

Prospective Study of Clinical Characteristics, Stroke Types and Aetiology of Stroke in Young

Manjesh Rathi, Suresh Kumar*

Department of Neurology, Sree Balaji Medical College & Hospital Affiliated to Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

*Corresponding author e-mail id: doc_suresh@yahoo.com

Abstract

The Present study includes to identify aetiology and types of stroke in young (15- 45 yrs) and to evaluate the clinical characteristics of stroke in young. Acute management, prognosis and long term strategies to prevent recurrence vary considerably depending on the aetiology and type of stroke . There are studies on stroke in young patients from a tertiary referral centre and most of these have involve ischaemic stroke, conducted before the widespread use of modern neuro-imaging methods; thus, with few exceptions, they did not identify stroke subtypes, aetiopathogenesis, and long term outcome. This present study focuses on one of the largest study of stroke in young patients and evaluated all young stroke patients for risk factors, aetiology, stroke subtypes and clinical features.

Keywords : aetiology, stroke, hemorrhage, echocardiography, cerebral angiography and homocysteine

1. Introduction

Stroke is one of the leading cause of morbidity and mortality. Stroke is the most common life- threatening neurological condition causing long-term disability and has enormous emotional and socioeconomic consequences in patients, their families and health services. Although stroke is considered to be a disease of the older population, it is not infrequent among adolescents and young adults [1–3]. According to Kittner et al. [4] the incidence of stroke is approximately 6/100,000 in Caucasians aged 15 –39 years and approximately 2.5 times higher in persons of African descent. According to M Gourie Devi's review article, in Indian population prevalence rates of strokes varying from 52-472 per 100000 persons, with the

exception of a very high rate of 842 among Parsis, a distinct ethnic community and overall annual incidence rates varied from 13-36 per 100000 population in various studies[10,15,16] .stroke in young has special significance in developing countries because of etiological variation from developed countries, and the affection of economically productive group . 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, non-communicable, 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. Stroke leaves the patients with residual disabilities like physical dependence, cognitive decline, depression, and seizures.

There is diversity in the incidence, aetiology and prognosis of stroke in young patients in India and Western countries. Studies of Indian immigrants to industrialized countries have shown that they are more susceptible than Caucasians to coronary artery disease and stroke[5]. The magnitude of this increased susceptibility is higher for young Indian adults than older adults. Young stroke patients constitute 15 – 30% of all stroke patients in India [5–11], as opposed to 3.0 –8.5% of all stroke patients in the West[12–17]; however, it should be borne in mind that India is demographically younger than the more developed countries of the West. The aetiology of stroke also varies from study to study, due to referral bias, differences in admission policy, patterns of providing and documenting emergency services, facilities available for investigation. The risk of cerebrovascular disease also differs between races at a younger age. The risk of subarachnoid hemorrhage (SAH) and intra cerebral hemorrhage (ICH) is higher in the non-white population. In addition, significant racial differences have been found in terms of the types and prognosis of stroke. Age wise segregation of cases in stroke is important as 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 apart from the conventional ones. They are also different from childhood strokes which have been classified as those occurring in less than fifteen years of age.

Acute management, prognosis and long term strategies to prevent recurrence vary considerably depending

on the aetiology and type of stroke [18]. There are very few studies from India on stroke in young patients from a tertiary referral centre [7,8,10,18], and most of these have involved ischemic stroke, conducted before the widespread use of modern neuro-imaging methods; thus, with few exceptions[5,7,11], they did not identify stroke subtypes, aetiopathogenesis, and long term outcome.

2. MATERIALS AND METHODS

Study Design: Prospective observational study

Setting: The study was conducted from Oct 2013 to Dec 2015 in the Department of Neurology, S.B.M.C.H, Chennai, a tertiary referral hospital receiving patients from southern India.

Selection of cases : A sample size of 351 pts of Stroke in Young who were admitted during the mentioned period (Oct 2013 to Dec 2015) were included in study.

