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STUDY OF CAUSES OF STROKE IN YOUNG POPULATION VISITING A TERTIARY CARE HOSPITAL WITH EMPHASIS ON VASCULAR IMAGING.

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ABSTRACT The results of a systematic analysis of patients aged 15-49 years attending stroke clinic in eastern India were evaluated based on based on clinical and imaging features from January 2012– June 2013. Out of 98 patients of stroke, the mean age of ischaemic and haemorrhagic stroke patients was 34.26 years and 32.81 years respectively. Of the 66 patients of ischaemic stroke, 10.4% had large artery atherosclerosis followed by cardio embolic (14.5%) and lacunar (8.3%). Among 32 haemorrhagic stroke patients, aneurysmal bleed (30%) was the most common aetiology. The stroke of other determined aetiology was 52% and in 14.5% aetiology was undetermined. It is evident that the nature and cause of stroke in young adults is different and unique, and they need different diagnostic work. Attempts must be made to formulate specific guidelines aimed at stroke detection, management, prevention, and rehabilitation in the young adults' population.

KEYWORDS : Stroke, Neuroimaging, CNS

INTRODUCTION:

A stroke is a clinical syndrome characterized by rapidly developing clinical symptoms and / or signs of focal and at times global (applies to patients in deep coma and those with subarachnoid hemorrhage) loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.[1] The impact of stroke on the individual's family and society is strongest when it affects a young adult. Previous hospital-based data from India indicated a high proportion of stroke in young adults (first-ever stroke onset <40 years of age), ranging between 15% and 30 % [2]. However, this number was biased because of preferential admission policy. In a recent well-designed population-based study [3], 8.8% of stroke subjects were young adults, which is similar to that seen in Western countries. Based on neuroimaging, recent studies in India have determined the stroke subtypes and the ratio of cerebral infarct to hemorrhage range as 1.86:1 to 2.21:1[3]. Cerebral hemorrhage is proportionately higher in the eastern Indian population than in Western countries, where the ratio of infarct to hemorrhage is 5:1. In up to 35 % patients of stroke in young adults, specific aetiological diagnoses may not be found. This may be explained by the insufficient extent and timing of investigation[4].

Currently, only few studies have addressed causes of stroke in developing countries like India where the burden of vascular risk factors like diabetes and hypertension is growing fast among younger population.

There are various classification systems for acute ischemic stroke. The TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification is based on clinical symptoms as well as results of further investigations. On this basis, a stroke is classified as being due to (a) thrombosis or embolism due to atherosclerosis of a large artery, (b) embolism of cardiac origin, (c) occlusion of a small blood vessel, (d) other determined cause and (e) undetermined cause[5].Many studies have examined the incidence of stroke in the young adults. However, only recent studies using CT have accurately identified the incidence of the major subtypes of stroke (cerebral infarction, intracerebral hemorrhage [ICH], and subarachnoid hemorrhage [SAH]). Still there is a paucity of literature regarding young adults' stroke, its neuroimaging findings and particularly vascular imaging characteristics in this subgroup of patients.

AIM AND OBJECTIVE

1. To evaluate the cases of stroke in age group 15-49 years by analyzing the history, clinical, and neuroimaging, in patients attending a tertiary care centre in eastern India.
2. Use of multi-modal vascular imaging (as available) to ascertain stroke aetiology.

MATERIALS AND METHODS

A non-randomized descriptive (cross-sectional) study of 98 consecutive patients of stroke who were admitted to the Department of Neurology in SSKMH (or were referred to the stroke clinic) fulfilling the WHO definition of stroke during study period of January 2012 to February 2013 was undertaken. Patients who were included in the study group had the following characteristics:

SUBJECT INCLUSION CRITERIA:

Subjects aged 15-49 years attending tertiary neurology centre, fulfilling WHO definition of stroke with imaging evidence (CT and MRI) suggestive of stroke.

