Review Article

Fifty years of stroke researches in India

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Abstract

Currently, the stroke incidence in India is much higher than Western industrialized countries. Large vessel intracranial atherosclerosis is the commonest cause of ischemic stroke in India. The common risk factors, that is, hypertension, diabetes, smoking, and dyslipidemia are quite prevalent and inadequately controlled; mainly because of poor public awareness and inadequate infrastructure. Only a small number of ischemic stroke cases are able to have the benefit of thrombolytic therapy. Benefits from stem cell therapy in established stroke cases are under evaluation. Presently, prevention of stroke is the best option considering the Indian scenario through control and/or avoiding risk factors of stroke. Interventional studies are an important need for this scenario.

Key Words

Burden of illness, outcome, pathology, risk factors, treatment and genetics

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Introduction

Worldwide, stroke is the commonest cause of mortality after coronary artery disease. Also, it is the commonest cause of chronic adult disability. The lifetime risk of stroke after 55 years of age is 1 in 5 for women and 1 in 6 for men.[1] More than four-fifth of all strokes occur in developing countries. This article aims to provide an overview of stroke disorder in India as derived through studies from 1968 to the present time.

Literature Search Strategy

We searched PubMed from 1968 to January 2015 with the words "stroke", "India", "population-based", "incidence", "prevalence", "case-fatality", "risk factors", "genetics", or "disability-adjusted life year". Relevant articles were also searched in the national journals, namely, Neurology India, Annals of Indian Academy of Neurology, Journal of Association of Physicians of India, Journal of Indian Medical Association, and Indian Journal of Medical Research.

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Epidemiology

Prevalence of stroke

The first community-based study of stroke was carried out in and around the town of Vellore, South India, between 1968 and 1969.[2] The second one was conducted in Rohtak, North India, during 1971-1974.[3] The very low prevalence rates (PRs) of stroke in these studies [Table 1] led to the belief that stroke was less frequent in India than in the Western countries. During the 1980s and 1990s, a spate of surveys was conducted in various parts of the country in both urban and rural communities [Table 1].[4-13] These surveys demonstrated that the crude PRs ranged from 1.27 to 2.20 per 1,000 persons. On the contrary, the study among the Parsis in Mumbai showed a substantially higher PR.[6] The divergence in rates could be due to the widely different age compositions of the populations studied. Age standardization with the US population as reference, used in some of these surveys, showed the PR between 2.44 and

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4.24 per 1,000. The somewhat higher age-standardized PR among the Parsis could be attributed to their distinct ethnicity. The age-standardized PRs used in the above surveys [Table 1], however, are not strictly comparable because the standardized populations themselves vary. Ideally, the standardization of epidemiological rates from non-North American and non-European populations should be calculated on the basis of the world standard population (WSP),[14] which represents a population age structure of third world countries. The community study on stroke conducted in the metropolitan city of Kolkata during 2003-2004 showed the crude PR to be 4.72 per 1,000 (men, 4.96 per 1,000; women, 4.44 per 1000; 95% confidence interval (CI), 4.15-5.34).[11] When age was standardized to the WSP, the PR was 5.45 per 1,000 (95% CI, 4.80-6.17) indicating there will be about five to six cases per 200 families considering on an average five members per family.

