Original Article

Risk factors, clinical characteristics, and outcomes of perinatal stroke in a Tertiary University Hospital

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ABSTRACT

الأهداف: استكشاف عوامل الخطر، الخصائص السريرية، والنتائج التنموية العصبية المرتبطة بالجلطة الدماغية لحديثي الولادة، بالإضافة إلى تقييم مخاطر الإصابة بالصرع، والتحكم في التشنجات، والوظيفة الإدراكية لدى الأطفال المتأثرين.

المنهجية: تمت مراجعة السجلات الطبية بأثر رجعي لـ 32 مريضًا تم تشخيصهم بجلطة الولادة في الفترة ما بين أكتوبر 2007 وأكتوبر 2020م.

النتائج: من بين 32 مريضًا، وُلد 27 منهم نتيجة حمل طبيعي، وكان (62.5%) منهم من آباء أقارب. وتم تسجيل أعراض أولية تشمل الشلل النصفي (56.25%)، التشنجات (37.5%)، ضيق التنفس (3.13%)، والمشي على أطراف الأصابع (3.13%). تم تشخيص 22 مريضًا بالصرع، مع تحقيق نجاح في السيطرة على التشنجات بنسبة 72.72%. أظهر تقييم نسبة الذكاء لـ 12 مريضًا تباينًا في الدرجات: 15.63% ضعف حدودي، 9.37% متوسط، 3.13% تحت المتوسط، و6.26% ضعف متوسط إلى شديد.

الخلاصة: كان الشلل النصفي هو العرض الأكثر شيوعًا، يليه التشنجات. أُصيب عدد من المرضى بالصرع، سجل معظمهم تحكمًا مرضيًا في التشنجات. وقد أظهر تقييم نسبة الذكاء وجود مستويات متفاوتة من الإعاقة الإدراكية، مما يبرز التأثيرات التنموية العصبية المعقدة الناتجة عن جلطة الولادة.

Objectives: To investigate the risk factors, clinical characteristics, and neurodevelopmental outcomes associated with perinatal stroke, as well as to assess the risk of epilepsy, seizure control, and cognitive function in children with perinatal stroke.

Methods: Data from 32 patients diagnosed with perinatal stroke between October 2007 and October 2020 were retrospectively reviewed.

Results: Of 32 patients, 27 were born after normal pregnancies, and 20 (62.5%) had consanguineous parents. Family histories of stroke, haematological disease, and epilepsy were noted in 3.13%, 3.13%, and 21.88%, respectively. Initial symptoms included hemiparesis (56.25%), seizures (37.5%), respiratory distress (3.13%), and tiptoe walking (3.13%). Epilepsy was diagnosed in 22 patients, with 72.72% achieving seizure control. Among 12 patients who underwent IQ testing, 15.63% had borderline impairment, 9.37% average IQ, 3.13% below-average IQ, and 6.26% moderate-to-severe impairment.

Conclusion: Hemiparesis was the most frequent presenting symptom, followed by seizures. Many patients developed epilepsy, with most achieving satisfactory seizure control. IQ testing revealed varying degrees of cognitive impairment, highlighting the complex neurodevelopmental effects of perinatal stroke.

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Perinatal stroke, which is a cerebrovascular event, occurs during cerebral blood flow disruption secondary to an ischaemic or haemorrhagic event between 20 weeks of foetal life and 28 postnatal days, with confirmation through neuroimaging.[1] It is more common among term and near-term infants;[2] further, its incidence ranges from 37 to 67 cases per 100,000.[3]

Males are more susceptible to perinatal stroke, which could be attributed to their larger birth size, hormonal differences, and higher risk of placental dysfunction.[4] Neonatal cerebral infarction accounts for 10%–15% of seizures among neonates and is recognised as the primary cause of congenital haemiplegia.[5] The clinical signs of perinatal stroke vary according to the age at diagnosis. Most patients with perinatal stroke present with seizures as the only symptom; however, some patients present with abnormalities in tone and movement.[6] Neonatal seizures are the most common clinical finding among patients with perinatal stroke.[2] Patients with perinatal stroke often have poor outcomes, with most survivors exhibiting permanent motor and mental disabilities.[7] Additionally, perinatal stroke is the most common cause of hemiparetic cerebral palsy, and many individuals present cognitive consequences and epilepsy, which are common even in children with delayed presentation.[7,8] However, the long-term risk of epilepsy and cognitive outcomes among children with perinatal stroke in Saudi Arabia remain unclear. Accordingly, this study aimed to outline the risk factors, clinical characteristics, and neurodevelopmental outcomes associated with perinatal stroke in Saudi Arabia. Furthermore, we aimed to assess the risk of epilepsy, seizure control, and cognitive function in children with perinatal stroke.

