ORIGINAL ARTICLE

Comparison of Risk Factors and Outcomes in Pediatric Posterior and Anterior Circulation Arterial Ischemic Stroke: A Cross-Sectional Analysis

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ABSTRACT

Objectives: Pediatric arterial ischemic stroke (AIS) is a rare but serious condition leading to significant neurological disability. AIS is classified into anterior circulation AIS (ACAIS) and posterior circulation AIS (PCAIS). Understanding the differences between these subtypes is essential for early diagnosis and effective management. This study aimed to evaluate the demographic, clinical, and laboratory characteristics of pediatric ACAIS and PCAIS, focusing on lipid profiles, prothrombotic factors, and SARS-CoV-2 prevalence.

Materials & Methods: A descriptive-analytical cross-sectional study was conducted on 34 children diagnosed with AIS at the Tabriz Children's Hospital from March 2020 to October 2021. Patients were categorized into ACAIS, PCAIS, and mixed, involving both anterior and posterior circulations based on neuroimaging findings. Demographic data, medical history, and laboratory parameters, including coagulation factors, lipid profiles, and SARS-CoV-2 antibodies, were analyzed. Statistical comparisons were performed using SPSS version 26, with a p-value of <0.05 considered statistically significant.

Results: Among the 34 patients, 73.5% were diagnosed with ACAIS, 20.6% with PCAIS, and 5.9% with both. PCAIS patients were older (median age: 8.0 vs. 2.0 years), and sex distribution varied, although not significantly. No significant differences were found in lipid profiles, coagulation factors, or SARS-CoV-2 prevalence between ACAIS and PCAIS groups.

Conclusion: No significant differences in demographic features, lipid profiles, or prothrombotic conditions were observed between ACAIS and PCAIS, suggesting that pediatric stroke mechanisms may differ from those in adults. Further large-scale studies are warranted to validate these findings and improve pediatric stroke management.

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Introduction

The term "stroke" refers to acute neurologic symptoms and signs caused by focal infarction in the central nervous system, occurring due to either hemorrhagic or ischemic events. While strokes are uncommon in children, they are a devastating condition and a leading cause of acquired neurological disability during childhood. The effects reach far beyond the individual, significantly influencing families and society as a whole. However, the diagnosis of pediatric stroke is often challenging and frequently delayed.

Ischemic strokes in children are classified into arterial ischemic stroke (AIS) and venous infarctions, including cerebral venous sinus thrombosis (CVST). Among these, AIS accounts for approximately 80% of all pediatric strokes (1-6). The incidence of pediatric

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AIS is increasing, particularly in developed countries, with rates estimated between one and three cases per 100,000 children annually (7-11). Advances in radiologic imaging with higher sensitivity have also revealed a higher prevalence of pediatric stroke than previously recognized (12).

AIS is further categorized into anterior circulation arterial ischemic stroke (ACAIS) and posterior circulation arterial ischemic stroke (PCAIS). Studies indicate that PCAIS is less common, with posterior circulation strokes accounting for approximately 15% of pediatric AIS cases (13). Unlike adult strokes, which are frequently caused by atherosclerosis, the etiology of childhood AIS is multifactorial. Major risk factors include congenital heart disease, non-atherosclerotic arteriopathies (e.g., Moyamoya disease), head and neck traumas, infections, including coronavirus disease-2019 (COVID-19), thrombophilia and other prothrombotic conditions, and sickle cell disease (3, 8, 14-18). Some studies suggest that screening for thrombophilia in pediatric AIS may help identify underlying risk factors (19).

Uohara et al. demonstrated that PCAIS carries a 5.3-fold increased recurrence risk compared to ACAIS, with recurrence rates of 19% vs. 4% (20). Similarly, Goeggel Simonetti et al. reported that PCAIS constitutes 18% of childhood strokes and is strongly associated with cervical dissections (20%) and trauma. Despite its high recurrence risk, PCAIS tends to present with milder symptoms and has a mortality rate comparable to ACAIS (21).

Understanding the differences between ACAIS and PCAIS, along with their risk factors, is critical for improving early diagnosis and reducing recurrence rates. Accordingly, this study aims to evaluate the demographic, clinical, and laboratory characteristics of pediatric ACAIS and PCAIS, providing further insights into these subtypes and their implications for management.

Materials & Methods

Study design and setting

This descriptive-analytical cross-sectional study was conducted at Tabriz Children's Hospital, a tertiary referral center in northwest Iran, between March 2020 and October 2021.

