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Factors influencing alzheimer's disease: A case-control study

Rusjini Rusjini [1*], **I Made Kariasa** [2], **Denissa Faradita Aryani** [1]

[1] Department of Medical Surgical Nursing, Faculty of Nursing, University of Indonesia, Indonesia
[2] Neuroscience Nursing Focus, Department of Medical Surgical, Faculty of Nursing, University of Indonesia, Indonesia

[*] **Corresponding author:** I Made Kariasa, Department of Medical Surgical Nursing, Faculty of Nursing, University of Indonesia, Indonesia.
Email: imadekariasa.mk@gmail.com

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Abstract

Background: As there are currently no curative treatments for Alzheimer's disease (AD) and other forms of dementia, focusing on risk factor reduction and primary prevention is essential.

Objectives: This study aimed to explore the factors that influence the occurrence of AD in comparison to other dementias.

Methods: We conducted a case-control study involving caregivers of Alzheimer's patients (n=60) and a control group of caregivers for individuals with other dementias (n=60). Participants were recruited from a hospital in Yogyakarta between January 2018 and December 31, 2023. An online questionnaire containing 62 questions was administered via Zoho Forms and analyzed using IBM SPSS Statistics 25.0. We employed chi-square tests, and logistic regression to identify factors associated with the incidence of AD relative to other dementias.

Results: Our findings indicated that an adequate dietary pattern (P=0.02; AOR=3.665; 95% CI=1.219-11.11) and age of 60 years or older (P=0.06; AOR=2.34; 95% CI=0.95-5.73) are significant risk factors for AD. Conversely, adequate sleep quality (P=0.03; AOR=0.24; 95% CI=0.07-0.87) and a history of stroke (P=0.00; AOR=0.07; 95% CI=0.02-0.26) were identified as protective factors against developing AD compared to other dementias. A poor diet can lead to systemic inflammation and oxidative stress, which may trigger neuroinflammation, including stroke. Additionally, increased tau load associated with being 60 years or older, along with poor sleep quality, can contribute to neuronal dysfunction and ultimately result in brain atrophy.

Conclusion: This study identifies moderate dietary habits and age over 60 as risk factors for AD, while adequate sleep quality and a history of stroke serve as protective factors. The insights gained from this research may serve as foundational data for further studies and provide guidelines for preventing the onset of AD.

Keywords: Aging, Alzheimer's disease, Diet, Sleep Quality, Stroke.

Introduction

Population aging is a global phenomenon affecting nearly every country in the world. In 2019, there were approximately 703 million individuals aged 65 and older, and this number is projected to reach 1.5 billion by 2050.[1] Notably, around 80% of the elderly population resides in low- and middle-income countries (LMICs). The combination of increased life expectancy and an aging demographic has led to a rise in non-communicable diseases.[2] In Indonesia, the elderly make up about 10.48% of the total population, with the Yogyakarta Special Region (DIY) having the highest proportion at 16.69%.[3]

Aging is characterized by the gradual accumulation of various molecular and cellular imperfections, which contribute to a decline in both physical and cognitive functions. This decline heightens the risk of diseases and ultimately leads to increased mortality rates. Alzheimer's disease (AD) and other forms of dementia pose a significant global challenge among age-related conditions.[4]

AD is a neurodegenerative disorder that accounts for 60-80% of dementia cases.[5-8] Experts predict that by 2050, the number of people living with AD and other forms of dementia could rise by an alarming 166%.[8] In Southeast Asia, Indonesia reported the highest number of AD and dementia patients in 2019, with expectations for a 244% increase in cases by 2050.[8] In DIY, the prevalence of dementia was recorded at 20.1% in 2016,[9] while in Sleman, it reached 63.2% among individuals aged 45 and older.[10] Alarmingly, fewer than 12% of caregivers can recognize memory loss as an early warning sign of AD, which contributes to the ongoing rise in cases across

Indonesia.[9,11]

The widespread prevalence of AD and other dementias significantly impacts care dependency, disability, mortality rates, economic costs, and the demands placed on caregivers. These conditions rank as the twenty-fifth leading cause of Disability-Adjusted Life Years (DALYs) and have seen the most substantial increase among the top 30 causes of DALYs from 2000 to 2019.[2] As population numbers grow, life expectancy rises, and risk factors become more prevalent, deaths attributed to AD and other dementias have surged, making them the seventh leading cause of death globally.[2] In Indonesia and Yogyakarta, these diseases are ranked nineteenth and twentieth in terms of age-related mortality rates.[12] The average survival time for individuals diagnosed with AD is approximately 5.8 years.[13]

