STROKE IN INDIA: ARE WE DIFFERENT FROM THE WORLD?

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Like all developing countries, stroke is fast emerging as a major public health problem in India.[1] Population-based estimates confirm a rising trend in both incidence and prevalence of stroke in India. These results are in contrast to data reported from western countries.

RISING INCIDENCE

The first population-based study in India to determine the incidence of stroke was conducted in the southern Indian town of Vellore in 1969-71, where a population of 258,576 in and around Vellore was kept under surveillance for two years. An incidence of 13 per 100,000 per year was obtained.[2] Soon thereafter, another study was carried out in the northern Indian town of Rohtak, Haryana, during 1971-1974. This was part of a World Health Organization (WHO) collaborative study involving 17 centers from 12 countries, aimed at collecting comprehensive and reliable data on cerebrovascular disease in various parts of world.[3,4] Case ascertainment was made using several overlapping sources of information by local doctors, regular inspection of local health center records, and examination of death certificates. An annual incidence of 33 per 100,000 (27 per 100,000 for first-ever strokes), was recorded. No incidence survey was reported in India for the next 30 years, until a survey from Kolkata in eastern India reported an age -adjusted annual stroke incidence of 105/100,000.[5] A recent community survey in Kolkata, carried out very methodically by the Indian Council of Medical Research, showed the average annual incidence of stroke as 145 per 100,000 persons per year.[6] This is the first survey that reported local stroke rates similar to or higher than many Western nations. These rates are also much higher than those reported previously from other parts of India. Incidence rates reported from other Asian countries have varied from 29/100,000 in Sri Lanka; 68/100,000 in Mongolia; and 370/100,000 in China, to as high as 523/100,000 in Jaboji, Japan.[7,8] Incidence rates previously reported in the western literature have been higher than reported from India, although these have declined from 146/100,000 in 1945-1949 to 81/100,000 in 1975-1979 (see Table1).[7-12] It is therefore clear that stroke incidence in India has been registering an upward trend in the last few decades, while the incidence of stroke in western countries has declined or plateaued.[12]

RISING PREVALENCE

Analysis of community surveys from different regions of India shows a crude stroke prevalence rate of about 203 per 100,000 population above 20 years of age, amounting to a total of about 1 million cases.[6] The male-to-female ratio was estimated to be 1.7.[6] However, a recently reported community survey[6] in Kolkata revealed a stroke prevalence rate of 545 per 100,000 population, which is equal to or higher than that reported from developed countries.[9-11] Interestingly, there is a marked difference in the reported prevalence rates between various countries and even across communities within the same nation. For example, in India the reported crude stroke prevalence has varied from 57/100,000 in Vellore (southern India), 45/100,000 in Rohtak (northern India), 143/100,000 in shepherds and cultivators in Kashmir (northern India), 147/100,000 in Kolkata (eastern India), and 222/100,000 in Hindus of Bombay (western India), to 843/100,000 in Bombay's Parsi community (Table 2).[11,13-16] Similarly, the point prevalence from two different cities in China, estimated within a span of 2 years, was found to vary from 620/100,000 to 1,188/100,000 population,[17,18] and from 398/100,000 to 3540/100,000 in Japan.[10,11] In Bangkok, the prevalence rate of stroke was found to be 690/100,000 population.[19] The point prevalence of stroke in USA has been reported to range from 612 to 1070/100,000.10 Table 3 is an overview of point prevalence of cerebrovascular disease per 100,000 population in various countries.[7] Variation in stroke prevalence even within the same country may be due to actual differences,

TABLE 1

Average crude annual incidence rate (per 100,000 population) from various countries

