https://doi.org/10.29309/TPMJ/2024.31.05.8053

The Professional Medical Journal
www.theprofesional.com
2024, Volume, 31 Issue, 05

ORIGINAL ARTICLE

Pediatric arterial ischemic stroke; Risk factors, clinical presentation and short-term outcome of patients presenting at a tertiary care hospital.

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Article Citation: Ibrahim S, Anjum M, Soomro S. Pediatric arterial ischemic stroke; Risk factors, clinical presentation and short-term outcome of patients presenting at a tertiary care hospital. Professional Med J 2024; 31(05):789-794. https://doi.org/10.29309/TPMJ/2024.31.05.8053

ABSTRACT… Objective: To determine the risk factors, clinical presentation and short term outcome in children presenting with arterial ischemic stroke at a tertiary care hospital. **Study Design:** Prospective Observational study. **Setting:** Medical Units of National Institute of Child Health, Karachi, Pakistan. **Period:** November 2022 October 2023. **Methods:** Children of either gender aged between 1 month to 12 years and admitted with the diagnosis of pediatric arterial ischemic stroke during the study duration were analyzed. Detailed medical and neurological examinations were performed. Routine work up and laboratory investigations were done. Modified Rankin Scale (MRS) scores at the time of enrollment, discharge and after 3 month follow-up were recorded. **Results:** In a total of 35 children, 21 (60.0%) were boys the mean age was 6.89±3.63 years. The most frequent presenting clinical features were focal neurological deficits noted in 29 (82.9%) children whereas fever, and fits were reported in 26 (74.3%), and 22 (62.9%) children, respectively. Right hemiplegia was observed in 15 (42.9%) children. Stroke was secondary to moyamoya 8 (22.9%), infections in 6 (17.1%) children. Mortality was reported among 3 (8.6%) children while 3 others lost during the follow ups. Comparison of mean mRS scores at the time of admission, discharge and after 3 months showed significant reduction ($p<0.001$). **Conclusion:** Focal neurological deficits were the predominant clinical features, with a significant incidence of associated fever and seizures. Moyamoya and infections emerged as primary causative factors. Despite a mortality rate of 8.6%, there was an overall improvement in outcomes, as evidenced by a significant reduction in Modified Rankin Scale scores at admission, discharge, and after three months.

Key words: Arterial Ischemic Stroke, Fever, Fits, Modified Rankin Scale, Moyamoya.

INTRODUCTION

Arterial ischemic stroke has been increasingly recognized as one of the important cause of mortality and significant morbidity in pediatric population.[1] The incidence of pediatric ischemic stroke is estimated to be 0.56 to 2.4 / 100,000 population / year.[2] Though rare in pediatric population but its overall incidence is on rise due to improvement in survival of children with risk factors and increase in its recognition.[3] Ischemic stroke accounts for 55% of cases in children while rest being hemorrhagic strokes.[2]

Clinical presentation of stroke mainly depends upon underlying systemic illness and territory of involved intracranial vessels.[4] Classically, stroke presents with acute focal neurological deficits like hemiplegia, speech abnormality or gait problem, but these clinical presentations also depend on child's age like young infants may present with irritability, lethargy, feeding difficulties, apnea and hypotonia.[5] Other important clinical presentations include seizures, altered consciousness, and fever.[2] Most common risk factors in pediatric population include central nervous system (CNS) infections, congenital heart diseases, acute systemic illnesses like sepsis, dehydration, hypoxia or acidosis, arteriopathies , heamoglobinopathies and trauma with on average half of the cases are cryptogenic.[6,7]

Early identification is important for provision of life saving treatments like thrombolysis or endovascular recanalization which is to be provided within 4-6 hours of onset of stroke , but in pediatric population diagnosis is usually

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Article received on: 08/11/2023
Accepted for publication: 16/01/2024

delayed with median duration of from onset of symptoms to the diagnosis is 22.7 hours in Canadian cohort.[8] Unlike adults who have uniform clinical presentations and underlying pathology, in pediatric population, there is heterogeneous etiology and variable presentation which poses delay in diagnosis and management.[7]

Stroke may lead to many neurological deficits like motor deficits, epilepsy, cognitive impairment with significant impact on daily life activities as well as cost of treatment and rehabilitation.[6] There are many outcome measures which have been used for classifying outcome severity including "Pediatric Evaluation of Disability Inventory (PEDI)", "modified Rankin Scale (MRS)" and "Pediatric Stroke Outcome Measure (PSOM)".[9] The objective of this study was to determine the risk factors, clinical presentation and short term outcome in children presenting with arterial ischemic stroke at a tertiary care hospitals.

