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Original Research Article

Predictors of outcome after childhood ischemic stroke at a referral neuroscience hospital in Bangladesh

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ABSTRACT

Background: Though stroke in the pediatric age group is not as common as in adults, it is now recognized as an important cause of morbidity and mortality in children. For proper management of childhood stroke, it is very important to know about the spectrum of clinical presentation, risk factors, and neuroimaging features that can affect the outcome following stroke. The aim of the study was to identify predictors of outcomes in children with ischemic stroke treated at a referral neuroscience hospital in Bangladesh.
Methods: A one-year prospective cohort study was conducted at the department of pediatric neurology, national institute of neurosciences and hospital (NINS and H), Dhaka, from March 2021 to February 2022. It involved 42 consecutive pediatric ischemic stroke patients aged 1 month to 18 years. Post-operative outcomes were assessed clinically, biochemically, and with imaging at discharge, 1 month, and 6 months post-discharge using the PSOM scale. Statistical analysis was performed using SPSS version 23.0, with significance set at $p<0.05$.
Results: In our pediatric ischemic stroke study (n=42), most patients (76.2%) were aged 1-5 years, with iron deficiency anemia (59.5%) as the predominant risk factor. Anterior circulation stroke was common (90.5%), and PSOM assessments showed 28.6% favorable outcomes at discharge, increasing to 76.2% at 6 months. Seizure, speech difficulty, altered consciousness, and CNS infection were linked to poorer outcomes ($p<0.005$).
Conclusions: Childhood stroke poses significant morbidity, with variable neurological outcomes. Factors like seizure, speech difficulty, altered consciousness, and CNS infection predict poorer outcomes.

Keywords: Pediatric ischemic stroke, Neuroimaging, Hemiparesis, PSOM, Referral neuroscience hospital

INTRODUCTION

Stroke is defined by the WHO as a rapid onset of neurological symptoms, lasting longer than 24 hours or leading to death, with a vascular origin.[1] Though stroke in the pediatric age group is not as common as in adults, it is now recognized as an important cause of morbidity and mortality in children. Childhood stroke differs from adult stroke in many facets, including clinical presentation, etiology, and treatment.[2] Considering the differences as well as the better capacity for recovery of the young brain, it becomes more evident that the outcome of children after stroke should be different from that of adults.[2,3]

The clinical presentation of childhood stroke is often subtle and nonspecific and can be attributed to other neurological disorders, and early neuroimaging may reveal normal findings. Hemiparesis is the most common presentation of AIS in childhood, and the middle cerebral artery (MCA) territory is the most common location of infarcts in children.[4] Certain clinical features are

associated with a poorer outcome. Children who present with seizures tend to have a worse prognosis for intellectual development and a higher incidence of recurrent seizures compared with children who do not have seizures during the acute phase.[5] In some studies, it was found that presentation with an altered level of consciousness predicted a worse outcome.[6,7]

The presence of multiple risk factors has been described in 25% of children with AIS, and their presence is associated with a poor outcome and recurrence.[8] Early identification of risk factors that affect the outcome allows for the rapid implementation of treatment and prevention of recurrence.[9]

Neuroimaging is a key tool in the diagnosis of stroke, allowing differentiation between a true stroke and a non-vascular stroke mimic, while also allowing further classification of the underlying cause.[10] MRI is recommended for further assessment of stroke and to identify the possible underlying cause. MRI of the brain helps to identify the presence of multiple infarcts, infarct localization, and involvement of the cortical and subcortical areas of the brain, which may affect the future outcome after stroke.

Treatment and outcomes of childhood stroke are largely dependent on etiology.[2] It is a widely held belief that the outcome in childhood stroke is better than in adults.[2] But this assumption is challenged by several studies showing that more than half of the survivors of childhood AIS have long-term physical disabilities and cognitive impairment.[11] Previously reported predictors of poor outcome include combined cortical and subcortical lesions, the use of seizure medication, and arteriopathies.[2]

Many stroke outcome measures are available for adults, but only one measure has been validated for pediatric stroke, the pediatric stroke outcome measure (PSOM) scale.[12,13] The outcome data are required for prognosis. This will support the improvement of treatment strategies, planning for preventive measures, and focusing on the early implementation of appropriate rehabilitation therapy to improve the quality of life of stroke survivors and decrease the risk of recurrence.

