Original Research Article

A study of ischemic stroke in young adults in tertiary care hospital in Salem

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Abstract

Background: Age is the most powerful predictor of the stroke. The incidence of stroke increases exponentially with age. It is now well known that stroke in young adults is not a rare event. Although the frequency of stroke is lower than in the general population, stroke is particularly dramatic in younger patients because it involves a previously healthy adult and the burden is extremely heavy on the spouse and the family. Stroke in young patients constitutes a challenge because of its social impact and also because of the large variety of associated diagnostic and therapeutic problems. The causes of stroke are more heterogeneous than in the older population.

Aim and objective: To study the clinical profile, vascular involvement, and etiologies in ischemic stroke.

Materials and methods: The study was conducted from January 2019 to July 2020 among the patients admitted to or consulted as outpatients in Government Mohan Kumaramangalam Medical College Hospital, Salem. All the patients aged between 16 and 40 years with clinical features suggestive of stroke were taken. All were subjected to a CT scan of the brain and patients with evidence of ischemic infarct were taken up for the study.

Results: CT scan brain was done in all patients. In many of the patients, MRI with MRA was done. The carotid territory was involved in about 80%, the vertebrobasilar territory was affected by 15%, and multiple territories were involved in about 5% of the patients. In 14 patients (22.22%), no cause was identified even after adequate investigations. Three patients found to have anticardiolipin antibodies IgM and IgG along with lupus anticoagulant and diagnosed to have antiphospholipid antibody syndrome (APLA) syndrome. Among this 1 had SLE and so secondary APLA and others were primary. One patient had a deficiency of protein C and S and one patient had hyperhomocysteinemia.

Conclusion: When the cause of ischemic stroke in a young adult is unclear after a thorough initial diagnostic evaluation, it is worthwhile to take a second look at the heart. Investigations should be tailored to suit the need of the particular case rather than a complete list of tests for all patients.

Key words

Ischemic stroke, Cardiac cause, Thromboembolism, Dyslipidemia.

Introduction

The World Health Organisation defines the Stroke as "rapidly developing clinical signs of focal disturbance of cerebral function, with symptoms lasting for 24 hours or longer or leading to death, with no apparent cause other than of vascular origin [1]. The National Institute of Neurological Disorders and Stroke (NINDS) applies the term " Stroke " to any one or all of a group of disorders including cerebral infarction, intracerebral hemorrhage, or subarachnoid hemorrhage [2]. The causes of stroke are more heterogeneous than in the older population. Cardiac disease, hematological disease, non-atherosclerotic arteriopathies, migraine, and drug abuse are more important causes for stroke in young adults than in adults. The differential diagnosis includes many genetic, congenital, metabolic, and systemic disorders that are rarely encountered in mature adult populations [3]. Brain and vascular location of lesions are somewhat different in the young. Cerebral infarcts tend to be more often limited to deep regions of cerebral hemispheres, especially striatocapsular region. Vascular occlusive lesions are more often intracranial, affecting especially supraclinoid internal carotid artery [4], proximal middle cerebral artery, and basilar artery [5]. Extracranial occlusive disease is much less common. The causes of stroke differ considerably with age [6].

Materials and methods

The study was conducted from January 2019 to July 2020 among the patients admitted to or consulted as outpatients in Government Mohan Kumaramangalam Medical College, Salem. All the patients aged between 16 and 40 years with clinical features suggestive of stroke were taken. All were subjected to a CT scan of the brain and patients with evidence of ischemic infarct were taken up for the study.

Inclusion criteria: All the patients aged between 16 and 40 years with clinical features suggestive of a stroke, Imaging showing ischemic infarcts in the brain.

Exclusion criteria: Imaging showing evidence of hemorrhage, Imaging showing evidence of venous infarct.