Methods. A retrospective chart review was conducted to examine the risk factors, clinical characteristics, and outcomes of patients with perinatal stroke at King Khalid University Hospital (KKUH), King Saud University Medical City (KSUMC), Riyadh, Saudi Arabia, between October 2007 and October 2020. We included pediatric patients aged 0–14 years with a diagnosis of perinatal stroke based on neuroradiological examination, encompassing both ischaemic and haemorrhagic types. We excluded children with acquired strokes, missing medical records, and lacking confirmatory neuroradiological study findings.

We collected data from the medical records of the included pediatric patients. Initially, 40 patients with presumed perinatal stroke were identified; among them, we excluded 5 due to insufficient data or loss to follow-up, while 3 were excluded because their strokes were determined to be related to acquired causes.

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The primary outcomes included risk factors, clinical characteristics, and neurodevelopmental outcomes associated with perinatal stroke. Secondary outcomes included the incidence of epilepsy, seizure control, and cognitive function.

Twelve patients underwent cognitive function assessment using the Stanford–Binet test, which is a standardised intelligence quotient (IQ) assessment tool. All statistical analyses were performed using SPSS version 22. Descriptive statistics were utilised to summarise the cohort characteristics and outcomes. Cases with incomplete data were excluded from the relevant analyses.

Results. This study included 32 patients diagnosed with perinatal stroke, including 15 males and 17 females (male-to-female ratio, 0.9:1). Furthermore, 28 patients were born through normal pregnancies. Among the 4 patients born through abnormal pregnancies, 2 had intrauterine growth restriction (IUGR), one was complicated by polyhydramnios, and one was complicated by pre-eclampsia. Additionally, 29 patients were born at term pregnancy, while 3 were late preterm.

The parents of 20 patients (62.5%) were consanguineous. Family histories of stroke, haematological disease, and epilepsy were observed in one (3.13%), one (3.13%), and 7 (21.88%) patients, respectively.

Four patients (12.5%) exhibited abnormalities on haematological screening. Among them, one patient presented with the heterozygous prothrombin G20210A mutation and was maintained on aspirin, another was a sickle-cell disease carrier, one was diagnosed with T-cell leukaemia at the age of 3 years, and the last patient had protein S deficiency.

Regarding maternal histories, there were 6 cases (18.75%) with hypothyroidism and 5 cases (15.63%) with recurrent abortions. Additionally, one patient each (3.13%) had a maternal history of myasthenia gravis, coronavirus disease 2019 infection, and epilepsy. The remaining 23 (71.88%) patients had no significant medical history (**Table 1**).

The initial stroke symptoms included hemiparesis, seizures, respiratory distress, and tiptoe walking in 18 (56.25%), 12 (37.5%), 1 (3.13%), and 1 (3.13%) patient, respectively. Stroke was diagnosed at birth, 1–12 months, 12–16 months, 2–3 years, and 3–5 years in 6 (18.75%), 4 (12.5%), 5 (15.62%), 8 (25%), and 3 (6.25%) patients, respectively. The age at stroke diagnosis was unknown in 6 patients (18.75%) (**Table 2**).

Table 1 - Demographics, family history, and pregnancy details of patients with perinatal stroke (N=32).

Characteristics	N	(%)
Males	15	(46.9)
Females	17	(53.1)
Maternal history		
Hypothyroidism	6	(18.75)
Recurrent abortions	5	(15.63)
Myasthenia gravis	1	(3.13)
COVID-19 infection	1	(3.13)
Epilepsy	1	(3.13)
Normal	23	(71.88)
Family history		
Seizures	7	(21.88)
Stroke	1	(3.13)
Haematological diseases	1	(3.13)
Congenital heart diseases	0	(0)
Renal diseases	0	(0)
Metabolic diseases	0	(0)
Immunological diseases	0	(0)
Liver/GI diseases	0	(0)
Consanguinity		
Consanguineous parents	20	(62.5)
Pregnancy		
Normal	28	(87.5)
Abnormal	4	(12.5)
Full term	29	(90.62)
Preterm	3	(9.37)

COVID-19, coronavirus disease 2019; GI, gastrointestinal

Table 2 - Initial stroke symptoms and age at stroke diagnosis (N=32).

First stroke symptoms:	N	(%)
Hemiparesis	18	(56.25)
Seizures	12	(37.5)
Respiratory distress	1	(3.13)
Tiptoe walking	1	(3.13)
Age at stroke diagnosis		
At birth	6	(18.75)
1–12 months	4	(12.5)
13–16 months	5	(15.62)
17-23 months	0	(0)
2–3 years	8	(25)
4–5 years	3	(6.25)
Unknown	6	(18.75)

Table 3 - Details of imaging in patients with perinatal stroke (N=32).