METHODS

This prospective observational study was conducted in 3 medical units of National Institute of Child Health, Karachi, Pakistan from November 2022 October 2023. Approval from "Institutional Ethical Committee" was acquired (Letter: IERB-51/2021). All children of either gender aged between 1 month to 12 years and admitted with the diagnosis of pediatric arterial ischemic stroke during the study duration were analyzed. Taken adopting consecutive, non probability sampling technique. Children who had post-traumatic or hemorrhagic stroke or venous insults were excluded. Approval was acquired from parent/guardian of each child included in the study.

Detailed medical and neurological examinations were done. Routine work up for arterial ischemic stroke according to hospital protocol was done like CBC, serum electrolytes, hemoglobin electrophoresis, echocardiography, lipid profile and thrombophiliac profile including protein C,S, anti thrombin III. CT/MRI and magnetic resonance angiography (MRA) were recorded. MRS at the time of enrollment, discharge and after 3 month follow-up were recorded. All study findings were recorded in a pre-designed proforma.

Data analysis was done using IBM-SPSS Statistics, version 26.0. Frequency and percentages were recorded for categorical variables like gender, symptoms, examination findings etc. Mean and standard deviation (SD) were calculated for numerical data such as age, vitals, lab values, GCS, and duration of symptoms. Chi-square test was applied to compare categorical data wheres analysis of variance was performed to compare mRS scores a different intervals. $P<0.05$ was considered significant.

RESULTS

In a total of 35 children, 21 (60.0%) were boys, representing a boys to girls ratio of 1.5:1. At the time of admission, the mean age and weight were 6.89±3.63 years (5 months to 12 years) and 15.89±5.85 kg (4 to 28 kg). Residential status of 23 (65.7%) children was urban. The most frequent presenting clinical features were focal neurological deficits noted in 29 (82.9%) children whereas fever, and fits were reported in 26 (74.3%), and 22 (62.9%) children respectively (Figure-1).

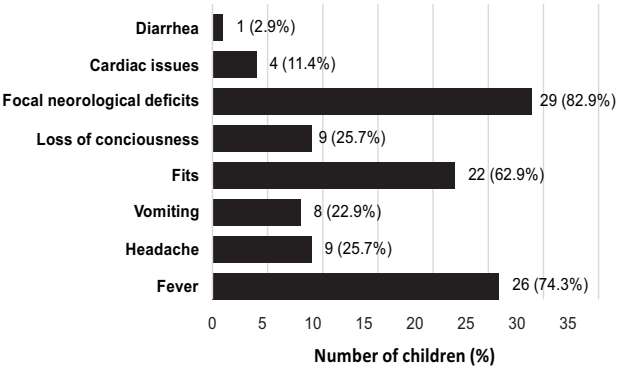

Figure-1. Frequency of sign, symptoms and clinical features

Involvement of cranial nerves was found in 7 children (3 cases of left sided facial palsy, 3 cases of right sided facial palsy, 1 case of visual loss). Right hemiplegia was observed in 15 (42.9%) children while left hemiplegia and quadriplegia noted in 10 (38.6%) and 3 (8.6%) children respectively. The mean Glasgow Coma Scale (GCS) score at the time of presentation was 12.88±2.80. Descriptive details of vitals and laboratory parameters are shown in Table-I.

Overall assessment showed that stroke was secondary to moyamoya 8 (22.9%), infections in 6 (17.1%), congenital heart defects 3 (8.9%), protein s and c deficiency 3 (8.6%), homocystinuria and sickle cell disease in 1 (2.9%) case each. No identifiable causes of arterial ischemic stroke were found among 13 (37.1%) children. Stroke recurrence was reported in 7 (20.0%) children while unilateral and bilateral involvement were observed among 17 (48.6%) and 11 (31.4%) children respectively. Comparison of demographic characteristics of children with arterial stroke are shown in Table-II.

