



NEUROIMAGING IN YOUNG STROKE: A HOSPITAL BASED STUDY

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ABSTRACT

Stroke is one of the most important public health problems with a global socio-economic impact and a major cause of disabilities. Stroke in young is a rare but catastrophic event. Stroke in young requires a different approach to investigate and treat. This is due to the different underlying etiology as compared to elders.

Methods: This hospital based cross sectional study was carried out in Assam Medical College & Hospital, a tertiary care hospital in Upper Assam to diagnose and categorize stroke in young (aged 15-45years) patients with CT or MRI and to find out the risk factors and etiology for young stroke with the help of clinico-biochemical parameters and imaging study.

Results: A total of 50 young stroke cases (23 male and 27 female) were studied during the study period. Mean age of the cases was 34.2 ±9.02 years with maximum numbers of cases in the age group of 15-25 years. Ischemic stroke accounted for 46 % followed by intracerebral hemorrhage (36 %), venous stroke (8%), spontaneous subarachnoid hemorrhage (6%) and mixed stroke (4%). Risk factors were detected in 74 % of the cases and hypertension was the most common risk factor found in 24 % cases. Most common site of ischemic stroke was in the MCA territory (43%) and multiterritorial infarcts were seen in 21.7 % of cases. Echocardiography was abnormal in 36% cases of ischemic stroke and rheumatic heart disease was the most common echocardiographic abnormality detected in the study. On ASCOD phenotyping, cardiogenic stroke was the most frequent etiologic subtype accounting for 39.1 % of all ischemic stroke cases. Atherosclerosis was found in 30.4 % of all cases of ischemic stroke followed by small vessel disease (8.7 %) and other causes (17.4 %). In our study, arterial dissection was seen in one (4.3 %) patient with ischemic stroke. Study showed, casual link between the etiologic phenotype & stroke was found in 52.2 % of the cases of ischemic stroke and causal link was uncertain in 26.1 % of the cases. In 17.4 % of the cases, causal link between the etiologic phenotype was unlikely. Eighteen (36%) cases were having intracerebral bleeding and 6% had Spontaneous subarachnoid hemorrhage. Basalganglia was the commonest location for a hemorrhagic stroke (44.4 %) followed by lobar bleed (28 %), primary intraventricular hemorrhage (16.7 %) and brainstem hemorrhage (5.1%). Various risk factors detected in the intracerebral hemorrhage were hypertension(22.2%) vascular anomalies(50%) pregnancy/puerperium 2(11.1 %), vasculitis 2(11.1%), obesity 1(5.6%), smoking 1(5.6 %) and undetermined in 16.7 % cases. Spontaneous subarachnoid hemorrhages were seen in 3 cases and an underlying aneurysm was identified in all the cases. In this study, 4 (3 male and 1 female) cases of venous stroke were encountered out of which there were 2 cases of combined dural venous sinus and cortical vein thrombosis and 1 case each of superior sagittal sinus and transverse/sigmoid sinus thrombosis.

Conclusion: Modifiable risk factors are common in young stroke patients. Brain imaging findings differ in young patients compared to that seen in middle-aged and elderly population, possibly because of the different etiologic spectrum

KEYWORDS : Young stroke, Neuroimaging, ischemia, hemorrhage

Introduction

Stroke is one of the most important public health problems with a global socio-economic impact and a major cause of disabilities. Stroke or CVA is a neurological deficit of sudden onset that is present for more than 24 hours and is attributable to a vascular cause. It is defined clinically wherein imaging studies play a diagnostic, corroborative & supportive role. While a specific definition of "young stroke" is lacking, the vast majority of authors consider "young stroke" to pertain to individuals less than 45 years of age. Stroke in young adults are relatively uncommon¹. The causes of stroke in young include varying pathologies which further necessitate the need for comprehensive investigations- laboratory as well as radiological. While a greater proportion of strokes are due to subarachnoid haemorrhage and intracranial haemorrhage in young adults (40–55%) compared to the general stroke population (15–20%),^{2,3} cerebral infarction is still most common. An increased risk of cerebral infarction among young adults with conventional vascular risk factors is observed, particularly in developing countries due to increasing smoking rates and urbanization⁴. Accurate etiological diagnosis is important to prevent future recurrences as many of the conditions are associated with modifiable risk factors or treatable pathologies. Previously undetermined etiology of stroke was by far the most prevalent, is now less frequent as a result of diagnostic improvements. Computer tomography (CT) and Magnetic resonance imaging (MRI) are the two most valuable tools in the diagnosis of stroke. Clinical examination alone cannot be used to specifically diagnose ischemic or hemorrhagic stroke which, however, is imperative as treatment approach to each entity varies markedly. Imaging findings, including the size, location, and vascular distribution of the infarction as well as the presence of bleeding, affects

