Chapter

Regional Burden and Region-Specific Stroke Risk Factors in Lower and Middle-Income Countries

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Abstract

In this chapter, we outline the trends in incidence, prevalence, and the burden of stroke in developing countries (lower- and middle-income countries—LMICs) over recent decades. We highlight the changes in risk factors and types of stroke (ischemic vs. hemorrhagic) in LMICs, comparing them to high-income countries (HIC). We will also use statistics from specific countries as case examples. The lack of resources and its impact on stroke management will be discussed. The authors include stroke physicians who are part of the World Stroke Organization Future Leaders Program and have carried out quality improvement projects in Sub-Saharan Africa, among other initiatives.

Keywords: stroke, intracerebral hemorrhage, lower and middle-income countries, epidemiology, incidence, prevalence, DALYs, burden, risk factors, developing countries

1. Introduction

Stroke is among the top 10 most common causes of death globally, being the third after ischemic heart disease and COVID-19, and accounting for approximately 10% of deaths worldwide [1]. Stroke is the leading cause of death in upper-middle-income countries (UMIC), the second leading cause of death in low-income countries (LIC), and the third leading cause of death in lower-middle-income countries (LMIC) [1]. Low- and middle-income countries constitute 89% of the global stroke burden as of 2025 [2]. Therefore, understanding the epidemiology of stroke in low- and middle-income countries is crucial in planning for developing strategies to reduce the global stroke burden. In this chapter, we explore the epidemiology of stroke in

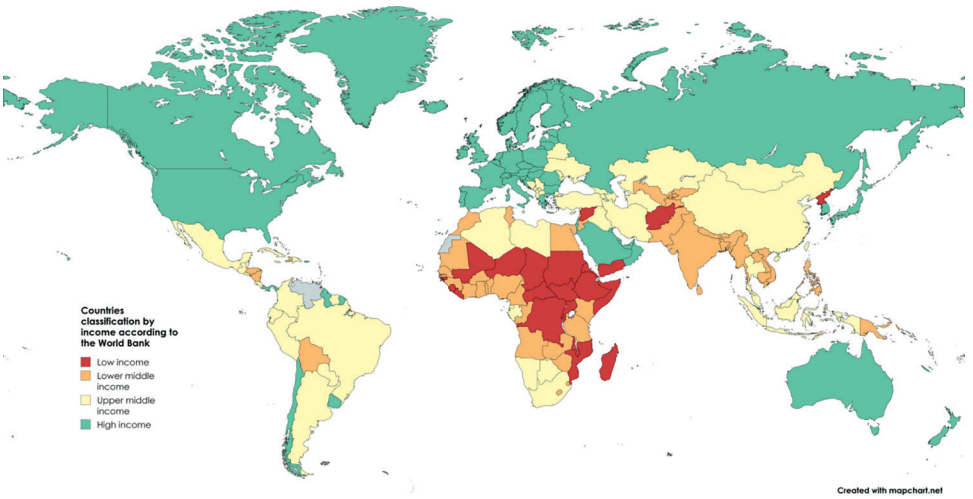

Figure 1.
Countries are classified by income according to the World Bank.

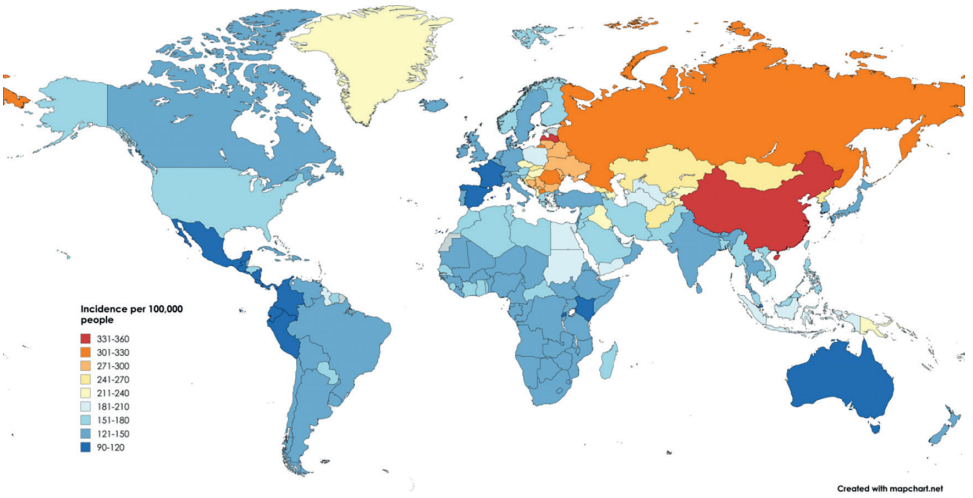

Figure 2.
Incidence of stroke per 100,000 population. Source: Adapted from Ref. [3].

a non-exhaustive list of low- and middle-income countries. A general overview of country classifications by income is provided in **Figure 1**, while **Figure 2** depicts the incidence of stroke worldwide.

2. Africa

2.1 Background

Africa is the second-largest and second most populous continent, consisting of 54 countries, an area of around 30 million km^2, and a population of around 1.2

billion. It is estimated to reach 2.2 billion for sub-Saharan Africa (SSA) by the year 2054 [4]. Africa's population is the youngest among the continents, with a median age of 19.7. Four African countries are densely populated with more than 100 million: Nigeria (>232 million), Ethiopia (>132 million), Egypt (>116 million), and the Democratic Republic of the Congo (>109 million), while the least populous country is Seychelles, with a population of around 130,000 [4].

