Risk factors of dementia cognitive symptoms among older patients in Vietnam: A cross-sectional study

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RISK FACTORS OF DEMENTIA COGNITIVE SYMPTOMS AMONG OLDER PATIENTS IN VIETNAM: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Dementia has emerged as a significant contributor to declining quality of life and stands as a prominent factor in the increase of disability and dependency among elderly populations globally. This study aimed to explore the relationship between cognitive symptoms of dementia and their risk factors in individuals aged 60 years and older among Vietnamese outpatients who visited Geriatrics Clinic at University Medical Center of Ho Chi Minh city, Vietnam.

Methods: 387 participants who were aged ≥ 60 years old were included in the cross-sectional study. Cognitive impairment was assessed by using the Mini Mental State Evaluation (MMSE) questionnaire. The functional limitations in activities of daily living (ADL) and Instrumental Activities of Daily Living (IADL), multimorbidity, and polypharmacy were also evaluated. Frailty was determined by The Canadian Study of Health and Aging Clinical Frailty Scale. Suffering dementia was determined when MMSE score was below 24 and IADL score less than 8.

Results: People with dementia cognitive symptoms accounted for 22.74 % of the cohort. The percentage increased with age, and was higher in women than in men. Factors that increased the odds of having dementia symptoms were older age, female, multimorbidity, Frailty Scale > Grade 4 and ADL dependency.

Conclusions: Age, female, multimorbidity, frailty and ADL dependency were considered as risk factors of dementia cognitive symptoms among the Vietnamese people aged 60 years and older.

Keywords cognitive impairment, dementia, frailty, MMSE, Vietnam

1. Background

Dementia is defined as a syndrome marked by ongoing decline in cognitive functions, potentially interfering with the ability to perform daily activities (1). This condition mainly affects older people and potentially leading to disability (1). Dementia presently impacts approximately 50 million individuals worldwide with nearly 60% of those residing in countries with low to moderate incomes (1). Regarding the elderly individuals aged 60 and over, dementia accounts for between 5 and 8% (1). The population afflicted with dementia is anticipated to increase to 82 million by 2030 and 152 million by 2050 (1). Dementia negatively affects the quality of life and has become one of the leading causes of disability and dependency among elderly individuals globally (2).

Some factors involved in the higher dementia prevalence among older patients such as age, gender, nutritional status, educational level, physical inactivity, smoking…have been studied (3, 4). Data retrieved from three nationwide cross-sectional surveys in China- a neighbouring Asian country to Vietnam- indicated that physical inactivity, midlife hypertension and low education were the three primary factors contributing to dementia within the Chinese population (3). Additionally, recent European studies suggested the involvement of frailty and activities of daily living (ADL) in the development of dementia (5, 6).

Early diagnosis of dementia in order to promote optimal management is essential. Besides, the risk factors of dementia development should be detected for proper and timely intervention to improve quality of life for the aged.

In Vietnam, few studies dementia and its risk factors in the elderly have been conducted while the proportion of Vietnamese older people has been rapidly increasing and would surpass 25% of the overall population by 2049 (7). A rare

cross-sectional study by Nguyen et al. in the Northern, Central and Southern region of Vietnam showed that the proportion of cognitive symptoms of dementia accounted for 46.4% among the Vietnamese elderly people and the symptoms were more common among older, female participants possessing lower education levels and having previously experienced stroke (8). To our knowledge, the association between frailty or ADL and dementia may have never been explored in Vietnamese population.

In light of limited data, we would like to clarify the relationship between cognitive symptoms of dementia and their risk factors in adults aged 60 years and older. Data from our study would provide new insights regarding the characteristics of dementia in Vietnamese people and contribute to implement effective management to prevent its development.

2. Materials and Methods

2.1 Study design and participants:

This cross-sectional study included 387 older individuals aged ≥ 60 years old who admitted to Geriatrics clinics at University Medical Center from September 2019 to May 2020. Participants were ineligible if they met any of the following criteria: acute pathology, cognitive impairment (unable to understand instructions and/or Mini Mental State Examination (9)). Sample size was calculated for a cross-sectional study with an unknown prevalence within the 95% confidence interval: $n = Z^2_{1-\alpha/2} \times [p \times (1 - p)/d^2]$. And the sample size required was at least 385 participants. The study protocol was approved by the local ethics committee of the University of Medicine and Pharmacy at Ho Chi Minh city, Vietnam (reference number: 626/ĐHYD-HĐĐĐ) and all participants provided informed consent for the study.

