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Sima Ataollahi Eshkoor[1,2], Tengku Aizan Hamid[1]*, Suzana Shahar[3] and Chan Yoke Mun[1]

[1]Malaysian Research Institute on Aging (MyAging), University Putra Malaysia, Serdang, Malaysia
[2]Iranian Research Center on Aging, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
[3]Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

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***Corresponding author:** Tengku Aizan Hamid, Malaysian Research Institute on Aging (MyAging), University Putra Malaysia, Serdang, Malaysia, E-mail: aizan@upm.edu.my

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Research Article

Predictive Factors of Severe Stage of Dementia among the Malaysian Elderly

Abstract

Background: The increase in life expectancy has particular relevance to conditions such as cognitive decline and dementia. Dementia is a chronic neurodegenerative disease that is on the rise globally. As the mechanism of dementia has not yet been understood completely; therefore, it is difficult to find a proper and exact cure. Many people with dementia gradually progress towards the severe stage and the identification of risk factors will help to better prediction, and prevention of the severe stage.

The context and purpose of the study: This study aimed to test the effects of hypercholesterolemia, hypertension (HT), diabetes mellitus (DM), and heart disease, as well as socio-demographic factors, and nutritional elements on the severe stage of dementia in the elderly. This study recruited 2322 subjects who were non-institutionalized Malaysian elderly. The hierarchy binary logistic regression analysis was used to predict the effects of suspected variables on the risk of severe stage of dementia in subjects.

Results: Approximately, 2.7% of samples experienced the severe stage of dementia. The results of the last step of analysis showed that age (odds ratio [OR]=2.44), and female gender (OR=3.12) increased significantly the risk of severe stage of dementia in subjects ($p<0.05$). Hypercholesterolemia (OR=0.25), phosphorous intake (OR=0.26), and the capability of counting (OR=0.37) reduced significantly the risk of severe stage of dementia.

Conclusions: It was concluded that age, and female gender were the factors, which increased the risk of severe stage of dementia in samples. On the other hand, hypercholesterolemia, phosphorous intake, and counting capability decreased the risk of severe stage of dementia in subjects. In addition, the rest of variables did not show any significant effects on the risk of severe stage of dementia in respondents.

Background

Dementia is a neurological degenerative disease [1]. It presents with disabilities, memory decline, language impairment, behavioral problems [1,2], and the depletion of many factors, including socialization, social relations, social activities [1,3], basic services and material resources [3]. It is the most common disabling disease in the elderly [4], and causes serious health problems in societies [5]. Because of the nature of disease, the majority of patients progress towards the severe stage within many years [6], which increases their health care consumption [1,2]. At this stage, there are many psychiatric and behavioral problems, prominent functional impairments, and dependency to others because of the impairment in daily living activities [6].

Nowadays, the average life expectancy has greatly extended over the last 50 years. The increased life expectancy results in a higher rate of individuals aged 65 years and above [7]. Almost 10% of Malaysian's population will be 60 years and above by 2020, which is due to improved health, longer life expectancy, and lower rate of mortality and fertility [8]. The increased rate of elderly population will enhance the number of cognitive decline and dementia [1,5,8]. It is expected that the number of people affected by dementia in worldwide will be over 100 million by 2050 and be double every 20 years. In Malaysia, the prevalence of dementia in the elderly has been reported differently, 22.4%, 8.3%, 6%, 2.5% and 36.5% in various research done in 2004, 2005, 2006, 2006 and 2007, respectively [9].

Since the etiology and pathogenesis of dementia are still unknown; no cure has been found so far [10]. Thus, the identification of exogenic and endogenic risk factors can help to better understand the pathogenesis of disease in which to predict, prevent and treat the disease. As chronic diseases, and

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nutritional elements can affect the risk of cognitive decline; therefore, this study assessed the effects of these variables and literacy skills on the risk of the progression of dementia towards the severe stage among the Malaysian elderly.

Materials and Methods

The main project (Project Code: NN-060-2013) was a heterogeneous survey entitled "TUA-Neuroprotective Model for Healthy Longevity among the Malaysian Elderly" and carried out in co-operation with the Universiti Kebangsaan Malaysia (UKM), and the Malaysian Research Institute on Ageing (MyAgeing), Universiti Putra Malaysia (UPM). The approval and permission for conducting the study were received from the Ethical Committee of the Universiti Kebangsaan Malaysia (UKM). This research was a part of the main project and recruited 2322 subjects who were the Malaysian elderly aged 60 years and above residing in non-institutional places. Samples were collected randomly, who were from four states of Malaysia, namely Kelantan, Selangor, Perak and Johor, and recruited through multistage random sampling. The states were selected on the basis of random sampling. The different ethnicities of samples were Malays, Chinese, Indians and others.

