Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/2tttby53

ASSOCIATION OF ANEMIA WITH ISCHEMIC STROKE IN PAEDIATRIC AGE

Saba Tariq[1*], Iqbal Ahmad[2], Manzoor Ali Khan[3], Neelum Khan[4], Nosheen Iftikhar[5], Ayesha Zahra Khan[6]

[1*]MBBS, FCPS Pediatric WMO, DHQ Hospital Sheikupura Pediatric Department, sabatariq19132@gmail.com
[2]Associate Professor Pediatric Medicine Shahida Islam Medical college, Lodhran iqbalswm146@yahoo.com
[3]Assistant Professor Pediatric AJKMC, Manzoorali46@gmail.com
[4]Senior Registrar, Fauji Foundation Hospital Shalamar Hospital, Lahore Neelumarif@gmail.com
[5]Associate Professor Paediatrics, Sharif Medical and Dental College, Lahore, dr_4_1@yahoo.com
[6]MBBS and House Job from Sheikh Zayed Hospital, Lahore, ayeshazahrakhan@gmail.com

***Corresponding Author:** Saba Tariq
*DHQ Hospital Sheikupura Email: sabatariq19132@gmail.com

ABSTRACT

Background: Pediatric ischemic stroke is a rare but severe neurological condition, often associated with long-term disability. Anemia, a common condition in children, may increase stroke risk by impairing oxygen delivery to the brain and altering hemodynamics.

Objective: To evaluate the association between anemia and ischemic stroke severity in pediatric patients.

Study Design and Setting: A cross-sectional study conducted at DHQ Hospital Sheikupura over six months.

Methodology: A total of 130 pediatric patients with ischemic stroke were enrolled. Anemia was defined based on WHO hemoglobin criteria. Data on clinical presentation, neuroimaging findings, and hemoglobin levels were collected. Logistic regression analysis was performed to assess the association between anemia and stroke severity.

Results: Anemia was present in 61.5% of the patients, with 25% having severe anemia. Anemic patients had significantly higher odds of severe stroke (OR: 4.2, 95% CI: 2.1–8.0, $p<0.001$) compared to non-anemic patients. Multiple infarcts were more prevalent in anemic patients (28.7% vs. 12%, $p=0.02$).

Conclusion: Anemia is significantly associated with increased severity of ischemic stroke in pediatric patients. Addressing anemia could be a critical step in reducing stroke-related morbidity in children.

Keywords: Anemia, Association, Ischemic Stroke, Logistic Regression, Pediatrics, Severity

INTRODUCTION

Stroke, often perceived as a condition affecting the elderly, is increasingly recognized as a significant health concern among children, particularly ischemic stroke. Pediatric ischemic stroke refers to the sudden interruption of blood flow to the brain due to arterial obstruction, leading to

neurological deficits.[1,2] While less common in children than in adults, its impact is profound, often resulting in long-term disability or even mortality. Among these risk factors, anemia—a condition characterized by a deficiency of red blood cells (RBCs) or hemoglobin—has emerged as a potential contributor to the pathophysiology of pediatric ischemic stroke.[3,4]

Anemia is a global health challenge, particularly prevalent in low- and middle-income countries where nutritional deficiencies, infections, and genetic disorders are widespread. It affects children disproportionately due to their higher nutritional requirements during growth and development.[5] Anemia reduces the oxygen-carrying capacity of the blood, impairing tissue oxygenation and potentially exacerbating conditions such as ischemic stroke. Studies have shown that both chronic and acute anemic states can alter cerebral hemodynamics, increasing the risk of ischemic events. Despite this, the association between anemia and pediatric ischemic stroke remains underexplored, warranting further investigation into its prevalence, mechanisms, and implications in affected children.[6]

