

Clinical Profile And Risk Factors of Cerebral Venous Sinus Thrombosis (CVST) in Sudan

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Research Article

Keywords: CVST, Risk factor, neurovascular, Sudan,

Posted Date: June 21st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-640264/v1>

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Abstract

Background

Cerebral venous sinus thrombosis (CVST) is relatively uncommon cause of stroke 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 is an observational cross-sectional multi-center hospital based study which covered 37 participants, in three major hospitals in khartoum, with radiologically confirmed Cerebral Venous Sinus Thrombosis (CVST)

Results

37 patients were included in this study, The mean age of patients was 38.5 ± 13.4 years, with minimum age of 23 years and maximum of 75 years, the largest group (n = 18, 48.6%) were in the range between "26–35" years, regarding gender distribution (n = 8; 21.6%) were males and the majority of patients were female (n = 29; 78.4%), 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 papilloedema was present in 83.8%. In this study 13.8% were pregnant, 31.0% were postpartum, OCPS user account for 27.%, and No risk factor present in 32.4%. 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 with heparin only 10.8%, while the new agents NOACs comprised only 8.1%.

Conclusion

The study concluded that 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.

Introduction

Cerebral venous sinus thrombosis is a condition with thrombosis in the cerebral veins and/or dural sinuses, it is an unusual site of thrombosis compared to arteries, but its importance relies on its potential morbidity. CVST tends to occur more in young adults and specifically in females of child bearing age, the incidence has increased recently most probably due to the improvement in radiological technique, but the precise incidence was not known yet⁽¹⁻³⁾. superior sagittal sinus and the 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 ⁽⁴⁾

There are several causes of CVST, even though the exact aetiology remains unidentified in about one-third of cases. Not uncommonly, some patients may have multiple risk factors. The most common causes of CVST are pregnancy and the puerperium, the contraceptive pill, coagulopathies and intracranial infections, medical causes of deep venous thrombosis, head and neck infections, cranial tumours, head injury including craniotomy, malignancies, severe dehydration, inflammatory bowel disease, connective tissue disorders, Behcets disease, sarcoidosis, nephrotic syndrome, and rarely Thyrotoxicosis. ⁽⁵⁻¹²⁾

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: headache, disorders of consciousness, focal neurological symptoms; motor and sensory deficits, seizures, cranial nerve palsies, these diverse Clinical manifestations, are the major reasons to delay the diagnosis ^(5,13-17). Differential diagnosis include Other causes of stroke and space occupying lesions are the major differential diagnosis. Also migraine, subarachnoid haemorrhage, CSF hypertension or hypotension mimic CVTS headache ⁽¹⁸⁾

Diagnosis relies on confirming the diagnosis and finding the cause of CVST thus initiating appropriate treatments to avoid recurrence ⁽¹⁵⁾. 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 disorder like space occupying lesions, this is done by (CT), it is useful to rule out tumour, subdural haematoma or abscess. The definitive imaging (MRI) combined with magnetic resonance venography (MRV) is currently the best method to confirm the diagnosis of CVT. ⁽¹⁹⁻²⁴⁾

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 ^(15,25)

The prognosis is variable from complete recovery to ending with some deficit, but the overall outcome was fairly good, Coma and intracerebral haemorrhage are independent predictors for poor outcome, this disease can be followed with a various complications like chronic headache which was the most common complication in (4.2%) of patients, recurrent seizures occurs in (1.1%), chronic intracranial hypertension in (0.9%), deep venous thrombosis in lower limbs in (0.9%), and most importantly and seriously and the major cause of death pulmonary thromboembolism in (0.4%), and arterial thrombosis in (0.7%) of patients ^(14,17,26-29)

Objectives:

To study Clinical Profile, Risk Factor, the treatment Of Cerebral Venous Sinus Thrombosis Among Sudanese Patients In Khartoum State, Sudan, Oct 2019-March 2020

Methods

This is an observational cross-sectional study, **37 participants** were included in the study with a diagnosis based on CT, MRI\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, it is considered the main tertiary referral teaching hospital for neurological disease in Sudan and received patients from all over the country, and has an established neurology team of registrars, specialist, and consultants “in neuromedicine and neurosurgery” providing round the clock services for adult neurology patients. 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 comprehensive, structural, close ended data collection form “Questionnaire”, This form 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 statistical package for social science (SPSS) for window version 24.0. Descriptive statistics in term 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”, P value of 0.05 or less is considered statistically significant.

