ORIGINAL ARTICLE

Analysis of Blood Biochemical Profiles in Elderly Women for Screening Dementia Diagnostic

Lisna Anisa Fitriana[1],Irma Darmawati1, Suci Tuty Putri[1], Septian Andriyani[1], Upik Rahmi[1], Erna Irawan[2], Elizabeth Ari Setyarini[3], Nita Fitria[4]

[1] Nursing Study Program, Faculty of Sport and Health Education, Indonesia University of Education, Bandung, 40154 West Java, Indonesia
[2] Nursing Study Program, Faculty of Nursing, Adhirajasa Reswara Sanjaya University, Bandung, 40124 West Java, Indonesia
[3] Nursing Study Program, Faculty of Nursing, Santo Borromeus University, Bandung, 40132 West Java, Indonesia
[4] Nursing Study Program, Faculty of Nursing, Padjadjaran University, Bandung, 45363 West Java, Indonesia.

ABSTRACT

Introduction: Beta-amyloid is widely recognized as a critical biomarker in diagnosing and monitoring the progression of dementia. However, the multifaceted nature of dementia suggests that other biochemical parameters may also play significant roles in its onset and development. Exploring these parameters can offer new insights into the mechanisms underlying dementia and pave the way for more comprehensive diagnostic and therapeutic strategies. This study aims to compare the blood biochemical profiles of elderly women with and without dementia. **Materials and methods:** This cross-sectional study included 80 women aged 60 to 100 years. Dementia was assessed using the Mini-Mental State Examination (MMSE) with a cut-off score of 23. High-Performance Liquid Chromatography (HPLC) combined with the Enzyme-Linked Immunosorbent Assay (ELISA) technique was employed to measure biochemical parameters, including amyloid beta-42 (Aβ42), acetylcholinesterase (AChE), brain-derived neurotrophic factor (BDNF), and superoxide dismutase (SOD). Statistical analyses were performed using the chi-square test and independent samples t-test. **Results:** Significant differences were observed in the plasma levels of biochemical markers between the two groups. Plasma amyloid beta-42 ($p < 0.001$), acetylcholinesterase ($p = 0.009$), BDNF ($p = 0.037$), and SOD ($p = 0.003$) were significantly altered in participants with dementia compared to those without dementia. **Conclusion:** This study highlights significant differences in plasma levels of amyloid beta-42, AChE, BDNF, and SOD between elderly women with and without dementia. These findings suggest that, in addition to Aβ42, AChE, BDNF, and SOD hold potential as biomarkers for dementia screening.
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Corresponding Author:
Lisna Anisa Fitriana, PhD
Email: lisna@upi.edu
Tel : (022) 2013163

INTRODUCTION

Dementia is a major public health concern, particularly among the elderly, with its prevalence increasing significantly with age. In Australia, the incidence of dementia rises from fewer than one per 1,000 individuals under the age of 60 to 71 per 1,000 among those aged 90 and older, underscoring the strong correlation between aging and the risk of developing this condition (1). Notably, women are disproportionately affected by dementia, with studies showing that nearly two-thirds of individuals living with the condition are female. This gender disparity becomes even more pronounced in advanced age groups, particularly among those aged 90 and older, where the prevalence of dementia in women significantly surpasses that in men (1,2).

The prevalence of dementia in elderly women, influenced by gender, is attributed to factors such as hypertension, hypercholesterolemia, and hormonal changes, which contribute to the increased risk. Understanding these gender-specific differences is crucial for developing targeted prevention and treatment strategies for dementia in elderly women (3). Dementia in elderly women highlights that women with a history of myocardial infarction are five times more vulnerable to dementia compared to those without such a history. This includes data from 59 subjects, with a significant representation of women in both the multi-infarct dementia and Alzheimer's disease groups. The study also emphasizes the link between cardiovascular abnormalities and dementia, demonstrating the complex relationship between gender, cardiovascular health,

and dementia prevalence in older adults (4).This paper highlights that the prevalence of Alzheimer's disease is higher in women, with 74.1% of patients over the age of 60 in Austria being women. It notes that women exhibit a broader spectrum of dementia-related behavioral symptoms, particularly depression. Biological factors, including brain morphology and postmenopausal hormonal changes, may contribute to this gender difference (5).

Beta-amyloid has long been recognized as a critical biomarker in the diagnosis and progression of dementia. Research indicates that women with dementia tend to have lower levels of amyloid beta-42 (Aβ42) in their cerebrospinal fluid compared to cognitively healthy women. For example, a study demonstrated that the Aβ42/Aβ40 ratio, a composite biomarker, exhibited high accuracy in predicting brain amyloid burden, with significant implications for diagnosing dementia in women. This disparity underscores the importance of gender-specific biomarkers in understanding the pathogenesis of dementia and developing targeted diagnostic and therapeutic strategies. Specifically, the measurement of plasma amyloid-β biomarkers, such as Aβ42 and Aβ40, has proven to be highly predictive of brain amyloid burden, offering potential applications in clinical practice (6,7).

