychiatry 2012; 21(1): 44-53.
22) Othman Z, Jamaluddin R, Alwi MNM, Ismail HI. Demographic and clinical factors associated with verbal memory performance in patients with schizophrenia in Hospital Universiti Sains Malaysia (HUSM), Malaysia ASEAN Journal of Psychiatry 2011; 12(2): 148-56.
23) Seidel UK, Gronewold J, Volsek M, Todica O, Kribben A, Bruck H2, Hermann DM. The prevalence, severity, and association with HbA1c and fibrinogen of cognitive impairment in chronic kidney disease. Kidney Int 2014; 85(3): 693-702.
24) Lee JH, Park BH, Park JW, Ka SO, Koh DH, Youm JH, Lee S, Park SK, Kwon KS. Elevated levels of serum endogenous secretory RAGE are associated with decreased glomerular filtration rate in healthy adults. International Medical Journal 2013; 20(1): 20-4.
25) Thimmaiah R, Murthy KK, Pinto D. Cognitive dysfunction in patients with renal failure requiring hemodialysis. Indian J Psychol Med 2012; 34(3): 237-41.
26) Cukor D, Ver Halen N, Rosenthal Asher D, Goldberg MA, Slyker J, Kimmel PL. A pilot investigation of cognitive improvement across a single hemodialysis treatment. J Nephrol 2013; 26(2): 323-330.
27) Costa AS, Tiffin-Richards FE, Holschbach B, *et al.* Clinical Predictors of Individual Cognitive Fluctuations in Patients Undergoing Hemodialysis. Am J Kidney Dis. 2014 Mar 27. pii: S0272-6386(14)00592-7.
28) Othman Z, Ismail SZ, Saring ARM, Jamaluddin R. Low diastolic blood pressure predicts depression in end stage renal disease patients on maintenance haemodialysis. International Medical Journal 2014; 21(1): 10-3.