

JFFR TERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH An official Publication of Human Journals



Human Journals **Review Article** September 2018 Vol.:13, Issue:2 © All rights are reserved by Bhukya Ramesh et al.

# Ischemic Stroke is the Third-Leading Cause of Death in India and Steps to Process of Regaining Possession and Resuscitation Therapy: A Systematic Case Review







www.ijppr.humanjournals.com

Keywords: Stroke, Resuscitation, Stereotype, Ischemic

#### ABSTRACT

Treating an acute stroke demands a great amount of financial and human resources. Stroke is the third leading cause of death in India and western countries. The aim of this study was to find out existing information about the latest therapeutic methods in treating an acute stroke. The study was conducted as a systematic review. The results and the theoretical information can be utilized by anyone working with a patient who has had a ischemic stroke. This case study review is a quantitative study which consists of eight studies. Most of the studies concentrated on medical interventions regarding acute stroke treatment. The results indicate that therapeutic care of an acute stroke involves resuscitation therapy with basic care of the patient and close collaboration with doctors. The results also indicate that the personnel need to have a fair understanding of medical interventions in order to notice complications and possible threats for the patient. One of the most elective ways in treating a stroke is preventive work in which doctors have a major role. Clinicians should share information about the risk factors of stroke and about how to minimize one's risk of having a stroke during one's lifetime. For most stroke survivors, the pattern of spontaneous neurological recovery of motor functions follows a relatively stereotype sequence of events; in which lower extremity function recover earliest and most completely followed by upper extremity and hand function. Return of tone usually precedes return of voluntary movement, proximal control precedes distal control, and mass movement patterns or synergy pattern precedes isolated coordinated volitional motor functions.

#### **INTRODUCTION:**

Stroke is a condition with unique epidemiological profile, consisting of high incidence and mortality rates, with a large proportion of survivors experiencing a significant amount of residual disability. However, stroke may have different meanings: for patients it is "the end of the road", for family it is "beginning of burden", for physicians it is opportunity for "investigation and intervention", for organizations it is "investment" and for nation it is "loss of disability adjusted life years." The first question that the family members ask when someone suffers from a stroke is "When is he going to walk". The degree of natural recovery after stroke is variable. However, there are two different but related ways that help the stroke survivor to improve after stroke. The first type of recovery, reduction in the extent of neurological impairment results from natural spontaneous recovery which usually account for early spontaneous improvement after stroke within first 3-6 months. This form of recovery manifests as improvement in motor control, language ability or other primary neurological functions. The underlying mechanisms include resolution of local edema, restoration of local toxins, restoration of circulation in ischemic penumbra, and recovery of partial damaged ischemic neurons. This sequence of recovery, however, can stop at any stage. The second type of recovery demonstrated in stroke survivors is the improved ability to perform daily functions in their environment, within the limitation of their physical impairment. The underlying mechanism to explain the second type of recovery is neuroplasticity. Brain plasticity is the ability of the nervous system to modify its structure and functional organization. The two most plausible forms of plasticity are, collateral sprouting of new synaptic connections and unmasking of previous latent pathways. Other mechanisms of plasticity include assumption of function by undamaged pathways, reverse ability from diastalsis, denervation supersensitivity, remyelination, and regenerative proximal sprouting of transacted neuronal axons.

#### How are insulin resistance, diabetes and CVD related?

Although diabetes is treatable, even when glucose levels are under control, it greatly increases the risk of heart disease and stroke. Pre-diabetes and subsequent type 2 diabetes usually result from insulin resistance. When insulin resistance or diabetes occur with other CVD risk factors (such as obesity, high blood pressure, abnormal cholesterol and high triglycerides), the risk of heart disease and stroke rises even more. Insulin resistance is associated with atherosclerosis (fatty buildups in arteries) and blood vessel disease, even

before diabetes is diagnosed. That's why it's important to prevent and control insulin resistance and diabetes. Obesity and physical inactivity are important risk factors for insulin resistance, diabetes and cardiovascular disease.

#### Metabolic syndrome:

People with the metabolic syndrome are at increased risk for developing diabetes and cardiovascular disease. A person has the metabolic syndrome if they have three or more of the following abnormalities:

- Waist circumference greater than 40 inches in men and 35 inches in women.
- Triglyceride level of 150 mg/dL, or higher
- HDL cholesterol level less than 40 mg/dL in men and 50 mg/dL in women
- Blood pressure of 130/85 mm Hg or higher
- Fasting glucose level of 110 mg/dL or higher.