Participants

The study population included all children aged one month to 15 years who were diagnosed with acute cerebral ischemia during the study period. A census sampling method was employed to include all eligible patients. Children were included if they exhibited clinical presentations of acute-onset focal neurological deficits suggestive of AIS and had radiologic confirmation of AIS via magnetic resonance imaging (MRI) or computed tomography (CT). All imaging findings were reviewed and confirmed by a multidisciplinary team, including pediatricians, pediatric neurologists, and neuroradiologists. Patients were excluded if they had a prior history of malignancy or an incomplete diagnostic workup. Written informed consent was obtained from the legal guardians of all participants.

Stroke classification

Patients were classified into three categories based on neuroimaging findings: Anterior circulation AIS (ACAIS), posterior circulation AIS (PCAIS), and combined AIS. ACAIS was defined as involving the internal carotid, middle cerebral, or anterior cerebral arteries. PCAIS referred to strokes involving the vertebral, basilar, cerebellar, or posterior cerebral arteries (21). Combined AIS included infarctions involving both anterior and posterior circulations.

Data collection

After obtaining written informed consent from parents or legal guardians, demographic and clinical data were collected using standardized forms. Information gathered included age, sex, prior medical history, recent trauma, and evidence of COVID-19 infection. Stroke characteristics were also documented based on clinical presentation and imaging findings.

Laboratory assessments

Peripheral venous blood samples were obtained under sterile conditions within 24 hours of admission. Laboratory evaluations included assessment of coagulation factors (protein C, protein S, antithrombin III, and antiphospholipid antibodies), lipid profile (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides), and SARS-CoV-2 antibodies to assess prior exposure to COVID-19. Coagulation parameters and SARS-CoV-2 antibodies were measured using standardized enzyme-linked immunosorbent assay (ELISA) kits, while lipid profiles were determined using automated biochemical analyzers according to standard protocols. All laboratory analyses were performed in the hospital's central laboratory by technicians blinded to the patients' stroke classification.

Statistical analysis

Data analysis was performed using SPSS software (version 26; IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages. Continuous variables were reported as mean ± standard deviation if normally distributed, or as median with interquartile range (IQR) if non-normally distributed. Group comparisons between ACAIS and PCAIS were conducted using the independent samples t-test or Mann–Whitney U test for continuous variables, and the Chi-square or Fisher's exact test for categorical variables. A p-value of <0.05 was considered statistically significant.

Results

Demographic and clinical characteristics

From March 2020 to October 2021, 34 children diagnosed with AIS were admitted to Tabriz Children's Hospital, Iran. Among these, 25 patients (73.5%) had ACAIS, seven patients (20.6%) had PCAIS, and two patients (5.9%) had combined ACAIS and PCAIS.

Although the median age was higher in the PCAIS group (8.0 years; IQR: 1.8–9.0), compared to the ACAIS group (2.0 years; IQR: 1.3–7.0), this difference was not statistically significant (p = 0.313). Males predominated in the PCAIS group (6 patients, 85.7%), while females were more common in the ACAIS group (14 patients, 56%), although the difference was also not statistically significant (p = 0.172) (Figure 1).

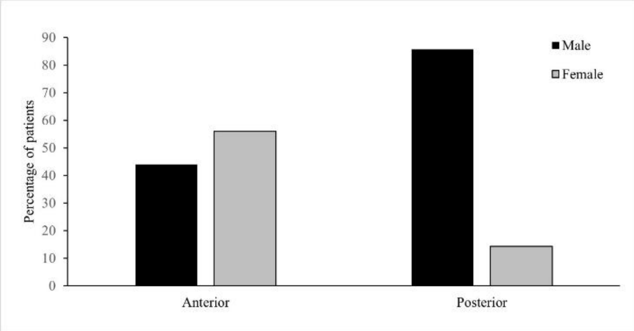

Figure 1. Gender distribution among patients with anterior and posterior circulation strokes (n = 32).
Data are presented as percentages. P-values were computed using Fisher's exact test. p = 0.172.

The prevalence of SARS-CoV-2 infection was one patient (14.6%) in the PCAIS group and three patients (11.1%) in the ACAIS group. Two patients (28.6%) in the PCAIS group had underlying heart disease, compared with four patients (14.8%) in the ACAIS group (Table 1).

