Cross-sectional Study

Clinical profile and risk factors of cerebral venous sinus thrombosis (CVST) in Sudan: A multicenter cross-sectional study

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ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is a relatively uncommon cause of stroke that mainly affects young ladies, with a wide spectrum of symptoms severity, and prognosis. In this study, we aim to study the clinical profile and Risk Factors of CVST among Sudanese patients in Khartoum state hospitals.

Methods: This was a multi-center cross-sectional hospital-based study that covered 37 participants in three major hospitals in Khartoum, with radiologically confirmed Cerebral Venous Sinus Thrombosis (CVST).

Results: About 37 patients were included in this study. The median age was 35 years; the range was 52 years, with a minimum age of 23 years and a maximum of 75 years. The commonest presenting feature was headache (n = 35; 94.6%), followed by blurring of vision (n = 25; 67.6%), while seizures is a presenting symptom in nearly half of the patients (n = 17; 45.9%), on examination papilledema was present in 83.8%. In this study 13.8% were pregnant, 31.0% were postpartum and OCPS users account for 27%. Regarding the involved sinus; Sagittal Venous Sinus and the transverse sinus were the most affected sinuses. Regarding treatment options: “low molecular weight heparin followed with warfarin” was found in 81.1%, followed by heparin in only 10.8%, while the new agents NOACs comprised only 8.1%.

Conclusion: Cerebral Venous Sinus Thrombosis is mainly a disease of child-bearing women, although significant proportions of men were affected. Cerebral Venous Sinus Thrombosis presents in a wide variety of signs and symptoms.

1. Introduction

In 1825, a 45-year-old male presented with headache and convulsions; on autopsy, thrombosis involving the superior sagittal sinus and lateral sinuses was discovered; this was the first case of Cerebral venous sinus thrombosis (CVST). Abercrombie (1828) reported the first case of postpartum CVST about three years later in a 24-year-old woman who developed headache and fever two weeks after delivery [1].

It is more common in young adults, particularly females of childbearing age. The estimated incidence has recently increased to 3–4 cases per million people, which may be attributed to increased awareness of the diagnosis and advancements in radiological techniques used in diagnosis [2–5]. Superior sagittal sinus and lateral sinuses are the main cerebral venous sinuses affected, while in about one-third of cases more than one sinus is affected. In a further one-third both sinuses and cerebral or cerebellar veins are involved [6]. Deep Cerebral Venous Thrombosis is thrombosis of deep venous outflow and is seen in 10% of cases of CVST [6].

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The most commonly identified risk factors are young age groups and the female gender. Also, antibiotics, dehydration, intracranial tumors, cancer, pregnancy/puerperium, oral contraceptives (OC), systemic diseases, thrombophilia, jugular thrombosis after catheterization, fibrous thyroiditis, idiopathic jugular vein stenosis, head trauma, arterio-venous malformations, surgery, and autoimmune disorders. Yet, associated conditions cannot be found in up to 30% of cases, and some patients might have multiple risk factors [7–10].

The clinical presentation depends on the involved sinuses, thrombus size, and extension, and if there is any venous collateral. The most common presenting symptoms and signs are headaches, disorders of consciousness, focal neurological symptoms; motor and sensory deficits, seizures, and cranial nerve palsies. These diverse Clinical manifestations are the major reasons to delay the diagnosis [11–16]. Major differential diagnosis includes other causes of stroke and space-occupying lesions. Also, migraine, subarachnoid hemorrhage, CSF hypertension, or hypertension mimic CVTS headache [17].

Diagnosis relies on confirming the diagnosis and finding the cause of CVST thus initiating appropriate treatments to avoid recurrence [14]. The confirmation of the diagnosis of CVT relies on the demonstration of thrombi in the cerebral veins and/or sinuses by neuroimaging and also to exclude other related disorders like space-occupying lesions, and this is done by (CT), as it is useful to rule out a tumor, subdural hematoma or abscess. Definitive imaging (MRI) combined with magnetic resonance venography (MRV) is currently the best method to confirm the diagnosis of CVT [18–23].