Inclusion Criteria

1. Patient in age group 15 -45 years
2. Clinical features of stroke
3. Neuroimaging shows stroke (Ischemic, Hemorrhagic, CVT)
4. Recurrent stroke

Exclusion Criteria

1. Patient outside the age group
2. Patient with head trauma
3. Patient with Transient Ischemic Attacks

All patients who meet the inclusion and exclusion criteria were taken into the study after taking an informed and written consent from the parents/attenders. Detailed history was taken and information collected which included Clinical features, risk factors, aetiology and coincident diseases. A thorough neurological examination was done. The test battery for diagnosis was individualized on a case to case basis depending on possible risk factors. The present study was mainly centred on stroke patients (

Ischemic, hemorrhagic and venous thrombosis) between 15 and 45 years of age. A sample size of 351 patients of Stroke in Young who were admitted during the mentioned period were examined in detail as per the standard protocol of Stroke in Young. Clinical features, risk factors of stroke, and diagnostic tests were evaluated in detail. Stroke was defined according to the criteria of World Health Organization [19]. Stroke types were defined based on the criteria of the Oxford Community Stroke Project [20]. The cases were categorized by etiology according to definitions described [4]:

- Cardio embolic stroke;
- Atherosclerosis;
- Non atherogenic arteriopathy/vasculopathy
- Hematological derangement;
- Stroke of undetermined etiology;
- Miscellaneous.

Pre-mature atherosclerosis was assumed if there were two or more risk factors for atherosclerotic disease in the absence of other identifiable causes of cerebral infarction. The risk factors for atherosclerosis included: Hypertension (sustained systolic blood pressure of >160mmHg and diastolic blood pressure of >90 mm Hg for at least one week after the stroke);

- Diabetes mellitus (history of disease requiring pharmacological or dietary intervention before the stroke);
- Transient ischemic attacks (TIA);
- Coronary artery disease;
- Hyperlipidemia (serum triglyceride concentration of >160mg%, cholesterol concentration of > 230 mg% and or high density lipoprotein concentration of <35mg%);
- Smoking;
- Peripheral vascular disease

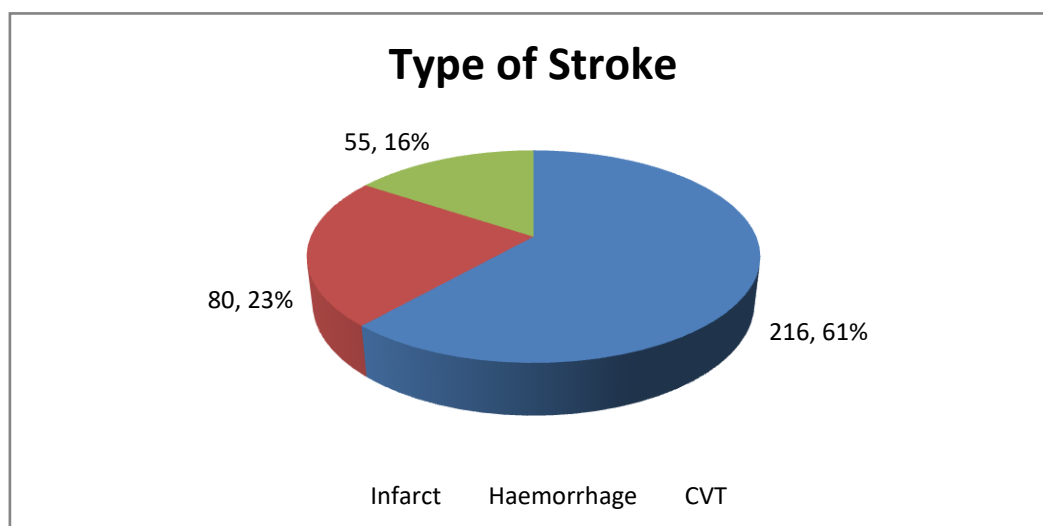
A stroke was attributed to coagulation defect which was defined as prolonged prothrombin time, partial thromboplastin and bleeding time, oral contraceptive pills (OCP) if the woman was using these at the time of stroke in the absence of other identifiable factors. Alcohol was considered as the cause of stroke if the patient had a history of excessive use of alcohol and had no other identifiable cause. Data from neuro imaging (computerized tomography, magnetic resonance imaging), carotid duplex study, digital subtraction cerebral angiography (DSA), magnetic resonance angiography (MRA) of cerebral vessels, cerebrospinal fluid evaluation, 24 -hour Holter monitoring, electrocardiography, echocardiography, chest X-Ray and laboratory tests (APLA, serum homocysteine level, serum lactate etc.) were reviewed.