The elderly who were living in institutions and bedridden, were excluded. Subjects were gathered at community halls or centers for interview and health screening. Written consent was taken from respondents prior to interview. The trained fieldworkers conducted a face-to-face interview. Questionnaires were used to collect data on socio-demography (age, gender, ethnicity, marital status, and educational level) and health status (self-reported chronic diseases and medical conditions). In addition, age was dichotomized into "less than 75 years" and "75 years and above". Participants were asked whether they had suspected diseases based on physician approval and/or taking medications. Then, respondents were coded as no (0) and yes (1).

In this study, the evaluation of nutritional dietary intake of vitamins and minerals was done by Diet History Questionnaires (DHQ) and Nutritionist Pro 3 [11,12]. Nutritionist ProVersion 3.1.0 software was used to analyse the nutrient intake from the Diet History Questionnaire (DHQ). In addition, the mini-mental mark less than 10 using the mini–mental state examination (MMSE) test was considered for the severe stage of dementia [13]. However, the present study predicted the risk of variables, including literacy skills, chronic diseases, socio-demographic factors, and nutritional vitamins and minerals on the severe stage of dementia in subjects. Based on education, samples were divided two groups as (0) who had no education and (1) who had one of three level of primary, secondary and tertiary education.

Statistical analysis

A four-step hierarchical binary logistic regression model using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) was used to determine the effects of demographic factors, literacy skills, some chronic diseases as well as minerals and vitamin intake on the severe stage of dementia. Prior to the hierarchical regression analyses, correlation tests were examined for confirming the existence of associations among dependent variable and covariates. No variables needed to be excluded due to collinearity and the problem of multicollinearity was ruled out. The first step of the analysis was about the effects of demographic factors on the severe stage of dementia. The second model was built on the Model 1 by adding literacy skills. In the third step, hypercholesterolemia was entered. The final model included minerals and vitamin intake. Odds ratios (OR) with 95% confidence intervals (95% CI) were computed. The critical level for rejection of the null hypothesis was considered to be a p value of 5%, two-tailed.

Results

Various analyses were run on data collected from 2322 subjects who were the Malaysian elderly and non-institutionalized. The prevalence of severe stage of dementia in subjects was 2.7% (95% CI: 2.07-3.43) (Table 1). The percentage of samples in the severe stage of dementia and variables has been summarized in table 2. Among the subjects, 1.37% had the severe stage with reading problems and 7.92% had the same stage without this problem. The prevalence of samples with or without a writing problem in the severe stage of dementia was 1.5% and 6.49%, respectively. In addition, the capability of counting was damaged in 1.62% of subjects, while it was non-damaged in 9.46% of subjects at the severe stage of dementia. It was found that 2.73% of subjects at the severe stage had a familial history of dementia and 2.45% of them reported no familial history of dementia.

The findings demonstrated that the presence and absence of hypertension among respondents at the severe stage of dementia were 1.71% and 3.5%, respectively. The coincidence rate of diabetes mellitus (DM) and heart disease with the severe stage of dementia among subjects was 2.02% and 2.48%, respectively. A higher rate of severe stage of dementia was found in females (4.03%) compared to males (1.28%). It was found that non-married subjects (4%) displayed a greater rate of the severe stage of dementia compared to married subjects (2.11%). In addition, the prevalence of the severe stage of dementia among educated respondents (1.55%) was less than non-educated respondents (7.02%). Among all samples, non-Malays (3.13%) had a higher rate of severe stage of dementia compared to Malays (2.45%). The prevalence of the severe stage of dementia once taking vitamins and minerals has also been summarized in Table 2.1, 2.2, 2.3.

The bivariate analysis established the presence of an association between the severe stage of dementia and

Table 1: Prevalence of the severe stage of dementia among 2322* elderly

Character	n	n (%)	95% C.I.
Severe Stage of Dementia			
Yes	62	2.7	2.07-3.43
No	2227	95.9	95.00-96.66

*Whole population 2332

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each variable by chi-square tests. The results showed the significant associations between the severe stage of dementia and the suspected variables of age (χ^2=24.69, p<0.001), gender (χ^2=17.74, p<0.001), education (χ^2=43.32, p<0.001), hypercholesterolemia (χ^2=7.27, p=0.007), and marital status (χ^2=7.58, p=0.006), as well as the intake of minerals including iron (χ^2=14.26, p<0.001), calcium (χ^2=4.57, p=0.033), and phosphorous (χ^2=26.65, p<0.001). The association between the severe stage of dementia and each of literacy skills including reading (χ^2=63.62, p<0.001), counting (χ^2=59.12, p<0.001), and writing (χ^2=46.35, p<0.001) was significant as well (Tables 2.1, 2.2, 2.3).