Assessment	N	(%)
MRA abnormality		
MRA scan	8	(25)
MRI/CT scan		
Left MCA	13	(40.63)
Right MCA	4	(12.5)
Others	15	(46.88)

MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; CT, computed tomography; MCA, middle cerebral artery

Among the included patients, 13 (40.63%) and 4 (12.5%) presented with left and right middle cerebral artery infarction, respectively, on magnetic resonance imaging. For the remaining 15 (46.88%) patients, more than one vascular territory was involved. Furthermore, 25% of the patients presented with abnormal findings on magnetic resonance angiography (**Table 3**).

Furthermore, 22 (68.75%) patients with perinatal stroke had epilepsy. Epilepsy onset occurred at birth, 1–6 months, 7 months–2 years, and 3–10 years in 4 (18.18%), 7 (31.81%), 6 (27.27%), and 5 (22.72%) patients, respectively. Among 11 patients (50%) who were taking anti-seizure medications (ASMs) for seizure control, 5 (22.72%) were seizure-free, with ASMs being discontinued; 3 (13.63%) had partially controlled seizures; and 2 (9.09%) had uncontrolled seizures (**Table 4**).

Twelve (37.5%) patients underwent IQ assessment using the Stanford–Binet test. Five patients (15.63%) had a score of 70–79 (borderline impairment), 3 (9.37%) had a score of 90–109 (average IQ), one (3.13%) had a score of 80–89 (below-average IQ), one (3.13%) had a score of 40–54 (moderate impairment), and one (3.13%) had a score of 35 (severe impairment) (**Table 5**).

Discussion. Parental consanguinity was present in 20 cases (62.5%), which is consistent with previous findings and highlights the high prevalence of consanguineous marriages in Saudi Arabia.[9] Perinatal stroke is associated with various maternal and pregnancy risk factors, including primiparity, infertility, smoking during pregnancy, thrombophilia, foetal growth restriction, maternal fever, pre-eclampsia, prolonged membrane rupture, and chorioamnionitis. In our cohort, the most prevalent maternal factors included IUGR, polyhydramnios, and pre-eclampsia during pregnancy. A few patients had a history of maternal hypothyroidism and recurrent abortions. Notable, perinatal stroke cannot be solely attributed to a single factor; instead, it is more likely to result from multifactorial interactions.[6,10,11]

Table 4 - Diagnosis of epilepsy, age at seizure onset, and assessment of seizure control in patients with perinatal stroke (N=32).

Diagnosis	N	(%)
Epilepsy	22	(68.75)
Age at onset of seizures		
Birth	4	(18.18)
1–6 months	7	(31.81)
7 months to 2 years	6	(27.27)
3–10 years	5	(22.72)
Seizures assessment		
Seizure-free (ASMs discontinued)	5	(22.72)
Controlled seizures (receiving ASMs)	11	(50)
Partially controlled seizures	3	(13.63)
Uncontrolled seizures	2	(9.09)
Unknown	1	(3.13)

ASMs - anti-seizure medications

Table 5 - IQ assessment results in patients with perinatal stroke (N=12).

IQ assessment	N	(%)
High average (110–119)	1	(3.13)
Average (90–109)	3	(9.37)
Low average (80–89)	1	(3.13)
Borderline impairment (70–79)	5	(15.63)
Moderately impaired (40–54)	1	(3.13)
Severely impaired (<40)	1	(3.13)

IQ - intelligence quotient

Patients with perinatal stroke may present with haematological disorders and coagulation abnormalities.[9,11] In our study, one patient had a Factor II (G20210A) mutation, which could have been a contributing factor. Regarding other haematological disorders, including sickle-cell disease carrier state, T-cell leukaemia, and mildly reduced levels of protein S, the relationship of these factors with perinatal stroke remains unclear.

The clinical presentations of perinatal stroke varied among patients. Early diagnosed cases often exhibited acute symptoms such as seizures, facilitating timely neuroimaging and diagnosis. In contrast, late-diagnosed cases were more likely to present with subtle symptoms, making diagnosis more challenging due to recall bias or incomplete clinical data. These factors could impact the accuracy of diagnosis and the understanding of long-term outcomes.

In our cohort, hemiparesis was the most common symptom of perinatal stroke, accounting for 59.35% of cases. Additionally, 37.5% of patients presented with seizures, which is consistent with a previous Saudi Arabian report indicating "motor defects" as the typical clinical presentation of perinatal stroke.[9] Contrastingly, other studies[10,11] have reported that neonatal seizures was the most common feature of perinatal stroke, with an incidence of 70%–90%, which is higher than that observed in our study.

Perinatal stroke can lead to the development of epilepsy, with 9.5%–67.2% of patients with perinatal stroke developing epilepsy.[12] In our study, 68.75% of patients were diagnosed with epilepsy, with the majority receiving their diagnosis within the first 6 months of life.