Geographically, historically, religiously, and ecosystem, Africa is divided into two different regions, namely North Africa (NA), composed of five countries, and SSA, comprising the rest of the African countries [5]. NA countries are mostly inhabited by Arabic/Semitic as well as Berber ethnicity, while SSA has a diversity of ethnicities, with the majority classified as Niger-Congo and Nilo-Saharan [6, 7]. The World Bank classifies most African countries as low-income countries (LIC) and middle-income countries, except for Seychelles. These include seven upper-middle-income countries (UMIC), 22 lower-middle-income countries (LMIC), and 24 low-income countries (LIC) [5].

2.2 Burden of stroke

Africa's Daily Adjusted Life Years (DALYs) following stroke is around 17.3 million [2]. Although much lower than Asia's, the actual numbers might be higher, especially since the epidemiology of Africa is changing owing to socio-demographic changes with many countries shifting to urbanization and lifestyle changes with changes in modifiable and non-modifiable vascular risk factors [8, 9].

There is still a scarcity of epidemiological data in many African countries owing to deficiencies in healthcare services, including a shortage of physicians and the absence of health facilities managing stroke, such as stroke units and centers [9, 10]. In a systematic review, it was found that epidemiological studies for stroke in Africa are mostly hospital-based studies and may not represent the actual incidence or prevalence, as patients with minor strokes or rapidly fatal strokes may not get hospitalized [9, 11]. Despite this bias, stroke accounts for 65% of different neurological disorders affecting hospitalized adults in Nigeria [12]. A rise in stroke admissions was reported in Tanzanian hospital-based studies (an increase from 23 to 86 per 100,000 over 27 years) as well as in Ghanaian studies (from 50 to 622 per 100,000 over 33 years) [13]. Such an increase in admission might highlight the increasing burden of stroke, more awareness of stroke, and the demographic shift from rural to urban in many African countries [9, 10, 14]. Other hospital-based studies found incidence ranging from 31 per 100,000 in Zimbabwe to 149 per 100,000 in Mozambique [15, 16]. Community studies in upper Egypt found an incidence of 181 and 250 per 100,000 [17, 18], whilst the incidence was 25 per 100,000 in Nigeria and between 108 and 316 per 100,000 in Tanzania [19, 20].

The prevalence of stroke varies greatly in different countries. The crude prevalence rate was as low as 15 per 100,000 population in rural Ethiopia [21], 42 in Tunisia [22], 114 in Nigeria [23], 243 in South Africa [24], 284 in Morocco [25], 460, and 1156 in two studies in Benin [26, 27], 922 and 963 in upper Egypt [28, 29]; and 1230 and 1460 along the Niger Delta region in Nigeria [30, 31]. The highest prevalence was 2300 per 100,000 population in Tanzania [32].

The incidence and prevalence for all kinds of strokes are on the rise compared to the rest of the world, and this could be explained based on demographic changes as in the case of increased longevity secondary to better control of communicable diseases and shifting in the community from rural to urban with its associated stress, modifiable vascular risk factors as sedentary lifestyle, food rich in carbohydrates and

fats with its associated dyslipidemia, hypertension, and diabetes [33, 34]. Moreover, if the study conducted in Tanzania, Hai as a rural area and Dar Es Salaam as an urban area, is generalized, according to Akinyemi et al., then one in six Africans will suffer a stroke every minute [34].

2.3 Burden of stroke in Africa (mortality, and fatality)

Stroke mortality in Africa is one of the highest in the world, ranging between 5.5 and 11% [35–37], and in some studies, the one-month case fatality exceeds 45% and might reach 83.3% [38]. This could be attributed to deficiencies in the proper implementation of stroke services in many African countries. There is a shortage of neurologists, and in many instances, general practitioners or even traditional and complementary medicine practitioners are first line in treating stroke [10, 39]. In addition, other shortfalls include delay in presentation, lack of reperfusion for ischemic stroke or surgical intervention for intracerebral hemorrhage, inadequate management of stroke-related complications such as pneumonia or sepsis, and lack of access to physiotherapy [10, 34].

2.4 Stroke subtype

Globally, rates of ischemic strokes (62.4%) are higher compared to intracerebral hemorrhage (27.9%) and subarachnoid hemorrhage (9.7%) [40]. This is also the case in Africa, including SSA, irrespective of age [9, 41–46]. In the INTERSTROKE study, hemorrhagic strokes accounted for 9% of cases seen in high-income countries (HIC) vs. 34% in African countries [47]. This reflects that a greater burden of hypertension is in Africa since it has been shown that the proportion of hemorrhagic strokes in a population correlates with the burden and severity of uncontrolled hypertension [47, 48].

2.5 Risk factors

Two major studies, INTERSTROKE and Stroke Investigative Research and Educational Network Study (SIREN), assessed stroke risk factors. For INTERSTROKE, it was conducted in Mozambique, Nigeria, South Africa, Sudan, and Uganda; for SIREN, it was conducted in Nigeria and Ghana. Despite the belief that communicable diseases such as HIV might share in a good sum of stroke risks in Africa, the two studies found that modifiable vascular risks are similar to developed world and are pivotal and more important in Africa [49, 50]. The two studies found that hypertension, dyslipidemia, diabetes mellitus, central obesity, cardiac disorders, smoking, an unhealthy diet rich in salt and protein, and poor in fresh leafy vegetables, as well as high alcohol consumption, physical inactivity, and psychosocial stress are all common contributors to stroke [49, 50].