2.2 **Procedure:**

Patients were physically examined on their visit. All the participants underwent a comprehensive geriatric assessment. The sociodemographic characteristics (gender, age, level of education, living place); comorbidity; body mass index (BMI); the information on the activities of daily living (ADL), the instrumental activities of daily living (IADL), and cognitive functions were collected.

Cognitive impairment was assessed using the MMSE questionnaire developed by Folstein et al.(9)- in the Vietnamese version. This tool is considered as the most commonly administered screening assessment of cognitive functioning (10). It comprises assessments of orientation, attention, memory, language, and visual-spatial skills, with a total score ranging from 0 to 30.

To evaluate the functional limitations in ADL, participants were asked regarding their capability to engage in bathing, dressing, toileting, feeding, transferring, and continence, as described by Katz et al. (11). ADL dependency was defined as dependency in at least one ADL.

IADL scale of Lawton and Brody consists of eight tasks: using the telephone, shopping, preparing meals, performing housekeeping chores, doing laundry, utilizing transportation, managing medication intake, and handling finances (12). Patients' IADL were scored according to the level of dependency on each of these activities.

In this study, we combined the IADL and MMSE for screening dementia, as suggested in the other studies (13-15). Specifically, participants were defined as cognitive symptoms of dementia cognitive impairment with MMSE score below 24 and IADL score less than 8.

Frailty status was identified by The Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale (16). This tool was employed due to its feasibility for research in older patients. Indeed, the Clinical Frailty Scale, a screening tool based on the clinical assessment, is less time-consuming. This measurement ranges from 1 (robust health) to 7 (complete functional dependence on others) (16) . In this study, participants were classified into two groups - grade 4 or below and above grade 4 – to examine the relation between frailty and dementia symptoms. This cut-off point was chosen based on the Frailty Scale indicating that participants with grade 5 are mildly frail ones (16).

Multimorbidity was regarded as the presence of two or more self-reported chronic diseases. And polypharmacy was described as patients' taking five or more medications simultaneously. BMI was calculated by using the measurements of height and weight (weight in kilograms divided by height squared in meters, m^2). BMI was classified into three categories based on the World Health Organization's recommendations for the Asia-Pacific region: underweight (<18.5 kg/m^2), normal weight (18.5–22.9 kg/m^2), and overweight (≥23 kg/m^2).

2.3 Statistical Analyses

The statistical analysis was conducted utilizing IBM SPSS version 26.0. Data normality was assessed using the Kolmogorov-Smirnov goodness-of-fit test. Comparisons among categorical variables were conducted using either the chi-square test or Fisher's exact test, as deemed appropriate. Since categorical variables did not follow a normal distribution, Mann-Whitney U tests were employed for comparison. Categorical variables are presented as frequencies (n) and percentages (%). Continuous variables are illustrated by using median and interquartile range. Univariate and binary logistic regression was applied to assess risk factors of having

dementia symptoms. All variables were examined for interaction and multicollinearity. Differences were considered to be significant for two-sided $p<0.05$.

3. Results

The main characteristics of the participants in the cohort are illustrated in table 1. There was an inverse association between age and MMSE total score (data not shown). Participants with lower education level had fewer MMSE total score (data not shown). When exploring the relation between gender and total MMSE score, females achived fewer scores than males ($p<0.05$, data not shown). The overall people with dementia cognitive symptoms accounted for 22.74 % of the cohort. Besides, the percentage was elevated in women than in men ($p = 0.021$) and increased with age ($p < 0.001$). Dementia cognitive symptoms were associated with BMI ($p=0.001$). People with dementia symptoms were found to have a lower level of education compared to robust ones ($p < 0.001$). There was no difference in the percentage of dementia cognitive symptoms between individuals residing in rural and urban settings. Married people are less likely to have dementia symptoms compared to the other groups ($p=0.026$).

