Established and Emerging Risk Factors of Stroke in Asian Countries: A Systematic Review

Phornanan Jarintanan[1], Nidhi Singh[1], Orasa Suthienkul [2], Pichit Boonkrong[3]

[1]Keerapat International School, Bangkok, Thailand

[2]Faculty of Public Health, Mahidol University, Bangkok,Thailand

[3]College of Biomedical Engineering, Rangsit University, Pathum Thani. Thailand

Correspondence: Pichit Boonkrong, 52/347 Muang-Ake Phaholyothin Rd., Lak-Hok, Muang, Pathumthani, Thailand, 12000. E-mail: pichit.bk@rsu.ac.th

Abstract

This paper aims to review the stroke situation regarding its risk factors in 16 Asian countries. From the stroke incidence in 2016 and 2019, it was found that the number of stroke cases per 100,000 people increased in 10 and decreased in 6 Asian countries. Low-middle income countries (LMICs) tend to have lower service and quality of healthcare compared to high-income countries (HICs), this significant difference in healthcare might be what causes the difference in stroke incidence. A systematic review was conducted for identifying and rating the frequency of stroke risk factors. Reviewing 15 selected papers, there are eight risk factors for stroke ranging from hypertension[15], diabetes[12], hypercholesterolemia/dyslipidemia[12], smoking[11], physical inactivity[7], obesity[7], air quality[2] to family history[1]. Age remains a significant risk factor for stroke, underscoring the importance of targeted preventive measures and healthcare interventions for older populations. China, as an example, has spread awareness and shown commitment to health issues and factors, adding institutions, and establishing a healthcare service for locations with more than 300,000. Studies have shown that women in LMICs are more likely to have a stroke at a young age compared to those in HICs, and could be influenced by cultural and social factors on women's health. Therefore, individuals could decrease stroke risk through healthy lifestyle choices, preventing hypertension, diabetes, and hypercholesterolemia/dyslipidemia. Lifestyle modifications including not smoking, maintaining a healthy diet, and exercising regularly should lower the risk of stroke occurrence in individuals. Simultaneously, national policies could lower stroke incidences by strengthening the stroke care ecosystem.

Keywords: Aging society, Asia, Public health, Risk factor, Stroke

Introduction

Stroke, a debilitating occurrence resulting from the disruption of cerebral blood supply or intracranial vessel rupture, causes profound brain damage and functional limitations. Commonly, the two main types of strokes include ischemic stroke (caused by blocked blood vessels), and hemorrhagic stroke (resulting from vessel rupture).[1] As a mounting cause of mortality, comprehending stroke risk factors is pivotal for formulating preventive measures, thereby enhancing public health, and mitigating the associated morbidity and mortality. Investigating and addressing these factors contribute to a strategic approach in minimizing the impact of strokes on individuals and society.

Asia has experienced an increase in stroke incidences, making it important to explore the factors contributing to this trend. Many researches in Asia showed that risk factors such as hypertension and lifestyle factors promote stroke occurrence.[3, 17] The variation in stroke incidence rates could be caused by the disparities of healthcare services between low-middle income countries and high-income countries. A notable trend surface as most low-middle income countries experience an increase in stroke incidences over the three-year period. Underscoring the need to explore the risk factors of stroke.

Regarding the stroke risk factors, there are currently 10 known risk factors worldwide, being hypertension, diabetes, high cholesterol, smoking, obesity, physical inactivity, excessive alcohol consumption, age, family history, and other medical conditions.[4, 9, 12] Generally, there are 4 main stroke contributors said by professionals, being hypertension, diabetes, high cholesterol, and smoking. Particularly for Asian countries, this paper gathers evidence for stroke risk factors using systematic review. Understanding the risk factors associated with stroke, people have to recognize the importance of maintaining a healthy lifestyle, managing chronic conditions (e.g., hypertension, diabetes), and adopting preventive measures toward reducing their risk of stroke.

From the aforementioned issues, it is essential to get a better understanding of associated risk factors of stroke toward the prevention. As the prevalence of strokes is frequently observed within the aging demographic, a discernible upward trajectory is evident in numerous Asian nations. Consequently, this investigation specifically directs its attention towards the examination of correlated risk factors prevalent among Asian countries. Subsequently, the guideline of systematic reviews of stroke risk factors was designed and illustrated through PRISMA principle.[43] Accordingly, the risk factors of stroke have been gathered and summarized. The discussion and conclusion are finally given.

While extant literature presents a variety of perspectives on stroke risk factors, this systematic review aims to consolidate predominant risk factors across diverse studies conducted in Asian countries. By synthesizing findings from a multitude of researches, this study aims to offer a comprehensive assessment of the key determinants contributing to stroke incidence in the Asian context.