Emerging biomarkers, including acetylcholinesterase (AChE), brain-derived neurotrophic factor (BDNF), and superoxide dismutase (SOD), are gaining significant attention for their potential roles in the diagnosis and understanding of dementia. AChE is essential for the breakdown of the neurotransmitter acetylcholine, and its reduced activity has been linked to cognitive decline in dementia patients. Research has shown that AChE levels can serve as an indicator of cholinergic dysfunction in dementia. BDNF, a neurotrophic factor critical for neurogenesis and synaptic plasticity, has lower serum levels in individuals with cognitive impairment, potentially reflecting underlying neurodegenerative processes. Moreover, SOD, an antioxidant enzyme, plays a protective role against oxidative stress, a key factor in the pathogenesis of dementia. Alterations in SOD levels have been observed in neurodegenerative diseases, supporting its potential as a biomarker for dementia (8,9). These biomarkers have the potential to improve diagnostic accuracy and offer valuable insights into the underlying mechanisms of dementia, thereby warranting further investigation into their clinical utility. Identifying potential biomarkers is essential for analyzing the levels and activity of these enzymes in the plasma of elderly women (10).

MATERIALS AND METHODS

Participants

Eighty elderly women participated in the study, with 40 diagnosed with dementia and the remaining 40 without dementia. Participants were recruited from three nursing homes in Bandung, Indonesia, where the majority of residents were women. The inclusion criteria were as follows: (a) participants must not have serious mental disorders, including schizophrenia, major depression with psychotic features, or delirium; (b) participants should not experience aphasia (loss of language ability) or severe sensory disorders affecting vision or hearing; and (c) participants must not have significant heart or lung diseases or cancer. Cognitive function was evaluated using the Mini-Mental State Examination, which consists of 30 questions, with a cut-off score of 23 to determine the presence of dementia. The study also examined sociodemographic factors such as marital status, education level, and age, while recording medical histories, including osteoarthritis, stroke, and hypertension.

Data Collection

Blood samples were collected using EDTA tubes containing heparin, with 3 ml drawn from each elderly woman, both with and without dementia. The samples were subsequently refrigerated at -8°C. The plasma levels of amyloid beta-42, acetylcholinesterase, BDNF, and SOD were analyzed at the Molecular Genetics Laboratory, Faculty of Medicine, Padjadjaran University. The analysis was performed using High-Performance Liquid Chromatography (HPLC) and Enzyme-Linked Immunosorbent Assay (ELISA) methods.

Ethical Clearance

This study has received ethical clearance from the PPNI West Java Nursing College with No.III/083/KEPK-SLE/STIKEP/PPNI/JABAR/X/2023.

Analytical Statistics

SPSS version 25 was used to analyze the data. The Kolmogorov-Smirnov test was applied to assess the data distribution. The independent samples t-test and chi-square test were used to compare the variables between the two groups.

RESULTS

There were no significant differences between the two groups for sociodemographic data, including age ($p = 0.594$), marital status ($p = 0.241$), hypertension ($p = 0.241$), osteoarthritis ($p = 0.546$), or stroke ($p =$

0.692) (Table I). The blood parameter results showed that plasma levels of amyloid beta-42 ($p < 0.001$), acetylcholinesterase ($p = 0.009$), BDNF ($p = 0.037$), and SOD ($p = 0.003$) were significantly associated with dementia (Table II). Levels of amyloid beta-42, acetylcholinesterase, and SOD were all lower in elderly dementia patients compared to those in the control group without dementia.

Table I: Sociodemographics profiles of respondents

Variable	Dementia (n=40)	Non-dementia (n=40)	p-value
MMSE (median, min-max)	18 (10-23)	26 (25-29)	<0.001*
Age (n, years, %)			
60-80	27 (50)	27 (50)	0.594
80-100	13 (50)	13 (50)	
Education (n, %)			
Low	38 (58.5)	27 (41.5)	0.002*
High	2 (13.3)	13 (86.7)	
Marital status (n, %)			
Married	2 (25)	6 (75)	0.263
Unmarried	38 (52.8)	34 (47.2)	
Hypertension (n, %)			
Yes	29 (55.8)	23 (44.2)	0.241
No	11 (39.3)	17 (60.7)	
Osteoarthritis (n, %)			
Yes	5 (38.5)	8 (61.5)	0.546
No	35 (52.2)	32 (47.8)	
Stroke (n, %)			
Yes	2 (50)	2 (50)	0.692
No	38 (50)	38 (50)	

*p< 0.05, chi-square

Table II: Blood biochemical profiles in women elderly with dementia and non-dementia

Variable	Dementia (n=40) Mean (SD)	Non-dementia (n=40) Mean (SD)	p-value
Amyloid beta-42 (pg/ml)	120.34 (36.0)	178.44 (82.91)	<0.001*
Acetylcholinesterase (pg/ml)	38.49 (28.92)	59.34 (43.01)	0.009*
BDNF (pg/ml)	554.30 (295.22)	711.79 (344.49)	0.037*
SOD (ng/ml)	2.18 (2.72)	4.20 (4.84)	0.003*

*p< 0.05, independent sample t-test and mann-whitney

DISCUSSION

Research indicates that elderly women with dementia exhibit significantly lower levels of amyloid beta-42 (Aβ42), acetylcholinesterase (AChE), brain-derived neurotrophic factor (BDNF), and superoxide dismutase (SOD) compared to a control group without dementia. These findings suggest that AChE, BDNF, and SOD could serve as potential biomarkers for diagnosing dementia in the future.