Written consent was taken from all the patients who participated in the study. Written permission was obtained from the Administrative authority of 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.

Results

This is a cross sectional Multicenter study covering 37 patients diagnosed with Cerebral Venous Sinus Thrombosis (CVST) .

Socio-Demographic characteristic

The mean age of patients was 38.5 ± 13.4 years (mean \pm SD)”, with minimum age of 23 years and maximum age of 75 years, the largest group (n = 18, 48.6%) were in the range between “26–35” years, The gender distribution (n = 8; 21.6%) were males and (n = 29; 78.4%) were female, with majority of patients were female, (n = 15; 40.5%) from rural area, while (n = 22; 59.5%) from urban area. 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)

The clinical presentation

Most of the patients presented with headache (n = 35; 94.6%) as a major presenting symptoms, 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%), 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 male and female in the clinical presentation was not statistically significance except in the unilateral weakness and cranial nerves involvement which show a p-value of 0.021 and 0.042 respectively. Most of the patients have papilloedema (n = 31; 83.8%), while (n = 12; 32.4%) have unilateral motor deficit, (n = 5; 13.5%) have unilateral sensory deficit, while only (n = 2; 5.4%) have cranial nerve involvement, (Table 2)

Regarding the risk factors

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

Concerning the finding on the imaging in relation to venous sinus involvement, most of the patient have "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 comprise (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, (Fig. 2)

However, the treatment options results were mainly constitute 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 noval oral anticoagulants "NOACs" comprised only (n = 3; 8.1%), (Fig. 3)

Table 1

Showing 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
	> 56	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

Table 2
 Showed the clinical presentation of the patients who were diagnosed with Cerebral Venous Sinus Thrombosis (CVST) (n = 37)

Clinical Presentation	Gender		Total	Percentage	P value
	Male	Female			
	n = 8	n = 29			
Headache	7	28	35	94.6	0.390
Unilateral Weakness	5	5	10	27.0	0.021*
Unilateral Numbness	1	4	5	13.5	0.708
Vomiting	2	9	11	29.7	0.555
Seizure	3	14	17	45.9	0.447
Blurred Vision	7	18	25	67.6	0.177
Speech Difficulties	2	2	4	10.8	0.197
Altered Level Of Consciousness	4	9	13	35.1	0.277
Unilateral Motor Focal Deficit	5	7	12	32.4	0.054
Unilateral Sensory Focal Deficit	1	4	5	13.5	0.708
Cranial Nerve Involvement	2	0	2	5.4	0.042*
Papilledema	8	23	31	83.8	0.204

* p value is significant "less than < 0.05"

p value was not significant "> 0.05"

Discussion

This is an observational cross-sectional Multicenter hospital based study covered 37 participants diagnosed with Cerebral Venous Sinus Thrombosis (CVST), and aimed to study 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 the half "48.6%" were in "26 to 35" years age group, and female constitutes 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 Cerebral venous thrombosis *Clinical presentation and outcome in*

prospective series from Sudan" which showed a mean age of 33.9 ± 11.8 , and female predominance of 80%⁽³⁰⁾, and also the same as other studies done in the regional area such as Iran, Oman and Saudi Arabia, and they concluded that Cerebral Venous Sinus Thrombosis (CVST) occurs predominantly in young female^(28,31-33) 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 higher level of clinical suspicion and detection of Cerebral Venous Sinus Thrombosis (CVST) at an early stage⁽¹⁷⁾