Hypertension was found to be a major contributor risk factor, and this might explain the higher rate of intracerebral hemorrhage in SSA. In Africa, more than 45% of the population above the age of 25 are hypertensives, and around 50% of hypertensives are unaware, undiagnosed, uncontrolled, and uncompliant [51]. Hypertension aggravates atherosclerosis by inducing complex vascular micro-aneurysm formation, lipohyalinosis, and micro atheroma, resulting in rupture or occlusion of the vessel, leading to intracerebral hemorrhage or ischemia, respectively.

Dyslipidemia was the second most common risk factor; meanwhile, and despite being one of the major causes of morbidity and mortality, yet cardiac disease came sixth in risk factors for stroke, with only 7% detected Atrial Fibrillation (AF) in the INTERSTROKE study, which is a much lower percentage for SSA if compared to NA. AF leads to uncoordinated contractions and stasis, most marked at the left atrial appendage [52]. This causes increased concentrations of fibrinogen, D-dimer, and von Willebrand factor, which are indicative of prothrombotic states and dislodgement of thrombus leading to cerebral infarction [52]. AF, coupled with other risk factors such as hypertension, cardiac diseases, tobacco smoking, and sleep apnea, further increases the likelihood of succumbing to a stroke [53]. Diabetes was ranked seventh and eighth for INTERSTROKE and SIREN, respectively [34]. It leads to atherosclerosis either alone or in combination with other atherogenic risk factors such as hypertension, obesity, and dyslipidemia, leading to thrombus formation [54]. Compared to the general population, individuals with diabetes have a fourfold higher risk of stroke.

Factors that affect the vessel wall integrity or the vascular content also play a role in stroke development. HIV is highly prevalent in SSA, with over 25 million adults now living with HIV infection [55]. With expanded access to anti-retroviral therapy (ART), people with HIV are living longer and experiencing fewer opportunistic infections, but conversely are experiencing an emerging rise in cardiovascular diseases, including stroke [55, 56]. HIV increases the risk of stroke through its inflammatory sequel to the endothelium, induced vasculitis, hypercoagulopathy, and the adverse effects of retroviral therapy (vasculopathy, induced dyslipidemia, and insulin resistance) [57, 58].

Rheumatic heart disease is by far the most important form of acquired heart disease in children and young adults in LMIC [59]. The predominant valvular lesion commonly associated with systemic embolization is mitral stenosis, usually observed in the third decade [60]. Mitral stenosis has a 30% risk of systemic thromboembolism leading to stroke, and the risk of recurrence is as high as 60% in the first year [61, 62]. In SSA, where the burden of rheumatic heart disease is high, it is an important risk factor for stroke in young adults that warrants studying [63, 64]. Two-thirds of sickle cell disease (SCD) patients are in Africa; it was found that SCD accounts for 4.2% of strokes in Africa. SCD is responsible for occluding distal circulation within the circle of Willis [65].

Many viral infections and febrile illnesses were reported to take place around 10 days before stroke in many Africans. In Nigeria and Ghana, 10% of stroke victims reported fever up to 4 weeks before stroke development; this highlights an unstudied role of viral infections and fever in stroke [66]. The COVID-19 burden on stroke showed a rising trend in many African countries. In one year since its declaration as a pandemic, 47 African countries reported 7.1 million infections, amounting to 2.5% of the global burden of COVID-19 [67]. COVID-19 affects the endothelium integrity as well as the angiotensin-converting enzyme receptors, with a further rise in the risk of blood pressure as well as coagulopathy, which in turn increases stroke risk directly or indirectly through augmenting risk factors such as uncontrolled blood pressure [68, 69].

2.6 Conclusion

The epidemiology of stroke in Africa needs further in-depth analysis and studies with two major defects, first is in-hospital-based data, which might be deficient

in representing the true country stroke status owing to that not all stroke cases are admitted, and of those not admitted and die out of stroke, stroke as a direct cause of death might not be properly stated in the registries, second, and despite that there is some community-based studies yet not covering all African countries.

Risk factors of stroke are nearly similar between different African countries and worldwide, with hypertension being a leading cause, and this might explain the prevalence of haemorrhagic stroke (HS) in SSA. Communicable diseases such as HIV and other forms of febrile viral infections might have some role in stroke development in African countries, and hematologic disorders, precisely SCD, account for a risk in stroke development in Africa compared to other countries worldwide.

3. China

3.1 Background

China is a country with a population of 1.4 billion people and is the second most populous country in the world after India. With rapid economic progress, the average life expectancy has increased from 33 years in 1960 to 79 years in 2022 [70]. With an aging population, stroke remains an important cause of mortality and morbidity.

Prevalence and incidence.

Between 1990 and 2019, the incidence of stroke in China increased by 123% to 276.7 per 100,000 person-years in 2019 [71]. The incidence is greater in the older population, with an estimated 500 per 100,000 person-years in people older than 40 years and as high as 2749 per 100,000 person-years after 80 years [72]. However, when the age of the overall population is considered, the age-standardized incidence rates decreased by 9.3% between 1990 and 2019 [71].