As the main aim of this study was to predict the risk of chronic diseases, literacy skills, socio-demographic factors, and the intake of minerals and vitamins on the severe stage of dementia, a four-step hierarchical regression analysis was applied (Table 3). It was found that the advanced age (p<0.01), female gender (p=0.001), and low level of education (p=0.001) are the significant risks of progression towards the severe stage of dementia in all steps (p<0.01). Meanwhile, we acknowledge the bias of MMSE on educational level. As an instance, the appropriate of cut-point of 26 has been established for age and educational level groups in a study, which was conducted by Ylikoski and co-workers [14,15].

Table 2.1: Prevalence of the severe stage of dementia and associations with socio-demographic factors and literacy skills

	Whole	n	n %	95% CI	χ^2	p value
Reading capability						
No	467	36	7.92	5.71-10.85	63.62	<0.001
Yes	1822	22	1.37	0.91-2.05		
Writing capability						
No	555	36	6.49	4.65-8.96	46.35	<0.001
Yes	1734	22	1.5	1.00-2.22		
Counting capability						
No	317	28	9.46	6.57-13.36	59.12	<0.001
Yes	1972	30	1.62	1.13-2.31		
History of Dementia						
No	2126	54	2.73	2.10-3.54	0.01	0.946
Yes	163	4	2.45	0.79-6.56		
Age Group						
Less than 75	1819	31	1.7	1.2-2.4	24.69	<0.001
75 and above	470	27	5.74	3.97-8.22		
Gender						
Males	1098	12	1.28	0.73-2.19	17.74	<0.001
Females	1191	46	4.03	3.02-5.35		
Marital status						
Singles	725	28	4.00	2.74-5.77	7.58	0.006
Married	1564	30	2.11	1.48-2.99		
Ethnicity						
Malays	1427	34	2.45	1.74-3.43	0.35	0.554
Non-Malays	862	24	3.13	2.11-4.58		
Educational level						
No	484	33	7.02	4.98-9.77	45.62	<0.001
Yes	1805	25	1.55	1.05-2.26		

Significant at the 0.05 level using the chi-square test

Table 2.2: Prevalence of the severe stage of dementia and associations with nutritional factors

	Whole	n	n%	95% CI	χ^2	p value
Potassium						
≤1500	1231	37	3.01	2.19-4.12	3.16	0.075
> 1500	941	17	1.81	1.13-2.88		
Calcium						
≤500 and less	1219	38	3.12	2.28-4.25	4.57	0.033
> 500	953	16	1.68	1.04-2.71		
Iron						
≤12	980	38	3.88	2.84-5.28	14.26	<0.001
> 12	1192	16	1.34	0.83-2.17		
Phosphorus						
≤700	363	23	6.34	4.26-9.33	26.65	<0.001
> 700	1809	31	1.71	1.21-2.42		
Beta Carotene						
≤6000	1717	44	2.56	1.91-3.42	0.20	0.657
> 6000	455	10	2.2	1.2-4.00		
Vit C						
≤90	1187	27	2.27	1.56-3.28	0.48	0.487
> 90	985	27	2.74	1.89-3.96		
Vit D						
≤0.3	1746	44	2.52	1.88-3.37	0.04	0.837
> 0.3	426	10	2.35	1.28-4.27		
Vit E						
≤5	1329	39	2.93	2.15-3.98	2.84	0.092
> 5	843	15	1.78	1.08-2.92		
Riboflavin						
≤1	805	22	2.73	1.81-4.1	0.32	0.571
> 1	1367	32	2.34	1.66-3.28		
Niacin						
10 and less	1141	34	2.98	2.14-4.14	2.42	0.120
Above 10	1031	20	1.94	1.26-2.98		
Folate						
≤100	1312	38	2.9	2.12-3.95	2.30	0.129
> 100	860	16	1.86	1.15-3.00		
Cobalamin						
≤1.5	617	21	3.4	2.23-5.14	2.99	0.084
> 1.5	1555	33	2.12	1.51-2.96		
Biotin						
≤1.5	1332	33	2.48	1.77-3.46	0.00	0.974
>1.5	840	21	2.5	1.64-3.79		
Sodium						
≤1500	1387	37	2.67	1.94-3.66	0.52	0.470
>1500	785	17	2.17	1.36-3.45		

Significant at the 0.05 level using the chi-square test

The effect of marital status on the severe stage of dementia was not significant (p=0.462). Adding literacy skills in step 2 showed the subjects with counting capability (p=0.021) was significantly at a lower risk of developing towards the severe stage of dementia. In addition, after adding hypercholesterolemia, hypertension, heart disease, and diabetes in step 3, hypercholesterolemia significantly decreased

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the risk of severe stage of dementia (p=0.001). Minerals and vitamins were added to model 4 and the results showed that phosphorous intake (p=0.008) significantly reduced the risk of progression towards the severe stage of dementia. The results have been summarized in Table 3.

