

# RISK FACTORS ASSOCIATED WITH ARTERIAL ISCHEMIC STROKE IN CHILDREN

<sup>1</sup>Essam Abdallah Albakrawi,<sup>2</sup> Ahmed Galal Syam,<sup>3</sup> Ahmed Hosny Mohamed

Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author: Essam A. Albakrawi, Email: alghaber81@gmail.com

## ABSTRACT

**Background:** Children have a more diverse and larger number of risk factors for arterial ischemic stroke (AIS) that differ significantly from adults which are predominated by hypertension, diabetes, and atherosclerosis. The aim of the present study was to inspect and conclude the most common risk factors and causes of AIS in children. **Patients and methods:** A prospective cohort study included 24 patients admitted to Pediatric Department, Faculty of Medicine, Zagazig University Hospitals. Full history taking, clinical and neurological examination and routine laboratory examination were performed. Neurological outcomes were graded by the site neurologists as no deficit, mild, moderate, or severe deficits and patients were followed up. **Results:** More than one half 58.3% of arterial ischemic stroke patients had single infraction, mainly at left side 45.8%, affected mainly Anterior circulation (58.3%). The vascular imaging artropathy subtype of Arterial Ischemic Stroke patients nearly two fifths was arteropathy type (12.5%) , Moyamoya, the same percent was arterial dissection. The outcome of treatment arterial ischemic stroke patients 37.5% of them became normal early. After follow up period one half of them became normal. Unfortunately 16.7% had severe deficit at early follow up and still at late follow up period. About 1 patient (4.2%) died pre discharge, 2 patients (8.3%) died post discharge, 2 patients (8.3%) related to ischemia, other patient (4.2%) unrelated ischemia. **Conclusion:** Cardiac lesion is the most risk factors associated with arterial ischemic stroke, followed by arteriopathy, prothrombin disorder and diabetes.

**Keywords:** Arterial ischemic stroke ; Risk factors ; Cardiac lesion

## INTRODUCTION

Stroke is a neurological injury caused by the occlusion or rupture of cerebral blood vessels. Stroke can be ischemic, hemorrhagic, or both. Ischemic stroke is more frequently caused by arterial occlusion, but it may also be caused by venous occlusion of cerebral veins or sinuses. Hemorrhagic stroke is the result of bleeding from a ruptured cerebral artery or from bleeding into the site of an acute ischemic stroke (AIS) (1).

Clinical presentation with altered levels of consciousness, headache or vomiting among older children predicted worse neurological outcomes. These symptoms may reflect large infarcts and increased intracranial pressure. As in the Danish registry, most acute deaths were related to malignant MCA syndrome, a condition of malignant edema within the infarcted brain tissue. Children with these presentations may therefore benefit from closer monitoring since it is crucial to identify malignant edema early, optimize neuroprotective care and provide life-saving early hemicraniectomy surgery when indicated (2).

In contrast to adults, in whom modifiable risk factors such as cigarette smoking, hypertension, diabetes, and hypercholesterolemia have been well-documented, risk factors for pediatric AIS are less well understood. Traditional pediatric stroke risk factors were initially identified in case series describing the high prevalence of congenital heart disease, sickle cell disease, infection and hyper-coagulable states among children with stroke (3).

Current strategies for acute management of childhood stroke rely on both pediatric and adult data that explore the treatment of hypertension, hypotension, hyperglycemia, and fever, as well as surveillance strategies to prevent complications such as cerebral swelling and seizures. Little is known about whether supportive care measures alter the effect of brain ischemia in children (4). However, traditional methods of neuroprotection are often used, and recent data on specific management challenges such as the role of early hemicraniectomy in large strokes are beginning to emerge (5). The current study aimed to inspect and conclude the most common risk factors and causes of AIS in children.

## PATIENTS AND METHODS

This prospective cohort study included 24 patients who admitted to Pediatric Department, Faculty of Medicine, Zagazig University. Approval of the ethical committee of Zagazig University was obtained.

