

Prevalence of Depression in Stroke Patients With Vascular Dementia in Universiti Kebangsaan Malaysia Medical Center

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SUMMARY

Objective: Depression among patients with vascular dementia is frequently overlooked and potentially causes significant morbidity. There is limited data in Malaysia on the subject and this study was conducted to determine the prevalence of depression in vascular dementia (VaD) in UKMMC.

Methods: This was a cross-sectional study involving diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) criteria and who had a mini mental state examination (MMSE) score of less than 26. All patients were interviewed, examined clinically and their previous brain computer tomography (CT) were reviewed. The prevalence of depression was determined using the Cornell scale of depression.

Results: A total of 76 patients were recruited with a mean age of 70.5 ± 9.5 years. The median duration of illness was 2.0 (1.0-4.8) years. The prevalence of depression in the study population was 31.6%. The patients with depression had a significant older mean age (74.5 ± 8.7 years old) compared to those without depression (68.6 ± 9.4 years old). Patients with large artery stroke of less than 3 years had significant higher frequency of depression (53.6%) compared to patients with small artery stroke (23.8%) and patients with right sided large artery stroke had significantly higher frequency of depression compared to left (70% vs. 44.4%). Median MMSE score (17.0) for depressed patients was significantly lower compared with median MMSE score (22.5) for non depressed patients. Median Barthel Index (30.0) for depressed patients was significantly lower compared with median Barthel score for non depressed patients.

Conclusions: Depression was prevalent among post stroke patients with VaD in UKMMC particularly for patients with older age, large artery stroke, right sided large artery stroke, low MMSE score and low Barthel Index. Early recognition of high risk patients is important in the holistic management of patients to prevent significant morbidity arising from depression.

KEY WORDS:

Depression, Dementia, Vascular dementia, Stroke, Malaysia, Cornell scale of depression

INTRODUCTION

Dementia is defined as a clinical condition or syndrome characterized by progressive decline in cognitive function that are severe enough to interfere with daily activities¹. Cognitive deficit include memory impairment plus at least one of the other cognitive domains, such as aphasia, apraxia, agnosia or disturbances in executive functioning¹. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) diagnostic criteria, vascular dementia manifests as memory impairment and one other cognitive disturbance such as aphasia, apraxia, agnosia or disturbances in executive functioning which require either focal neurological signs and symptoms or laboratory evidence of focal neurological damage (for example, multiple infarction involving cortex and underlying white matter) in the absence of delirium². Vascular dementia (VaD) is the second most common dementia after Alzheimer's disease. Vascular dementia makes up 10 to 20 percent of cases of dementia in North America and Europe^{3,4}. The prevalence of VaD among Hisayama residents aged 65 or older was estimated at 3.8%. The rate was 2.2 times higher than Alzheimer's disease⁵. Population study done in Utah, USA also shown that depression was more common among VaD patients than AD patient which is 32.3% and 20.1% respectively⁶. A population study in Arab community in Israel further confirmed that depression among VaD is higher among Asian which shows 86% of VaD patient had depressive symptoms compared to 57% of Alzheimer disease⁷. In a local study by Glamcevski et al, depression was seen in 65% (mild 50%, moderate to severe 15%) of patients 3-6 month post stroke⁸. In that study, there were significant association between advanced age, ethnicity, non use of traditional medication, non religiousness and social disability but there is no significant association between gender, previous education level, type and length of previous employment and side of lesion. However demented patients who had dementia prior to stroke were excluded in this study⁸. Sulaiman et al. in another study of post stroke

This article was accepted: 3 January 2013

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depression (PSD) in Malaysia found that there is no significant association between age, gender, marital status, ethnic groups and occupational status with PSD but there is an association between left hemisphere lesion and physical functional impairment⁹. In patients with VaD developing post stroke, the onset of depression leads to more morbidity and distress to caregivers¹⁰.

There are limited local data looking at depression in VaD patients. This study will determine the prevalence of depression among VaD patients and the factors associated with depression in VaD patients.