Based on neuroimaging findings, the patients were assigned to subtypes of stroke, i.e. hemorrhagic vs. ischemic stroke. Ischemic stroke were divided into various subtypes as per TOAST classification (Trial of Org 10172 in Acute Stroke Treatment).The TOAST classification denotes five subtypes of ischemic stroke: (1) large-artery atherosclerosis,(2) cardioembolism, (3) small-vessel occlusion, (4) stroke of other determined aetiology, and (5) stroke of undetermined aetiology.

3. Results

The total no of patient admitted for stroke in young in age group 15-45 years were 351 from October 2013 to December 2015 in the Department of Neurology. Patient were divided in different groups based on types of stroke, gender and age group

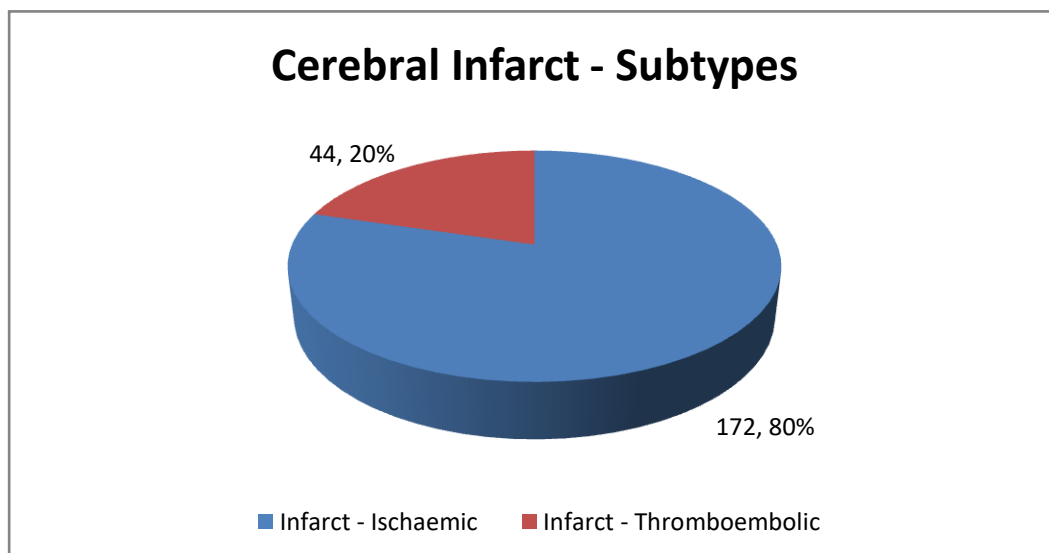
Type of Stroke



Type of Stroke	Number	%
Infarct	216	61.54
Haemorrhage	80	22.79
CVT	55	15.67
Total	351	100

In our study, 351 stroke patients was the sample size. Majority of the sample contained infarct type (n=216, 61.54%) followed by haemorrhage type (n=80, 22.79%) and rest (55, 15.67%) were CVT type of stroke.