Stroke is an leading cause of mortality and morbidity in children. For proper management of childhood stroke, it is very important to know about the spectrum of clinical presentation, risk factors, and neuroimaging features that can affect the outcome following stroke. So, this study aims to evaluate the factors that influence the outcomes of childhood ischemic stroke.

Objectives

The aim of the study was to identify predictors of outcomes in children with ischemic stroke treated at a referral neuroscience hospital in Bangladesh.

METHODS

This observational study was conducted at the NINS and H, Sher-E-Bangla Nagar, Dhaka, over a 12-month period from March 1, 2021, to February 28, 2022. The study population comprised approximately 42 consecutive patients aged 1 month to 18 years with childhood ischemic stroke who were admitted or attended the outpatient department during the study period.

Inclusion criteria

Children aged 1 month to 18 years with sudden onset of neurological deficit and radiological evidence of ischemic stroke, patients providing appropriate consent were included in study.

Exclusion criteria

Patients with clinical signs of focal disturbance of cerebral function lasting less than 24 hours, patients with cerebral venous sinus thrombosis, post-operative patients of cranial surgery and patients with other comorbid neurological conditions such as ischemic stroke with cerebral palsy, ICSOL were excluded.

Institutional approval was obtained from the Ethical committee of national institute of neurosciences and hospital (NINS and H), and ethical issues were addressed according to the Helsinki declaration. Pre-study assessments included detailed history taking, physical and neurological examinations, and radiological evaluations corroborated with expert opinions from the department of neuroradiology, NINS and H.

Diagnosis was based on history, clinical, and neuroradiological findings as per the inclusion criteria. The following information was collected and recorded: age, sex, socioeconomic status, clinical presentation, perinatal details, family history, developmental status, physical examination findings, neuroradiological findings, other relevant investigations, and treatment history.

Neurological outcomes were assessed using the PSOM scale at discharge, 1 month, and 6 months post-discharge. Statistical analysis was performed using SPSS version 22.0. Qualitative data were expressed as frequencies and percentages, while quantitative data were presented as mean±SD, minimum, and maximum. Chi-square tests were used to compare qualitative variables, and one-way ANOVA and chi-square tests were used to compare quantitative variables. A p value less than 0.05 was considered statistically significant. Informed written consent was obtained from the parents of all participants, ensuring confidentiality and explaining the risks and benefits of the study.

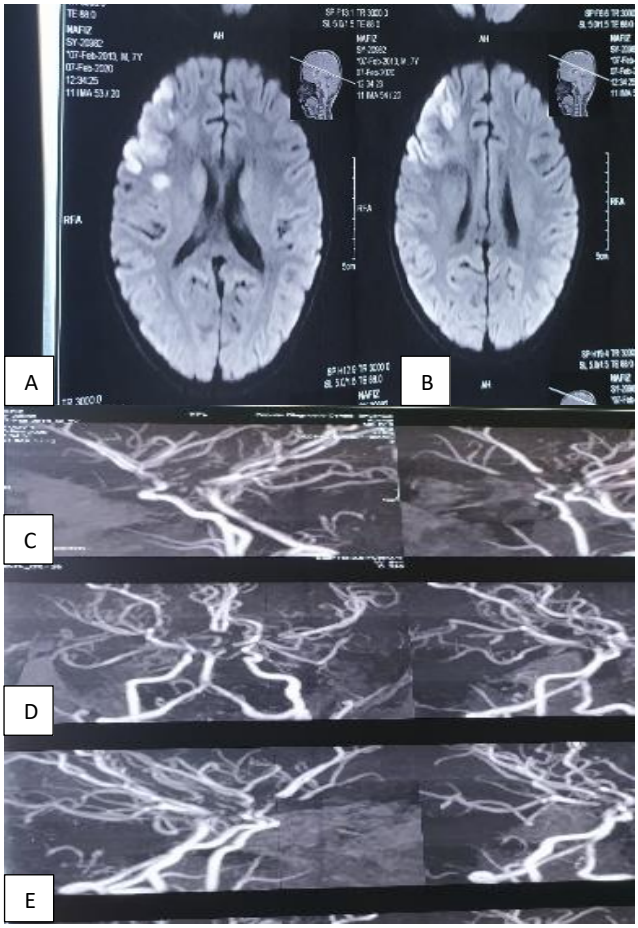

Figure 2 (A-E): MRI of brain including MRA of a 7-year-old child (Nafiz) with Moya Moya disease.