Bladder or bowel incontinence was found in 2 (5.8%) children. Speech impairment was observed in 13 (37.2%) cases. Echocardiography examination revealed Tetralogy of Fallot in 2 (5.7%) children while left ventricular dysfunction was also noted among 2 (5.7%) children. Multiple infarcts were reported in 14 (40.0%) children. Meningeal enhancement as associate finding was noted in 4 (11.4%0 children. Mortality was reported among 3 (8.6%) children while 3 others lost during the follow ups. Comparison of mean mRS scores at the time of admission, discharge and after 3 months are shown in Table-III and it showed significant reduction ($p<0.001$)

Parameters	Mean±Standard Deviation	Minimum	Maximum
Respiratory rate (respiratins/minute)	26.89±6.0	18	40
Heart rate (beats/minute)	115.72±22.39	70	150
Systolic blood pressure (mmHg)	98.82±15.04	70	135
Diastolic blood pressure (mmHg)	59.18±15.72	36	98
Temperature (^{0}F)	100.50±1.87	97	102
Hemoglobin (g/dl)	10.44±2.62	4.2	14.2
Total leukocytes count (/ul)	12313±5412	3800	30000
Platelets (10^9/L)	446±175	94	751
Urea (mg/dl)	25.40±11.69	10	54
Creatinine (mg/dl)	0.28±0.10	0.20	0.50
Na (mEq/L)	134.20±4.77	130	148
K (mEq/L)	4.20±0.84	2.0	5.6
Albumin (g/dl)	3.60±0.53	3	4
PT (sec)	15.41±2.66	13.0	20.90
APTT (sec)	33.60±2.83	26	37
INR (sec)	1.07±0.39	0.10	1.40
Triglyceride (mg/dl)	137.67±92.44	66	242
Cholesterol (mg/dl)	133.67±15.01	125	151

Table-I. Descriptive details of vitals and laboratory parameters (n=35)

Demographics		Arterial Ischemic Stroke			P-Value
		Unilateral	Bilateral	Recurrent	
Gender	Boys	12 (70.6%)	6 (54.5%)	3 (42.9%)	0.409
	Girls	5 (29.4%)	5 (45.5%)	4 (57.1%)	
Age	≤5	9 (52.9%)	2 (18.2%)	3 (42.9%)	0.183
	6-12	8 (47.1%)	9 (81.8%)	4 (5.1%)	
Residence	Rural	7 (41.2%)	4 (36.4%)	1 (14.3%)	0.444
	Urban	10 (58.8%)	7 (63.6%)	6 (85.7%)	

Table-II. Comparison of demographic characteristics of children with arterial ischemic stroke (n=35)

	Admission (n=35)	Discharge (n=34)	After 3 Months (n=29)	P-Value
MRS Scores	4.80±0.41	4.50±0.79	2.90±1.57	<0.001

Table-III. mRS scores during the course of the study

DISCUSSION

The gender distribution among children with arterial ischemic stroke showed a predominance of boys, with a ratio of 1.5:1. This observation aligns with existing literature suggesting a potential gender-based susceptibility to arterial ischemic stroke in pediatric cases.[10,11] The mean age at the time of admission was 6.89±3.63 year. Fink et al analyzing children with posterior arterial ischemic stroke revealed the median age of the children to be 7.9 year.[12] Uohara et al reported the median age of 7.7 year for overall arterial ischemic stroke among children.[13] Further investigation into whether age plays a role in the vulnerability to pediatric arterial ischemic stroke is needed.