Methodology

This study aims to explore the stroke risk factors within the Asian context, with a specific focus on prevalent contributors such as hypertension, diabetes, high cholesterol, and smoking. By doing so, it seeks to underscore the critical importance of comprehending these factors in order to effectively mitigate the increasing burden of stroke within the region. The systematic review was employed as the main research tool. The PRISMA diagram for eligibility criteria regarding stroke risk factors includes a detailed flowchart outlining the study selection process as shown in Figure 1. Focusing on the stroke incidences in Asian countries, the process of undertaking the systematics reviews of stroke risk factors and individual concerns is presented in the following steps:
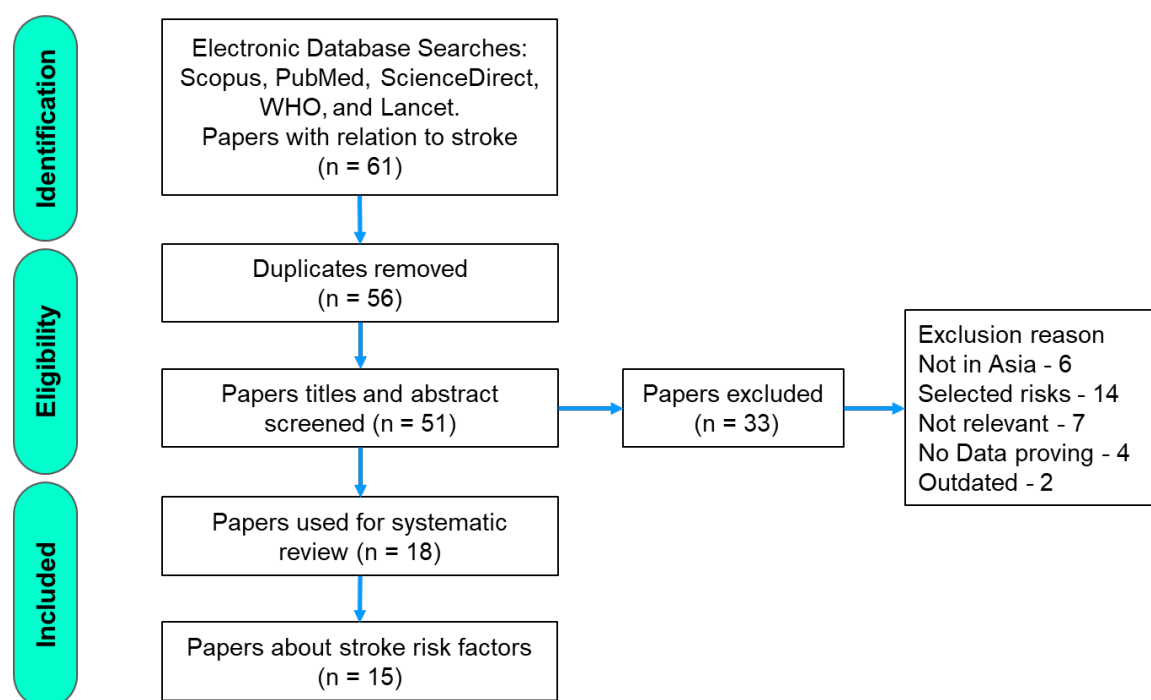

Figure 1. PRISMA diagram presenting eligibility criteria for the study of stroke risk factors

Step 1: Check the existing reviews – To start conducting a systematic review, the eligibility criteria, relevant databases, and search strategy were initially scanned from the existing reviews. It was found that the numbers of stroke cases in many countries are continuously increasing over time and it poses a risk to decline an individuals' health.

Step 2: Identify research question – The existing reviews mentioned about stroke burden, mortality and risk factors. The research questions include

1) What are some stroke risk factors in which Asian countries face?

2) How does each factor have the impact on stroke incidences?

3) How would individuals be aware of stroke risk factors and strategies to prevent stroke occurrence?

Step 3: Define inclusion and exclusion criteria – To ensure the reliability and validity of the review, specific eligibility criteria are applied to select studies for inclusion. In Figure 2, the flow chart shows the eligibility criteria processing the filtering and selection of papers which are used in this systematic review. Factors such as duplicates, not in Asia, selected risks, not relevant, no data, and outdated were screened in each paper to determine its exclusion. From there, 18 papers were selected, with 15 of them on the topic of stroke risk factors, which is used in Figure 3.

Step 4: Search for relevant studies – Keywords such as "Stroke", "Stroke Incidence", "Risk Factors", "Stroke in Asia" and "Epidemiology" were used in this systematic review to find relevant studies. A comprehensive search was made in databases such as Scopus, PubMed, and ScienceDirect. In our study, we leveraged The Lancet as a reputable source for accessing original research and review articles pertaining to stroke epidemiology and interventions. Additionally, we utilized the World Health Organization (WHO) platform to gather essential public health data and guidelines relevant to our investigation into stroke risk factors. This search process has allowed relevant studies to be gathered, containing valuable information for this systematic review.

