

PREVALENCE OF CEREBRAL VENOUS SINUS THROMBOSIS IN PATIENTS PRESENTED WITH SECONDARY HEADACHE

Dr. Filzah Yousuf Qureshi^{1*}, Dr. Bashir A. Soomro², Dr. Nashmina Bashir Soomro³, Dr. Rabiah Nisar Usmani⁴, Dr. Rabia Mubarak Sheikh⁵

¹ Neurology Resident (FCPS), Department of Neurology, Ziauddin University Hospital, Karachi, Pakistan. Email: filzahq@gmail.com

² Professor of Neurology, Department of Neurology, Ziauddin University Hospital, Karachi, Pakistan. Email: bashir.soomro@zu.edu.pk

³ Senior House Officer (SHO), Emergency Medicine Department, Milton Keynes University Hospital NHS Foundation Trust, United Kingdom.

Email: nashminabashir97@gmail.com

⁴ Neurology Resident (MD), Department of Neurology, Ziauddin University Hospital, Karachi, Pakistan. Email: rabihanisar@gmail.com

⁵ Resident Neurology (MD), Department of Neurology, Ziauddin University Hospital, Karachi, Pakistan. Email: dr.sheikh19@gmail.com

*Corresponding Author: Dr. Filzah Yousuf Qureshi, Email: filzahq@gmail.com

ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is a rare but life-threatening secondary headache disorder. Sometimes it is difficult to diagnose because its clinical picture is variable, especially if no local neurological signs are present. The authors in this study found, from a hospital-based perspective, the prevalence of CVST in patients with clinically suspected secondary headache and described the clinical, radiological, treatment and short-term outcome characteristics.

Methods: This was a cross-sectional study with 100 patients between 18-60 years coming to the Department of Neurology, Ziauddin University Hospital, Karachi. Convenience sampling was used to recruit the participants. Eligible patients were those with clinically suspected secondary headache who underwent MRI as a part of usual care. Demographic data, characteristics of headache, neurologic manifestations, imaging results, treatment, and discharge outcomes were documented. SPSS 25 was used for data analysis. $P \leq 0.05$ considered significant.

Results: Mean age was 36.8 ± 11.4 years, females were 62%. Prevalence of CVST was 15.0% in 15 patients. CVST was significantly related to severe headache ($p=0.008$). Visual loss ($p=0.021$), loss of consciousness ($p=0.020$), loss of movement control ($p=0.005$), and seizures ($p<0.001$) were also significantly associated with CVST. The most frequent involvement was with the superior sagittal sinus. 93.3% received anticoagulation, 80% improved at discharge.

Conclusions: CVST was an important cause of secondary headache. CVST was strongly associated with severe headache and neurological red flags which can help to prompt timely clinical suspicion and suitable neuroimaging.

KEYWORDS: Cerebral Venous Sinus Thrombosis; Headache; Vascular Headaches; Prevalence; Magnetic Resonance Imaging.

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a rare, but potentially serious, cerebrovascular disorder characterized by a thrombosis of the cerebral veins or dural venous sinuses. In its presentation it is variable, with headache often being the first, or most prominent, symptom. CVST can be missed when patients with headache present to emergency services, as the presentation may mimic a primary headache disorder, especially in the absence of focal neurological deficits, seizures or altered consciousness [1].

CVST headaches can be caused by increased ICP, venous congestion, decreased CSF absorption or intracranial complications. Recent evidence has also shown the link between cerebral venous thrombosis and spontaneous intracranial hypotension, highlighting the varied mechanisms in which venous thrombosis can manifest as secondary headache [2]. Clinical features of CVST are extremely heterogeneous in patients with new onset headache and headache could be the initial sign of onset of CVST [3]. This variability can pose a challenge in diagnosis as patients with seemingly uncomplicated headache may have intracranial venous disease [4].

More than just the burden of cerebral venous thrombosis diagnosis and therapy, headache may continue after the acute stage [5]. The headache following CVT has, therefore, become an important outcome following the acute thrombotic event [6]. The persistence and diversity of headache patterns after CVT again assures the relationship between cerebral venous pathology and headache syndromes [7].

CVST is rare in the general population, but there is evidence of variation between settings and across time in population-based studies [8]. Epidemiological studies have also shown that CVST is seen in all age groups and all demographic groups, so it's important to have the diagnostic suspicion in the at-risk patient [9]. Recent data

from emergency departments have identified CVST as a low-prevalence, high-risk disorder with a variable presentation which may explain difficulties in diagnosis [10].