Incidence rates of stroke

Only a few surveys were conducted in India where annual incidence rates (AIRs) of stroke were determined. They are listed in Table 2. Studies prior to 2003 included only stroke survivors (SS) and not stroke death cases.[3,9,10] Additionally, these earlier studies included recurrent stroke cases and there were paucities of information about AIR of first-ever-in-a-lifetime stroke. On the other hand, the Kolkata study[11] captured for the first time both the SS and stroke-related deaths. The AIR of first-ever stroke therein was 123.15 per 100,000 (men, 99.54 per 100, 000; women, 149.49 per 100, 000) persons per year (95% CI, 102.46-232.50; age-standardized rate to the WSP, 145.30; 95% CI, 120.39-174.74). Subsequently, prospective population-based stroke registries were reported from Mumbai[15] and from Trivandrum.[16] The Mumbai study reported AIR of 148 per 100,000 persons (95% CI, 120-170); when age standardized to the Segi's 1996 world population, the AIR was 154 per 100,000.[15] Age-standardized AIRs in Trivandrum study[16] per 100,000 were 135 (95% CI, 123-146) for total, 135 (95% CI, 122-148) for urban, and 138 (95% CI, 112-164) for rural populations. The age-standardized AIRs were 74.8 (95% CI, 66.3-83.2), 10.1 (95% CI, 7.0-13.2), and 4.2 (95% CI, 2.2-6.1) for ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage, respectively. The AIRs of stroke in India, as observed in the Kolkata, Mumbai, and Trivandrum studies are higher than that in United States (107 per 100,000 per year),[17] European countries (61-111 per 100,000 per year),[18-21] and Australia (99 per 100,000 per year);[22] but similar to that reported from one Chinese city (Changasha).[23]

Mortality in stroke

Stroke is one of the leading causes of death in India. Joshi *et al*.,[24] determined mortality due to chronic diseases through verbal autopsy in a population of 180,162 residing in 45 villages of Andhra Pradesh. Stroke was the cause of death in 13% very similar to death due to coronary artery disease (14%).[24] The 30-day case fatality rate (CFR) in Kolkata[11] was 41.08%

Table 1: Prevalence (PR) of stroke in major Indian studies

Place	Rural/urban	Year	Population, *n*	PR per 1,000*	AS-PR per 1,000
North Rohtak, Haryana[3]	Urban	1971–1974	79,046	0.44	
Kuthar Valley, Kashmir[4]	Rural	1986	63,645	1.43	2.44#
Ballabgarh, Haryana[5]	Rural	1986	48,798	0.88	
West Mumbai (Parsis)[6]	Urban	1985	14,010	8.42	4.24#
Mumbai[7]	Urban	1997	145,456	2.20	
East Malda, WB[8]	Rural	1989-1990	37,286	1.26	
Baruipur, WB[9]	Rural	1992-1993	20,842	1.47	
Kolkata[10]	Urban	1998-1999	50,291	1.47	3.34‡
Kolkata[11]	Urban	2003-2004	52,377	4.72	5.45†
South Vellore[2]	Rural	1968-1969	258,576	0.57	
Gowribidanur, Karnataka[12]	Rural	1982-1984	57,660	0.52	
Bangalore[13]	Rural	1993-1995	51,055	1.65	2.62¹
Bangalore[13]	Urban	1993-1995	51,502	1,36	

PR = Prevalence rate, AS-PR = age-standardized PR, WB = West Bengal. *Crude PR, #US population of 1960, ‡US population of 1996, †world standard population, ¹not mentioned

Table 2: Annual incidence rates (AIR) of stroke in India

Place	Rural/urban	Year	Population, *n*	AIR per 100,000*	AS-AIR per 100,000
Rohtak, Haryana[3]	Urban	1971–1974	79,046	33	
Kolkata[10]	Urban	1998–1999	50,291	36	105#
Baruipur, WB[9]	Rural	1993–1998	20,842	124	262†
Kolkata[11]	Urban	2003–2005	52,377	123	145.3‡
Mumbai[15]	Urban (age 25–94+)	2005–2006	156,861	148	154¹
Trivandrum[16]	Urban	2005	741,307	116.4	135‡
Trivandrum[16]	Rural	2005	184,560	119.4	138‡

AS-AIR = Age-standardized AIR, WB = West Bengal. *Crude AIR, #US population in 1996, †US population in 1990, ‡age-standardized to world standard population, ¹Segi's world population of 1996

(men, 38.18%; women, 43.24%), significantly higher than that seen in the industrialized Western countries (17-33%).[17-20,22] Inadequacy of prompt medical care in the poor and lesion severity could be reasons for the high stroke-related case fatality.[21,25] Genetic factors might also be responsible because there is greater susceptibility and higher mortality to stroke among UK residents of Indian descent.[26] The rates are especially higher among women, perhaps because women outlive men (Census India, 2001) and exhibit higher prevalence of uncontrolled hypertension than men.[27] Incidentally, the 28-day CFR of stroke in Mumbai[15] was 29.8%. In Trivandrum, the 28-day CFRs were 24.5% for urban and 37.1% for rural populations.[16] Further analysis demonstrated that in the first 7-10 days of stroke, fatality occurs among 20% in Kerala and 33% in Kolkata.[28]

