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Original Article

Factors associated with newly diagnosed ischemic stroke among people with type 2 diabetes mellitus in Thailand: A population-based case-control study

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Abstract

Stroke is a leading cause of mortality and disability-adjusted life years. Its incidence is rising across Asia, with ischemic stroke accounting for approximately 80% of total stroke cases in Thailand. Stroke often leads to long-term disabilities, including impairments in speech, communication, and cognitive function. The aim of this study was to investigate risk factors associated with newly diagnosed ischemic stroke. A matched case-control study was conducted, including 154 newly diagnosed ischemic stroke cases and 183 non-stroke controls, all with type 2 diabetes mellitus (T2DM). Data were collected between February and September 2022 (post-COVID-19 period) using a structured questionnaire covering socio-demographics, lifestyle factors, perceived social support, and self-care management (SCM). Multivariable logistic regression models were used to estimate adjusted odds ratios (aOR) with 95% confidence intervals (CI). The majority of participants were female (60.8%), Buddhist (92.9%), and agriculturists (66.5%), with a mean age of 58.9 (±9.9) years. Factors associated with ischemic stroke included male (aOR: 3.53; 95%CI: 1.73–7.21), Buddhism (aOR: 3.53, 95%CI: 1.11–11.25), sedentary occupation (aOR: 5.78; 95%CI: 2.61–12.81), and T2DM duration >10 years (aOR: 6.19, 95%CI: 3.55–10.80). Protective factors included age ≥60 years (aOR=0.55, 95%CI: 0.31–0.98) and moderate SCM levels (aOR=0.45, 95%CI: 0.26–0.80). This study highlighted that prolonged T2DM and sedentary occupations significantly contributed to ischemic stroke risk. Targeted prevention strategies, including lifestyle modifications and enhanced diabetes self-care management, may help reduce the burden of ischemic stroke.

Keywords: Diabetes mellitus, stroke, risk factors, sedentary lifestyle, self-care management

Introduction

Stroke is the second leading cause of death and the third cause of combined death and disability. Its burden has been increasing rapidly in low-income (LICs) and middle-income countries (MICs) [1]. Between 1990 and 2019, the global burden of stroke increased significantly, with a 70% rise in incidence (12.2 million new cases), an 85% increase in prevalence (101 million cases), a 43% rise in mortality (7 million deaths), and a 32% increase in disability-adjusted life years (DALYs) (143 million DALYs) [2]. In Asia, the incidence rate of stroke ranges from 116 to 483 per 100,000 population per year [3].

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Ischemic stroke, which accounts for approximately 62% of all stroke cases, is caused by arterial occlusion leading to brain tissue necrosis due to insufficient blood flow [4,5]. This type of stroke results in significant morbidity, including long-term physical impairments and cognitive deficits such as post-stroke cognitive impairment (PSCI) and post-stroke dementia (PSD) [6,7], as well as significant physical impairments [8-10]. Globally, ischemic stroke accounts for 7.6 million new cases annually, with over 58% occurring in individuals under the age of 70, and is responsible for 3.3 million deaths and over 63 million DALYs per year [5]. Despite a decline in the age-standardized mortality rate from 61 to 49 per 100,000 population between 1990 and 2019, the incidence rate increased from 96 to 105 per 100,000 population [4]. The risk factors for stroke are categorized into non-modifiable, semi-modifiable, and modifiable factors. Non-modifiable risk factors include age, sex [6,11], and family history [12], while semi-modifiable factors encompass hypertension, diabetes mellitus, dyslipidemia [13,14], and environmental factors such as air pollution [2,15]. Modifiable risk factors, including obesity, smoking, alcohol consumption, and physical inactivity, play a crucial role in stroke prevention [2,15]. Understanding the most important risk factors in specific population is critical for stroke prevention.

Thailand, an upper-middle-income country undergoing demographic shifts toward an aging society [16,17], faces an increasing burden of non-communicable diseases, including hypertension, type 2 diabetes mellitus (T2DM), and stroke [18]. Stroke remains a major public health concern and a leading cause of mortality in Thailand, with a higher prevalence in males [19]. The overall prevalence of stroke is estimated at 1.3% [6], with ischemic stroke accounting for approximately 80% of all cases [19]. Despite the significant impact of ischemic stroke in Thailand, research on its associated risk factors remains limited. A review identified only eight relevant studies in Thailand, including four nationwide analyses, three regional studies focusing on the central region, and one study in the northeast region [19-26]. However, these studies did not specifically examine ischemic stroke or account for regional variations of which most of the studies were conducted in a lower northeast province focusing on non-specific stroke. Therefore, the aim of this study was to investigate factors associated with newly diagnosed ischemic stroke in upper-north region of Thailand.

Methods

Study design, setting and sampling

A case-control study was conducted in Sakon Nakhon, an upper-northeast province of Thailand with approximately 1.2 million inhabitants and annual per capita income of 2,100 USD [27]. The incidence rate of stroke in this province is approximately 295.4 per 100,000 population per year [28]. The study was conducted at Sakon Nakhon Provincial Hospital (case group) and Subdistrict Health Promoting Hospitals (SHPHs) (control group) between February 21 to September 30, 2022, to identify factors associated with newly diagnosed ischemic stroke. The sample size was determined using a statistical formula for logistic regression [29], considering an odds ratio of 2.8, a 95% confidence level (α=0.05), and a statistical power of 80% (β=0.8) [14]. A 1:1 case-to-control ratio was applied, requiring a minimum of 150 participants in each group. Cases comprised individuals newly diagnosed with ischemic stroke, while controls were matched based on relevant demographic and clinical criteria. This study used consecutive sampling (i.e., collecting data at the specified period).