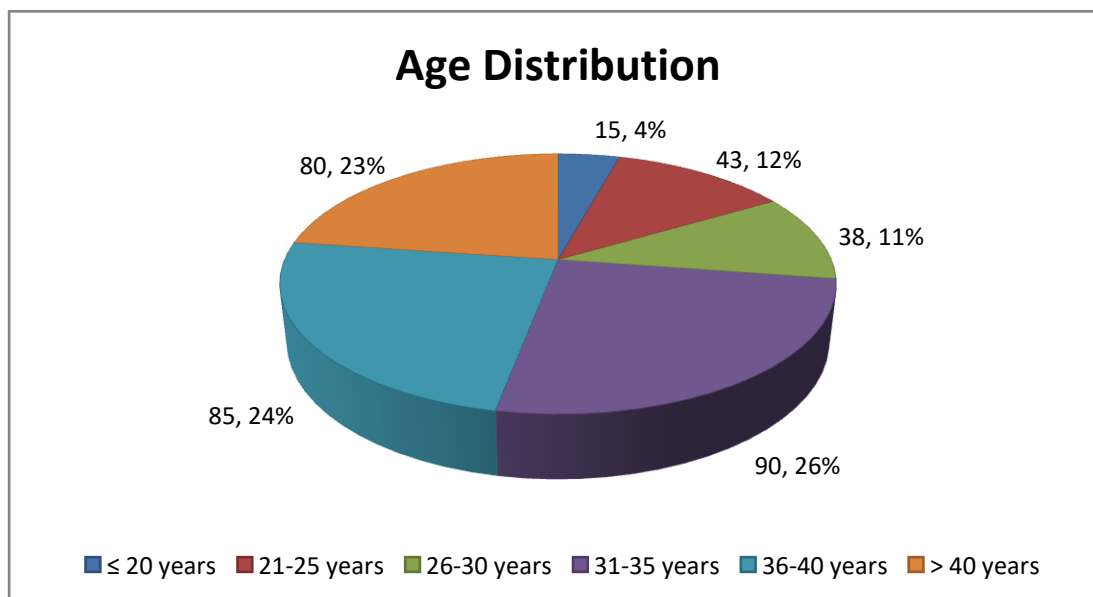
Cerebral Infarct – Subtypes



Cerebral Infarct - Subtypes	Number	%
Infarct - Ischaemic	172	79.63
Infarct - Thromboembolic	44	20.37
Total	216	100

Among the cerebral infarct patients, Majority belonged to ischaemic type (n=172, 79.63%) followed by thromboembolic type of stroke (n=44, 20.37%).

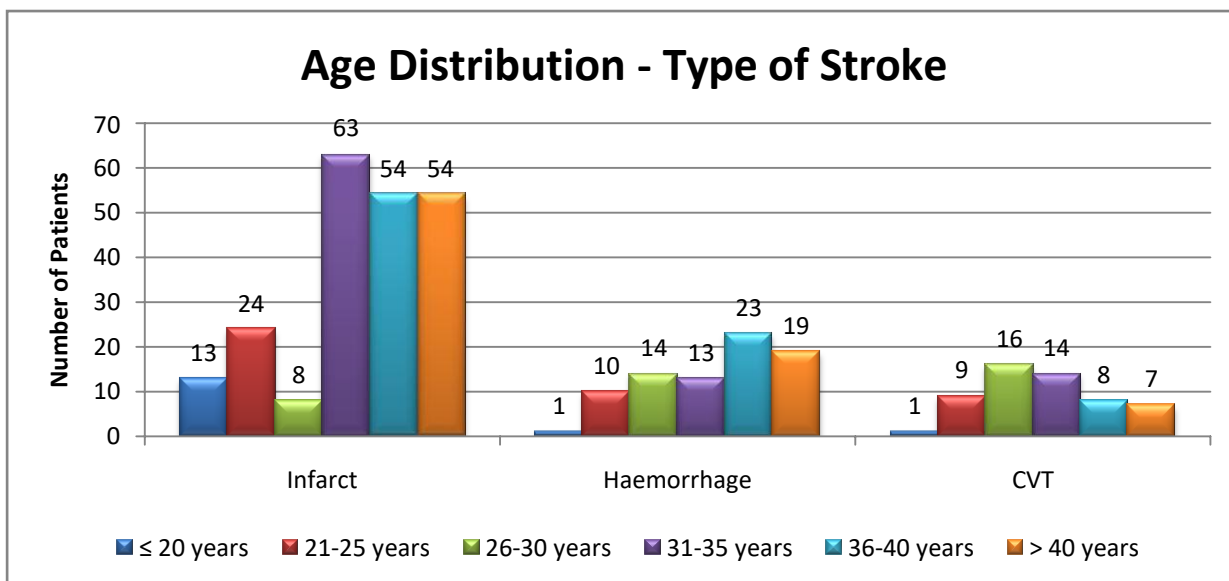
Age Distribution



Age Distribution	Combined	%
15-20 years	15	4.27
21-25 years	43	12.25
26-30 years	38	10.83
31-35 years	90	25.64
36-40 years	85	24.22
41-45 years	80	22.79
Total	351	100

When analysed based on age distribution it was found that majority of stroke patients belonged to 31 -35 years age class interval (n=90, 25.64%) followed by 36 -40 years age class interval(n=85, 24.22%).