The global economic burden associated with AD and other dementias was estimated at $1.3 trillion in 2019, with projections suggesting an increase to $2.8 trillion by 2030. Informal caregiving typically involves providing 5 to 8 hours of daily support for Activities of Daily Living (ADLs) and supervision, primarily by family members or caregivers.[2] Families bear approximately 70% of the lifetime costs related to AD, encompassing long-term care expenses and the value of unpaid caregiving.[7]

Sporadic AD emerges from a complex interplay of various factors and typically involves both positive and negative interactions across three key areas: psychosocial health, physical health, and brain health.[14] Risk factors for AD can be divided into two categories: non-modifiable factors such as age, genetics, and family history, and modifiable factors that include cardiovascular health, smoking habits, physical activity levels, dietary choices, education, social and cognitive engagement, traumatic brain injuries, as well as other influences like poor sleep quality and exposure to air pollution.[7]

In Indonesia, modifiable risk factors -particularly low education levels, smoking, and physical inactivity- are most prevalent among the larger population. Research indicates that individuals exhibiting a combination of these factors face a 54.3% increased risk of developing AD.[15] Moreover, the prevalence of other modifiable risk factors such as hypertension, diabetes, obesity, and mental health disorders remains alarmingly high in the country. In Jatinangor, engaging in cognitive, social, recreational, and physical activities has been shown to significantly lower the incidence of dementia.[16] In Yogyakarta, various risk factors contribute to the occurrence of AD and other dementias. These include high systolic blood pressure, unhealthy dietary habits, excessive sugar intake, smoking, obesity, air pollution, elevated cholesterol levels, low physical activity, and alcohol consumption.[12] Specific factors have been linked to increased incidence rates: age,[10] gender,[17] diabetes, smoking, hearing loss, depression,[18] education,[19] work activities, leisure activities,[16] sleep quality,[20] and language use.[21]

As there are currently no curative treatments available for AD and other forms of dementia, it is crucial to focus on reducing risk factors and implementing primary prevention strategies.[2] The progression of AD's tends to be faster in low-income and lower-middle-income countries due to aging populations, increased life expectancy, and a higher prevalence of associated risk factors. While enhancing well-being is an essential aspect of dementia care, maintaining physical health and mitigating risk factors can help decrease both the incidence of AD and the burden on caregivers.[22]

Although there has been extensive research on AD's risk factors in high-income countries, there is a notable lack of studies in lower-middle-income countries like Indonesia, particularly regarding the comparison between the factors influencing AD and those affecting other types of dementia.

Objectives

The aim of this research was to explore the factors influencing the occurrence of AD in relation to other forms of dementia.

Methods

Study Design

This study employed a case-control design, focusing on two groups of outpatients at the memory clinic of Sardjito Hospital in Yogyakarta. The research was conducted from January 2018 to December 2023, in alignment with the average survival rate of 5.8 years for patients diagnosed with AD.[13] A non-probability sampling method, specifically purposive sampling, was utilized during the period from November to December 2023.

To determine the sample size, we applied a single measurement unpaired categorical etiological multivariate formula, using the odds ratio (OR) as a basis for estimating the desired outcome.[23-25] Following a 1:1 comparison of the case and control groups, the average sample size derived from seven previous studies[10,16-21] indicated that 60 respondents would be required for each group.

In this study, caregivers -specifically spouses or children- who had been living with and caring for the patient for more than five years prior to the diagnosis were classified as cases if the patient had AD or Alzheimer's dementia

(ICD-10 codes G30 or F00). Conversely, the control group comprised patients diagnosed with other forms of dementia (ICD-10 codes F01, F02, F03).

Inclusion criteria for the case group required that patients meet the specified ICD-10 codes for AD. For the control group, inclusion was based on the presence of other dementia diagnoses. Exclusion criteria encompassed patients with cognitive impairments due to mixed dementia (a combination of Alzheimer's and other dementias), mental disorders, brain tumors, or those who declined to participate in the study.