Patients and criteria

The case and control groups have been diagnosed with T2DM for more than one year from medical record. The case group included individuals with a first-time ischemic stroke diagnosis (ICD-10 codes I630-I639), as confirmed by physician through computerized tomography scan (CT scan) or magnetic resonance imaging (MRI) within seven days of onset [30] and admitted to the stroke unit at Sakon Nakhon Provincial Hospital. Ischemic stroke was confirmed using CT scan or MRI based on standard diagnostic criteria [31,32]. CT scans were primarily used to exclude hemorrhagic stroke and identify early ischemic changes, including loss of gray-white matter differentiation, sulcal effacement due to cytotoxic edema, and the hyperdense artery sign indicating acute thrombosis. Established ischemic infarcts were characterized by well-defined hypodense regions in a vascular distribution, often with mass effect in the subacute phase. MRI was performed for cases requiring more detailed assessment of infarct evolution and lesion characterization. Diffusion-weighted imaging (DWI) was used to detect acute ischemia, with infarcted areas appearing hyperintense and exhibiting restricted diffusion on apparent diffusion coefficient (ADC) maps [31,32]. These imaging modalities ensured accurate diagnosis and classification of ischemic stroke, facilitating appropriate patient management and inclusion in the study. Moreover, only individuals of Thai ethnicity, confirmed by national identification card, aged between 18 and 75 years and able to communicate in Thai were eligible. Additionally, they were able to communicate in Thai. Controls were selected from the same community for at least one year as the cases who were registered at SHPHs, and no prior diagnosis of ischemic stroke. Matching was done based on sex and age group. Patients from both groups were excluded if they had cognitive impairment, defined as dementia, major depression, and schizophrenia, had a diabetes complication (such as diabetes retinopathy), were getting pregnant, or refused from the study. The flow diagram for the enrolment of study participants is presented in **Figure 1**.

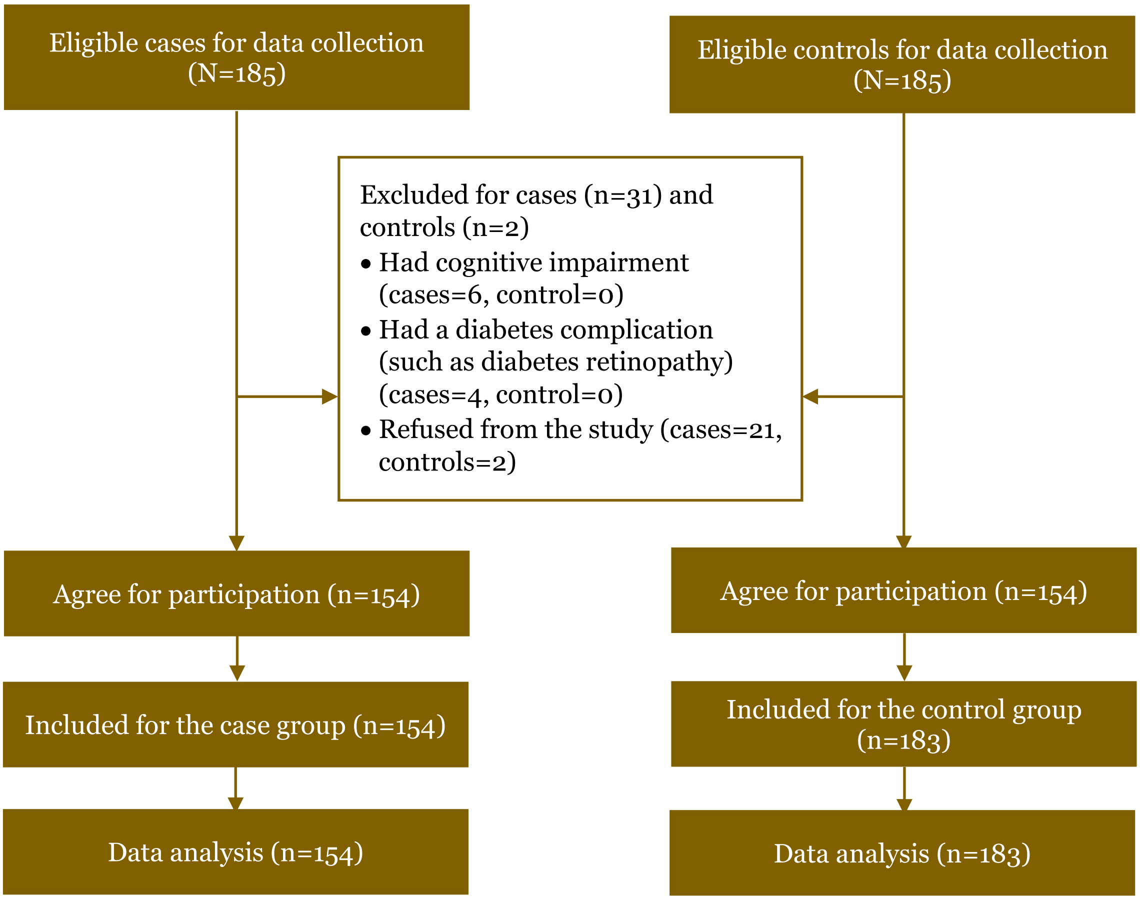

Figure 1. Flow diagram for the enrolment of study participants.

