REVIEW

Stroke in Asia: geographical variations and temporal trends

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ABSTRACT

Asian countries are in various stages of epidemiological transition and therefore exhibit a great diversity in disease patterns. Collectively, they comprise almost two-third of the world's total mortality due to stroke. The purpose of this review is to explore existing epidemiological data on stroke, highlight the temporal trends in stroke epidemiology in various regions of Asia and predict future patterns based on these observations. Our search revealed that there is a lack of good epidemiological data from most Asian countries. Whatever data exist are not comparable due to lack of standardised methodology for ascertaining stroke and its subtypes. For this and other reasons, these estimates exhibit country-to-country variation and also within-country variability. We have also reviewed temporal trends in stroke incidence and prevalence in 12 Asian countries and the evolution of stroke subtypes over the past two decades. Important observations include a rise in stroke incidence in most Asian countries, an earlier age at onset compared with the West, a relative increase in the proportion of ischaemic strokes and a decline in haemorrhagic strokes. Among ischaemic stroke subtypes, lacunar strokes, which were once the commonest variety, are now declining. Emerging data suggest that large artery atherosclerosis and in particular that of intracranial vessels is the predominant aetiology in most Asian countries. The review also identified important gender differences in terms of stroke risk factors, prevalence and outcomes. There is need for sound epidemiological data from most countries to understand the disease better and plan policy-level interventions to decrease the burden. We identify a need for standard format or guidelines for conducting stroke epidemiological studies especially in developing Asian countries. This region must be identified as a priority region for stroke-related interventions and preventive strategies by global healthcare authorities and organisations.

INTRODUCTION

Although the age-standardised mortality due to stroke has shown a downward trend in the past two decades, the absolute numbers affected by this devastating condition are on the rise, particularly in low-to-middle income countries.[1] The Asian continent harbours almost two-thirds of the world's population, and in 2002 East Asia alone comprised 60% of the world's total mortality due to stroke.[2]

Asia is home to a very diverse population both in terms of ethnic variability and socioeconomic differences, with countries in various stages of development and epidemiological transition. The burden of cerebrovascular disease, therefore, is also expected to exhibit geographical variability. This burden is also expected to go up further as Asian countries undergo development, their populations age and there is a change in lifestyle factors.[3] South Asian countries (India, Pakistan, Bangladesh and Sri Lanka) constitute 22% of world's population and 40% of the developing world, and are the most affected regions probably accounting for more than 40% of global stroke deaths.[4] Therefore, global burden of stroke and stroke-related deaths cannot be substantially reduced without interventions in Asia. Analysis of existing data is mandatory to identify current and future trends in stroke epidemiology in this part of the world.

Many regional or multinational studies (registries or cohorts) are in progress or recently completed, including stroke in young Asian women study (8 Asian countries), Asian cerebral venous thrombosis (CVT) registry (13 Asian countries) and INTERSTROKE (a global case–control study with more than 20 000 cases and controls from Asia).[5 6] These studies indicate growing collaboration and infrastructure development in developing Asian countries. Current emphasis by United Nations (UNO) and WHO on non-communicable diseases including stroke is likely to translate into more epidemiological research in this region. It is high time we analysed epidemiological data related to stroke in Asia, identified areas of research collaboration among Asian countries and set priorities for future research and advocacy in this region.

Available stroke data from Asia are largely confined by geographical boundaries of individual countries. The objective of this review is to explore the existing data on stroke from selected Asian countries, summarise the evolution of stroke epidemiology in these countries over the past 20 years and predict future patterns based on these observations. Four of these countries are from Far East Asia (China, Japan, Korea and Taiwan), three from South East Asia (Thailand, Singapore and Malaysia), three from South Asia (Pakistan, India and Bangladesh) and two from the Middle East (Iran and Israel). These 12 countries represent more than 75% of Asian population. This review looks at various themes across major parts of Asia to identify areas for future interventions.

Search strategy

For the purpose of this review, we restricted our search to 12 Asian countries, ensuring that we get adequate representation from all regions of Asia. A detailed search for all articles published since 1990 was conducted using two search engines, PubMed

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and Google Scholar. The following keywords were used along with the name of each country to identify relevant articles: "stroke", "cerebrovascular disease", "incidence of stroke", "prevalence of stroke", "stroke epidemiology", "temporal trends in stroke", "stroke subtypes", "ischemic strokes", "intracranial hemorrhage", "lacunar strokes", "large artery strokes" and "cardioembolic strokes". The search was restricted only to English language. Abstracts from the search were screened, and all articles on stroke epidemiology were selected. Both longitudinal and cross-sectional studies were included in this review.

