

Original Article

Clinical Spectrum and Neuroimaging Characteristics of Arterial Ischemic Stroke in Childhood: Experience in a Tertiary Care Hospital

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Abstract

Background: Arterial ischemic stroke in children is rare but may be associated with mortality and significant neurological morbidity. Clinical manifestations and underlying etiology of pediatric ischemic stroke differ from adult stroke. This study aimed to detect the common presentations with their neuroimaging characteristics along with probable etiology of pediatric stroke in a tertiary care hospital of Bangladesh. **Materials and Methods:** This cross-sectional observational study was conducted in Dhaka Medical College Hospital (DMCH) during period of June 2017 to December 2020 among 65 children aged 29 days to 14 years diagnosed with acute arterial ischemic stroke. Children with acute onset of focal neurological sign with evidence of acute parenchymal ischemic infarction on brain MRI were included as study population. Children diagnosed with hemorrhagic stroke, history of perinatal stroke and cerebral venous sinus thrombosis (CVST) were excluded from the study. **Results:** Majority of studied children came from rural areas with male predominance. Hemiparesis was the most common presenting feature, then speech disturbance, headache, seizure, visual disturbance and behavioral abnormalities. Thirty-four percent had history of recurrence. Arteriopathy was present among 37% of studied population and moyamoya disease was the common variety. Single infarction with unilateral distribution was seen on radiology imaging among 74% of studied population. Moyamoya disease as etiology and presence of multiple infarcts with bilateral distribution on neuroimage were significantly associated with stroke recurrence. **Conclusion:** Early diagnosis of pediatric stroke and early search of underlying etiology is essential to prevent mortality, long term neurological morbidity and further recurrence.

Key words: Arterial ischemic stroke; Neuroimage; Arteriopathy

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Introduction

Stroke is a neurological injury caused by the occlusion or rupture of cerebral blood vessels which can result in both focal and global neurological impairments including hemiparesis to seizure. The reported incidence of pediatric stroke including

both ischemic and hemorrhagic cause ranges from 1.2–13 cases/100,000/year with a case fatality rate approximately 4%.¹⁻³ Arterial Ischemic Stroke (AIS) comprises fifty percent of total cause of stroke in children which differs from adult where 80–85% of

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strokes are ischemic.^{4,5} Compared to adult pediatric populations have more and diverse risk factors. Adult AIS is predominantly associated with hypertension, diabetes, hypercholesterolemia etc.⁶

Most often multiple factors coexist behind the etiopathology of pediatric stroke. Presence of multiple factors and low level of suspicion from the pediatrician sometimes make delayed diagnosis; one report has shown 19 out of 45 pediatric strokes failed to receive a correct diagnosis until 15 hours to 3 months from the initial presentation.⁷ But it is well-established that early suspicion and identification of risk factors will be associated with early intervention that can prevent mortality and morbidity associated with pediatric stroke. Around 10–25% of pediatric stroke will die, roughly 25% associated with recurrence and as much as 66% associated with significant morbidity like persistent neurologic deficits, learning disorders, speech problems and subsequent development of epilepsy.⁸ Epilepsy develops in about one-third of survivors of young stroke within the first decade of attack which may add a huge burden on families.⁹ In the recent decade there is a lot of advancement of neuroimaging facilities that leads to early hospitalization and early diagnosis.¹⁰ Besides the rising of awareness and diagnostic facilities prevalence of risk factors have changed a lot over time due to change of life style, increment of childhood obesity associated with cardiovascular risk factors, prevalence of survival of congenital heart defects improved due to advancement of cardiac care which is associated with increased risk of cardiovascular risk of AIS in young adults. Cerebral arteriopathy is the leading cause of childhood stroke and most of the cases remain undiagnosed due to lack of proper diagnostic facilities in low-income countries.

Pediatric stroke remains as an emerging field of study in the developing countries and the advancement of diagnostic facilities open the opportunity to identify and confirm the risk factors associated with stroke. But in still half of the cases etiology and risk factors remain undetermined despite adequate work up. When the knowledge of childhood stroke etiology and risk factors remain insufficient the diagnostic and management procedures will remain underdeveloped.

This study aimed to describe the clinical pattern and probable etiology for childhood AIS and also assesses the relationship of clinical findings and recurrence with demography, etiology and infarct characteristics.