Patients' details regarding age, sex, family history, risk factors like hypertension diabetes mellitus, hypercholesterolemia, valvular heart disease, atrial fibrillation, trauma, smoking, substance abuse were recorded. The onset and details of the symptoms and clinical signs were recorded. All patients underwent a basic examination protocol that included complete blood counts, erythrocyte sedimentation rate, blood glucose, urea, creatinine, electrolytes, lipid profile (triglycerides, total cholesterol, and fractions) CT brain, chest x-ray, electrocardiogram; transthoracic echocardiogram. MRI brain with MRA, B-mode carotid ultrasonography, carotid, and vertebral Doppler study had been done in many patients. Other laboratory tests such as homocysteine, fibrinogen, prothrombin time, partial activated thromboplastin time, antinuclear antibodies, anticardiolipin antibody, lupus anticoagulant autoantibodies (anti-SM, anti-SSA, and anti-RNA), were done in selected patients. Specific studies for the detection of natural anticoagulant deficiency, such as measurement of protein C, protein S, and antithrombin III, were carried out for patients with an undetermined diagnosis and when personal or family history indicated a prothrombotic disorder.

Results

Among 63 patients, the maximum number of patients was in the age group between 31 and 40 years. Among 63 patients, there were 41 (65.08%) males and 22 (34.92%) females (**Table – 1**).

Table - 1: Age distribution in study group.

Age group in years	No. of patients	%
16 – 20 years	7	11.11%
21 – 30 years	20	31.74%
31 - 40 years	36	57.14%

Table - 2: Clinical features.

Clinical Features	No. of Patients	%
Weakness	59	93.65%
Sensory disturbances	27	42.85%
Speech disturbances	38	60.32%
Altered sensorium	9	14.29%
Convulsions	8	12.70%
Headache	12	19.05%
Visual disturbances	6	9.52%
Giddiness	11	17.46%
Cerebellar symptoms	7	11 .11%

Table - 3: Location of infarctions.

Location of Infarctions	No. of patients	%
MCAterritory	47	74.6%
PCA territory	6	9.52%
Basilar artery	1	1.59%
PICA territory	3	4.76%
SCA territory	1	1.59%
ACA territory	2	3.17%
Multiple territories	3	4.76%

The clinical features of all the patients were studied. The commonest presentation was the weakness of the extremities with or without speech disturbances and sensory complaints. The other symptoms associated with weakness were convulsions, headache, giddiness, fever, altered sensorium, and visual disturbances. Few patients mainly presented with headaches or seizures and subsequently found to have infarcts on imaging (**Table – 2**).

Table - 4: Etiology groups for the stroke.

Etiology Group	No. of Patients	%
Cardioembolism	18	28.57%
Atherosclerosis	9	14 .29%
Nonatherosclerotic Arteriopathies	11	17.46%
Hematological	7	11.11%
Miscellaneous	4	6.35%
Unknown Cause	14	22.22%

Table - 5: Specific diseases causing cardioembolism.

Specific disease	No. of Patients	%
Rheumatic heart disease	9	14.29 %
Prosthetic valve	4	6.35%
Dilated cardiomyopathy	1	1.59 %
Acute Myocardial infarction	1	1.59 %
Infective endocarditis	1	1.59 %
Atrial septal defect	2	3.17 %
TOTAL	**18**	**28.57%**

Table - 6: Risk factors for atherosclerosis.

Risk factors	No. of Patients	%
Diabetes	5	7.94 %
Hypertension	7	11.11%
Hyperlipidemia	10	15.87%
Smoking / alcoholism	14	22.22 %
Carotid plaques	3	4.76 %

Table - 7: Non-atherosclerotic arteriopathies.

Specific disease	No. of Patients	%
Dissection	1	1.59%
Takayasu arteritis	1	1.59%
Infective arteritis	4	6.35%
Systemic Lupus Erythematosus	3	4.76%
Bechet's disease	2	3.17%
TOTAL	**11**	**17.46%**

Table - 8: Hematological diseases.

Specific disease	No. of Patients	%
Myeloproliferative Disorder	1	1.59 %
Antiphospholipid antibody syndrome	3	4.76 %
Protein C, S defiency	1	1.59%
Hyperhomocysteinemia	1	1.59%
Snakebite	1	1.59 %
TOTAL	**7**	**11.11%**

CT scan brain was done in all patients. In many of the patients, MRI with MRA was done. The carotid territory was involved in about 80%, the vertebrobasilar territory was affected by 15%, and multiple territories were involved in about 5% of the patients (**Table – 3**).

In 14 patients (22.22%), no cause was identified even after adequate investigations (**Table – 4**).

Of the identifiable causes, Cardioembolism was the single most common etiology. The rheumatic mitral valvular disease was the most important cause followed by a prosthetic valve or cardiac surgery. Transthoracic echocardiography was done in almost all patients (**Table – 5**).