Stroke Subtypes and Etiologies

Based on neuroimaging findings, recent studies have determined the stroke subtypes and the ratio of cerebral infarct to hemorrhage range as 1.86:1-2.21:1.[10,11] Hence, cerebral hemorrhage is proportionately much higher in the Eastern Indian community than in Western countries, where the ratio of infarct to hemorrhage is 5:1. Suitable neuroimaging data were available only in 50-60% of cases in these surveys. Incidentally, the high incidence of cerebral hemorrhage also has been noted among Chinese.[23] The Kolkata study[11] demonstrated that the basal ganglia-thalamic region was, by far, the commonest site (75%) of hemorrhage. In contrast, the subcortical region was the commonest site of infarction (75.6%). This predilection for subcortical infarct also is common in other Asian races. A study based on noninvasive tests to determine subtypes of ischemic stroke from a hospital-based registry of Southern India has attributed 41% of strokes to large artery atherosclerosis, 18% to lacunar causes, 10% to cardioembolic causes, and 4% to causes such as Takayasu syndrome, MoyaMoya disease, carotid dissection, hyperhomocysteinemia, anticardiolipin antibody, and protein S deficiency. The rest 27% of the cases of ischemic stroke were of undetermined origin.[29] Among cardioembolic stroke, rheumatic heart disease (29%) and ischemic heart disease (27%) are predominant causes.[29] In a clinicoradiological study among young strokes,[30] the common site of arterial occlusion was the supraclinoid internal carotid artery, whereas, narrowing or occlusion of major neck vessels occurred in only 10.8% cases. Few other Indian studies trying to detect underlying vascular pathology have shown variable findings. An earlier study in the 1060s from western-central India based on conventional angiograms had documented significant stenosis and occlusion in extracranial vessels similar to that observed in the Western countries.[31] But studies conducted in the last decade in large academic centers from northern and southern India both have documented a high frequency of intracranial vessels affected on the basis of noninvasive vascular studies.[29,32] This is consistent with findings in other Oriental countries. The Indian Collaborative Acute Stroke Study (ICASS); a multicentric study conducted among 2,162 admitted stroke patients across southern, northern, and western India; observed ischemic stroke in 77%, hemorrhagic stroke in 22%, and unspecified stroke in 1% cases based on cerebral computed tomography (CT).[33]

Hence, in India, the pooled data incorporating all the studies reveal that ischemic stroke occurs in 68-80% and hemorrhagic stroke in 20-32%. Ischemic stroke comprise large vessel (41%), lacunar (18%), cardioembolic (10%), other determined (10%), and undetermined (20%) subtypes. The extracranial carotid disease is the etiological factor in 25-26% and intracranial carotid disease in 30% of ischemic stroke cases.[34]

Stroke in Young

Previous hospital-based data from India observed a high proportion of young stroke (first-ever stroke onset below 40 years of age), ranging between 15 and 30%.[30] In a recent study at All India Institute of Medical Sciences (AIIMS), out of the 2,634 patients admitted for ischemic stroke, 440 (16.7%) were in the age range of 18-45 years and majority (83.4%) were male.[36] However, this figure was biased because of preferential admission policy. In the well-designed population-based study,[11] 8.8% of stroke subjects were young, which is similar to that seen in Western countries.[35] In the late 1960s, however, a population-based study from Southern India found that 25% of stroke patients were less than 40 years of age, and this included young women with cerebral venous thrombosis (CVT) occurring in the postpartum stage.[37] CVT was found to be 12 times more common in India than in Western countries. An angiographically proven study reported that 50% of the total cases of stroke in young women were related to pregnancy and puerperium, 95% of which were due to CVT.[37] MoyaMoya disease, common among the Orientals, is also reported from India, but there is no epidemiological data or a large clinical series on it.[38] Takayasu's arteritis[39] is also often noted among Indians where the genders were almost equally affected. Stroke occurs in 40% of children and adolescents (4-15 years of age) with Takayasu's arteritis. The subclavian arteries are occluded more often than the carotids, leading to posterior circulation stroke.[40] Although tuberculosis is endemic in India, the disease in a prospective study of young stroke affected only 8% of subjects.[41]