Study tools and study variables

A structured questionnaire was used for both cases and controls, comprising five sections: socio-demographics, the Alcohol Use Disorders Identification Test (AUDIT), self-care management (SCM), the Revised Thai Multi-Dimensional Scale of Perceived Social Support (r-T-MSPSS), and the Fagerström Test for Nicotine Dependence (FTND). The questionnaire was reviewed for content validity by three experts in public health, epidemiology, and clinical medicine and pretested for reliability among individuals in a community near Sakon Nakhon (n=30). Both content validity and reliability scores were deemed acceptable.

The socio-demographic section included information on age (measure by years), gender (male and female), education level (primary school or less, secondary school, and higher education), marital status (single, married, divorced, and widowed), occupation (agriculturist, daily workers, self-employers, civil servants, unemployed, and housewives), alcohol consumption (never had alcohol, quit alcohol, and currently take alcohol), smoking status (never smoked, quit smoking, and current smoker), family history of paralysis (yes and no), family history of cardiovascular disease (yes and no), and duration of T2DM (in years).

The AUDIT, developed by the World Health Organization [33], was used to evaluate alcohol consumption, potential dependence, and alcohol-related harm. It consisted of ten items scored from 0 to 4, except for questions nine and ten, which were scored as 0, 2, or 4. Total scores were categorized as low-risk consumption (score 1–7), hazardous or harmful consumption (score 8–14), and moderate to severe alcohol use disorder (score 15 or more). The Thai version of the AUDIT, translated by the Thai Health Promotion Foundation with Cronbach's alpha coefficient of 0.86 [34] was used in this study. The Cronbach's alpha coefficient for the present study was 0.91.

The SCM section, developed by Han *et al.* [35], measured self-care behaviors, motivation, and self-efficacy, based on Orem's model and Motivational Interviewing. The instrument comprised 20 items on a 4-point scale (1–4), a total possible score ranged from 20 to 80. The total scores were categorized using Bloom's classification [36]: 20–47 (low SCM), 48–63 (moderate SCM), and 64–80 (high SCM). The English version was translated into Thai using a backward-forward translation process and the validation of Thai version had Cronbach's alpha coefficient of 0.77.

The r-T-MSPSS, originally developed by Zimet *et al.* [37] and translated into Thai by Wongpakaran *et al.* [38] with Cronbach's alpha coefficient of 0.91, was used assessed perceived social support from three sources (family, friend, and significant others). It consisted of 12 items on a 7-point Likert scale (7=very strongly agree, 1=very strongly disagree). A total score ranged from 12 to 84 and categorized as low perceived social support (score 12–36), moderate perceived social support (score 37–60), and high perceived social support (score 61–84) [39]. The Cronbach's alpha coefficient for this study was 0.94.

The FTND, modified by Heatherton *et al.* [40] and translated into Thai by Klinsophon *et al.* [41], with Cronbach's alpha coefficient of 0.52, was used to assess the nicotine dependence using six items that evaluate the quantity of cigarette consumption, each scored from zero to three. Total scores ranged from 0 to 10 were categorized as very low dependence (score 1–2), low dependence (score 3–4), moderate dependence (score 5), high dependence (score 6–7), and very high dependence (score 8 or more). The Cronbach's alpha coefficient for this study was 0.61.

Data collection procedures

Following approval from the relevant ethics committees, permission to collect data was obtained from the director of Sakon Nakhon Provincial Hospital (Stroke Unit) and from the heads of SHPHs where control participants resided. Subsequently, the head nurse of the Stroke Unit was contacted to facilitate case identification and recruitment, while the directors of SHPHs in the same geographic areas as the cases were approached to recruit control participants. After ischemic stroke (case group) and non-ischemic stroke (control group) diagnoses were confirmed by a physician through CT-scan or MRI, all participants were provided with both oral and written information regarding the study. Informed consent was obtained voluntarily before participation. Data collection was conducted using self-reported questionnaire, which required 15 to 20 minutes to complete in a private setting. For case participants, informed consent procedures and data collection were conducted within the Stroke Unit. For control participants, these procedures took place in a designated room near the selected SHPHs. The investigators provided standardized instructions, addressed any uncertainties, and reviewed the completed questionnaires to ensure accuracy and completeness of the collected data.

Statistical analysis

Cross-tabulations and Chi-squared tests were used to analyze relationships between categorical variables in the case and control groups, with *p*-values indicating significance. Univariable logistic regression was conducted to assess individual relationships between independent variables and ischemic stroke. Variables with $p<0.05$ in univariable regression were included in multivariable regression analysis (age and sex were also included as confounders). Due to highly correlated (collinearity) with smoking and alcohol consumption variables, the AUDIT and FTND levels were not included in the logistic regression analysis. Crude odds ratios (OR), adjusted odds ratios (aOR), and 95% confidence intervals (CIs) were calculated to examine the associations between risk factors and ischemic stroke. All tests were two-sided with statistical significance set at $p<0.05$.