Researchers estimate that 47 million Americans have the metabolic syndrome. Risk increases with age. Age-adjusted prevalence for adults is 23.7 percent. Mexican-Americans have the highest prevalence at 31.9 percent. If you have three or more of these conditions or have a brother, sister or parent with diabetes, you should be tested regularly for diabetes (i.e., blood Glucose level fasting and postprandial). In addition, experts recommend that all adults over age 45 should have a fasting blood glucose test every three years, and more often if they have several risk factors. According to the National Indian stroke association, the population has increased by 34 percent since 1980. Studies indicate that they have a higher rate of hemorrhagic strokes at a younger age than adult age. One study found that hemorrhagic strokes occurred more commonly in 35 years age group people. Different Prevalence of Risk Factors have for stroke when compared with other countries. For instance, they have strokes at younger ages. Diabetes is more prevalent among south India, with estimates that 30 percent of adults have the disease and as many as half do not know.

The prevalence of previously diagnosed diabetes in India wide between ages 24–74 was 2.4 times greater than other western countries. Heavy alcohol use occurs in 40 percent of men age 18–39, and the stroke Database found that 24 percent of Indians have heavy alcohol

intake compared to seventeen percent in non-Indians. Obesity is more prevalent among Indian people. The American Heart Association reports that about western countries 75 percent of American men and 72 percent of women ages 20 and older were overweight or obese and 29 percent of men and 40 percent of women were obese. The National Health and Nutrition Examination Survey reported that 65 percent of American men and 74 percent of American women did not participate in leisure time physical activity.

Rehab centers across the country are using innovative advances in rehab science. These therapies can either supplement or replacement of traditional therapy. Traditional therapy is intended to progress very slowly to prevent abnormal movement. The new therapies are aggressive, focusing on forced movement, repetition and intensity. They also rely on technological advances. "The more intensive the therapy the better," says Dr. Robert Teasel, professor and chief of the Department of Physical Medicine and Rehabilitation at St. Joseph's Health Care in London, Ontario. Teasel reviewed over 10000 stroke rehab trials in all over countries to states that took place from 1988 to 2017. He says that four new therapies showed better results than conventional therapy in two or more randomized controlled trials. Those therapies are constraint-induced movement therapy, biofeedback, electrical stimulation and partially supported treadmill training. These advances all await large, definitive trials to confirm the promising results from these smaller studies. All of these therapies, with the exception of constraint induced movement, are reimbursable by Medicare.

#### Making you move: Constraint-induced movement therapy:

Constraint-induced movement therapy (CI) forces the use of the affected side by restraining the unaffected side. With CI therapy, the therapist constrains the survivor's unaffected arm in a sling. The survivor then uses his or her affected arm repetitively and intensively for two weeks. This therapy deals after a stroke, a survivor tries unsuccessfully to use the affected side. Their initial failure discourages them from using that side. Therapy lasted six hours a day, five days a week, for three weeks. The patient can raise her arm, hold a bottle steady in her hand and feed her/himself cookies with her left hand. "In order to use CI therapy, survivors need to be able to extend their wrists and move their arm and their fingers. Numerous small studies show CI therapy improves movement on the affected side. A June 2005 study published in Stroke: Journal of the Indian Heart Association also showed that brain activity actually improves with the treatment. "This finding offers hope to researchers

who believe it may be possible to stimulate or manipulate brain areas to take over lost functions, a process known as cortical reorganization

#### The benefits of biofeedback:

The concept of biofeedback is as simple as looking in the mirror to watch yourself move your arm or leg. It's a visual reinforcement that you are moving your limbs in a desired way. After a stroke, it is common for survivors to move their arms or legs abnormally.

### Case study:

In biofeedback, a wire electrode connected to a metal plate is attached to the skin over an arm or leg muscle. When the survivor moves this muscle, an electrical signal travels from the electrode to an attached monitor, where it produces a particular image. The survivor gets reinforcement every time he or she moves the muscle and creates this image. Biofeedback gives a visual cue that the survivor is moving muscles in a desired way. After his stroke in 2005. In rehab, a therapist attached an electrode to the bicep muscle in his arm and attached the wire to a monitor. When Rocket moved that muscle, a line would move up on a graph on the monitor screen. The more he moved the bicep muscle, the higher the line climbed on the screen. Biofeedback is helpful in isolating which muscle to use when two opposing muscles are working against each other after a stroke. For example, a survivor may not be able to open his first if one muscle in his hand is working to open the hand, but an opposing muscle is overactive. After isolating which muscle needs to be relaxed in order to allow the opposing muscle to do its job, the therapist attaches an electrode to the overactive muscle. Every time that muscle relaxes, an image appears on a screen. The survivor receives visual feedback that teaches him to relax the correct muscle. Biofeedback has been used for pain management for years. There are no risks with biofeedback, it can train a survivor to open his or her hand by extending the fingers and relaxing the finger flexors and its main drawback is it's usually not helpful for learning a functional task like drinking from a cup. So, biofeedback can improve motor control but does not focus on improved functional use.