Appraisal of current epidemiological data

Online supplementary table S1 provides a review of the most important stroke studies from these countries with details of recruitment period, methodology of stroke subtype classification, study design (hospital registries or population based) and definition of stroke and study shortcomings.[7–18] It is evident that there is lack of robust epidemiological data from most Asian countries. There are wide variations in study designs, case ascertainment and stroke definitions. It is important to know how this figure for incidence or prevalence has been standardised. Use of different standard populations can change the figures substantially. This table elaborates which standard population has been used. Because of this difference, the incidence reports are not as easily comparable as these statements sound. Reader has to understand this limitation of standardisation. These variations identify a lack of standard format or guidelines for conducting stroke epidemiological studies.

Incidence and prevalence

Table 1 provides estimates of stroke prevalence and incidence from these Asian countries[7 11–24] No prevalence data are reported from Malaysia, Japan, Iran and Israel while no incidence data from Thailand, Bangladesh and Israel could be found. Data from China and India (more than 50% of Asian population) are most robust and reliable. Reported prevalence of stroke is comparable from China and India. Very high prevalence in Pakistan and Singapore could be related to methodological issues including case ascertainment and definition. These data need confirmation by sound and reliable studies. Incidence data are comparable from China, Japan, Korea, India and Singapore ranging from 116 to 219 per 100 000 per year. Reported incidence data from Pakistan are not based on a population-based study, but it is an estimate from physician's survey. These data are neither accurate nor reliable. Low incidence in Malaysia and high incidence in Taiwan and Iran (one study) need reconfirmation by sound and reliable studies.

These data set again highlight the methodological issues in conducting and reporting these studies, which could be addressed by implementation of standardised protocols and methods throughout the continent.

Table 1 Stroke prevalence and incidence in selected Asian countries

Country	Study period	Prevalence	Incidence
Japan*	2002–2005	Not available	145/100 000/year[7]
China*	1985–1991	260–719/100 000[19]	116–219/100 000/year[19]
Korea*	2004–5	1590/100 000 (age adjusted >35 years)[11]	216/100 000/year[11]
Taiwan*	1986–1990	1642/100 000 (age >36 years)[20]	329/100 000/year[12]
Thailand*	2010	1850/100 000[13]	Not available
Malaysia*	2010–2011	Not available	67/100 000/year[14]
Singapore*	2001–2003	3650/100 000[21]	180/100 000/year[21]
India*	2003–2005	545/100 000[15]	145/100 000/year[15]
Bangladesh*		300/100 000 (age >40 years)[22]	Not available
Pakistan*	1998	4800/100 000 (age adjusted >45 years)[23]	250/100 000/year[24]
Iran*	2006, 2010	Not available	103–203/100 000/year[17 18]
Israel*	Not available	Not available	Not available

*Latest published estimates are reported here.

Stroke types and subtypes

Table 2 shows the frequencies of stroke types (ischaemic vs haemorrhage) and subtypes of ischaemic stroke (large vessel, small vessel and cardioembolic).[25–41] It is obvious that the frequency of haemorrhagic stroke (labelled as intracerebral haemorrhage in many reports) is still high compared with reports from the Western countries. Haemorrhagic stroke still accounts for 20–30% cases of all strokes in these countries, except Israel, Iran and Thailand. Among ischaemic stroke, China, Taiwan and Pakistan have a high proportion of small vessel disease, while Japan, Korea and Malaysia have a higher proportion of large vessel disease. Israel, Iran and Japan also have a high frequency of cardioembolic stroke. The major issue with these data is again lack of standardisation. Only a few studies used TOAST classification. Most of the studies are hospital-based registries.

Temporal trends

It is extremely important to study temporal trends in stroke incidence and stroke types/subtypes to predict future outlook and future interventions. In this section, we will provide a brief account of changing trends in these Asian countries. A summary of these trends is provided in online supplementary table S4.

Japan: One of the best evidence about stroke epidemiology from Asia comes from Japan. In the 1950s, Japan used to have the highest mortality due to stroke, but it has since declined steeply.[42 43] Despite this, stroke still remains the third most common cause of death in Japan.[44] The Hisayama stroke registry is one of their most established cohorts.[45] They report a decline in the incidence of ischemic[46] as well as haemorrhagic strokes over time,[47] although the decline was steeper before the 1970s and since then has been less sharp. The Miyakojima study conducted in another area of Japan reports no major changes in incidence of stroke and all its subtypes from 1988–1991 to 2002–2005.[7] The relative proportion of ischaemic strokes has increased over time compared with haemorrhagic strokes, which has shown a steady decline. The Hisayama cohort suggests that lacunar strokes have shown a significant decrease over time, whereas the incidences of the other two subtypes have not shown much change.[48]