Results

Characteristics of patients

A total of 154 newly diagnosed ischemic stroke cases with T2DM and 183 of non-stroke individuals with T2DM as controls included in this study and their characteristics are presented in (**Table 1)** The majority of participants were female (60.8%) and the mean age was 58.9 years (±9.9). Most participants were Buddhists (92.9%), married (78.0%), had a primary education or less (76.3%), worked as agriculturists (66.5%), never smoked (73.6%), never consumed alcohol (61.4%), had no family history of paralysis (92.6%), and had no family history of cardiovascular disease (97.3%) (**Table 1**). A greater proportion of cases had a duration of T2DM for 11 or more years (69.5%), while 72.7% of controls had a duration of 10 years or less.

There was no significant difference in the proportion of age, education level, family history of paralysis, family history of cardiovascular disease, and r-T-MSPSS Level in the case and control groups (**Table 1**). Univariate analyses indicated sex, religion, education level, occupation, smoking status, alcohol consumption status, self-care management level and duration of T2DM were associated with the incidence of ischemic stroke (**Table 2**).

Factors associated with newly diagnosed ischemic stroke

Our univariable logistic regression several factors were significantly associated with an increased risk of ischemic stroke (**Table 2**). Males had a higher likelihood of stroke compared to females (OR: 4.21; 95%CI: 2.64–6.71, $p<0.001$). Being Buddhist was also linked to a greater risk compared to Christianity (OR: 3.45; 95%CI: 1.26–9.48, $p=0.016$). Individuals with higher education levels had increased odds of ischemic stroke compared to those with primary education or less (OR: 2.96; 95%CI: 1.18–7.44, $p=0.021$). Occupational factors played a significant role, with those in sedentary jobs having a markedly higher risk than those in active occupations (OR: 4.67; 95%CI: 2.59–8.43, $p<0.001$). Lifestyle behaviors such as smoking and alcohol consumption were also important contributors; former smokers (OR: 2.82; 95%CI: 1.36–5.87, $p=0.006$) and current smokers (OR: 4.33; 95%CI: 2.26–8.29, $p<0.001$) had a significantly higher risk compared to never smokers. Similarly, former alcohol drinkers (OR: 2.54; 95%CI: 1.33–4.85, $p=0.005$) and current drinkers (OR: 2.61; 95%CI: 1.55–4.40, $p<0.001$) had greater odds of ischemic stroke. The strongest risk factor identified was a longer duration of T2DM ≥11 years, which was associated with a sixfold increase in risk (OR: 6.06; 95%CI: 3.77–9.71, $p<0.001$) (**Table 2**).

In contrast, one factors appeared to be protective against ischemic stroke (**Table 2**). Moderate level of SCM was associated with a reduced risk compared to low SCM levels (OR: 0.53; 95%CI: 0.33–0.83, $p=0.006$) (**Table 2**).

In multivariate, all variables with $p<0.05$ in univariable regression were included together with sex and age as the confounders. After included these variables together with sex and age as the confounders, our multivariate analysis revealed that sex, religion, age, occupation, SCM level, and duration of T2DM were associated with the incidence of ischemic stroke (**Table 2**). Male was associated with a 3.53 times higher risk compared to females (aOR: 3.53, 95%CI: 1.73–7.21) (**Table 2**). Buddhism was linked to a 3.53 times higher risk compared to Christianity (aOR: 3.53, 95%CI: 1.11–11.25). Individuals with a sedentary occupation had a 5.78 times higher risk compared to those with an active occupation (aOR: 5.78, 95%CI: 2.61–12.81). In addition, having T2DM for more than 10 years was associated with a 6.19 times higher risk of ischemic stroke compared to those with a duration of 10 years or less (aOR: 6.19, 95%CI: 3.55–10.80) (**Table 2**).

Protective factors included being aged 60 years or older, which was associated with a 55% lower risk compared to those aged 59 years or younger (aOR: 0.55, 95%CI: 0.31–0.98). Furthermore, having a moderate level of SCM was associated with 45% lower risk of ischemic stroke compared to a low level of SCM (aOR: 0.45, 95%CI: 0.26–0.80) (**Table 2**). The summary of the aOR and 95%CI included in multivariate analysis is presenting in forest plot in (**Figure 2**).

Table 1. Characteristics of the case and control group (n=337)