Treatment involves initial anticoagulation with UFH or LMWH followed by a vitamin K antagonist even in the presence of ICH. The optimal duration of therapeutic anticoagulation following CVST is unknown but can follow the rules for deep venous thrombosis [14,24].

The prognosis is variable from complete recovery to ending with some deficit, but the overall outcome is fairly good. Coma and intracerebral hemorrhage are independent predictors of poor outcome. This disease can be followed by various complications like a chronic headache which was the most common complication in (4.2%) of patients, recurrent seizures in (1.1%), chronic intracranial hypertension in (0.9%), deep venous thrombosis in lower limbs in (0.9%), arterial thrombosis in (0.7%), and the major cause of death; pulmonary thromboembolism in (0.4%) of patients [13,16,25–28].

So, because CVST is a rare disease that, if detected and treated early, can significantly improve the outcome, we set out to investigate the clinical profile, risk factors, and treatment of Cerebral Venous Sinus Thrombosis among Sudanese patients in Khartoum State, Sudan.

2. Methods

This was a multi-center cross-sectional study. 37 participants were included in the study with a diagnosis based on CT, MRI, or MRV, from three major hospitals in the Capital, the National Center for Neurological Disease, Soba university hospital, and Omdurman Teaching hospital. NCNS located in Khartoum city is considered the main tertiary team of registrars, specialists, and consultants “in neuro medicine and neurosurgery” providing services for adult neurology patients during day and night, while the other two hospitals are considered general secondary hospitals with a lot of facilities and departments specialized in neurology. This study was conducted from October 2019–March 2020. Data was collected using a comprehensive, structural, close-ended data collection form “Questionnaire”. This form was designed to cover the data of demographic, clinical, treatment, and risk factors from all patients under the study. The data was coded and entered for analysis using the statistical package for social science (SPSS) for window version 24.0. Descriptive statistics in terms of frequency tables with percentages and graphs were calculated for categorical data. Means and standard deviations were computed with relevant graphical representation for quantitative data “scaled data”; a P value of 0.05 or less is considered statistically significant. The Chi-square test uses to test association between clinical presentation and gender with Fisher’s exact test used when chi square was violated.

Written consent was taken from all the patients who participated in the study. Written permission was obtained from the administrative authority of the National Center for Neurological Disease, Omdurman Teaching hospital, and Soba university hospital. Study data/information will be used for the research purposes only, the privacy issues were intentionally considered.

This study is fully compliant with the STROCSS 2021 criteria [29].

3. Results

This was a cross-sectional multicenter study covering 37 patients diagnosed with Cerebral Venous Sinus Thrombosis (CVST).

3.1. Socio-demographic characteristic

The median age was 35 years; the range was 52 years with an IQR of 16 years a minimum age of 23 years and maximum age of 75 years. The largest group (n = 18, 48.6%) was in the range between “26–35” years. The gender distribution; (n = 8; 21.6%) were males and (n = 29; 78.4%) were female, with the majority of patients being female, (n = 15; 40.5%) from rural areas, while (n = 22; 59.5%) from urban areas. Concerning the educational level, the majority of patients were in a secondary level education (n = 14; 37.8%) followed by a university level of education (n = 12; 32.4%) and “16.2%” had no formal education. Regarding the occupation, most of the patients were not employees (n = 21; 56.8%). The majority of the patients were married (n = 30; 81.1%) regarding marital status (Table 1).

