POOR COGNITIVE RESERVE STATUS AS PREDICTORS OF MEMORY IMPAIRMENT AMONG ELDERLY

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**Cite this as:** Harahap HS, Indrayana Y. Poor cognitive reserve status as predictors of memory impairment among elderly. Malang Neurology Journal; 2023.9:102-106. DOI: http://dx.doi.org/10.21776/ub.mnj.2023.009.02.6

**ABSTRACT**

**Background:** Cognitive impairment in the elderly population is commonly associated with age-associated neurodegenerative processes in the brain. The integrity of the cognitive reserve status may be an important factor that can compensate this age-associated neurodegenerative processes.

**Objective:** To investigate the predictor role of poor cognitive reserve status on memory impairment among elderly subpopulation in Mataram, West Nusa Tenggara.

**Methods:** This cross-sectional study involved elderly subjects recruited at Panti Jompo Tresna Werdha Puspa Karma. Data collected included age, gender, hypertension, diabetes, cognitive reserve status (years of education, leisure activity, occupation, and exercise), and memory status. Memory status obtained based on scores of 3 neuropsychological tests (wordlist memory task, recall, and recognition tests). Subjects with normal memory status had normal scores on at least 2 of the 3 neuropsychological tests. Multivariate regression analysis was performed to examine the role of cognitive reserve as a predictor of memory impairment in subjects.

**Results:** In Model 1 of multivariate regression analysis, the main predictors for memory impairment in elderly subjects are shorter years of education (odds ratio: 13.1; 95% confidence interval: 1.8 – 95.0) and absence of leisure activity (odds ratio: 5.9; 1.2 – 28.8). In model 2, the main predictors for memory impairment are consistently shorter years of education (OR: 11.0; 95% CI: 1.4 – 84.0) and absence of leisure activity (OR: 5.3; 95% CI: 1.0 – 27.7).

**Conclusion:** Shorter years of education and the absence of leisure activity were predictors for memory impairment in the subpopulation of the elderly in Mataram, West Nusa Tenggara.

**Keywords:** Cognitive reserve, memory impairment, neurodegeneration, brain aging

**Introduction**

Cognitive impairment is a common health problem in the elderly population, with a prevalence between 5.1 and 41%.\(^1\) Although generally found in the form of mild cognitive impairment (MCI), conversion to dementia is also quite high, at 10% per year.\(^2\) When it comes to dementia, where memory impairment is the most prominent clinical symptom, the elderly will lose their independence in carrying out their daily functional and social activities which results in an increase in the health, economic, and social burdens of their families. In fact, early identification of memory disorders and their determinants and adequate management are useful for slowing the progression of cognitive decline in the elderly.\(^3\)

Theoretically, cognitive impairment in healthy elderly is related to the occurrence of age-associated neurodegenerative processes in the brain. The main finding resulting from this age-associated neurodegenerative process is the occurrence of atrophy in various regions of the brain that play an important role in carrying out cognitive function. Brain atrophy in the hippocampus and prefrontal cortex causes memory impairment.\(^4\) Brain atrophy that occurs with increasing age is morphologically characterized by a decrease in the substantia volume of the cerebral cortex, widening of the sulci and reduced gyrus, and ventricular enlargement.\(^5\) Abnormal protein deposition in the brain, such as β-amyloid, tau protein, and neurofibrillary tangles, is also considered to contribute to age-associated neurodegenerative processes in the elderly. This opinion is supported by the results of a post-mortem study which showed that deposition of these abnormal proteins was also found in 30% of the elderly with intact cognitive function.\(^6\) Vulnerability to the occurrence of these neurodegenerative processes will increase with the presence of vascular risk factors in the elderly.\(^7\)

Among the well-known vascular risk factors, hypertension and diabetes mellitus are the most important risk factors for abnormal protein deposition in the elderly as previously described.\(^8\) These two vascular risk factors are also known to be independent risk factors for vascular dementia and Alzheimer’s dementia.\(^9\) The presence of hypertension and diabetes mellitus contributes to chronic hypoperfusion in various brain areas. Hypoperfusion in the hippocampal area that underlies memory impairment in the elderly is a common finding in the elderly with vascular dementia. An imaging study showed that chronic hypoperfusion induced...
by hypertension and diabetes mellitus was correlated with the occurrence of brain atrophy with the characteristics described previously. As previously stated, healthy elderly people whose brain imaging results show brain atrophy do not always have memory problems. An important factor that can explain this phenomenon is the intact cognitive reserve status in the elderly, even in the presence of the previously mentioned vascular risk factors. Cognitive reserve reflects the ability of the brain in the elderly to compensate for the effects of age-related neurodegenerative processes, such as brain atrophy, which allows the elderly to maintain optimal cognitive function and functional and social capacities. Several factors that play a dominant role in determining a person's cognitive status include years of education, leisure activity, occupation, and exercise. Previous studies have shown that elderly people with memory impairment generally have poor cognitive reserve status. Thus, poor cognitive reserve status also has the potential to be a predictor of memory disorders in the elderly population. This study aims to investigate the predictor role of poor cognitive reserve status in the elderly subpopulation in Mataram, West Nusa Tenggara, on the progression of their memory impairment.