Characteristics	Total (n=337) n (%)	Cases (n=154) n (%)	Controls (n=183) n (%)	χ^2	*p*-value
Overall	337	154 (45.7)	183 (54.3)		
Sex				38.451	<0.001*
Male	132 (39.2)	88 (57.1)	44 (24.0)		
Female	205 (60.8)	66 (42.9)	139 (76.0)		
Religion				6.438	0.011*
Buddhism	313 (92.9)	149 (96.8)	164 (89.6)		
Christianity	24 (7.1)	5 (3.2)	19 (10.4)		
Age (years)				1.049	0.592
≤50	59 (17.5)	30 (19.5)	29 (15.9)		
51–60	117 (34.7)	50 (32.5)	67 (36.6)		
≥61	161 (47.8)	74 (48.0)	87 (47.5)		
Mean±SD	58.9±9.9	58.5±11.1	59.3±8.9		
(min, max)	(21, 75)	(21, 75)	(28, 75)		
Marital status				11.812	0.008*
Single	15 (4.5)	4 (2.6)	11 (6.0)		
Married	263 (78.0)	123 (79.9)	140 (76.5)		
Divorced	44 (13.0)	15 (9.7)	29 (15.9)		
Widowed	15 (4.5)	12 (7.8)	3 (1.6)		
Education level				5.745	0.057
Primary school or less	257 (76.3)	112 (72.7)	145 (79.2)		
Secondary school	57 (16.9)	26 (16.9)	31 (17.0)		
Higher education	23 (6.8)	16 (10.4)	7 (3.8)		
Occupation				45.494	<0.001*
Agriculturists	224 (66.5)	76 (49.4)	148 (80.8)		
Daily workers	33 (9.8)	22 (14.3)	11 (6.0)		
Self-employers	20 (5.9)	12 (7.8)	8 (4.4)		
Civil servants	19 (5.6)	13 (8.4)	6 (3.3)		
Unemployed	31 (9.2)	27 (17.5)	4 (2.2)		
Housewives	10 (3.0)	4 (2.6)	6 (3.3)		
Family history of paralysis				0.031	0.859
No	312 (92.6)	143 (92.9)	169 (92.3)		
Yes	25 (7.4)	11 (7.1)	14 (7.7)		
Family history of cardiovascular disease				0.361	0.547
No	328 (97.3)	149 (96.8)	179 (97.8)		
Yes	9 (2.7)	5 (3.2)	4 (2.2)		
Smoking				26.179	<0.001*
Never smoked	248 (73.6)	93 (60.4)	155 (84.7)		
Quit smoking	35 (10.4)	22 (14.3)	13 (7.1)		
Current smoker	54 (16.0)	39 (25.3)	15 (8.2)		
FTND level				20.322	<0.001*
Never smoked or quit smoking	283 (84.0)	115 (74.7)	168 (91.8)		
High dependence (6–7 points)	20 (5.9)	17 (11.0)	3 (1.6)		
Very high dependence (≥8 points)	34 (10.1)	22 (14.3)	12 (6.6)		

Characteristics	Total (n=337) n (%)	Cases (n=154) n (%)	Controls (n=183) n (%)	χ^2	*p*-value
Alcohol consumption				17.453	<0.001*
Never had alcohol	207 (61.4)	76 (49.4)	131 (71.6)		
Quit alcohol	47 (14.0)	28 (18.2)	19 (10.4)		
Currently take alcohol	83 (24.6)	50 (32.4)	33 (18.0)		
AUDIT level				3.574	0.167
Never had alcohol or quit alcohol (0 point)	254 (75.4)	123 (79.9)	131 (71.6)		
Low-risk consumption (1–7 points)	70 (20.8)	25 (16.2)	45 (24.6)		
Harmful alcohol consumption (≥8 points)	13 (3.8)	6 (3.9)	7 (3.8)		
Self-care management level				8.890	0.012*
Low (20–47 points)	123 (36.5)	69 (44.8)	54 (29.5)		
Moderate (48–63 points)	201 (59.6)	81 (52.6)	120 (65.6)		
High (64–80 points)	13 (3.9)	4 (2.6)	9 (4.9)		
Mean±SD	50.3±7.9	48.9±7.8	51.6±7.7		
(min, max)	(30, 72)	(30, 69)	(33, 72)		
r-T-MSPSS level				3.082	0.214
Low (12–36 points)	12 (3.6)	3 (2.0)	9 (4.9)		
Moderate (37–60 points)	110 (32.6)	47 (30.5)	63 (34.4)		
High (61-84 points)	215 (63.8)	104 (67.5)	111 (60.7)		
Mean±SD	64.6±13.2	66.0±12.7	63.5±13.5		
(min, max)	(16, 84)	(36, 84)	(16, 84)		
Duration of type 2 diabetes mellitus				59.730	<0.001*
≤10 years	180 (53.4)	47 (30.5)	133 (72.7)		
≥11 years	157 (46.6)	107 (69.5)	50 (27.3)		
Mean±SD	8.6±7.5	9.9±9.4	8.1±6.7		
(min, max)	(1, 40)	(1, 40)	(1, 30)		

AUDIT: alcohol use disorders identification test; FTND: fagerström test for nicotine dependence; SD: standard deviation; r-T-MSPSS: the revised multi-dimensional scale of perceived social support

*Significance level of $p<0.05$

Table 2. Univariable and multivariable analyses showing risk factors of ischemic stroke (n=337)

Characteristics	Ischemic stroke		Odds ratio (95% confidence intervals)	*p*-value	Adjusted odds ratio (95% confidence intervals)	*p*-value
	Yes (n=154) n (%)	No(n=183) n (%)				
Sex						
Male	88 (57.1)	44 (24.0)	4.21 (2.64–6.71)	<0.001*	3.53 (1.73–7.21)	<0.001*
Female *(Reference group, R)*	66 (42.9)	139 (76.0)	1		1	
Religion						
Buddhism	149 (96.8)	164 (89.6)	3.45 (1.26–9.48)	0.016*	3.53 (1.11–11.25)	0.033*
Christianity *(R)*	5 (3.2)	19 (10.4)	1		1	
Age (years)						
≤59 *(R)*	78 (50.6)	92 (50.3)	1		1	
≥60	76 (49.4)	91(49.7)	0.99 (0.64–1.51)	0.945	0.55 (0.31–0.98)	0.043*
Marital status						
Never marri*(R)*	4 (2.6)	11 (6.0)	1			
Ever married	150 (97.4)	172 (94.0)	2.40 (0.75–7.69)	0.141		