Of the 3.94 million incident strokes in 2019, 2.87 million were ischemic strokes, 0.85 million were intracerebral hemorrhages, and 0.22 million were subarachnoid hemorrhages [71]. The increase in stroke incidence was the highest in ischemic stroke (226.5%), followed by subarachnoid hemorrhage (35.6% and intracerebral hemorrhage (17.6%) [71]. However, age-standardized incidence rates of intracerebral hemorrhage and subarachnoid hemorrhage had decreased, whilst ischemic stroke increased between 1990 and 2019 [71].

The prevalence of stroke was on the rise as well. In 2019, the prevalence of stroke was 28.8 million, a 147% rise from 1990. The increase in prevalence was largest in ischemic stroke (24.8 million, 195% increase) compared to intracerebral hemorrhage (4.4 million, 43% increase) and subarachnoid hemorrhage (1.5 million, 55% increase) [71]. The prevalence rate increased in people ≥60 years but decreased in people <60 years, highlighting the major contribution of aging to the burden of stroke in China [71].

3.2 Outcomes after stroke

Despite an increase in the number of deaths due to stroke and mortality rate since the 1990s, age-standardized mortality had reduced in all subtypes of stroke, with the largest decline in subarachnoid hemorrhage (reduction of 84%) followed by intracerebral hemorrhage (reduction of 48%) and ischemic stroke (reduction of 3%) [71]. This may be due to a gradual but substantial improvement in the quality

of stroke care [73, 74]. The prognosis of acute stroke patients appeared to be better compared to HICs, in part due to the younger age of onset and milder stroke [74, 75]. Disability-adjusted life years (DALYs) of stroke have increased steadily since 1990. However, there is a reduction in the age-standardized DALY rate by 42% between 1990 and 2019 [71]. The economic burden of stroke is massive. In 2018, the direct costs of stroke were ¥247.8 billion (purchasing power parity-$PPP 58.6 billion), and the indirect costs were ¥704.4 billion ($PPP 166.5 billion) [76]. As approximately 70% of stroke costs come from public funding, this constitutes a significant economic burden on the Chinese economy [76].

3.3 Risk factors for stroke

Hypertension, dyslipidemia, diabetes mellitus, excessive alcohol intake, air pollution, high salt, and low fruit and vegetable diet are the most common risk factors for stroke [49, 77, 78]. Hypertension is highly prevalent, affecting 28% of the population. Between 2002 and 2014, the number of people with hypertension nearly doubled from 153 million to 300 million [79]. In addition, less than 20% of patients with hypertension had adequate blood pressure control [80].

Dyslipidemia and diabetes mellitus are common, affecting 34% and 11% of the population, respectively, and are poorly controlled [81, 82]. Lifestyle factors put men at higher risk of stroke as well. As high as two-thirds of men are smokers and one-third drink alcohol weekly compared to <5% in women [83, 84].

3.4 Geographical differences

Geographical location was a factor that contributed to the burden of stroke in China [77, 85]. The incidence of stroke was the highest in the northeastern (441–486/100,000 person-years) and the lowest in the southern region (81–136/100,000 person-years) [86]. The higher incidence of stroke may be associated with a higher prevalence of hypertension in the northeastern and northern regions [87]. In addition, there is a higher proportion of smoking and alcohol consumption in the northeast region [77]. Dietary differences contribute to a higher incidence of stroke, where the northern Chinese diet is high in salted vegetables, and the southern Chinese diet is characterized by high intakes of vegetables and fruits and lower salt intake [88].

Rural areas had a higher incidence and prevalence of stroke due to differences in prevalence of risk factors and their treatment [77, 85, 89, 90]. The awareness, treatment, and control of hypertension, diabetes mellitus, and dyslipidemia are less optimal in the rural areas [79, 81, 82, 87]. Smoking prevalence is higher, whilst consumption of vegetables and fruits is lower in rural areas [91]. In addition, the common domestic use of coal and wood as fuels in rural areas contributes to the release of fine particulate matter (PM) and increases the risk of stroke mortality [92].

3.5 Conclusions

Due to an aging population, the overall incidence and prevalence of stroke have been on the rise. Hypertension is a major risk factor for stroke and is poorly controlled. There are vast geographical differences in the burden of stroke and its risk factors between different regions and rural–urban differences. These factors should be considered with planning health policies to reduce the stroke burden.

4. Europe

4.1 Background

Europe has a population of 742 million as of 2023, having diverse demographic trends across its regions. The European Union (EU), comprising 27 member states, has a population of 448 million people. Europe's median age is among the highest globally, with 21% of the population being aged 65 and over, and a life expectancy of 81.5 years in 2023, with important variations between regions and countries. Eastern European countries, most of them being considered low- to middle-income countries, present distinct demographic characteristics influenced by their socioeconomic and historical factors, marked by demographic decline, high level of emigration, and lower life expectancy when compared with Western Europe [93]. The health care systems of this region exhibit notable differences, with funding and access to services being higher in Western countries, infrastructure and health education levels in the population being lower in Eastern European countries when compared to Western countries. According to the World Bank, globally there are 132 countries classified as low- or middle-income countries (LMICs), seven LMICs being from Europe, most of them from Eastern and Southern Europe [5].

4.2 Burden of stroke

Eastern Europe recorded the highest number of stroke cases, followed by Western and Central Europe. Between 2010 and 2019, the incidence rates remained stable across all these subregions; however, age-standardized incidence rates showed a consistent decline in all the subregions, except for the individuals from Eastern and Central Europe below 70 years, where rates remained unchanged. Eastern Europe had the highest age-standardized incidence rate, 2.75 times greater than in Western Europe, despite a significant reduction in incidence rates across all subregions over the past decades. The total number of prevalent stroke cases rose by 4%, reaching more than 14 million cases between 2010 and 2019. Ischemic stroke accounted for 78.9%, while intracerebral hemorrhages and subarachnoid hemorrhages made up 14.4% and 10.6%, respectively.