RESULTS

Table 1 shows that a maximum of 32 (76.2%) cases were in the age group of 1-5 years, followed by 9 (21.4%) cases in the age group of 5-10 years. The mean age of the cases 38.4±35.8 months. Regarding gender distribution, male-female ratio was 1.3:1. The 24 (57.1%) children were boys, and 18 (42.9%) were girls. Most of the children were from middle-class and poor families.

Table 2 shows that acute stroke (81%), i.e., 1st attack, was more common than recurrent stroke (19%). The most common clinical presentation was hemiparesis 38 (90.5%), followed by facial palsy 26 (61.9%), speech difficulty 22 (52.4%), vomiting 16 (38.1%), seizure 11 (26.2%), and headache 6 (14.3%).

Table 3 reveals that common risk factor was iron deficiency anemia 25 (59.5%), followed by vasculopathy 9 (21.4%), trauma 12 (28.6%), cardiac disorders 3 (7.1%), etc.

Table 4 reveals that anterior circulation stroke 38 (90.5%) was more common than posterior circulation stroke, and unilateral infarct 38 (90.5%) was more common than bilateral and multiple infarcts. Infarct laterality was almost equal, involving both right (50%) and left (40.5%). The most common area of infarction was the involvement of capsuloganglionic area and both cortical and subcortical areas. The MCA territory was the most common site of stroke, with 35 (83.3%) cases.

Table 5 shows that only 12 (28.6%) patients had favorable outcome at discharge, but at 6-month follow-up, about 32 (76.2%) patients achieved favorable outcome. There was no death during the follow-up period.

Table 6 reveals that seizure, speech difficulty, altered level of consciousness, and CNS infection were associated with poor outcomes. P value was significant at<0.005.

Table 1: Demographic profile of the study subjects, (n=42).

Variables		N	Percentage (%)
Age (in years)	1 month-5	32	76.2
	5-10	9	21.4
	10-18	1	2.4
	Mean (months)	38.4±35.8	
	Min-max	0.80-14.0	
Gender	Male	24	57.1
	Female	18	42.9
Socio-economic status	Poor	18	42.9
	Middle class	23	54.8
	Affluent	1	2.4
Living area	Rural	26	61.9
	Urban	16	38.1

Table 2: Clinical features of the study subjects, (n=42).

Variables		N	Percentage (%)
No. of attack	First attack	34	81.0
	Recurrent attack	8	19.0

Continued.

Variables		N	Percentage (%)
Focal neurological feature	Hemiparesis	-	-
	Right sided	21	50.0
	Left sided	17	40.5
	Mono-paresis	4	9.5
	Facial palsy	26	61.9
	Speech difficulty	22	52.4
	Visual disturbance	2	4.8
Global neurological feature	Altered level of consciousness	4	9.5
	Seizure	11	26.2
	Vomiting	16	38.1
	Headache	6	14.3
Other features	Fever	4	9.5

Table 3: Risk factors of the study subjects, (n=42).

Variables	N	Percentage (%)
H/O any congenital/acquired heart disease	3	7.1
Vasculopathy (Moya Moya)	9	21.4
Iron deficiency anemias	25	59.5
Metabolic (suspected mitochondrial)	1	2.4
Sturge Weber syndrome	1	2.4
Infection (Encephalitis)	3	7.1
Trauma	12	28.6

Table 4: Radiological features among the study cases, (n=42).

Radiological features		N	Percentage (%)
Infarction	Bilateral	3	7.1
	Right side	21	50.0
	Left side	17	40.5
Circulation involvement	MCA	35	83.3
	ACA + MCA	3	7.1
	PCA	4	9.5
Vessel involvement	Small artery	23	54.8
	Large artery	19	45.2
Area involvement	Cortical	2	4.8
	Subcortical	1	2.4
	Cortical and subcortical	19	45.2
	Capsuloganglionic	19	45.2
	Brain stem	1	2.45

Table 5: Outcome measure by PSOM at discharge at 1 month and at 6 months, (n=42).