#### A shocking therapy: Functional electrical stimulation:

Functional electrical stimulation delivers a shock to the survivor's muscle. The shock activates nerves and makes the muscle move. Theoretically, the brain may be able to recapture and relearn this movement without the stimulation. We don't know exactly why

electrical stimulation works, just that it does. Electrodes can be placed on the wrist extensor muscles of the forearm, for example. The patient relaxes the hand, then contracts the wrist extensor muscle to cause movement. This movement triggers an electric shock to the wrist extensor muscle, which causes greater movement of the hand than the patient could make. Electrical stimulation can be used on all parts of the body, including the shoulders and legs. Chuck used electrical stimulation two to three times a day for about 30 minutes each time. As he improved, he started to use it four times a day for 30 minutes. Now he has returned to work, so he only uses it once every few months. The electric shock "can range from a mild tingling sensation to almost a burning sensation depending on the intensity I set on the unit.

#### A case for support: Treadmill training with partial body support:

Partially supported treadmill training helps survivors learn to walk again although neither their legs nor upper body can support them. Therapists hope this will rewire the brain, so survivors can eventually make these movements on their own. In treadmill therapy, the therapist places the survivor in a harness with their legs suspended over a treadmill. The harness eliminates the risk of falling. One therapist stands by the survivor and moves their affected leg forward on the treadmill to keep pace with the unaffected leg. A second therapist operates the treadmill. The drawback is that this training requires two therapists, making it more expensive than conventional therapy. This type of treadmill training is available at large academic centers around the country, like the Rehabilitation Institute of Chicago. Even patients who can't extend their wrists or fingers on their own can still use this orthotic. They do need some shoulder and elbow movement. Since the F.T.M. Arm Training Program works for survivors with limited movement in their hand and fingers, it can prepare survivors to qualify for constraint induced therapy. First case study using the orthotic in Mumbai. Their therapists or doctors tell them they are not making progress.

#### **Stem Cell Implants:**

Animal studies of stem cell implants have also been initiated. Since stem cells can regenerate and change into other types of cells, researchers are hoping they will stimulate other cells to grow in the brain and form new connections among cells to help restore motor function. The risk of treatment in humans and animals is that both humans and animals need an immunosuppressant to keep their bodies from rejecting cells taken from other animals. A breakthrough in research has been to remove cells from bone marrow in rats and re-inject

them in the same rats' brain cells. The rats don't reject these cells like they do foreign cell injections. Scientists hope neural growth factors and stem cell injections may be used successfully alongside physical therapy to promote recovery from stroke.

Know the warnings and signs of stroke:

- Sudden numbness or weakness of the face, arm or leg, especially on one side of the body
- Sudden trouble seeing in one or both eyes
- Sudden confusion, trouble speaking or understanding
- Sudden trouble walking, dizziness, loss of balance or coordination
- Sudden severe headache with no known cause

Rehabilitation Services Long-term rehabilitation services are important in helping heart disease and stroke patients recover as fully as possible and return to a fulfilling quality of life. Stroke patients may need speech therapy, occupational therapy, and physical therapy to help restore cognitive and physical functioning. Heart disease patients may need cardiac rehabilitation services such as exercise and strength training, nutrition and weight loss counseling, and support for smoking cessation and other lifestyle changes that can improve quality of life and help prevent another acute cardiac event. Rehabilitation services are often hospital-based but may also be offered through independent medical and rehabilitation clinics. As with many types of preventive and medical services, rehabilitation services tend to be more available and accessible in larger cities and metropolitan areas than in small towns and rural areas. Communities that lack these services locally may be able to improve access for local residents by arranging for visiting service providers to be available 1 day per week, or by coordinating transportation to rehabilitation providers in nearby cities or towns. Nutrition and Dietetics Dietary patterns and nutritional status are both very important in the prevention and treatment of heart disease and stroke. Both macronutrients (e.g., total calories and fat consumption) and micronutrients (e.g., sodium, calcium, iron, and vitamins) have been linked to the development of high blood pressure, high cholesterol, diabetes, and obesity. Professional nutrition services are a vital link in community efforts to prevent heart disease and stroke risk factors and to manage risk conditions after they develop. Nutrition and dietetic services related to primary prevention of heart disease and stroke may include: 1)

healthy meal planning for institutions such as schools, hospitals, nursing homes, and worksites; 2) nutrition education classes offered through public health departments, schools, hospitals, community centers and senior centers; 3) professional nutrition counseling offered as an adjunct to primary medical care; 4) diet planning offered through fitness and weightloss centers. Social Environment Handbook 20. For people who need to minimize the negative consequences of biomedical risk factors, professional nutrition services can be a critical resource. Nutritionists and registered dieticians can provide detailed nutritional assessments, weekly meal plans and specific treatment recommendations for adults with high blood pressure, high blood cholesterol, diabetes or obesity. These services may be offered through public health departments, primary care physician offices, specialist physician offices (such as cardiologists and endocrinologists), or more uncommonly, through private independent nutrition practices.

#### Recommendations

In patients with suspicion of acute stroke, the treatment of high blood pressure is not recommended in the extra-hospital environment, if <220 (PAS) or <120 mmHg.

(DBP) is maintained, with the exception of certain urgent situations (founded clinical suspicion of left cardiac insufficiency, acute coronary syndrome or aortic dissection). If the decision is taken to treat it, sudden and intense decreases of the BP will be avoided (more than 20% in < 24 hours).