Data collection involved searching for eligible respondents within the Medical Records Installation and reviewing their medical files through the hospital's electronic medical records system. Researchers then contacted potential participants directly or via WhatsApp to explain the study's objectives, benefits, and compensation for participation. An online form was sent to respondents through WhatsApp, which they could complete and sign if they agreed to participate. For those who encountered difficulties filling out the form, researchers provided assistance via phone calls or by accompanying them to the memory clinic. Figure 1 illustrates the flowchart detailing the research process.

Instrumentation

The primary tool for data collection was an online questionnaire consisting of 62 questions, designed using Zoho Forms by the research team. This questionnaire explored various aspects of participants' lifestyles, including their habits, physical activity levels, language use, and leisure activities. Additionally, we incorporated the Sleep Quality Questionnaire (KKT), developed by Evi Karota in Jakarta. This instrument evaluates seven key sleep parameters: total hours of sleep at night, time taken to fall asleep, frequency of awakenings, feelings of refreshment upon waking, depth of sleep, overall satisfaction with nighttime sleep, and daytime tiredness or sleepiness. We also included a question that allowed participants to self-report their perception of sleep quality, categorizing it as either good or poor.[26]

The content validity of the KKT questionnaire was assessed by three experts from Prince of Songkla University in Thailand, specializing in Sleep and Medical Science, Psychological Nursing, and Gerontological Nursing. Reliability testing for the KKT was conducted using test-retest Pearson correlation coefficients for the seven sleep parameters, yielding the following results: total hours of sleep at night (0.96), time to start sleeping (0.89), frequency of awakening (0.94), feeling refreshed when waking up (0.85), depth of sleep (0.98), satisfaction with sleep (0.92), and daytime tiredness (0.83).[26] All questionnaires were retested using the product moment correlation formula on 60 respondents with mixed-type dementia and mild cognitive impairment. The average validity scores were as follows: lifestyle habits (0.48), physical activity (0.41), language use (0.92), leisure activities (0.51), and KKT (0.61). Overall, the questionnaire instrument was deemed reliable, achieving an average Cronbach's alpha coefficient of 0.7496.

Data Analysis

Data analysis was performed using IBM SPSS Statistics version 25.0. Chi-Square test was employed for bivariate analysis involving two categories. For analyses involving more than two categories, logistic regression was applied. Specifically, the Backward LR method within the predictive framework was used for multivariate analysis.[27]

Ethical Considerations

This study received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Public Health, and Nursing at Universitas Gadjah Mada (UGM), under approval number KE/FK/1653/EC/2023 dated October 20, 2023. Additionally, we obtained research permission from RSUP Dr. Sardjito Yogyakarta, with permit number DP.04.03/D.XI.2/27025/2023 dated November 2, 2023.

Results

The study involved 120 participants, comprising 60 cases and 60 controls, all of whom were subjected to univariate analysis. The results, summarized in Table 1, reveal significant differences between the cases and controls across various factors, including age at diagnosis, history of stroke, Down syndrome, smoking habits, dietary practices, levels of physical activity, and sleep quality. However, for other variables such as gender, number of children, history of traumatic brain injury, family history of dementia, obesity, elevated cholesterol levels, diabetes, hypertension, heart disease, COVID-19, dental and oral diseases, alcohol consumption, tea or coffee intake, marital status, income level, education, hearing loss, symptoms of stress or depression, language use, and leisure activities, there were minimal differences observed between the two groups.

Table 2 illustrates that individuals with a balanced diet, adequate sleep quality, and a history of stroke are at a higher risk of developing AD compared to other forms of dementia when age is controlled for (≥60 years). Specifically, a healthy diet was associated with an increased risk of AD (P=0.02; AOR=3.665; 95% CI=1.219-11.11), as

was being aged 60 years or older (P=0.06; AOR=2.34; 95% CI=0.95-5.73). Conversely, adequate sleep quality (P=0.03; AOR=0.24; 95% CI=0.07-0.87) and a history of stroke (P=0.00; AOR=0.07; 95% CI=0.02-0.26) were identified as protective factors against AD when compared to other dementias.