The clinical presentation of arterial ischemic stroke in these children manifested predominantly as focal neurological deficits (82.9%), fever (74.3%), and fits (62.9%). These findings underscore the diverse clinical features associated with pediatric arterial ischemic stroke, emphasizing the need for comprehensive clinical evaluation when suspecting such cases. Children with strokes typically exhibit focal neurological deficits, commonly presenting as hemiplegia and/or focal seizures.[14] Recognizing these signs in pediatric cases poses a challenge, as symptoms are often misconstrued as more prevalent neurological or systemic disorders. Notably, emergency room physicians display less accuracy in identifying strokes in children compared to adults.[15] While various highly sensitive stroke screening tools exist for adults, their efficacy diminishes in the pediatric population.[16] Discriminating symptoms such as focal weakness, seizures, ataxia, and difficulties in speech or walking become crucial in distinguishing stroke from common mimics like migraines in children.[17] The development of more effective screening tools holds promise in mitigating diagnostic delays, ultimately enhancing the timely implementation of acute therapies for pediatric stroke patients.[18] The neurological complications observed, such as cranial nerve involvement, bladder or bowel incontinence, speech impairment, and the presence of multiple infarcts, highlight the complexity of pediatric arterial ischemic stroke and its potential impact on various organ systems. Additionally, the echocardiography findings, including Tetralogy of Fallot and left ventricular dysfunction, suggest a need for a multidisciplinary approach in managing these cases. Cardiac conditions linked to stroke span a diverse range of acquired or congenital diseases. A study conducted by Rodan et al, involving 135 patients diagnosed with congenital heart diseases and acute ischemic stroke from the Canadian Pediatric Ischemic Stroke Registry, revealed a notable 10-year recurrence rate of 27%. This finding underscores the importance of recognizing and addressing cardiac factors in the context of stroke, especially in individuals with congenital heart diseases, for a more comprehensive understanding and management of the associated risks.[19]

The improvement in mean mRS scores from admission to discharge and after 3 months ($p<0.001$) is a positive outcome, indicating the potential for recovery and rehabilitation in these cases. The mRS is a clinician-reported measure assessing global disability, serves as a widely utilized tool for evaluating outcomes in stroke patients and as a key endpoint in randomized clinical trials. 20 Despite its broad application, there exists extensive evidence validating the mRS, dispersed across a substantial yet fragmented body of literature. This underscores the need for comprehensive synthesis and analysis of existing research to further enhance our understanding and confidence in the mRS as a reliable and robust metric for assessing stroke-related disability and outcomes. Data has shown that outcomes following acute ischemic stroke in both children and young adults show no significant differences in terms of mortality, disability, quality of life, or psychological and social variables.[21] This may suggests a comparable impact of arterial ischemic stroke on these aspects in different age groups. Understanding these similarities in long-term outcomes can contribute to the development of more inclusive and effective strategies for post-stroke care across different age ranges.

The mortality rate of 8.6% is a concerning aspect of the study, emphasizing the severity of pediatric

arterial ischemic stroke and the challenges in its management. Seven year data from Singapore analyzing pediatric stroke for an average follow up period of 33.2 months revealed no mortality but only 42.3% children achieved full recover. These findings show that long-term neurological and functional abnormalities are quite frequent among surviving pediatric stroke cases.[22] A study by Beslow et al reported overall in-hospital mortality following arterial ischemic stroke as 2.6%.[23] We did not observe any case of in-hospital mortality in this study. The prevalence of fatal outcomes following arterial ischemic stroke in different groups of pediatric patients varies significantly, spanning from 1% to nearly 32%. This wide range underscores the heterogeneity of outcomes and highlights the importance of further research to understand the factors contributing to this variability. Exploring the determinants of mortality in pediatric AIS cases is crucial for developing targeted interventions and improving overall prognosis in affected children.

Several potential limitations warrant consideration in interpreting the findings of this research on pediatric arterial ischemic stroke. The relatively small sample size of 35 children may limit the generalizability of the results to a broader pediatric population. Additionally, the single-center nature of the study, conducted in a tertiary care hospital, may introduce selection bias and limit the external validity of the findings. Furthermore, the short-term follow-up duration may not capture the full spectrum of outcomes and long-term consequences associated with pediatric arterial ischemic stroke. Despite these limitations, the study provides valuable insights, but caution should be exercised in extrapolating the findings to a more diverse and extensive pediatric population.

CONCLUSION

Focal neurological deficits were the predominant clinical features, with a significant incidence of associated fever and seizures. Moyamoya and infections emerged as primary causative factors. Despite a mortality rate of 8.6%, there was an overall improvement in outcomes, as evidenced by a significant reduction in Modified Rankin Scale scores at admission, discharge, and after three months.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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2	Misbah Anjum	Study concept, Methodology.	
3	Shazia Soomro	Proof reading, Critical review.	