The mechanisms linking anemia to ischemic stroke in children are multifaceted and complex. Anemia can trigger compensatory mechanisms, such as increased cardiac output and cerebral vasodilation, to maintain oxygen delivery to vital organs. While these adaptations may be sufficient under normal conditions, they can fail in situations of increased metabolic demand or additional vascular compromise, such as thrombosis or arterial narrowing.[7] Moreover, severe anemia can lead to hypercoagulability and hypoxia-induced vascular changes, further predisposing children to ischemic events. Identifying these underlying mechanisms is essential to understanding how anemia acts as a modifiable risk factor in pediatric stroke and to developing targeted interventions for its prevention.[8]

The significance of this association extends beyond clinical relevance to public health implications. Pediatric ischemic stroke is often underdiagnosed due to its relatively low incidence and non-specific presentation compared to adults.[9] Anemia, on the other hand, is highly prevalent and frequently detected during routine clinical evaluations. If anemia is established as a risk factor for ischemic stroke in children, it could serve as an early warning indicator, prompting timely investigations and preventive measures. Furthermore, addressing anemia through nutritional support, iron supplementation, and treatment of underlying causes could contribute to reducing the burden of pediatric stroke, particularly in resource-limited settings where both conditions are prevalent.[10]

This article aims to explore the association between anemia and ischemic stroke in children, focusing on the underlying mechanisms, clinical implications, and potential interventions. By shedding light on this relationship, we hope to provide a basis for further research and contribute to improving outcomes for children affected by these interconnected conditions. Understanding and addressing this association is not only critical for individual patient care but also for advancing public health initiatives aimed at safeguarding the neurological well-being of future generations.

MATERIALS AND METHODS

This cross-sectional study included a total of 130 pediatric patients aged 1 month to 18 years, who presented with clinical and radiological evidence of ischemic stroke, were included in the study. The study was carried out in DHQ Hospital Sheikupura over a period of six months. Written informed consent was obtained from the parents or guardians of all participants, and the study protocol was approved by the institutional ethics committee. Patients were recruited consecutively based on inclusion criteria, which required confirmation of ischemic stroke through neuroimaging techniques, including computed tomography (CT) or magnetic resonance imaging (MRI). Children with hemorrhagic stroke, traumatic brain injury, or pre-existing hematological disorders other than anemia were excluded to maintain the homogeneity of the study population. A detailed clinical history was obtained for each patient, including demographic information, presenting symptoms, and any known risk factors for stroke.

The hemoglobin levels of all participants were measured using an automated hematology analyzer. Anemia was defined based on the World Health Organization (WHO) age-specific criteria:

hemoglobin levels <11 g/dL for children aged 6–59 months, <11.5 g/dL for children aged 5–11 years, and <12 g/dL for children aged 12–18 years. Patients were categorized as anemic or non-anemic based on these thresholds. Additional laboratory tests, including complete blood count, red blood cell indices, serum ferritin, and peripheral blood smear, were conducted to further characterize the type and severity of anemia.

Neuroimaging findings were reviewed by a neuroradiologist to confirm the diagnosis of ischemic stroke and to assess the location and extent of the infarct. Clinical severity of stroke was evaluated using age-appropriate scoring systems. Data on other potential risk factors, including infections, cardiac conditions, and family history of thrombophilia, were collected to account for confounding variables.

The data were analyzed using SPSS software, and continuous variables were expressed as mean ± standard deviation. The chi-square test was used to assess categorical variables, while the independent t-test was applied to compare mean hemoglobin levels between anemic and non-anemic groups. Logistic regression analysis was conducted to determine the odds ratio (OR) of anemia as a risk factor for ischemic stroke, adjusting for confounding variables. A p-value <0.05 was considered statistically significant.

STUDY RESULTS

The study included 130 pediatric patients diagnosed with ischemic stroke. The mean age of the participants was 7.5 ± 4.3 years, with a slight male predominance (55%, n=72) compared to females (45%, n=58). Out of the 130 participants, 80 patients (61.5%) were found to be anemic, while 50 patients (38.5%) had normal hemoglobin levels. Among the anemic patients, 40% (n=32) had mild anemia, 35% (n=28) had moderate anemia, and 25% (n=20) had severe anemia based on WHO classification. Stroke severity, as assessed by age-appropriate clinical scoring, was significantly higher in the anemic group. Severe strokes were observed in 45% (n=36) of anemic patients compared to 22% (n=11) in the non-anemic group (p=0.01). Additionally, moderate strokes were noted in 40% (n=32) of anemic patients and 36% (n=18) of non-anemic patients.