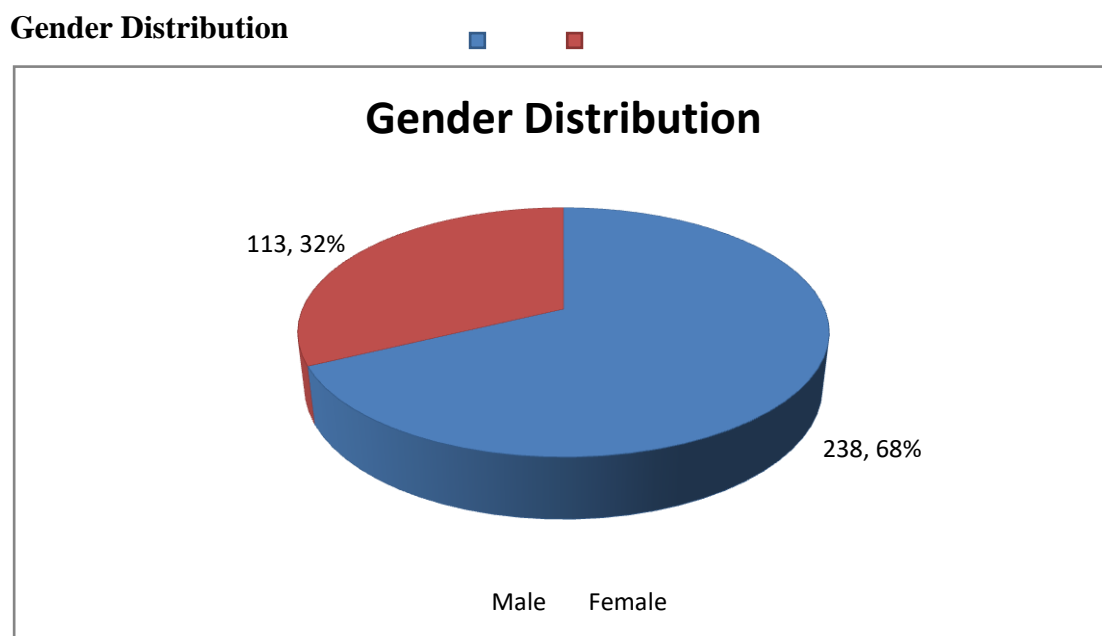
Age Distribution - Type of Stroke



Age Distribution - Type of Stroke	Infarct	%	Haemorrhage	%	CVT	%	Combined	%
15-20 years	13	6.02	1	1.25	1	1.82	15	4.27
21-25 years	24	11.11	10	12.50	9	16.36	43	12.25
26-30 years	8	3.70	14	17.50	16	29.09	38	10.83
31-35 years	63	29.17	13	16.25	14	25.45	90	25.64
36-40 years	54	25.00	23	28.75	8	14.55	85	24.22
41-45 years	54	25.00	19	23.75	7	12.73	80	22.79
Total	216	100	80	100	55	100	351	100

Age Distribution - Type of Stroke	Infarct	Haemorrhage	CVT
N	216	80	55
Mean	34.95	35.16	31.73
SD	7.79	6.97	7.09
P Value One Way ANOVA	0.8250		

When age distribution was matched against type of stroke it was found that majority of infarct patients belonged to 31-35 years age class interval(n=63, 29.19%) with a mean age of 34.95 years, majority of hemorrhage patients belonged to 36-40 years age class interval(n=23, 28.75%) with a mean age of 35.16 years and majority of CVT patients belonged to 26 -30 years age class interval(n=16, 29.09%) with a mean age of 31.73 years. The association between the stroke groups and age distribution is considered to be not statistically significant since $p > 0.05$ as per one way ANOVA test.



Gender Distribution	Number	%
Male	238	67.81
Female	113	32.19
Total	351	100

When analyzed based on gender distribution it was found that majority of stroke patients belonged to male gender class interval (n=238, 67.81%) followed by female gender class interval

(n=113, 32.19%).

