

ORIGINAL ARTICLE

Etiological Risk Factors Profile of Arterial Ischemic Stroke in Children at A Tertiary Care Children's Hospital

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ABSTRACT

Objective: To determine the etiological risk factors of arterial ischemic stroke (AIS) in children.

Study Design: An observational cohort study.

Place and Duration of the Study: Neurology department of "The Children's Hospital and Institute of Child Health, Multan", from January 2020 to December 2020.

Methods: Children in the age group from one month of age to 12 years with a history of acute onset of focal neurological deficit of upper motor nerve and positive findings on neuroimaging were included in the study. The workup included baseline lab testing, neuroimaging, cardiac evaluation, and cerebro-spinal fluid (CSF) laboratory testing. We used predesigned proforma for recording the patient's details and the possible etiology of the stroke.

Results: In a total of 84 children, 28 (33.3%) were male and 56 (66.7%) were female. Age ranged from 4 months to 11 years with a mean age of 3.4 ± 2.2 years. Etiological risk factors identified in 62 (73.8%) patients and were remained undetermined in 22 (26.2%) patients. The risk factors identified were central nervous system infection arteriopathy in 22 (26.2%), iron deficiency anemia 20 (23.8%), cardiac disorders 11 (13.1%), moyamoya disease in 5 (6.0%), and mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes in 4 (4.8%) patients.

Practical Implications: It is essential to know the etiology of risk factors responsible for AIS as the management and prognosis are directly influenced by them.

Conclusion: Infection-associated arteriopathy was the most common etiological risk factor for arterial ischemic stroke in our study population.

Keywords: Anemia, arterial ischemic stroke, central nervous system, moyamoya.

INTRODUCTION

Arterial ischemic stroke (AIS) is a medical emergency and is a significant cause of morbidity and mortality in children. The AIS is defined as: "(1) A neurological deficit related to the perfusion territory of a cerebral artery and (2) Neuroradiological evidence of an ischemic lesion."¹ Strokes are broadly categorized as ischemic and hemorrhagic strokes. An ischemic stroke is further subdivided into arterial stroke and venous stroke.¹ According to recent data, childhood stroke incidence is 6 per 100,000 children per year.²

Children suffer from strokes for different reasons than the adult population as there is a diversity of risk factors responsible for AIS in children. The common risk factors for paediatric ischemic stroke are heart disease, arteriopathies (primary, secondary), hematological, hypercoagulable states, and neurometabolic disorders.³ The children of developing countries developed strokes because of the above mentioned risk factors but the central nervous system infections is the leading cause.³ After a thorough investigation, the cause of stroke remains unidentified in a significant number of cases.⁴

Prompt diagnosis of pediatric AIS remains a challenge for general pediatricians. The reasons include not having suspicion of the diagnosis in mind, non-specific clinical symptoms, and the lack of adequate neuroimaging facilities.⁵ The symptoms of AIS are age-dependent, patients younger than one year present mainly with seizures and a change in their mental state. In older children, hemiparesis most frequent presenting symptom (80%) while ataxia is seen in about 10% of children.⁵ Most children who suffer from arterial ischemic stroke become neurological handicapped in the domain of motor, and cognition, and become epileptic. Stroke-specific mortality is estimated to be around 5% while families of stroked children suffer from grave psychological and economic issues.⁶

Early diagnosis and management are very crucial as the prognosis is directly dependent on it. Keeping in mind, a slogan "TIME IS BRAIN" is floated regarding time management in this medical emergency of stroke.^{7,8}

There are no definite recommendations exist for the acute treatment and secondary prevention after AIS in children. Most of treatment practices are mainly adopted from the adult population.⁹ Pakistani data about childhood AIS are scarce. This study was performed to determine the etiological risk factors of arterial ischemic stroke (AIS) in children. We aimed to address how childhood arterial-ischemic strokes are etiologically characterized in our region.

METHODOLOGY

This observational cohort study was conducted from January 2020 to December 2020 in the Pediatric Neurology unit of "The Children Hospital and Institute of Child Health, Multan", a tertiary care referral hospital of South Punjab, Pakistan. After satisfying the hospital's "Ethical Review Committee", and taking informed consent from the parents or guardians, we started enrollment of the cases.

Children in the age group from one month of age to 12 years with a history of acute onset of focal neurological deficit of upper motor nerve and positive findings on neuroimaging were included in the study. We used our institution's protocol for the diagnosis and management of Paediatric Arterial Ischemic stroke in our children. Computed tomography (CT) scan of the brain, baseline lab investigations, fasting lipid profile, electrography and echocardiography were done in each patient on the first day of admission, and an "magnetic resonance imaging (MRI)" of the brain and "magnetic resonance angiography (MRA)" within a week. When clinical history and physical examination suggestive cerebrospinal fluid analysis, prothrombotic factors level testing, "magnetic resonance spectroscopy (MRS)", and neurometabolic testing were planned at a second-tier level. We advised low molecular weight heparin (LMWH) or aspirin for up to 1 week while waiting for further etiological evaluation.

We designed a proforma for the recording of patient demographic data, signs and symptoms, neuroimaging findings, laboratory investigations, and responsible etiological risk factors. We grouped the study population into 3 age groups, 1) 1 month to

2 years 2) 2 to 5 years, and 3) 5 to 12 years. The data was analyzed by using "Statistical Package for Social Sciences (SPSS)" version 26.00. The categorical variables were presented as proportions and continuous variables were calculated as mean, and standard deviation.