Table 1. Demographic and clinical characteristics of patients with anterior and posterior circulation acute ischemic stroke

Characteristics	Anterior stroke (n = 25)	Posterior stroke (n = 7)	P-value
Sex, n (%)			
Male	11 (44.0 %)	6 (85.7 %)	0.172[b]
Female	14 (56.0%)	1 (14.3%)	
Age (years) [a]	2.0 (1.3 – 7.0)	8.0 (1.8 – 9.0)	0.313[c]
SARS-CoV-2, n (%)	3 (12 %)	1 (14.6 %)	0.64[b]
CHD, n (%)	4 (14.8%)	2 (28.6%)	0.57[b]

Abbreviations: CHD: Congenital Heart Disease
[a] Values are presented as median (interquartile range).
[b] P-values were calculated using Fisher's exact test.
[c] P-value was calculated using the Mann–Whitney U test.

Table 2. Lipid profile and prothrombotic factors levels in patients with anterior and posterior circulation acute ischemic stroke

Characteristics	Anterior stroke (n = 25)	Posterior stroke (n = 7)	P-value
Triglyceride (mg/dl)	99.28 ± 4.5	112.14 ± 19.3	0.526
Cholesterol (mg/dl)	139.28 ± 4.8	127.14 ± 5.3	0.340
Antithrombin III (%)	114.68 ± 1.8	115.43 ± 7.3	0.835
Protein S (%)	96.84 ± 3.89	94.11 ± 1.68	0.777
Protein C (IU/dL)	95.56 ± 3.4	82.33 ± 6.14	0.057

Note: Values are presented as mean ± standard deviation.
Statistical test: Independent samples t-test was used for all comparisons.

Lipid profile

Serum triglyceride and cholesterol levels were within normal ranges in both groups, with no significant differences between them (triglycerides: p = 0.526; cholesterol: p = 0.340) (Table 2, Figure 2).

Prothrombotic factors

Antithrombin III levels in both the PCAIS and ACAIS groups were within normal ranges, with no significant difference between them (p = 0.835). However, one case of antithrombin III deficiency was observed in a male neonate with PCAIS.

Protein S levels also did not show a significant difference between the PCAIS and ACAIS groups (p = 0.777). Protein S deficiency was observed in only one patient, a 7-year-old girl with combined posterior and ACAIS.

Protein C levels were below the normal range in three patients: Two with ACAIS and one with PCAIS. Otherwise, protein C levels were within normal limits, with no significant difference between groups (p = 0.057) (Table 2, Figure 3).

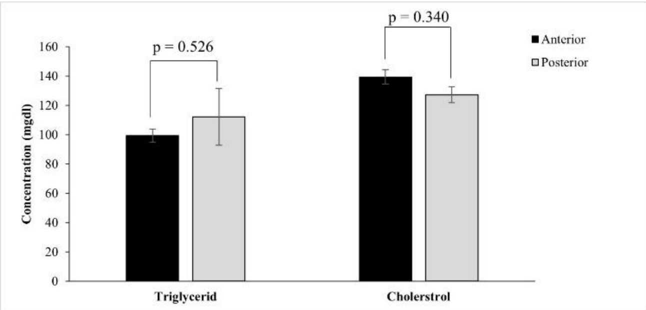

Figure 2. Lipid profile concentrations in patients with anterior and posterior circulation strokes (n = 32).
Data are presented as mean ± SD. P-values were computed using independent samples t-tests. Triglycerides: p = 0.526; Cholesterol: p = 0.340.

Antiphospholipid antibodies were not detected in the serum of any patients, and no prothrombotic conditions were observed in SARS-CoV-2-positive patients.

One case of hemorrhagic transformation was observed in a 7-year-old boy with ACAIS who tested positive for SARS-CoV-2 antibodies.

Overall, no statistically significant differences were found in demographic characteristics, lipid profiles, prothrombotic factors, or SARS-CoV-2 prevalence between the PCAIS and ACAIS groups.

