

Review Article

Stroke in Young in India

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Stroke in young has special significance in developing countries. This is so because some etiologies like cardioembolic infections are more common than in developed countries, and the affection of economically productive group adds further to the overall disease burden. The paper discusses the burden of stroke in young and its implications in a developing country like India along with an approach to identifying different causes that are known to occur in this age group.

1. Introduction

Stroke in young poses a major health problem. WHO defines stroke as an event caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue [1]. The most common symptom of a stroke is sudden weakness or numbness of the face, arm, or leg, most often on one side of the body, occurring in 90% of the strokes [2]. Other symptoms include confusion; difficulty speaking or understanding speech; difficulty seeing with one or both eyes; difficulty walking, dizziness, and loss of balance or coordination; severe headache with no known cause; fainting or unconsciousness. The effects of a stroke depend on which part of the brain is injured and how severely it is affected. A very severe stroke can cause sudden death.

Globally, stroke is the third commonest cause of mortality [3] and the fourth leading cause of disease burden [4]. It makes an important contribution to morbidity, mortality, and disability in developed as well as developing countries. In recent years, there has been increasing economic and demographic development in developing countries resulting in a shift from diseases caused by poverty toward chronic, noncommunicable, lifestyle-related diseases [5]. This happening in the younger age group adds to the social burden, and as such these patients merit special

attention in diagnostic, therapeutic, and preventive care. It leaves the patients with residual disabilities like physical dependence, cognitive decline, depression, and seizures. The review discusses the burden of stroke in young and its implications in a developing country like India along with approach to identifying different causes that are known to occur in this age group.

2. What Is So Special about Stroke Occurring in Young?

Age wise segregation of cases in stroke is important due to several reasons. Age has been shown to have a strong association with the incidence of stroke. While the peak age of stroke occurrence is 55–65 years [6], events occurring at a younger age assume importance in being occurring in a productive age group and having a different set of causes which have to be looked into apart from the conventional ones (Tables 1, 2, and 3). They are also different from childhood strokes which have been classified as those occurring in less than fifteen years of age.

Cerebral venous thrombosis and rheumatic heart disease are the leading causes of stroke in the young in India [18]. Tubercular meningitis leading to arteritis or autoimmune angiitis are also important stroke risk factors in young [19, 20]. Other Indian studies that have reported risk factors

TABLE 1: Causes of stroke in young-Ischemic.

Cardioembolic		Vasculitis		Others	
Common	Less common	Common	Less common	Common	Less common
Rheumatic heart disease	Patent foramen ovale	Infections	Polyarteritis nodosa	Atherosclerotic vascular disease	MELAS
Prosthetic valve	Myxoma and other tumors	Antiphospholipid antibody syndrome [7, 8]	Takayasu's arteritis	Arterial dissection	Prothrombotic states
Atrial fibrillation	Acute myocardial infarction	Systemic lupus erythematosus	Wegener's granulomatosis		Sickle cell disorder
Bacterial endocarditis	Mitral valve prolapsed				Protein C/S deficiency [9]
	Atrial and ventricular septal defects				Fibromuscular dysplasia [10]
					Polycythemia vera
					Antithrombin III deficiency [11]
					Paroxysmal
					Nocturnal Hemoglobinuria
					CADASIL and CARASIL [12]
					Fabry's disease
					Familial hypercholesterolemia [13]
					Thrombophilia [14]
					Hyperhomocytinemia [15]
					Migraine [16]
					Hyperthyroidism [17]

TABLE 2: Causes of stroke in young-Hemorrhagic.

Common	Less common
Arterio venous malformations	Moya moya syndrome
Saccular aneurysms	Arteritis (septic or mycotic)
Bleeding disorders	Intracerebral tumors
Anticoagulants	Substance abuse like cocaine

TABLE 3: Causes of stroke in young-Venous.