Epilepsy onset occurred at various intervals relative to the timing of perinatal stroke. Among patients with early-diagnosed perinatal stroke, epilepsy onset predominantly occurred within the neonatal period or during the first 6 months, highlighting a strong temporal association between the acute cerebrovascular event and subsequent seizure development. In contrast, patients with late-diagnosed perinatal stroke often exhibited epilepsy onset several years after the initial event, suggesting that delayed seizure manifestation may result from progressive neurodevelopmental changes or evolving post-stroke sequelae. Follow-up durations ranged from 2 to 10 years, encompassing both early-onset epilepsy associated with neonatal presentations and late-onset epilepsy arising during later stages of childhood.

Seven patients with epilepsy had a family history of epilepsy, which has been suggested to be a risk factor for epilepsy development; however, its role in the development of epilepsy among patients with perinatal stroke remains unclear.[12,13] In our study, 72.7% of patients achieved seizure control, which is higher than the rate reported in a previous study (64%).[13]

In our cohort, 12 patients aged 4–14 years underwent IQ assessment using the Stanford–Binet test. The scores of most patients ranged within borderline or delayed impairment, which is consistent with previous reports of low IQ scores and cognitive impairment among children with perinatal stroke. Furthermore, individuals who experienced left-hemisphere stroke associated with epilepsy had relatively worse IQ scores.[14,15] Despite the small sample size, our findings provide significant insights into the effects of perinatal stroke on cognitive function in children.

Our findings highlight the complex nature of perinatal stroke and its effects on neurodevelopment. Moreover, the observed associations of perinatal stroke with parental consanguinity and various maternal and pregnancy-related factors demonstrate the multifactorial aetiology of perinatal stroke, which suggests that a combination of genetic predisposition

and environmental influences may contribute to its onset.

Moreover, the high prevalence of epilepsy among patients with perinatal stroke emphasises the significant burden of seizure disorders in this population. The early onset of epilepsy in most of the patients demonstrates the importance of vigilant monitoring and prompt intervention to achieve seizure control. Effective seizure management not only alleviates immediate risks but also crucially contributes towards mitigating the long-term neurocognitive consequences associated with recurrent seizures.

Furthermore, the cognitive impairments observed in children with perinatal stroke highlight the far-reaching impact of this condition on developmental outcomes. Additionally, the observed range of cognitive impairment, from borderline to delayed impairment, highlights the heterogeneous nature of neurodevelopmental sequelae following perinatal stroke. This underscores the critical need for tailored neurodevelopmental assessments and targeted interventions for addressing specific cognitive deficits and promoting optimal cognitive functioning in affected individuals. Furthermore, evidence suggests that early therapeutic interventions, such as targeted physical and cognitive therapies implemented during critical periods of brain plasticity, can significantly reduce long-term neurodevelopmental challenges. These interventions not only enhance functional outcomes but also lessen the overall burden of developmental delays in affected children.[16]

Although mortality is an important outcome of perinatal stroke, no deaths were recorded in our cohort. However, the retrospective nature of this study may have led to incomplete data on mortality, and future research should address this critical outcome.

There were discrepancies between our results and those of earlier studies, which could be attributed to our small sample size or differences in cultural and demographic factors.

This study has several limitations. The retrospective design and dependence on medical records may have resulted in missing or incomplete data. Furthermore, the single-center nature of the study and relatively small sample size restrict the generalizability of the findings. The limited follow-up period may also have led to an underestimation of the true incidence of epilepsy and other long-term outcomes. Additionally, the reliance on hospital-based patient identification introduces potential selection bias, as it likely over represents more severe cases requiring specialized care or hospitalization. Consequently, this cohort may not accurately reflect the general population, potentially overlooking milder or undiagnosed cases of perinatal stroke.

Despite these limitations, our study contributes to the existing literature by providing a detailed assessment of the incidence of epilepsy, seizure onset, and cognitive function among patients with perinatal stroke. Furthermore, the use of standardised assessment tools, including the Stanford–Binet test, enhances the validity of our neurodevelopmental evaluations. Additionally, our study addresses a gap in the literature by focusing on a local population in Saudi Arabia, and thus provides valuable insights into the epidemiology and clinical characteristics of perinatal stroke in this region.

Conclusions. Our study highlights the heterogenous nature of perinatal stroke and its significant impact on neurodevelopment. Our findings demonstrate the importance of early identification and management of risk factors associated with perinatal stroke, as well as comprehensive neurodevelopmental assessment in order to optimize long-term outcomes in affected children. Further large-scale multicentre studies are warranted to elucidate the underlying mechanisms and improve management strategies for patients with perinatal stroke.

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