The most common symptom was headache which is present in up to 94.6% of the patients in this study, which is nearly same to "Cerebral venous thrombosis *Clinical presentation and outcome in prospective series from Sudan*" 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%^(18,23). 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 by 67.6% and 45.9% respectively. Blurring of vision was found to be higher in our study more than what is reported by other studies 13.5% and 10%^(14,27). Seizure reported nearly the same 47% in another study from Netherlands (14) and more than what is reported by International Study on Cerebral Vein and Dural Sinus (ISCVT) which is 39.3%⁽²⁷⁾, altered level of consciousness occurred in 35.1% slightly the same to one study reported it as 39%⁽¹⁴⁾, vomiting occurred in 29.7% the same like 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%^(14,28,32), sensory affection occurred less than the motor one by 13.5% and less likely speech difficulties which comprised only 10.8 less than what is reported by International Study on Cerebral Vein and Dural Sinus (ISCVT) which is 13.5%⁽²⁷⁾. On the other hand, cranial nerve involvement was present in just 5.4% of the patients, which is far less than another study from Saudi Arabia 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 significant difference between male and female; p value 0.021, 0.041 respectively, that means they tend to occur more in male, the reasons for this most probably attributed to anatomical variation in venous systems between male and female

Most of them have papilloedema 83.8%, nearly the same what is reported by "Cerebral venous thrombosis *Clinical presentation and outcome in prospective series from Sudan*" which is 86.7%, in contrast to other study from Oman and Netherlands which reported only 39.0% and 41% of patient with papilloedema respectively^(14, 28)

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 comparison to the International Study on Cerebral Vein and Dural Sinus (ISCVT), which showed that pregnancy accounted for 6.3% of cases, While postpartum accounted for 13.8%⁽²⁷⁾, a possible explanations for these difference is that our birth rates are higher than that in the west, another reasons for this high percentage in our study may be related to some traditional habits in our community specified to a married women something like sawna called "*Dukhan*" that leads to steaming and profuse fluid loss through sweating which lead to more fluid loss, dehydration and increase 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, and most of the cases identified postnatally - in agreement with our study results⁽³⁵⁾. A more identifiable risk factor which is the use of an OCPs by ladies for different reasons, in this study it was accounted for 27.6% while in the international 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 more than in our countries, generally the risk was associated with the combined OCPs. Malignancy was reported as 8.1% nearly the same as in International Study on Cerebral Vein and Dural Sinus (ISCVT) "7.4%", in this study two third was CNS tumour and one third was solid tumors outside the CNS Breast cancer"⁽²⁷⁾. A 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%^(27,28,31). No case of diagnosed thrombophilia or connective tissue disease with tendency to thrombose or systemic disease "e.g. thyrotoxicosis, IBD" was reported in this study unlike other studies which comprises substantial proportions of the cases. Surprizingly 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 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, this may be due to inability to obtain complete workup for all the causes of Cerebral Venous Sinus Thrombosis (CVST) by our patient because of a financial issues, since some of the investigations are not present in our country and needed to be sent for outside, and if present they was so expensive^(27, 28, 31, 32).

Regarding the result from the imaging MRI/MRV, the most common involved sinuses in this study was the "Sagittal Venous Sinus (SSS) + the transverse sinus" thrombosis which account for 37.8% followed with Sagittal Venous Sinus (SSS) thrombosis 29.7%, the transverse sinus 10.8%, sigmoid sinus thrombosis 8.1% nearly the same to the result of a study from Oman, Iran and India, and differ to the result from Saudi Arabia and International Study on Cerebral Vein and Dural Sinus (ISCVT)^(14, 16, 27, 28, 31, 33)

Concerning the treatment options, most of the patients received LMWH followed by warfarin 81.1% which is similar to the number given in the International Study on Cerebral Vein and Dural Sinus (ISCVT) and a study from Oman^(27, 28), while small percentage was given the Noval Oral anticoagulants "NOACs" 8.1%,

this can be explained by the cost effect of these new drugs, although they donot need close monitoring with a blood test “INR” like warfarin.

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 with blurred vision, seizures and vomiting. On examination most of the patients have papilloedema followed with 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 with warfarin was the major treatment options. However, unilateral weakness and cranial nerves involvement were more likely to occur in male

Limitations

Further Research especially “A Prospective Study” with large sample size Is Required For Better Characterization, Outcome and prognosis Assessment

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: Noval “non vitamin-K antagonist” oral anticoagulants

OCPs: Oral contraceptive pills

UFH: Unfractionated heparin,,, VTE: Venous thromboembolism

Declarations

Availability of data and materials

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

Ethical Considerations

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

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors participated in planning the study, data collection, results and discussion sections.