If the BP has to be reduced, the intravenous route and when this is not possible, oral route, will preferably be used. In those cases where there is low blood pressure, the presence of another serious concomitant disease will be ruled out and it will be treated according to the etiology.

#### Supplementary oxygen therapy:

Hypoxemia during the acute stroke phase seems to be associated with an increase of the risk of death<sup>15</sup>, so the administration of supplementary oxygen to hypoxic patients is recommended. This is a recommended practice based on clinical experience and consensus, as there is no evidence. More controversial is the use of supplementary oxygen in nordoxepin patients with acute stroke. The increase of oxygenation of the brain tissue has been considered as a logical option in the management of acute stroke for more than 40 years<sup>55</sup>.

The administration of norm baric oxygen (NBO) is easy to apply, non-invasive and can be used in extra-hospital environments during the initial phases of acute stroke. Studies in animals suggest that hyperoxia could slow down the cerebral infarction process and therefore increase the time frame during which reperfusion treatment can be applied<sup>16,15</sup>. On other hand, the application of oxygen is not risk-free: the formation of toxic free radicals 158, a possible increase in the risk of infections and a delay in the mobilization of the patient, are some of the potential adverse effects associated with its use.

# Summary of evidence

	There is no evidence that supplementary oxygen improves mortality or		
1	disability in non-hypoxic patients with light or moderate stroke and it		
	even seems to increase the mortality		
	even seems to mercuse the mortunity.		
	There is no evidence, either, that supplementary oxygen improves		
2	There is no evidence, ender, that supprementary oxygen improves		
	mortality		
	monanty.		

# Recommendations

А	The routine use of supplemental oxygen is not recommended in people with
	Suspected acute stroke.
В	Patients with suspicion of acute stroke must receive supplemental oxygen if
	there are clinical signs of hypoxia or to maintain an oxygen saturation of 94-
	98%, except in those patients with risks of hypersonic respiratory failure, In
	whom a saturation of 88 to 92% will be maintained.

# Antiplatelet treatment:

Antiplatelets can reduce the volume of brain damage causes the ischemia, so early administration could reduce mortality and sequelae caused by the stroke, and also the risk of recurrence. Antiplatelets in the treatment of acute stroke<sup>12</sup>. Studies were excluded from the review about treatment with antiplatelets in patients with primary intracranial hemorrhage or known subarachnoid hemorrhage, although those studies that did not appropriately differentiate ischemic or hemorrhagic stroke before the randomization, are included. It included a sample of 43,041 patients originating from 12 studies. Two of these, the CAST and the IST (administration of aspirin, started within 48 hours after the establishment of the stroke in doses of 160 to 300 mg a day), contributed to 94% of the data. The results of the

review showed that there was a significant reduction of the risk of death or dependence at the end of the follow-up in the group treated with antiplatelets (OR=0.95; 95% CI: 0.91 to 0.99). For every 1000 patients treated with aspirin, 13 negative results were avoided. Antiplatelet Agents Aspirin & Dipyridamole Clopidogrel vs. Aspirin Clopidogrel vs. Aspirin and Clopidogrel Relative risk reduction (RRR) in secondary stroke prevention 18% 20-24% 8.7% 6.4%.

 Table 1. Risk of stroke 2, 7 and 90 days after a TIA (ABCD2 risk table)

Risk score	2 days	7 days	90 days
Low risk (0-3)	1%	1.2%	3.1%
Moderate risk (4-5)	4.1%	5.9%	9.8%
High risk (6-7)	8.1%	11.7%	17.8%

The ABCD2 scale presents a total score range from 0 to 7 for the following components or independent risk predictors<sup>73</sup>:

- Age: >60 years (1 point)
- Blood pressure: SBP >140 mmHg or DBP >90 mmHg (1 point)

• Clinical features: Focal weakness (2 points) or speech alterations without focal weakness (1 point)

- Duration of symptoms: 60 minutes (2 points), 59-10 minutes (1 point)
- Diabetes mellitus: (1 point)

Ischemic strokes can be divided into two different types: transient ischemic attack (TIA) or a stroke which is caused by an embolus or thrombus. Embolus or thrombus caused strokes can be divided into five different subtypes based on the cause of the stroke (see Figure 1). The percentage indicates the proportion of a certain stroke type from all ischemic strokes.



# **Figure 1: Ischemic stroke subtypes**

However, it must be considered that the environment where the rehabilitation is provided may change throughout the rehabilitation process, depending on each patient's specific needs, without losing coordination or continuity. Most of the recovery that patients will experience takes place in the first three months after the stroke.

