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Cerebral Venous Sinus Thrombosis in Pediatrics with Closed Head Injury: A Systematic Review and Meta-analysis

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Abstract

This study aims to systematically review the current literature on pediatric cerebral venous sinus thrombosis (CVST) following closed head injury and to evaluate the clinical management of these patients. Systemic review of the literature was conducted using the following databases: PubMed, Google Scholar, Microsoft Academic, Clinical Trials, Cochrane Library, and Web of Science. All databases were searched from their date of inception to June 2022. Inclusion criteria were applied to identify articles reporting on pediatric patients with CVST following closed head injury. Out of the articles screened, 23 met the inclusion criteria, reporting on 23 pediatric patients with CVST. Falls were the most common cause of traumatic CVST (52.2%), followed by motor vehicle accidents (30.4%). Nausea and vomiting were the most common presenting symptoms (71.4%), and magnetic resonance venogram was the most common diagnostic method (43.5%). Multisinus involvement was noted in 52.2% of cases. Patients with falls from height were more likely to receive conservative management than those with nonfall mechanisms of injury ($p < 0.05$). Pediatric CVST following closed head injury is a rare condition, with only case reports available in the literature. Prompt diagnosis and early treatment can lead to good survival and neurological outcomes. In severe cases, neurosurgical intervention may be necessary to prevent mortality and severe morbidity. This review highlights the need for further research to establish evidence-based management guidelines for this rare but potentially serious condition in the pediatric population.

Keywords
- CVST
- sinus
- thrombosis
- conservative
- intervention

Introduction

Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening complication that can occur in children following a head injury. CVST is the formation of a blood clot within the venous sinuses of the brain, leading to impaired blood flow and accumulation of intracranial pressure. While CVST is relatively rare in

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children, with an annual incidence of 0.6 in every 100,000, it is more common in newborns, accounting for 30 to 50% of all pediatric cases.[1]

There are multiple causes of CVST in the pediatric population, including infection, hypercoagulable states, dehydration, and head trauma. Falls are the most common cause of CVST in children, especially in older age groups.[2] The diagnosis of CVST following a head injury can be challenging due to the rarity of occurrence and the variable presentation of symptoms. Therefore, healthcare providers should have a high index of suspicion for CVST in pediatric patients who have sustained a head injury, especially in newborns.[3]

The symptoms of CVST in children vary depending on the age group. In newborns, seizures and altered mental status are more common, while headache, vomiting, lethargy, and 6th nerve palsy are more common in older children and adolescents.[2] Close neuro-observation and early diagnosis are critical in those patients. Imaging studies, such as magnetic resonance venography (MRV) or computed tomography (CT) venography, are the gold standard for diagnosing CVST. Treatment for CVST includes anticoagulation therapy to prevent further clot formation and to promote the dissolution of the existing clot. In severe cases, mechanical thrombectomy or decompressive craniectomy may be required.[4]

CVST is a complex and challenging condition to manage, particularly in children, due to the potential for severe neurological sequelae and the rarity of the condition. It is essential to recognize the symptoms and promptly diagnose CVST in children to prevent severe complications such as cerebral hemorrhage, cerebral edema, and death.[4,5]

Management of CVST in children following head trauma requires a multidisciplinary approach involving pediatricians, neurologists, neurosurgeons, and hematologists. Anticoagulation therapy is the mainstay of treatment for CVST in children. Heparin is typically the first-line therapy, followed by oral anticoagulants such as warfarin or novel oral anticoagulants.[5] The duration of anticoagulation therapy depends on the etiology of CVST and the individual patient's risk factors. In some cases, catheter-based interventions such as thrombolysis, thrombectomy, or stenting may be necessary to restore normal venous drainage and reduce intracranial pressure.[3]

While the majority of children with CVST after head injury have a good prognosis with appropriate treatment, some patients may experience long-term neurological deficits, cognitive impairments, or disability. Therefore, early diagnosis and prompt treatment are essential to minimize the risk of adverse outcomes.[5]

Despite the potential seriousness of CVST in pediatric patients, the literature on children with CVST after closed head injury and its management is limited to single case reports. Therefore, the purpose of this study is to conduct a systematic review to examine the clinical presentation, diagnosis, and treatment outcomes of pediatric cases with CVST following a closed head injury. By analyzing the available data, this study aims to provide valuable insights that can guide clinical decision-making and improve outcomes for this rare but serious condition.[6]

Materials and Methods

Search Strategy

The present literature review was performed by using the following databases: PubMed, Google Scholar, Microsoft Academic, Clinical Trials, Cochrane Library, and Web of Science. All databases were searched from their date of inception to June 2021. The keywords used were "Pediatric," "Child," "Children," "Cerebral Sinus Thrombosis," "Cerebral sinus occlusion," "Closed Head Injury," "Cerebral Sinus Venous Thrombosis," "CSVT," "Cerebral sinus occlusion and closed head injury," "Venous occlusion and closed head injury," "Sinus thrombosis and cranial trauma," "Sinus venous thrombosis and cranial trauma."