This study highlights a significant disparity in Aβ42 levels between women with dementia and those without. These findings are consistent with previous research showing that dementia patients have lower plasma Aβ42 levels compared to cognitively healthy individuals. Additionally, significant differences in plasma Aβ42 levels and the Aβ42/Aβ40 ratio were observed between the dementia and cognitively normal groups (11). Plasma levels of Aβ42 have been shown to have profound significance in relation to cognitive health, where lower Aβ42 levels are associated with cognitive decline. A study on elderly individuals in China emphasized that Aβ42 levels could serve as a peripheral biomarker for Alzheimer's disease (12). Furthermore, Aβ42, AChE, and BDNF are key components in the pathology of Alzheimer's disease. Elevated Aβ42 levels are also associated with an increased risk of Alzheimer's disease. Aβ42 levels not only reflect neurological status but also have the potential to serve as an early diagnostic tool. Understanding the interactions between Aβ42 and other biomarkers is crucial, as AChE influences neurotransmission and BDNF contributes to neuroplasticity. To develop more effective diagnostic and therapeutic strategies, it is important to explore the combination of these biomarkers (13).

It is important to note that amyloid beta (Aβ) is the primary protein responsible for the formation of senile plaques in the brain, as demonstrated by foundational research on dementia. This study also reveals a relationship between plasma acetylcholinesterase (AChE) levels and dementia, which is consistent with research on cortical AChE activity, showing a significant decline, particularly in the temporal region. These enzymes play a crucial role in language comprehension, executive function, and both verbal and nonverbal memory. In the clinical stage of mild cognitive impairment (MCI), cholinergic dysfunction acts as an early indicator, preceding the onset of dementia. The effects of this dysfunction, particularly in the temporal neocortex, have been associated with impaired neuropsychological performance (14). Impaired memory performance and behavioral abnormalities are caused by structural lesions of the basal cholinergic neurons in the forebrain or by the administration of muscarinic and nicotinic AChE receptor antagonists. In dementia patients, an association was observed between lower MMSE scores and reduced AChE activity in the amygdala and cortex. Cortical AChE activity showed a significant correlation with working memory and attention scores, but not with long-term memory function (15).

This study also found that women with dementia had lower levels of BDNF. This finding supports previous research indicating a significant difference in BDNF levels between the dementia group and the cognitively normal group. Specifically, the dementia group exhibited lower levels of BDNF compared to the cognitively normal group (16). Meta-analysis studies show serum BDNF levels are significantly lower in patients with dementia than in healthy groups (17).BDNF plays an important role in the nervous system, including improving cognitive function, memory, neurogenesis, and neuronal transmission at the synapse (18). When nerve damage in dementia becomes extensive, protective factors and other mechanisms are unable to maintain stable BDNF levels. Compared to healthy controls, patients with

dementia exhibited significantly lower serum BDNF levels, attributed to the depletion of cognitive reserve, irreversible neuronal damage caused by reduced BDNF, and failed compensatory mechanisms (16).

The last parameter is SOD. The study revealed a significant difference in plasma SOD levels between the two groups. This finding is consistent with research showing significant differences in SOD activity between the sexes in both the control group and dementia patients (20). The hallmark lesions of dementia are caused by oxidative stress, which may contribute to various somatic and psychiatric pathological conditions (21). Dementia and other mortality factors in the elderly are exacerbated by low levels of SOD. A wealth of evidence suggests that specific brain networks undergo neurodegeneration in response to this deficiency.

Oxidative stress plays a significant role in brain damage in individuals with dementia. The biological effects of these highly reactive substances are regulated by antioxidant defense systems, including vitamins E and C, carotenoids, metabolites such as glutathione and uric acid, and antioxidant enzymes. SOD combats free radicals and reactive oxygen species (ROS) by promoting the production of hydrogen peroxide from superoxide radicals, thereby protecting the brain from injury (22). Dementia-related reductions in cerebrospinal fluid SOD activity may indicate impaired radical defense mechanisms, with potential pathophysiological implications (23).

CONCLUSION

Significant differences in plasma levels of Aβ42, AChE, BDNF, and SOD were identified between elderly women with and without dementia. This study highlights the potential of not only Aβ42, but also AChE, BDNF, and SOD, as valuable biomarkers for dementia screening. However, further research involving larger sample sizes is necessary to better define the precise relationship and enhance diagnostic accuracy.

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