In a hospital-based study of pediatric age group (1 month-18 years) from a tertiary center in northern India, majority cases were of acute ischemic stroke followed by intracerebral hemorrhage (12.7%) and CVT (8.9%).[42] The commonest etiology in cases with ischemic stroke were neuroinfections (40%), prothrombotic state (8%), arteriopathy (6.5%), arterial dissection (5%), miscellaneous (4.83%), and cryptogenic (21%). Only about 9% of subjects died.

In another study of younger subjects (18-50 years; mean age, 41.6 years) with hemorrhagic stroke from the same center has been studied.[43] The subjects were predominantly male. The important risk factors were hypertension (57%), hypocholestreomia (34%), alcohol (15.5%), and anticoagulants (3.5%). Underlying etiologies were hypertension (79%), vascular malformation (4%), coagulopthay (4%), CVT (2%), thrombocytopenia (0.7%), vasculitis (0.5%), and cryptogenic stroke (9%). About 2.5% subject died and only 35% had good outcomes. Overall outcome was related to volume of intracerebral hemorrhage, Glasgow Coma Scale, and leukocyte count on admission.

Risk Factors

Age is an important nonmodifiable risk factor for stroke. The mean age of stroke onset in India (i. e., 63 years) is lower than that in Western countries (68 years in the USA and 71 in Italy).[34] This is due to inadequate control of the common modifiable risk factors and also due to added existence of nontraditional risk factors. There were several studies in India determining risk factors of stroke. A multicentric, hospital-based, case-control study in the 1990s revealed that diabetes mellitus, hypertension, tobacco use, and low hemoglobin, rather than cholesterol level, were the most important risk factors of ischemic stroke.[7] Sridharan[44] analyzed the risk factors of ischemic stroke including patients of all age groups. Hypertension, electrocardiogram (ECG) abnormality, heart disease of any type, diabetes, smoking, and alcohol were associated with stroke. Low high-density lipoprotein (HDL) and elevated low-density lipoprotein (LDL):HDL ratio was observed among stroke patients.[44] The major risk factors identified in a recent North Indian study were hypertension (a diastolic blood pressure >95 mmHg), hyperglycemia, tobacco use, and low hemoglobin levels (<10 g%).[45] Another community-based study on biochemical risk factors from North India among urban, rural, and semiurban people has documented elevated levels of fasting blood glucose, cholesterol, triglycerides, and low HDL with urbanization.[46] A case-control study from the same region has produced similar results and documented low consumption of fruits and vegetables, sedentary lifestyles, and psychological stress as contributory factors.[47] A study from south India on young stroke found smoking, elevated systolic blood pressure, diabetes, and lower HDL cholesterol as important risk factors. The presence of at least or more than three metabolic syndrome components were associated strongly with stroke compared with hospital and community controls.[48] Another recent data revealed that diabetes mellitus, hypertension, heart disease, current smoking, and long-term heavy alcohol consumption are major risk factors for stroke in young adults as in elder population.[49] Gunaratne *et al*., observed that South Asians living in UK are known to have an atherogenic lipid profile, which includes raised triglycerides, low HDL cholesterol, and raised lipoprotein a levels.[50] Incidentally, several hospital-based and community-based studies have identified hypertension as the most important risk factor.[7,10,45,51-53] All these studies indicate the importance of controlling hypertension and biochemical risk factors and avoiding smoking. The pattern of tobacco consumption is commoner among less educated persons by nearly 2.69 times and prevalent among families with lower socioeconomic stratum.[54] India faces a double burden of tobacco exposure, with 15-20% prevalence of smoking and up to 40% of people having the habit of chewing tobacco. A large number of those who chew tobacco are women.[34] Among women of advanced age, the high incidence and case fatality of stroke had a strong correlation with the high prevalence of hypertension.[11,27] This indicates that less attention is paid to women's health in this country with insufficient control of hypertension.[10] Trigger factors were present in 44.2% of acute stroke patients. Psychological stress (17.6%), acute alcohol abuse (10.7%), and clinical infections (8.3%) were the most common triggers.[55] In a study in the 1980s, the important predisposing factors for CVT were thought to be poor socioeconomic status and consumption of illicit liquor.[56] A recent data on CVT revealed anemia, hyperhomocysteinemia, alcoholism, oral contraceptive use, and postpartum state as the most common risk factors.[57] Several epidemiological studies showed some association between atherosclerosis or cardiac disease and past infection with *Chlamydia pneumoniae* (*C. pneumoniae*),[58-61] raising the possibility that infection-related immune reaction is the trigger for acute stroke. A study from south India found significantly elevated *C. pneumoniae* immunoglobulin A (IgG) and IgA antibodies in acute ischemic stroke with hyperhomocysteinemia.[60] Another study, this time from north India, demonstrated association of IgA antibodies to *C. pneumoniae* in patients with acute ischemic stroke.[61] However, large-scale prospective studies are required to prove the causative role of *C. pneumoniae* in acute stroke.