Step 5: Include studies based on pre-defined criteria – The abstracts, conclusion, along with relevant parts of each identified paper were reviewed to determine the suitability for inclusion in this systematic review. Differentiating relevant studies from those which are not, and removing duplicates found within the search ensuring unique information.

955

Step 6: Extract information from included studies – The incidence rates of Asian countries were gathered from the WHO of the years 2016 and 2019. To capture current trends and patterns in stroke incidence, we narrowly focused on the years 2016 to 2019. This allowed us to stay within the parameters of our study and provide an updated analysis of the most relevant data that was available during the study period. In addition, the frequencies of stroke risk factors were examined from selected papers. Among the known risk factors, eight key factors were found to have an association with stroke occurrence in Asian countries: hypertension, diabetes, hypercholesterolemia/dyslipidemia, smoking, physical inactivity, obesity, air quality, and family history.

Step 7: Combine the useful information – The observed increase in incidence of stroke across Asian countries underlines the importance of stroke prevention. To address this issue, there were 8 known risk factors found in Asia, ranging from those known to be the biggest to the least contributors of stroke occurrence. From there, the 8 stroke risk factors were researched on how their mechanisms contribute to stroke.

Step 8: Discuss and concluded overall findings - The eight known risk factors have shown a connection to stroke occurrence through many different mechanisms. Understanding the underlying factors of stroke could help contribute to strategies on how to prevent stroke occurrence. To properly decrease stroke incidences in Asia, promoting health services, and individual health literacy to spread awareness of stroke risk factors are crucial to have a healthier society.

Results

Variantion in Stroke Incidence across 16 Asian Nations

Statistically, Figure 2. shows and compares the stroke incidence per 100,000 people from 16 Asian countries, especially in 2016 and 2019.[2, 3] Over three years, there was an increasing stroke incidence trend in 10 Asian countries including Sri Lanka, Vietnam, Indonesia, Philippines, Syria, Turkey, Japan, Uzbekistan, Iraq, and Pakistan. On the other hand, there was a decrease trend in 6 Asian countries including, China, South Korea, Taiwan, Thailand, India, and Afghanistan.
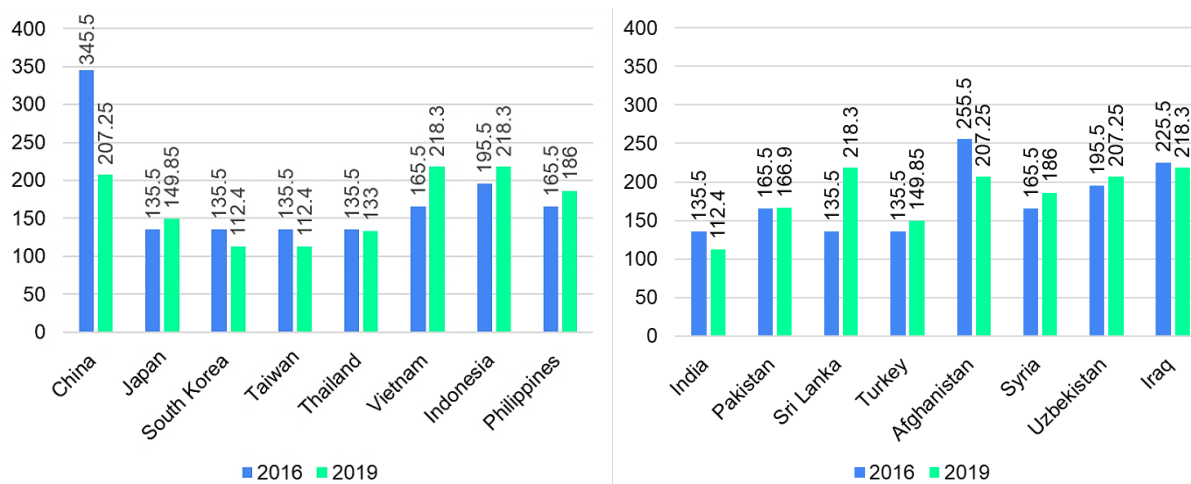
Figure 2. Stroke incidence per 100,000 people from 16 Asian countries

Notably, China exhibited the most substantial reduction among the 16 Asian countries, transitioning from an approximate 345.5 incidences in 2016 to 207.25 incidences in 2019. Similarly, the number of stroke incidences in Afghanistan significantly decreased from around 255.5 in 2016 to 207.25 in 2019.[2] In contrast, Vietnam and Sri Lanka showed a notable increase of stroke incidences within the three years, from 165.5 to 218.3 and 135.5 to 218.3, respectively.[3] However, there was a slight variation in stroke incidences among other countries.