Discussion

Dietary history emerged as a significant risk factor influencing the likelihood of developing AD relative to other types of dementia. The cognitive protective effects associated with certain dietary patterns may be attributed to their antioxidant, anti-inflammatory, and anti-diabetic properties, along with sufficient intake of monounsaturated fats. Increased fish consumption has also been linked to a reduced risk of AD.[28] Furthermore, older adults over 75 living in rural areas who consume fewer fruits are at a heightened risk for dementia (OR=4.62; 95% CI=1.18-18.02).[16] While a Western diet poses a known risk for AD, adherence to a Mediterranean or ketogenic diet -along with supplementation of omega-3 fatty acids and probiotics- can provide protective benefits for individuals with mild to moderate AD.[29] Maintaining a healthy diet rich in whole, unprocessed plant-based foods throughout life may significantly lower the risk of dementia in later years.[30]

Age was identified as a critical factor influencing the incidence of AD in this study. This finding aligns with existing research indicating that elderly individuals in Yogyakarta face a 2.3 to 2.7 times higher risk of dementia between the ages of 70 and 79 years, a 3.8 to 6.2 times higher risk at ages 80 to 89 years, and an alarming 12.4 times higher risk for those aged 90 years and above compared to individuals aged 60 to 69 years.[11] A similar study conducted in Sleman found that individuals aged 60 have a 3.4 times greater risk of developing dementia.[10] Moreover, those aged 75 years and older experience a significantly elevated risk, 2.8 times more likely to develop dementia compared to those aged 60 to 74 years (OR=2.75; 95% CI=1.70-4.46).[16] Age ≥60 years was identified as the second most significant risk factor for AD compared to other dementias.

The mechanisms underlying age-related brain aging include mitochondrial dysfunction, glucose hypometabolism, immune and inflammatory responses, accumulation of amyloid beta (Aβ), dyslipidemia, degeneration of white matter, and reduced regenerative capacity.[31] For individuals aged ≥65 years, the probability of developing late-onset AD is approximately 3%, which escalates to over 30% by age ≥85 years.[32] Consequently, age remains the primary non-modifiable risk factor for AD.[7,11,16,33,34]

Sleep quality plays a crucial role in protecting against AD compared to other forms of dementia. Research indicates that sleep deprivation can lead to increased production of amyloid-β (Aβ) and the release of tau proteins, while simultaneously hindering the clearance of these substances from cerebrospinal fluid. This process contributes to the formation of amyloid plaques and tau pathology, both of which are hallmarks of AD. Additionally, sleep disturbances may exacerbate inflammation and metabolic dysfunction, further elevating Aβ and tau levels and promoting neurodegeneration. During the extended asymptomatic preclinical phase of AD, sleep disturbances are believed to have a dual role: they can act as indicators of AD pathology while also increasing the risk of developing the disease.[35] Conditions that disrupt sleep affect brain regions responsible for regulating sleep-wake cycles and circadian rhythms.[36] Insomnia, sleep behavior disorders, and insufficient sleep duration significantly heighten the risk of AD and other dementias.[37] For individuals aged 50 to 69, sleeping less than six hours a night raises the risk of dementia by 30%.[38] Fragmented sleep, which has been linked to cognitive decline and memory issues, is also associated with a greater likelihood of developing AD.[39]