Inclusion and Exclusion Criteria

This study focuses on pediatric patients less than 18 years of age diagnosed with CVST following closed head injuries, regardless of the mechanism of trauma. Only studies published in the English language were eligible for inclusion in this systematic review. The search strategy utilized various electronic databases and relevant articles were identified. After the initial screening process, the selected studies underwent critical screening by two independent authors using established inclusion criteria. Studies without sufficient data and unclear methodology were excluded from the final analysis, and duplicate publications were removed including non-English and adult studies (►**Supplementary Fig. S1** [available in the online version]). The aim of this study is to synthesize the current literature on the clinical presentation, diagnosis, and treatment outcomes of CVST in pediatric patients following closed head injuries, to inform evidence-based management strategies and to guide future research in this area.

Data Extraction

In this systematic review, three independent reviewers screened the titles and abstracts of potentially eligible studies based on the inclusion and exclusion criteria. Three reviewers then assessed the full text of each study to extract data using multiple variables that aligned with the study's objectives. These variables included the type of article, author's name, publication year, and sample size. Demographic data of the patients, such as age, sex, past medical history, and medication history, were also collected. Mechanism of injury, presenting signs and symptoms, Glasgow Coma Scale (GCS) score at arrival, and any changes in GCS during hospitalization were recorded if available. Radiological findings and diagnostic methods used for the diagnosis of CVST were noted. Management was classified into surgical and nonsurgical interventions. The aim of this systematic review is to provide a comprehensive synthesis of the current literature on CVST in pediatric patients following closed head injuries to guide clinical decision-making and to inform future research in this field.

Statistical Analysis

Following data collection, statistical analysis was conducted using SPSS version 23. Cross-tabulations and the chi-squared method were employed to analyze the data. The collected

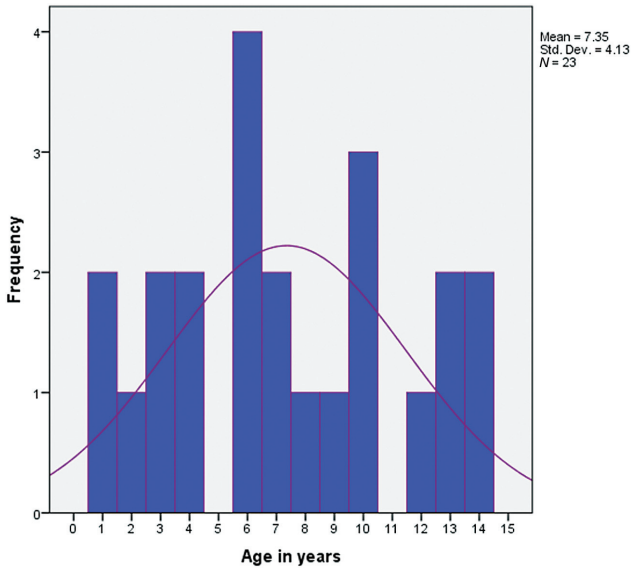

Fig. 1 Histogram for the frequency distribution of the age in years for the selected pediatric patients.

data were presented using graphical representations such as bar charts, which were used to depict different categorized variables, such as age and sex and their relationship to each other. The aim of this statistical analysis was to identify any significant associations between different variables and to provide a clear overview of the collected data, allowing for a more comprehensive understanding of the clinical presentation, diagnosis, and treatment outcomes of CVST in pediatric patients following closed head injuries.