Materials and Methods

This cross-sectional observational study was conducted in Dhaka Medical College Hospital (DMCH) during period of June 2017 to December 2020 among 65 children aged 29 days to 14 years diagnosed with acute arterial ischemic stroke. Children with acute onset of focal neurological sign with evidence of acute parenchymal ischemic infarction on brain MRI were included as study population. Children diagnosed with hemorrhagic stroke, history of perinatal stroke and cerebral venous sinus thrombosis (CSVT) were excluded from the study. Complete history, general, physical and neurological examinations was done for all enrolled patients. A patient, who matched the inclusion and exclusion criteria according to history, physical examination and freely gave their informed consent, was selected for the study. All children underwent for Magnetic resonance imaging (MRI) of brain to detect and localize the infarct and other necessary investigations was done according to indication. Data were processed and analyzed using computer software SPSS (Statistical Package for Social Science) version 21.0. The data presented on categorical scale are expressed as frequency and corresponding percentage, while the quantitative data are presented as mean and standard deviation (\pm SD). Qualitative variables were assessed with chi-square test and the quantitative variables were analyzed with Student's t-test or one way ANOVA as applicable. A p value of ≤ 0.05 will be considered significant.

Results

Total 65 patients with arterial ischemic stroke were studied. Table I shows their baseline characteristics where we found a male predominance and majority came from rural areas with mean age 64.60 ± 27.49 and mean duration of illness 4.35 ± 1.32 .

Table II has shown the common clinical presentations of studied population which displayed hemiparesis as the most prominent features then speech disturbance, headache, seizure, visual disturbance and behavioral

abnormalities. Twenty patients (33.80%) came with recurrent attack.

Table I: Baseline characteristics of the study population

Characteristics of patients	Mean ± SD
<i>Age of stroke (months)</i>	64.60 ± 27.49
<i>Duration of illness (days)</i>	4.35 ± 1.32
<i>Residence</i>	Number (%)
Urban	16 (24.6)
Rural	49 (75.4)
<i>Sex</i>	Number (%)
Male	40 (61.5)
Female	25 (38.5)

Table III analyzes the neuroimaging findings of the study population where we found 73.85% have single infarct with unilateral distribution. Majority located anteriorly in left hemispheres and MCA is the common vascular territory involved in the process of infarct formation.

Table II: Clinical findings of study population

Characteristics of patients	Number (%)
<i>Mode of presentation</i>	Total 65 (100)
Hemiparesis	63 (97.00)
Speech disturbance	43 (66.15)
Headache	35 (53.85)
Seizure	34 (52.30)
Visual disturbance	10 (15.38)
Memory loss	10 (15.38)
Behavioral problem	10 (15.38)
Fever	21(32.30)
<i>Recurrence</i>	Total 65 (100)
First attack	43 (66.20)
Recurrent attack	22 (33.80)

Table IV shows the common etiological risk factors of the study population which shows arteriopathy as the most common single etiological factors involved in the pathogenesis of stroke which is present among 24 patients (36.92), next common risk factors were hematological disorders (iron deficiency anemia), CNS infection, cardiac disorder, prothrombotic and metabolic disorder. Among the arteriopathy we found moyamoya disease and focal cerebral arteriopathy is most common. Figure 1 has shown that a good

number of patients (25) present with multiple risk factors simultaneously. We also found no risk factors at all among six patients.

Table V shows the distribution of risk factors that influence the recurrence of stroke. We found arteriopathy (moyamoya disease), multiple number of infarcts and bilateral distribution of infarct significantly associated with recurrence of stroke.

Table III: Neuroimaging findings of study population

Neuroimaging findings	Number (%)
<i>Number of infarcts</i>	
Single	48 (73.85)
Multiple	15 (23.07)
No infarct	02 (03.07)
<i>Laterality of infarct</i>	
Unilateral	50 (76.92)
Bilateral	13 (20.00)
<i>Lesion distribution</i>	
Anterior	40 (61.50)
Posterior	15 (23.10)
Both	08 (12.30)
No infarct	02 (03.10)
<i>Site of infarct</i>	
Left	40 (61.50)
Right	10 (15.38)
Both	13 (18.50)
<i>Vascular territory</i>	
MCA (Full)	24 (37.00)
MCA (Partial)	12 (18.50)
PCA	09 (13.80)
ACA	02 (03.10)
Vertebrobasillar	04 (06.20)
Multiple	12 (18.50)
Normal	02 (03.00)
<i>MRA findings</i>	
Moyamoya disease	15 (23.10)
Focal cerebral arteriopathy	06 (09.20)
Unspecified arteriopathy	03 (04.60)
AVM	02 (03.10)
Arterial dissection	01 (01.50)
Normal	38 (58.50)