SUBJECT EXCLUSION CRITERIA:

- Head injury patients
- Intracranial Space Occupying Lesions (tumor/SDH/EDH)
- Any CNS infection
- Known case of demyelinating disease
- Any case with static encephalopathy or significant metabolic derangement.

METHOD OF STUDY:

All consecutive stroke patients aged 15-49 years attending Stroke Clinic and Neurology OPD, neurology wards of BIN, SSKM hospital, were evaluated for age, gender, risk factors, family history, type of neurodeficit and neurological examination. An informed written consent was taken, and blood samples were drawn in fasting condition for evaluation of biochemical parameters like lipid profile, and blood sugar level. Further, radiological assessment including ECG, 2D echocardiography, carotid and/ or vertebral doppler and neuroimaging (CT and/or MRI/DSA) were conducted in all cases. All subjects were treated with conservative management and necessary physiotherapy. All the drugs used were commercially available and tried & tested.

Vascular imaging using intracranial MRA was offered to all patients depending on affordability. Digital Subtraction Angiography (DSA) was done in all patients suspected to have vascular malformations.

Further, if no obvious source of cardio embolic stroke was found, then DSA again was offered to evaluate for the cause of stroke. DSA was done using Philips Alleva FD 70/70 machine. DSA was done in patient with the following features:

1. All patients of Subarachnoid Hemorrhage (SAH)
2. Patients with recurrent / crescendo (Transient Ischaemic Attack) TIAs in the same territory
3. Suspected carotid or vertebral artery dissection when MRI (Magnetic Resonance Imaging) is inconclusive
4. Patients with intracerebral bleed when an underlying AVM (Arteriovenous malformation) is suspected (peripheral location of the bleed, no evidence or history of hypertension, recurrent bleeds in the same territory, etc.)

DATA ANALYSIS METHOD:
All case report forms were checked for completeness and inappropriate or illogical responses. The forms were entered using Microsoft 2007 Excel worksheet. The databases were validated, and all inconsistencies and differences were resolved.

OBSERVATIONS
All consecutive stroke patients who were admitted in neuromedicine ward or referred to stroke clinic, fulfilled the inclusion criteria and were subjected to a thorough clinical and neurological examination. With the help of data thus accumulated ancillary testing was done to evaluate the cause of stroke in this age group. Further vascular imaging was performed to look for aneurysms, arterio-venous malformations, and arterial stenosis and to establish diagnoses such as arterial dissections.

Age and demographic characteristics:
In the present study a total of 66 patients (67.3%) out of total 98 were found to have ischaemic stroke, and 32 patients (32.7%) had haemorrhagic stroke. The ratio of ischaemic to haemorrhagic stroke in study was 2.1:1. The youngest patient in the study was 16 years old in ischaemic subgroup and 17 years old in haemorrhagic subgroup at the time of presentation. The mean age of ischaemic and haemorrhagic stroke patients were 34.26 years and 32.81 years, respectively. Of the total 98 patients studied, 37 were females and 61 were males. In ischaemic subgroup 40 patients (60.6%) were males and 26 patients (39.4%) were females. In the haemorrhagic stroke subgroup, of a total of 32 patients, 21 patients (65.6%) were males while 11 patients (34.4%) were females.

Presenting features:
As depicted in Table 1, out of 98 patients studied, the most common presenting feature of stroke was motor paresis (43.9%), followed by headache (16.3%), followed by seizures and ataxia (11.2% each).

Table 1. Presenting features of Ischaemic and haemorrhagic stroke.

Presenting Features	Ischemic	Haemorrhagic	Total
Headache	4(6%)	12 (37.5%)	16 (16.3%)
Seizure	3(4.5%))	8(25%)	11 (11.2 %)
Cognitive deficit	3(4.5%)	0	3(3.1%)
Motor paresis	38(57%)	5(15.6%)	43 (43.9%)
Ataxia	9(13.6%)	2(6.2%)	11(11.2%)
Hemianopia	4(6%)	1(3.1%)	5(5.1 %)
Loss of consciousness	3(4.5%)	4(12.5%)	7(7.1%)
Paraesthesia	2(3%)	0	2(2%)
Total	66	32	98

Imaging characteristics:
As depicted in Table 2, a CT scan of the brain was done in 93 patients (94.8%) and MRI in 74 patients (75%), MRA in 74 patients and DSA in 63 patients, Carotid Doppler in 98 patients, CTA in 2 patients and 2D echo in 98 patients.

