Characteristics and Factors that Predict Alzheimer's Disease of Early-onset Dementia in Neurological Institute of Thailand

Jakkree Kanpittaya,
Jedsada Khieukhajee

Abstract

Introduction: Early-onset dementia (EOD), occurring in individuals under 65, is a growing public health concern. In Thailand, data on EOD, particularly distinguishing Alzheimer's disease (AD) from non-AD dementia subtypes, are limited. This study aimed to investigate EOD's prevalence, characteristics, and associated factors at the Neurological Institute of Thailand.

Methods: A retrospective study was conducted on patients diagnosed with dementia before age 65 between 2018 and 2022. Data collection included demographic data, comorbidities, cognitive assessments (TMSE, MOCA), neuroimaging (MTA scores, Fazekas scale), and lab results. Statistical comparisons were made between AD and non-AD groups.

Results: Among 199 patients, AD was the most common form of dementia (54.7%). The AD group had fewer males (43.2% vs. 63%, $p = 0.006$) and a higher median age of onset (58 vs. 54 years, $p = 0.005$). Memory and attention impairments were more impaired in AD ($p < 0.001$). MTA scores were higher in AD, and Fazekas scores in non-AD groups ($p < 0.001$).

Conclusions: Early-onset AD is the most common EOD in this study, while non-AD dementias, particularly vascular dementia, are linked to more vascular risk factors. Early diagnosis and management of these factors are essential for improving outcomes.

Keywords: Characteristics, Predicting factors, Alzheimer's disease ,Early-onset dementia

Jakkree Kanpittaya, Jedsada Khieukhajee
Department of Neurology, Neurological Institute of Thailand, Bangkok, Thailand

Corresponding author:
Jakkree Kanpittaya, M.D.
Department of Neurology, Neurological Institute of Thailand, 312, Ratchawithi Road, Thung Phaya Thai, Ratchathewi, Bangkok 10400, Thailand
Tel.: 66-2306-9899, Fax: 66-2354-7085
E-mail: kanpittaya@hotmail.com

รับต้นฉบับ 17 เมษายน 2568, ปรับปรุงต้นฉบับ 1 สิงหาคม 2568, ตอบรับต้นฉบับตีพิมพ์ 16 สิงหาคม 2568

Introduction

Dementia is a growing public health concern worldwide that significantly impacts society from both medical and socio-economic perspectives. In Thailand, the rising elderly population has drawn much attention to age-related dementia[1,2] however, early-onset dementia (EOD), which occurs in individuals younger than 65 years, remains under-recognized.

EOD presents unique challenges for the affected individuals and their families, as the early onset often coincides with the prime working years. This leads to increased financial strain and caregiver burdens[3]. Studies estimate the prevalence of EOD to be approximately 119 per 100,000 people aged 30-64 years, with varying prevalence rates depending on countries' income levels. Thailand, classified as a middle-income country, is expected to have a relatively high prevalence of EOD compared to other regions[4].

A recent study in Thailand found that EOD accounted for approximately 17% of all dementia cases, with 44% being Alzheimer's disease (AD), 16% vascular dementia, 8% frontotemporal dementia, and 6.5% posterior cortical atrophy. Alzheimer's disease remains the most prevalent form of EOD[1]. Accurate and timely diagnosis is critical for managing AD[3,5,6] especially in early-onset cases, as new therapeutic options, such as disease-modifying therapy, become available[7].

Despite its significance, data on the prevalence and associated factors for EOD in Thailand remain limited. Most studies have focused on elderly populations, leaving a gap in understanding the clinical characteristics and risk factors for younger patients with dementia. This study aims to fill that gap by investigating EOD's characteristics and associated risk factors, with a specific focus on Alzheimer's disease and other non-AD dementia types, at the Neurological Institute of Thailand. The results of this study will help inform the development of early diagnosis and intervention strategies, ultimately improving patient outcomes and easing the burden on families and caregivers.