Risk Factors for Stroke

Following the PRISMA framework given in the previous section to a comprehensive understanding of stroke etiology, the systematic review was conducted to evaluate and synthesize the existing evidence on stroke risk factors. Summarizing data from different studies on risk factors for stroke, Figure 3. presents the frequency of risk factors found in Asian countries from 15 literatures.[3-17] There are 8 risk factors ranging from highest to lowest frequencies of appearance: hypertension (15), diabetes (12), hypercholesterolemia / dyslipidemia (12), smoking (11), physical inactivity (7), obesity (7), air quality (2) and family history (1).
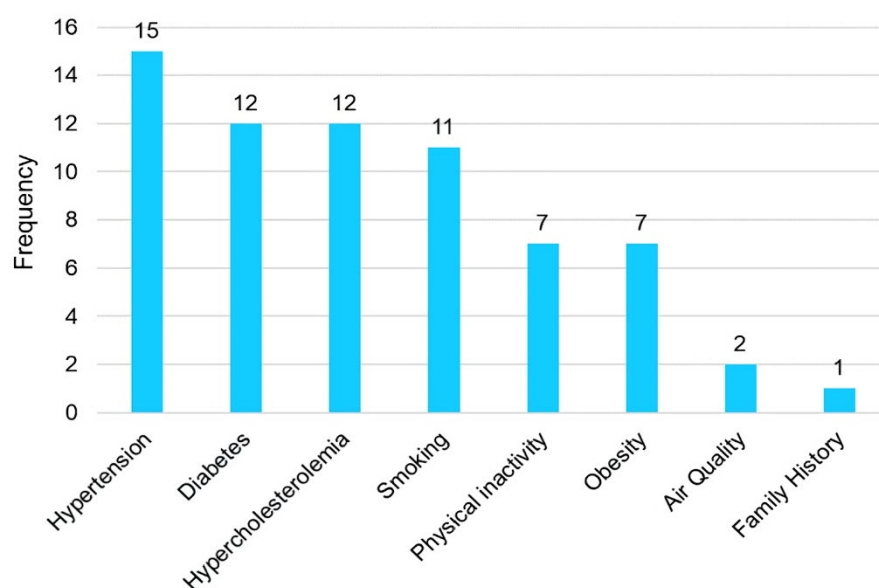
Figure 3. Frequencies of stroke risk factors mentioned in 15 literatures

1. Hypertension: Hypertension, defined by elevated blood pressure (BP ≥140/90 mmHg), is prevalent in individuals with heart disease, heart attacks, and strokes.[20] It emerged as the most common risk factor in 15 stroke research papers. Hypertension damages blood vessels, particularly arteries. In normal instances, arteries are flexible, strong, and have a smooth inner lining that helps blood flow to organs and tissues delivering vital nutrients and oxygen. However, high blood pressure could impair the arterial lining causing plaques which reduces elasticity and narrows blood vessels, restricting blood flow.[19] Unhealthy artery walls could develop aneurysms, which, if ruptured, can lead to internal bleeding. Strokes happen when the brain does not have sufficient oxygen and nutrients, killing the brain cells.[18, 20] Hypertension leads to stroke through many mechanisms, including alterations in intracerebral artery endothelium and smooth muscle function, increased permeability of the blood–brain barrier, formation of local blood clots, ischemic lesions, lacunar infarcts from focal narrowing, and a higher chance of intracerebral hemorrhages.[18] However, the elderly with hypertension tends to have higher risk of stroke.

2. Diabetes: Diabetes leads to the development of atherosclerosis, accumulation of plaques and fatty materials in the arteries. This condition damages the inner lining of blood vessels making them vulnerable to clot formation resulting in reduced blood flow to the brain,

risking a stroke happening. Furthermore, diabetes could also lead to development of cerebral small vessel diseases (CSVD), affecting the blood vessels in the brain and increasing the chances of stroke.[21, 22] Hyperglycemia or elevated blood sugar levels damages blood vessels and causes inflammation, leading to atherosclerosis and other vascular complications. Adding on, hyperglycemia can affect blood viscosity and clotting factors increasing the risk of plaque formation and blocking blood flow to the brain.[21]

3. **Hypercholesterolemia/ Dyslipidemia**: Dyslipidemia, abnormal levels of lipids (cholesterol and triglycerides) in blood, increases the risk of stroke from its plaque formations and atherosclerosis.[23, 24, 25] This condition could impair endothelial function, which is where the blood vessel inner lining regulates blood flow and maintains vascular health. The production of nitric oxide which is a molecule crucial for dilating blood vessels and regulating blood pressure would be disrupted. Diminishing sensitivity of the baroreflex, a mechanism in which baroreceptors detect changes in blood pressure and trigger the parasympathetic nervous system to counteract these changes. Reducing the sensitivity leads to the development of hypertension.[21, 25, 26] Additionally, dyslipidemia can decrease the distensibility or elasticity of arteries, impairing their ability to expand according to blood flow and resulting in elevated blood pressure.[23]