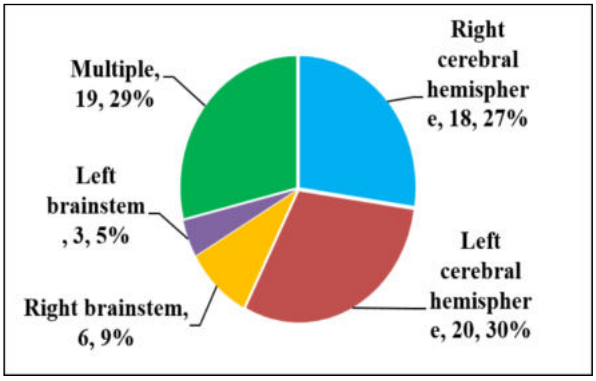
Table 2. Patients who underwent neuroimaging, vascular imaging and transthoracic 2D echocardiography.

Imaging	Type of Test (in Number of Patients)	Normal
Neuroimaging	CT-93; MRI-74	
Vascular Imaging	MRA-74/98; DSA-63/98; Carotid Doppler-(98); CTA-2	MRA-38; DSA-10; Carotid Doppler-72
2D Echo	98	2D Echo -72

Topography of stroke
Stroke in anterior versus posterior circulation and stroke topography on imaging is depicted in Figure 1. Out of total 66 patients of ischaemic stroke, 60.61% patients had stroke in the anterior circulation. Posterior circulation stroke was seen in 10.61% patients of ischaemic stroke. A total of 28.8% patients of ischaemic stroke suffered from a stroke in both anterior and posterior circulations. Regarding the topography of the ischaemic stroke cases, 27.3% patients suffered from right cerebral infarction while left cerebral infarction occurred in 30.3% patients. Infarcts at multiple locations were seen in 28.8% patients. Brainstem involvement was seen in 7% patients and cerebellum was involved in 6% cases or patients.

Out of 32 patients of haemorrhagic stroke, lobar bleed was seen in 13 patients (40.6%), cerebellar in 2 patients (6.3%), thalamic bleed in 5 patients (15.6%), basal ganglia in 5 patients (15.6 %), and subarachnoid bleed in 3 patients. Bleed in multiple areas was seen in 2 patients, while brainstem bleed was also seen in 2 patients. A total of 98 patients were present in this study.

Figure 1.



Specific imaging characteristics for stroke aetiologies:
2D echocardiography: Out of the 98 cases or patients, 2D Echocardiography done. It helped in establishing diagnosis of cardio embolic stroke in 8 patients. Various aetiologies were RHD (Rheumatic Heart Disease): MS (Mitral Stenosis) (moderate) in 3 patients, RHD: MS (severe) in 1 patient and ischaemic DCM (Dilated Cardiomyopathy) in 3 patients. Other findings on 2D echo were left ventricular hypertrophy (LVH) in 15.3% patients and pulmonary artery hypertension (PAH) in 3.1% patients.

Carotid Doppler findings: Of the 98 patients of stroke, carotid doppler were normal in 72 patients (73.5 %). Carotid stenosis was found in 10 patients in which 6 were unilateral and 4 were bilateral. One patient was found to have carotid stenosis with thrombus. Bilateral carotid stenosis with plaque was seen in 4 patients. 11 patients had raised intimal medial thickness (IMT) but without other changes of atherosclerosis. Distal flow reduction suggestive of dissection of carotid artery was present in 3 patients and false lumen in 2 patients.

