Childhood stroke: A prospective study on risk factors, clinical profile, and short-term outcome in a tertiary care hospital in Eastern India

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Abstract

Background: Childhood stroke is an acute onset neurological sign or symptom attributable to focal brain infarction or haemorrhage. It is an under-studied entity and is scarcely reported from India.

Objectives: To evaluate the risk factors, clinical profile and short-term outcome (after a 6-month follow-up) of childhood stroke in a tertiary care hospital of Eastern India.

Method: This observational, prospective study was conducted on 50 patients aged 2 months to 12 years over a period of 18 months. Data on history, examination, relevant investigations, radio-imaging and follow-up was taken and recorded on a pre-formed proforma and analysed.

Results: Out of the 50 cases, 23 (46%) had arterial ischaemic stroke (AIS), 12 (24%) had cerebral sino-venous thrombosis (CSVT) and 15 (30%) had haemorrhagic stroke (HS). The common risk factors were infection (30%) and vascular disorder (24%), including arteriopathy and vascular malformation. Common presentations were seizures (78%) and hemiparesis (70%). Eight (16%) cases died. Although none died among AIS and CSVT cases, there was statistically significant mortality in HS ($p<0.001$). After 6-month follow-up of discharged cases (n=42), partial neurological recovery was noted in 64.3%.

Conclusions: AIS was the most common type of stroke. Commonest risk factor was infection and commonest presentation was seizure. Mortality was observed only in HS. Majority achieved partial neurological recovery on short-term follow-up.

(Key words: Arterial ischaemic stroke, Cerebral sino-venous thrombosis, Haemorrhagic stroke, Eastern India, Infection)

Introduction

Stroke is an acute onset neurological sign or symptom attributable to focal brain infarction or haemorrhage[1]. The reported incidence of stroke is between 1.3–13/100,000/year[2]. The preferred way for classifying stroke is conventional (ischaemic and haemorrhagic). Ischaemic stroke is of 2 types, arterial ischaemic stroke (AIS) and venous infarction caused by cerebral sino-venous thrombosis (CSVT)[3,4]. Childhood stroke remains an under-studied entity. To the best of our best knowledge, longitudinal studies on childhood stroke are not well described from eastern India.

Objectives

To describe the clinical profile, risk factors and short-term outcome of childhood stroke from eastern India.

Method

This observational, prospective study was conducted from March 2020 to July 2021 in a tertiary care hospital in Kolkata, West Bengal, Eastern India.

Inclusion criteria: a) Children aged between 2 months to 12 years. b) Children must have recent clinical and radiological evidence of stroke.

Exclusion criteria: a) Children having perinatal stroke; b) Children suffering from hypoxic ischaemic event; c) Paraparesis / Paraplegia; d) Brain/spinal cord trauma.

During the initial 12 months of the study period, all children aged 2 months to 12 years who had presentations suggestive of stroke were enrolled and those satisfying the inclusion and exclusion criteria were included in the study. All study participants were evaluated by proper history taking, general and systemic examination, including detailed neurological examination. In the neurological examination, emphasis was given to

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higher function, cranial nerve, and sensory-motor system examination.

Relevant laboratory investigations were sent to the institute's laboratories as per study proforma. Special investigations like serology (antinuclear antibody, antineutrophil cytoplasmic antibody, antiphospholipid antibody), thrombophilia profile (protein C and protein S deficiency, homocysteine, Factor V Leiden mutation) and coagulation factor deficiency (Factors VIII and IX deficiency) were done. Along with this, appropriate neuro-imaging was planned. Non-contrast computed tomography (NCCT) and contrast-enhanced computed tomography (CECT) of brain were done for HS and tuberculous meningitis (TBM) respectively. Magnetic resonance imaging (MRI) of brain was done for all cases. Magnetic resonance angiography (MRA) was considered for AIS and HS and magnetic resonance venography (MRV) for CSVT.