MATERIALS AND METHODS

A cross-sectional study was conducted at the UKMMC, from May 2010 till February 2011. The study was conducted after approval from UKM ethical committee. All ischemic stroke patients within past 6 years and have VaD according to DSM IV who fulfilled the inclusion criteria were recruited from the medical wards, neurology clinic, psychiatry clinic or referral cases from non-medical wards. Patients and caregivers were given detailed explanation regarding the study and informed consent was obtained. The confidentiality of the patient and caregivers was warranted. Patients who met the inclusion criteria were recruited into the study after obtaining their consent. The consent was taken from the next of kin for patients with the MMSE score of 10 and below. Patients were excluded if there are underlying bipolar disorder, depression, pre-existing psychosis aphasia, delirious or Alzheimer disease.

The history and socio-demographic data were obtained from the patients. Physical examination and mini mental state examination (MMSE) were conducted on every subject. The computer tomography (CT) of the brain performed during the period of hospitalization were reviewed. Barthel Index was used to assess physical disability and followed by an interview using a questionnaire based on Cornell Scale for depression in dementia. The data analysis was performed using the SPSS version 19. Test for normality was performed using the Shapiro-Wilk test. Quantitative and qualitative demographic characteristic were summarized and data were tabulated. All distributed numerical data were expressed as mean \pm standard deviation (SD), median and percentage. Student t-test was used to analyze continuous variables that were normally distributed. For non-normally distributed data, Mann-Whitney U test was used. Chi-square and Fisher's exact test were used to analyze discrete variables. Binary logistic regression was used for analysis of multivariate model. A p value of <0.05 was deemed as statistically significant.

Mini mental state examination (MMSE)

MMSE is a brief 30 point questionnaire used to test the cognition of the patient. It was introduced by Folstein *et al* in 1975. MMSE consists of 5 parts which are orientation, registration, attention & calculation, recall and language. The full score is 30. A score of less than 26 is considered dementia. Mitchell *et al.* found that the sensitivity was 79.8%, specificity was 81.3%, positive predictive value was 81.3% and negative predictive value was 73.0%¹¹.

Barthel Index

Barthel Index is a index of independence. The instrument is used easily by a non physician and consistent with the ability of individuals to perform daily activities. There are 10 items in Barthel index consist of feeding, bathing, grooming, dressing, bowel continence, bladder continence, toilet use, transfer from bed to chair, mobility, and ability to climb stairs. The full score of Barthel index is 100. The patient who scores 100 in the Barthel index is totally independent. The higher the score reflect the higher independent of the patient¹². Barthel Index score was divided into 4 categories according to their level of functioning: very severe dependence (Barthel Index score 0-39), severe dependence (Barthel Index score 40-59), moderately independence (Barthel Index score 60-84) and almost complete independence (Barthel Index score 85-100)¹³.

Cornell Scale for depression in dementia

The Cornell Scale for depression in dementia was introduced by Alexopoulos and colleague from Cornell University Medical college in 1985. The scale was designed to utilize information obtained from the patients' caregivers and from a brief interview with the patient¹⁴.

The Cornell scale is a 19-item instrument consists of 5 major parts which are mood related signs, behavioral disturbance, physical signs, cyclic functions and ideational disturbance designed for the rating of symptom of depression in demented¹⁴. Score 0 for absent symptom, 1 for mild symptom and 2 for severe symptom. The maximum score is 38 points. A score of 8 or more out of 38 is suggestive of significant depressive symptoms. The Cornell scale of depression is a better scale with a sensitivity and specificity of 93% and 97% compared with the geriatric depression scale¹⁵.

Radiological Assessment

Infarction in brain CT was further divided into small artery stroke and large artery stroke¹⁶. Small artery stroke is defined as occlusion of small end arteries that penetrate the brain which results in focal, deeply located area of infarction that included lacunar infarctions and Binswanger disease. Lacunar infarct is defined as infarcts in the territories of small arteries whereas Binswanger disease is defined as symmetrical demyelination of white matters due to vascular causes. Large artery stroke is defined as occlusion of large cerebral arteries which results in regions of ischemic involvement¹⁶.