Magnetic Resonance Angiography (MRA) findings: As depicted in Table 3, out of the total 75 MRAs done, 38(50.66%) MRAs were normal. Steno-occlusive disease of intracranial vessels was seen in 5 patients (6.66%), venous sinus thrombosis was seen in 5 patients (6.66%) and dissections of the cervical segment of the internal carotid artery (ICA) were seen in 7 patients (9.33 %).

Table 3.MRA findings

MRA findings	Number of patients
Steno-occlusive disease of intracranial vessels with collaterals	5 (6.66%)
Venous sinus thrombosis	5(6.66%)
Dissections (all cervical)	7(9.33%)
Decreased flow in major aortic arch vessels with collaterals	4(5.1%)
Atherosclerosis of carotid arteries	7(9.33%)
Intracranial Aneurysms	2(2.6%)
Ectasia of Intracranial artery with aneurysmal dilatation	2(2.6%)
Arteriovenous malformations (AVM)	3(4%)
Other vascular abnormalities	2 (2.6%)
Normal	38 (50.66%)
Total	**75**

DSA findings: As depicted in Table 4, out of the 98Patients, DSA was done in 63 patients (64 .28 %). 10 patients (15.8 %) had no abnormality on DSA.

Table 4. DSA findings

Findings on DSA	No of patients
Steno-occlusive disease of distal ICA and PCA	2 (3.1%)
Steno-occlusive disease affecting distal ICA only	4(6.3%)
Venous sinus thrombosis	2 (3.1%)
Non visualization of aortic arch vessels with extensive collateralization	6(9.2%)

Dissection of cervical carotid artery	9(14.28%)
Dissection of vertebral artery	2(3.1 %)
Thinned out intracranial vessels with beading	2(3.1 %)
Cut –off stenosis of MCA	2(3.1 %)
Atherosclerotic narrowing of carotids with plaques (unilateral)	6 (9.2 %)
Atherosclerotic narrowing of carotids bilateral with plaques	3(4.7%)
Intracranial aneurysm s	6 (9.2%)
Intracranial AVM	7 (11.2%)
Other abnormalities	2 (3.1%)
Normal	10(15.8%)
Total	**63**

DISCUSSION

At least one modality of neuroimaging (CT scan or MRI) was done in all patients. Few studies have reported topography of ischaemic stroke among young adults. These studies have shown that anterior circulation strokes are more frequent than those involving posterior circulation. Out of 66 patients of ischaemic stroke, 60.61% patients had stroke in anterior circulation while posterior circulation stroke was seen in 10.61% patients and total of 28.8% patients of ischaemic stroke suffered from a stroke in both circulations.

Topographically in ischaemic stroke patients 27.3% suffered from right cerebral infarction while left cerebral infarction occurred in 30.3% patients. Infarcts at multiple locations were seen in 28.8% patients. Brainstem involvement was seen in a total of 7%patients while cerebellum was involved in 6% patients. In the Helsinki Stroke registry in topography of infarcts in young adults' anterior circulation, left hemispheric infarcts were more common than right. However, we found a higher number of patients (28.8%) having stroke in both territories. This finding could be explained as a large number of patients suffered from diseases such as atherosclerosis, small vessel occlusion, venous sinus thrombosis, cardio embolism, Moyamoya disease and Takayasu arteritis etc., which are diffuse processes and may involve both circulations.

Out of the 32 cases or patients of haemorrhagic stroke (fig 2), lobar bleed was seen in 13 (40.6%) patients, cerebellar in 2 (6.3%) patients, thalamic bleed in 5(15.6%) patients, basal ganglia in 5 (15.6 %) patients, and subarachnoid bleed in 3 patients. Bleed in multiple areas was seen in 2 patients while brainstem bleed was also seen in 2 patients. In a study of 200 patients with age range of 15 to 40 years, the most common locations of ICHs were lobar in 110 patients (55%), basal ganglia/internal capsule in 43 patients (22%), the brain stem in 26 patients (13%), cerebellum in 10 patients (5%), intraventricular in 8 patients (4%), and multiple in 3 patients (1.5%)[6,7].