Risk factor according to gender in Ischemic group

Risk factor	Male (n=172)	Female (n=44)	P value
Hypertension (90)	78	12	0.0230
Smoking (56)	56	0	< 0.0001
Alcohol (52)	52	0	0.0002
Diabetes Mellitus (79)	46	33	< 0.0001
Serum cholesterol (>240mg%) (56)	38	18	0.0110
Serum Triglyceride (>160mg%) (69)	48	21	0.0119
Coronary artery disease (38)	32	6	0.4399
Carotid artery disease (43)	32	11	0.3431
Transient Ischemic attack (37)	26	11	0.1205
Family history (16)	12	4	0.6328
Obesity (62)	42	20	0.0059
OSA ()	23	13	0.0120

Hypertension

The incidence of hypertension among male patients with ischemic infarct was 45.35 % (n=78). In the female patients with ischemic infarct the incidence of hypertension was 27.27 % (n=12). The association between the ischemic infarct gender groups and hypertension status is considered to be statistically significant since p value is 0.0230 as per chi squared test. The increased incidence of hypertension in male patients with ischemic infarct was meaningfully and significantly more compared to female patients with ischemic infarct by 1.66 times with a difference of 18.08 percentage points.

Smoking

The incidence of smoking among male patients with ischemic infarct was 32.56 % (n=56). In the female patients with ischemic infarct the incidence of smoking was 0.00 % (n=0). The association between the ischemic infarct gender groups and smoking status is considered to be statistically significant since p value is < 0.0001 as per chi squared test. The increased incidence of smoking in male patients with ischemic infarct was meaningfully and significantly more compared to female patients with ischemic infarct by >33 times with a difference of 32.56 percentage points.

Alcohol Intake

The incidence of alcohol intake among male patients with ischemic infarct was 30.23 % (n=52). In the female patients with ischemic infarct the incidence of alcohol intake was 0.00 % (n=0). The association between the ischemic infarct gender groups and alcohol intake status is considered to be statistically significant since p value is 0.0002 as per chi squared test. The increased incidence of alcohol intake in male patients with ischemic infarct was meaningfully and significantly more compared to female patients with ischemic infarct by >30 times with a difference of 30.23 percentage points.

Diabetes Mellitus

The incidence of diabetes among male patients with ischemic infarct was 26.74 % (n=46). In the female patients with ischemic infarct the incidence of diabetes was 75.00 % (n=33). The association between the ischemic infarct gender groups and diabetes status is considered to be statistically significant since p value is < 0.0001 as per chi squared test. The decreased incidence of diabetes in male patients with ischemic infarct was meaningfully and significantly less compared to female patients with ischemic infarct by 2.80 times with a difference of 48.26 percentage points.

Serum Cholesterol (>240mg%)

The incidence of Serum Cholesterol (>240mg%) among male patients with ischemic infarct was 22.09 % (n=38). In the female patients with ischemic infarct the incidence of Serum Cholesterol (>240mg%) was 40.91 % (n=18). The association between the ischemic infarct gender groups and Serum Cholesterol (>240mg%) status is considered to be statistically significant since p value is 0.0110 as per chi squared test. The decreased incidence of Serum Cholesterol (>240mg%) in male patients with ischemic infarct was meaningfully and significantly less compared to female patients with ischemic infarct by 1.85 times with a difference of 18.82 percentage points.

Serum Triglycerides (>160mg%)

The incidence of Serum Triglycerides(>160mg%) among male patients with ischemic infarct was 27.91 % (n=48). In the female patients with ischemic infarct the incidence of Serum Triglycerides(>160mg%) was 47.73 % (n=21). The association between the ischemic infarct gender groups and Serum Triglycerides(>160mg%) status is considered to be statistically significant since p value is 0.0119 as per chi squared test. The decreased incidence of Serum Triglycerides(>160mg%) in male patients with ischemic infarct was meaningfully and significantly less compared to female patients with ischemic infarct by 1.71 times with a difference of 19.82 percentage points.

CAD(Coronary artery disease)

The incidence of CAD among male patients with ischemic infarct was 18.60 % (n=32). In the female patients with ischemic infarct the incidence of CAD was 13.64 % (n=6). The association between the ischemic infarct gender groups and CAD status is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

Carotid Artery Disease

The incidence of carotid artery disease among male patients with ischemic infarct was 18.60 % (n=32). In the female patients with ischemic infarct the incidence of carotid artery disease was 25.00 % (n=11). The association between the ischemic infarct gender groups and carotid artery disease status is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

TIA (Transient ischemic attack)