Methods

This retrospective, cross-sectional study was conducted at the Neurological Institute of Thailand. The aim was to evaluate the clinical characteristics, proportion, and associated factors of early-onset dementia (EOD), focusing on distinguishing Alzheimer's disease (AD) from non-AD dementias. Data were extracted from medical records of patients treated between January 2018 and December 2022.

The study included patients diagnosed with dementia based on the International Classification of Diseases, 10th Revision (ICD-10) criteria in the hospital database. Patients were included if they were diagnosed with dementia before the age of 65 and who received treatments at the Neurological Institute of Thailand. Dementia subtypes were differentiated using general guidelines for dementia classification to ensure consistent diagnosis. Patients were excluded if their medical records lacked essential clinical or cognitive data or if there were comorbidities that could obscure the dementia diagnosis, such as severe psychiatric illness or substance abuse.

Data were collected retrospectively from both outpatient and inpatient medical records. The demographic data collection included age, sex, and education level. Information on comorbidities and associated risk factors was also gathered, including

Type 2 diabetes mellitus (DM), hypertension, hyperlipidemia, coronary artery disease, smoking, alcohol consumption, and family history of dementia. Clinical data on cognitive symptoms were recorded, with particular attention to memory, language, visuospatial ability, attention, and executive function. Cognitive function was assessed using the Thai Mental State Examination (TMSE)[8] and the Montreal Cognitive Assessment (MOCA) scores[9] to evaluate the degree of cognitive impairment. Neuroimaging data were obtained from brain magnetic resonance imaging (MRI) reports, explicitly focusing on medial temporal atrophy (MTA) scores[10] and Fazekas scale ratings[11] for white matter hyperintensities.

Additionally, laboratory data such as fasting blood glucose, hemoglobin, and lipid profiles were included in the analysis. The primary outcome was to identify the proportion and clinical characteristics of Alzheimer's disease and non-Alzheimer's disease in patients with early-onset dementia (EOD) diagnosed at the Neurological Institute of Thailand between 2018 and 2022. The secondary outcome was to determine the significant factors associated with the development of Alzheimer's disease compared to non-AD dementia.

Descriptive statistics were used to summarize demographic characteristics, clinical findings, and cognitive assessments. Continuous variables were expressed as mean ± SD in normally distributed data and medians and interquartile ranges (IQR) in non-normally distributed data. In contrast, categorical variables were reported as frequencies and percentages.

The chi-square test was used to compare categorical variables between the AD and non-AD groups; continuous variables were compared using the Mann-Whitney U test for non-normally distributed data, and an independent t-test was performed for normally distributed continuous variables. Finally, the multivariate analysis was performed, and logistic regression was applied to identify independent risk factors associated with Alzheimer's disease. A p-value of <0.05 was considered statistically significant. Statistical analyses were conducted using SPSS version 17.0 (SPSS et al., Illinois, USA).

Result

1. Demographic data

Table 1 summarizes 199 participants. The median age at first presentation was 57 (IQR=8) years, with 51.3% of the patients being male (n = 102). The median number of education years was 12 (IQR = 10). The median score of the Thai Mental State Examination (TMSE) was 19 (IQR=12), and the mean score for the Montreal Cognitive Assessment (MOCA) was 14 ±4.

Table 1 Patients demographics data and baseline characteristics

Demographic data	
Age at first presentation, median (IQR)	57(8)
Sex	
Male, n (%)	102 (51.3)
Female, n (%)	97(48.7)
Educationyear, median (IQR)	12(10)
TMSE, Median (IQR)	19(12)
MOCA, mean +- SD	14.14 ± 4.8
Diabetes mellitus, n (%)	69(34.7)
Hypertention, n (%)	34(17.1)
Hyperlipidemia, n (%)	48(24.1)
Coronary artery disease, n (%)	13(6.5)
Smoke, n (%)	38(19.2)
Alcohol, n (%)	42(21.2)
Diagnosis	
AD and variant	118 (60.3)
-AD, n (%)	109(54.8)
-LV PPA, n (%)	3 (1.5)
-PCA, n (%)	6(3)
Non AD	81(30.6)
-VAD, n (%)	57(28.6)
-DLB, n (%)	3(1.5)
-FTD, n (%)	10 (5)
-Huntington, n (%)	6 (3)
-CBS, n (%)	5 (2.5)