Results

A total of 23 articles were included in this study, which examined pediatric patients with traumatic CVST. The study population had a mean age of 7.4 years (standard deviation [SD] = 4.4 years) with a range from 12 months to 14 years. The frequency distribution of the age in years for the selected pediatric patients was presented in ►**Fig. 1**. The mean GCS score was 13 (SD = 3.4), and the mean length of stay in the hospital was 9 days (SD = 5.7) as shown in ►**Table 1**. The characteristics of the included patients shown in ►**Table 2**. In

Table 1 Descriptive statistics of the included cases

	n	Minimum	Maximum	Mean	SD
Age in years	23	0.12	14.00	7.4449	4.44374
GCS at presentation	17	3	15	13.06	3.418
Length of stay in days	13	2	21	9.23	5.747

Abbreviations: GCS, Glasgow Coma Scale; SD, standard deviation.

Table 2 Characteristics of the included cases

		n	%
Gender	Female	10	43.5
	Male	13	56.5
Past medical history	Yes	2	8.7
	No	21	91.3
Past medications history	Yes	1	4.3
	No	22	95.7
Mechanism of injury	Fall	12	52.2
	Motor vehicle collision	7	30.4
	Strike to head	3	13.0
	Polytrauma/blast	1	4.3
Final outcome	Symptoms resolved	18	81.8
	Impairment of attention	0	0.0
	Impairment of memory	0	0.0
	Impairment of language functions	1	4.5
	Hemiparesis	2	9.1
	Seizures	0	0.0
	Death	1	4.5

Table 3 Number of sinuses involved based on radiological report of the included cases

		n	Response %	% of cases
Vessel's involvement	Single sinus	11	16.9	47.8
	Multi sinuses	12	18.5	52.2
	Straight sinus	3	4.6	13.0
	Transverse sinuses	11	16.9	47.8
	Sagittal sinus	8	12.3	34.8
	Sigmoid sinus	13	20.0	56.5
	Jugular vein	5	7.7	21.7
	Bilateral cavernous sinuses	1	1.5	4.3
	Superior ophthalmic veins	1	1.5	4.3

total, 23 patients were included in the study, and 43.5% of them were female. Falls were the most common cause of traumatic CVST in the pediatric population, accounting for 52.2% of cases, followed by motor vehicle collisions (30.4%) and trauma due to a strike to the head (13%). The majority of patients (81.8%) had more than three quadrants of their symptoms resolved, while 9.1% had hemiparesis, and 4.5% had impairment of language functions. One patient out of 23 passed away. ►**Supplementary Table S1** (available in the online version) shows the presenting signs and symptoms of pediatric patients with CVST and closed head injury. Nausea and vomiting were the most commonly reported symptoms (71.4% of cases), followed by headaches (52.4%), loss of consciousness (33.3%), and drowsiness (23.8%). Scalp abrasions/lacerations and bilateral papilledema were each seen in 14.3% of the cases. In addition, 38% of patients developed nick stiffness, diplopia, and lethargy. The most common radiological method used to diagnose CVST in pediatrics was MRV, accounting for 43.5% as presented in ►**Supplementary Table S2** (available in the online version).

Sinus involvement is shown in ►**Table 3**. The study showed that CVST occurred in multiple sinuses in 52.2% of cases, while 47.8% of cases occurred in a single sinus. Sigmoid sinuses were the most commonly affected sinus (56.5%), followed by transverse sinuses (47.8%), sagittal sinus (34.8%), jugular vein (21.7%), straight sinus (13%), and bilateral cavernous sinuses and superior ophthalmic veins (8.6%).

Skull fracture was the second most common finding on the scan, accounting for 43.5% of cases, followed by edema (21.7%), subdural and epidural hematoma (13% each), subarachnoid hemorrhage, and signs of impaired venous drainage (4.3% each; ►**Supplementary Table S3** [available in the online version]). There was no association with any of the study group patients having an intraparenchymal hemorrhage (►**Table 4**).

Conservative management was used for 35.3% of females and 46.7% of males. Patients who experienced falls from a height were treated with conservative management compared with other mechanisms of injury ($p < 0.05$). Craniectomy and craniotomy with or without evacuation of hematoma were the most common surgical interventions, accounting for 66.6% of cases. Other interventions, such as the elevation of bony fragments and external ventricular drain, accounted for 33.4% (►**Table 5**).