Table IV: Risk factors present among study population

Risk factors category	Number (%)
Arteriopathy	24 (36.92)
Hematological disorder	19 (29.23)
CNS infection	12 (18.50)
Cardiac disorder	11 (16.92)
Acute systemic condition	09 (13.85)
Prothrombotic disorder	03 (04.60)
Chronic head & neck disorder	02 (03.10)
Metabolic disorder	02 (03.10)

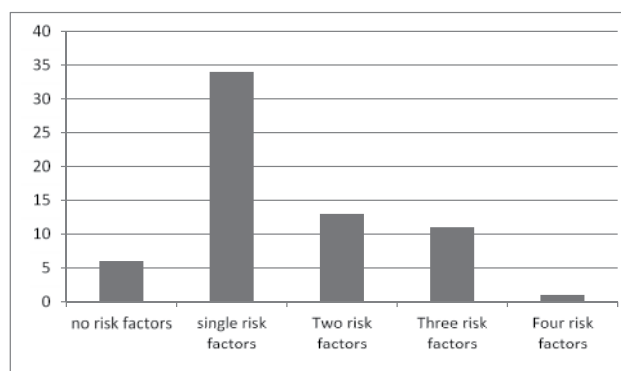


Fig 1. Distribution of study population according to number of risk factors

Table V: Factors influencing recurrence of stroke

Risk factors	Single attack (43)	Recurrent attack (22)	p values
<i>Age at stroke</i>	61.98 (28.42)	69.73 (25.40)	0.29
<i>Risk factors</i>			
Arteriopathy	12 (27.9)	12 (54.54)	0.003*
Prothrombotic states	00 (0.0)	03 (100)	
No risk factors	06 (100)	00 (0.0)	
<i>Area of infarct</i>			
Anterior	28 (70.0)	12 (30.0)	0.005*
Posterior	13 (86.7)	02 (13.3)	
Both	02 (25.0)	06 (75.0)	
No infarct	0 (0.0)	02 (100)	
<i>Number of infarcts</i>			
Single	38 (77.6)	11 (22.4)	0.002*
Multiple	05 (33.3)	10 (66.7)	
<i>Laterality of infarct</i>			
Unilateral	38 (74.5)	13 (25.5)	0.18
Bilateral	05 (38.5)	08 (61.5)	
<i>Site of infarct</i>			
Left	31 (77.5)	09 (22.5)	0.017*
Right	08 (61.5)	05 (38.5)	
Both	04 (33.3)	08 (66.7)	
<i>MRA findings</i>			
Moyamoya disease	05 (33.30)	10 (66.70)	0.002*
AVM	00 (00.00)	02 (100.0)	
Normal	31 (81.60)	07 (18.40)	
<i>Number of risk factors</i>			
No risk factors	6 (100.0)	00 (0.00)	0.09
Single risk factors	22 (64.7)	12 (35.3)	
Two risk factors	10 (76.9)	03 (23.1)	
Three risk factors	05 (45.5)	06 (54.5)	
Four risk factors	00 (0.0)	01 (100.0)	

Discussion

Stroke in children is as much as common of childhood brain tumor and hold the one of the top ten positions of childhood mortality and morbidity.^{11,12} Survivors of pediatric stroke may experience lifelong disabilities in motor, speech, cognitive and behavioral functions. So knowledge about the range of preventable risk factors is crucial to prevent the mortality and morbidity related to pediatric stroke.¹³ Here in this study we assess the common clinical presentations, the underlying risk factors and the factors that influence the recurrence of stroke among the children with arterial ischemic stroke. We found that hospital admissions with AIS is higher among the male. This male predominance of pediatric stroke was also observed in the studies done by Nowak-Gottl et al¹⁴ and Warren et al¹⁵. The age of onset of pediatric stroke in this studied population is as early as 20 months of age with the mean age of presentation 64.60 ± 27.49 in months. Here our majority of children with stroke came from rural background of lower to middle socioeconomic background. Though this finding is not a recognizable risk factor but it is proved that infection acts as a nidus for the formation of thrombus which is more prevalent among the low socioeconomic background. Chiang & Cheng¹⁶ have found higher prevalence of stroke amongst the urban people of lowest household income level. AIS in all groups including neonatal and childhood has a higher prevalence among males and black people.¹⁷ Clinical manifestations of AIS in children are variable depending on age, underlying etiology and involvement of vascular territory.¹⁸ Focal neurologic deficits like hemiparesis, hemisensory loss, cranial nerve palsy, seizure headache are the most common presentation of AIS in children. Infant may present with seizure, lethargy, apnea without having focal neurologic deficits.¹⁸ Here in our study we found hemiparesis as the most common presentations which is evident among 63 (97%) cases; next common presentations were aphasia (66.15%), headache (53.85%), seizure (52.30%) and visual disturbance, memory loss and behavioral problem were noticed among 15.38% of children. Fever was documented during presentation among 33.80% of children with AIS. Hidalgo MJ et al have the same observation in their study where they found 79% with