both acute and long-term treatment decisions. In addition, information about the possible degree of reversibility of ischemic injury, the status of intracranial vessels, and cerebral hemodynamic status can be obtained from modern imaging studies. CT imaging is the initial screening tool to rule out hemorrhagic stroke or other stroke mimics viz tumours, infection, etc. Other advantages are the rapidity of imaging and wider availability. Newer modifications like CT angiography and CT perfusion are also being used in the imaging of ischemic stroke with better characterization of lesion and cerebral vasculature. MR imaging is being increasingly used for the evaluation of stroke. Even though it is thought to be relatively insensitive to diagnose hyperacute hemorrhage but with T2 and T2* sequences it can be used to rule out hyperacute hemorrhage as has been pointed out in some studies.^{5,6} Echocardiography is helpful in the diagnosis of various cardiac diseases in a case of suspected cardioembolic stroke.

Methods

This hospital based cross sectional study was carried out in Assam Medical College & Hospital, a tertiary care hospital in Upper Assam, from July 1st 2015 to June 30th 2016 to diagnose and categorize stroke in young patients with CT or MRI and to find out the risk factors and etiology for young stroke with the help of clinico-biochemical parameters and imaging study. Stroke patients who were between 15 to 45 years of age were included in this study. All young stroke patients were undergone detail history, clinical examination, biochemical tests and various neuroimaging. All included patients were initially undergone computed tomography (CT) scan and subsequently undergone magnetic resonance imaging (MRI), magnetic resonance venography (MRV), CT angiography, and digital subtraction

angiography (DSA) whenever necessary. To find out the risk factors and causes of stroke in young, we also did various tests like routine hemogram, blood glucose test, serum lipid profile, viral markers, blood venereal disease research laboratory (VDRL), electrocardiogram (ECG), echocardiography, carotid Doppler, and chest X-ray. Detailed coagulation profile and vasculitis profile, cerebrospinal fluid (CSF) analysis for CSF-VDRL were done in appropriate situations. Strokes were classified as cerebral infarction, ICH, SAH, venous stroke and mixed. Cerebral infarction was classified according to their vascular territory involvement, type of vessels (small /large vessels) involve and lacunar or cortical stroke. Haemorrhagic stroke were categorized as basal ganglionic, lobar, thalamic, pontine, cerebellar, and intraventricular (primary, or secondary).Cerebral venous thrombosis (CVT) and strokes where there was both haemorrhage and infarct were kept in mixed category. The study protocol was approved by the institutional ethical committee.

Results

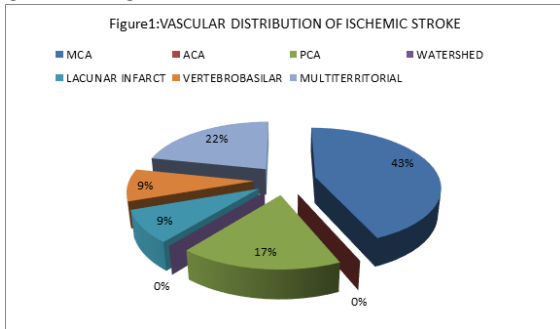
A total of 50 young stroke cases were admitted during the study period. Mean age of the cases was 34.2±9.02 years with maximum numbers of cases in the age group of 15-25 years. In this study, 23 (46 %) of young stroke cases were males and 27(54 %) were females. Ischemic stroke accounted for 46 % followed by intracerebral hemorrhage (36 %). Venous stroke and spontaneous subarachnoid hemorrhage accounted for 8 % and 6 % of the cases respectively. We also encountered 2(4%) cases of mixed stroke having both hemorrhagic and ischemic components. In this study, 74 % of the cases had one or more than one risk factors and hypertension was the commonest risk factor present in 24 % of all cases. Multiple risk factors were seen in 10 % of all cases. Smoking as a risk factor was noted in 10 % of the cases. Pregnancy/puerperium as risk factor was present in 10 % of all cases. Table 1 showing prevalence of various risk factors in young stroke as per stroke subtypes.

Table1:Prevalence of various risk factors in young stroke as per stroke subtypes.