Outcome	Favorable (0.5/10)	Unfavorable (≥1/10)	Death
At discharge	12 (28.6%)	30 (71.4%)	0
At 1 month	25 (59.5%)	17 (40.5%)	0
At 6 months	32 (76.2%)	10 (23.8%)	0

Table 6: Outcome predictor of pediatric stroke (clinical features and risk factors).

Variables	PSOM at discharge favorable/ unfavorable outcome unadjusted OR 95% CI	P value	PSOM at 3 month favorable/ unfavorable outcome unadjusted OR 95% CI	P value
Clinical profile				
Right sided hemiparesis	2.61 (0.66-10.61)	0.153	3.92 (0.678-22.70)	0.116
Left sided hemiparesis	0.357 (0.09-1.41)	0.127	0.436 (0.075-2.52)	0.302
Monoparesis	1.22 (0.114-13.06)	0.68	0.765 (0.635-0.921)	0.371

Continued.

Variables	PSOM at discharge favorable/ unfavorable outcome unadjusted OR 95% CI	P value	PSOM at 3 month favorable/ unfavorable outcome unadjusted OR 95% CI	P value
Seizure	0.20 (0.045-0.882)	0.036	1.97 (0.374-10.39)	0.348
Headache	0.769 (0.121-4.88)	0.561	0.75 (0.614-0.916)	0.215
Facial nerve palsy	2.00 (0.512-7.81)	0.255	1.11 (0.233-5.54)	0.615
Visual disturbance	0.70 (0.57-0.857)	0.5	0.784 (0.662-0.928)	0.789
Speech difficulty	10.00 (1.83-54.59)	0.004	12.09 (1.30-111.65)	0.014
Altered consciousness	0.684 (0.551-0.849)	0.245	0.118 (0.047-0.295)	0.001
Risk factors				
Congenital/acquired heart disease	0.786 (0.065-9.56)	0.646	9.66 (0.750-124.59)	0.106
Moya Moya	0.75 90.154-3.65)	0.509	0.73 (0.591-0.910)	0.12
CNS infection (meningoencephalitis)	0.70 (0.571-0.857)	0.505	0.167 (0.08-0.346)	0.04
Iron deficiency anaemia	0.707 (0.581-0.861)	0.714	0.189 (0.097-0.369)	0.211
H/O recent trauma	1.28 (0.281-5.891)	0.531	0.778 (0.131-4.61)	0.578

DISCUSSION

The study was conducted over one year in the department of pediatric neurology, NINS and H. A total of 42 patients were included. Most of the patients, 32 (76.25%), were below 5 years of age, and the mean age was 38.4±35.8 months. Parakh et al also observed similar results (70% of patients were below 5 years, with a mean age of 52.84±50.99 months).[15] Tham et al, Uzunhan et al and Mallick et al also observed almost similar results.[6,15,16] Male patients were slightly higher in the present study, 24 (57.1%). This finding was similar to Patra et al (61.8% male) and Parakh et al (64% male), which were conducted in India.[14,17] However, in most of the published literature, the male-female ratio was almost equal.[15,18]

Recurrent stroke was found to be slightly higher in the present study, 8 (19%), compared to Lehman et al (8.6%).[19] This difference was possibly due to a lack of definitive treatment according to etiology.

The common symptoms of acute stroke in the present study included hemiparesis (90%), hemiparesis with hemifacial weakness (62%), followed by speech or language disturbance (52%), and altered mental status in 10% of children. Seizures at stroke onset are more common in children than adults, affecting 15% to 25%, especially in those <6 years of age.[6] In our study, seizure was a presenting feature in 26% of patients.

In this study, the common risk factors of ischemic stroke were iron deficiency anemia (59.5%), followed by vasculopathy (21.4%), infection (7.1%), and cardiac disorders (7.1%). Lee et al also observed similar findings.[20] In contrast, Pergami et al observed that cardiac disorders (31%) and hypercoagulability states (13%) were more common.[9] In the current study, vasculopathy was a more common etiology in contradiction to the common ones like cardiac defects, which is probably due to referral bias of more Moya Moya cases and the search for etiology in every case with MRA angiography in this center. Bleeding disorders and prothrombotic conditions were not evaluated in most of the children due to financial constraints. This is why hypercoagulability was found less commonly, and the etiology remained undetermined in a quarter of children in the present study.