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Figures

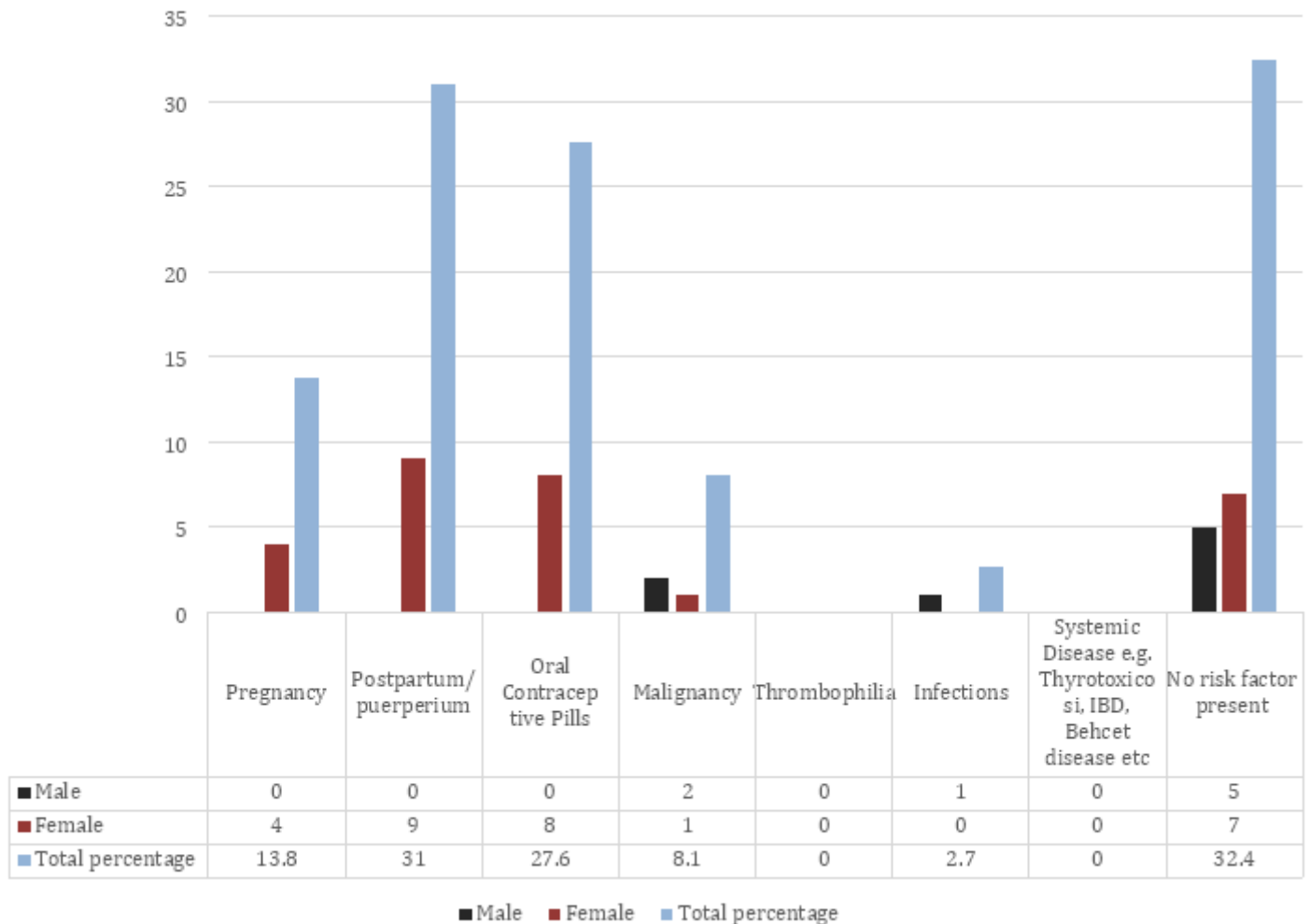


Figure 1

Shows the distribution of the patients according to their risk factors for Cerebral Venous Sinus Thrombosis (CVST)