4. **Smoking**: Smoking can contribute to the development of atherosclerosis, or a buildup of plaques in the arteries. The plaques narrow down and harden arteries, blocking blood flow to the brain resulting in an increased risk of stroke.[27] One of the cigarettes main components, Nicotine, stimulates the release of catecholamines including adrenaline, raising heart rate and blood pressure (BP).[28] Increase of workload on the heart with the increase of BP causes strain on arteries, potentially leading to blood clots and increasing the risk of ischemic or hemorrhagic stroke. Smoking-induced vasoconstriction or the narrowing of blood vessels impairs blood flow to the brain. This affects the body's natural ability to break down blood clots. This disruption in endogenous fibrinolysis delays the delivery of plasminogen activators to the clot, hindering the breakdown of blood clots and leading to inefficiency which can contribute to stroke.[27, 29]

5. **Obesity and Physical Inactivity**: Obesity, with a BMI of 30 or higher, is linked to hypertension through various mechanisms, including sympathetic nervous system activation, increased renal sodium reabsorption, and activation of the renin-angiotensin system.[30] These

mechanisms disrupt pressure regulation, leading to inadequate blood pressure control. Moreover, obesity causes volume expansion by increasing sodium and water retention in the kidneys, straining the cardiovascular system and increasing blood pressure.[30, 33] Individuals with a BMI greater than 35 kg/m2 are 93 times more likely to have diabetes.[34] Excess adipose tissue in the body can lead to insulin resistance, which contributes to the development of type 2 diabetes, a stroke risk factor.[34] Insulin resistance happens when the body's cells are unable to respond effectively to insulin, a hormone responsible for regulating blood sugar levels.[21] As a result, the pancreas produces more insulin to compensate and maintain normal blood sugar levels, which puts strain on the pancreas. Regular physical activity plays a critical role in reducing blood pressure and the risk of hypertension.[32] Exercise lowers resting blood pressure and improves blood vessel dilation.[31] Additionally, declining physical activity levels among the elderly contribute to hypertension, while engaging in physical activity also helps reduce obesity, a shared risk factor for hypertension and stroke.[32]

6. Air Quality and Family History: Air Quality is a relevant stroke risk, with particulate matter (PM2.5) and gaseous pollutants, such as, sulfur dioxide (SO2), ozone (O3), carbon monoxide (CO), and nitrogen dioxide (NO2) being capable of infiltrating lung alveoli and brain cells.[4] Family history is a partially understood factor, but studies indicate that if siblings have experienced a stroke, the likelihood of stroke occurrence is also increased. The shared environmental factors in the household of siblings contribute to the presence of common stroke risk factors among siblings.[35]

Discussion

The synthesis of data from 15 literatures provided valuable insights into the frequencies of stroke risk factors across Asian countries. The analysis revealed hypertension, diabetes, hypercholesterolemia/dyslipidemia, and smoking as the most prevalent risk factors, underscoring the complex nature of stroke causation. Notably, disparities in the stroke incidences observed across different countries highlight the complex interplay of socioeconomic, cultural, and healthcare factors influencing stroke risk. These variations underscore the importance of prevention and management strategies that address the specific risk factor profiles of diverse populations. Moreover, the identification of regional disparities in

risk factor prevalence suggests the need for targeted interventions aimed at addressing underlying determinants such as access to healthcare, health literacy, and lifestyle factors.

China, as an example, has established Stroke Centers, Training Programs, Integration of Chinese and Western Medicine, Health Literacy Improvement, National Initiatives, Policy and Legislation, Infrastructure Development, Public Awareness Campaigns, and Collaboration with International Organizations. Through these prevention and management strategies, they were able to reduce the incidence rate of stroke from 2016 to 2019. Their objectives include establishing stroke centers in locations and prefectures with a population greater than 300,000 providing thrombolytic technology for stroke treatment. They also offer training programs for stroke treatment technology and stroke first aid personnel, along with improving health literacy to enhance understanding of stroke prevention and treatment. Infrastructure investment includes promoting physical activity through sports facilities and educating people about the benefits of exercise through workplace programs and media campaigns.[37, 38]

Lower to middle income countries have a trend for stroke incidences increasing between the three-year gap. The main difference between low-middle income countries (LMICs) and high-income countries (HICs) are the differences in their healthcare services, quality, and access. LMICs lack the proper diagnostic techniques, which leads to underdiagnosis and underreporting of stroke cases, resulting in limited awareness of stroke risk factors.[36, 40] Adding on to that, studies have shown that women in LMICs are more likely to have a stroke at young age compared to those in HICs (China, Japan, South Korea, Taiwan and Iraq), possibly highlighting the difference in healthcare access, healthcare services, and influence of cultural and social factors on women's health.[40] Nevertheless, it is a challenge for both LMICs and HICs to deal with the stroke incidences in aging population which is growing constantly and is vulnerable to stroke.