Table 4 Association of the type of management for pediatric patients with cerebral venous sinus thrombosis secondary to closed head injury with regard to the following categories ($n = 23$)

Characteristic	Type of management, *n* (%)		*p*-Value
	Conservative	Intervention	
Gender			0.192
Male	7 (46.7%)	6 (75%)	
Female	8 (35.3%)	2 (25%)	
Age			0.278
Below 7-year-old	6 (40%)	5 (62.5%)	
7-Year-old or above	9 (60%)	3 (37.5%)	
Mechanism of trauma			< 0.05
Fall from height	10 (66.7%)	2 (25%)	
Nonfall trauma	5 (33.3%)	6 (75%)	

Table 5 Surgical interventions in pediatric CVST cases

		n	Response %	% of cases
Intervention	Elevation of bony fragments	1	16.7	20.0
	External ventricular drain	1	16.7	20.0
	Decompressive craniectomy	2	33.3	40.0
	Craniotomy ± evacuation of hematoma	2	33.3	40.0

Abbreviation: CVST, cerebral venous sinus thrombosis.

Discussion

CVST is a rare but severe neurological condition characterized by the formation of a blood clot in the cerebral venous sinuses, which can lead to a variety of complications such as seizures, hemorrhage, and increased intracranial pressure. CVST is more common in adults, but it can also affect children, and it is known to occur after head injury.[2] It is important to note that while CVST is a serious condition, it is still relatively rare. One study estimated the incidence of CVST in children after closed head injury to be around 0.5% of all cases. However, due to the potentially severe consequences of CVST, it is important for healthcare providers to be aware of the condition and to consider it as a possible complication in any pediatric patient who has suffered a closed head injury. In this article, we discuss the epidemiology, etiology, clinical presentation, diagnosis, and management of CVST in pediatric patients with closed head injury. Twenty-four articles met our inclusion criteria with 23 children.

CVST and Patient Demographics

The epidemiology of CVST in pediatric patients with closed head injury is not well understood; however, it is more common in adults. The demographics of pediatric patients with CVST after a closed head injury can vary depending on the population being studied. Several studies have looked at this population, and findings suggest that the condition is more common in boys than girls, with a male-to-female ratio of approximately 1.5:1.[5]

In this study, the age of patients ranged from 12 months to 14 years, while prior research has demonstrated that 30 to 50% of cases of CVST occur in neonates.[2,3] The duration of hospital stays for our patients varied from 2 to 21 days, with our study being the first to highlight the hospital stay in pediatric CVST cases to the best of our knowledge. In terms of gender distribution, our review found a relatively equal ratio between males and females, which differs from a study by Mishra et al showing a male predominance (60–70%) in pediatric CVST cases.[4] A Canadian Pediatric Stroke Registry Analysis showed that neonates accounted for 43% of children diagnosed with CVST, and 54% of those were younger than 1 year old.[5] The increased risk of CVST in neonates may be due to various factors, such as damage to the dural venous sinuses during delivery, a prothrombotic state, and dehydration. Infection is a significant cause of CVST in children, while hypoxia may play a considerable role in neonates.[6]

Presenting Signs and Symptoms

The clinical presentation of CVST in pediatric patients with closed head injury can vary widely depending on the location and extent of the thrombus. Symptoms may include headache, vomiting, seizures, focal neurological deficits, and altered mental status. In some cases, CVST can present with a nonspecific clinical picture, making it difficult to diagnose. Therefore, a high level of suspicion is required in pediatric patients with closed head injury, particularly if there are persistent or worsening symptoms.

A previous study reported that children with CVST commonly had an injury in the sixth cranial nerve palsy; they might present with symptoms like progressive headaches, papilledema, and diplopia.[7] In comparison to our study nausea and vomiting come first as the most common symptoms then headache was the second symptom that occurs in a patient with CVST. Moreover, the differentiation between the symptoms related to the primary head injury and the CVST is always difficult. Both conditions might present similarly. Headache related to an isolated CVST is typically described as diffuse and often progresses in severity over days to weeks. Changing the headache characteristic may suggest an underlying sequel or complication related to the CVST including subarachnoid hemorrhage or intracerebral hematoma.[8,9] Isolated headache without focal neurological findings or papilledema occurs in up to 25% of patients with CVST and presents a significant diagnostic challenge.[8,9] Moreover, papilledema and diplopia represent 14.3 and 9.5%, respectively.[8,9] In a previous case report, a child was readmitted on the 10th day after discharge with a complain of new vomiting. The results of the laboratory tests were normal. Due to concern regarding the progression of the previous sinus thrombosis, had an MRV, and it showed a recovery of the flow signal in the right sigmoid sinus.[10]