3.2. The clinical presentation

Most of the patients presented with headache (n = 35; 94.6%) as a major presenting symptom, followed by blurring of vision (n = 25; 67.6%), while seizures was a presenting symptom in nearly half of the patients (n = 17; 45.9%), altered level of consciousness occurred in (n = 13; 35.1%), vomiting in (n = 11; 29.7%), unilateral weakness in (n = 10; 27.0%), unilateral numbness in (n = 5; 13.5%) and less likely speech difficulties which comprised only (n = 4; 10.8%) and symptoms related to cranial nerve involvement (5.4%). However, the difference between males and females in the clinical presentation was not statistically

| Table 1  | Showed the Demographic characteristics of the patients who were diagnosed with Cerebral Venous Sinus Thrombosis (CVST) (n = 37). |
|----------|-------------------------------------------------------------------------------------------------|
| Demographic data | Frequency | Percentage % |
| Age Group | | |
| < 25 | 3 | 8.1 |
| 26–35 | 18 | 48.6 |
| 36–45 | 9 | 24.3 |
| 46–55 | 2 | 5.4 |
| >55 | 5 | 13.5 |
| Gender | | |
| Male | 8 | 21.6 |
| Female | 29 | 78.4 |
| Educational Level | | |
| Illiterate | 6 | 16.2 |
| Basic/primary | 5 | 13.5 |
| Secondary | 14 | 37.8 |
| University/post Graduate | 12 | 32.4 |
| Working status | | |
| Worker | 15 | 40.5 |
| Retired | 1 | 2.7 |
| not worker | 21 | 56.8 |
| Marital status | | |
| Single | 3 | 8.1 |
| Married | 30 | 81.1 |
| Widower | 4 | 10.8 |
| Divorced | 0 | 0 |
| Residence | | |
| Rural | 15 | 40.5 |
| Urban | 22 | 59.5 |
significant except in the unilateral weakness and cranial nerves involvement which showed a p-value of 0.021 and 0.042 respectively. Most of the patients had papilledema (n=31; 83.8%), while (n=12; 32.4%) had unilateral motor deficit, (n=5; 13.5%) had unilateral sensory deficit, while only (n=2; 5.4%) had cranial nerve involvement (Table 2).

3.3. Regarding the risk factors

Postpartum period comprised nearly the third (n=9 out of 29 females; 31%), followed by ladies with the use of OCPs (n=8 out of 29 females; 27.6%), while (n=4 out of 29 females; 13.8%) were pregnant. Malignancy was found in (n=3; 8.1%) “Two CNS tumors and one breast tumor”, while infection “mastoiditis” was found in only one patient (n=1; 2.7%). No risk factor identified was present in about a third of the patients (n=12; 32.4%) (Fig. 1).

Concerning the finding on the imaging about venous sinus involvement, most of the patients had “sagittal Venous Sinus (SSS) plus transverse sinus” involvement (n=14; 37.8%), followed by the Sagittal Venous Sinus (SSS) only (n=11; 29.7%), then Transverse sinus (n=4; 10.8%), while sigmoid sinus thrombosis only and “Sagittal Venous Sinus (SSS) plus sigmoid sinus thrombosis plus transverse sinus thrombosis” both comprised (n=3; 8.1%). Less likely the occurrence of “transverse sinus thrombosis with sigmoid sinus thrombosis” and “Sagittal Venous Sinus (SSS) with Transverse sinus thrombosis with Straight sinus thrombosis” with only one case identified (n=1; 2.7%) while no case was reported with cavernous sinus thrombosis (Table 3).

However, the treatment options results were mainly constituted of low molecular weight heparin followed with warfarin in (n=30; 81.1%), followed with heparin only (n=4; 10.8%), while the new agents’ novel oral anticoagulants “NOACs” comprised only (n=3; 8.1%).

4. Discussion

We found that CVST among Sudanese Patients in Khartoum State is mainly a disease of child-bearing women, although significant proportions of men were affected. Headache was the commonest presenting symptoms followed by blurred vision, seizures, and vomiting. Concerning risk factors, we found; Postpartum, Oral contraceptive pills “OCPs” and Pregnancy to be the most common predisposing factors. We also found treatment with LMWH followed by warfarin to be the major treatment option. Our study is an observational cross-sectional Multicenter hospital-based study that covered 37 patients diagnosed with Cerebral Venous Sinus Thrombosis (CVST), and aimed to study the clinical profile and Risk Factors of Cerebral sinus thrombosis among Sudanese patients in Khartoum state and conducted in three major hospitals; NCNS, Soba University Hospital, and Omdurman Teaching Hospital, during the period October 2019–March 2020.