Limited health literacy has been associated with negative health outcomes, which could be poor health status, increased hospitalizations, and higher healthcare costs. Individuals who lack health literacy may struggle to understand health-related materials such as medication instructions or health education materials, potentially leading to medication errors and adverse outcomes. A study in Malaysia conducted in a hospital showed that the knowledge regarding health literacy was low among healthcare professionals. With attitude scores being relatively high, although there were still some negative attitudes towards health literacy. Common constraints found in the study was the lack of time, training, and resources, thus leading to not

optimal health literacy. Indonesians were more likely to smoke, while Thais were more likely to drink.[41, 42] This demonstrates the behaviors of individuals in Asian countries, with some not knowing the factors of which could cause heavy burden and diseases. Improving health literacy is an important goal for a healthier society, with strategies including improved health education, patient communication, and health-related materials.

Developing successful prevention methods requires a thorough understanding of individual concerns regarding stroke risk factors. A person's risk of stroke is mostly determined by their lifestyle decisions and personal habits. A number of risk factors for stroke, including obesity, diabetes, and hypertension, can be brought on by smoking, physical inactivity, and poor dietary choices. Furthermore, one of the most important factors in preventing stroke is health literacy, or the capacity to comprehend and apply health information. Low health literacy can make it difficult for a person to properly manage their risk factors, follow preventive guidelines, or identify the warning signs and symptoms of a stroke. Consequently, lowering the burden of stroke requires interventions that enhance health literacy, encourage healthier lifestyle choices, and raise people's knowledge of their personal risk factors for stroke. Techniques like focused health education campaigns, neighborhood outreach programs, and the distribution of easily comprehensible health information can enable people to take charge of their health and lower their risk of stroke.

Although this study offers insightful information about stroke risk factors in Asian nations, there are a few limitations that should be taken into account. First off, relying solely on publicly accessible data sources could lead differences in data gathering techniques and possible underreporting, especially in areas with limited healthcare systems. Additionally, the systematic review approach, while rigorous, may inadvertently exclude relevant studies not indexed in selected databases or published in languages other than English, limiting the inclusivity of our analysis. To provide a more thorough understanding of stroke epidemiology and to inspire more focused intervention techniques, future research efforts ought to tackle these constraints.

Conclusoin

Several Asian countries have an increased incidence for stroke, especially those in low to middle income countries (LMICs), needing effective prevention strategies. Some countries have however been able to stabilize or decrease their stroke incidence rate over the three-year period, suggesting that it is possible to prevent stroke incidences. Many risk factors contribute to strokes, such as hypertension, diabetes, dyslipidemia, and smoking. LMICs have many

challenges to decrease their incidence rate due to the lack of healthcare services and access. Looking at the difference in healthcare between countries is important to reduce stroke incidences and improve health in LMICs. Addressing these differences in public health capacities is crucial for developing tailored strategies that account for the unique challenges faced by both LMICs and HICs in mitigating the burden of stroke within their aging populations. As stroke is a medical emergency that requires prompt intervention for optimal outcomes, health literacy plays a crucial role in stroke prevention, recognition, and management. Improving health literacy for stroke intervention, awareness of risk factors, recognition of symptoms, medication adherence, clear communication, and accessible resources should be promoted for ultimately reducing the burden of stroke.

Author Contributions

Jarintanan and Signh, screened and selected the relevant papers based on the eligibility criteria in Figure 2. Suthienkul and Boonkrong designed and supervised the study and structure of manuscript. Jarintanan and Boonkrong analyzed, synthesized and summarized the qualitative content. All authors read and approved the manuscript prior to submission for publication.

Source of Funding

There is no funding for this study.

Conflicts of Interest

There is no conflict of interest.

References

1.   Centers for Disease Control and Prevention, Spain. About Stroke. Available from: www.cdc.gov/stroke/about.htm#Ischemic, accessed 15 June, 2023.

2.   GBD 2016 Stroke Collaborate. Global, regional, and national burden of stroke, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019; 18(5): 439-58.

3.   GBD 2019 Stroke Collaborate. Global, regional, and national burden of stroke and its risk factors, 19902019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021; 20(5): 391-02.

4.   Turana Y, Tengkawan J, Chia YC, Nathaniel M, Wang JG, Sukonthasarn A, et al; HOPE Asia Network. Hypertension and stroke in Asia: A comprehensive review from HOPE Asia. J Clin Hypertens (Greenwich) 2021; 23(3) : 513-21. DOI: 10.1111/jch.14099

5.   Venketasubramanian N, Yoon BW, Pandian J, Navarro JC. Stroke Epidemiology in South, East, and South-East Asia: A Review. J Stroke 2017; 19(3): 286-94. DOI: 10.5853/jos.2017.00234

6.   Kim YD, Jung YH, Saposnik G. Traditional Risk Factors for Stroke in East Asia. J Stroke 2016; 18(3): 273-85. DOI: 10.5853/jos.2016.00885

7.   Venketasubramanian N. The epidemiology of Stroke in ASEAN countries – A review. Neurol J Southeast Asia 1998; 3(2); 105-18.