Table 1 Baseline characteristics of the participants

Variables	All (n= 387)	Dementia symptoms (n= 88)	Without dementia symptoms (n= 299)	p value[1]
Age (years)	71.00 ± 10.00	77.00 ± 13.00	69.00 ± 7.00	**< 0.001**
Gender, n (%)				
Male	132 (34.11)	21 (23.86)	111 (37.12)	**0.021**
Female	255 (65.89)	67 (76.14)	188 (73.73)	
Age group, n (%)				
<70 years	169 (43.67)	18 (20.45)	151 (50.50)	
70 – 79 years	163 (42.12)	34 (38.64)	129 (43.14)	**< 0.001**
≥80 years	55 (14.21)	36 (40.92)	19 (6.35)	

BMI, n (%)[2]				
Underweight	39 (10.08)	18 (20.45)	21 (7.02)	
Normal weight	183 (47.29)	35 (39.77)	148 (49.50)	**0.001**
Overweight	165 (42.64)	35 (39.77)	130 (43.48)	
Education, n (%)				
Primary School	240 (62.02)	76 (86.36)	164 (54.85)	
Secondary School	80 (20.67)	6 (6.82)	74 (24.75)	
High School	53 (13.70)	6 (6.82)	47 (15.72)	**< 0.001**
University	11 (2.84)	0	11 (3.68)	
Postgraduate school	3 (0.78)	0	3 (1.00)	
Living place, n(%)				
Rural	273 (70.54)	62 (70.45)	211 (70.57)	0.984
Urban	114 (29.46)	26 (29.55)	88 (29.43)	
Current marital status, n(%)				
Married	253 (65.37)	47 (53.41)	206 (68.90)	
Widowed	130 (33.59)	40 (45.45)	90 (30.10)	**0.026**
Divorced	4 (1.04)	1 (1.14)	3 (1.00)	
Living alone, n(%)	18 (4.65)	5 (5.68)	13 (4.35)	0.712

Note: Categorical variables are described as frequencies (percentages). Continuous variables are described by using median (Interquartile range). Comparisons were conducted using the chi-square test or Fisher's exact test for categorical variables across categorical variables. Abbreviations: BMI=body mass index

[1] With dementia group versus without dementia

[2]BMI was classified as underweight (<18.5 kg/m^2), normal weight (18.5–22.9 kg/m^2), overweight (≥ 23 kg/m^2)

Table 2 outlines the overview of participants' medical conditions. Hypertension and prior stroke were more frequently recorded in people with dementia symptoms compared to the other group ($p < 0.05$). Participants with dementia cognitive symptoms are more prone to have polypharmacy and multimorbidity compared to those without dementia ($p<0.001$). Besides, people with Frailty Scale > Grade 4 tended to have dementia symptoms compared to the robust. Dementia symptoms were significantly associated with ADL dependency ($p < 0.001$).

Table 2: Health condition, Frailty Scale, and ADL dependency according to dementia symptoms

Variables	All (n=387)	Dementia symptoms (n= 88)	Without dementia symptoms (n= 299)	p value

Health condition, n (%)				
Hypertension	273 (70.45)	80 (90.91)	193 (64.55)	**< 0.001**
Diabetes mellitus	127 (32.82)	31 (35.23)	96 (32.11)	0.584
Dyslipidemia	207 (53.49)	43 (48.86)	164 (54.85)	0.322
Coronary artery disease	74 (19.12)	22 (25.00)	52 (17.39)	0.111
Heart failure	6 (1.55)	1 (1.14)	1 (1.67)	0.721
Atrial fibrillation	4 (1.03)	1 (1.14)	3 (1.00)	0.914
Prior stroke	22 (5. 68)	11 (12.50)	11 (3.68)	**0.002**
Chronic kidney disease	43 (11.11)	10 (11.36)	33 (11.04)	0.932
Parkinson	4 (1.03)	2 (2.27)	2 (0.67)	0.584
Multimorbidity, n (%)	331 (85.53)	86 (97.73)	245 (81.94)	**< 0.001**
Multiple drug use, n (%)	298 (77.00)	76 (86.36)	222 (74.25)	**0.018**
Frailty Scale, n (%)				**< 0.001**
≤ Grade 4	347 (89.66)	59 (67.05)	288 (96.32)	
> Grade 4	40 (10.34)	29 (32.95)	11 (3.68)	
ADL dependency, n (%)	40 (10.34)	33 (37.50)	7 (2.34)	**< 0.001**

Note: Categorical variables are described as frequencies (percentages). Comparisons were conducted using the chi-square test or Fisher's exact test for categorical variables across categorical variables. Abbreviations: ADL=activities of daily living

Finally, univariate and multivariate regression analyses were used to determine the risks factors of dementia symptoms for the cohort (table 3). As can be seen in the adjusted model, factors that increased the odds of having dementia symptoms were older age, female, multimorbidity, Frailty Scale > Grade 4 and ADL dependency.