We have not found any other RCT focused exclusively on the treatment of anxiety in patients after a stroke. The guidelines consulted recommendation considering normal therapies (both psychological and pharmacological) in managing anxiety after a stroke Anxiety frequently occurs concomitantly with depression, so it is considered advisable to evaluate its presence when any other form of mood alteration is detected, treating it in the normal way<sup>28</sup>. The research articles had a variety of topics and they discussed acute stroke care more or less. The results show clearly that acute stroke treatment is bound to medicine quite profoundly which raises some interesting thoughts about the nursing care and nurse's role in acute stroke treatment. While acute stroke treatment is bound to medicine, the patient needs a lot of nursing care in everyday activities.

#### Sequelae and common complications after a stroke:

Patients who have suffered a stroke may experience a large variety of limitations and complications that may perhaps hinder their optimal recovery.

# Table 2. Sequelae and common complications in the follow-up after a stroke

Sequel	lae and	physical	complications
Seque	ac and	physical	comprisedions

Most frequent	Less frequent	
Total or partial motor	• Sight alterations	
Sensory alterations	• Epilepsy	
Language alterations	Central post stroke pain	
• Fatigue	Deep venous thrombosis	
Osteoporosis	Fecal incontinent	
Shoulder pain	Pressure ulcers	
• Falls / fractures	• Urinary infections	
Spasticity	• Lung infections	
Urinary incontinence	Constipation	
Contractions	• Dysphasia	
Hemiplegic shoulder subluxation		
Sexual dysfunction		
=	Mood alterations	
	uman	
Most frequent	Less frequent	
Depression	• Emotionalism	
• Anxiety		
	Cognitive alterations	
Most frequent	Less frequent	
• Dementia	• Apraxia	
• Attention deficits	• Alteration of upper executive	
	functions	
Memory alteration	Spatial neglect	
	Agnosia (visual and anosognosia)	

# Falls:

Falls, both in hospital and in the community, are normal in patients who have suffered a stroke 257-260. It is estimated that up to 73% suffer at least one fall during the first six months after discharge 204. Apart from the high incidence of falls, there is a greater loss of bone mineral density, especially in the hemiparetic side 200, so, apart from the interventions required to reduce the incidence of falls, interventions are also required to limit their consequences.

Intervention	RQ (95% CI)	RQ (95% CI)
1. Multiple component exercises (when		
focused on 2 or more of the following		
categories: strength,equilibrium,flexibility)		
2. Group exercises	0.78 (0.71 to 0.86)	0.83 (0.72 to 0.97)

# **CONCLUSION:**

Stroke is the third leading cause of death in India and in all Western countries. The financial costs are profound and they are estimated to rise every year. Intensive is bound to medicine and the need for effective collaboration between patients and doctors is important. While this study did not fully answer the set research question it raised some questions which can be adapted to following few implications for future research. Acute stroke care will be a great challenge for the future because it has been predicted that more and more people will contract stroke during their lifetime. Ongoing research for new and more effective medical interventions and therapy for stroke study will ensure that patients will have better chances of survival and recovery from a stroke. Finally, in India, the stroke ratio highest compare with the other countries and these are the therapies should follow and treat and control maximum level of the stroke cases. In north India there has to some variations are there compare with the South and East Indian states mostly in India Mumbai and Chennai cities were raised stroke conditions as per the data followed by the Indian stroke association records. Hypertension patients are 35%, diabetes patients are 35% and dyslipidemia patients are 15% are mostly suffering with ischemic stroke. Common risk factors e.g. Diabetes and Hypertension, Lipids can be decisively blamed in only less than 50% of CVD. Especially with causative intracranial and cardioembolic causes are common in East than West India.

# **REFERENCES:**

1. Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Au R, Kannel WB, et al. The lifetime risk of stroke: Estimates from the Framinham Study. Stroke. 2006; 37:345–50.

2. Abraham J, Rao PS, Inbaraj SG, Shetty G, Jose CJ. An epidemiological study of hemiplegia due to stroke in South India. Stroke. 1970; 1:477–81.

3. Bansal BC, Parkash C, Jain AL, Brahmanandan KR. Cerebrovascular disease in young individuals below the age of 40 years. Neurol India. 1973; 21:11–8.

4. Razdan S, Kaul RL, Motta A, Kaul S. Cerebrovascular disease in rural Kashmir, India. Stroke. 1989; 20:1691–3.

5. Kapoor SK, Banerjee AK. Prevalence of common neurological diseases in a rural community of India. Indian J Community Med. 1989;14:171–6.

6. Bharucha NE, Bharucha EP, Bharucha AE, Bhise AV, Schoenberg BS. Prevalence of stroke in the Parsi community of Bombay. Stroke. 1988; 19:60–2.

7. Dalal PM. Studies in young and elderly: Risk factors and strategies for stroke prevention. J Assoc Physicians India. 1997;45:125–31.

8. Das SK, Sanyal K. Neuroepidemiology of major neurological disorders in rural Bengal. Neurol India. 1996;44:47–58.

9. Saha SP, Bhattacharya S, Das SK, Maity B, Roy T, Raut DK. Epidemiological study of neurological disorders in a rural population of Eastern India. J Indian Med Assoc. 2003;101:299–300. 302-4.