Common	Less common
Pregnancy	Prothrombotic states
Postpartum	Red blood cell disorders
Dehydration	Behcet's disease
Oral contraceptive	Connective tissue disease
Other prothrombotic states	

among the young include coagulopathy, elevated lipoprotein (a), homocysteine, and elevated anticardiolipin antibodies [21–25]. Some Indian studies have reported interesting causes of stroke, like viper envenomation, and also suggested mechanisms like squatting whilst on the toilet as an important triggering factor for stroke in Indians, by raising the blood pressure [26, 27]. A recent study from Pakistan [28] in 50 young stroke patients also found infective meningitis including tuberculosis meningitis and bacterial meningitis as

the leading cause of stroke (34%). The second most common cause was cardioembolism (20%) comprising Valvular heart diseases (14%), Cardiomyopathies (4%), and atrial myxoma (2%). Hypertension was found in 14% cases. Pregnancy-related causes (including Pregnancy-induced hypertension and puerperal sepsis) were 12%. Systemic lupus erythematosus and nephritic syndrome was 4% each. Various causes which constitute 4% or less were grouped together as miscellaneous and they include hyperhomocysteinemia and hyperlipidaemias.

While the data from several studies worldwide in young stroke population have realized that conventional risk factors for all strokes still are most prevailing in young strokes as well and while more than a decade-old Baltimore Washington [29] study found cardiac embolism (31.1%), hematologic and other (19.8%) small vessel (lacunar) disease (19.8%), nonatherosclerotic vasculopathy (11.3%), illicit drug use (9.4%), oral contraceptive use (5.2%), large artery atherosclerotic disease (3.8%), and migraine (1.4%) in their 428 young ischemic stroke patients, a later case series from Rome [30] confirmed smoking in 56% of patients, hypertension in 23%, dyslipidemia in 15%, migraine in 26%, and diabetes mellitus in 2% in 394 young ischemic stroke patients. Diabetes, hypertension, heart disease, current smoking, and long-term heavy alcohol consumption are major risk factors for stroke in young adults as in elder population [31].

Data on primary intracerebral hemorrhage (ICH) in young is scarce in India. Mehndiratta et al. [32] found

TABLE 4: Studies on stroke conducted in India.

Study	Setting	Results	Comments
Abraham et al. [48], 1970, Vellore	Rural and urban, community-based, all stroke prevalence	Prevalence: 56.9/100,000	25% of the stroke patients were below the age of 40 years.
Bansal et al. [49], 1975, Rohtak	Urban, community-based study, all stroke prevalence	Population: 79,046 Prevalence: 44/100,000	
GourieDevi et al. [50], 1987, Karnataka	Rural, community based study, all stroke prevalence	Population: 57,660 Prevalence: 52/100,000	
Razdan et al. [37], 1989, Kashmir	Rural, community based study, all stroke prevalence	Population: 63,645 Prevalence: 143/100,000	10.9% of age group 15–39 years (prevalence rate 41/100,000)
Dalal et al. [51], 1989, Mumbai	Urban, hospital based study, 1963–1968 and 1978–1982	Case fatality rate changed from 32 to 12% over this period	Studied only young stroke
Nayak et al. [52], 1997, Kerela	Hospital based, retrospective, 15–45 years of age	177 patients from 1988 to 1994.	Studied clinical features and risk factors in young
Mumbai stroke registry [53]	Population based, urban, Jan to Dec 2005, all age groups	Population: 1, 86,000 Crude incidence rate: 148/100, 000	77% ischemic, hypertension in 25.3%
JIPMER stroke registry [53]	Hospital based, 2005, all age groups	105 in six months	36.2% patients <40 years of age
Trivendrum stroke registry [53]	Population-based, urban and rural, 2005, all age groups	Population: 925,867 Crude incidence rate: 97.9/100,000 urban, 81.3/100,000 rural	Stroke in young 4.3%
Das et al. [36], 2007, Kolkata	Population based, urban, 2003–2005, all age groups	Population: 52 377 Annual incidence rate (AIR)123/100,000/year	AIR in <40 years 4.22/100,000/year
Lipska et al. [41], 2007, Kerala	Case control study, 15–45 years, ischemic stroke	214 cases, 195 controls,	Metabolic syndrome and smoking-associated ischemic stroke in young
Dalal et al. [54], 2008, Mumbai	Population based study, all stroke types, Jan 2005–Dec 2006	Population: 156,861 Annual incidence 145/100,000 in >25 years of age	
Nagaraja et al. [55], 2009, Bangalore	Hospital based, all stroke types	1174 patients	18% less than 40 years of age
S. Kaul et al. [56], 2009, Hyderabad	Hospital based, 2001–2005, all stroke types	Annual incidence of stroke 145/100,000	10–15% of stroke in young