8.   Hata J, Kiyohara Y. Epidemiology of stroke and coronary artery disease in Asia. Circ J 2013; 77(8): 1923-32. DOI: 10.1253/circj.cj-13-0786

9.   Xia X, Yue W, Chao B, Li M, Cao L, Wang L, et al. Prevalence and risk factors of stroke in the elderly in Northern China: National Stroke Screening Survey. J Neurol 2019; 266(6): 1449-58. DOI: 10.1007/s00415019-09281-5

10.   Sharma VK, Tsivgoulis G, Teoh HL, Ong BK, Chan BP. Stroke risk factors and outcomes among various Asian ethnic groups in Singapore. J Stroke Cerebrovasc Dis 2012; 21(4): 299-04. DOI: 10.1016/j.jstrokecerebrovasdis.2010.08.010

11.   Rajeev Ojha, Dongya Huang, Hedi An, Lian Zuo, Wenxia Zhu. Young ischemic stroke in South Asia: A review. Journal of Stroke and Cerebrovascular Diseases 2014; 23(7): 1753-159.

12.   Chin YY, Sakinah H, Aryati A, Hassan BM. Prevalence, risk factors and secondary prevention of stroke recurrence in eight countries from south, east and southeast asia: a scoping review. Med J Malaysia 2018; 73(2): 90-99.

13.   Lin X, Wang H, Rong X, Huang R, Peng Y. Exploring stroke risk and prevention in China: insights from an outlier. Aging (Albany NY) 2021; 13(11): 15659-73. DOI: 10.18632/aging.203096

14.   Qi W, Ma J, Guan T, Zhao D, Abu-Hanna A, Schut M, et al. Risk Factors for Incident Stroke and Its Subtypes in China: A Prospective Study. J Am Heart Assoc 2020; 9(21): 1-19. DOI: 10.1161/JAHA.120.016352

15.   Venketasubramanian N, Tan LC, Sahadevan S, Chin JJ, Krishnamoorthy ES, Hong CY, Saw SM. Prevalence of stroke among Chinese, Malay, and Indian Singaporeans: a community-based tri-racial cross-sectional survey. Stroke 2005; 36(3): 551-6. DOI: 10.1161/01.STR.0000155687.18818.13

16.   Shahbandi A, Shobeiri P, Azadnajafabad S, Saeedi Moghaddam S, Sharifnejad Tehrani Y, Ebrahimi N, et al. Burden of stroke in North Africa and Middle East, 1990 to 2019: a systematic analysis for the global burden of disease study 2019. BMC Neurol 2022; 22(1): 1-11. DOI: 10.1186/s12883-022-02793-0

17.   El-Hajj M, Salameh P, Rachidi S, Hosseini H. The epidemiology of stroke in the Middle East. Eur Stroke J 2016;1(3):180-98. DOI: 10.1177/2396987316654338

18.   Johansson BB. Hypertension mechanisms causing stroke. Clin Exp Pharmacol Physiol 1999; 26(7): 563-5. DOI: 10.1046/j.1440-1681.1999.03081.x

19.   American Heart Association, USA. How High Blood Pressure Can Lead to Stroke. Available from: www.heart.org/en/health-topics/high-blood-pressure/health-threats-from-high-blood-pressure/how-highblood-pressure-can-lead-to-stroke, accessed 25 June, 2023.

20.   Stroke Association, England and Wales. High Blood Pressure. Available from: www.stroke.org.uk/whatis-stroke/are-you-at-risk-of-stroke/high-blood-pressure, accessed 25 June, 2023.

21.   Chen R, Ovbiagele B, Feng W. Diabetes and Stroke: Epidemiology, Pathophysiology, Pharmaceuticals and Outcomes. Am J Med Sci 2016; 351(4): 380-6. DOI: 10.1016/j.amjms.2016.01.011

22.   Stroke Association, England and Wales. Diabetes. Available from: www.stroke.org.uk/what-is-stroke/areyou-at-risk-of-stroke/diabetes, accessed 26 June, 2023.

23.   Khan RSU, Nawaz M, Khan S, Raza HA, Nazir T, Anwar MS, et al. Prevalence of Dyslipidemia in Ischemic Stroke Patients: A Single-Center Prospective Study From Pakistan. Cureus 2022;14(6):1-6. DOI: 10.7759/cureus.25880

24.   Stroke Association, England and Wales. High Cholesterol. Available from: www.stroke.org.uk/what-isstroke/are-you-at-risk-of-stroke/high-cholesterol#:~:text=on%20your%20health.,Why%20does%20high%20cholesterol%20increase%20your%20risk%20of%20stroke%3F,of%20a%20blood%20clot%20developing, accessed 29 June, 2023.