10. Banerjee TK, Mukherjee CS, Sarkhel A. Stroke in the urban population of Calcutta: An epidemiological study. Neuroepidemiology. 2001; 20:201–7

11. Das SK, Banerjee TK, Biswas A, Roy T, Raut DK, Mukherjee CS, et al. A prospective community-based study of stroke in Kolkata, India. Stroke. 2007; 38:906–10

12. Gourie-Devi M, Rao VN, Prakash R. Neuroepidemiology study in semi urban and rural areas in South India: Pattern of neurological disorders including motor neuron disease. In: Gourie-Devi M, editor. Motor Neuron Disease: Global Clinical Patterns and International Research. New Delhi: Oxford and IBH Publishing; 1987. pp. 11–22.

13. Gourie-Devi M, Gururaj G, Satishchandra P, Subbakrishna DK. Prevalence of neurological disorders in Bangalore, India: A community-based study with comparison between urban and rural areas. Neuroepidemiology. 2004; 23:261–8.

14. Ahmad OB, Boschi-Pinto C, Lopez AD, Christopher JL, Murray CJ, Lozano R, et al. Age standardization of rates: A new WHO standard. Geneva, Switzerland: World Health Organization. GPE Discussion Paper Series No 31, EIP/GPE/EBD;

15. Dalal PM, Malik S, Bhattacharjee M, Trivedi ND, Vairale J, Bhat P, et al. Population-based stroke survey in Mumbai, India: Incidence and 28-day case fatality. Neuroepidemiology. 2008; 31:254–61

16. Sridharan SE, Unnikrishnan JP, Sukumaran S, Sylaia PN, Nayak SD, Sarma PS, et al. Incidence, types, risk factors, and outcome of stroke in a developing country: The Trivandrum Stroke Registry. Stroke. 2009; 40:1212–8

17. Brown RD, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Stroke incidence, prevalence, and survival: Secular trends in Rochester, Minnesota, through 1989. Stroke. 1996; 27:373–80

18. Rothwell PM, Coull AJ, Giles MF, Howard SC, Silver LE, Bull LM, et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study) Lancet. 2004;363:1925–33

19. Kolominsky-Rabas PL, Sarti C, Heuschmann PU, Graf C, Siemonsen S, Neundoerfer B, et al. A prospective community-based study of stroke in Germany — The Erlanger Stroke Project (ESPro): Incidence and case fatality at 1, 3, and 12 months. Stroke. 1998;29:2501–6.

20. Syme PD, Byrne AW, Chen R, Devenny R, Forbes JF. Community-based study of stroke incidence in a Scottish population: The Scottish Borders Stroke Study. Stroke. 2005;36:1837

21. Tsiskaridze A, Djibuti M, van Melle G, Lomidze G, Apridonidze S, Gaurashvili I, et al. Stroke incidence and 30-day case fatality in a suburb of Tbilisi: Result of the first prospective population-based study in Georgia. Stroke. 2004;35:2523–8.]

22. Thrift AG, Dewey HM, MacDonnell RA, McNeil JJ, Donnan GA. Incidence of the major stroke subtypes: Initial findings from the North East Melbourne stroke incidence study (NEMESIS) Stroke. 2001;32:1732–8.

23. Jiang B, Wang WZ, Chen H, Hong Z, Yang QD, Wu SP, et al. Incidence and trends of stroke and its subtypes in China: Results from three large cities. Stroke. 2006;37:63–8

24. Joshi R, Cardona M, Iyengar S, Sukumar A, Raju CR, Raju KR, et al. Chronic diseases now a leading cause of death in rural India — mortality data from the Andhra Pradesh Rural Health Initiative. Int J Epidemiol. 2006;35:1522–9.

25. Jacobs BS, Boden-Albala B, Lin IF, Sacco RL. Stroke in the young in the Northern Manhattan Stroke Study. Stroke. 2002;33:2789–93.

26. Balarajan R. Ethnic differences in mortality from ischemic heart disease and cerebrovascular disease in England and Wales. BMJ. 1991;302:560–4.

27. Das SK, Sanyal K, Basu A. Study of urban community survey in India: Growing trend of high prevalence of hypertension in a developing country. Int J Med Sci. 2005;2:70–8.

28. Ray BK, Hazra A, Ghosal M, Banerjee T, Chaudhuri A, Singh V, et al. Early and delayed fatality of stroke in Kolkata, India: Results from a 7-year longitudinal population-based study. J Stroke Cerebrovascular Dis. 2013;22:281–9.

29. Kaul S, Sunitha P, Suvarna A, Meena AK, Uma M, Reddy JM. Subtypes of ischemic stroke in a metropolitan city of south India (one-year data from hospital-based stroke registry) Neurol India. 2002;50:S8–14.