RESULTS

A total of 76 patients were recruited in this study. They consisted of 34 (44.7%) females and 42 (55.3%) males. There were 38 (50%) Chinese, 32 (42.1%) Malays, 5 (6.6%) Indians and 1 (1.3%) other races in this study. The overall mean age of this study population was 70.5 ± 9.5 years. The mean age of onset of stroke was 67.5 ± 9.5 years, with the median duration of illness of 2.0 (1.0-4.8) years.

Majority of the study population 46 (60.5%) has primary school education followed by 23 (30.3%) with secondary school education, 2 (2.6%) with tertiary educational and 5 (6.6%) had no formal education.

Twenty nine (38.2%) of the study population has hypertension while 2.6% has diabetes mellitus. There was only 1 (1.3%) patient who has ischemic heart disease. Thirty one (40.8%) of the study population has both diabetes and hypertension while 5 (6.6%) of study population has diabetes, hypertension and ischemic heart disease. Previous history of depression was present in 2 (2.6%) patients which was already cured and no longer on follow up. Three (3.9%) patients had family history of stroke while 1 (1.3%) patient had a family history of dementia. Twenty two (29.0%) patients in study population had a stroke which was less than a year duration whereas most of them (71.0%) had stroke more than a year (table I).

Computer tomography of study population was divided into small artery stroke and large artery stroke. Forty three (56.6%) patients had large artery stroke while the remainder had small artery stroke. The left hemisphere was mainly involved in 40.8% of the study population (table II).

In this study, 47.3% and 30.2% of the study population was moderate and mild dementia using MMSE score. 27.6% and 7.9% of the study population were very severely dependent and severe dependent respectively. The moderately independent category accounted for 11.8% of the study population whereas 52.6% of patients were almost completely independent.

The prevalence of depression among VaD in this study population was 31.6% (24) with equal number of male and female patients. The breakdown score of patients with depression were in the table 8. The median age was 77 (68-81) years old. The ethnic distribution for depression was 14 (36.8%) Chinese compared to 9 (28.1%) Malays. There were 15 (32.6%) patients with primary school education level who presented with depression in this study. There were 7 (30.4%) patients with secondary school education. Two (40%) patients did not receive any formal education. However, there were no tertiary education patients who were depressed. Among the depressed patients, 10 (32.3%) patients had one pre-existing medical illness. Ten (30.3%) of depressed patients had two pre-existing medical illnesses. There was only 1 (20%) patient with diabetes mellitus, hypertension and ischemic heart disease. None of the patients with depression had family history of dementia or previous history of depression. There was only 1 (33.3%) patient who had family history of stroke (table III).

There were no significant association with gender, race, religion, educational level, premorbid medical conditions, previous history depression and family history of stroke.

The patients with depression had a significant older mean age (74.5 ± 8.7 years old) compared to those without depression (68.6 ± 9.4 years old) in this study ($p < 0.011$).

The depressed patients had 39.5% (17) of large artery stroke and 21.2% (7) of small artery stroke patients. The side of hemisphere involved was divided to right side, left side or bilateral involvement. The right sided hemispheric involvement had the highest number of depressed patients, 47.8% (11). Half of the right sided large artery stroke patients

Table I: Baseline characteristic of the study population

		Study population n (%)
Age (mean \pm SD)		70.5 \pm 9.5
	41-50	2.0 (2.6)
	51-60	9.0 (11.8)
	61-70	25.0 (32.9)
	71-80	30.0 (39.5)
	81-90	10.0 (13.2)
Age of Onset		67.5 \pm 9.5
Gender	Male	42.0 (55.3)
	Female	34.0 (44.7)
Race	Malay	32.0 (42.1)
	Chinese	38.0 (50.0)
	Indian	5.0 (6.6)
	Other	1.0 (1.3)
Duration of illness in years median (interquartile range)		2.0 (1.0-4.8)
Education	Nil	5.0 (6.6)
	Primary School	46.0 (60.5)
	Secondary School	23.0 (30.3)
	Tertiary Education	2.0 (2.6)
Co-morbid medical condition	None	7.0 (9.2)
	Hypertension	29.0 (38.2)
	Diabetes Mellitus	2.0 (2.6)
	IHD	1.0 (1.3)
	Coexisting diabetes Mellitus & hypertension	31.0 (40.8)
	Coexisting diabetes mellitus, hypertension & ischemic heart disease	5.0 (6.6)
	Previous depression	2.0 (2.6)
Family history of stroke	3.0 (3.9)	
Family history of dementia	1.0 (1.3)	