Discussion

The number of older adults who suffer from dementia is on the rise worldwide [16]. As dementia is not a curable disease [17], further studies are required to identify the risk factors of progression of the disease and to know how to improve patients' quality of life. Such research may prevent or delay the progression of disease towards the severe stage. This study evaluated the effects of chronic diseases, vitamins, minerals and socio-demographic factors on the risk of progression towards the severe stage of dementia in the Malaysian elderly.

Table 2.3: Prevalence of the severe stage of dementia and associations with some chronic diseases

	Whole	n	n%	95% CI	χ^2	p value
Hypertension						
No	1246	36	3.05	2.2-4.2	1.40	0.237
Yes	1043	22	1.71	1.12-2.57		
Hypercholesterolemia						
No	1703	52	3.29	2.52-4.28	7.27	0.007
Yes	586	6	1.02	0.40-2.33		
Diabetes Mellitus						
No	1745	47	2.92	2.2-3.85	0.76	0.384
Yes	544	11	2.02	1.07-3.7		
Heart Disease						
No	2087	53	2.73	2.09-3.55	0.00	0.956
Yes	202	5	2.48	0.92-6.00		

Significant at the 0.05 level using the chi-square test.

The final model showed that age, female gender, hypercholesterolemia, and phosphorous intake were the significant predictors of the severe stage of dementia in subjects. In addition, counting capability was prominently associated with a lower risk of severe stage of dementia at the second model. The significant effect of age on the severe stage of dementia indicated the progression of disease with advancing age, which can be due to the brain aging and cognitive decline [18]. Age-related physiological, psychological and social changes in the elderly can promote dementia and the progression of disease. Factors including infection, inflammation [19], vascular problems [20], nutritional deficiencies [21], and taking or not taking medications [22] in older adults can enhance the risk of cognitive decline and its progression towards the severe stage of dementia. The findings of this study indicated that the number of the severe stage of dementia in females is higher than males, which is consistent with works before. One explanation can be the difference of hormones between males and females [23]. The longer life expectancy of women than men seems to be the greatest factor in which to increase the rate of dementia among women [23,24]. Living longer increases the risk of facing to stresses such as the loss of loved ones and even jobs, which may aggravate cognitive decline and its progression. In addition, lifestyles [25,26], co-morbidities, and medications may cause such differences in the number of patients at the severe stage of dementia between genders [14].

In this study, counting capability significantly reduced at the severe stage of dementia. One possible explanation is that the brain damages more in the parts of counting capability compared to writing and reading skills. It is probably due to the neuronal loss in specific lobes of the brain, which in return affects counting capability [27]. In addition, lower counting ability can be due to the loss of memory in subjects as well.

Table 3: Prevalence of the severe stage of dementia and associations derived by logistic regression analysis

	Model 1			Model 2			Model 3			Model 4		
Variables	B	SE	OR	B	SE	OR	B	SE	OR	B	SE	OR
Age	1.091*	0.309	2.98	0.949*	0.313	2.58	0.863*	0.315	2.37	0.890*	0.323	2.44
Marital status	0.233	0.317	1.26	0.317	0.322	1.37	0.345	0.326	1.41	0.339	0.337	1.40
Education	-1.058*	0.311	0.35	-0.092*	0.419	0.91	-0.116*	0.419	0.89	-0.008*	0.441	0.99
Gender	1.364*	0.404	3.91	1.321*	0.403	3.75	1.415*	0.403	4.12	1.137*	0.413	3.12
Reading capability				-0.987	0.567	0.37	-0.954	0.558	0.39	-1.087	0.567	0.34
Writing capability				0.080	0.549	1.08	0.065	0.542	1.07	0.163	0.541	1.18
Counting capability				-0.861**	0.372	0.42	-0.846**	0.370	0.43	-0.987**	0.385	0.37
Hypercholesterolemia							-1.415*	0.529	0.24	-1.387*	0.534	0.25
Calcium										-0.042	0.378	0.96
Phosphorous										-1.336*	0.384	0.26
Niacin										0.428	0.391	1.53
Folate										0.268	0.377	1.31
Cobalamin										-0.202	0.327	0.82
Potassium										0.152	0.428	1.16
Iron										-0.739	0.396	0.48
Vitamin E										0.084	0.391	1.00