30. Chopra JS, Prabhakar S, Sodhi JS. Stroke in young: A clinic-radiological study. Neurol India. 1979b;27:160–9.

31. Dalal PM, Shah PM, Aiyar RR, Kikani BT. Cerebrovascular disease in west central India. A report on angiographic findings from a prospective study. Br Med J. 1968;3:769–74.

32. Padma MV, Gaikwad S, Jain S, Maheswari MC, Misra NK. Distribution of vascular lesions in ischemic stroke: A magnetic resonance angiographic study. Natl Med J India. 1997;10:217.

33. Dalal PM. Burden of stroke: Indian perspective. Int J Stroke. 2006;1:164-6

34. Wasay M, Khatri IA, Kaul S. Stroke in South Asian countries. Nat Rev Neurol. 2014;10:135-43

35. Blecic S, Bogousslavsky J. Stroke in young adults. In: Barnett HJ, Mohr JP, Stein BM, Atsu FM, editors. Stroke: Pathophysiology, diagnosis and Management. 3rd ed. New York: Churchill Livingstone; 1998. pp. 1001–12.

36. Dash D, Bhashin A, Pandit AK, Tripathi M, Bhatia R, Prasad K, et al. Risk factors and etiologies of ischemic strokes in young patients: A tertiary hospital study in north India. J Stroke. 2014;16:173–7.

37. Bansal BC, Gupta RR, Prakash C. Stroke during pregnancy and puerperium in young females below the age of 40 years as a result of cerebral venous sinus thrombosis. Jpn Heart J. 1980;21:171–83

38. Gosalakkat JA. Moyamoya disease: A review. Neurol India. 2002;50:6-10

39. Sharma BK, Sagar S, Sing AP, Suri S. Takayashu arteritis in India. Heart Vessels Suppl. 1992;7:37-43

40. Kothari SS. Takayasu's arteritis in children: A review. Images Pediatr Cardiol. 2002;9:4-23.

41. Dalal PM. Strokes in the young in west central India. Adv Neurol. 1979;25:339–48.

42. Kalita J, Goyal G, Misra UK. Experience of pediatric stroke from a tertiary medical centre in North India. J Neurol Sci. 2013;325:67–73.

43. Kalita J, Goyal G, Kumar P, Misra UK. Intracerebral hemorrhage in young from a tertiary neurological centre in North India. J Neurol Sci. 2014;336:42–7.

44. Sridharan R. Risk factors for ischemic stroke

45. Kulshrestha M, Vidyanand Analysis of risk factors and outcomes of cerebrovascular disease in northern India. J Clin Diagn Res. 2013;7:127–31

46. Nongkynrih B, Acharya A, Ramakrishnan L, Ritvik, Anand K, Shah B. Profile of biochemical risk factors for non-communicable diseases in urban, rural and periurban Haryana, India. J Assoc Physicians India. 2008;56:165–70.

47. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart. 2008;94:16–26

48. Lipska K, Sylaja PN, Sarma PS, Thankappan KR, Kutty VR, Vasan RS, et al. Risk factors for acute ischemic stroke in young adults in South India. J Neurol Neurosurg Psychiatry. 2007;78:959.

49. Hassan KM, Verma A, Prakash A, Chandran V, Kumar S, Banerji A. Prevalence and association of lifestyle factors with extracranial carotid atherosclerosis in non-cardioembolic anterior circulation strokes in adult males less than 50 years: One-year cross-sectional study. Ann Indian Acad Neurol. 2013;16:516–20

50. Gunaratne A, Patel JV, Potluri R, Gammon B, Jessani S, Hughes EA, et al. Increased 5-year mortality in the migrant South Asian stroke patients with diabetes mellitus in the United Kingdom: The West Birmingham Stroke Project. Int J Clin Pract. 2008;62:197–201

51. Bhattacharya S, Saha SP, Basu A, Das SK. A 5 year prospective study of incidence, morbidity and mortality profile of stroke in a rural community of eastern India. J Indian Med Assoc. 2005;103:655–9.

52. Basu AK, Pal SK, Saha S, Bandopadhyay R, Mukherjee SC, Sarkar P. Risk factor analysis in ischemic stroke: A hospital-based study. J Indian Med Assoc. 2005;103:586–588.

53. Banerjee TK, Chowdhury D, Das A, Sekhar A, Roy D, Sen S. Analysis of hospital-based registry in a neurological centre in Kolkata. J Indian Med Assoc. 2005;103:665–8

54. Subramanian SV, Nandy S, Kelly M, Gordon D, Davey Smith G. Patterns and distribution of tobacco consumption in India: Cross sectional multilevel evidence from the 1998-9 national family health survey. BMJ. 2004;328:801–5

55. Sharma A, Prasad K, Padma MV, Tripathi M, Bhatia R, Singh MB, et al. Prevalence of triggering factors in acute stroke: Hospital-based observational cross-sectional study. J Stroke Cerebrovascular Disc. 2015;24:337–47.