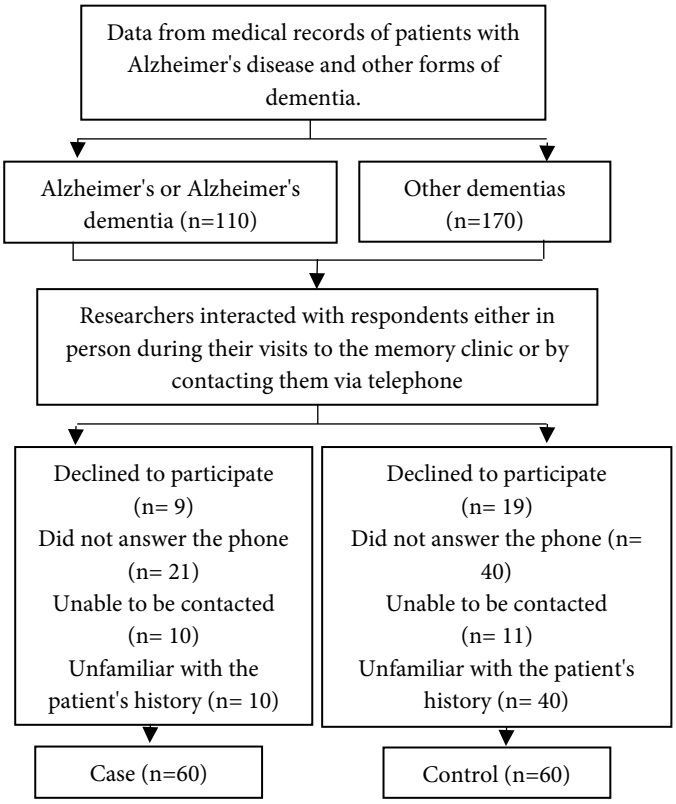

Figure 1. Flowchart of the research process

Table 1. Univariable associations between potential risk factors and alzheimer's disease in the total sample (n = 120)

Variable		**Case**, n=60		**Control**, n=60		P-value*	OR	95% CI
		n	(%)	n	(%)			
Sex	Male	33	27.5	37	30.8	0.58	1.32	(0.64-2.73)
	Female	27	22.5	23	19.2			
Age of diagnosis	<60 years	19	15.8	31	25.8	0.04	2.31	(1.10-4.85)
	≥60 years	41	34.2	29	24.2			
Number of children	≥ 3 children	24	20	29	24.2	0.64		
	1-2 children	32	26.7	27	22.5	0.35	1.43	(0.68-3.02)
	Childless	4	3.3	4	3.3	0.8	1.21	(0.27-5.35)
History of traumatic brain injury	No	37	30.8	44	36.7	0.24	1.71	(0.79-3.71)
	Yes	23	19.2	16	13.3			
Family history of Alzheimer or dementia	No	42	35	48	40	0.29	1.71	(0.74-3.97)
	Yes	18	15	12	10			
Stroke history	No	57	47.5	37	30.8	0.00	0.09	(002-0.30)
	Yes	3	2.5	23	19.2			
Down syndrome history	No	59	49.2	60	50	1	0.50	(0.41-0.59)
	Yes	1	0.8	0	0			
Obesity history	No	51	42.5	49	40.8	0.81	0.79	(0.30-2.06)
	Yes	9	7.5	11	9.2			
High cholesterol history	No	41	34.2	38	31.7	0.7	0.80	(0.38-1.71)
	Yes	19	15.8	22	18.3			
Diabetes history	No	43	35.8	45	37.5	0.84	1.19	(0.53-2.67)
	Yes	17	14.2	15	12.5			
Hypertension history	No	36	30	35	29.2	1	0.93	(0.45-1.93)
	Yes	24	20	25	20.8			
Cardiovascular disease history	No	52	43.3	52	43.3	1	1.00	(0.35-2.87)
	Yes	8	6.7	8	6.7			
Covid-19 history	No	49	40.8	46	38.3	0.65	0.74	(0.30-1.79)
	Yes	11	9.2	14	11.7			
Dental and oral disease history	No	56	46.7	55	45.8	1	0.79	(0.20-3.08)
	Yes	4	3.3	5	4.2			
Smoking history	Never	45	37.6	34	28.3	0.09		
	Smoking and quit	10	8.3	11	9.2	0.45	0.69	(0.26-1.80)
	< 20 packs/year	1	0.8	1	0.8	0.85	0.76	(0.05-12.52)
	≥ 20 packs/year	4	3.3	14	11.7	0.01	0.22	(0.07-0.72)
Alcohol consumption	Never	55	45.9	51	42.5	0.37	0.41	(0.12-1.42)
	Drinking and quit	4	3.3	9	7.5	0.16		
	< 14 glass/2 weeks	1	0.8	0	0	1		
	≥ 14 glass/2 weeks	0	0	0	0	0		
Tea consumption	1-2 cups/day	28	23.3	29	24.2	0.98		
	> 2 cups/day	11	9.2	11	9.2	0.94	1.04	(0.39-2.77)
	Never or < 1 cups/day	21	17.5	20	16.6	0.84	1.09	(0.49-2.43)
Coffee consumption	1-2 cups/day	10	8.3	18	15	0.22		
	> 2 cups/day	3	2.5	2	1.7	0.32	2.70	(0.39-18.96)
	Never or < 1 cups/day	47	39.2	40	33.3	0.1	2.12	(0.88-5.10)
Diet history	Good	39	32.5	46	38.3	0.13		
	Moderate	20	16.7	11	9.2	0.08	2.15	(0.92-5.02)
	Poor	1	0.8	3	2.5	0.43	0.39	(0.04-3.93)