Capsuloganglionic and combined cortical-subcortical areas were the common (45%) sites of infarction observed in the present study, with almost equal involvement of the left (40%) and right hemispheres (50%). DeVeber et al also observed almost similar results.[21] Single infarct (90%) was more common than multiple infarcts (10%) in the current study, which corresponds with other studies.[21] Anterior circulation stroke was more common (90%) than posterior circulation stroke (10%) observed in the present study. Pergami et al also observed similar findings (ant. cir 68%, post. cir 23%, both cir. 9%).[9] The MCA territory was the commonest (83.3%) site of stroke observed in the present study, which corresponds to previous studies.[14]

At discharge, 12 patients (28.6%) had a favorable outcome (PSOM 0-0.5), and 30 patients (71.4%) had an unfavorable outcome (PSOM 1-5). At the 6-month follow-up, no patient died; the outcome was favorable (PSOM 0-0.5) for 32 (76.2%) patients and unfavorable (PSOM 1-4) for 10 (23.8%) patients. At the time of discharge, the disability level (59.5% moderate to severe disability) in the present study was similar to Tham et al and Parakh et al (64% and 65%, respectively).[14,15] Finally, among all stroke patients, no patient died during discharge or follow-up period, which was not similar to previous studies where death was a common outcome variable in ischemic stroke.[14,22]

Even if it is widely believed that brain plasticity can lead to improved outcomes following acquired brain injury at an early age, recent studies suggest that children before 1

to 2 years of age have worse neurocognitive and motor outcomes.[6,23,24] There is increasing evidence to support the hypothesis that younger age at the time of stroke is a predictor of a worse outcome, particularly for cognitive and neuropsychological domains.[25] In contrast to the above-mentioned studies, we have not found any correlation between age at stroke and neurological outcome. In our study, outcome was found equal in relation to sex, socioeconomic status, or residence.

Recurrent stroke is a predictive factor for poor outcome, as reported in other series.[26] Certain clinical features are associated with poorer outcomes. Children who present with seizures tend to have a worse prognosis for intellectual development and a higher incidence of recurrent seizures compared with children who do not have seizures during the acute phase.[5] In our study, initial presentation with seizure had a poor outcome. But there was no history of seizure recurrence during the follow-up period. Symptoms such as altered levels of consciousness, headache, or vomiting among older children predicted worse neurological outcomes. So, in our study, seizure (chi-square test; p=0.036), speech difficulty (chi-square test; p=0.004), altered level of consciousness (chi-square test; p=0.001), and CNS infection (meningoencephalitis) (chi-square test; p=0.04) were predictive factors for poor outcome.

Many studies have identified neuroimaging features that might influence the outcome: large artery stroke, bilateral infarcts, and involvement of basal ganglia were associated with poor outcomes.[27,28] We have not found any correlation between infarct number, infarct laterality, involvement of circulation (ACA, MCA and PCA), or small versus large vessel stroke and a poorer neurological outcome.

Limitations

This study had some limitations-Sample size was small, potentially affecting the generalizability of the findings. Single center study, limiting the generalizability of the results to other settings. Follow-up period was very short, possibly overlooking long-term effects or complications. All investigations were not available due to the COVID-19 pandemic situation, potentially leading to incomplete data. The study was conducted in a tertiary care hospital or referral center, so prevalence may be higher than the general population in hospital-based studies. Hence, data cannot be projected to the general population, for which population-based studies are necessary.

CONCLUSION

In this study, ischemic stroke was more common in children under 5 years of age, with a slight male predominance. Hemiparesis, speech difficulty, and seizures were the most common clinical presentations of childhood ischemic stroke, and the MCA territory was the most common site of infarction. The neurological outcome after pediatric ischemic stroke was variable, with a favorable outcome in about two-thirds of the patients. Initial presentation with seizures, speech difficulty, altered level of consciousness, and stroke associated with CNS infection (meningoencephalitis) were predictive factors for poor outcome.

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