Risk factor	Stroke subtype					Total
	Ischaemic	Hemorrhagic	SAH	Venous stroke	Mixed	
Diabetes	1	0	0	0	0	1 (2%)
Hypertension	4	4	3	0	1	12(24%)
Obesity	0	1	0	1	0	2(4%)
Smoking	3	1	0	1	0	5(10%)
SLE	1	0	0	0	0	1(2%)
Dyslipidemia	3	0	0	0	0	3(6%)
Vasculitis	0	2	0	0	0	2(4%)
Pregnancy/puerperium	2	2	0	0	0	4(8%)
Hyperhomocystenemia	1	0	0	0	0	1(2%)
Multifactorial	2	1	0	2	0	5(10%)
None	6	7	0	0	1	14(26%)
Total	23	18	3	4	2	50

Ischemic stroke

In this study, ischaemic stroke was found in 46 % cases, among which 56.5 % of cases were in the acute stage which was followed by subacute and chronic stages constituting 30 % and 13 % respectively. In this study, MCA territory was the most common site for infarction accounting for 43 % of all cases. Multiterritorial infarcts were the next most common ischemic stroke accounting for 21.7 % of all cases. Figure 1 showing vascular distribution of ischemic stroke.



Echocardiography was done in all ischemic and mixed stroke and abnormalities were detected in 9(36%) cases. Among the 9 patients 7 had rheumatic heart disease and other two patients had VSD and ASD.

ASCOD phenotyping of ischemic stroke patients

The ASCOD system classifies patients of ischemic stroke into 5 phenotypes, Atherosclerosis; Small vessel disease; Cardiac pathology; other causes and dissection. Each phenotype is further divided into grades on the basis of degree of causality between each phenotype and stroke. In our study, cardiogenic stroke was the most frequent etiologic subtype accounting for 39.1 % of all ischemic stroke cases. Atherosclerosis accounted for 30.4 % of all cases of ischemic stroke; small vessel disease accounted for 8.7 % of all cases of ischemic stroke; other causes accounted for 17.4 %. In our study, arterial dissection was seen in one (4.3 %) patient with ischemic stroke. In our study, in 52.2 % of the cases of ischemic stroke a definite causal link was found between the etiologic phenotype & stroke. Causal link was uncertain in 26.1 % of the cases. In 17.4 % of the cases, causal link between the etiologic phenotype was unlikely. In 1 case (4.3 %), the diagnostic workup was incomplete. Table2 showing ASCOD phenotypic classification of ischemic stroke patients.

Table 2: ASCOD phenotype of ischemic stroke cases

ASCOD phenotype	GRADE OF ASCOD				Total	
	Causal link certain	Causal link uncertain	Causal link unlikely	Insufficient workup		
Atherosclerosis	3	4	0	0	7	30.4 %
Small vessel disease	0	2	0	0	2	8.7 %
Cardiogenic	5	0	4	0	9	39.1 %
Others	3	0	0	1	4	17.4 %
Dissection	1	0	0	0	1	4.3 %
Total	12	6	4	1	23	100 %

Haemorrhagic stroke

In our study, 18(36%) cases had intracerebral hemorrhage,3(6%) had spontaneous subarachnoid hemorrhage (SAH). In this study, subacute stage of hematoma was found in 72.2 % of all hemorrhagic stroke cases which was followed by chronic and acute stages constituting 22.2 % and 5.6 % cases respectively. Basal ganglia was the commonest location for a hemorrhagic stroke accounting for 44.4 % of all cases followed by lobar bleed 28 %, primary intraventricular hemorrhage 16.7 % and brainstem hemorrhage in 5.1%. In this study, arteriovenous malformations were found in 6(33.3 %) cases and cavernous malformations were identified in 3(16.7%) haemorrhagic cases. Among the 18 cases of intraparenchymal hemorrhage, a structural vascular lesion was found in 9 cases (50 %). Among the cases with hemorrhagic stroke, hypertension was detected in 4(22.2%) cases. Other risk factors detected in the intracerebral hemorrhage were pregnancy/puerperium 2(11.1 %), vasculitis 2(11.1%), obesity 1(5.6%) and smoking 1(5.6 %). In 3 cases, the etiology remained undetermined (16.7 %). In this study, 3 cases of spontaneous subarachnoid hemorrhage were encountered and an underlying aneurysm was identified in all the cases.

Venous stroke

In this study, 4 (3 male and 1 female) cases of venous stroke were encountered out of which there were 2 cases of combined dural venous sinus and cortical vein thrombosis and 1 case each of superior sagittal sinus and transverse/sigmoid sinus thrombosis. All three cases were having hemorrhagic infarct.