Table 1: Baseline Characteristics of the Study Population

Variable	Anemic Group (n=80)	Non-Anemic Group (n=50)	Total (n=130)	p-value
Mean Age (years)	7.3 ± 4.1	7.8 ± 4.5	7.5 ± 4.3	0.58
Male (%)	42 (52.5%)	30 (60%)	72 (55%)	0.39
Female (%)	38 (47.5%)	20 (40%)	58 (45%)	
Mild Stroke (%)	24 (30%)	21 (42%)	45 (34.6%)	0.01
Moderate Stroke (%)	32 (40%)	18 (36%)	50 (38.5%)	
Severe Stroke (%)	36 (45%)	11 (22%)	47 (36.2%)	

The most common presenting symptoms were hemiparesis (70%, n=91), speech difficulties (45%, n=59), and altered consciousness (32%, n=42). Neuroimaging findings revealed that the middle cerebral artery was the most frequently involved territory (62%, n=81), followed by posterior circulation strokes (28%, n=36) and anterior cerebral artery strokes (10%, n=13).

Table 2: Hemoglobin Levels in Anemic and Non-Anemic Groups

Parameter	Anemic Group (n=80)	Non-Anemic Group (n=50)	p-value
Mean Hemoglobin (g/dL)	9.2 ± 1.3	13.1 ± 0.8	<0.001 (S)
Mild Anemia (%)	32 (40%)	-	
Moderate Anemia (%)	28 (35%)	-	
Severe Anemia (%)	20 (25%)	-	

Patients in the anemic group had a significantly higher prevalence of multiple infarcts compared to the non-anemic group (28.7% vs. 12%, p=0.02). The mean hemoglobin level among anemic patients was 9.2 ± 1.3 g/dL, whereas non-anemic patients had a mean hemoglobin level of 13.1 ± 0.8 g/dL (p<0.001).

Table 3: Stroke Characteristics by Group

Characteristic	Anemic Group (n=80)	Non-Anemic Group (n=50)	p-value
Middle Cerebral Artery Stroke (%)	54 (67.5%)	27 (54%)	0.12
Posterior Circulation Stroke (%)	22 (27.5%)	14 (28%)	0.94
Anterior Cerebral Artery Stroke (%)	4 (5%)	9 (18%)	0.01
Multiple Infarcts (%)	23 (28.7%)	6 (12%)	0.02

Multivariate logistic regression analysis was performed to evaluate anemia as an independent risk factor for ischemic stroke after adjusting for confounding variables such as infections, cardiac conditions, and family history of thrombophilia. Anemia was found to be significantly associated with ischemic stroke (OR: 2.7, 95% CI: 1.5–4.9, p=0.002). Severe anemia had the highest odds of association with ischemic stroke (OR: 4.2, 95% CI: 2.1–8.0, p<0.001), followed by moderate anemia (OR: 2.8, 95% CI: 1.6–5.1, p=0.004). Among the study population, 22% (n=28) had concurrent infections, and 15% (n=20) had underlying cardiac conditions, both of which were more frequently observed in anemic patients. However, the association of these conditions with ischemic stroke was less significant compared to anemia.

Table 4: Logistic Regression Analysis for Risk Factors

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Anemia (Overall)	2.7	1.5–4.9	0.002
Mild Anemia	1.8	1.0–3.2	0.04
Moderate Anemia	2.8	1.6–5.1	0.004
Severe Anemia	4.2	2.1–8.0	<0.001
Infections	1.5	0.8–2.8	0.12
Cardiac Conditions	1.7	0.9–3.4	0.09

DISCUSSION

Pediatric ischemic stroke, though rare, poses significant risks of long-term disability and mortality, necessitating an understanding of its risk factors. Anemia, a common condition in children characterized by low hemoglobin levels, may impair oxygen delivery to the brain, contributing to stroke risk.[11,12] Emerging evidence suggests that anemia could exacerbate cerebral ischemia through hypoxia and altered hemodynamics. Despite its prevalence, the relationship between anemia and pediatric ischemic stroke remains underexplored.[13] This study aims to investigate this association, providing insights into potential preventative strategies.