Physical activity	Highly active	3	2.6	1	0.8	0.19		
	Active	1	0.8	3	2.6	0.18	0.11	(0.01-2.73)
	Moderate	10	8.3	10	8.3	0.38	0.33	(0.03-3.78)
	Low	28	23.3	18	15	0.58	0.52	(0.05-5.38)
	Sedentary	18	15	28	23.3	0.2	0.21	(0.02-2.22)
Marital status	Married	50	41.7	49	40.8	1	0.89	(0.35-2.29)
	Unmarried/ divorce	10	8.3	11	9.2			
Occupation	Non-manual	46	38.3	39	32.5	0.23	0.57	(0.25-1.26)
	Manual	14	11.7	21	17.5			
Income	≥ IDR 2.500.000,00	39	32.5	36	30	0.71		
	< IDR 2.500.000,00	14	11.7	18	15	0.44	0.72	(0.31-1.65)
	No income	7	5.8	6	5	0.9	1.08	(0.33-3.50)
Length of education	> 12 years	32	26.7	37	30.8	0.38		
	7-12 years	24	20	17	14.2	0.22	1.63	(0.75-3.56)
	0-6 years	4	3.3	6	5	0.71	0.77	(0.20-2.98)
Hearing problems	No	43	35.8	44	36.7	1	1.10	(0.49-2.42)
	Yes	17	14.2	16	13.3			
Stress symptoms	No	29	24.2	36	30	0.27	1.60	(0.78-3.31)
	Yes	31	25.8	24	20			
Depression symptoms	No	55	45.8	56	46.7	1	1.27	(0.33-4.99)
	Yes	5	4.2	4	3.3			
Language use	≥ 3 languages	46	38.4	43	35.8	0.81		
	2 languages	7	5.8	8	6.7	0.72	0.82	(0.27-2.45)
	1 language	7	5.8	9	7.5	0.56	0.73	(0.25-2.12)
Leisure activity	Highly active	0	0	0	0			
	Active	3	2.5	3	2.6	0.61		
	Moderate	15	12.5	13	10.8	0.87	1.15	(0.19-6.74)
	Low	24	20	31	25.8	0.77	0.77	(0.14-4.18)
	Sedentary	18	15	13	10.8	0.72	1.39	(0.24-7.99)
Sleep quality	Good	52	43.4	40	33.4	0.02		
	Moderate	4	3.3	16	13.3	0.01	0.19	(0.06-0.62)
	Poor	4	3.3	4	3.3	0.72	0.77	(0.18-3.27)

* Groups were compared using the chi-squared test and logistic regression. OR: Odds Ratio

Table 2. Multivariable models for the total sample (n = 120)

Variable		Case		Control		P-value	Crude OR	(95% CI)	B	P-value	Adjusted OR	(95% CI)
		n	(%)	n	(%)							
Age of diagnosis	<60 years	19	15.8	31	25.8							
	≥60 years	41	34.2	29	24.2	0.04	2.31	(1.10-4.85)	0.849	0.064	2.340	(0.95-5.73)
Stroke history	No	57	47.5	37	30.8							
	Yes	3	2.5	23	19.2	0.000	0.09	(0.02-0.30)	-2.725	0.00	0.066	(0.016-0.261)
Diet history	Good	39	32.5	46	38.3	0.13				0.064		
	Moderate	20	16.7	11	9.2	0.08	2.15	(0.92-5.02)	1.299	0.022	3.665	(1.219-11.11)
	Poor	1	0.8	3	2.5	0.43	0.39	(0.04-3.93)	-0.357	0.804	0.700	(0.04-11.77)
Sleep quality	Good	52	43.4	40	33.4	0.02				0.096		
	Moderate	4	3.3	16	13.3	0.01	0.19	(0.06-0.62)	-1.417	0.030	0.243	(0.07-0.87)
	Poor	4	3.3	4	3.3	0.72	0.77	(0.18-3.27)	-0.239	0.778	0.787	(0.15-4.14)
	Constant								-0.102			

Multivariable models incorporate age, stroke, diet, sleep quality history, and all risk factors with ORs < 0.25 from the univariable models [Table 1], OR: odds ratio, AOR: adjusted odds ratio, 95% CI: 95% confidence interval.