The incidence of TIA among male patients with ischemic infarct was 15.12 % (n=26). In the female patients with ischemic infarct the incidence of TIA was 25.00 % (n=11). The association between the ischemic infarct gender groups and TIA status is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

Family History

The incidence of family history among male patients with ischemic infarct was 6.98 % (n=12). In the female patients with ischemic infarct the incidence of family history was 9.09 % (n=4). The association between the ischemic infarct gender groups and family history status is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

Discussion

The present study covered the one of the largest number of cases of stroke in young from India so far reported, including hemorrhagic ,ischemic and

venous strokes. All patient were treated as per standard protocol for stroke in young. Most of our cases were from Chennai and surrounding rural areas of Tamilnadu and Andhra Pradesh.

Comparison of various Indian studies

S.No	Authors	Year	Common Etiology	Comments
1	Chopra et	1979	Atherosclerotic occlusive disease	Infection, nonspecificarteritis,D M,HTN, contribute very little
2	Dalal et al	1989	Atherosclerosis	HTN, DM, tobacco and low Hb were found to be important risk factor
3	Srinivasan et al	1984	Neurosyphilis, C VT	This has not been confirmed in any other studies
4	Nagaraja	1997	APLA	23% of all young patient positive anticardiolipin antibody
5	Mehndira tta et al	2004	Cardioembolic stroke	29.3% had cardioembolic stroke
6	Padma et al	2014	Other determined cause and undetermined causes	57% had undetermined causes

7	Present study	2016	Atherosclerotic occlusive disease, Cardioembolic, CVT	-Incidence of CVT is high in our study -OSA incidence is higher
---	---------------	------	-------------------------------------------------------	--------------------------------------------------------------------

OSA-Obstructive sleep apnea, HTN-Hypertension, DM-Diabetes

Melitis

Various studies of stroke in young patients from India were compared for risk factors and etiologies found in various parts of India. Most of these studies were done in the pre CT era, except for that of Nagaraja et al, Mehndirata et al and the present study. Nagaraja et al in their study found that 23% of the young stroke patients had positive anticardiolipin antibodies. In our study, only 9 patients out of 171 ischemic stroke (5.26%) patients had positive anticardiolipin antibody.

Srinivasan et al reported meningo vascular syphilis as an important risk factor for strokes in young in South India (10); but our study did not find a single case of meningo vascular syphilis causing stroke in young patients. This is expected, as neurosyphilis is much rarer today's world as compared 1980s. Mehndiratta et al conducted a study in a university hospital in north india in 127 patients. Ischemic stroke accounted for 85.8% of the young patients of young stroke, while 14.2% had spontaneous intracerebral hemorrhage (ICH). In our study ischemic stroke accounts for 61.53%, spontaneous intracranial hemorrhage in 22.79% and CVT in 15.63%. Their study didn't include CVT cases.

CONCLUSION

This is one of the largest studies of stroke in young patients from India. The major risk factors for stroke in our young patients were hypertension, hypercholesterolemia, hypertriglyceridemia, smoking and alcohol. Oral contraceptives and illicit drug use were infrequent risk factors, unlike the results reported in Western studies. Atherosclerotic occlusive disease Cardioembolic stroke, vasculitis, homocysteinemia state were the common causes of ischemic stroke. Incidence of CVT is higher in young patients as compared to previous studies due to easy availability of MRI/MRA/MRV. About 3.98% of our patients posed diagnostic and therapeutic challenges, in which the exact cause of stroke could not be discerned. Further role of TEE is advocated as routine for all stroke in young. OSA/Obesity was significantly related to stroke in young. We advocate a battery of tests in stroke in young before labelling them cryptogenic stroke.

Funding: No funding sources

Ethical approval: The study was approved by the Institutional Ethics Committee

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

The encouragement and support from Bharath University, Chennai is gratefully acknowledged. For provided the laboratory facilities to carry out the research work.