Characteristics	Ischemic stroke		Odds ratio (95% confidence intervals)	*p*-value	Adjusted odds ratio (95% confidence intervals)	*p*-value
	Yes (n=154) n (%)	No(n=183) n (%)				
Education level						
Primary school or less *(R)*	112 (72.7)	145 (79.2)	1		1	
Secondary school	26 (16.9)	31 (17.0)	1.09 (0.61–1.93)	0.780	0.64 (0.30–1.37)	0.249
Higher education	16 (10.4)	7 (3.8)	2.96 (1.18–7.44)	0.021*	0.43 (0.13–1.45)	0.174
Occupation						
Active occupation *(R)*	102 (66.2)	165 (90.2)	1		1	
Sedentary occupation	52 (33.8)	18 (9.8)	4.67 (2.59–8.43)	<0.001*	5.78 (2.61–12.81)	<0.001*
Family history of paralysis						
No *(R)*	143 (92.9)	169 (92.3)	1			
Yes	11 (7.1)	14 (7.7)	0.93 (0.41–2.11)	0.859		
Family history of cardiovascular disease						
No *(R)*	149 (96.8)	179 (97.8)	1			
Yes	5 (3.2)	4 (2.2)	1.50 (0.40–5.69)	0.550		
Smoking						
Never smoked *(R)*	93 (60.4)	155 (84.7)	1		1	
Quit smoking	22 (14.3)	13 (7.1)	2.82 (1.36–5.87)	0.006*	1.04 (0.38–2.88)	0.933
Current smoker	39 (25.3)	15 (8.2)	4.33 (2.26–8.29)	<0.001*	1.48 (0.60–3.61)	0.393
Alcohol consumption						
Never had alcohol *(R)*	76 (49.4)	131 (71.6)	1		1	
Quit alcohol	28 (18.2)	19 (10.4)	2.54 (1.33–4.85)	0.005*	1.38 (0.56–3.41)	0.481
Currently take alcohol	50 (32.5)	33 (18.0)	2.61 (1.55–4.40)	<0.001*	1.51 (0.72–3.15)	0.273
Self-care management (SCM) level						
Low (20–47 points) *(R)*	69 (44.8)	54 (29.5)	1		1	
Moderate (48–63 points)	81 (52.6)	120 (65.6)	0.53 (0.33–0.83)	0.006*	0.45 (0.26–0.80)	0.007*
High (64–80 points)	4 (2.6)	9 (4.9)	0.35 (0.10–1.19)	0.093	0.53 (0.13–2.23)	0.387
The revised multi-dimensional scale of perceived social support level						
Low (12–36 points) *(R)*	3 (2.0)	9 (4.9)	1			
Moderate (37–60 points)	47 (30.5)	63 (34.4)	2.23 (0.57–8.72)	0.246		
High (61–84 points)	104 (67.5)	111 (60.7)	2.81 (0.74–10.67)	0.129		
Duration of type 2 diabetes mellitus (T2DM)						
≤10 years *(R)*	47 (30.5)	133 (72.7)	1		1	
≥11 years	107 (69.5)	50 (27.3)	6.06 (3.77–9.71)	<0.001*	6.19 (3.55–10.80)	<0.001*

*Significance level of $p<0.05$

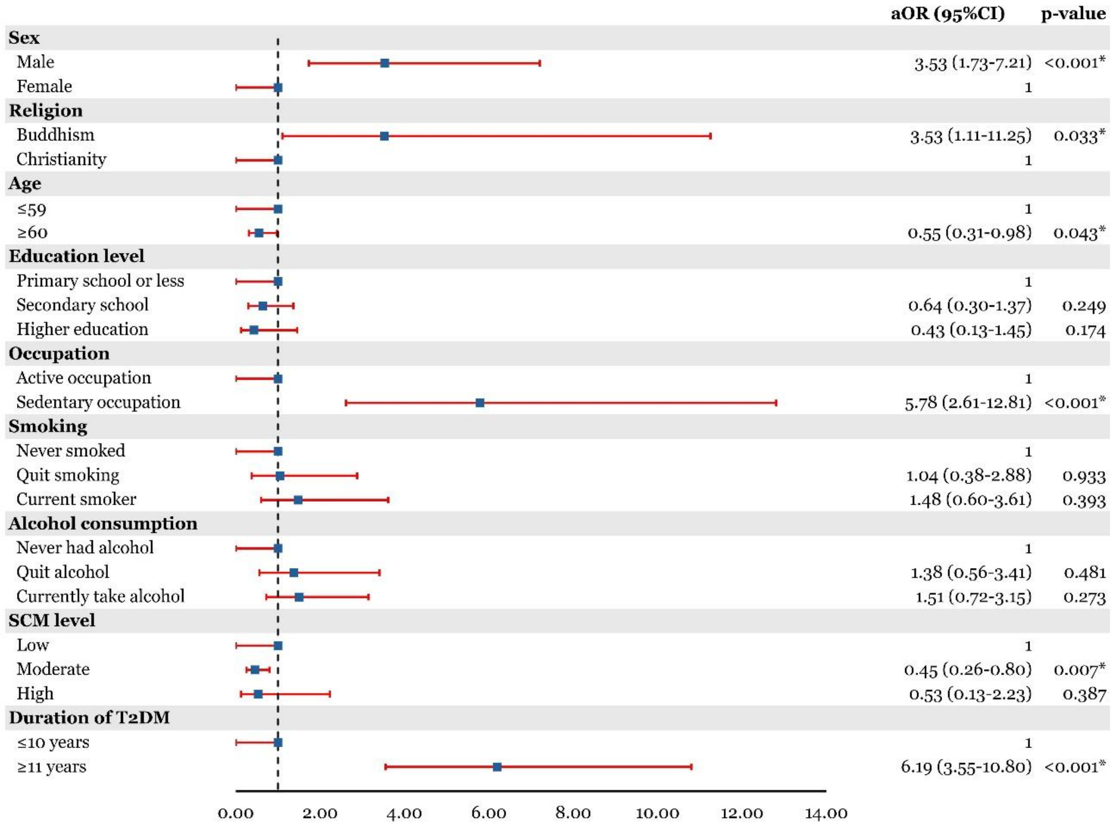

Figure 2. Forest plot displaying the adjusted odds ratios (aOR) and 95% confidence intervals (CI) for ischemic stroke risk factors.