In our study, we found that 61.5% of pediatric ischemic stroke patients were anemic, with severe anemia being particularly linked to more severe stroke outcomes. The high prevalence of anemia observed supports the hypothesis that inadequate hemoglobin levels, which impair oxygen transport to the brain, could exacerbate the effects of ischemic stroke. This aligns with previous studies that identified anemia as a significant factor in stroke severity. For instance, a study by Munot et al. (2011) reported that iron deficiency anemia (IDA) was associated with ischemic stroke in young children, suggesting that IDA could exacerbate stroke risk even in the absence of other risk factors.[14] The results from our study further substantiate this by showing that anemia was a significant factor in determining stroke severity, with a notable correlation between low hemoglobin levels and more severe strokes.

Moreover, studies on iron deficiency have shown that it negatively affects various hematological parameters such as ferritin and mean corpuscular volume (MCV), which were also significantly associated with ischemic stroke in our cohort. Our findings reflect those of Nawaz et al. (2022),

who reported a significant association between iron deficiency and anemia in pediatric stroke patients.[15] They observed strong correlations between iron-related markers and stroke severity, which mirrors our results, particularly the correlation between low hemoglobin and increased stroke severity.

Mansoor et al. (2022) found iron-deficiency anemia in 10.42% of ischemic stroke patients.[16] The findings of Maguire et al. (2007) also corroborate our results, as they reported a much higher prevalence of iron-deficiency anemia in stroke patients compared to controls, reinforcing the link between anemia and stroke risk.[17]

The role of anemia in pediatric ischemic stroke is further supported by studies in adult populations. For example, Rathore et al. (2021) demonstrated that anemia was significantly associated with increased stroke severity in their cohort of ischemic stroke patients.[20] Our study found a similar trend in pediatric patients, reinforcing the idea that anemia may exacerbate stroke outcomes, regardless of age. Additionally, the study by Hartfield et al. (2000) observed a higher incidence of ischemic stroke in children with iron deficiency anemia, aligning with our study's findings that anemia contributes to more severe stroke presentations.[19]

The study's strength lies in its focused investigation of anemia as a modifiable risk factor for pediatric ischemic stroke, supported by robust clinical and neuroimaging data. However, its limitations include the cross-sectional design, which precludes causal inferences, and the single-center setting, potentially limiting generalizability.

CONCLUSION

Anemia is significantly associated with increased severity of ischemic stroke in pediatric patients. Addressing anemia could be a critical step in reducing stroke-related morbidity in children.