2. Comorbidities

Among these patients, 34.7% (n = 69) had a diagnosis of type 2 DM, 17.1% (n = 34) had hypertension, and 24.1% (n = 48) had hyperlipidemia. Coronary artery disease was present in 6.5% (n = 13) of the participants. Furthermore, 19.2% (n = 38) of the patients reported smoking, and 21.2% (n = 42) had a history of alcohol consumption.

3. Proportion of Dementia Types

In this study, a total of 199 participants were analyzed, with 118 (59.3%) diagnosed with Alzheimer's disease (AD) and its variants, and 81 (40.7%) diagnosed with non-AD dementia. Among the total participants, 54.8% (n = 109) were diagnosed with typical amnestic AD., some participants were diagnosed with AD variants, including posterior cortical

atrophy (PCA) in 3% (n = 6) and logopenic primary progressive aphasia (LV PPA) in 1.5% (n = 3).

Among the non-AD dementia cases, the most common cause was vascular dementia (VAD), affecting 28.6% of all participants (n = 57). Other types of non-AD dementia included frontotemporal dementia (FTD) in 5% (n = 10), Huntington's disease in 3% (n = 6), corticobasal syndrome (CBS) in 2.5% (n = 5), and dementia with Lewy bodies (DLB) in 1.5% (n = 3).

4. Characteristics and associated factors of Early-onset dementia in AD and non-AD groups

Table 2 compares demographic characteristics, risk factors, and clinical parameters between Alzheimer's disease (AD) and non-AD groups.

Table 2 Comparison of Characteristic and Predicting factor between AD and non-AD patients

	Data			
	AD=118	Non AD=81	total 199	P value
Sex(male)	51(43.2%)	51(63%)		0.006
Age, median (IQR)	58(7)	54.5(9)	57(8)	0.005
Education year, median (IQR)	12(10)	12(10)	12(10)	0.687
BMI, mean +- SD	22.6(5)	22.8(5)	22.6(5)	0.268
Smoke, n (%)	16(13.7%)	22(27.2%)	38(19.2%)	0.018
Alcohol, n (%)	20(17.1%)	22(27.2%)	42(21.2%)	0.88
Diabetes mellitus, n (%)	32(27.1%)	37(45.7%)	69(34.7%)	0.007
Hypertention, n (%)	18(15.3%)	16(19.8%)	34(17.1%)	0.407
Hyperlipidemia, n (%)	21(17.8%)	27(33.3%)	48(24.1%)	0.012
Coronary artery disease, n (%)	7(5.9%)	6(7.4%)	13(6.5%)	0.679
Major depressive disorder, n (%)	4(3.4%)	4(4.9%)	8(4%)	0.59
First main present symptom				
Memory impairment, n (%)	116(98.3%)	66(81.5%)		<0.001
Executive impairment, n (%)	33(28%)	20(24.7%)		0.608
Visuospatial impairment, n (%)	19(16.1%)	11Z(13.61%)	30(15.1%)	0.625
Language problem, n (%)	10(8.5%)	13(16%)	23(11.6%)	0.101
Attention impairment, n (%)	39(33.5%)	5(6.2%)	44(22.1%)	<0.001
Social impairment, n (%)	8(6.8%)	10(12.3%)	18(9%)	0.179
Cognitive assesment				
TMSE, median (IQR)	17(14)	21(11)	19(12)	0.009
Orientation, median (IQR)	3(3)	5(3)	4(3)	0.001
Regist, median (IQR)	3(1)	3(0)	3(1)	0.008
Attention, median (IQR)	3(5)	5(5)	5(5)	0.097
Calculation, median (IQR)	1(1)	1(2)	1(2)	0.047
Language, median (IQR)	7(5)	8(3)	7(4)	0.215
Recall, median (IQR)	0(0)	0(1)	0(1)	0.019
Moca	13(7)	16(6)	14(8)	0.02
Executive, median (IQR)	0(1)	0(1)	0(1)	0.93
Visuospatial, median (IQR)	1(1)	1(2)	1(1)	0.93
Memory, median (IQR)	0((0)	0(2)	0(1)	0.018
MIS, median (IQR)	3(6)	5(8)	3(7)	0.014
Language, median (IQR)	3(1)	4(2)	3(1)	0.14
Attention, median (IQR)	3(3)	4(2)	4(3)	0.088
Orientation, median (IQR)	4(3)	5(2)	4.5(3)	0.039