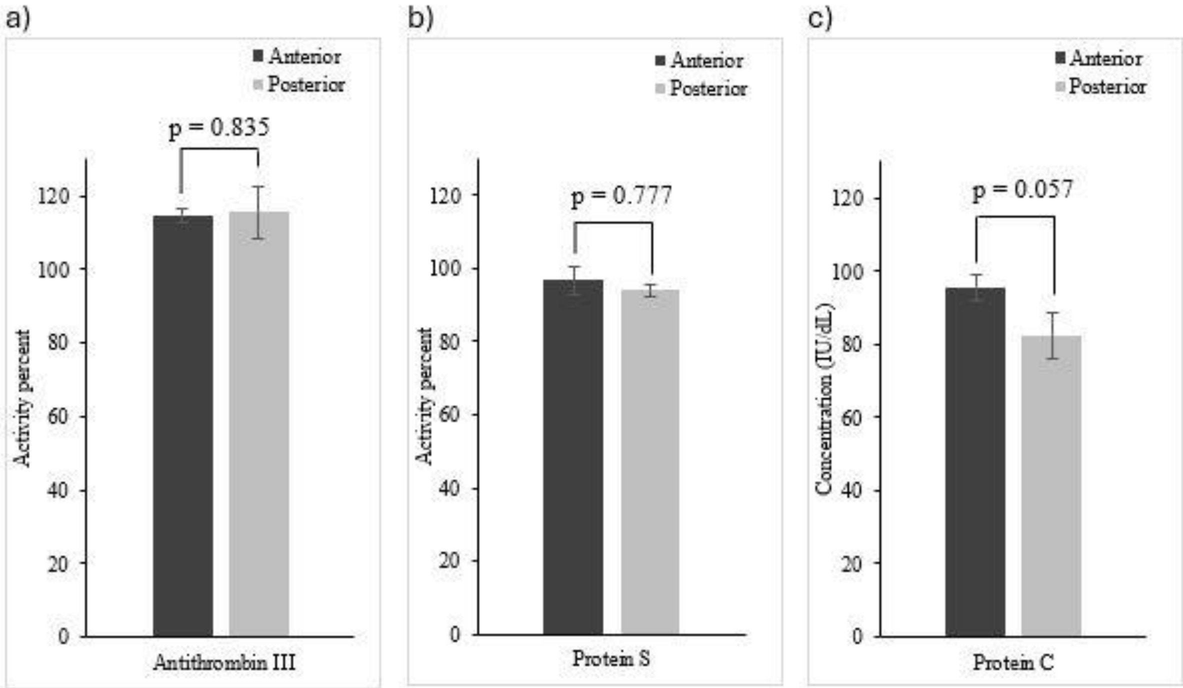

Figure 3. Comparison of prothrombotic factor levels in patients with anterior and posterior circulation strokes (n = 32).
Data are shown as mean ± SD. P-values were computed using independent samples t-tests. Antithrombin III: p = 0.835; Protein S: p = 0.777; Protein C: p = 0.057.

Discussion

This cross-sectional, descriptive-analytical study aimed to assess and compare the serum levels of protein C, protein S, antithrombin III, antiphospholipid antibodies, lipid profiles, and SARS-CoV-2 antibodies in children diagnosed with PCAIS and ACAIS.

The present findings align with previous studies, indicating that patients with PCAIS tend to be older (21). Although males were more prevalent in the PCAIS group and females in the ACAIS group, the differences were not statistically significant. This observation is consistent with the findings of Mallick et al., but differs from the IPSS (Golomb et al.) study, which reported a male predominance in AIS cases (8, 22). One possible explanation for the male predominance in AIS is a higher prevalence of arterial dissections in males. However, no dissections were identified in the current cohort.

Additionally, the IPSS study was not population-based, and ethnic variations may have influenced its findings. While some studies have noted a male predominance in PCAIS, they did not account for dissections (13, 15, 20). For instance, Simonetti et al. found that male predominance in PCAIS disappeared after correcting for dissections (21).

Research indicates that dyslipidemia is more prevalent in children with AIS than in the general pediatric population (23, 24). However, no prior studies have specifically examined dyslipidemia in the context of ACAIS versus PCAIS in children. In a study by Yang et al., analyzing446 AIS cases in young adults in China between 2001 and 2010, variations in risk factors were observed between PCAIS and ACAIS groups. Notably, higher total cholesterol levels were associated with poorer short-term outcomes in the ACAIS group. (25). Subramanian et al., using data from the Registry of the Canadian Stroke Network, employed multivariable logistic regression and found no significant association between hyperlipidemia and AIS subtype (odds ratio: 1.10; 95% CI: 0.99–1.21) (26). Similarly, Zurcher et al., who compared 466 PCAIS cases with 983 ACAIS cases, observed no significant difference in the prevalence of hypercholesterolemia between the two groups (27). In line with these findings, the present study also found no correlation between triglyceride or cholesterol levels and AIS in children.