Methods

Subjects and study design

This cross-sectional study involved elderly subjects who were recruited at the Panti Jompo Tresna Werda Puspa Karma, Mataram, West Nusa Tenggara. This study was conducted between July and December 2021. Data were obtained through interviews with subjects and this was conducted by well-trained nurses. Inclusion criteria for subjects were those aged 60 years and over, literate, voluntary participating, and fully conscious. Meanwhile, the exclusion criteria for subjects were those with visual and hearing impairments that could not be corrected and those who decided not to continue their participation in the study. This study has received ethical approval from Komisi Etik Penelitian Kesehatan, Universitas Mataram (Register number: 223/UN18.07/ETIK/2021). All subjects provided written informed consent prior to their participation.

Demographic characteristics and vascular risk factors

In this study, data regarding the demographic characteristics (age and gender) and vascular risk factors (hypertension and diabetes mellitus) of the subjects were collected. Data regarding age was continuous data expressed in mean with standard deviations and then grouped into 3 groups, namely 60-69 years, 70-79 years, and ≥ 80 years, respectively. Gender was categorized into male and female. Subjects were categorized as having hypertension if they reported a previous history of hypertension and/or were currently taking antihypertensive drugs. In addition, subjects were categorized as having diabetes mellitus if they reported a previous history of diabetes mellitus and/or were currently taking antidiabetic drugs.

Cognitive reserve status

Data representing cognitive reserve status collected in this study included years of education, current occupation, leisure activity, and exercise. Years of education was a continuous variable expressed in mean ± SD and then categorized into groups with years of education ≤ 12 years and > 12 years. Subjects were categorized as having an occupation if they currently have an occupation that was routinely carried out to meet their daily economic needs. Subjects were categorized as having leisure activity if they currently continue to carry out daily physical activities to maintain their health.

Memory status

The memory status of the subjects was determined based on scores from several neuropsychological tests consisting of wordlist memory task, wordlist memory recall, and wordlist memory recognition. The Wordlist memory task consisted of 3 series of tests, where in each series, each subject was asked to read and remember 10 words on the stimulus card shown by the examiner. At the end of each series of tests, the subject was asked to try to recall these 10 words. In each series, these 10 words given to the subject were the same but were shown in random order. The results of this test had a total score of 30 and the subjects with a score of 16-30 were categorized as having normal memory function.

Wordlist memory recall was carried out after the subjects underwent several different neuropsychological tests aimed at other purposes. In this test, the subject was asked to recall 10 words that were previously tested in the wordlist memory task. The results of this test had a total score of 10 and subjects with a score of 4-10 were categorized as having normal memory function.

Wordlist memory recognition was performed after the subject completed the wordlist memory recall test. In this test, the examiner added another 10 words, in addition to the 10 words previously given in the wordlist memory task. Then, the subject was asked to determine whether each word shown by the examiner in a certain order was part of the 10 wordlist that had been tested in the previous wordlist memory task or not. The final score was obtained by dividing the number of words correctly stated by the subject. The results of this test had a total score of 10 and subjects with a score of 8-10 were categorized as having normal memory function.

Based on the results of the 3 neuropsychological tests above, the subjects were further categorized as having normal memory status if they had normal scores on at least 2 of the 3 neuropsychological tests. The cut-off point for normal values in each of these neuropsychological tests was determined based on the results of a previous study.

Data analysis

The first analysis was carried out to investigate differences in mean and/or proportion of demographic characteristics (age and gender), cognitive reserve status (years of education, leisure activity, occupation, and exercise), vascular risk factors (hypertension and diabetes mellitus), and scores on memory function tests (wordlist memory task, wordlist memory recall, and wordlist memory recognition) between subjects with normal memory function and those with impaired memory function. Statistical analysis used for this purpose included independent t-test, chi-square test, Fisher exact test, and Mann-Whitney test. For continuous data, independent t-test was used if the mean value of the tested variables was normally distributed.
If the mean value of the variables examined was not normally distributed, then the statistical analysis used was the Mann-Whitney test.