Discussion

The aim of the present study was to investigate factors associated with people newly diagnosed with ischemic stroke in Thailand. The results identified non-modifiable factors (gender, duration of T2DM, and age), semi-modifiable factors (Buddhism and sedentary occupation), and modifiable factors (SCM) were significantly associated with ischemic stroke. The mean age of ischemic stroke cases in this study was 58.5 (±11.1) years, with the majority of participants aged 60 years or younger (52.0%), which aligns with findings from previous studies [5,20,23,30]. Approximately 60% of participants were male, which is similar with other studies [20-22]. Furthermore, most patients were married and had a primary level of education, consistent with prior research [20,22]. These demographic similarities suggested that the findings of this study could be generalized to other contexts.

Diabetes can lead to a range of microvascular and macrovascular complications, including stroke [42]. The pathophysiologic mechanisms of diabetes contributes to stroke primarily involve three major pathways: large artery atherosclerosis, cerebral small vessel disease (SVD), and cardiac embolism [42]. In large artery atherosclerosis, diabetes accelerates the atherosclerotic process through dyslipidemia, uncontrolled hyperglycemia, and insulin resistance. Consequently, this leads to impaired distal perfusion and artery-to-artery embolism, increasing the risk of ischemic stroke. In cerebral small vessel disease (SVD), both diabetes and prediabetes contribute to cerebral microvascular dysfunction, increasing the risk of lacunar and hemorrhagic strokes [42]. Key contributing factors include hyperglycemia, insulin resistance, obesity, and hypertension [11,42-44], with increased arterial stiffness further exacerbating the condition. Oxidative stress, inflammation, and endothelial dysfunction also play crucial roles in the pathogenesis of cerebral SVD, contributing to the damage of small blood vessels in the brain [11, 42]. In cardiac embolism, diabetes increases the risk of atrial fibrillation, a leading cause of cardioembolic stroke [42]. In addition, individuals with diabetes tend to have more comorbidities than those without diabetes, including obesity, hypertension, and a longer duration of diabetes, all of which are associated with an increased risk of stroke [11,35,42-47]. Furthermore, complications related to diabetes, such as stroke, may even be presented at the time of diabetes diagnosis [42]. People with diabetes may be population-at-risk for some complications, like stroke. They are in need of screening and intervening in advance.

Prolonged T2DM (11 years or more) was a potential risk factor for ischemic stroke in this study. Previous studies have also demonstrated that diabetes duration significantly increases stroke risk [35,45-47]. For instance, individuals with diabetes for over 10 years face a threefold higher risk of ischemic stroke, with an annual increase of 3% [45]. Similarly, a diabetes duration of eight years or more is associated with an elevated risk of 1-year stroke recurrence following ischemic stroke or transient ischemic attack [46]. Additional studies have linked prolonged diabetes with higher stroke risk in people with atrial fibrillation, especially when accompanied by poor glycemic control (HbA1c>7%) [47]. These findings underscored the importance of screening for ischemic stroke in individuals with prolonged T2DM.

Sedentary lifestyle or physical inactivity involve minimal to no physical activity and is defined as any waking behavior with an energy expenditure of ≤1.5 metabolic equivalents while in a sitting, reclining, or lying posture [48]. This includes activities such as using a computer and sitting at school or work [48,49]. A sedentary lifestyle linked to various metabolic dysfunctions, including elevated plasma triglycerides, reduced high-density lipoprotein cholesterol, and decreased insulin sensitivity [48]. Physical inactivity lowers lipoprotein lipase activity, contributing to metabolic disorders, including hypertension, diabetes mellitus, obesity, or coronary artery disease [48]. This modifiable factor shall be improved by an appropriate program, e.g. diabetes knowledge and community-based intervention [50].

This study also found that having a sedentary occupation significantly increased the risk of ischemic stroke, include professions such as self-employers, civil servants, and unemployed. Previous studies, sedentary lifestyle is strongly associated with an increased risk of cardiovascular disease, cancer, premature mortality, and stroke [48,49]. Prolonged sedentary behavior, such as sitting for more than eight hours daily [51], or computer use more than four hours daily [52], has been associated with an increased risk of stroke. In addition, prolonged sitting sessions lasting more than 17 minutes were associated with a higher risk of stroke compared to shorter bouts of less than eight minutes [49]. However, individuals who engaged in at least 25 minutes of moderate-to-vigorous physical activity per day had a 43% lower risk of stroke [49]. Although individuals in sedentary occupations may not face high physical workloads, they are often exposed to other risk factors, including reduced physical activity, environmental stressors, and psychosocial pressures, which may contribute to stroke risk [20]. Further research is needed to determine whether the relationship between sedentary occupation and ischemic stroke is causal or influenced by confounding variables.