### **Inclusion and exclusion criteria:**

Patients in age between 29 days to 18 years with Acute arterial ischemic stroke. While, patients < 29 days or > 18 years and children with congenital hemiplegia.

All patients were subjected to full history taking, clinical examination and routine blood tests were performed. Initial brain magnetic resonance imaging/angiography and echocardiograms were reviewed.

Risk factors in the major categories were as follows:

- Arteriopathy included dissection, post-varicella, vasculitis, moyamoya, transient cerebralarteriopathy and non-specific arteriopathy and were defined based on a published consensusbased system (6).
- Cardiac included congenital, acquired, and procedure-related (stroke within 7 days of cardiacsurgery/catheterization) or isolated PFO in older children.
- Prothrombotic included laboratorydefined abnormalities in coagulation testing results referencing concurrent age-matched normalvalues and parameters (7) or prothrombotic medications.
- Acute illness risk factors included for all children, bacterial sepsis, shock (cardiovascular collapse), extracorporeal membrane oxygenation (ECMO), head or neck trauma,meningitis, vascular malformations (arteriovenous malformation (AVM) or aneurysm), primarycerebral haemorrhage, hydrocephalus, intracranial surgery and established migraine history.

Outcomes & Follow up:

Neurological outcomes were graded by the site neurologists as no deficit (normal), mild, moderate, or severe deficits and patients were followed up.

Statistical analysis:

Data analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data qualitative represent as number and percentage , quantitative continues group represent by mean  $\pm$  SD. Differences between quantitative independent multiple by ANOVA or Kruskal Wallis., P value was set at  $<0.05$  for significant results &  $<0.001$  for high significant result.

## RESULTS

The present study showed the variability of focal manifestation among studied patientsmost frequent one was hemiparesis (62.5%), followed bySpeech disturbance41.7% thenFacial weakness 33.3% ;the least manifestation wasAtaxia (16.7%) among Arterial Ischemic Stroke group (Figure 1).

The most frequent risk factor was cardiac lesion followed by arteriopathy and prothrombin disorder (41.7%,37.5%, 29.2%) respectively ;the least recorded risk factor was diabetic (4.2%) among arterial ischemic stroke group (Table 1).

More than one half 58.3% of arterial ischemic stroke patients had single infraction, mainly at left side 45.8%, affected mainly Anterior circulation (58.3%) (Table 2).

The vascular imaging artropathy subtype of Arterial Ischemic Stroke patients nearly two fifths was arteropathy type (12.5%), Moyamoya, the same percent was arterial dissection (Figure 2).

Regarding the outcome of treatment arterial ischemic stroke patients 37.5% of them became normal early. After follow up period one half of them became normal. Unfortunately 16.7% had severe deficit at early follow up and still at late follow up period (Table 3).

Concerning mortality among AIS patients showed that 1 patient(4.2%) died pre discharge, 2 patients (8.3%) died post discharge, 2 patients (8.3%) related to ischemia, other patient (4.2%) unrelated ischemia (Table 4).