REFERENCES

1. Bonita R, Mendis S, Truelsen T, Bogousslavsky J, Toole J, Yatsu F. The global stroke initiative. *Lancet Neurology*. 2004; 3: 391 –3. [PubMed]
2. Fratiglioni L, Wayne M E, Schoenberg D G et al: Mortality from Cerebrovascular Disease, International Comparisons and Temporal Trends. *Neuroepidemiology*, 1983: 2; 101 - 62. KurtzkeJF: In: Mcdowell FH et al.(eds.) *Cerebrovascular Survey Report NINCDS/ NIHPubl. Health Services USA,1985; 1–34*
3. Adams HP Jr, Kappelle LJ, BillerJ et al: M. Ischemic stroke in young adults. Experience in 32 patients enrolled in the Iowa Registry of strokeinyoungadults. *Arch Neurol*,1995;52(5): 491 – 95
4. Kittner SJ, Stern BJ, Wozniak M et al: Cerebral infarction in young adults: the Baltimore-Washington Cooperative Young Stroke Study. *Neurology*, 1998;50(4);890 -94
5. Srinivasan K: Ischemic Cerebrovascular Disease in the Young. Two common causes in India. *Stroke*, 1984: 15(4): 733 - 35
6. Bansal B C, Prakash C, Jain AL, Brahma nandam KR: Cerebro- vascular disease in young individuals below the age of 40 years. *Neuro India*, 1973; 21(1):11 -18
7. Chopra JS, Prabhakar S: Clinical features and risk factors in stroke in young. *Act A Neuro IScand*,1979; 60(5):289 - 300
8. Radhakrishnan K, Ashok PP, Sridharan R, Mouseme: Stroke in the young: Incidence and pattern in Benghazi, Libya, *ActaNeuroIScand*,1986; 73(4):434 - 38
9. OsuntokunBO, Bademosi O, Akinkugbe et al: Incidence of stroke in an African Country: results from the Stroke RegistryatIbadan, Nigeria,1973- 1975. *Stroke*, 1979;10(2):205 -7
10. Dalal PM: Strokes (CVD) in the young. In Chopra JS, Jaganathan K, Sawhney IMS (eds). *Advances in Neurology*. Amsterdam Excerpta Medica, 1990: 73 - 84
11. Dalal PM: Stroke in the young in West Central India. InGoldstein LB. New York: RavenPress, 1979:339 - 48
12. LenoC, BercianoJ, CombarrosOetal: A prospective study of stroke in young adults in Cantabria, Spain. *Stroke*,1993;24(6): 792 -95
13. Lidegaard, Some, Andersen MV: Cerebral thromboembolism among young women and men in Denmark,1977 -1982. *Stroke*,1986;17(4): 670 -75

14. Nencini P, Inzitari D, Baruffi MC et al: Incidence of stroke in young adults in Florence, Italy. *Stroke*,1988; 14:110 - 14
15. Bevan H, Sharma K, Bradley W: Stroke in young adults. *Stroke*, 1990;21(3): 382 -86
16. Hart RG, Miller VT: Cerebral Infarct in young adults: A practical approach. *Stroke*,1983; 14: 110 -14
17. Bogousslavsky J, Pierre P: Ischemic stroke in patients under age 45. *Neurol Clin*,1992; 10(1): 113 -24
18. Nayak SD, Nair M, Radhakrishnan K, Sarma PS, Ischemic stroke in the young adult: Clinical features, risk factors and outcome. *NatlMed J India*, 1997;10(3): 107 -12
19. Hatano S: Experience from multicentre stroke register. A preliminary report. *Bull WHO*, 1986; 54:541 - 53
20. Oxfordshire Community Stroke Project: Incidence of stroke in Oxfordshire: First year experience of community of stroke register. *Br Med J*, 1988; 287: 713 -17
21. Bevan H, Sharma K, Bradley W: Stroke in young adults. *Stroke*. 1990;21(3): 382 -86
22. Philip B, Gorelick M, Schneck L, Berglund F: Status of lipids risk factor for stroke. *Neuroepidemiology*, 1997; 16:107 - 15
23. Carolei A, Marini C, Ferranti et al: A prospective study of cerebral ischemia in the young. Analysis of pathogenic determinants. The National Research Council Study Group Stroke. 1993;24(3): 362 -67
24. Alvarez J,Matias- Guis J, Sumalla J et al: Ischemic stroke in young adults. Analysis of etiological subgroups. *ActaNeuroIScand*,1989; 80(1):28 -34
25. Lanzionog, Andreolia, Di Pasquale G et al: Etio pathogenesis and prognosis of cerebral ischemis in the young and adults. A survey of 155 treated patients. *ActaNeuroIScand*, 1991; 84(4):321-25.