Atherosclerotic vasculopathy was diagnosed as the cause of cerebral infarction in 9 patients (14.29%). Atherogenic risk factors were present in all of these patients except one. Some patients with a possible diagnosis of atherosclerotic vasculopathy were demonstrated by plaque formation in the carotid arteries and some by the presence of risk factors (**Table – 6**).

The main cause of non-atherosclerotic arteriopathy was vasculitis due to infective causes like tuberculosis or AIDS. In this study, 3 known SLE patients presented with features of stroke, one patient with posterior cerebral artery. One young female presented with features of stroke and was detected to have absent radial pulses and imaging showed features of Takayasu's arteritis. Two young male patients had oral and mucocutaneous ulcers, keratitis, and stroke and subsequently diagnosed to have neurobechet's disease. Another patient presented with left hemiplegia and severe neck pain and MRA and carotid Doppler showed the double lumen and carotid artery dissection was diagnosed (**Table – 7**).

Hemostatic tests were performed on 18 (28.58%) of the 63 patients in whom the cause of the neurologic episode was unexplained; Hematological causes had been found in 7 (11.11%) patients. It includes hyperviscosity syndromes like myeloproliferative disease in 1 patient. He presented with stroke and severe anemia and thrombocytopenia and bone marrow study revealed the diagnosis. Three patients found to have anticardiolipin antibodies IgM and IgG along with lupus anticoagulant and diagnosed to have antiphospholipid antibody syndrome (APLA syndrome. Among this 1 had SLE and so secondary APLA and others were primary. One patient had a deficiency of protein C and S and one patient had hyperhomocysteinemia (**Table – 8**).

Discussion

Regardless of the percentage of cases occurring among young individuals, most authors today agree that among victims of stroke, young people are not rare. Another common conclusion is the existence of a much broader spectrum of pathologies involved in stroke etiology among young patients compared with patients older than 50 years. However, available studies do not agree about the upper age limit to consider a patient "young," which varies between 30 and 50 years [7]. The causes and the proportion with 'no obvious cause' depend on these factors, and all these can change as the years go by and as more causes are discovered. A cardiogenic cerebral embolus is one of the most common causes of stroke in the young, accounting for up to one-third of the cases. In this study, 28.57 % of the cases of cerebral infarction were of cardiac origin [8]. In In this study, rheumatic heart disease was the leading cardiac cause of ischemic stroke.