56. Srinivasan K. Cerebral venous and arterial thrombosis in pregnancy and puerperium. A study of 135 patients. Angiology. 1983;34:731–46

57. Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VC, Mridula KR, et al. Risk factors, clinical profile, and long-term outcome of 428 patients of cerebral sinus venous thrombosis: Insights from Nizam's Institute Venous Stroke Registry, Hyderabad (India) Neurol India. 2012;60:154–9

58. Thom DH, Grayston JT, Siscovick DS, Wang SP, Weiss NS, Daling JR. Association of prior infection with Chlamydia pneumoniae and angiographically demonstrated coronary artery disease. JAMA. 1992;268:68–72.

59. Melnick SL, Shahar E, Folsom AR, Grayston JT, Sorlie PD, Wang SP, et al. Past infection by Chlamydia pneumonia strain TWAR and asymptomatic carotid atherosclerosis. Atherosclerosis Risk in Communities (ARIC) Study Investigators. Am J Med. 1993;95:499–504

60. Srinivasrao Bandaru VC, Kaul S, Boddu DB, Vemu L, Neeraja M. Hyperhomocysteinemia associated with Chlamydia pneumonia infection in ischemic stroke: A hospital-based study from South India. Neurol Asia. 2009;14:1–5.

61. Rai NK, Choudhary R, Bhatia R, Singh MB, Tripathi M, Prasad M, et al. Chlamydia pneumoniae seropositivity in adults with acute ischemic stroke: A case-control study. Ann Indian Acad Neurol. 2011;14:93–7.

62. Paul N, Das S, Hazra A, Ghosal MK, Ray BK, Banerjee TK, et al. Depression among stroke survivors: A community-based, prospective study from Kolkata, India. Am J Geriatr Psychiatry. 2013;21:821–31.

63. Das S, Paul N, Hazra A, Ghosal M, Ray BK, Banerjee TK, et al. Cognitive dysfunction in stroke survivors: A community-based prospective study from Kolkata, India. J Stroke Cerebrovasc Dis. 2013;22:1233–42.

64. Ghosal MK, Burman P, Singh V, Das S, Paul N, Ray BK, et al. Correlates of functional outcome among stroke survivors in a developing country — a prospective community-based study from India. J Stroke Cerebrovasc Dis. 2014;23:2614–21.

65. Shah B. Assessment of Burden of Non-Communicable Diseases. New Delhi: Indian Council of Medical Research; 2004.

66. Banerjee TK, Dutta S, Ray BK, Ghosal M, Hazra A, Chaudhuri A, et al. Disease burden of stroke in Kolkata, India: Derivation of disability-adjusted life years by a direct method. Neuroepidemiology. 2013;41:88–93

67. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systemic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380:2197–223

68. Das K, Mandal GP, Dutta AK, Mukherjee B, Mukherjee BB. Awareness of warning symptoms and risk factors of stroke in the general population and in survivors of stroke. J Clin Neurosci. 2007;14:12–6

69. Pandian JD, Jaison A, Deepak SS, Kalra G, Shamser S, Lincoln DJ, et al. Public awareness of warning symptoms, risk factors, and treatment of stroke in northwest India. Stroke. 2005;36:644–8

70. Menon B, Swaroop JJ, Deepika HK, Conjeevaram J, Munisusmitha K. Poor awareness of stroke — A hospital-based study from South India: An urgent need for awareness programs. J Stroke Cerebrovasc Dis. 2014;23:2091–8.

71. Srivastab AK, Prasad K. A study of factors delaying hospital arrival of patients with acute stroke. Neurol India. 2001;49:272–6

72. Rural Energy Health Transportation System. Commissioner of family welfare, Government of Andhra Pradesh (India) [Last accessed on 2008 Mar 4].

73. Singh SK. Review of urban transportation in India. J Public Transp. 2005;8:79–97.

74. Pandian JD, Kalra G, Jaison A, Deepak SS, Shamsher S, Padala S, et al. Factors delaying admission to a hospital-based stroke unit in India. J Stroke Cerebrovasc Dis. 2006;15:81–7.

75. Padma MV, Singh MB, Bhatia R, Srivastava A, Tripathi M, Shukla G, et al. Hyperacute thrombolysis with IV rtPA of acute ischemic stroke: Efficacy and safety profile of 54 patients at a tertiary referral center in a developing country. Neurol India. 2007;55:46–9

76. Pandian JD, Sudhan P. Stroke epidemiology and stroke care services in India. J Stroke. 2013;15:128–34.

77. Pandian JD, Toor G, Arora R, Kaur P, Dheeraj KV, Bhullar RS, et al. Complementary and alternative medicine treatments among stroke patients in India. Top Stroke Rehabil. 2012;19:384–94.

78. Cramer SC. Repairing the human brain after stroke. II. Restorative therapies. Ann Neurol. 2008;63:549–60.

79. Bhasin A, Srivastava MV, Bhatia R, Mohanty S, Kumaran SS, Bose S. Autologous intravenous mononuclear stem cell therapy in chronic ischemic stroke. J Stem Cells Regen Med. 2012; 8:181–9.