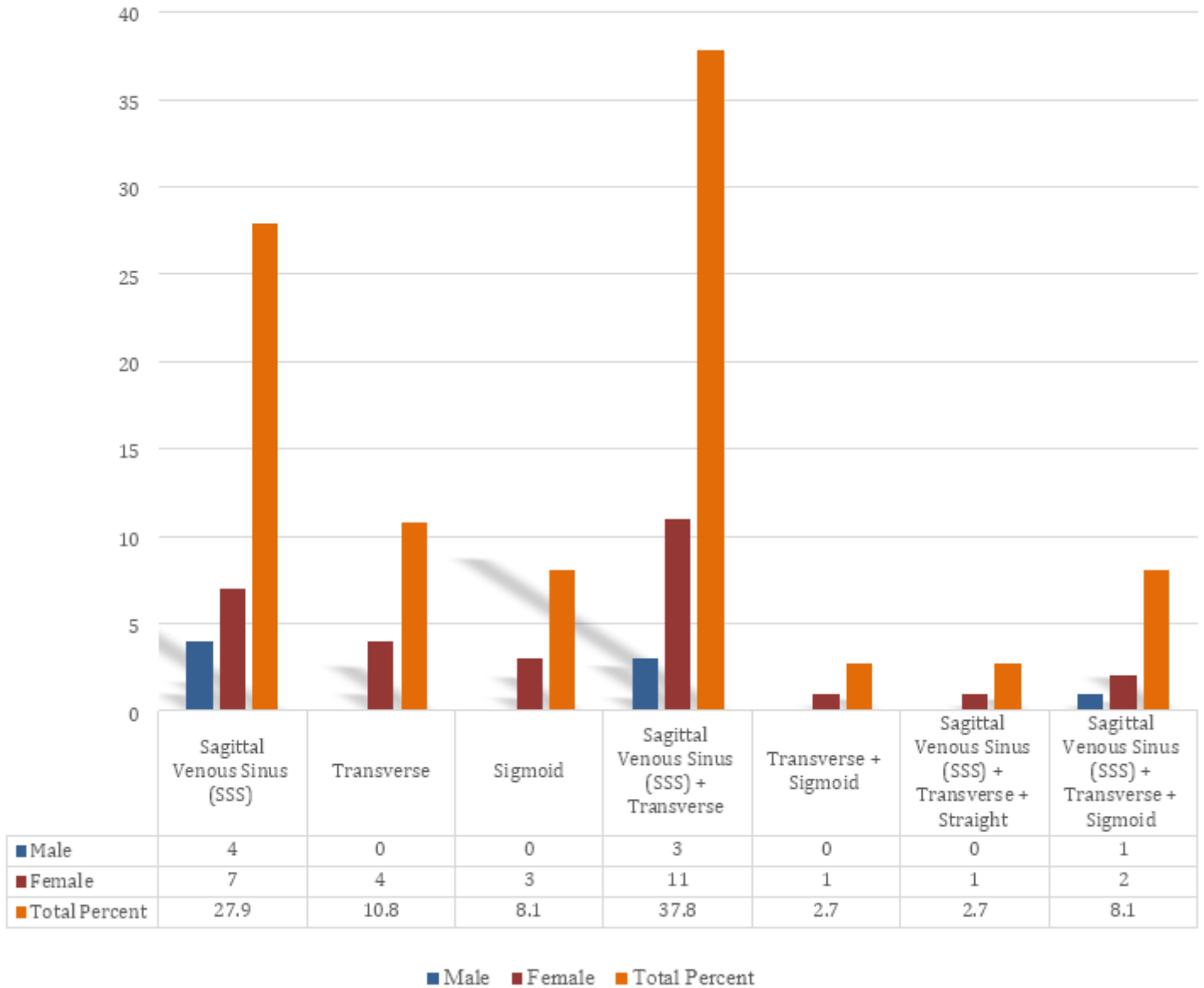


Figure 2

Shows the distribution of the patients with Cerebral Venous Sinus Thrombosis (CVST) according to the affected venous sinus from the imaging