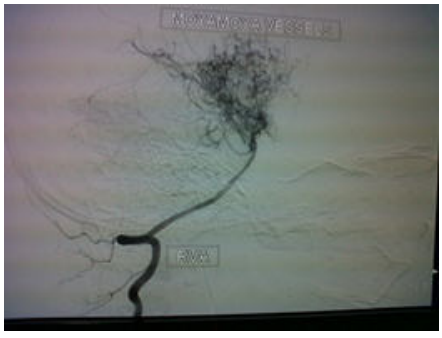
Figure 2: Aetiology of haemorrhagic stroke

Features on transthoracic 2D echocardiography: Cardio embolic stroke is the most frequent subtype in young adults and accounts for up to 46% of ischemic infarcts in this age grouping western literature. Imaging findings typically show a single large vessel occlusion from a solitary embolus or small scattered infarcts in multiple territories from showering of emboli.

In this study out of 98 2D echocardiographies done, 2D echo helped in establishing diagnosis of cardio embolic stroke in 14.5 % patients of ischaemic stroke. Various aetiologies were RHD: MS (moderate) in 3 patients, RHD: MS (severe) in 1 case or patient and ischaemic DCM in 3 patients. Other findings on 2D echo were left ventricular hypertrophy (LVH) in 15.3% patients and PAH in 3.1% patients. Thus, 2D echo was a useful modality for diagnosing high risk cardio embolic cases and should be considered when large stroke is diagnosed on neuroimaging in initial stages so that appropriate treatment strategies can be adopted. Data from several studies indicate cardio embolism causes 13-35% of strokes [8].

About 30–60% of strokes are caused by atherosclerotic disease involving the extra cranial carotid arteries usually within 2 cm of the carotid bifurcation.9 out of the 98 patients of stroke, carotid Doppler findings were normal in 72 patients (73.5 %). Carotid Doppler helped in identifying 6 patients of atherosclerosis in ischaemic subgroup correctly, though underestimation and overestimation of degree of stenosis was a significant drawback. Features suggestive of cervicocephalic arterial dissection (fig 3) was correctly identified in 5 patients by carotid Doppler.

Figure 3: Long segment narrowing of left ICA suggestive of intracranial dissection



Out of the total 78 MRAs done, 38 patients (50.66%) MRAs were normal. Steno-occlusive disease of intracranial vessels was seen in 5 patients (6.66%), venous sinus thrombosis was seen in 5 patients (6.66%) and dissections of cervical segment of ICA were seen in 7 patients (9.33 %). Features suggestive of nonspecific aortoarteritis were detected in 4 (5.1%) patients. Atherosclerosis was seen in 7 patients (9.3 %). Aneurysms of intracranial vessels were successfully detected in 2 patients and AVMs in 3 patients. Other vascular abnormalities included ectasia and dilatations of intracranial ICA (2 patients) and stenosis of MCA in 2 patients. Both of these abnormalities fell in the undetermined aetiology group.

DSA was done in 63 patients (64 .28 %). 10 patients (15.8 %) had no abnormality on DSA. Bilateral atherosclerosis of carotid arteries was seen in 3 patients and unilateral atherosclerosis in 6 patients. Features suggestive of Moyamoya disease (steno-occlusive disease of distal ICA) were seen in 6 patients, of which 2 patients had involvement of the PCA also. Features suggestive of aortoarteritis were seen in 6 patients. Only 2 (3.1%) patients of venous sinus thrombosis were subjected to DSA in which DSA was successful in detecting venous sinus thrombosis. Features suggestive of vasculitis, i.e. beading and thinning of intracranial vessels, were seen in 2 patients. Dissections were detected in 11 patients, of which 2 were vertebral and 9 were carotid dissections. Intracranial aneurysms (fig 4 & 5) were found in 6 patients (9.2%), while AVMs (fig 6) were detected in 7 patients (11.2 %).