When examining all the regions in Europe, the absolute number of stroke cases increased in Western and Central Europe but remained stable in Eastern Europe. Overall age-standardized prevalence rates declined across all subregions. However, there was an approximately 4% rise in age-standardized prevalence among individuals under 70 in Eastern and Central Europe. Eastern Europe had the highest age-standardized prevalence rate, which was 1.8 times greater than in Western Europe. Regarding stroke-related deaths, the absolute number increased significantly in Western Europe, while remaining stable in Eastern Europe, but still at a higher level compared to the other regions. Although, Eastern Europe had the highest age-adjusted mortality rate, it also experienced the most significant decline in mortality rates between 2010 and 2019, with a decrease of more than 20%, this improvement being caused mainly by better health policies, higher levels of investments and better quality of care [94, 95].

The total disability-adjusted life years lost (DALYs) rates have been declining across Europe, in both genders, over the timespan of 30 years, between 1990 and 2019, with the Eastern European region experiencing the highest burden of disease from ischemic and hemorrhagic (intracerebral and subarachnoid hemorrhage (SAH))

stroke, followed by Central Europe. In 1990, DALY rates for the female gender were approximately identical in Eastern Europe and Central Europe and higher by 25–26% than in Western Europe. As the years passed, Central Europe observed the highest reduction of stroke burden in women, reducing the gap with Western Europe to 9%, while Eastern Europe experienced an increase from 26–32% in 2019. The burden of disease is greater in men (with a male–female ratio of 1.3 in Western Europe and 1.5 in Eastern Europe in 2019) and the difference in stroke burden across regions is also higher in the male population, with Eastern Europe having the lowest decline in stroke incidence and DALYs, by 16% from 1990 to 2019.

All the countries in Central and Eastern Europe experienced a decline in disease burden [96], although they had different trends and patterns. The smallest decrease was observed in LMICs like Montenegro (−5%), North Macedonia (−16%), Bosnia and Herzegovina (−19%), and Albania (−28%), with North Macedonia having the highest health loss due to stroke in 2019, which is 7.7 times higher than the rates in Western Europe. There is a substantial variation in stroke burden between the countries from the Central and Eastern European regions. The variation was larger among the Central European countries, and it was driven mainly by the very high stroke burden rates of three Balkan countries, those being North Macedonia, Montenegro, and Serbia. A possible explanation for this may be related to the fact that the highest rates of years of life lost (YLLs) due to stroke are found in North Macedonia, Montenegro, and Serbia, suggesting differences in the quality of acute stroke care in those countries compared to the rest of Central Europe.

4.3 Stroke subtypes

There are differences reported about the relative proportions of each stroke based on pathophysiological subtypes in various regions and countries of Europe, as previously reported on a global scale [97]. There were countries where the proportion of total stroke burden due to intracerebral hemorrhage reached 75% in Montenegro and 71% in Albania among men in 2019. Among Eastern European countries, Moldova had a higher proportion of stroke burden due to intracerebral hemorrhage, which may be related to greater total stroke burden due to YLLs in these countries (up to 90%). While the proportion of total stroke burden from SAH did not vary as much as for the other pathological subtypes, the lack of access to treatments for ruptured cerebral aneurysms and the sequelae of SAH likely contributes to a disproportionate burden of YLLs in Eastern and Central Europe.

5. India

5.1 Burden of stroke

India is the most populous country in the world, with a population of 1.45 billion people [98]. Life expectancy in India has increased beyond 60 years of age, which has led to a progressive increase in noncommunicable age-related disorders [99, 100]. Stroke burden is increasing in India, and it is the fourth leading cause of death and the fifth leading cause of disability in the country [101]. The Indian Global Burden of Disease Study 1990–2019 estimated stroke to be the largest contributor to disability-adjusted life years (DALYs) with an approximate contribution of 37.9% [102]. The incidence of stroke in India is between 105 and 152/100,000 people per year [103],

and the age and sex-standardized mortality rate is 82.4 per 100,000 person-years [104]. The one-month fatality from stroke ranges between 18 and 42% (4), which is much higher than in developed nations.

A recent systematic review by Jones et al. [101] found that the median age of stroke patients in India was 62.2 years, with a male preponderance (59%), with a higher stroke incidence in men. Lower female representation could likely be due to gender discrimination in access to healthcare, with studies revealing that it was worse for women, with a male-to-female sex ratio of 1.69 for outpatient visits [105]. The mean age for stroke occurrence was lower in Indian patients compared to the global average [106]. Approximately 20% of first-ever stroke patients admitted were found to be younger than 40 years of age. The annual stroke incidence in individuals between 18 and 49 years was found to be 46 per 100,000 person-years [107], which was significantly greater than the European (5–15 per 100,000) and American population (20 per 100,000) [108]. Strokes in this economically productive age group lead to multiple social, emotional, economic, vocational, and physical considerations [109].

Although the one-month case fatality rate ranged between 18 and 42%, higher death rates were found in men compared to women. Also, the Million Death Study [110] found that approximately 33% of premature stroke deaths were reported from the Eastern part of the country which could be attributable to ethnic differences (higher rates of hypertension and dietary habits of increased salt intake).