Table 3: Logistic regression analysis for dementia and related factors

Variables	**Univariate**		**Multivariate**	
	OR (95% CI)	p value	OR (95% CI)	p value
Age	1.162 (1.115 – 1.209)	**< 0.001**	1.111 (1.059 – 1.165)	**< 0.001**
Gender, female vs male	1.884 (1.094 – 3.244)	**0.022**	2.128 (1.090 – 4.155)	**0.027**
Multimorbidity	9.478 (2.262- 39.705)	**0.002**	4.847 (1.114 – 21.091)	**0.035**
Frailty Scale ≤ Grade 4 > Grade 4	 reference 12.869 (6.088 – 27.201)	 **< 0.001**	 reference 2.870 (1.099 – 7.493)	 **0.031**

ADL dependency	25.029 (10.539 – 59.442)	**< 0.001**	6.867 (2.535 – 18.603)	**< 0.001**

Note: Unless otherwise specified, data are presented as odds ratio (OR) and 95% confidence interval (CI); Abbreviations: ADL=activities of daily living

4. Discussion

Although the dementia and its risk factors among older persons in Vietnam have been reported before (8), as far as we are aware, this study marks the first investigation in Vietnam, which examines either frailty or ADL to further address their relevance to the risk of having dementia in Vietnamese elderly.

In our study, frailty was significantly associated with dementia cognitive symptoms. In this viewpoint, the elevated markers of inflammation such as C-reactive protein or proinflammatory interleukins provide a biological framework from which the syndrome of frailty evolves (17). Also, the inflammation may trigger the neurodegenerative and vascular damages which were in correlation with cognitive decline and dementia (18). Frailty and cognitive decline might share some common etiologies, for instance, a few factors associated with the development of frailty such as diabetes or brain infarcts which have been thought to be related to both frailty (19) and Alzheimer's disease (20). Both cross-sectional and longitudinal studies have indicated that frailty serves as a predictor of cognitive disorders (21).

We confirmed a significant correlation between ADL dependency and cognitive symptoms of dementia. The finding has some correspondence with an earlier study by Fauth et al., in which they found that ADL was a predictor for dementia after controlling for global cognitive status (22). Several mechanisms can be responsible for this association. Some factors exacerbating dementia development was supposed to cause the reductions in physical performance associated with daily functioning (23, 24). Schneider et al. demonstrated that neurofibrillary tangles in the substantia

nigra were related to gait impairment – one of the most important of parkinsonian signs in older persons without idiopathic Parkinson's disease (23). Some scientists have indicated that gait disorder or rigidity was associated with impaired cognitive function and risk of dementia (24). These findings support the notion that there may be a shared etiology in brain pathology between cognitive impairment and physical performance tasks. Besides, there was an increase in the percentage of ADL in parallel with the levels of dementia in our study. In accordance, Giebel et al. documented a decline in activities of daily living (ADL) performance throughout the progression of dementia (25).

Subjects with cognitive symptoms of dementia were more prone to have a history of hypertension or prior stroke compared to the robust. This outcome was similar to the result by other authors, suggesting an increasing risk of dementia in people with hypertension (26). The literature on these longitudinal studies, in which the participants were followed for decades, has indicated that people with a history of high blood pressure were likely to develop dementia (27). Hypertension-induced microvascular lesions may lead to subcortical and periventricular white matter damage, microinfarcts, and microhemorrhages, which have proven to be closely correlated with the cognitive dysfunctions (27). Besides, stroke survivors would be at higher risk of cognitive impairment development, as described in earlier studies (28). In clinical research, a great deal of effort has been devoted to control hypertension for limiting stroke and cognitive impairment prevalence. In a meta-analysis, Rouch et al. confirmed that antihypertensive drugs may decrease the incidence of dementia and prevent the cognitive decline (29). Also, nonrandomized observational studies including the Rotterdam study (30), Cache County Study (31), Indianapolis study(32), and Kungsholmen study(33) demonstrated that antihypertensive medication could protect the cognitive functions from declining.

The result from this study would, therefore, highlight the need for an appropriate management of hypertension in order to prevent dementia development among the elderly.