Numerous studies support the idea that sleep disturbances are a risk factor for cognitive impairment related to probable AD, although the specifics of this relationship can vary based on the sleep parameters assessed, such as total sleep time. Discrepancies in findings across studies may arise from subjective reports of sleep duration and quality, which contrast with objective measures obtained through polysomnography and actigraphy. Conditions such as obstructive sleep apnea, insomnia, and restless legs syndrome/periodic leg movement disorder (RLS/PLMD) have also been linked to an increased risk of future cognitive decline.[35]

Interestingly, a history of stroke has been identified as a protective factor influencing the incidence of AD compared to other dementias. Individuals who have experienced a stroke exhibit a reduced risk of developing AD by 0.07 times compared to those without such a history (OR=0.07; 95% CI=0.017-0.26). In this study, it was noted that 16.7% of participants in the control group had a history of stroke, with many suffering from vascular dementia. While only 2.5% of patients were in the case group, the data confirmed that stroke is a significant factor impacting the incidence of AD. Stroke can trigger a chronic inflammatory response that releases compounds contributing to the development of amyloid beta plaques and neurofibrillary tangles. Lacunar infarction, often resulting from cerebral endothelial dysfunction and inadequate brain perfusion, further complicates this relationship.[14] Classic vascular risk factors during midlife are also linked to increased deposition of brain amyloid, highlighting the intricate connection between vascular health and neurodegenerative processes.[40] Neurovascular disorders stemming from cerebrovascular disease can lead to decreased cerebral blood flow, disrupt the blood-brain barrier, and cause selective brain atrophy. These changes can result in direct neuronal damage and indirectly promote Aβ accumulation.[28]

This research represents the first study to compare the factors influencing AD with other forms of dementia in Indonesia. However, there are several limitations to consider. These include potential biases in case and control selection, recall bias, confounding bias, respondent bias, and the risk of fraudulent questionnaire responses. To minimize case and control selection bias, respondents were chosen from a single hospital. Recall bias may arise from patients' varying abilities to accurately remember past information. While there is a possibility of respondent bias or dishonesty in completing online questionnaires, researchers mitigated this risk by administering the questionnaires in the outpatient clinic and guiding respondents over the phone when they were at home. The absence of clearly defined confounding factors and matching variables in this study presents a significant risk of confounding bias. Therefore, it is advisable to adopt a case-control study design that accounts for confounders and matches variables between groups, or to consider a cohort study design.

Conclusions

Demographic factors such as age, brain health factors like stroke, physical health aspects including dietary patterns, and psychosocial elements such as sleep quality all significantly influence the incidence of AD compared to other dementias. This highlights that AD is affected by multiple interconnected factors. There is an urgent need for early education on healthy dietary practices, quality sleep, and stroke prevention as part of proactive measures to reduce the incidence of AD, particularly in the Special Region of Yogyakarta.

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Competing interests

The authors declare that they have no competing interests.

Abbreviations

Alzheimer's Disease: AD; Adjusted Odds Ratio: AOR; Odds Ratio: OR; Confidence Interval: CI; Dietary Approaches to Stop Hypertension: DASH; Hazard Ratio: HR; Mediterranean-DASH Intervention for Neurodegenerative Delay: MIND; Coronavirus disease 2019: COVID-19; Sleep Quality Questionnaire: KKT.

Authors' contributions

IMK, DFA and RR: Conceptualization, methodology, writing original draft and editing. IMK, DFA and RR: Conceptualization, methodology, data curation, validation, and editing. IMK, DFA and RR: Methodology, supervision, data curation, visualization, investigation, validation. All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

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Role of the funding source

None.

Availability of data and materials

The data used in this study are available from the corresponding author on request.

Ethics approval and consent to participate

This study received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Public Health, and Nursing at Universitas Gadjah Mada (UGM), under approval number KE/FK/1653/EC/2023 dated October 20, 2023. Additionally, we obtained research permission from RSUP Dr. Sardjito Yogyakarta, with permit number DP.04.03/D.XI.2/27025/2023 dated November 2, 2023.

Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

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