5.2 Stroke subtypes

The rates of ischemic stroke varied between 65 and 84%, with large artery and small vessel stroke subtypes being more common than cardioembolic ones [104]. This could, in part, be due to the greater prevalence of intracranial atherosclerotic disease among Asian (and Indian) stroke patients [111]. Among other determined etiologies, stroke due to infectious diseases, although uncommon, was more common than elsewhere, with tuberculosis, fungal infections, and infective endocarditis being the leading culprits [111]. Tuberculosis causes stroke involving the basal ganglia secondary to tubercular meningitis associated with basal arachnoiditis around the circle of Willis. Thrombocytopenia with viral infections like dengue has occasionally led to intracerebral hemorrhage (ICH) [112]. The rate of ICH was found to be between 20 and 32% [104], which is higher than in Western countries. Overall, the rate of ICH was found to be the highest in Asia among all continents [113].

Although cerebral venous sinus thrombosis (CVT) [114] is an uncommon cause of stroke in India, it was found to affect predominantly young people (median age—31 years) and is more prevalent during the summer months [114, 115]. The risk factors mostly identified were anemia, oral contraceptives, pregnancy, puerperium, and central nervous system (CNS) infections [115]. Another study found that among pregnant CVT patients, 34% had more than one CVT-predisposing prothrombotic factor [116].

5.3 Conclusion

High-quality epidemiological stroke data from India is heterogeneous and incomplete since it is only representative of four out of the 29 states and seven union territories of the country. To further identify the stroke burden in India, future, more detailed studies following the WHO STEPS framework [117] would be required.

6. South America and the Caribbean

6.1 Background

Stroke is a leading cause of morbidity and mortality in Latin America and the Caribbean (LAC). With a population exceeding 666 million [118] (World Meter, 2025), the region's socioeconomic, cultural, and geographic diversity results in significant variations in stroke incidence, prevalence, etiology, risk factors, healthcare, and outcomes. Stroke poses a major public health challenge due to its high burden on healthcare systems and its impact on individuals and families [119].

6.2 Incidence and mortality rates

Stroke epidemiology in LAC is characterized by considerable regional variability, with stroke incidence rates differing widely across countries. A pooled analysis of data from multiple studies indicated an overall incidence of 255 stroke cases per 100,000 person-years in South America, with men exhibiting higher rates (261 per 100,000) compared to women (217 per 100,000) [120]. This regional variability in stroke incidence reflects differences in healthcare infrastructure, socioeconomic status, and the prevalence of risk factors.

Data from a systematic review spanning from 1997 to 2021 reported an annual stroke incidence of 119 cases per 100,000 individuals across LAC, with a prevalence of 3060 cases per 100,000 individuals [121]. In contrast, earlier population-based studies have shown that stroke incidence varied from 0.35 to 1.83 per 1000 individuals annually, while prevalence ranged between 1.74 and 6.51 per 1000 individuals [122].

This variation underscores the changing landscape of stroke epidemiology in the region, with differences in data collection methods and healthcare access contributing to evolving figures.

In 2019, LAC accounted for the fourth largest stroke burden globally, with 6.8 million disability-adjusted life years (DALYs). The majority of this burden was attributed to premature deaths (89.5% of DALYs), and intracerebral hemorrhage emerged as the leading cause of overall stroke burden, responsible for 42% of DALYs. Ischemic stroke, on the other hand, was the leading cause of disability, contributing to 69% of years lived with disability [123].

6.3 Younger people

Several studies have identified an unfavorable temporal trend in stroke incidence among younger people in LAC, particularly among young women. While the global incidence of stroke declined in older people between 2010 and 2019, a similar trend was not observed in younger people in LAC. Instead, the incidence of stroke has risen. This has been linked to increasing rates of conventional risk factors, such as arterial hypertension, obesity, physical inactivity, dyslipidemia, diabetes mellitus, and smoking, alongside emerging factors like air pollution, long working hours, and stress. Moreover, better access to acute stroke care and improved patient awareness have also contributed to the rising numbers [124].

6.4 Risk factors and population-attributable fractions

The high burden of stroke in LAC can largely be attributed to modifiable risk factors. Arterial hypertension remains the most significant contributor to stroke risk in the region, responsible for approximately 53% of the population-attributable fraction [123]. Obesity is another key risk factor, contributing to 37% of stroke cases. These risk factors are particularly influential in hemorrhagic strokes, which disproportionately affect women and older adults [123].

In lower-income countries within LAC, household air pollution is emerging as a critical risk factor, further complicating the stroke epidemiology in these settings. The higher prevalence of metabolic conditions, including high blood pressure and elevated body mass index, combined with limited access to prevention and treatment, particularly in rural areas, exacerbates the stroke burden in these nations [122, 123].

6.5 Case fatality and mortality trends

The case-fatality rate for stroke in LAC remains alarmingly high, with studies indicating rates ranging from 20 to 40% depending on the country. In particular, the 30-day case-fatality rate following a first stroke was reported as 21.1% in recent analyses. The high mortality rates are compounded by limited access to specialized acute stroke care, including thrombolysis and mechanical thrombectomy, and also by a lack of sufficient post-stroke rehabilitation, especially in lower-resource settings [119, 121, 125].