Immediate outcome after admission was analysed by considering discharge and mortality. Cases who were discharged, were followed up after 6 months for neurological outcome by assessing 4 neurological parameters viz. residual motor deficit, cranial nerve palsy, seizure and recurrent stroke and classified as:

1. No neurological recovery: Presence of more than 1 parameter.

2. Partial neurological recovery: Presence of any one parameter.

3. Complete neurological recovery: Absence of all parameters

Ethical issues: Approval for the study was obtained from the Institutional Ethics Committee of the Institute of Postgraduate Medical Education and Research, Kolkata, India (No. IPGME&R/ IEC/ 2020/359) dated 28/4/2020. Witten informed consent was obtained from the parents/guardians of the participating children and informed assent from children 7-12 years of age.

Statistical analysis: Data were entered into a Microsoft Excel spread sheet. Categorical variables were expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test, as appropriate. Continuous variables were expressed as Minimum, Maximum, Mean, Median and Standard Deviation. The statistical software SPSS version 22 was used for the analysis. p-value less than 0.05 was considered as significant.

Results

Among the 50 cases of childhood stroke, 2 (4%) were less than 1 year, 20 (40%) were between 1-5 years and 28 (56%) were older than 5 years. Minimum and maximum ages were 0.6 years (7 months) and 11.2 years respectively. Mean age, median age and standard deviation were 6.01 years, 6.25 years and 3.23 years respectively; 27 (54 %) were male and 23 (46%) were female (male: female = 1.2:1). In this study 23 (46%) had AIS, 12 (24%) had CSVT and 15 (30%) had HS. Although AIS had an association with higher age (>5yrs), this finding was not statistically significant (p = 0.629).

Table 1 shows the distribution of cases according to risk factor. Infection (30%) was the most common risk factor followed by vascular disorder (24%) including arteriopathy and vascular malformation, haematological disorder (22%), cardiac disorder (4%) and others (4%) and in 8 (16%) cases, risk factor was idiopathic. The most common risk factors for AIS, CSVT and HS were arteriopathy (30%, n=23), infection (67%, n=12), and haematological disorder (47%, n=15) respectively. CSVT had higher association with infection which was statistically significant (p=0.006). Most common specific risk factor for AIS, CSVT and HS were TBM (21.7%, n=23), orbital cellulitis (50%, n=12) and haemophilia (20%, n=15) respectively (Table 1).

Most common presentation was seizure (78%) followed by hemiparesis (70%), fever (50%), headache (44%), altered sensorium (40%), squint (36%), vomiting (34%), ptosis (8%) and aphasia (6%). Most common individual presentations for AIS and HS were hemiparesis (95%, n=23) and altered sensorium (80%, n=15), respectively both of which were statistically significant. Seizure (100%, n=12) was the most common presentation in CSVT; squint was statistically associated with it (p <0.001). Vomiting was significantly low in AIS (p =0.015) and fever was significantly low in HS (p =0.020) (Table 2).

Most common territory involvement was middle cerebral artery (MCA) (28 cases, 56%) followed by internal carotid artery (12 cases, 24%), both anterior cerebral artery (ACA) and MCA (6 cases, 12%), multiple territories (3 cases, 6%), and cerebellar (1case, 2%) (Figure 1).

Table 1: ***Distribution of cases according to risk factor***

Stroke Type	Category	Specific risk factor	Frequency (%)
Arterial ischaemic stroke (AIS)	*Vascular (30%)*	Vasculitis	03 (13.0)
		APLA syndrome	02 (08.7)
		Moya moya disease	02 (08.7)
	Infection (26%)	Tuberculous meningitis	05 (21.7)
		Viral meningoencephalitis	01 (04.3)
	Cardiac (~9%)	Cyanotic CHD	01 (04.3)
		Dilated cardiomyopathy	01 (04.3)
	Haematological (~4%)	Sickle cell disease	01 (04.3)
	Others (~9%)	Homocystinuria	01 (04.3)
		Mitochondrial	01 (04.3)
	Idiopathic (~22%)	Idiopathic	05 (21.7)
		Total	**23 (100.0)**
Cerebral sino-venous thrombosis (CSVT)	*Infection (~67%)*	Orbital cellulitis	06 (50.0)
		Dehydration	02 (16.7)
	Haematological (25%)	SRNS	02 (16.7)
		Factor V Leiden	01 (08.3)
	Idiopathic (~8%)	Idiopathic	01 (08.3)
		Total	**12 (100.0)**
Haemorrhagic stroke (HS)	*Haematological (~47%)*	Haemophilia	03 (20.0)
		Hepatic disease	02 (13.3)
		Leukaemia	02 (13.3)
	Vascular (~33%)	Arterio-venous malformation	02 (13.3)
		Cavernous malformation	01 (06.7)
		Choroid plexus angioma	01 (06.7)
		Vasculitis	01 (06.7)
	Infection (7%)	Sepsis	01 (06.7)
	Idiopathic (13%)	Idiopathic	02 (13.3)
		Total	**15 (100.0)**