ICH in their 18 (14.2%) of 127 young stroke patients. Most common etiology was ruptured aneurysm (44.4%) followed by ruptured Arteriovenous Malformations (AVM) and hypertension (22.2% each) and eclampsia in 11.1%. Causes of ICH in young in other parts of the world have yielded variable results. The Hemorrhagic Stroke Project (HSP) [33] had 217 out of 1714 patients with primary ICH. The independent risk factors found were hypertension, diabetes, menopause, current cigarette smoking, alcoholic drinks > or =2/day, caffeinated drinks > or =5/day, and caffeine in drugs.

3. Why Its Identification Is Important in Developing Countries Like India?

By 2050, it is anticipated that 80% of stroke events will occur in people living in developing regions of the world [34, 35]. Interestingly, the Kolkata study sample consisted

of mainly younger people (>80% were aged <60 years) who are active in the workforce. When stroke occurs in the main income earner in the household, there may be enormous consequences for the welfare of the family [36]. Indian studies have shown that about 10% to 15% of strokes occur in people below the age of 40 years [37]. It is believed that the average age of patients with stroke in developing countries is 15 years younger than that in developed countries [38, 39]. In India, nearly one-fifth of patients with first ever strokes admitted to hospitals are aged <40 years [40]. However, in the Trivandrum Stroke Registry [41], only 3.8% of incident strokes occurred in people aged <40 years, 9.5% aged <50 years, and 18.1% aged <55 years; these data are very similar to that in another community-based study from northeastern India [36] and those from developed countries [42]. The reported occurrence of stroke in the young, therefore, appears to be largely an artifact related to hospital-based case ascertainment [43].

4. What Information Do We Have So Far about Stroke in Young in India?

Literature is available suggesting that risk of coronary artery disease (CAD) is higher in Indians especially in the young population [44, 45]. While we know that the risk factors for stroke and coronary artery disease are same, recent studies show that the risk of stroke may be comparable to other populations [46, 47]. A number of well-designed prevalence studies of stroke were carried out in hospital and community in various parts of the country in the past and recently, which have not only looked at risk factors but also focused upon the young stroke population [41]. Table 4 shows the studies conducted in various parts of India.

While these studies do reflect the enthusiasm of neurologists and stroke specialists in India to acquire knowledge about stroke in young and stroke at large, the wider community-based study is still wanting. The conventional risk factors still play an important role in causation of stroke in young [41], and genetic causation studies have evaluated MTHFR polymorphisms [57, 58], alpha1 antichymotrypsin [59], -344C/T aldosterone synthase (CYP11B2) [60], Phosphodiesterase 4D (PDE4D) [61], Prothrombin G20210A [62], eNOS [63], and Angiotensin-converting enzyme [64] gene mutation in Indian stroke patients. These might assume a greater importance in patients with family history of stroke and young patients.

5. What Information Is Still Needed from Studies?

More robust evidence is still required to dispel the myth that young Indians are more susceptible to stroke [65]. The areas which require more information and insights are intracerebral hemorrhage, cerebral venous sinus thrombosis in young apart from ischemic stroke which forms the majority and also the focus of stroke studies. Not only this, the less conventional risk factors like migraine [16] and patent foramen ovale [66], emerging factors like arterial dissection [67], and established but less studied causes like peripartum [68, 69] and infection [70, 71] need greater evidence from India as well.

6. Limitations of the Review

As mentioned, definite answers are still required to answer whether young Indians have increased susceptibility to stroke. Most of the studies have a heterogeneous population are hospital-based data with admission and selection bias. Future studies should aim for a multicentric well-defined prospective evaluation on representative population samples to acquire robust answers.

7. Conclusion

While it might turn out through more evidence that stroke in young Indians might not be very different from that in other countries, the implications in a developing country are

many. Preventive measures could aid immensely in bringing down costs and emotional burden on the family. But this would need prior and correct identification of burden and risk factors prevailing in the community. Of added interest would be risk factors, both acquired and genetic, which are unique to this geographic area.

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