RESULTS

During the study period, 84 children were enrolled. Male patients were 28 (33.3%) females were 56 (66.7%) and male to female ratio was 1:2. The Age group ranged from 4 months to 11 years with the mean age was 3.4 ± 2.2 years. Age group stratification showed that patients who were younger than 2 years were 42 (50.0%), 2-5 years of age were 22 (26.2%) and above 5 to 12 years were 20 (23.8%) as shown in table-1.

Table 1: Gender and Age Groups distribution (n=84)

Study Variables	No. (%)
Sex	
Male	28 (33.3%)
Female	56 (66.7%)
Age groups	
1 month to < 2 years	42 (50.0%)
2 to 5 years	22 (26.2%)
>5 to 12 years	20 (23.8%)

The hemiparesis was present in all patients (100%), seizures in 48 (57%), low GCS in 24 (28.6%), and facial nerve palsy in 33 (39%) patients. Forty-four (52%) of children had a history of moderate to high-grade fever.

Table 2: Frequency of Clinical Presentations

Clinical features	Number (%)
Hemiparesis	84 (100%)
Facial weakness	33 (39.3%)
Aphasia	8 (9.5%)
Fever	44 (52.4%)
Encephalopathy	24 (28.6%)
Seizure	48 (57.1%)

Complete blood count showed that 20 (23.8%) children were anemic with a mean hemoglobin concentration was 9.1 ± 2.5 gm/dL. Keeping in mind the diagnosis of CNS infection, cerebro-spinal fluid examination was done in 42 (50.0%) cases and the result showed pleocytosis in 22 (26.2%) with a median cell count of 40 cells, protein of 80 mg/dL, and glucose of 28 mg/dL.

CT was used as the first imaging modality in all patients (100%), whereas MRI brain and MRA were done in 55 (65.5%) subjects. The MRS was done in 10 (11.9%) patients, with suspicion of the diagnosis of "mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS)". Neuroimaging results showed that left middle cerebral artery territorial infarcts occurred in 30 (36%), and right hemispheric infarcts in 22 (26.2%) children.

We were able to identify risk factors in 62 (73.8%) patients. The risk factors of arteriopathy in 5 (6.0%), cardiac disorders in 11 (13.1%), CNS Infection in 22 (26.2%), iron deficiency anemia in 20 (23.8%), and MELAS in 4 (4.8%) patients. The etiological risk factor remained undetermined in 22 (26.2%) cases.

Table 3: Risk factors for childhood AIS (n=84)

Risk factors for AIS	No. (%)
Infection-associated arteriopathy	22 (26.2%)
Cardiovascular etiology	11 (13.1%)
Moyamoya disease	5 (6.0%)
MELAS	4 (4.8%)
Anemia (iron deficiency)	20 (23.8%)
Undetermined etiology	22 (26.2%)

DISCUSSION

The arterial ischemic Stroke is an acute condition and is a medical emergency. It has a very high morbidity ratio in children and has a

grave socioeconomic burden on the families. The diagnosis is challenging since the symptoms can be non-specific and diagnostic methods pose additional difficulties. Because of these reasons, the diagnosis of ischemic stroke is often delayed in the pediatric age group.¹⁰ Our study showed that 76.2% of patients were below 5 years of age which is consistent with the international literature.¹¹ Acute hemiplegia is the predominant (77%) clinical presentation of stroke.¹² CNS infection-associated arteriopathy is the number one (26.2% cases) etiological risk factor of AIS in our study population. Tuberculous meningitis and bacterial meningitis were the most common CNS Infection. This could be due the fact that children in our part of the world are more prone to infections because of many reasons including low socioeconomic condition, poor hygiene, poor valued nutrition, and lack of adequate primary immunization. One study from India showed that CNS infections are responsible for stroke in 41%, primary arteriopathy in 26%, and heart disease in 6% of cases.¹³ In a study conducted at a single center, the results showed that cardiac disease in 17%, followed by head trauma in 13%, vasculopathies in 7.5%, and CNS infection in 4% of cases, were responsible for aetiological factors for AIS in the subject population.¹⁴

Tuberculous meningitis is the most common risk factor for arterial-ischemic stroke in our study. The literature also described that tuberculous meningitis causing stroke as a complication in about 20%-60% of patients.¹⁵ A Pakistani study showed a higher percentage of stroke (66%) because of iron deficiency anemia.¹⁶ Cardiac disorder accounted for 12-28% of childhood with stroke.¹⁷ A study carried out between 2000 and 2010 that analyzed 76 patients detected 15.7% of strokes of unknown cause.¹⁸ Many Studies showed that often, more than one risk factors are present in the same patient.^{19,20} The five-year cumulative risk of stroke recurrence was 19% among children with AIS according to another study.²⁰ The chance of recurrence depends on the underlying causes and risk factors. Children with more than one demonstrable risk factor have a recurrence chance of 42%, compared to only 6% to 8%, if no or only one risk factor is present.²¹

More than 60% of survivors have persistent neurological phenomena that are more or less interfere with activities in their daily life activities. The mortality of the arterial infarct ranges in children from 2% to 11%.²² It is essential to know the etiology risk factors responsible for AIS as the management and prognosis are directly influenced by them. There is no evidence or consensus on the acute treatment and secondary prevention of arterial infarction in children.²³ Our study also had limitations such as it has a small sample size, a single-center study, and a lack of availability of funds for prothrombotic workup in all study children.

CONCLUSION

Children less than 5 years of age and predominantly females were the main bulk of the sufferers of arterial ischemic stroke. CNS infection is the most common etiology responsible for arterial ischemic stroke. Utmost importance should be to emphasize the preventive measures of arterial ischemic stroke by good personal hygiene, good nutrition, and vaccination in the paediatric age groups.

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