Figure 4: NCCT showing hypertensive intracranial bleed

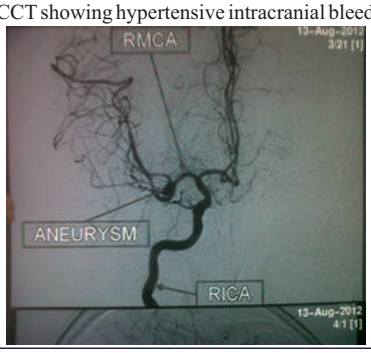


Figure 5: DSA image showing right MCA aneurysm

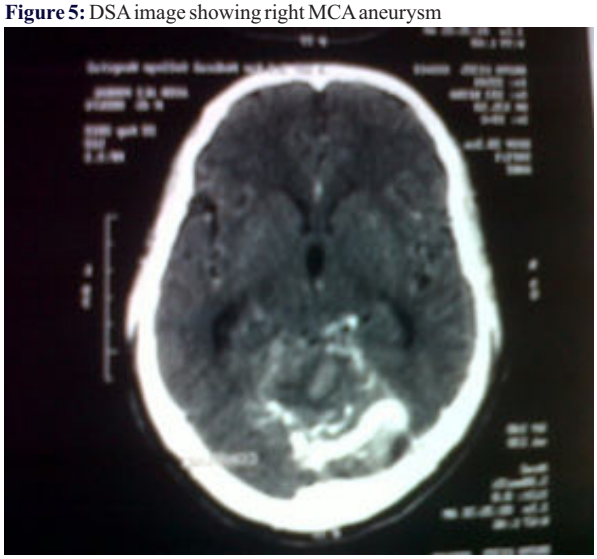
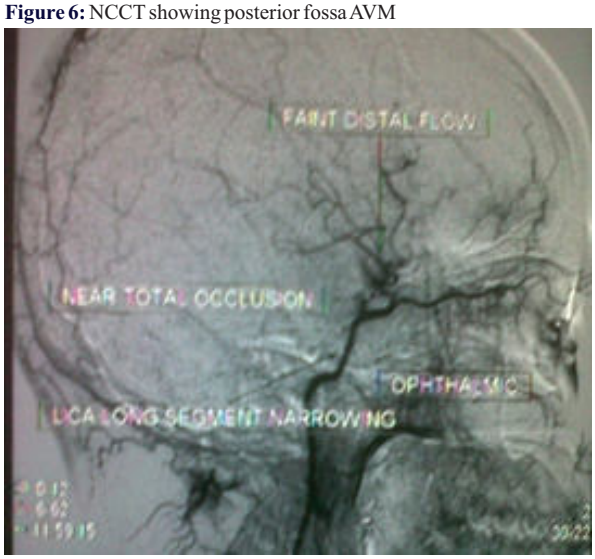


Figure 6: NCCT showing posterior fossa AVM

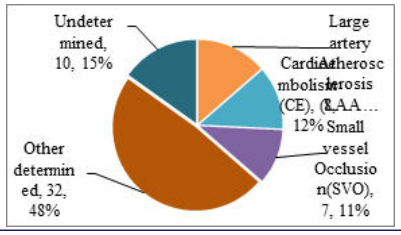


Aetiological classification of stroke

As per trial of ORG-1782 classification for stroke mechanisms in ischaemic stroke, 9 patients suffered from large artery atherosclerosis (13.6%) patients and 8 (12.1%) patients suffered from cardio embolic stroke. Small vessel occlusion was seen in 7 patients (10.6%). The other determined aetiologies in 32(48.5%) patients consisted of a heterogeneous group of patients comprising diagnoses of arterial dissection (16.6%), nonspecific aortoarteritis in 6 patients (9.09%), Moyamoya syndrome in 6 patients (9.09%), cerebral venous thrombosis in 5 patients (7.5%) CADASIL (3.03%) and vasculitis in 1(1.5%). In 10(15.2%) patients, stroke aetiologies could not be ascertained because of incomplete and/or negative investigations.