Table II: Brain CT finding of stroke in study population

		Study population n (%)
Side of Hemisphere Involved		70.5 \pm 9.5
	Left	31 (40.8)
	Right	23 (30.3)
	Bilateral	22 (28.9)
Site	Right sided large artery stroke	18 (23.7)
	Left sided large artery stroke	25 (32.9)
	Small artery stroke	33 (43.4)

were depressed compared with 32% (8) of the left sided large artery stroke patients.

There was no significant association with large artery stroke, site of large artery stroke and side of hemispheric involvement.

Further analysis on the duration of stroke was based on previous longitudinal study of PSD which was conducted up

Table III: Demography comparison between those with depression and non depression

		Depression n =24(%)	No Depression n=52 (%)	p value
Gender	Male	12 (28.6)	30 (71.4)	0.531*
	Female	12 (35.3)	22 (64.7)	
Race	Malay	9 (28.1)	23 (71.9)	0.654**
	Chinese	14 (36.8)	24 (63.2)	
	Indian & Other	1 (16.7)	5 (83.3)	
Education	Nil	2 (40)	3 (60)	0.999**
	Primary School	15 (32.6)	31 (67.4)	
	Secondary School	7 (30.4)	16 (69.6)	
	Tertiary Education (college-university)	0	2 (100)	
Co-morbid Medical Condition	Not known Illness	3 (42.9)	4 (57.1)	0.890**
	One preexisting medical illness	10 (32.3)	21 (67.7)	
	Two pre-existing medical illnesses	10 (30.3)	23 (69.7)	
	Three pre-existing medical illnesses	1 (20)	4 (80)	
Previous depression	No	24 (32.4)	50 (67.6)	0.839***
	Yes	0	2 (100)	
Family history of stroke	No	23 (31.5)	50 (68.5)	0.999***
	Yes	1 (33.3)	2 (66.7)	
Family history of dementia	No	24 (32)	51 (68)	0.999***
	Yes	0	1 (100)	

Table IV: Brain CT comparison between depressed and non depressed patients with stroke less than 3 years

Infarction less than 3years		Depression n=20 (%)	No Depression n=29 (%)	p value
Large artery stroke		15 (53.6)	13 (46.4)	0.045*
Small artery stroke		5 (23.8)	16 (55.2)	
Side of Hemisphere Involved	Right	8 (61.5)	5 (38.5)	0.197**
	Left	8 (38.1)	13 (61.9)	
	Bilateral	4 (26.7)	11 (73.3)	
Side	Right sided large artery stroke	7 (70%)	3 (30%)	0.046**
	Left sided large artery stroke	8 (44.4)	10 (55.6)	
	Small artery stroke	5 (23.8)	16 (55.2)	

Table V: Multivariate model predicting depression in study population

		P value	OR	95% Lower	CI Upper
Age		0.05	1.119	1.000	1.252
Race	Non Malays (0)	0.091	0.203	0.032	1.291
	Malays (1)				
Education	Nil (0)	0.507			
	Primary school (1)	0.490	3.397	0.105	109.36
	Secondary school (2)	0.170	25.597	0.250	2622.59
	tertiary school (3)	0.392	5.663	0.107	299.033
Co-morbid medical illness	≤ 2 disease (1)	0.251	0.356	0.061	2.080
	> 2 disease (0)				
Barthel Index		0.007	0.945	0.908	0.985
MMSE		0.315	1.103	0.877	1.504
Type of infarct	Large artery stroke (1) Small artery stroke (0)	0.030	57.719	1.493	2231.11

to 3 years²⁴. Hence, the duration of stroke was divided to more or less than 3 year. Patients with large artery stroke of less than 3 years had higher frequency of depression (53.6%) compared to patients with small artery stroke (23.8%) ($p=0.045$). Patients who had right sided large artery stroke had higher frequency of depression that is 70% compared to left sided large artery stroke, 44.4 % and small artery stroke, 23.8% ($p=0.046$). (Table IV)