However, in studies from developed countries paradoxical embolism occurring in patients with ASD or PFO is now diagnosed as the leading cardiac cause of ischemic stroke in young adults [9]. In the group of cardioembolic infarctions, the subgroup with synthetic valve prostheses represented one-fifth of the total cases and was the most numerous. Considering cerebral embolisms as a whole for all ages, non-rheumatic atrial fibrillation is the most frequent cause, a fact that is not observed in young patients [10]. In young patients with stroke, rheumatic heart disease is predominant with or without atrial fibrillation. It should be pointed out that rheumatic heart disease was the most important cause since all patients with synthetic valve prosthesis had rheumatic lesions [11]. Atrial fibrillation was present in 3 cases of RHD with mitral stenosis. In 3 cases (two with prosthetic valve and one with MS and atrial fibrillation) stroke occurred a few days after the cessation or decrease in the dose of anticoagulant therapy with warfarin [12]. It should be pointed out that this expressive proportion was obtained without the aid of special techniques such as contrast echocardiography or transesophageal study, which are known to greatly increase the chance of identifying sources often inaccessible by conventional study (patent foramen ovale, atrial septum aneurysm, etc.) [13]. We found that 14.29 % of the young patients with cerebral infarction had an atherosclerotic cause; the majority of these were more than 35 years of age. Our experience is similar to that in other surveys [14]. Different criteria for the diagnosis of atherosclerosis have been used. In some studies, diagnosis is based upon the existence of risk factors, while other evidence of atherosclerotic disease with imaging techniques is required for diagnosis. This may be one of the reasons why there is such a wide range of atherosclerosis being reported as the cause of ischemic stroke in young adults, with as little as 5 percent to as much as 50 percent of cases being attributed to atherosclerosis in different series [15]. The percent of atherosclerosis in this study was 14.29% based on the existence of risk factors or the detection of plaque in carotid or vertebrobasilar arteries. According to most investigators, the number of atherothrombotic infarctions is small among young patients. The high incidence among older patients is in contrast to patients younger than 30 years. In this study, lacunar infarctions were significantly more numerous in the 30- to 40-year age range compared with the 15- to 29-year age range [16]. The significant increase in the proportion of lacunar infarctions observed here from 30 to 40 years may suggest that degenerative arteriolar alterations occur earlier than expected in patients with severe systemic arterial hypertension [17]. We found 15.87 % of patients had hyperlipidemia. Systemic hypertension, diabetes, alcoholism, and smoking were found in a significant proportion of patients to contribute atherosclerotic process.[18]This is another major group of the causes of ischemic stroke. Non-atherosclerotic arteriopathies may be due to non-inflammatory diseases like dissection, fibromuscular dysplasia, homocystinuria, Marfan syndrome, or inflammatory diseases like vasculitis due to infections or systemic connective tissue disorders like SLE, or other conditions such as Takayasu's disease or Bechet's disease [19]. Numerous rare etiologies including reversible cerebral angiopathies fall into this category [20]. In some recent studies, arterial dissection is diagnosed as the cause of ischemic stroke of the young adults in up to 20% of cases Recent interest and enthusiasm have led to erroneous over diagnosis of the cervical carotid artery dissection, based on nonspecific arteriographic abnormalities. The arteriographic features of carotid dissection have been recently reviewed. Blood disorders have been implicated in 5% to 10% of ischemic stroke, with an increased frequency in younger patients [21]. Most disorders are associated with an increased thrombotic tendency and therefore, an increased risk of ischemic stroke. Typically, patients to be screened for coagulation defects will have a prior history of one or more unexplained thromboembolic events. The yield for diagnosing a hypercoagulable state is typically greatest for young stroke patients or those with a family history of thrombosis and who have no other

explanations for their stroke (cryptogenic stroke) [22]. Hematological disorders have been considered to be the cause of ischemic stroke in 2-16% of cases, most often 5 – 9%. However, this was 11.11 % in this study. Protein C, protein S, AT III, and fibrinogen levels may be altered in the setting of acute thrombosis [23]. Therefore, laboratory testing for these conditions should be deferred until several weeks after an acute thrombotic episode. If they were tested in the acute phase, then they should be repeated. However, because protein C and protein S are vitamin K-dependent proteins, these assays are not reliable in patients treated with oral anticoagulants. Similarly, AT III measurements are unreliable in patients receiving heparin [24]. Investigation for APLA syndrome is warranted if a history of deep vein thrombosis, pulmonary embolism, acute ischemia, myocardial infarction, or stroke (especially when recurrent) exists in a younger individual or the absence of other risk factors. The definition of migraine-induced stroke applied in studies conducted thus far has been inconsistent and probably explains why cerebral infarctions in the young attributed to "migrainous infarction" have varied between 1.2% and 25%. In this study only 1.59% of the patients), based on the criteria of the International Headache Society, fulfilled the criteria for migrainous infarction [25]. OCP has been considered to be the cause of ischemic stroke in 2-5% of cases of young adults. However, it is considered a lower priority diagnosis, and a thorough workup rule out of higher priority diagnosis, i.e. cardiac, atherosclerotic, non-atherosclerotic vasculopathy, and hematological causes is required before OCP can be diagnosed as the cause of stroke [26]. A Finnish study suggested that alcohol was a frequent contributing factor in the development of stroke; in a survey of patients with cerebral infarction, 40% had been intoxicated during the previous 24 hours. In our series, 7(11.11%) of the patients were moderate to heavy drinkers of alcohol [27].

Conclusion

The ischemic strokes among young patients were caused by a broad spectrum of diseases. All young patients with stroke deserve detailed evaluation to determine the etiology. Aggressive evaluation leads to etiological diagnosis and so proper acute management as well as long term care. When the cause of ischemic stroke in a young adult is unclear after a thorough initial diagnostic evaluation, it is worthwhile to take a second look at the heart. Investigations should be tailored to suit the need of the particular case rather than a complete list of tests for all patients.