Second, a bivariate analysis was conducted to examine the individual relationship between each component of cognitive reserve (years of education, occupation, leisure activity, and exercise) with the memory status of the subjects and the results were presented as odds ratio (OR) with 95% confidence interval (CI). Finally, multivariate regression analysis was performed to examine the role of cognitive reserve as a predictor of memory impairment in subjects after controlling for several covariates, including demographic variables (age and gender) for Model 1 and plus vascular risk factors (hypertension and diabetes mellitus) for Model 2 and the results were reported as OR with 95% CI. All statistical analysis were performed using a computer program and statistical significance was set at p ≤ 0.05.

**Results**

There were 226 elderly people managed by Panti Sosial Tresna Werdha Puspa Karma, Mataram. Of these, 66 subjects met the inclusion criteria. Most of the subjects who did not meet the inclusion criteria were due to their reluctance to participate in the study after receiving information regarding the research procedure and due to their illiteracy. Of the 66 subjects who met the inclusion criteria, 11 of them were excluded due to their refusal to continue their participation in the study so that their data collected was incomplete. Thus, the final number of subjects who were able to complete their participation in this study was 55 subjects (n = 55).

Table 1 shows the results of the first analysis examining differences in mean values and/or proportions in terms of demographic characteristics, cognitive reserve status, and vascular risk factors and neuropsychological test results between subjects with normal and impaired memory status. This study indicates that subjects with memory impairment have a higher mean age, shorter mean years of education and lower mean scores on all neuropsychological tests for memory domains than those with normal memory function. This study also demonstrates that older age, shorter years of education, absence of leisure activities, hypertension, and diabetes mellitus have significantly higher proportions in the memory impaired group compared to the normal memory function group.

Table 2 shows the second analysis that examines the relationship between years of education, occupation, leisure activity, and exercise and memory status of subjects in which the results are presented as OR (95% CI) with a significance of p ≤ 0.05. This study shows that the risk for memory impairment was significantly higher in elderly subjects with shorter years of education (OR: 15.3; 95% CI: 3.0 – 77.0; p = 0.001) and those with no leisure activity (OR: 9.9; 95% CI: 2.8 – 34.8; p = 0.001). Other components of cognitive reserve, including the absence of occupation and exercise, are not the main determinants of memory impairment (p > 0.05).

Table 3 shows the results of the third analysis, namely the multivariate logistic regression analysis which tested whether each component of cognitive reserve was a predictor for memory impairment in elderly subjects after adjustment by controlling for other variables.

**Table 1. Subjects Characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Memory status</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Impaired</td>
</tr>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>68.91 ± 5.98</td>
<td>78.26 ± 12.17</td>
</tr>
<tr>
<td>Age, n (%)</td>
<td>2 (20.0)</td>
<td>8 (80.0)</td>
</tr>
<tr>
<td>≥80 years</td>
<td>14 (63.6)</td>
<td>8 (36.4)</td>
</tr>
<tr>
<td>70 – 79 years</td>
<td>16 (69.6)</td>
<td>7 (30.4)</td>
</tr>
<tr>
<td>60 – 69 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>28 (60.9)</td>
<td>18 (39.1)</td>
</tr>
<tr>
<td>Male</td>
<td>4 (44.4)</td>
<td>5 (55.6)</td>
</tr>
<tr>
<td>Leisure activities, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>26 (78.8)</td>
<td>7 (21.2)</td>
</tr>
<tr>
<td>No</td>
<td>6 (21.2)</td>
<td>16 (77.8)</td>
</tr>
<tr>
<td>Occupation, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Workers</td>
<td>7 (87.5)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Non-workers</td>
<td>25 (53.2)</td>
<td>22 (46.8)</td>
</tr>
<tr>
<td>Exercise, n (%)</td>
<td></td>
<td></td>
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<td>Yes</td>
<td>31 (60.8)</td>
<td>20 (39.2)</td>
</tr>
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<td>No</td>
<td>1 (25.0)</td>
<td>3 (75.0)</td>
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<tr>
<td><strong>Vascular risk factors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Hypertension, n (%)</td>
<td></td>
<td></td>
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<td>Yes</td>
<td>18 (48.6)</td>
<td>19 (51.4)</td>
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<tr>
<td>No</td>
<td>14 (77.8)</td>
<td>4 (22.2)</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td></td>
<td></td>
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<td>Yes</td>
<td>9 (90.0)</td>
<td>1 (10.0)</td>
</tr>
<tr>
<td>No</td>
<td>23 (51.1)</td>
<td>22 (48.9)</td>
</tr>
<tr>
<td><strong>Cognitive evaluation scores</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wordlist memory task, mean ± SD</td>
<td>16.22 ± 4.32</td>
<td>7.36 ± 4.42</td>
</tr>
<tr>
<td>Wordlist memory recall, mean ± SD</td>
<td>6.03 ± 1.83</td>
<td>1.91 ± 1.72</td>
</tr>
<tr>
<td>Wordlist memory recognition, mean ± SD</td>
<td>9.47 ± 0.69</td>
<td>5.89 ± 3.40</td>
</tr>
</tbody>
</table>