Study	Reference number	Year	Crude Incidence rate
Rochster (USA)	(12)	1945-1949	146
Rochster (USA)	(12)	1975-1979	81
Auckland (Newzealand)	(54)	1981-1982	94
Shibata (Japan)	(10)	1976-1978	142
Benghazi (Libya)	(55)	1983-1984	100
Oxford (UK)	(56)	1981-1982	101
Beijing (China)	(10)	1980-1981	370
Zerifin (Israel)	(10)	1971-1974	140
Colombo (Sri Lanka)	(10)	1971-1974	29
Rohtak ,(India)	(11)	1971-1974	33
Vellore (India)	(3)	1969-1971	13
Kolkata (India)	(5)	1998-1999	105
Kolkata (India)	(6	2003-2005	145

as some areas can have a higher stroke prevalence than others, popularly referred to as "stroke belts", as found in the southeastern United States.[20] However, the variation may also represent methodological differences, as well as time trends, as the surveys have been conducted at different points in time. It is thus obvious that stroke prevalence in India has been steadily rising in the last few decades and is particularly high in elderly patients.[6]

EXPLANATIONS FOR LOW STROKE INCIDENCE AND PREVALENCE IN EARLIER STUDIES

Average life expectancy for Indians is lower than that of American, European and Japanese populations, which excludes the population at highest risk for stroke, thereby bringing down the prevalence rate. This was confirmed in the Rohtak Study where, despite the low overall incidence of 33/100,000, it was 356/100,000 (over ten-fold higher) in patients 70 years of age or older.[11] Recent community surveys for stroke in India identified 320 cases in 145,456 persons, indicating a crude prevalence rate (CPR) of 220/100,000 population. For the elderly (55-65 years) population in the same study, the CPR was 700 per 100,000.[14] It is possible that the predominantly young population of India dilutes overall stroke prevalence. This is also reinforced by stroke estimates among the Parsis of Bombay, a well educated and generally prosperous community with a relatively long life span, whose crude stroke prevalence was found to be 843/100,000.15 Another reason for low stroke prevalence in India could be because prevalence misses those who died from stroke.[12] As stroke mortality in India is expected to be high given inadequate medical facilities, the prevalence figures might be an underestimate. However, with increased longevity and better medical care, prevalence is fast rising and matching western figures.[6]

STROKE RISK FACTORS IN INDIA

By and large, risk factors for stroke are similar all over the world. Epidemiological studies in India have found hypertension, diabetes and cigarette smoking as the leading risk factors for stroke.[17-19] In 1989, the Indian Council of Medical Research (ICMR) sponsored a multi-center prospective case-control study on risk factors in cerebral infarction in different regions of India. A standardized, pre-tested protocol was used for collecting baseline and follow up data with well defined inclusion and exclusion criteria. Hypertension, diabetes mellitus, tobacco use and, interestingly, low concentration of hemoglobin were the most important risk factors for ischemic stroke, for both sexes, and in the young as well as the elderly.[21] Also in 1989, a WHO task force report on stroke found hypertension, smoking, elevated blood lipid levels, and diabetes, as important modifiable risk factors for ischemic stroke in India.[22] A study from Chennai in southern India revealed similar observations on hypertension, heart disease of any type, diabetes mellitus, smoking, and low HDL-cholesterol as significant risk factors.[23]

Most studies carried out in India show that about 10% to 15% of strokes occur in the population below 40 years, which is a higher proportion compared with other countries.[16,23] This could be due to many local etiological factors. Many years ago, causes contributing to stroke in

TABLE 2

Crude prevalence rate of cerebrovascular disease, as assessed by surveying for hemiplegia. [8]

Zones	City/Area	R/U/SU	Total subjects	PR/ 100,000	AA
North	Kashmir	R	63,645	145	74
	Rohtak	U	79, 046	44	46
	1975/1988	R	51,165	23	45
	Ballabhagarh	R	4,786	125	NA
West	Bombay	U(Parsi)	14,010	843	424
	Bombay	U	5,723	245	NA
	Bombay	U	318,552	222	NA
	Bombay14	U	145, 456	220	NA
South	Vellore	R	258,576	57	84
	Gowribidanur	R	57, 660	52	NA
East	Bengal (Malda)	R	37,286	126	NA
	Bengal (Calcutta)[5]	U	50,291	147	334
	Bihar (Chotanagpur)	R	5,806	103	NA
	Assam (Guwahati)	SU	14,200	270	NA
	Bengal(Kolkata)[6]	U	52,377	495	535