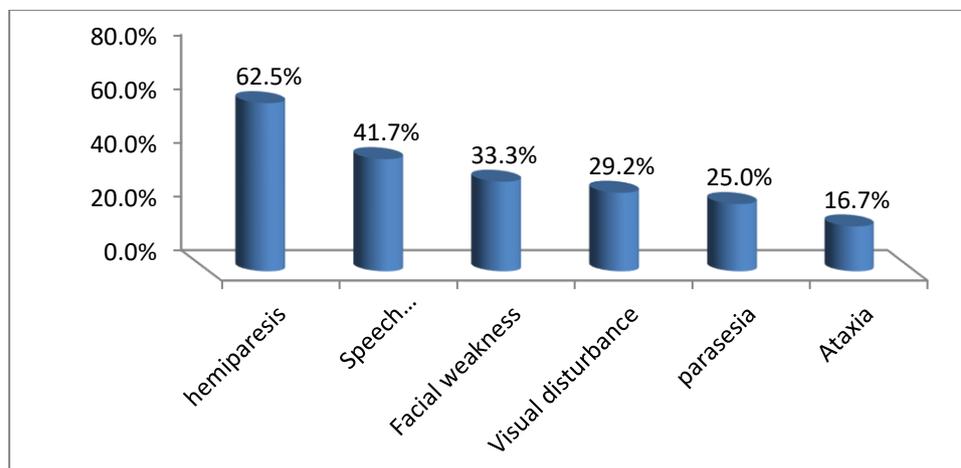


Figure (1):Percent of focal manifestations among Arterial Ischemic Stroke group

Table (1): Frequency of risk factors among arterial ischemic stroke group (n=24)

variables	Risk factors			
	yes		no	
	n.	%	n.	%
diabetic	1	4.2%	23	95.8%
Cardiac	10	41.7%	14	58.3%
Arteriopathy	9	37.5%	15	62.5%
Prothrombin disorder	7	29.2%	17	70.8%
Acute illness	4	16.7%	20	83.3%
Chronic headache	2	8.3%	22	91.7%
Tumor	4	16.7%	20	83.3%

Table (2): Frequency of brain imaging among arterial ischemic stroke group

variables	brain imaging (n=24)			
	yes		no	
	n.	%	n.	%
Single infraction	14	58.3%	10	41.7%
Multiple infraction	10	41.7%	14	58.3%
Leftside	11	45.8%	13	54.2%
Rightside	9	37.5%	15	62.5%
bilateral	4	16.7%	20	83.3%
Anterior circulation	14	58.3%	10	41.7%
Postcirculation	5	20.8%	19	79.2%
Both	4	16.7%	20	83.3%

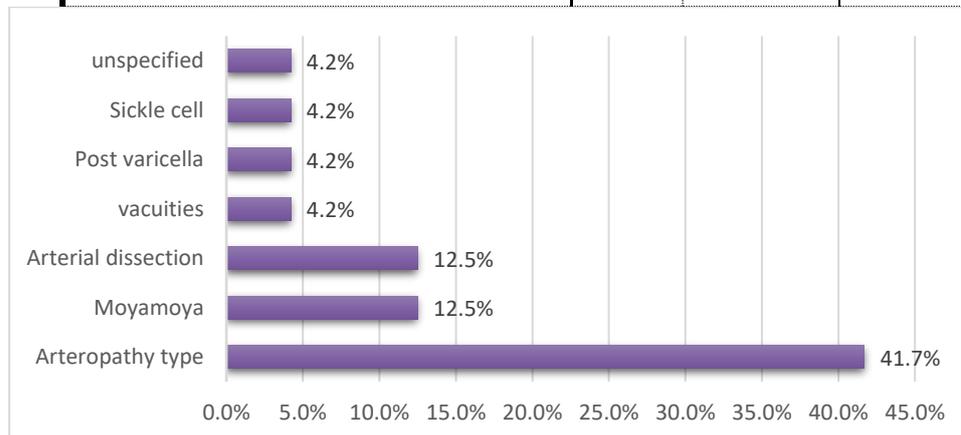


Figure (2): Vascular imaging arteriopathy subtype among AIS group

Table (3): Prognosis of arterial ischemic stroke patients (n=24)

variables	outcome (n=24)			
	yes		no	
	n.	%	n.	%
<b>Early outcome</b>				
normal	9	37.5%	15	62.5%
mild deficit	6	25.0%	18	75.0%
moderate deficit	5	20.8%	19	79.2%
severe deficit	4	16.7%	20	83.3%
<b>late outcome</b>				
normal	12	50.0%	12	50.0%
Mild deficit	4	16.7%	20	83.3%
Moderate deficit	4	16.7%	20	83.3%
Severe deficit	4	16.7%	20	83.3%
seizures	4	16.7%	20	83.3%