Outcome of Stroke

According to recent studies, 55-70% of SS become fully independent by 1 year and 7-15.7% remained completely disabled.[11,51] Prominent residual spasticity was noted in 46% of cases; it was severe in one-third cases.[53] Among those who had speech dysfunction, complete recovery was reported in 47% of cases, and there was no improvement in 12%.[38] Post-stroke seizure was observed in about 2% of cases.[11] The low incidence of post-stroke seizure may be related to predominantly subcortical involvement. A comprehensive 4-year prospective study on SS was conducted in the city of Kolkata from 2006 to 2010. Early fatality among a cohort of stroke affected subjects was higher compared to developed countries. About 70.45% of death was primarily due to index stroke and 19.27% due to recurrent stroke. The rest were due to other causes. After 5 years, the fatality become similar to developed countries such as Sweden, Denmark, and Australia; indicating affected subjects prefer secondary preventive measure than primary prevention.[28] In that study, approximately one-third developed post-stroke depression (PSD), similar to developed countries. Delayed peak of PSD suggested later realization of underlying disability.[62] The period PR of post-stroke mild cognitive impairment (MCI) was 6.05% at baseline, and 10.6% of the former converted to post-stroke dementia annually. Survival analysis showed a greater risk of death of post-stroke dementia patients as compared to non-demented SS (hazard ratio, 2.65; 95% CI, 1.72-6.15).[63] SS of female gender and with neuropsychiatric disturbances had poor functional outcome, while education correlated with better outcome.[64]

Burden of Illness of Stroke

For chronic illnesses; only prevalence, incidence, and mortality data are not enough to express burden of illness, since disability from the disease is also an important burden parameter. The disability-adjusted life year (DALY) is currently the most important time-based measure of burden of a chronic disease incorporating both disability and mortality. According to the global data from 2004 covering 192 World Health Organization (WHO) member countries, the stroke-related DALY loss ranged from 160 per 100,000 person-years in the Seychelles to 2,192 per 100,000 person-years in Mongolia. During that period, the stroke-related DALY loss in India was 597.6 per 100,000 person-years.[65] However, direct derivation of DALY from our stroke database demonstrated that overall DALYs lost due to stroke were 795.57 per 100,000 person-years (730.43 in men and 552.86 in women).[66]

The old incidence-based approach for DALY estimation was used in the above data. Prevalence-based global burden of disease (GBD) study 2010 methodology is now considered to be more comprehensive for DALY calculation and should be utilized in future studies.[67]

Public Awareness Regarding Stroke

Warning symptoms of stroke

In India, awareness of the warning symptoms of stroke among general public is far from satisfactory. Surveys in the last decade revealed that about one-fourth of the urban and one-third of rural respondents who were unaffected had no knowledge of any warning symptom of stroke. Only 55% of the urban population was aware of one warning symptom of stroke; 16.2% were aware of two symptoms; and only 6.2% could identify three symptoms. Analysis has shown that improved socioeconomic status and higher education raise awareness of the warning symptoms of stroke for both rural and urban subjects.[68-69]