Reports have suggested an increased incidence of AIS associated with COVID-19, caused by SARS-CoV-2, particularly when compared to influenza. Although rare in children, AIS linked to COVID-19 often occurs in the presence of underlying risk factors (28-34). Hypothesized mechanisms include thrombotic complications, multisystem inflammatory syndrome in children (MIS-C), vasculopathy, and direct endothelial dysfunction caused by the virus (18, 35-40). Finsterer et al. (2022) studied 455 COVID-19 patients with ischemic stroke and found that anterior cerebral artery territories were predominantly affected (41). However, this study observed no significant difference in the prevalence of ACAIS versus PCAIS in pediatric COVID-19 cases. This discrepancy may be attributed to differences in stroke mechanisms between children and adults, racial variations, or the small sample size of the present study.

Prothrombotic conditions, such as deficiencies in protein C, protein S, or antithrombin III, hyperlipoproteinemia, and the presence of antiphospholipid antibodies, are well-recognized risk factors for pediatric stroke and are closely associated with both mortality and recurrence of AIS (3, 42-45). The IPSS study reported a higher prevalence of hematologic conditions, including prothrombotic disorders, in ACAIS compared to PCAIS (7% vs. 2%, $p < 0.001$) (21). However, this research found no significant association between prothrombotic conditions and AIS. Furthermore, none of the studied patients tested positive for antiphospholipid antibodies.

Limitations

This study has several limitations that should be acknowledged. First, the small sample size of 34 patients limits the generalizability of the findings, as a larger cohort may provide more statistically robust conclusions regarding differences between ACAIS and PCAIS. Second, the study was conducted at a single center, which may not thoroughly represent the broader pediatric AIS population, particularly in different geographic regions with varying risk factors and healthcare access.

Another limitation is the cross-sectional nature of the study, restricting the ability to establish causal relationships between lipid profiles, prothrombotic factors, and AIS subtypes. Longitudinal studies are needed to assess long-term implications and recurrence risks. Additionally, while this study analyzed key laboratory parameters, other potential contributing factors, such as genetic predispositions, inflammatory markers, and detailed vascular imaging findings (e.g., arterial dissection or vasculopathy), were not extensively evaluated.

The study period also coincided with the COVID-19 pandemic, which may have influenced the observed prevalence of SARS-CoV-2 antibodies and their potential role in AIS. However, the small number of SARS-CoV-2-positive cases limits any definitive conclusions regarding its impact on pediatric stroke.

Lastly, given the heterogeneity of pediatric AIS etiology, a more comprehensive multicenter study with a larger sample size and broader scope of risk factors is warranted to validate the obtained findings and provide deeper insights into the mechanisms underlying pediatric ACAIS and PCAIS.

In Conclusion

This study highlights the importance of understanding pediatric AIS, focusing on the differences between ACAIS and PCAIS. The obtained findings show no significant differences in demographic characteristics, lipid profiles, or prothrombotic factors between the two groups, suggesting that the mechanisms underlying pediatric stroke may differ from those in adults.

Given the multifactorial causes of pediatric stroke, early diagnosis and tailored management are crucial for improving outcomes. Future research should involve larger studies to validate these results and examine the long-term effects of pediatric AIS. A deeper understanding of pediatric stroke can lead to timely interventions, lower recurrence rates, and better support for affected children and their families.

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This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1400.504).

Authors' Contributions

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Investigation: Amirreza Jahanshahi, Mahsa Niknam, Shahram Sadeghvand, Sepehr Mahmoudi Azar, Atiyeh Ghassemi.

Methodology: Mahsa Niknam, Sina Raeisi, Khatereh Rezazadeh.

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Supervision: Amirreza Jahanshahi, Shahram Sadeghvand.

Validation: Shahram Sadeghvand, Sina Raeisi, Khatereh Rezazadeh.

Writing–original draft: Mahsa Niknam, Sepehr Mahmoudi Azar, Atiyeh Ghassemi, Khatereh Rezazadeh.

Writing–review & editing: Amirreza Jahanshahi, Mahsa Niknam, Sina Raeisi, Shahram Sadeghvand, Sepehr Mahmoudi Azar, Atiyeh Ghassemi, Khatereh Rezazadeh.

Conflicts of Interest

The authors declared no conflicts of interest.

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