Discussion

Many studies have been carried out regarding stroke in the young and imaging features. The conclusion reached by depends upon the number of cases studied, the geographic areas encompassed, the type of researchers and the scope of diagnostic modalities used to evaluate the patients enrolled in series. This study was conducted in Assam Medical College and Hospital, Dibrugarh. We evaluated 50 cases of stroke in young patients aged between 15 and 45 years in a period of one year using Computed Tomography and/or Magnetic resonance imaging and echocardiography. In this study, mean age of presentation was 29.92 years with maximum numbers of cases in the age group of 15-25 years. In this study, females outnumbered males; 54 % of the subjects were females and 46 % were males. Even though our study did not correlate with the studies of P. P. Subha *et al*⁷, O Oyinloye *et al*⁵, Dževdet Smajlović⁹ who reported a male predominance in their series. But our study correlated with the study conducted by K. Spengos *et al* (2010)¹⁰ who found a female predominance at ages under 30. In this study, prevalence & frequency of the traditional risk factors namely diabetes, hypertension, smoking, obesity & hyperlipidemia were specifically looked for and presence of other risk factors was assessed with the help of clinico-biochemical parameters. In this study, traditional risk factors of stroke were found in 70% cases. Hypertension was noted to be the commonest risk factor present in 24 % of all cases. Prevalence of current smoking and dyslipidemia was noted in 10 % and 6 % cases respectively. Diabetes was found in 1 case and obesity in 2 patients. Our study also correlated with the studies of Dževdet Smajlović⁹ who found high prevalence of smoking, hypertension, dyslipidemia in patients with young stroke. Another study from Trivandrum Medical College, Kerala in 2015 reported hypertension is the leading risk factor of young stroke(80%) followed by smoking (40%), hyperlipidemia (33.3%), and cardiac diseases (33.3%).⁷ Our study also correlated with the study of S. Roditis *et al*¹¹ who reported hypertension and tobacco use to be the most frequent risk factors in young stroke. Another important risk factor of young stroke is Pregnancy/puerperium. Study conducted by Z Moatti *et al*¹² and J Tate *et al*¹³ reported preeclampsia/eclampsia as important risk factors for stroke in pregnancy. M Khan *et al*¹⁴ also highlighted that majority of the hemorrhages in pregnancy are secondary to hypertensive disorders of pregnancy. In our study, pregnancy/puerperium as a risk factor was found in 4 patients accounting for 8 % of the cases. Gestational hypertension was found in 2 cases and essential

hypertension was found in 1 case. Vasculitis, SLE and hyperhomocystenemia are important risk factors of young stroke. We reported vasculitis in 2 patients and SLE and hyperhomocystenemia in 1 case each.

Ischemic stroke

In our study, cerebral infarction was the most common cause of stroke in young (46%) which is identical to the previous studies. Dževdet Smajlović, P.P. Subha *et al*, Dayna Griffiths *et al*.¹⁵ In our study, anterior circulation stroke accounted for 43.5 % of all cases, posterior circulation stroke accounted for 26.1 % of all cases and infarcts involving both territories accounted for 21.7 % of all cases. Similar pattern of distribution of infarcts were reported by Dash *et al*¹⁶, R Ji *et al*¹⁷. Echocardiographic abnormalities were found in 9 (39.1 %) cases of ischemic stroke. Thus in this study, 39.1 % had stroke due to probable cardioembolism. Similar incidence was reported by R Rosaria *et al*¹⁸, R Ji *et al* (2013), K Sher *et al*¹⁹. Out of 9 cases of cardioembolism, there were 7 cases of rheumatic valvular heart disease. However this is in contrast with the results of studies from developed countries where etiologies such as patent foramen ovale (PFO) or atrial septal defects (ASD) were more common than valvular heart disease as a cause of stroke as reported by R Ji *et al* (2013) and J Putaala *et al*.²⁰ Banerjee *et al*²¹ and D. Dash *et al* reported high frequency of rheumatic valvular disease among young stroke patients. We classified the cases of ischemic stroke with the ASCOD phenotyping system proposed by Amarenco *et al*.²² The ASCOD system classifies patients of ischemic stroke into 5 phenotypes of: Atherosclerosis; Small vessel disease; Cardiac pathology; other causes and dissection. Each phenotype is further divided into grades on the basis of degree of causality between each phenotype and stroke. In our study, atherosclerosis accounted for 30.4 % of all cases of ischemic stroke; small vessel disease accounted for 8.7 % of all cases of ischemic stroke; cardiac pathology accounted for 39.1 % of all cases of ischemic stroke; other causes accounted for 17.4 % of all cases of ischemic stroke and dissection accounted for 4.3 % of all cases of ischemic stroke. Cardioembolic stroke by far the most common etiological subtype of stroke found in our study is similar to the previously reported study by R Ji *et al* and K Sher *et al*. High frequency of atherosclerosis in young stroke patients was reported by YN Zhang *et al*²³ and Mehndiratta *et al*²⁴. Table3 showing etiological subtype of ischaemic stroke among young in different studies.