*p<0.01; **p< 0.05

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Phosphorous intake reduced the risk of developing dementia towards the severe stage in subjects. Inorganic phosphor is an essential nutrient in cells to retain cellular structures, cellular functions, energy metabolism, cell signaling, biological reactions, and cellular homoeostasis [28]. The contribution of phosphor into cellular structures and enzymes, can affect brain plasticity, synaptic efficacy, and brain functions such as learning and memory [29]. Phosphorous is a basic part of universal energy currency in living cells, adenosine triphosphate (ATP), which plays the central role in brain bioenergetics, function and neurodegeneration [30]. Our result was paradox to a research before, which reported high dietary inorganic phosphate can perturb normal brain growth [31]. In this project, hypercholesterolemia showed a significant effect to reduce the risk of progression towards the severe stage of dementia. This impact can be related to a specific type of cholesterol and correspond effects on blood vessels in the brain [32]. Cholesterol is a very high requirement for the CNS, which contains 23% of the total cholesterol in the body. Furthermore, the effects of cholesterol on the myelin sheaths [33], synaptogenesis, the maintenance of synaptic connections [34], and the release of neurotransmitters [33] may play roles in lower risk of severe stage of dementia [33,34]. Cholesterol likely affects cognitive function via the contribution to the formation of cell membranes, steroid hormones and vitamin D. Besides, gender and aging can mediate the effect of cholesterol on cognition through changing the uptake and biosynthesis of cholesterol in the body, brain regions and CNS cell types [33]. The activities of genes such as ABCA1 and CYP46 may impact the flow of cholesterol through neurons, which in turn affects the progression of dementia towards the severe stage of dementia [33,35]. However, paradoxical reports showed that the increased cholesterol level in the brain increases the risk of dementia [36,37]. One possible explanation can be the presence of the specific types of cholesterol, which may accelerate the deposition of amyloid-β (A-β) peptides in the brain. However, the exact effects and mechanism of cholesterol are still unclear [33,38].

According to the results, sodium has no significant impact on the brain tissue to cause the severe stage of dementia. The prominent effect of sodium on dementia in other research may reflect its mediator influence. For example, the correlation of sodium with hypertension and heart disease can trigger the onset of dementia in the vascular type [39]. Despite several research indicating the effects of diabetes mellitus [40], heart diseases [41], and hypertension [42,43] on the progression of dementia, our results did not establish such correlations between these types of diseases with the severe stage of dementia. It seems that those factors contributing to the onset of dementia are probably different to those, which have roles in the progression of dementia towards the severe stage.

Despite a paradoxical report [44], no correlation was found between ethnicity and the progression of dementia towards the severe stage. It is likely due to confounding factors that may interfere with the effect of ethnicity on the progression of dementia. The effect of ethnicity is probably through cultural factors, which may trigger the onset of dementia. The effect of ethnicity on health is due to the impact of socioeconomic status, education, health beliefs and migration [45]. In addition, genetic predisposing factors and childhood IQ change the risk of dementia among people [46]. As the elderly with dementia are different from those without dementia in biological, psychological, behavioural, economic and social circumstances; therefore, a broad orientation is needed over this literature.

Limitations of study

The findings of the present study should be considered in light of its limitations, which can affect the interpretation of data in the elderly at the severe stage of dementia. First was the difficulty in collecting accurate self-reported data from subjects who were at the severe stage. Cross-sectional design of the study was second limitation and confined to determine the exact effects of variables on the severe stage of dementia. Meanwhile, the physical and psychological co-morbidities of respondents can limit the appropriate assessment of risk factors for the progression of dementia towards the severe stage. However, further researches are needed to identify the exact causes and risk factors for the progression of dementia towards the severe stage.

Conclusion

It was concluded that age, female gender, hypercholesterolemia and phosphorous intake were the significant factors affecting the risk of the severe stage of dementia in subjects. While, age and female gender significantly increased the risk of severe stage of dementia, hypercholesterolemia and phosphorous intake affected negatively the progression of dementia towards the severe stage. Furthermore, the loss of counting capability was significantly observed at the severe stage of dementia. However, a better understanding of risk factors for the progression of dementia can reduce the burden of the severe stage; therefore, further investigations are required to improve our knowledge.

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