25.   Otsuka T, Takada H, Nishiyama Y, Kodani E, Saiki Y, Kato K, et al. Dyslipidemia and the Risk of Developing Hypertension in a Working-Age Male Population. J Am Heart Assoc 2016; 5(3): 1-9. DOI: 10.1161/JAHA.115.003053

26.   Perrault LP, Mahlberg F, Breugnot C, Bidouard J-P, Villeneuve N, Vilaine J-P, et al. Hypercholesterolemia increases coronary endothelial dysfunction, lipid content, and accelerated atherosclerosis after heart transplantation. Arterioscler Thromb Vasc Biol 2000; 20(3): 728–36.

27.   Shah RS, Cole JW. Smoking and stroke: the more you smoke the more you stroke. Expert Rev Cardiovasc Ther 2010; 8(7): 917–32. DOI: 10.1586/erc.10.56

28.   Lee J, Cooke JP. The role of nicotine in the pathogenesis of atherosclerosis. Atherosclerosis 2011; 215(2): 281-3. DOI: 10.1016/j.atherosclerosis.2011.01.003

29.   Gue YX, Gorog DA. Importance of Endogenous Fibrinolysis in Platelet Thrombus Formation. Int J Mol Sci 2017; 18(9): 1-15. DOI: 10.3390/ijms18091850

30.   Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. Exp Ther Med 2016; 12(4): 2395-99. DOI: 10.3892/etm.2016.3667

31.   Mayo Clinic, USA. Exercise: A drug-free approach to lowering high blood pressure. Mayo clinic. 2021. Available from: https://www.mayoclinic.org/diseases-conditions/high-blood-pressure/in-depth/high-bloodpressure/art-20045206#:~:text=Regular%20exercise%20makes%20the%20heart,This%20lowers%20blood%20pressure, accessed 1 July, 2023.

32.   Hayes P, Ferrara A, Keating A, McKnight K, O'Regan A. Physical activity and hypertension. Rev Cardiovasc Med 2022;23(9): 1-13.

33.   Barnes AS. The epidemic of obesity and diabetes: trends and treatments. Tex Heart Inst J 2011; 38(2): 1424.

34.   Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity? Curr Opin Endocrinol Diabetes Obes 2012; 19(2): 81-7. DOI: 10.1097/MED.0b013e3283514e13

35.   Choi JC, Lee JS, Kang SY, Kang JH, Bae JM. Family history and risk for ischemic stroke: sibling history is more strongly correlated with the disease than parental history. J Neurol Sci 2009; 284(1-2): 29-32. DOI: 10.1016/j.jns.2009.03.015

36.   Yan LL, Li C, Chen J, Miranda JJ, Luo R, Bettger J, et al. Prevention, management, and rehabilitation of stroke in low- and middle-income countries. eNeurologicalSci 2016; 2: 21-30. DOI: 10.1016/j.ensci.2016.02.011

37.   Chao BH, Tu WJ, Wang LD; Stroke Prevention Project Committee, National Health Commission of the People's Republic of China. Initial establishment of a stroke management model in China: 10 years (20112020) of Stroke Prevention Project Committee, National Health Commission. Chin Med J (Engl) 2021; 134(20): 2418-20. DOI: 10.1097/CM9.0000000000001856

38.   Chen S, Ma J, Hong J, Chen C, Yang Y, Yang Z, et al. A public health milestone: China publishes new Physical Activity and Sedentary Behaviour Guidelines. Journal of Activity, Sedentary and Sleep Behaviors 2022; 1(1): 1-6.

39.   Rahbar MH, Medrano M, Diaz-Garelli F, Gonzalez Villaman C, Saroukhani S, Kim S, et al. Younger age of stroke in low-middle income countries is related to healthcare access and quality. Ann Clin Transl Neurol 2022; 9(3): 415-27. DOI: 10.1002/acn3.51507

40.   Rajah R, Hassali MAA, Murugiah MK. A systematic review of the prevalence of limited health literacy in Southeast Asian countries. Public Health 2019; 167: 8–15.

41.   Rajah R, Hassali MA, Lim CJ. Health Literacy-Related Knowledge, Attitude, and Perceived Barriers: A Cross-sectional Study among Physicians, Pharmacists, and Nurses in Public Hospitals of Penang, Malaysia. Front Public Health 2017; 5: 1-6.

42.   Institute for Population and Social Research; Mahidol University. Health Behaviors. In Andrew Jonathan Hall: Thai Health 2015: Health Frauds. 1st. Nonthaburi: Ban Tai Soi Design; 2015. 18-20. Available from: https://www.hiso.or.th/hiso/picture/reportHealth/ThaiHealth2015/eng2015_7.pdf, accessed 5 June, 2023.

43.   Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71. DOI: 10.1136/bmj.n71