The average age for most large-scale cerebral venous sinus thrombosis (CVST) studies is between 37 and 39 years, although this can affect any age. Maximum numbers of patients, nearly half “48.6%” were in the “26 to 35” years age group, and a females constituted the majority of the patients with a percentage of 78.4% and exceeded the male in all age groups. The age and gender distribution were relevant to a study which is done here in Sudan which showed a mean age of 33.9 ± 11.8, and female predominance of 80% [30]. Also, the same as other studies done in the regional area such as Iran, Oman, and Saudi Arabia, concluded that Cerebral Venous Sinus Thrombosis (CVST) occurs predominantly in young females [27] [31] [32] [33]. Only two studies from India revealed a male predominance [16] [17], one of them attributed this probably due to rising consumption of alcohol by men, improvement in obstetric care, and a higher level of clinical suspicion and detection of Cerebral Venous Sinus Thrombosis (CVST) at an early stage [16].

The most common symptom was headache which is present in up to 94.6% of the patients in this study, which is to the same as “Cerebral venous thrombosis which showed that all the patients presented with headache [30], and slightly more than what is reported in almost all the studies of Cerebral Venous Sinus Thrombosis (CVST) regionally and internationally, as it has been reported in the range of 70%–90% [17] (22) and in one case report from Turkey a case of Cerebral Venous Sinus Thrombosis (CVST) has been misdiagnosed as subarachnoid hemorrhage because he was presenting with headache only [34], so headache must be taken seriously and should be investigated thoroughly, especially in high-risk groups.

Other common presentations in this study also occur nearly in concordance with the current literature. Blurring of vision and seizures presented as 67.6% and 45.9% respectively. The Blurring of vision was found to be higher in our study than what is reported by other studies 13.5% and 10% [13] [26]. Seizure was reported as nearly the same as 47% in another study from the Netherlands [13] and more than what is reported by the International Study on Cerebral Vein and Dural Sinus (ISCVT) which is 39.3% [26]. Altered level of consciousness occurred in 35.1% slightly the same as one study reported as 39% [14]. Vomiting occurred in 29.7%, the same as in a study from Saudi Arabia 26.9% [32]. Focal neurological deficit occurred in 32.4% less than other studies 53.8%, 46% and 48.0% [13] [28] [32]. Sensory affection occurred less than motor by 13.5%, and less likely speech difficulties which comprised only 10.8% less than what is reported by an International Study on Cerebral Vein and Dural Sinus (ISCVT) which is 13.5% [26]. On the other hand, cranial nerve involvement was present in 5.4% of the patients, which is less than another study from Saudi Arabia which was reported as 38.8% [32]. As general focal neurological findings, cranial nerve palsies are usually the common findings in almost all the series of Cerebral Venous Sinus Thrombosis (CVST), however, unilateral weakness and cranial nerves involvement show a significant difference between males and females; p-value 0.021, 0.041 respectively, which might indicate the tendency to occur more in male. The reasons for this might be attributed to an anatomical variation in venous systems between males and females.

Most of the patients had papilledema 83.8%, nearly the same as what is reported by Idris MNA et al. which is 86.7%, in contrast to other study from Oman and Netherlands which reported only 39.0% and 41% of patients with papilledema respectively [13] [27] [30].