APLA syndrome: Anti-phospholipid antibody syndrome, CHD: Congenital heart disease, SRNS: Steroid resistant nephrotic syndrome

Table 2: ***Presentations in different stroke types***

Presentation	Stroke type			p-value
	AIS (n=23) Frequency (%)	**CSVT (n=12) Frequency (%)**	**HS (n=15) Frequency (%)**	
Hemiparesis	22 (95.0)	01 (08.3)	12 (80.0)	**<0.001**
Seizure	15 (65.2)	12 (100.0)	12 (80.0)	0.055
Altered sensorium	07 (30.4)	01 (08.3)	12 (80.0)	**<0.001**
Vomiting	03 (13.0)	06 (50.0)	08 (53.3)	**0.015**
Fever	14 (60.9)	08 (66.7)	03 (20.0)	**0.020**
Headache	08 (34.8)	08 (66.7)	06 (40.0)	0.183
Aphasia	03 (13.0)	0 (0)	0 (0)	0.317
Squint	04 (17.4)	11 (91.7)	03 (20.0)	**<0.001**
Ptosis	02 (08.7)	0 (0)	02 (13.3)	0.676

AIS: arterial ischaemic stroke, CSVT: cerebral sino-venous thrombosis, HS: haemorrhagic stroke

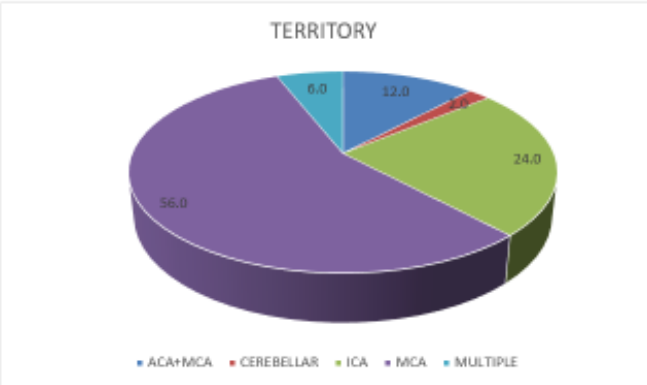

Figure 1: ***Distribution of cases according to territory involvement***
ACA: Anterior cerebral artery, MCA: Middle cerebral artery, ICA: Internal carotid artery

Sixteen (32%) cases had 7th nerve palsy and 12 (24%) had 6th nerve palsy. We had 2 patients with Moya Moya disease with childhood stroke (Figure 2A-2C)