6.6 Economic impact and cost of stroke care

The financial burden of stroke treatment is another critical issue in LAC. A multicenter study assessed the direct costs associated with acute ischemic stroke treatment in various LAC countries [126]. The analysis revealed significant cost disparities, with costs ranging from I$ 5902 in Peru to I$ 27,488 in Brazil for the same treatment. The study further highlighted the variations in costs for different treatment modalities, including medical treatment, intravenous thrombolysis, mechanical thrombectomy, and the combination of both, with costs ranging from I$ 9735 to I$ 30,153 depending on the treatment approach. These cost differences reflect the diversity in healthcare systems, access to treatment, and regional disparities in economic resources. Addressing these disparities through targeted interventions, improving access to care, and optimizing healthcare spending are essential to improving stroke outcomes across LAC [126].

6.7 Conclusion

Stroke continues to impose a significant burden on public health in Latin America and the Caribbean, with increasing incidence rates, high mortality and case-fatality rates, and substantial regional disparities in care. The rising prevalence of risk factors such as arterial hypertension, obesity, and diabetes mellitus, compounded by emerging environmental risks, calls for urgent public health action. Furthermore, disparities in access to care and the economic burden of stroke treatment must be addressed through more equitable healthcare policies, better prevention strategies, and efficient allocation of resources.

Improving stroke outcomes in LAC will require comprehensive approaches that target modifiable risk factors, enhance stroke care infrastructure, and ensure more equitable access to treatment, especially in underserved areas. As stroke epidemiology continues to evolve, ongoing research and collaboration will be crucial to developing effective strategies for reducing the stroke burden in this diverse and rapidly changing region.

7. Southeast Asia

7.1 Background

Southeast Asia (SEA) represents a diverse sub-region of Asia, encompassing 11 nations: Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste, and Vietnam. The region spans approximately 4.5 million square kilometers and hosts a population exceeding 680 million, making it one of the world's most densely populated regions [4]. Population projections indicate continued growth, with expectations of reaching 760 million by 2050, driven by high birth rates and improving life expectancy [127].

The region exhibits remarkable cultural, ethnic, and linguistic diversity, predominantly composed of Austronesian, Austroasiatic, Tai-Kadai, and Sino-Tibetan ethnic groups. The religious landscape is equally varied, with Islam, Buddhism, Christianity, and Hinduism serving as major faiths. Economically, SEA presents a spectrum ranging from low-income countries to upper-middle-income nations, with Singapore standing as the region's sole high-income country [127].

7.2 Epidemiological patterns and disease burden

The Global Burden of Disease Study 2019 revealed that stroke remains the second leading cause of death in Southeast Asia, with low-income countries experiencing a significantly higher burden than high-income nations [128]. Specifically, World Bank low-income countries faced 3.6 times higher age-standardized stroke mortality rates (95% CI: 3.5–3.8) and 3.7 times higher disability-adjusted life year (DALY) rates (95% CI: 3.5–3.9), exceeding the global average of 11.6% [128]. The disparity is further emphasized by the fact that 86.0% (85.9–86.9) of all stroke-related deaths and 89.0% (88.9–89.3) of stroke-related DALYs occurred in lower-income, lower-middle-income, and upper-middle-income countries [128]. A comprehensive WHO report published in 2021 highlights that the burden is particularly significant in low- and middle-income countries, which account for over 85% of global stroke mortality [129].

Southeast Asian countries show significant variations in stroke burden, with Indonesia demonstrating the highest mortality rate of 193.3 per 100,000 person-years, followed by Myanmar (165.4), Lao PDR (141.3), and Cambodia (137.8). The middle-range countries include the Philippines (109.6) and Vietnam (124.5), while Malaysia shows a lower rate at 84.3 per 100,000 person-years [7]. The lowest mortality rates are observed in Singapore (47.9), Thailand (62.8), and Brunei (68.6) per 100,000 person-years. Regarding stroke incidence, limited data are available for Southeast Asian countries, with Malaysia reporting the lowest rate at 67 per 100,000 person-years, Vietnam at 250 per 100,000 person-years, and Singapore at 180 per 100,000 person-years [104]. When examining DALYs lost, a similar pattern emerges

with Indonesia showing the highest burden, followed by Myanmar, Lao PDR, and Cambodia, while Singapore demonstrates the lowest burden in the region [104].

7.3 Young stroke

The burden of stroke among young adults (aged ≤50 years) has emerged as a significant public health challenge in Southeast Asia, with epidemiological data indicating substantially higher prevalence rates compared to Western populations [128]. This concerning trend is attributed to a complex interplay of modifiable risk factors, including increasing prevalence of hypertension and diabetes mellitus at younger ages, rapid urbanization-associated lifestyle changes, and region-specific genetic predispositions. Recent epidemiological surveillance data demonstrate that Southeast Asia bears a disproportionate burden of young stroke, with urbanization and socioeconomic transitions driving significant shifts in dietary patterns and physical activity levels [5]. Moreover, the healthcare infrastructure challenges, particularly in resource-limited settings, contribute to delayed diagnosis and suboptimal risk factor management [5]. These findings underscore the urgent need for targeted public health interventions, emphasizing primary prevention strategies and early risk factor modification, to address this emerging epidemic in the region.

7.4 Cerebrovascular disease patterns

Intracranial arterial stenosis (ICAS) patterns in Southeast Asia demonstrate distinct characteristics. Hospital-based studies from Southeast Asian countries show varying distributions, with Indonesia reporting high rates of large artery atherosclerosis at 59.6% [130], while Singapore shows a predominance of small vessel disease at 47.9% [131]. Traditional cardiovascular risk factors remain consistent with other Asian regions, though the impact may vary across different Southeast Asian populations.