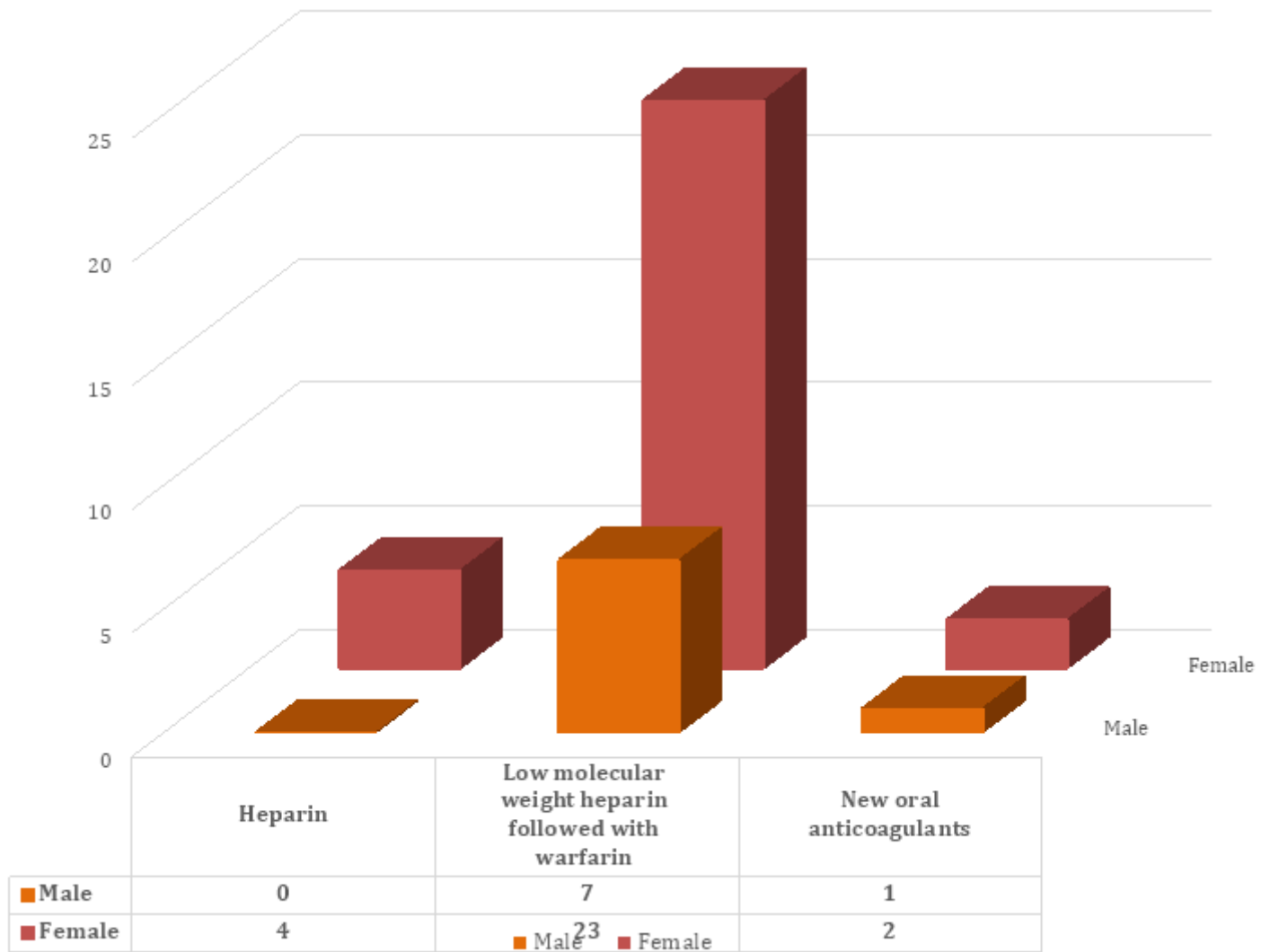


Figure 3

Shows the distribution of the patients with Cerebral Venous Sinus Thrombosis (CVST) according to the treatment options p value was not significant " > 0.05 "