However, the risk factor profile was almost similar to other studies done in regional areas as in Saudi Arabia as well as internationally. Of the risk factors, pregnancy and the postpartum period accounted for a large proportion of the cases with Cerebral Venous Sinus Thrombosis (CVST), they accounted for 13.8% and 31% of all female cases in our study respectively. This is in contrast to the International Study on Cerebral Vein and Dural Sinus (ISCVT), which showed that pregnancy

| Clinical Presentation (%) | Gender | Total (%) | P value |
|---------------------------|--------|-----------|---------|
| Headache                  | 7(27.5%) | 28(96.6) | 35(94.6) | .3 |
| Unilateral Weakness       | 5(62.5%) | 5(17.2)  | 10(27)  | .02* |
| Unilateral Numberness     | 1(12.5%) | 4(13.8)  | 5(13.5) | .7 |
| Vomiting                  | 2(25%)   | 9(31)    | 11(29.7) | .5 |
| Seizure                   | 3(37.5%) | 4(14.8)  | 7(14.9) | .4 |
| Blurred Vision            | 7(87.5%) | 18(62.1) | 25(67.6) | .1 |
| Speech Difficulties       | 2(25%)   | 2(6.9)   | 4(10.6) | 1 |
| Altered Level Of Consciousness | 4(50%)   | 9(31)    | 13(35.1) | .2 |

*P value is significant “less than <0.05”

Table 2

showed the clinical presentation of the patients who were diagnosed with Cerebral Venous Sinus Thrombosis (CVST) (n = 37).
accounted for 6.3% of cases, while postpartum accounted for 13.8% [26]. A possible explanation for these differences is that the birth rates here, in Sudan, are higher than that in the west. Another reason for this high percentage in our study might be related to some traditional habits in our community, specified to married women, something like Sawna called “Dukhan” that leads to steaming and profuse fluid loss through sweating, which leads to dehydration and increase the viscosity of the blood in the ladies who are already in a hypercoagulable state. A related study published in 2015 from Sudan showed that the incidence of pregnancy-related Cerebral Venous Sinus Thrombosis (CVST) is 0.01 per 100,000, with most of the cases identified postnatally as in agreement with our study results [35]. A more identifiable risk factor is the use of OCPs by ladies for different reasons. In this study, it accounted for 27.6%, while in an international Study on Cerebral Vein and Dural Sinus (ISCVT) it was 54.3%. This can be explained by the wide use of OCPs in the west, and the lower level of sexual education about the use of OCPs in Sudan. Generally, the risk was associated with the combined OCPs. Malignancy was reported as 8.1%, nearly the same as in an International Study on Cerebral Vein and Dural Sinus (ISCVT) “7.4%”. In this study two-thirds were CNS tumors and one third was a solid tumor outside the CNS; a Breast cancer” [26]. One case of infection was reported in our study “2.7%”, and it was mastoiditis “infection of the mastoid bone” less than what is reported in other studies 8.8% and 12.3% [26,27][31]. No case of diagnose0d thrombophilia or connective tissue disease with a tendency to thromboses or systemic disease “e.g., thyrotoxicosis, IBD” was reported in this study, unlike other studies which comprise substantial proportions of the cases. Surprisingly no identifiable cause was reported in 32.4% of the cases which is similar to a study from Oman 35% and far more than what is reported by an International Study on Cerebral Vein and Dural Sinus (ISCVT), and by a study from Iran and Saudi Arabia, which are 12.5%, 12.9% and 11.5% respectively. Although third of the cases are known to be of unknown etiology, this result may be due to the inability to obtain complete workup for all the causes of Cerebral Venous Sinus Thrombosis (CVST) by our patients because of financial issues, since some of the investigations are not present in our country, and need to be sent for outside the country. Yet, even if present inside, the expensive prices still resemble a barrier [26,27,31,32].