	Data			
	AD=118	Non AD=81	total 199	P value
Neuroimaging				
MTA, median (IQR)	2(1)	0(1)	1(2)	<0.001
Falzeka, median (IQR)	0(1)	2(3)	1(2)	<0.001
Labaratory				
WBC, median (IQR)	6900(2770)	7200(2400)	7185(2575)	0.317
HB, mean +- SD	13.1(1.8)	13.5(1.2)	13.4(1.2)	0.029
HCT, median (IQR)	40.7(4.5)	41.4(3.8)	41(4.37)	0.066
Plt, mean +- SD	307000(10500)	325000(83000)	320000(92500)	0.558
BUN, median (IQR)	13(6)	14(7)	13(6)	0.13
Cr, median (IQR)	0.71(0.29)	0.72(0.27)	0.71(0.29)	0.368
AST, median (IQR)	23(8)	19(10)	22(9)	0.58
ALT, median (IQR)	18(10)	18(13)	18(10)	0.976
Glucose, median (IQR)	92.5(16)	102(27)	98(21)	0.001
TFT, median (IQR)	1.04(0.587)	1.04(1.11)	1.04(0.72)	0.43
B12, median (IQR)	644(407)	592(338)	625(377)	0.377

4.1 Baseline characteristics

The median age at presentation was significantly higher in the AD group (median 58, IQR 7) compared to the non-AD group (median = 54.5, IQR 9) (p = 0.005). The proportion of males was significantly lower in the AD group (43.2%) compared to the non-AD group (63%) (*p* = 0.006). The median number of education years was similar between the AD group (median = 12, IQR = 10) and the non-AD group (median = 12, IQR = 10).

4.2 Risk Factors and Comorbidities

The proportion of smoking was significantly higher in the non-AD group (27.2%) compared to the AD group (13.7%), suggesting a stronger association between smoking and non-AD dementias (*p* = 0.018). This finding may relate to vascular dementia. In contrast, there is no difference in alcohol consumption between both groups (p-value = 0.88). For comorbidities, the proportion of type 2 DM was higher in the non-AD group (45.7%) compared to the AD group (27.1%) (p-value = 0.007). In addition, hyperlipidemia was also more common in the non-AD group (33.3%) compared to the AD group (17.8%) (p-value = 0.012). However, there is no significant difference in hypertension (p-value = 0.407), coronary artery disease (p-value = 0.679), or major depressive disorder (p-value = 0.59) between both groups.

4.3 Presenting Symptoms

Memory impairment was more frequent in the AD group (98.3%) compared to the non-AD group (81.5%) (p-value < 0.001). Furthermore, attention impairment was significantly more common in the AD group (33.5%) compared to the non-AD group (6.2%) (p < 0.001). There were no statistically significant differences between the two groups regarding executive, visuospatial, or social impairment.