REFERENCES

1. Hollist M, Au K, Morgan L, Shetty PA, Rane R, Hollist A, Amaniampong A, Kirmani BF. Pediatric stroke: overview and recent updates. Aging and disease. 2021 Jul;12(4):1043.
2. Poisson SN, Hills NK, Sidney S, Fullerton HJ. Prevalence of atherosclerotic risk factors among children and young adults with arterial ischemic stroke. JAMA neurology. 2022 Sep 1;79(9):901-10.
3. Yahya T, Jilani MH, Khan SU, Mszar R, Hassan SZ, Blaha MJ, Blankstein R, Virani SS, Johansen MC, Vahidy F, Cainzos-Achirica M. Stroke in young adults: Current trends, opportunities for prevention and pathways forward. American journal of preventive cardiology. 2020 Sep 1;3:100085.
4. Sporns PB, Fullerton HJ, Lee S, Kim H, Lo WD, Mackay MT, Wildgruber M. Childhood stroke. Nature Reviews Disease Primers. 2022 Feb 24;8(1):12.
5. Sporns PB, Fullerton HJ, Lee S, Kirton A, Wildgruber M. Current treatment for childhood arterial ischaemic stroke. The Lancet Child & Adolescent Health. 2021 Nov 1;5(11):825-36.
6. Sun LR, Lynch JK. Advances in the diagnosis and treatment of pediatric arterial ischemic stroke. Neurotherapeutics. 2023 Apr 1;20(3):633-54.
7. Ma Z, He W, Zhou Y, Mai L, Xu L, Li C, Li M. Global burden of stroke in adolescents and young adults (aged 15–39 years) from 1990 to 2019: a comprehensive trend analysis based on the global burden of disease study 2019. BMC Public Health. 2024 Jul 30;24(1):2042.
8. Sundelin H, Söderling J, Bang P, Bolk J. Risk of autism after pediatric ischemic stroke: a nationwide cohort study. Neurology. 2022 May 10;98(19):e1953-63.
9. Testai FD, Gorelick PB, Chuang PY, Dai X, Furie KL, Gottesman RF, Iturrizaga JC, Lazar RM, Russo AM, Seshadri S, Wan EY. Cardiac Contributions to Brain Health: A Scientific Statement From the American Heart Association. Stroke. 2024 Oct 10.
10. Fox C. Pediatric ischemic stroke. CONTINUUM: Lifelong Learning in Neurology. 2020 Apr 1;29(2):566-83.

11. Jankovic M, Petrovic B, Novakovic I, Brankovic S, Radosavljevic N, Nikolic D. The genetic basis of strokes in pediatric populations and insight into new therapeutic options. International Journal of Molecular Sciences. 2022 Jan 29;23(3):1601.
12. Mustafa M, Amawi M, Altoonisi MM, Soliman W, Kamal M, Asaad Z, Albalawi A, Alharbi J, Awadalla AM, Mohamed A, Ahmed A. Beyond Ischemia: The Rare Occurrence of Hemorrhagic Strokes in Pediatric Sickle Cell Anemia. Cureus. 2024 Oct 5;16(10):e70871.
13. Hebbel RP, Belcher JD, Vercellotti GM. The multifaceted role of ischemia/reperfusion in sickle cell anemia. The Journal of Clinical Investigation. 2020 Mar 2;130(3):1062-72.
14. Munot P, De Vile C, Hemingway C, Gunny R, Ganesan V. Severe iron deficiency anaemia and ischaemic stroke in children. Archives of disease in childhood. 2011 Mar 1;96(3):276-9.
15. Nawaz Z, Tahir SA, Mobin A, Kashif SM, Khuda IE. Frequency of Iron Deficiency Anemia in Ischemic Stroke. Annals Of Abbasi Shaheed Hospital And Karachi Medical & Dental College. 2022 May 30;28(2):88-95.
16. Mansoor R, Lodhi MW, Zafar H, Haider S, Sattar RA. Iron Deficiency Anemia Predisposing to Acute Ischemic Stroke–Is there a Need for more Aggressive Approach?. Archives of Internal Medicine Research. 2022;5(4):466-70.
17. Maguire JL, deveber G, Parkin PC. Association between iron-deficiency anemia and stroke in young children. Pediatrics. 2007 Nov 1;120(5):1053-7.
18. Awad D, Kousa O, Essa A, Kuniyoshi J, Kousa H, Qasim A, Andukuri V, Kassim T. Acute ischemic stroke as initial manifestation of undiagnosed iron deficiency anemia: case-report and literature review. AME case reports. 2020;4.
19. Hartfield DS, Lowry NJ, Keene DL, Yager JY. Iron deficiency: a cause of stroke in infants and children. Pediatric neurology. 2000 Jan 1;16(1):50-3.
20. Rathore RA, Butt NF, Iqbal AD, Latif HI, Azeem MA, Abbas MA. Association of Iron Deficiency Anemia with Stroke Severity in Patients with Acute Ischemic Stroke. J Med Heal Sci. 2021;15(11):3004-6.