Compared to above mentioned studies, the recent survey reveals no meaningful improvement of knowledge among general public regarding stroke, and hence there is an urgent need for stepping up awareness drive in our country.[70]

Hospitalization and transportation

Poor recognition of early stroke symptoms and low perception of threat lead to delayed arrival of stroke subjects at hospitals; only one-fourth arrived within 6 h. In a major urban center, the median time to casualty arrival was 7.66 h, with 25% of cases arriving within 3 h and 49% of cases arriving within 6 h. Distance from hospital, contact with a local doctor, and low threat perceptions of symptoms were independent factors for delay in arrival.[71] A rural-based study documented that the mean arrival time of stroke patients was 34 ± 6 h.[68] The arrival time was influenced by distance from the hospital, education, socioeconomic status, family history of stroke, and advice of friends and local doctor. Transportation of stroke subjects is an important issue in management. Poor availability of transport in rural areas and congestion in urban areas are considered constraints or barriers to immediate hospitalization and initiation of treatment.[72-73] A hospital-based study from northwest India has documented that only 12% of patients came by ambulance.[74]

Treatment in Stroke

Because of cost of therapy and delayed hospital admission, thrombolytic therapy (recombinant tissue plasminogen activator (rtPA)) has been possible in only a very small number of acute ischemic stroke cases in India. Padma *et al*., published a paper in 2007 about their 4-year experience on 54 ischemic stroke cases with rtPA.[75] Due to availability of a small available "therapeutic time window", they were administered rtPA without their coagulation profile being checked; still the outcome has generally been good. In our country, where all the investigations are not readily available, a modified approach to thrombolytic therapy is warranted. Over the years, the utilization of rtPA has increased all across the country, but the use is restricted only to urban centers. At present, in India there are approximately 100 centers which are able to provide intravenous rtPA treatment and 55 centers capable of performing intra-arterial or mechanical thrombolysis.[76] Stroke unit has a multidisciplinary team comprising medical, nursing, physiotherapy, occupational therapy, speech therapy, and social workers. It has been amply demonstrated that patients treated in stroke units have substantially better outcome of acute stroke. In India, there are about 35 dedicated stroke units and that too available in private hospitals mainly.[76] There is an urgent need to set up quite a number of such stroke units across the country. India is the hub for generic pharmaceutical industries and antiplatelets, antihypertensives, antidiabetics, statins, etc., are readily purchasable over-the-counter. Monitoring of oral anticoagulant therapy is a major problem for cardioembolic stroke in India. The monitoring facilities exist mainly in city-based hospitals and laboratories. Newer oral anticoagulants are used mainly for rich patients who could afford.[76] Unfortunately, there are many poor people in our country who cannot afford even the common stroke-related medications. Rehabilitation in India relies heavily on physiotherapists. Till 2011, there were 32,800 physiotherapists registered in Indian Association of Physiotherapists, 3,000 occupational therapists registered in Indian Association of Occupational Therapists, and 1,700 speech therapists registered in Indian Association of Speech Therapists. Only a very few centers have organized in-hospital and outpatient rehabilitation facilities in the country. Untrained or half-trained physiotherapists fill this very large lacuna in our stroke rehabilitation.[76] One study has shown that more than one-third of the SS opted for complimentary or alternative medicine. This included ayurvedic massage, intravenous fluids, herbal medicines, homeopathy, witchcraft, acupuncture, opium intake, and other nonconventional treatments.[77]

Stem Cell in Ischemic Stroke

There is potential benefit of stem cell in chronic ischemic stroke.[78-79] It is postulated that stem cells operate not only through forming neurons at the infarct zone, but rather as cellular mediators of many of biological mechanisms that could provide a favorable recovery of neurological disease. In AIIMS, Delhi, a study was conducted using autologous mononuclear stem cell (MNC) transplantation in patients with chronic ischemic stroke using clinical scores and functional imaging. The rationale was that the intravenously administered stem cells will help in upregulation of growth factors within the body and brain making the host environment conducive for behavioral recovery in the form of 'learning'.[78] They observed that autologous bone marrow-derived MNC are safe in chronic ischemic stroke. MNC with physiotherapy regime in chronic ischemic stroke led to a trend of improvement in clinical and functional magnetic resonance imaging (fMRI) scores at 8 weeks as compared to physiotherapy alone and the changes lasted till 24 weeks.[80]