Abbreviations: R, Rural; U, Urban; SU, Semiurban; PR, Prevalence rate; AA, Age-adjusted to US population

the young were reported as meningo-vascular syphilis in men, puerperal cerebral venous thrombosis in women, and rheumatic heart disease in both sexes.[24] A disturbed equilibrium in coagulation and fibrinolysis has been suggested in the pathogenesis of non-embolic cerebral infarction in the young.[25] Other studies have incriminated subacute tubercular meningitis with arteritis, or autoimmune angiitis, as an important risk factor in India.[26] More recently reported risk factors among the young include viper envenomation, elevated lipoprotein(a) levels, and elevated anticardiolipin antibodies.[27-29] A recent Indian study has suggested that squatting during toilet use, common throughout India, raises blood pressure and could be an important triggering factor for stroke.[30]

STROKE SUBTYPES IN INDIA

There is insufficient information on the proportion of ischemic and hemorrhagic strokes from India, as most studies have not included neuroimaging. However, in our own stroke database of 1500 patients at Nizam's Institute of Medical Sciences in Hyderabad, 85% patients have ischemic stroke. In a population-based study done in Kolkata, infarction was found in 68% of cases.[6]

Many studies have shown that there are significant racial-ethnic differences in the distribution of atherosclerosis lesions leading to ischemic stroke.[31-39] Chinese,[31-33] Japanese,[34,35] Hispanics, and blacks [36,37] have a greater preponderance of intracranial atherosclerosis than whites. There is not much data on stroke subtypes and their risk factors from India, as most stroke patients are not fully investigated due to various reasons. Even those who are investigated are not generally enrolled in systematic registries for publication in the medical literature. A well-organized stroke registry can provide much information and insight into these problems.[39-41] For the past few years, the stroke registry at Nizam's Institute of Medical Sciences has been studying various stroke subtypes in India and their associated risk factors. Based on our experience of three years, intracranial large artery atherosclerotic disease seems to be the most common stroke mechanism in India, followed by lacunar, cardioembolic, and extracranial carotid disease, respectively.[42,43] Two earlier studies from India, one based on conventional angiography and the other on magnetic resonance angiography (MRA) also reported a high frequency of intracranial lesions.[44,45] Interestingly, while intracranial disease is very uncommon in the West (<5%) and extracranial carotid artery disease is uncommon in Far Eastern countries such as China and Japan (<5%), both vascular patterns are fairly well represented in Indian stroke patients and this may be called the "Indian pattern." Common risk factors for the development of large- and small-artery disease are similar and constitute hypertension, diabetes, and smoking.[46] No significant differences have been found in risk factors between extra- and intra-cranial large artery disease.[47] For cardioembolic stroke, rheumatic heart disease and ischemic heart disease seem to be the dominant risk factors in India.[48]

STROKE MORTALITY

WHO estimated that in 1990, out of a total of 9.4 million deaths in India, 619,000 were due to stroke. This gives a stroke mortality rate of 73 per 100,000 (estimated total population 849 million). For comparison, this figure is 22 times the number of deaths from malaria, 1.4 times that due to tuberculosis, 4 times that due to rheumatic heart disease, and almost equal that due to ischemic heart disease.[49] It is believed that 1.2% of total deaths in India are due to stroke. Compared with developed nations, stroke mortality rates among Indians have been found to be two to three times higher, suggesting thereby that Indians are at a higher risk of stroke-related death than Caucasians.[50] The greater susceptibility of Indians to stroke has also been found in a study of Indians settled in

TABLE 3

Cerebrovascular disease – point prevalence rate per 100,000 population. [10]

Location	Years	Crude	Age-adjusted (US)
Honolulu, Hawaii, USA	1967-1970	1,070	NA
Rochester, USA[12]	1970	612	NA
Hiroshima-Nagasaki, Japan	1973	3,540	NA
Hisayama, Japan	1961	398	569
Jaboji, Japan	1971	2093	2071
Beijing, China	1981	1188	1285
Six cities, China	1983	620	719
Bangkok ,Thailand	1983	690	NA
Taiwan	1988	1,642	NA
India (Vellore)	1968-1969	56.9	NA
India (Overall)[6]	2001	203	NA

the United Kingdom.[51] In this report, immigrants to England and Wales from the Indian subcontinent had a higher risk of dying due to stroke (53% higher for males and 25% higher for females) than the average local population. Reasons for the increased susceptibility of Indians to stroke are not clear. However, a study from Bombay has reported a significant drop in case fatality rates for all strokes (from 32% to 12%), resulting in higher rates of survival (68% to 88%).[52] There is a need to initiate steps to collect data on morbidity and mortality due to stroke in the country, as a first step towards control measures.[47]