There was significant association of depression with MMSE score and Barthel index. Median MMSE score (17) for depressed patients was significantly lower compared with median MMSE score (22.5) for non depressed patients ($p=0.013$). Median Barthel Index (30) for depressed patients was significantly lower compared with median Barthel Index (100) for non depressed patients ($p<0.0001$).

In multivariate analysis, the Barthel Index (odd ratio 0.945, 95% CI 0.908-0.985) and type of infarct (odd ratio 57.719 95% CI 1.493-2231.11) were significantly associated with depression (table V).

DISCUSSION

Stroke is the third leading cause of death in many developed countries. Many stroke survivors are left with physical and psychological disabilities. Prevalence of VaD was high following stroke¹⁷. Depression among VaD patients had not been extensively studied in Malaysia although there have been limited reports on post stroke depression^{8,9}.

Prevalence of depression with VaD in study population was 31.6% with equal number of male and female patients. The prevalence of depression is much lower than post stroke depression study documented (36%)⁹. Al Jawad *et al.* also shown a higher rate of depression around 67% in the elderly care home for normal cognitive and borderline demented patients¹⁸. A population study in Arab community showed 86% of depressed patients among VaD patients⁷. However, the finding of many studies found that the prevalence of post stroke depression in hospital setting range from 25% to 70% with a highest range around 30-40%²⁹. Our study had almost similar prevalence compared to the findings of other studies. The frequency of depression in the VaD patients in our study reduces with the duration of the stroke. The proportion of depressed patients with stroke less than 3 years were 40.8% (20) compared to the proportion of depressed patients with stroke more than 3 years which was 14.8% (4). This pattern was also noted in Robinson's prospective study which showed a steady reduction in the trend of depression rate where 14% of patients with major depression remained depressed at 1year follow up and none were depressed at 2 year follow up⁵⁴. Robinson *et al.* proposed that the natural duration of depression was between 6 months to 1 year whereas the duration of minor depression was variable⁵⁴. This finding suggested that patient with depression symptom need to be extensively follow up by psychiatrics and treatment should be started early if depression symptoms not improved or showed suicidal idea that may be life threatening. This study showed our patients had a mean age of 70.5 ± 9.5 years, while the mean age of onset of stroke was 67.5 ± 9.5 years with a median duration of illness of 2 (1.0-4.8) years. The

commonest age categories of study population were between 61-70 and 71-80 which consisted of 32.9% and 39.5%. This was comparable in the prevalence study done to detect dementia and depression in elderly care home by Al-Jawad where the main proportion of study population were 60-69 and 70-79 years which were 41.3% and 41.9% respectively¹⁸. The difference was the setting was at an elderly care home where the admission only allowed at 60 years or older. Al-Jawad *et al.* used the Elderly Cognitive Assessment Questionnaire (ECAQ) to detect dementia rather than MMSE and DSM IV criteria for dementia¹⁸. Our study population had only 14.5% patients with the age below 60. This finding was comparable to the studies in Europe, Canada and North America where prevalence of VaD increases with age^{3,19,20}. A local post stroke depression prevalence study conducted in 1998 and 2000 in University Malaysia Medical Centre (UMMC) had a mean age of 56.8 years ± 12.5 years and 57.7 ± 12.3 years respectively which is considerably younger than our study population^{8,9}. The proportion of Malay patients in our study (42.1%) was lower compared to the study done by Al-Jawad *et al.* (46.7%) and lower among Indian patients (7.1% vs. 24.0%)¹⁸. Our study had a higher subgroup of Chinese patients compared to the study done by Al-Jawad *et al.* (50.0% vs. 29.3%). However, a post-stroke depression study done by Glamcevski *et al.* showed different racial properties with Indians (25%), Malays (22%) and Chinese (51%)⁸. Another study done by Sulaiman *et al.* reported the racial distribution comprising of 38% Chinese, 34% Malays, 24% Indians and 2% others⁹. This is probably a reflection of different racial distribution from the underlying catchment areas of the two hospitals. Interestingly, we found that a high proportion (50%) of our VaD patients were of Chinese ethnicity. This could be a reflection of the local population in Cheras, where Chinese is the major population.