4.4 Cognitive Assessment

The median TMSE score was significantly lower in the AD group (median = 17, IQR = 14) than in the non-AD group (median = 21, IQR = 11) (*p-value* = 0.009). The orientation score was also significantly lower in the AD group (median = 3, IQR = 3) than in the non-AD group (median = 5, IQR = 3) (*p-value* = 0.001).In contrast, the attention, language, and recall scores showed no significant difference between the groups.

The overall mean MOCA score was significantly lower in the AD group (mean = 13.3 ± 5.04) compared to the non-AD group (mean = 15.44 ± 4.21) (p = 0.022). The sub-score analysis showed that memory score was significantly lower in the AD group (median = 0, IQR = 0) compared to the non-AD group (median = 0, IQR = 2) (p = 0.018). Memory impairment, as reflected in the Memory Index Score (MIS), was also significantly lower in the AD group (median = 3, IQR = 6) compared to the non-AD group (median = 5, IQR = 8) (p = 0.014). Moreover, the orientation score was significantly lower in the AD group (median = 4, IQR = 3) compared to the non-AD group (median = 5, IQR = 2) (p = 0.039). There was no significant difference between the AD and non-AD groups for the executive domain, visuospatial, language, and attention scores.

4.5 Neuroimaging

Neuroimaging findings showed significant differences between the AD and non-AD groups. Medial temporal atrophy (MTA) scores were significantly more significant in the AD g+roup (median = 2, IQR = 1) compared to the non-AD group (median = 0, IQR = 1) (p-value < 0.001). Fazekas scores were also significantly higher in the non-AD group (median = 2, IQR = 1) compared to the AD group (median = 0, IQR = 1) (p-value < 0.001).

4.6 Laboratory Results

The hemoglobin (Hb) level was significantly lower in the AD group (mean = 13.11 ± 1.12) compared to the non-AD group (mean = 13.54 ± 0.94) (p-value = 0.037). Fasting blood glucose was also significantly lower in the AD group (median = 92.5, IQR = 16) compared to the non-AD group (median = 102, IQR = 27) (p-value = 0.001).

Discussion

This study provides a comprehensive comparison between Alzheimer's disease (AD) and non-AD dementia patients, explicitly focusing on the proportion, associated characteristics, and risk factors of cognitive impairment. Our findings revealed significant differences in both comorbidities and cognitive outcomes between the two groups.

Associated Factors

The findings of this study indicate that hyperlipidemia and diabetes mellitus were significantly more proportion in the non-AD group, suggesting a stronger association with non-AD dementias, particularly vascular dementia. This aligns with previous research linking vascular risk factors, such as hyperlipidemia and diabetes, to non-AD dementias, where vascular pathology contributes to cognitive decline through mechanisms such as ischemia and white matter changes[12].

Smoking was also more common in the non-AD group, supporting its association with vascular-related cognitive decline. Smoking is known to promote atherosclerosis and reduce cerebral blood flow, increasing the risk of vascular dementia[13].

Cognitive Impairment

As expected, memory impairment was significantly more proportion in the AD group. AD is characterized by early and progressive memory loss due to hippocampal and cortical degeneration. In contrast, the non-AD group exhibited a broader range of initial symptoms, including visuospatial and executive impairments, consistent with the heterogeneity seen in other forms of dementia, such as Lewy body dementia and frontotemporal dementia (FTD).

Our cognitive scores (TMSE and MOCA) analysis highlights significant distinctions between the AD and non-AD groups. The AD group had significantly lower TMSE and MOCA scores, particularly in memory-related sub-scores. The significant difference in the Memory Index Score (MIS) between the AD and non-AD groups can be attributed to the distinct neurodegenerative patterns in Alzheimer's disease. In AD Alzheimer's disease, memory impairment is primarily related to encoding difficulties, which do not significantly improve with cueing. AD is often associated with hippocampal atrophy and hypometabolism, which are critical for encoding new information[14].