LONG-TERM OUTCOME

Not many studies have been done to address this question, but limited data suggests that recurrence may be higher in India due to poor compliance with treatment and control of risk factors.[53] Functional outcome in Indian patients has also been reported to be poor. Among stroke survivors, only about one-third are fully independent in their daily activities of living while more than one-fourth cases are bedridden. Poor outcome in functional recovery is likely due to lack of rehabilitation and related treatment facilities.[53]

EPIDEMIOLOGICAL CHALLENGES

Earlier epidemiological stroke studies have suffered from shortcomings and inconsistencies. Because of variable case definition, data instruments, and methodology, it is possible that the observed variation in incidence and prevalence rates of stroke is an artifact attributable to sampling error, difference in study methodology, or changes in sample demography. Also, there is always potential for human error, especially as much of the data collection is done by non-specialist personnel. This highlights the need for extreme care and caution in training epidemiological data collectors and holding regular appraisals of the personnel involved.

STROKE SERVICES IN INDIA

Many parts of India lack organized stroke services. Government health planners have so far focused mainly on diseases related to infection and malnutrition. Secondly, low educational levels adversely affect risk identification, and compliance with steps for stroke prevention. In the last decade, about fifty stroke units have sprung up in various cities of India. However, the majority of Indians live in villages, where they cannot even afford or avail a CT scan of the brain. General practitioners provide most stroke-related care in India. Home and traditional treatment of stroke is also an accepted practice in the rural areas of India. Many strange culture-specific beliefs about stroke treatment are in existence; a popular one is that massage with fresh pigeon's blood can cure the paralysis.[27]

STROKE THROMBOLYSIS IN INDIA

Only in 2006 was tissue plasminogen activator (tPA) approved for use in acute ischemic stroke in India. At present, approximately 15 stroke units in India use tPA. Thus far, approximately 400 patients have received intravenous tPA in different centres across the country.

Intrarterial thrombolysis therapy is being used in approximately 10 centers in India with good results.[27] Most centers are in the private sector, although some public sector university hospitals have also been running successful thrombolysis programs. Barriers towards stroke thrombolysis are due to lack of infrastructure, lack of awareness, and poor affordability. However, it is clear that hyperacute thrombolysis in acute ischemic stroke is feasible in urban private and public sector tertiary hospitals, and can be widely used if a greater number of dedicated stroke teams and stroke units become available, and the cost of drug is reduced.

CONCLUSIONS

The last few decades have seen a rise in the incidence and prevalence of stroke in India, attributable to increasing life span, urbanization, and better survival, and the rates are now matching western figures. Hypertension, diabetes and smoking are the three major risk factors for stroke in India, as elsewhere. Low hemoglobin and low HDL cholesterol have also been identified as risk factors. Stroke in the young constitutes a higher proportion of stroke patients in India than in other countries, possibly due to the age structure of the population, and also perhaps from a preponderance of risk factors including infections, rheumatic heart disease, and cerebral venous sinus thrombosis. Ischemic heart disease is emerging as a major cardiac risk factor for ischemic stroke in India, while rheumatic heart disease continues to be a significant risk factor. As in most parts of the world, ischemic strokes predominate over intracerebral hemorrhage in India. Among ischemic strokes, intracranial atherosclerosis is the major stroke mechanism, although all other stroke mechanisms also contribute to stroke. Stroke is expected to assume epidemic proportions in India in the coming years and will strain its already limited health care infrastructure. Public education and strict control of risk factors at a primary care level is the most appropriate strategy for India to meet the growing challenge of stroke.

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