Male was also a significant risk factor for ischemic stroke. Sex-related differences are evident in stroke incidence, clinical outcomes, and risk factors. [53,54]. The incidence of stroke has been rising in both sexes; however, it remains more prevalent in men, whereas women tend to experience more severe strokes with higher rates of post-stroke complications and mortality compared to men. [53,54]. Both biological and sociocultural factors contribute to this disparity. These differences are largely attributed to variations in sex hormones, such as testosterone and estrogen, play a role in stroke pathophysiology. Estrogen promotes vasodilation and enhances blood flow, whereas testosterone exerts vasoconstrictive effects [53-56]. While sociocultural factors, such as higher rates of smoking and alcohol consumption among males, further elevate their risk [52-54]. Efforts to reduce stroke risk in males should focus on discouraging smoking and excessive alcohol consumption.

The result showed that smoking was not a risk factor contributing to stroke in this population. Even though top ten risk of a non-communicable disease covers smoking consumption [57], including stroke [2,3,5,11,57], especially among people with socially marginalized populations [58]. One study demonstrated that smoking is related to quality of life among stroke survivors [59], while some studies show there is no association between quality of life and stroke [14,60,61] (**Table 3**). When analyzing crude data, smoking seems to be significantly associated with stroke. However, after adjustment of some confounders, there was no effect of smoking and stroke. It might be that the participants in this study had similar average age between cases and controls (58.5 and 59.3, respectively). Young adults have thought that

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benefit of smoking is an engagement in the society and for reducing stress and for relaxation, whereas older adults may not need to relief stress using smoking [62]. Future study focusing in details of using smoking, such as doses, smoking behavior, and type might be beneficial for understanding the dose-response relationship of smoking and social contexts.

The present study found that individuals aged 60 years or older had a lower risk of ischemic stroke, contrasting with findings from previous studies [63-68]. Age is widely recognized as a major non-modifiable risk factor for stroke, with incidence increasing significantly with advancing age [63]. Older stroke patients generally experience higher mortality, greater morbidity, and poorer functional recovery than younger individuals [64]. Aging is considered the strongest risk factor for incident stroke, with the risk doubling every 10 years after age 55 [65]. Moreover, over 70% of all strokes, or approximately three in four cases, occur in individuals aged 65 years or older [4,65,66]. However, recent studies have reported a rising incidence of ischemic stroke in younger populations [5,12], particularly among individuals aged 20 to 54 years [12], while hemorrhagic stroke incidence has been observed to increase after age 45 [12], underscoring the complex relationship between age and stroke. Differences between the findings of this study and previous research may be attributable to variations in study populations, methodologies, and healthcare access, all of which could influence stroke risk across age groups. Further research is needed to explore potential protective factors in older populations and to refine the understanding of the evolving epidemiology of ischemic stroke across different age groups.

Table 3. Summaries of the conflicting results of smoking and age as risk factors for ischemic stroke

Finding from this study	Similar results	Conflicting results
Smoking as not a risk factor	Hanchaiphiboolkul *et al.* [14] Matsushita *et al.* [60] Funahashi *q.* [61]	GBD 2019 Stroke Collaborators. Global [2] Suwanwela *et al.* [3] Feigin *et al.* [5] Jarintanan *et al.* [11] WHO [57] Abdulsalam *et al.* [59]
Aged 60 year or older as a protective factor	NA	Zhang *et al.* [4] Feigin *et al.* [5] Boehme *et al.* [12] Techasuwanna *et al.* [20] Hunter *et al.* [63] Roy-O'Reilly *et al.* [64] Yousufuddin *et al.* [65] Kelly-Hayes [66] Akyea *et al.* [67] Asplund *et al.* [68]

NA: not available; GBD: Global Burden of Diseases; WHO: World Health Organization

However, several limitations should be noted. The reliance on self-reported data may have introduced recall bias, and stroke cases managed outside hospital settings were excluded, potentially introducing selection bias. Furthermore, the study did not account for stroke severity, which may influence the observed associations. Future research should aim to address these limitations by including more diverse samples and exploring causal relationships between identified risk factors and ischemic stroke. A qualitative study focusing on individuals with ischemic stroke may also provide deeper insights into additional risk factors.

Conclusion

Prolonged diabetes and sedentary occupations are significant contributors to ischemic stroke incidence. Moderate levels of self-care management, including adherence to medical appointments and medications, as well as lifestyle adjustments, may act as protective factors. Additionally, older age (≥60 years) appears to confer some protective effect. Community-based prevention programs, such as diabetes self-care management education, could empower individuals to adopt healthier lifestyles. Early intervention targeting at-risk populations, particularly those with prolonged diabetes or sedentary lifestyles, is essential to reduce the incidence of ischemic stroke.

Ethics approval

Ethical approval was obtained from the Sakon Nakhon Provincial Hospital Ethics Committee (COA026/2564) and Kasetsart University Chalermphrakiat Sakon Nakhon Province Campus Ethics Committee (Kucsc.HE-64-008). The study adhered to the ethical principles outlined in the Declaration of Helsinki. Permissions were also obtained from the director of Sakon Nakhon Provincial Hospital, the head nurse of the stroke unit, and the directors of the selected SHPHs. Prior to participation, all participants were provided with both oral and written information about the study. They signed informed consent forms voluntarily at the stroke unit (for cases) and at a designated room near the selected SHPHs (for controls). Participants were informed of their right to withdraw from the study at any time without consequences. Confidentiality was strictly maintained, and participant data were anonymized throughout the study.

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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