China and Hong Kong: In 2010, cerebrovascular disease was ranked as the third highest cause of mortality in urban and the first highest in rural China.[49] Jiang *et al*[50] reported temporal trends, with the incidence of intracranial haemorrhages decreasing through the 1990s and that of ischaemic strokes increasing. The Sino-MONICA Beijing[51] project analysed more than 14 000 strokes in Beijing from 1994 to 2004 and reports a similar trend in stroke subtypes. The burden of intracranial atherosclerosis is also substantial in China, with as many as 33–50% of patients with stroke affected by it.[52] A recent study

Table 2 Stroke subtypes as reported from various Asian studies

	Stroke types (proportion of all strokes %)		Ischaemic stroke subtype (proportion of all ischaemic strokes %)		
Country	Ischaemic stroke	Haemorrhagic stroke	Large artery	Small vessel	Cardioembolic
Japan[25 26]	65–74	26–34	54.1	21.0	22.9
China[27 28]	75	25	21.5	40.6	7.5
Korea[11]	76	24	36.1	25.4	17.1
Taiwan[29 30]	71	28	14.6	39.4	12
Malaysia[33]	73–80	18–27	59	28.3	3.4
Singapore[34 35]	76–80	19–24	41	35	10
India[16 36]	74–80	20–32	41	18	10
Bangladesh[37]	61–80	20–39	Not available	Not available	Not available
Pakistan[38]	79	21	26–31	43	6–8
Iran[18 39]	82	17	Not available	Not available	20–31
Israel[40 41]	90	10	5–9	15–28	21–34

reports this aetiology in 46.6% of the 2864 stroke subjects studied and concludes that it is the most common vascular lesion in Chinese patients with cerebrovascular disease.[53] There is also evidence to suggest that cardioembolic strokes have also increased in China in the past decade.[54] Among Hong Kong Chinese, recent trend suggests a decrease in incidence of ischaemic strokes, whereas there is a reported increase in haemorrhagic strokes among those between 35 and 44 years of age.[55]

Korea: According to the Korean Stroke Society's report,[11] the proportion of ischaemic strokes admissions has increased from 64.7% in 2000 to 76.1% in 2009. The proportion of haemorrhagic strokes has gone down steadily. According to these data, large artery atherosclerosis was and still remains the predominant aetiology found in 36.1% of patients with ischaemic stroke. Small vessel disease has shown a downward trend, whereas cardioembolism increased during this time. The study also reports a predominant intracranial atherosclerosis, although extracranial disease tended to show a rising trend over the study period. Slightly older data from 1999 to 2007 also show an increase in intracranial disease burden over time.[56]

Taiwan: A recently published study has shown a temporal rise in the burden associated with ischaemic strokes in Taiwan from 2000 to 2005.[57] Recent data suggest that the incidence of haemorrhagic strokes is higher in Taiwan compared with the white and black populations of North America and Europe but lower than the incidence reported from China and Japan.[33] Compared with data from 1995, lacunar stroke proportion has gone up from 29% and that of cardioembolism has come down.[58]

Thailand: Stroke is among the top three leading causes of mortality in Thailand.[59] In 1998, a study conducted on elderly Thai population revealed a prevalence of 1.12%.[60] The frequency of haemorrhagic stroke decreased from 22% (in 2003) to 13% (in 2012).[61 31] Among ischaemic stroke subtypes, recent data suggest a very high percentage of intracranial atherosclerosis (52.6% of all ischaemic strokes) as the predominant aetiology.[32]

Malaysia: According to the most recent estimates, stroke is the fifth leading cause of death in Malaysia.[14] The National Stroke Registry reports ischaemic strokes as the predominant variety found in 73.3% of all patients with stroke.[33] This proportion has not changed since the late 1990s when a hospital-based study reported ischaemic strokes in 72%.[62] The proportion of small vessel disease is reported as declining trend from 62% (2003) to 28% (2012).[33]

Singapore: Stroke is the fourth leading cause of death in Singapore.[21] When temporal trend was analysed between 2000 and 2005, no significant changes were seen in the relative proportions of the stroke subtypes.

India: Data from India report consistent trends in stroke incidence and types/subtypes. The variations in frequencies of haemorrhagic stroke and small vessel diseases are largely attributed to geographical variations.

Bangladesh: Stroke is the third leading cause of death in Bangladesh.[37] No data are available on ischaemic stroke subtypes so far. No data are reported addressing temporal trends related to stroke from Bangladesh.

Pakistan: Recently, a multicentre stroke registry was analysed by our stroke group,[63] and large artery atherosclerosis seems to have taken over as the predominant subtype found in 35.7% subjects followed by small vessel disease. Cardioembolic strokes have also gone up in proportion to 11.8% from 6 to 8% previously reported. Wasay *et al*[64] evaluated the temporal trends for intracerebral haemorrhage from 1988 to 2005 using hospital-based data. They concluded that the number of hospital admissions went up significantly over time, proportion of female victims increased and age at onset decreased by about 5 years.