Table 3: Different study showing etiological subtype of ischaemic stroke among young patients

Study	No. of cases	Atherosclerosis	Cardioembolic	Smallvessel diseases	Other determined etiology	Undetermined etiology
R Renna <i>et al</i> (2014)	150	11.3 %	24 %	8 %	27.3 %	29.3 %
D Dash <i>et al</i> (2014)	440	4.9 %	14 %	6.8 %	17.3 %	57 %
K Sher <i>et al</i> (2013)	75	20 %	25.3 %	16 %	22.7 %	16 %
YN Zhang <i>et al</i> (2012)	109	57 %	18 %	5.5 %	15 %	4.5 %
J Putaala <i>et al</i> (2009)	1008	8 %	20 %	14 %	25 %	33 %
Telman <i>et al</i> (2008)	87	6 %	23 %	15 %	26 %	30 %
Varona <i>et al</i> (2007)	272	21 %	17 %	17 %	9 %	36 %
Lipska <i>et al</i> (2007)	214	13 %	25 %	8 %	11 %	44 %

Hemorrhagic stroke

We encountered 18 cases of intraparenchymal hemorrhage and 3 cases of spontaneous subarachnoid hemorrhage making a combined percentage of 42 %. Similar prevalence of hemorrhagic stroke was reported by the studies of C Marini *et al*.²⁵ In our study, hypertension was the single most common risk factor accounting for 22.2 % of all the cases of hemorrhagic stroke. Similar findings were reported by Riku-Jaakko Koivunen²⁶, Jayantee Kalita *et al*²⁷, Edward Feldmann *et al*²⁸ and S-L Lai *et al*²⁹. Other risk factors of haemorrhagic stroke in this study were AVM (33.3 %), cavernoma (16.7 %), Pregnancy/puerperium (11.1 %), vasculitis (11.1%) and smoking (5.6 %). In our study, we encountered 3 cases of spontaneous subarachnoid hemorrhage accounting for 6 % of all cases out of which 2 were females and 1 was a male. In this regard, our study correlated well with the studies of Y A Bokhari *et al*³⁰, A Keedy *et al*³¹, B Ogungbo *et al*³² who reported a higher frequency of females in their series. In our study, 1st patient with SAH revealed a ruptured aneurysm in the A2 bifurcation of left ACA on MR Angiography. The 2nd patient revealed aneurysm in the anterior communicating artery and the 3rd patient revealed aneurysms in the anterior communicating artery and M2 segment of right MCA on MR Angiography. Our study correlated well with the studies of S Y Kim *et al*³³ and A Keedy *et al*³⁴ who reported a higher incidence of ACA territory aneurysms in young adults with spontaneous subarachnoid hemorrhage.

Venous stroke

In our study we reported 4 cases (3 male and 1 female) of venous stroke i.e. infarction secondary to cerebral venous thrombosis constituting 8 % of all cases. Out of 4 cases, there were 2 cases of combined dural venous sinus and cortical vein thrombosis and 1 case each of superior sagittal sinus and transverse/sigmoid sinus thrombosis. In all the 4 cases MRI revealed hemorrhagic infarcts in venous territories. Our study was consistent with the study of M Wasay *et al*³⁵ who reported presence of hemorrhagic infarcts as one of the strongest predictors of cerebral venous thrombosis. We searched for risk factors of venous stroke by doing complete blood count, chemistry panel, ESR, and measures of the prothrombin time and activated partial thromboplastin time and other pro-coagulant tests. After detail work-up we did not find any obvious derangement.

Conclusion

Stroke in young is a rare but catastrophic event. Modifiable risk factors are common in young stroke patients. The variety of causes of stroke in young further entails the need for comprehensive neuroimaging. Brain imaging findings differ in young patients compared to that seen in middle-aged and elderly population, possibly because of the different etiologic spectrum.

Source of interest: Nil

Conflict of interest: Nil

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