In contrast, non-AD dementias, such as vascular dementia or frontotemporal dementia, more often exhibit retrieval-related memory impairments. Retrieval difficulties may improve with cueing, as these impairments are linked to dysfunction in subcortical structures and the hippocampal-parietal-frontal network rather than the encoding deficits seen in AD[15]. Therefore, the lower MIS in AD patients, compared to non-AD patients, can be attributed to their profound encoding deficits linked to hippocampal pathology, distinguishing it from retrieval deficits typical of non-AD dementias.

The significant difference in orientation scores between the AD and non-AD groups highlights temporal orientation as a valuable marker for dementia severity, particularly in Alzheimer's disease (AD). Impairment in orientation has been shown to predict daily functioning and is associated with caregiver burden. Temporal disorientation is highly sensitive for detecting dementia, though less specific[14]. Our findings align with this, as AD patients showed more significant temporal orientation deficits, reflecting hippocampal and medial temporal lobe deterioration typical of AD. However, orientation is less helpful in identifying mild cognitive impairment, as it becomes more pronounced only in later stages of dementia[15]. However, attention scores did not significantly differ between the groups, suggesting that attention-related cognitive domains may be similarly affected across both dementia types.

Laboratory Findings

The significant differences in hemoglobin levels and fasting blood glucose between the AD and non-AD groups are intriguing. Lower hemoglobin levels in the AD group suggest a relationship between anemia and cognitive decline, as anemia has been associated with reduced oxygen supply to the brain, which may exacerbate neurodegeneration[16]. The higher fasting blood glucose levels in the non-AD group are particularly noteworthy. Non-AD dementias, particularly vascular dementia (VAD), are more strongly associated with metabolic disorders, such as Type 2 DM and insulin resistance. Elevated FBS in the non-AD group may reflect the higher proportion of diabetes in these patients, as diabetes and impaired glucose metabolism are well-established risk factors for vascular damage and subsequent cognitive decline.

Limitations and Future Directions

There are minor limitations to this study. First, the small sample size, particularly in the non-AD group, may limit the generalizability of the findings. Additionally, the retrospective nature of the study may introduce bias, particularly in the self-reported risk factors such as smoking and alcohol consumption. Future studies should include a larger and more diverse cohort to explore these relationships further.

Moreover, while this study focused on traditional risk factors and cognitive assessments, with diagnosis based on established criteria and clinical assessments, it would be valuable to include biomarker data in future research to provide a more detailed characterization of the underlying neuropathology in AD and non-AD dementias.

Conclusion

This study identified the key clinical characteristics of early-onset Alzheimer's disease (AD) and non-Alzheimer's disease dementias in patients under 65 at the Neurological Institute of Thailand. Alzheimer's disease was the most proportion form of dementia, vascular dementia was the most common non-AD subtypes, strongly associated with vascular risk factors such as Type 2 DM and hyperlipidemia. Early identification of these clinical features and risk factors is crucial for improving diagnosis, guiding treatment, and managing outcomes in patients with early-onset dementia.

Acknowledgments

The authors would like to express their gratitude to all the staff and participants involved in the study for their invaluable contributions.

Statement of Ethics

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Approval for the study was obtained from the Institutional review board of the Neurological Institute of Thailand No.67016. Due to the retrospective nature of the study, the Ethics Committee waived informed consent. All patient data were anonymized to maintain confidentiality.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Funding Sources

This study received financial support from the Neurological Institute of Thailand, Department of Medical Services, Ministry of Public Health, Thailand. The funder had no role in the study design, data collection, data analysis, decision to publish, or preparation of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Author Contributions

Dr. Jakkree Kanpittaya conducted the study plan and data gathering, and the statistical analysis was performed by Dr.Jakkree and Dr.Jedsada.The authors acknowledge the use of ChatGPT, developed by OpenAI, to assist in drafting sections of this manuscript, including the abstract, introduction, methods, results, discussion, and overall editing. The final manuscript was reviewed and approved by all authors.

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