Table (4): Mortality of arterial ischemic stroke patients (n=24)

variables	mortality (n.24)			
	yes		no	
	n.	%	n.	%
<b>Time of death</b>				
Death pre discharge	1	4.2%	23	95.8%
Death post discharge	2	8.3%	22	91.7%
Total deaths	3	12.5%	21	87.5%
<b>Cause of deaths</b>				
Related ischemia	2	8.3%	22	91.7%
Unrelated ischemia	1	4.2%	23	95.8%

**DISCUSSION:**

Childhood arterial ischemic stroke (AIS) causes lifelong disabilities in the majority of affected children (8). Ischemic stroke is no longer a disease affecting just elderly people, since one-fourth of ischemic strokes occur in working-aged individuals in the high-income countries. The burden of pediatric stroke may be increasing further, since multiple recent studies have reported increasing incidence of ischemic strokes particularly at pediatric ages, while incidence at older ages has been declining during the same period (9,10).

Globally almost half of the entire stroke burden now affects children given that they have a greater likelihood to survive their strokes with long life spans ahead and because strokes occur at younger ages in low- and middle-income countries (11).

In the present study, there was variability in focal manifestation among studied patients, most frequent one was hemiparesis (62.5%), followed by Speech disturbance 41.7%, then Facial weakness 33.3%; the least manifestation was Ataxia (16.7%) among Arterial Ischemic Stroke group. One quarter of case had vertigo in addition one quarter of case had vomiting and nausea. Gerstl et al. (12) found the results of their study confirm that non-specific symptoms such as headache or vomiting and seizures may complicate the diagnosis of childhood stroke. Concomitant non specific symptoms such as headache, vertigo, vomiting, and decreased levels of consciousness were especially common in children and adolescents. More than half of infants presented with seizures.

Also, uncontrolled case series suggest that non-atherosclerotic arteriopathies and cardiac disorders are the most commonly identified causes (13,14). DeVeber et al. (15) found arteriopathy was documented in half of those who underwent vascular imaging (49%). Approximately half (45%) of the children without vascular imaging presented with an obvious cardiac condition. The most common definable arteriopathies were dissection (13%), post-varicella angiopathy (12%), transient cerebral

arteriopathy (8%) and moyamoya disease (8%). Acute illnesses, present in 48% of cases, included sepsis, meningitis, and major trauma.

The presence of these modifiable risk factors offers opportunities for secondary prevention in young adults, while the opportunities for secondary prevention in children are far more limited. The difference in presumed risk factors is even more pronounced in neonates. The identification of stroke risk factors in neonates has been limited, but pregnancy, particularly in the months just before delivery, is a relatively hypercoagulable state (16). This may contribute to clotting in the placenta, which, in turn, might serve as a source of embolus to the fetus/newborn. A 2016 case-control study of infants with neonatal arterial ischemic stroke found that their mothers had experienced more intrapartum complications when compared with controls (17).

Mackay et al. (13), Mallick et al. (14), Wintermark et al. (18) found that arteriopathies are the most frequently identified cause of stroke, accounting for 18–53% of index events in prospective observational studies.

Chiang and Cheng (19) found the most common risk factors were vascular diseases (26.3%), infection (14.0%), cardiac disorders (9.1%) and Central Nervous System (CNS) neoplasms (7.6%). Other risk factors included hematological diseases, renal diseases, child abuse or shaken baby, autoimmune diseases, metabolic disorders and head trauma. In addition, old history of cerebral palsy, major traumatic brain injury or long-term ventilator dependent respiratory failure is also important risk of pediatric stroke (5.1%).

The present study showed that 1 patient (4.2%) died pre discharge, 2 patients (8.3%) died post discharge with total deaths 12.5%, 2 patients (8.3%) related to ischemia, other patient (4.2%) unrelated ischemia. This came in agreement with Chiang and Cheng (19) reported that roughly 10–25% of children with a stroke will die and up to 25% of children will have a recurrence. A study using the Global Burden of Disease (GBD) methods reported the mortality ratio was about 20% (11).

#### CONCLUSION

Cardiac lesion is the most risk factors associated with arterial ischemic stroke, followed by arteriopathy, prothrombin disorder and diabetes.

No Conflict of interest.

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