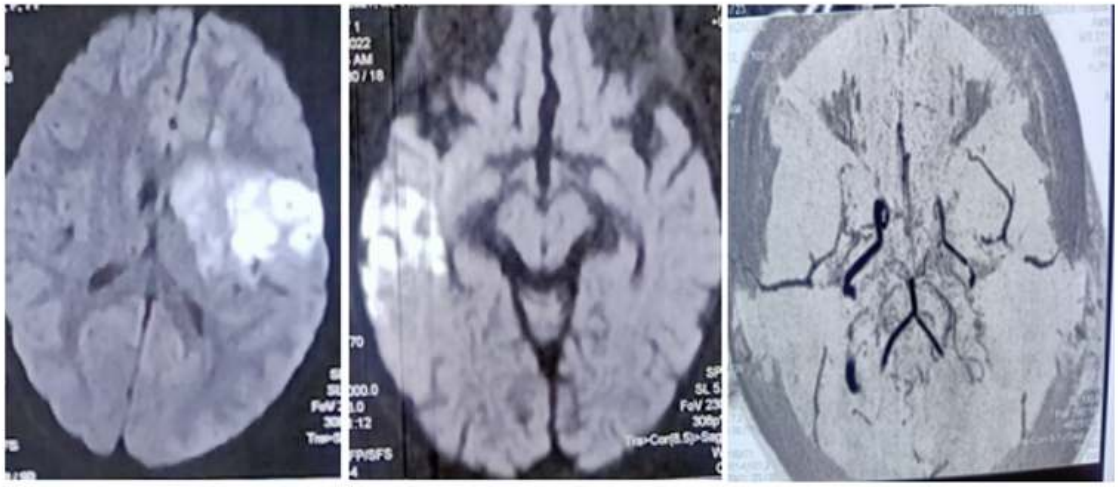

Figure 2: ***MRI image of Moyamoya disease showing- a) diffusion restriction in left parietal region, b) diffusion restriction in right temporal region and c) susceptibility weighted image – multiple bilateral collaterals around circle of Willis***

Immediate outcome after admission was as follows: 8 (16%) cases died and 42 (84%) cases were discharged. Although none died among AIS and CSVT cases, there was a statistically significant ($p<0.001$) mortality (8, 53.3%) in HS (Table 3).

Table 3: ***Outcome after admission in different stroke types***

Outcome	Stroke type			Total n (%)	p-value
	AIS n (%)	CSVT n (%)	HS n (%)		
Discharge	23 (100.0)	12 (100.0)	07 (46.7)	42 (84.0)	<0.001
Died	0 (0)	0 (0)	08 (53.3)	08 (16.0)	
Total	23 (100.0)	12 (100.0)	15 (100.0)	50 (100.0)	

After 6-months follow-up of discharged cases (n=42), the major neurological outcome was partial recovery (64.3%). The majority achieved partial recovery in case of AIS (86.9%) and HS (71.4%), although CSVT (n=12) had a significantly higher prevalence of complete recovery (83%, p =0.000) (Table 4).

Table 4: ***Outcome (neurological recovery) of discharged cases at 6 months follow up***

Outcome at 6 month follow-up	Stroke type			Total n (%)	p-value
	AIS n (%)	CSVT n (%)	HS n (%)		
No recovery	02 (08.7)	0(0)	02 (28.6)	04 (09.5)	0.000
Partial recovery	20 (87.0)	02 (16.7)	05 (71.4)	27 (64.3)	
Complete recovery	01(04.4)	10 (83.3)	0 (0)	11 (26.2)	
Total	23 (100,0)	12 (100,0)	07 (100.0)	42 (100.0)	

Discussion:

Stroke is a less studied entity in the childhood population. It is a cerebrovascular disorder resulting in focal cerebral injury. It is one of the prominent causes of acquired brain injury leading to neurologic emergency[5]. It has been receiving great attention in recent years because of significant morbidity and mortality associated with it. In this study, 50 cases of childhood stroke were studied and evaluated. Majority of cases (56%) were more than 5 years of age and very low prevalence (4%) was observed in infancy. These findings were consistent with studies by Kalita J, *et al*[6] and Vyas S, *et al*[7] where they found that peak prevalence was after 5 years of age. The present study revealed almost equal prevalence in case of

gender (M: F=1.2:1) which was similar to the observation of the study by Lee EH, *et al*[8].

In our study (n=50), the commonest stroke type was AIS (46%) followed by HS (30%) and CSVT (24%) which was similar to studies by Jeong G, *et al*[9] and Parakh M, *et al*[10] where AIS was more prevalent than others. In our study, all stroke types (AIS, CSVT and HS) were almost equally prevalent in the 1-5-year age group (35% vs 30% vs 35%; n=20) whereas AIS was more common than CSVT and HS in the more than 5-year age group (53.57% vs 21.43 vs 25%; n=28). This was similar to studies by Kalita J, *et al*[6] and Vyas S, *et al*[7] where AIS was more prevalent in older children (>5 years age group). However, a study by Chiang KL, *et al*[11] found that AIS was more prevalent in all age groups.