Role of stem cells in acute ischemic stroke

Open-label studies using autologous MNCs were transplanted in 11 subacute ischemic stroke patients within 1 week to 1 month.[81] Subjects were regularly followed-up till 1 year, based on standard clinical scales, neuroimaging (MRI and positron emission tomography (PET)), and electrophysiology (electroencephalography (EEG)). Favorable outcomes were

noticed in 64% of cases and no serious adverse events were documented.

Role of Tea

Worldwide, tea is the commonest beverage after water. A study from India has shown beneficial effect that tea consumption of 450 ml or more than or equal to three cups per day was associated with reduction of the incidence of recurrent ischemic stroke, significant decrement of systolic blood pressure, better control of fasting hyperglycemia, and lowering down of the level of total cholesterol and LDL level in subjects with hypercholesterolemia.[82]

Caregiving

Increasing stroke cases in India induces burden on caregivers (CGs) who are usually women. CGs' stress includes financial, physical, psychological, and family burden.[83] The stress is greater among slum dwellers and less educated families. Urinary incontinence, morbidity at 28 days, and moderate-to-severe neurological deficit on admission inflict major stress.[84] Other factors includes long care giving hours, anxiety, disturbed night sleep, financial stress, younger age, and female gender. In India, organized counseling for CGs is rare and it should be part of rehabilitation process.

Genetics of Stroke

Certain rare single gene disorders do lead to stroke in young individuals without known risk factors, and they include CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), Fabry's disease, sickle cell disease, etc.[85] However, in the common multifactorial stroke cases, genetic contribution is polygenic. Most human genetic studies have focused on polymorphic variants that promote stroke predisposing phenotypes or mediators. Several candidate genes have been found to be associated with stroke.[85] In India, relationships of some of these candidate genes with stroke disorder were determined in case-control studies. The association of *PDE4D* (a gene involved in inflammatory pathway) gene polymorphisms was investigated in a south Indian population.[86] Single nucleotide polymorphism (SNP) 83 showed significant association with two stroke subtypes; intracranial large artery atherosclerosis and small artery occlusion. In another case-control study, apolipoprotein E gene (gene involved with lipid metabolism) was evaluated in patients of stroke where high frequency of apo ε 4 allele (30% in cases and 11% in controls) was observed (odds ratio (OR) 4.2).[87] The authors concluded that presence of apo ε 4 allele along with elevated triglycerides, hypertension, and age could predict the development of stroke. Another case-control study revealed that angiotensin-converting enzyme (ACE) gene I/D polymorphism contributes to the risk of developing stroke, especially with intracranial large artery atherosclerosis.[88] MTHFR C677T mutations (MTHFR gene is involved with homocysteine metabolism) was found to be strongly associated with arterial stroke, especially in young onset stroke.[89]

Conclusion

In contrast to industrialized Western countries where there has been a steady decline in stroke over the past 30 years,[90] India is currently facing the challenge of a high stroke incidence. The major reason is that the common risk factors of stroke, namely, hypertension, diabetes, smoking, and dyslipidemia are not being adequately controlled. Public awareness in this regard is still quite poor in our society. Cardiovascular disease including stroke, which comprised 19% of death in India in 2001-2003, is estimated to rise to 36% by 2030. On 4th January 2008, the Ministry of Health has launched the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), which includes development of public awareness and improvement of logistic facilities right from the grassroot level to deal with the various noncommunicable diseases. The program, if implemented successfully, will achieve the WHO target of 25% reduction in cardiovascular disease and stroke by the year 2025.[91-92] However, at present, India needs more interventional studies to find out the efficacy of preventive agents such as antihypertensives and antiplatelets, and study on awareness and attitude of people from various ethnic groups.

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Conflict of interest

There are no conflicts of interest.

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