7.5 Distinctive vascular conditions

While Moyamoya disease (MMD) is less commonly reported in Southeast Asia compared to East Asia, other vascular conditions show regional significance. Studies from Thailand have documented cases of cerebral gnathostomiasis, a parasitic infestation unique to the region that can cause subarachnoid hemorrhage and migratory intracerebral hemorrhage [132]. The pattern of arterial dissections in Southeast Asian populations remains understudied compared to East Asian cohorts.

7.6 Infection-related cerebrovascular complications

Southeast Asia faces unique challenges from tropical infectious diseases affecting cerebrovascular health. Dengue hemorrhagic fever, prevalent in the region, can result in intracranial hemorrhage due to thrombocytopenia [133]. Recent studies have also highlighted the impact of COVID-19 on stroke presentations in Southeast Asian healthcare systems [134].

7.7 Less common vascular conditions

In Southeast Asia, radiation vasculopathy presents a significant clinical challenge, particularly due to the high prevalence of nasopharyngeal carcinoma (NPC) in the

region [135]. Studies from Southeast Asian centers, particularly in Singapore and Malaysia, have reported favorable experiences with carotid artery stenting (CAS) for radiation-induced carotid artery stenosis [136]. A meta-analysis demonstrated that NPC patients treated with radiation therapy had an increased risk of carotid stenosis, with a relative risk of 4.17 ($p < 0.00001$) compared to non-irradiated patients [137]. Regional institutions have adopted surveillance strategies using carotid ultrasound screening one year after radiation therapy, with close monitoring for disease progression.

7.8 Future directions

The challenges in Southeast Asian stroke care require targeted interventions focusing on strengthening primary prevention, particularly for young stroke patients. Key priorities include developing telemedicine networks to bridge urban–rural divides, training more stroke specialists, and establishing more acute stroke units in underserved areas. Healthcare financing reforms are needed to reduce out-of-pocket expenses for acute stroke treatments, while regional collaboration could optimize resource utilization and improve access to advanced therapies.

7.9 Conclusion

Southeast Asia faces unique challenges in stroke care, marked by significant healthcare disparities across countries and a concerning trend of increasing young stroke incidence. While some nations have established comprehensive stroke systems, many struggle with limited resources and healthcare access. Success in addressing these challenges will require a sustained commitment to improving infrastructure, increasing specialized workforce capacity, and implementing targeted public health interventions that consider the region's socioeconomic diversity and unique disease patterns.

8. COVID-19 and stroke

COVID-19 significantly impacted stroke care worldwide, but its effects have been especially severe in LMICs, where healthcare systems were already under strain.

The pathophysiology of stroke in COVID-19 patients is multifactorial and complex, involving both direct and indirect effects of the virus on the vascular and nervous systems. SARS-CoV-2, the virus responsible for COVID-19, binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in endothelial cells, neurons, and glial tissue. This interaction can trigger widespread endothelial dysfunction and inflammation, leading to a prothrombotic state. The exaggerated immune response, or "cytokine storm," seen in severe cases, leads to elevated levels of inflammatory markers like IL-6 and C-reactive protein (CRP), further promoting coagulation and platelet activation. Additionally, COVID-19 is associated with increased levels of D-dimer and fibrinogen, indicating hypercoagulability and increased risk of thromboembolic events, including large vessel occlusion strokes. Cardiac complications such as arrhythmias and myocarditis may also increase the risk of cardioembolic strokes. In some cases, autoimmune mechanisms and antiphospholipid antibodies may also play a role. Together, these factors contribute to an increased incidence of ischemic stroke, particularly in younger patients without traditional risk factors, underlining the need for vigilance and early intervention in COVID-19-associated stroke [138–140].

However, in LMICs, limited access to diagnostic tools, delayed hospital presentations, and shortages of trained personnel often hinder timely diagnosis and treatment [141]. Lockdowns and fear of infection further discouraged patients from seeking urgent care, leading to a rise in untreated or late-presenting strokes. Telemedicine, which offered a lifeline in high-income settings, remained inaccessible to many in LMICs due to technological and infrastructural barriers. Moreover, many of the existing stroke units were reallocated to manage the pandemic, and this further compromised the stroke care. As a result, mortality and disability from stroke increased disproportionately in these regions.

Addressing this crisis requires targeted strategies, such as strengthening stroke care pathways, investing in public awareness, and ensuring equitable access to acute stroke interventions, even during pandemics. The COVID-19 experience highlights the urgent need to build resilient stroke systems in LMICs that can withstand future global health emergencies.

9. Summary of stroke in low- and middle-income countries

Stroke poses a significant and growing public health challenge in low- and middle-income countries (LMICs), where rising incidence rates are fueled by urbanization, sedentary lifestyles, and diets high in salt and fat. Hypertension, diabetes, and limited awareness of risk factors contribute to the burden, compounded by inadequate healthcare infrastructure for timely diagnosis, acute treatment, and rehabilitation. LMICs face higher stroke-related mortality and disability rates compared to high-income nations, as limited access to specialized care, costly therapies, and scarce rehabilitation services exacerbate outcomes. Economic strains on families due to medical expenses and lost income further deepen the crisis. Addressing this requires targeted investments in preventive measures, affordable management of chronic conditions, and strengthening healthcare systems to improve acute care and long-term support for survivors.

Conflict of interest

The authors declare no conflict of interest.

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