Iran: In 2001, the Khorasan Stroke Registry was established with the view to study stroke incidence and patterns in Southern Khorasan. This study reported a rise in incidence of stroke from 84.16 to 103.23/100 000 population per year from 2001 to 2005. No substantial temporal changes in stroke types/subtypes are reported.[65]

Israel: The National Acute Stroke Israeli (NASIS) registry has recently published their results on 6279 patients with stroke from 28 hospitals across the country.[40] There has not been much change in stroke type/subtype proportions from 2004 to 2010. The authors also report a significant decline in the proportion of small vessel strokes in elderly subjects (>85 years of age) from 2004 to 2010.

Having reviewed the stroke data from individual countries, the following observations can be made. There is lack of robust epidemiological data from most Asian countries. There is an increase in absolute number of stroke cases, although the incidence of stroke has come down in countries such as Japan. Ischaemic strokes are the predominant subtype in all countries and increasing in relative proportion. Haemorrhagic strokes have in the past accounted for more than a third of all strokes in Asian countries, particularly in East and South Asia. However, they have decreased in proportion over time. Large artery atherosclerosis is the predominant aetiology in most East Asian, South East Asian and South Asian countries.

Atherosclerosis is, in most cases, affecting the intracranial vasculature and is suggested to be the most common cause of stroke in Asians.[66] There are some data to suggest the high and rising burden of cardioembolic strokes, particularly from China and the Middle East.[67]

Gender differences

Differences exist between men and women in terms of risk factors and stroke prevalence in Asian countries. A recent study from Korea found more atrial fibrillation in Korean women with stroke compared with men in all ages, and more diabetes in women greater than 65 years of age.[68] The risk factors in younger women particularly during pregnancy and puerperium are different. This region probably represents highest prevalence area of pregnancy and postpartum stroke.[69] A prior study by our group demonstrated that among pregnancy-related strokes in women from five Asian countries, cortical venous thrombosis accounted for almost half of all cases.[69] Gender differences exist in terms of stroke outcomes also. A recent study from China[70] demonstrates many gender differences, the most significant of which was a higher dependency level at 1 year postischaemic stroke among women compared with men. Stroke in women is poorly reported in South Asia. Stroke is the leading cause of death in women above age 60 years in South Asia.[71]

Mean age at stroke onset and young stroke

The mean age of stroke in some Asian countries (Pakistan 59 years; China 60 years; India 63 years) is less compared with the Western countries (USA 68 years; Italy 71 years).[4] There are data to suggest that the onset of stroke and ischaemic heart disease is almost 10 years earlier in this region.[4] A population-based study carried out in Masshad (Iran) in 2006[18] reported that ischaemic strokes were occurring one decade earlier than in the Western countries. Some of the Indian studies have shown that about 10–15% of strokes occur in population below the age of 40 years.[72] Prasad *et al*[73] have reviewed data from Indian studies on young stroke, and they conclude that although traditional risk factors are also quite abundant in this age group, cardioembolic, venous and cryptogenic stroke make up a substantial proportion of all strokes. Wasay *et al*[5] describe strokes in young women from eight Asian countries and report cortical venous thrombosis as the predominant cause of stroke in this group. Large artery atherosclerosis and cardioembolism were the other important causes identified in this study. From Taiwan, Lee *et al*[74] found other determined and undetermined aetiologies to make up a significant proportion of stroke in the young with small vessel and cardioembolism being other important causes. Ghandehari reports cardioembolism as the proximate aetiology in 54% of young Iranian patients with stroke.[75]

CONCLUSION

Pattern of stroke in Asia shows geographical diversity and is evolving with time. The absolute burden of the condition is rising, and measures need to be taken to address risk factors for atherosclerosis, which is the predominant mechanism of stroke in this region. There is need for sound epidemiological data from most countries to understand the disease better and plan policy-level interventions to decrease the burden. We identify a need for standard format or guidelines for conducting stroke epidemiological studies especially in developing Asian countries. Future research should focus on better epidemiological studies to gauge the true burden of the condition. Comparative studies between various Asian regions may help elucidate mechanisms of stroke that are specific to race and ethnicity. Global burden of stroke and stroke-related deaths cannot be substantially reduced without interventions in Asia, especially in South Asia and China. This region must be identified as a priority region for stroke-related interventions and preventive strategies by the WHO, World Stroke Organization (WSO) and other global healthcare authorities and organisations. We propose that the WSO or Asia-Pacific Stroke Organization should develop and publish these guidelines. Standardisation of future stroke epidemiological research across Asian countries should become a priority area for stroke researchers and organisations in Asia. This will definitely lead to a better understanding of stroke epidemiology in this region.

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