In our study the commonest risk factor was infection (30%) followed by vascular disorder (24%) including arteriopathy and vascular malformation. Patra C, *et al*[4] and Kalita J, *et al*[6] reported infection as the commonest risk factor of stroke. Contrarily, Lee EH *et al*[8] and Jeong G, *et al*[9] found that arteriopathy was the commonest risk factor. In current study, in AIS (n=23), commonest risk factor was vascular disorder (30%). Lee EH, *et al*[8] and Sood A, *et al*[12] found that vascular disorder was the commonest risk factor for AIS whereas Chand P, *et al*[13] found cardiac disease as the commonest risk factor. In CSVT (n=12), the commonest risk factor was infection (67%) followed by haematological disorder (25%) which was consistent with study by Sebire G, *et al*[14]. In HS (n=15), commonest risk factor was haematological disorder (47%) followed by vascular disorder mainly vascular malformation. This was similar to the study by Makhija S, *et al*[15]. Sharma S, *et al*[16] found vitamin K deficiency related bleeding disorder as the commonest risk factor but Beslow LA, *et al*[17] found vascular malformation as commonest risk factor of HS. Most common individual risk factor for AIS, CSVT and HS were TBM, orbital cellulitis and haemophilia respectively.

Overall, commonest presentation was seizure (78%) followed by hemiparesis (70%). Parakh M, *et al*[10] and Chand P, *et al*[12] found that seizure was the commonest presentation but Patra C, *et al*[4] and Lee EH *et al*[8] reported hemiparesis as commonest presentation followed by seizure. Among AIS (n=23) commonest presentation was hemiparesis (95%) which was similar to studies by Jeong J, *et al*[9] and Mallick AA, *et al*[18]. In CSVT (n=12), seizure (100%) was the commonest presentation. Sebire G, *et al*[14] reported seizure as the commonest presentation. Among HS (n=15), all had a common presentation of seizure, hemiparesis and altered sensorium (80% each). Parakh M, *et al*[10] found that all HS cases had seizures and altered sensorium followed by hemiparesis.

In our study, the commonest cranial nerve involvement was 7th nerve palsy (32%) followed by 6th nerve palsy (24%). Studies by Vyas S, *et al*[7] and Parakh M, *et al*[10] also reported that 7th cranial nerve palsy was the commonest palsy. The commonest territory involvement was MCA (56%), followed by internal carotid artery (24%). Similar observations were found in studies by Kalita J, *et al*[6] and Parakh M, *et al*[10].

Overall mortality was 16% and 84% cases were discharged after treatment. This was comparable to the study by Patra C, *et al*[4] who found a mortality of 15%. Statistically significant ($p<0.001$) mortality (53.3%) was noted in HS (n=15) but there was no mortality in AIS and CSVT. Similar high mortality in HS in contrast to AIS was reported by Vyas S, *et al*[7] and Chiang KL, *et al*[11]. In our study, after 6 months follow up of discharged cases (n= 42), there was no mortality; 64.3% achieved partial recovery 26.2% achieved complete recovery and 9.5% had no recovery. Similar findings were observed by Ogeng'o JA, *et al*[19] in their study (n=32) where they found that 53% cases had some neurological deficit. In all age group, major outcome after 6 months follow up was partial recovery. Kalita J, *et al*[6] and Chand P, *et al*[13] found poor outcome in the young age group. Majority achieved partial recovery in case of AIS and HS although CSVT (n=12) had significantly higher prevalence of complete recovery (83%, $p =0.000$). Christerson S, *et al*[20], Karalok ZS, *et al*[21] and others[22,23] found that mild neurological deficit (partial recovery) was more common in ischaemic stroke than in HS due to higher mortality in HS. Vyas S, *et al*[7] also observed higher prevalence of partial recovery in ischaemic stroke than in HS. Future research with a larger sample size, long term follow up and treatment is needed to further substantiate the results of this study.

Conclusions

From this hospital based, observational, prospective study it can be concluded that the commonest stroke type was AIS. Common risk factor was infection and it was also a statistically significant risk factor for CSVT. Seizure was the commonest presentation followed by hemiparesis although statistically significant presentation for AIS, CSVT and HS was hemiparesis, squint and altered sensorium respectively. Statistically significant mortality was observed in HS whereas AIS and CSVT had no mortality. Commonest short-term outcome was partial neurological recovery whereas majority of CSVT cases recovered completely.

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