As depicted in Figure 7, out of the total 10 patients of undetermined aetiology, 2 patients remained undiagnosed after extensive investigations including bubble contrast ECHO and trans oesophageal echocardiography (TOE), Holter monitoring and checks for coagulation abnormalities. In the remaining 9 patients, the cause remained unidentified due to lack of complete work up.

Figure 7.



In a study on stroke in young adults[10] from Sri Chithra Tirunal Institute of Medical Sciences and Technology (SCIMST), Trivandrum, patients of ischemic stroke were classified based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria: 25.2% patients had cardio embolic stroke, 12.6% had large artery atherosclerosis and 7.5% had lacunar infarcts. Strokes due to other determined etiology were 11.2% (7.0% arterial dissection, and one patient each with lupus erythematous, primary antiphospholipid antibody syndrome and protein S deficiency). 4 patients had stroke due to other causes (one case each of Moyamoya disease, Takayasu's arteritis, fibro muscular dysplasia and nephritic syndrome). In comparison to these figures (Figure 1 and Figure 7) we had a lower rate of cardio embolic stroke, lower rate of cardio embolism (12.2%) patients, perhaps due to a referral bias as we conducted the study in a tertiary care neurology specialty hospital. We had similar rates of atherosclerotic disease and small vessel occlusion disease as the SCIMST study. We had a higher rate of other determined etiologies in this study as compared to the SCIMST study. Other determined etiologies comprised of a heterogenous group of disorders including 6 patients (9.1%) of nonspecific aortoarteritis, 6 patients (9.1%) of Moyamoya, 5 patients (7.3%) of cerebral venous sinus thrombosis (1 protein S deficiency, 1 protein C deficiency, I Factor V Leiden mutation, I polycythemia, I undiagnosed coagulopathy), 11 patients (16.6%) of dissection of extra cranial arteries (9 carotid arteries, 2 vertebral arteries). These findings show a higher percentage of dissection as aetiology of young adults' stroke as compared to the above-mentioned study, perhaps owing to higher frequency of DSA done in this study. Similarly, we had a higher rate of nonspecific aortoarteritis and Moyamoya in the study compared to Western literature where these conditions account for less than 1% of stroke in young adults, perhaps due to higher prevalence in the study population. Percentages of patients with large-artery atherosclerosis according to TOAST classification in studies have ranged from 6% to 21%, the highest proportion being in young adult Koreans [11]. One European study that used 49 as the upper age limit, reported relatively large proportions of large-artery atherosclerosis (15%) [12].

A high number of atherosclerotic stroke patients similar to above studies were found due to Asian population considered in the first study and higher age group in European study.

Cerebral small-vessel disease is generally related to older age and presence of hypertension or diabetes. Percentages of small-vessel disease in young adults ranged thus from 2% to 9% in most studies [13,14].

A higher percentage (10.6 %) of patients was observed to be suffering from small vessel occlusion, perhaps due to a high prevalence of hypertension in the study. With an incidence rate of only about 2.6 to 3.0 per 1,00,000 inhabitants in the general population,[15] the most important cause of stroke in young adults— and naturally in the other determined TOAST-group—is cervical artery dissection (CAD), accounting for 10% to 24% of ischemic strokes in large and mostly recent patient series from numerous geographic regions. Study findings showed a large number of arterial dissections similar to western studies perhaps because a large number of patients underwent DSA, which has higher sensitivity in recognizing dissections.

CONCLUSION

The aetiological diagnosis of stroke in young adults needs a different and more complex diagnostic work up than does stroke in older adults. The wide variety of causes of stroke in the young adults necessitates a careful diagnostic approach and a battery of investigative approaches. Multimodal vascular imaging including DSA may aid in diagnosis of causes such as arterial dissection which have a different management strategy Vis a Vis other causes. Studies comparing the cost-effectiveness of different strategies (e.g., Comprehensive versus staged versus clinically oriented) are also needed to search for the causes of stroke in this age group.

Finally, attempts must be made to formulate specific guidelines aimed at stroke detection, management, prevention, and rehabilitation in the young adult's population, which do not exist at present.

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