References

1. Abraham J, Shetty G, Jose CJ. Strokes in the young. Stroke, 1971; 2: 258-267.
2. Adams HP Jr, Butler MJ, Biller J, Toffol GJ. Non-hemorrhagic cerebral infarction in young adults. Arch Neurol., 1986 Aug; 43(8): 793-796.
3. Adams HP Jr, Kappelle LJ. Biller ischemic stroke in young adults. Experience in 329 patients enrolled in the Iowa Registry of stroke in young adults. Arch Neurol., 1995 May; 52(5): 491-495.
4. Adams HP, Butler MJ, Biller J. Non-hemorrhagic cerebral infarction in young adults Arch Neurol., 1986; 43: 793.
5. Amarenco P, Duyckaerts C. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. **N** Engl J Med., 1992; 326: 221-225.
6. Bansal BC, Prakash C. Cerebrovascular diseases in young below 40 years. Neurol India, 1973; 21: 11-18.
7. Bansal BC, Good AK, Bonsal CB. Familial hyperlipidemia in stroke in young. Stroke, 1986; 17: 1142.
8. Bevan H, Sharma K, Bradley W. Stroke in the young adults. Stroke, 1990; 21: 382 – 386.
9. Biller J, Hinton WL, Adams Jr HP, et al. Cervicocepphalic arterial dissections; a ten-year experience. Arch Neurol., 1986; 43: 1234.
10. Biller J, Johnson MR, Adams HP, et al.

Echocardiographic evaluation of young adults with nonhemorrhagic cerebral infarction. Stroke, 1986; 17: 608-612.
11. Bogousslavsky J, Regli F. Ischemic stroke in young adults; Causes and prognosis. Arch Neurol., 1987; 44: 479.
12. Bogousslavsky J, Pierre P. Ischemic stroke in patients under age 45. Neurol Clin., 1992; 10: 113-124.
13. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Register: analysis of 1000 consecutive patients with the first stroke. Stroke, 1988 Sep; 19(9): 1083-1092.
14. Bruno A, Adams HP, Biller J, et al. Cerebral infarction due to moyamoya disease in young adults. Stroke, 1988; 19: 826 – 833.
15. Caplan LR, Zarins CK, Hematti M. Spontaneous dissection on extracranial carotid and vertebral arteries. Stroke, 1995; 16: 1030-1038.
16. Chopra JS, Prabhakar SL. Clinical features, and risk factors in stroke in young. Ada Neurol Scmd., 1979; 6a: 285 -300.
17. Collaborative Group study for stroke in young women. Oral contraceptives and stroke in young women. JAMA, 1975; 231: 718-722.
18. Fisher D, stringers K, Liberpoulos K. MR angiography, and conventional angiography in carotid artery dissections. Int Angiol., 1996; 15: 20-25.
19. Futrell N, Millikan C. Frequency, etiology, and prevention of stroke in patients with systemic lupus erythematosus. Stroke, 1989; 20b: 583-591.
20. Gilon D, Buonanno FS. Lack of evidence of an association between mitral-valve prolapse and stroke in young patients. N Engl J Med., 1999 Jul 1; 341(1): 8-13.
21. Griffin JH, Evatt B, Zimmerman TS, Kleiss AJ. Deficiency of protein C in congenital thrombotic disease. J Clin Invest., 1981; 68: 1370-1373.
22. Hart RG, Kanter MC. Hematological disorders and ischemic stroke. Stroke, 1990; 21: 1111 -1121.
23. Hart RG, Freeman GL. Stroke in young people –The heart of the matter. West J Med., 1987; 146: 596-597.
24. Kohrman MH, Huttenlocher PR. Takayasu's arteritis: a treatable cause of stroke in young. Ped Neurol., 1986; 2: 154-158.
25. Masi M, Edelman E, st John Sutton. Transient patency of foramen ovale in young patients with stroke of unknown etiology. Circulation, 1988, 78: 601.
26. Midlands L, Brosset C, Habib G, Khalil R. Cerebral infarction in patients aged 16 to 35 years: a prospective study of 52 cases. Press Med., 1994; 23: 1603 -1608.
27. Radhakrishnan K, Ashok PP, Sridharan R, Mousa ME. Stroke in the young: incidence and pattern in Benghazi, Libya. Acta Neurol Scand., 1986 Apr; 73(4): 434-438.