motor involvement, 45% with seizure and headache among 10% of studied population.¹⁹ The IPSS study also found focal signs of motor involvement 82%, diffuse signs in 64% and epileptic seizures in 31%.²⁰ Some international studies have found hemiparesis as the most frequent presentation (94%) and seizures are present in 20% to 48% cases.^{18,21} Regarding etiology of AIS there are different sets of genetic and non-genetic risk factors which may be related to the causation of AIS in children. Multiple risk factors may coexist in a single patient. Common risk factors for the causation of AIS in children include arteriopathy, congenital heart defects, hematological abnormalities, sickle cell disease, metabolic and genetic disorder.^{22,23} Here in our study most common identified risk factors are arteriopathy (36.92%), hematological disorder (29.23%), CNS infection (18.50%), cardiac disorder (16.92%), acute systemic condition (13.85%), prothrombotic disorder (4.6%), chronic head and neck disorder and metabolic disorder (3.10%). We did not find any identifiable risk factor among 6 (9.2%) patients. A great number of patients 26 (40%) had more than one risk factors in the studies of Chiang & Cheng¹⁶, Mackay et al²² and Fullerton et al²⁴ have the same observation where they also found vascular disorder as the most common risk factors. Among the vascular disorders moyamoya disease is the major cause of ischemic stroke in our study which is 66.7% of total arteriopathy diagnosed among the studied population. Though the sickle cell disease is the most common hematologic disorder responsible for ischemic stroke, in South East Asian region it is not prevalent. In our study we found 19 (29.23%) patients with moderate to severe grade of iron deficiency anemia in patients with ischemic stroke. We found 3 (4.6%) patients with prothrombotic disorder. Congenital heart disease accounted 12 (16.92%) in stroke patients in our study which matched with the findings of the study of Ganesan et al²³ and deVeber et al²⁵. Tetralogy of Fallots and persistent foramen ovale are the most common forms of cardiac disorders associated with AIS in our studied group. CNS infection was found to be the third most common associated condition in our studied population and the identified common pathogens were streptococci and mycobacterium tuberculosis. Lee et al²⁶ also have

the similar observation; besides these two organisms they found influenza as the most frequent pathogens involved in AIS in children. Among the metabolic disorder we found one case of homocystinuria and one mitochondrial disorder presented with AIS. Among 65 of total studied population, we found 22 (33.80%) had the recurrent attacks and most of the recurrence occurred within 6 months of first attack. Percentage of recurrence in our study is a bit higher than the international level. A study on pediatric patients of USA demonstrated 10.3% stroke recurrence including 4% from anterior circulation and 19% from posterior circulation.²⁷ Another report of the national institute of neurologic disorders and stroke workshop on perinatal and childhood stroke noticed stroke recurrence rate in children ranges from 20% to 40%.²⁸ Lack of proper etiological evaluation may be the main cause of our higher percentage of recurrence. Here in our study, we found high rates of recurrence in children with arteriopathy, particularly in moyamoya disease, 3 cases of prothrombotic states protein C and protein S deficiency associated with recurrence within one year of initial attack. Neuroimaging factors that contribute to evaluate the risk of recurrence are the presence of multiple infarcts with bilateral distribution. Fullerton et al²⁴ and Sarecka-Hujar & Kopyta²⁹ also had the same observations; they found arteriopathy, prothrombotic states, and presence of multiple risk factors significantly associated with AIS recurrence. Though stroke is rare in children but its multifactorial etiology and heterogeneity of clinical presentation makes difficult to diagnose straight forward, so strong suspicion and methodical etiological survey is very much crucial to prevent its immediate and long-term morbidity.

Childhood stroke is not uncommon in our country but lack of awareness about the presentation and probable etiology delays the diagnosis and ultimately complicate the outcome of disease, so it is very crucial to search the underlying etiology and probable risk factors of recurrence to prevent immediate and late complications.

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