Regarding the results from the imaging MRI/MRV, the most common involved sinuses in this study were the “Sagittal Venous Sinus (SSS) + the transverse sinus” thrombosis which accounts for 37.8%, followed by Sagittal Venous Sinus (SSS) thrombosis 29.7%, the transverse sinus 10.8%, sigmoid sinus thrombosis 8.1%. Nearly the same as the result of a study from Oman, Iran, and India, and differ from the result from Saudi Arabia and an International Study on Cerebral Vein and Dural Sinus (ISCVT) [13,15,26,27,31,33]. We didn’t find any case of Deep Cerebral Venous Sinus Thrombosis in our patients, unlike an international study on cerebral vein and Dural sinus thrombosis (ISCVT), where it was seen in 10% of patients. This might be due to our small sample size. Further studies are needed to investigate possible explanations. Concerning the treatment options, most of the patients received LMWH followed by warfarin 81.1% followed by Sagittal Venous Sinus (SSS) thrombosis 29.7%, the transverse sinus 10.8%, sigmoid sinus thrombosis 8.1%. Nearly the same as the result of a study from Oman, Iran, and India, and differ from the result from Saudi Arabia and an International Study on Cerebral Vein and Dural Sinus (ISCVT) [13,15,26,27,31,33]. We didn’t find any case of Deep Cerebral Venous Sinus Thrombosis in our patients, unlike an international study on cerebral vein and Dural sinus thrombosis (ISCVT), where it was seen in 10% of patients. This might be due to our small sample size. Further studies are needed to investigate possible explanations. Concerning the treatment options, most of the patients received LMWH followed by warfarin 81.1% which is similar to the number given in an International Study on Cerebral Vein and Dural Sinus (ISCVT) and a study from Oman [26,27], while a small percentage was given the Novel Oral anticoagu-

5. Limitations

The sample size wasn’t large enough due to the lack of resources and...
logistics, low incidence of the disease, and the low awareness of patients, in that many of them do not attend the hospital to receive treatment due to lack of education and the presence of financial burdens. Further Research specifically “A Prospective Study” with large sample size is required For Better Characterization, Outcome and prognosis Assessment.

6. Conclusion

The study concluded that Cerebral Venous Sinus Thrombosis (CVST) is mainly a disease of child-bearing women, although significant proportions of men were affected. Cerebral Venous Sinus Thrombosis (CVST) presents in a wide variety of signs and symptoms. Headache was the commonest presenting symptoms followed by blurred vision, seizures and vomiting. On examination most of the patients have papilledema followed by unilateral motor deficit. Postpartum, Oral contraceptive pills “OCPs” and Pregnancy were found to be the most common predisposing factors for Cerebral Venous Sinus Thrombosis (CVST). After imaging, The Sagittal Venous Sinus (SSS) and the transverse sinuses were the most affected sinuses. Concerning treatment, LMWH followed by warfarin were the major treatment options. Unilateral weakness and cranial nerves involvement were more likely to occur in males.

Ethical approval

Written permission was obtained from the administrative authority of National Center for Neurological Disease, Omdurman Teaching hospital and Soba university hospital.

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The study was self-funded

Author contribution

All authors participated in planning the study, data collection, analysis, writing and revising the manuscript.

Registration of research studies

Name of the registry:
Unique Identifying number or registration ID:
Hyperlink to your specific registration (must be publicly accessible and will be checked):

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Consent

Written and verbal consents to participate and to publish the study were obtained from all participants before conducting.

Availability of data and materials

The materials datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

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Declaration of competing interest

Authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jamsu.2022.104891.

Abbreviations

CNS Central nervous system
CSF Cerebrospinal fluid
CT Computed tomography
CVST Cerebral venous sinus thrombosis
CVT Cerebral venous thrombosis
DOACs Direct oral anticoagulants
IBD Inflammatory bowel diseases
ISCVT International Study on Cerebral Vein and Dural Sinus Thrombosis
LMWH Low molecular weight heparin
MRI Magnetic resonance imaging
MRV Magnetic resonance venography
NCNS National center for neurological diseases
NOACs Novel “non-vitamin-K antagonist” oral anticoagulants
OCPs Oral contraceptive pills
UFH Unfractionated heparin, VTE: Venous thromboembolism

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