More than half (56.6%) of study population had large artery stroke and the remaining was small artery stroke. Sulaiman *et al.* study documented left and right hemisphere involvement of almost 40% and bilateral hemispheric involvement of nearly 20%⁹. In comparison, our study showed a higher percentage of patients with bilateral hemispheric involvement (28.9%), left hemisphere (40.8%) and right hemisphere (30.3%).

MMSE scores in the study population ranges from 8 to 25. Moderate dementia consisted of 47.3% whereas 30.2% consisted of borderline dementia and severe dementia only consisted of 22.5%¹⁷. In this study, 27.6% and 7.9% of the study population were severely dependent and moderately dependent respectively using Barthel Index. Sulaiman *et al.* using the Modified Rankin Scale to measure disability found 18% of patients with moderate severe disability and 22% with moderate disability. There were no patients with severe disability in his study population. There was 52.6% of patients in our study who were completely independent compared to 8% with no significant disability in the study done by Sulaiman *et al.*⁹. The disadvantage in comparing the disability score between the 2 studies is attributed to the different scales for measuring disability as there are 5 grades in modified Rankin Scale whereas there are only 4 categories in the Barthel Index.

Frequency of depression among females was slightly higher than male (35.3% vs. 28.6%) in study population although depression was not significantly associated with gender ($p=0.531$). A study in the Arab community also showed similar findings where women were more likely to be depressed than men among VaD patients²³. The Aging, Demographics and Memory Study (ADAMS) found slightly higher prevalence of depression among female demented patients than males (11.44% vs. 10.19%)²¹. A local study did not show that females have a higher frequency of post stroke depression study^{8,9}.

In the study population, frequency of depression among Chinese (36.8%) was higher than Malays (28.1%), Indian and others (16.7%). Glamcevski *et al.* found higher frequency among Chinese compared with Malays and Indian which was 83%, 55.6% and 30% respectively⁸. Al-Jawad *et al.* found a similar rate of depression among Chinese and Malays in an elderly care home (61.6% and 60.8% respectively) but the Chinese had a higher rate of depression¹⁸. These racial differences was also seen in ADAMS population study at Utah, USA where whites and Hispanics had higher prevalence than African American²¹.

Most of the patients in study population had primary school education which accounted for 60.5% followed by secondary school (30.3%). There was no significant association between educational levels with depression. Pohjasvaara *et al.* found no significant association between educational level with depression²². Low education levels were significantly associated with both anxiety and depression in Nord-Trøndelag Health Study 1995–1997 (HUNT 2) study although the study did not specifically targeted for VaD patients²³.

There was several study limitation for this study as all data were collected by a single observer which may increase the risk of observer bias. Another limitation is that some of the variables were based on patients' recollection, particularly the first presentation of VaD. The medical records unfortunately do not always have thorough and detailed documentation of the necessary data required for the study. Patient with very severe dementia MMSE 0-3 need to be excluded as MMSE was unable to be assessed. CT scan may not be as sensitive as magnetic resonance imaging (MRI) in detecting of small areas of stroke.

CONCLUSIONS AND CLINICAL IMPLICATIONS

This is the first cross-sectional study done to determine the prevalence of the depression in post stroke patients with vascular dementia in UKMMC, Malaysia. This study showed that the prevalence of depression was 31.6% among VaD patients in our centre. Factors found to be associated with depression were functional impairment (as measured by Barthel Index), severity of cognitive impairment (measured by MMSE), type of infarct, age and right sided large artery stroke. Depression is not uncommon among post stroke patients with VaD. Depression poses significant morbidity to the patients. Early recognition of high risk patients is important in the holistic management of patients to prevent significant morbidity arising from depression.

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