Notes: *Independent t test, aChi-square test, bFisher exact test, cMann-Whitney test, *significant results (p < 0.05). SD: standard deviation

In Model 1, after controlling for age and gender, the main predictors for memory impairment in elderly subjects are shorter years of education (OR: 13.1; 95% CI: 1.8 – 95.0; p = 0.011) and absence of leisure activity (OR: 5.9; 95% CI: 1.2 – 28.8; p = 0.027), whereas the absence of work and exercise do not increase the risk of memory impairment.

In model 2, after controlling for age, gender, hypertension, and diabetes, the main predictors for memory impairment are consistently shorter years of education (OR: 11.0; 95% CI: 1.4 – 84.0; p = 0.020) and absence of leisure activity (OR: 5.3; 95% CI: 1.0 – 27.7; p = 0.048).
The most important clinical outcome of a good cognitive reserve status that should be obtained by the elderly is their optimal ability to carry out daily functional and social activities. Furthermore, this optimal clinical outcome will enable the elderly to maintain a high level of independence to carry out daily physical activities without becoming a health, economic, and social burden for their families. In general, cognitive reserve status is determined by many factors, but the most important are the level of education, occupation, leisure activity, and exercise. However, this study showed that both occupation and exercise did not increase the risk for memory impairment in the elderly. This result was not in accordance with the findings of previous studies. Exercise with a relatively high intensity can theoretically increase the production of brain-derived neurotrophic factor (BDNF) in various regions of the brain, including the hippocampus, which is protective of cognitive function through its effect in facilitating neuronal plasticity in these brain areas. The complex occupation that the elderly have in theory will support their brains in constructing efficient memory functions, including memory function. One of the forms of compensation the elderly do is to maintain a high level of independence to carry out daily physical activities without becoming a health, economic, and social burden for their families. Furthermore, this study showed that hypertension and diabetes mellitus were predictors for memory impairment in the elderly, both as predictors of cognitive impairment and as modulators of other predictors of cognitive impairment.

The results of this study are valuable to add to previous studies. This study also indicated that hypertension and diabetes mellitus did not contribute significantly to modulating the role of poor cognitive reserve as a predictor of memory impairment in the elderly. This result was in accordance with the findings of a previous study. A systematic review conducted by Meusel et al. showed that diabetes mellitus and hypertension had a negative effect on cognitive function, including memory function, through their effect on chronic brain hypoperfusion which resulted in the degradation of white matter integrity and gray matter atrophy in the hippocampus area. Among the well-identified vascular risk factors, hypertension was the main risk factor for impaired cognitive function, including memory impairment in elderly. Further longitudinal studies are still needed to determine the role of hypertension and diabetes mellitus in cognitive impairment in the elderly, both as predictors of cognitive impairment and as modulators of other predictors of cognitive impairment.

The results of this study are valuable to add to previous studies. However, this study has several limitations. First, since this study used a small sample size, generalization of the results of this study to different populations should be carried out with caution. Second, the absence of detailed quantification of the intensity of the components of cognitive reserve, especially the components of occupation and exercise, may affect the results of statistical analysis obtained in this study. Third, the data on the characteristics of the subjects obtained in this study were mostly based on recall from the subjects, which has the potential to cause recall bias. Thus, further studies with a larger sample size and with a more detailed operational definition of each component of cognitive reserve need to be carried out. Longitudinal studies also need to be conducted to investigate the effect of poor cognitive reserve in the elderly on the progression of their memory impairment over a certain period.

**Conclusion**

This study showed that shorter years of education and the absence of leisure activity which was a representation of poor cognitive reserve were predictors for memory impairment in the population of the elderly in the province of West Nusa Tenggara. The predictor role of these two components of poor cognitive reserve was independent, not modulated by demographic characteristics and vascular risk factors possessed by the elderly studied.
Longitudinal studies are needed to confirm the effect of poor cognitive reserve in the elderly on the progression of their memory impairment.

Acknowledgement

We would like to acknowledge contribution of Head of Panti Panti Jompo Tresna Wardha Puspa Karma, Mataram, who supported the implementation of the study.

Conflict of interest

The authors declare that there is no conflict of interest in this study.

References