Multimorbidity was associated with dementia in the present study. From a cross-sectional analysis among Scottish population, elderly individuals with dementia were found to have a higher likelihood of experiencing comorbidity and polypharmacy compared to those without dementia(34). Older adults with multimorbidity usually receive many interventions of various types, or many medications, and are therefore at risk of polypharmacy. This condition may lead to a higher exposure to potentially inappropriate medicine (PIM) use, which is related to dementia (35, 36). For instance, sedatives or anticholinergics may impair the cognitive function (37, 38). Medical records of all outpatient attendees at The National Geriatric Hospital in Vietnam showed that PIM use was common in patients with dementia (41,4% of those patients) (37). Also, 21.4% of patients with dementia attending the memory clinics were reported to have been prescribed PIMs in Australia (39). Higher exposure to PIM use would cause persistent cognitive impairment and, therefore, was associated with higher risk of developing dementia (40). In our perspective, attempting to control an appropriate number of effective drugs prescribed among older adults with multimorbidity is very likely to be able to prevent the dementia onset. In addition, adequate caution should be exercised when administrating medications that may negatively affect cognitive functions.

Some limitations should be acknowledged in this study. Our resources were limited. We could only conduct the investigation in the city's major clinic where there are sufficient number of geriatrics and necessary equipment for diagnosis. Our analyses reflect the profile from only one particular place; therefore, they cannot be extrapolated to the general population. Besides, being a cross-sectional study, it does

not allow for establishing causal relationships. Also, Diagnostic and Statistical Manual-5 (DSM-5) criteria, a better tool to diagnose dementia, was not applied in this study due to the lack of neurological specialists and funding.

Despite such limitations, this study contributes a crucial aspect to the understanding of dementia and its risk factors among the Vietnamese population. In previous studies, the association between frailty or the functional limitations in activities of daily living (ADL) and dementia cognitive symptoms had been relatively less investigated than other very common, significant risk factors such as age, gender or educational levels. Hence, the outcomes of the study may support the relatively few published works concerning that relation. Nearly 75% and even higher percentage of patients with moderate to severe dementia, are not recognized by primary care physicians (41). Therefore, screening tests are helpful for detection of patients with high risks of dementia in clinical settings. The study may further highlight the importance of screening the "dementia cognitive symptoms" in older population who have high risks of that condition. When the patient has such symptoms, further steps should be performed to confirm the diagnosis of dementia (by using Diagnostic and Statistical Manual-5 (DSM-5) criteria, for instance).

Future prospective studies using a broader panel of risk factors of dementia with DSM-5 criteria is highly recommended to fully verify their relevance to dementia.

5. Conclusion

This study confirms the association of age, female, multimorbidity, frailty and ADL dependency with dementia in Vietnamese people aged 60 years and older. Our findings provide an overview of dementia and its risk factors in Vietnamese older adults. The outcomes also emphasize the need of screening the "dementia cognitive symptoms" in these patients and managing the modifiable factors to prevent or, at

least, partially delay dementia development. Yet, further longitudinal studies would be performed to clarify the causal relationships between dementia and other possible risk factors.

Abbreviations:

- **MMSE**: Mini Mental State Evaluation,

- **ADL**: activities of daily living,

- **IADL**: Instrumental Activities of Daily Living,

- **BMI**: body mass index,

- **CSHA**: The Canadian Study of Health and Aging.

Ethics approval and consent to participate

The study design was revised and approved by the Ethical Committee of University of Medicine and Pharmacy at Ho Chi Minh city following the Declaration of Helsinki, last updated in 2008.

Consent for publication

Written informed consent was obtained from all patients for the publication of this research, and copies of the written consents are available for review by the Editor-in-Chief of this journal.

Availability of data and material

The datasets are available from the corresponding author upon reasonable request.

Competing interests

The author(s) declare that they have no competing interests.

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Authors' contributions

- Dr. HTBT contributed to the conception and design of the study, data collection, drafting of the manuscript, and revision of the final manuscript.

- Dr. THNT took part in conception of the study, and collected data.

- Dr NNHMT drafting of the manuscript revision and litureture reviewing

- Dr NVT took part in the conception and design of the study

- Dr NHLT conducted data analysis and wrote draft manuscripts.

- Dr. CDH took part in the conception and design of the study, revision, and approval of the final manuscript.

All authors have reviewed and approved the final manuscript.

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