Radiological Findings

The diagnosis of CVST in pediatric patients with closed head injury can be challenging, and a high index of suspicion is required. A detailed clinical history and physical examination are essential, and imaging studies, such as MRI or CT, are necessary to confirm the diagnosis. MRI is the preferred imaging modality, as it has a higher sensitivity for the detection of thrombi in the cerebral venous sinuses. In this review, we found that MRV was the most common radiological method used to diagnose CVST in pediatrics. CT scan and MRI were used as well. Another study showed

that CT and MRI come first and MR venogram was only used for selected cases to rule out vasculopathy.[11]

We discussed in this review the numbers of sinuses involved that were not previously well illustrated in the literature. Based on the radiological report of the included cases, the involvement of single and multiple sinuses was nearly the same. The sigmoid sinus, transverse sinus, and sagittal sinus are the most common then come all the other sinuses. In contrast, another study showed that multiple sinuses were involved in most cases and the transverse sinus was the most commonly involved sinus.[7]

The study found that the most radiological finding in a child with CVST was thrombosis only followed by skull fracture, while another study showed a higher percentage of brain lesions and intraventricular hemorrhage.[7]

Management of CVST

The management of CVST in pediatric patients with closed head injury requires a comprehensive, multidisciplinary approach aimed at preventing further thrombus formation, managing underlying medical conditions, and reducing the risk of complications such as intracranial hemorrhage. Anticoagulation, thrombolysis, and surgical intervention are potential treatment options. However, the use of anticoagulants in pediatric patients is controversial due to their increased risk of bleeding complications. Thrombolysis is reserved for patients with severe or life-threatening symptoms, while surgical intervention is considered in cases of massive intracranial hemorrhage or persistent venous occlusion.

In this study, we investigated the relationship between patient sex, age, mechanism of trauma, and the type of management (conservative versus surgical intervention) in treating children with CVST. We found no correlation between patient sex (p-value = 0.192) or age (p-value = 0.278) and the type of management. However, we did observe a correlation between the mechanism of trauma and the type of management. Specifically, the majority of CVST cases caused by falls were treated conservatively, while the majority of nonfall trauma cases received an intervention.[8,9] In total, eight patients underwent surgical intervention, which included decompressive craniectomy, craniotomy with or without hemorrhage evacuation, and elevation of bony fragments and external ventricular drain.[10]

Emergent decompressive craniotomy or other neurosurgical interventions have been shown to be the most effective treatment in severe forms of CVST to prevent mortality and severe morbidity.[12,13] In our review, both decompressive craniectomy and craniotomy with or without hemorrhage evacuation were commonly performed in children with CVST. In a study of adult patients with CVST, decompressive craniectomy was found to be a viable treatment option for large venous infarcts, with very good outcomes expected, especially if performed early and in those under 40 years of age. The modified Rankin Scale (mRs) continued to improve even after 6 months, with 77% of survivors achieving an mRs of less than or equal to 2 at 1-year follow-up. CVST is a rare but potentially life-threatening condition that can occur in pediatric patients with closed head injury. A high level of suspicion is required, and prompt diagnosis and management are crucial to prevent complications and improve outcomes. The choice of management strategy depends on the severity of the condition, underlying medical conditions, and risk of bleeding complications in the pediatric population. Neurosurgical interventions such as decompressive craniectomy can be a life-saving option in severe cases of CVST, and prompt intervention can significantly improve outcomes.[14]

Limitations

We believe that there are several limitations of this study. The sample size was small, with only 23 patients meeting the inclusion criteria. This limited the ability to conduct subgroup analyses and draw robust conclusions. As pediatric CVST in closed head injury is a rare condition, larger studies involving multiple trauma centers should be developed to increase the number of cases studied. Additionally, the study may be subject to publication bias due to the reliance on individual case reports. Further studies, including large, prospective, multicenter studies, are needed to address these limitations and provide a more systematic and comprehensive understanding of CVST in closed head injuries in pediatrics.

Conclusion

In conclusion, this study highlights that CVST in the pediatric population following closed head injury is a rare condition. The review of 23 cases showed that conservative management was the preferred treatment option, and both management options (conservative versus surgical intervention) resulted in good outcomes for pediatric cases with CVST. While this study sheds some light on this rare condition in the pediatric population, further research is necessary to improve our understanding of its management and outcomes. Additional studies are recommended to investigate larger patient populations and to address the limitations of the current study to develop more comprehensive and evidence-based treatment guidelines for this rare traumatic condition in pediatrics.

Conflict of Interest
None declared.

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