Although it was known that headache can be linked to CVST, there was still not enough evidence to determine the percentage of patients who presented with a headache as the primary presenting symptom, and who were subsequently diagnosed with CVST in the local clinical setting. So, this study was done with the aim of finding the prevalence rate of CVST in patients with secondary headache. The study was performed with the aim of providing local evidence that would have lent support to the earlier suspicion, proper imaging and rapid diagnosis and prevention of neurological complications.

METHODS

The cross-sectional study was conducted in Department of Neurology, Ziauddin University Hospital, Karachi during a period of 6 months. The sample size was calculated to be 100 patients was calculated using the OpenEpi sample size software, assuming cerebral venous sinus thrombosis prevalence of 15% in patients presenting with secondary headache, with 7% margin of error and 95% confidence level. Non-probability consecutive sampling technique was used in the recruitment of the participants. All patients, irrespective of gender, between 18 and 60 years of age, who met the operational definition of secondary headache and who had already been recommended for magnetic resonance imaging in the course of their clinical care by the patient's treating neurologist were recruited. Patients with history of trauma or neurologic diseases, diabetes mellitus, hypertension, ischemic heart disease, rheumatoid arthritis, other inflammatory brain diseases and contraindications for MRI (e.g., pacemaker, metal implants or severe claustrophobia) were excluded. All eligible participants signed written informed consent. Demographic data such as age, gender, residence, education and employment status was taken. Weight was measured with a digital weighing machine and height was measured using stadiometer and BMI was calculated. The characteristics of the headache, such as frequency, duration, severity (on a Visual Analog Scale), and suspected underlying pathology were recorded. Patients were also assessed for clinical features of CVST such as nausea, vomiting, visual loss, motor impairment, loss of consciousness and seizures. The MRI results were analysed to see if CVST was present or not. For CVST cases, the involved sinus, type of treatment received and clinical status at discharge were documented. SPSS 25 was used for data analysis. Quantitative variables were described as mean and standard deviation; qualitative variables were summarised as frequencies and percentages. Potential effect modifiers were controlled by stratification and a chi-square test was performed after stratification. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

One hundred patients with clinically suspected secondary headache were enrolled in the study. The mean age of the participants was 36.8 ± 11.4 years and 62% of these were females. The age group of 31-45 years was the largest age group with the majority of patients. Over half the patients experienced headache of subacute type, and about one-fifth of the patients experienced severe headache. Demographic and clinical characteristics of study population are listed in **Table I**.

Of 100 patients, 15 (15.0%) were found to have cerebral venous sinus thrombosis on neuroimaging. CVST was more common in patients with severe headache than in patients with mild or moderate headache. CVST was found to be statistically significant with the headache severity ($p=0.008$). CVST was also significantly associated with visual loss, loss of consciousness, motor impairment and seizures. CVST was most closely correlated with seizures ($p<0.001$). There was no significant correlation with age group, sex, place of residence, headache duration, nausea or vomiting. The clinical characteristics according to CVST status are presented in **Table II**.

The most common venous sinus in CVST was the superior sagittal sinus among the 15 patients who had CVST. Most of the CVST-positive patients were treated with anticoagulation, and most of them were clinically better at the time of discharge. The summary of radiological distribution, treatment received and short-term clinical outcomes of patients with confirmed CVST are presented in **Table III**.

Table I: Demographic and clinical characteristics of patients presenting with secondary headache (n=100)

Variables	Frequency (%) / Mean $\pm$ SD
Age, years	36.8 $\pm$ 11.4
Age groups	
18 to 30 years	32 (32.0)
31 to 45 years	40 (40.0)
46 to 60 years	28 (28.0)
Gender	
Male	38 (38.0)
Female	62 (62.0)
Residence	
Urban	73 (73.0)
Rural	27 (27.0)
Employment status	

Employed	48 (48.0)
Unemployed	52 (52.0)
BMI category	
Normal	42 (42.0)
Overweight	39 (39.0)
Obese	19 (19.0)
Headache severity (VAS)	
Mild	18 (18.0)
Moderate	43 (43.0)
Severe	39 (39.0)
Headache duration	
Acute	28 (28.0)
Subacute	55 (55.0)
Chronic	17 (17.0)
Nausea	46 (46.0)
Vomiting	38 (38.0)
Visual loss	21 (21.0)
Loss of consciousness	12 (12.0)
Loss of control over movement	10 (10.0)
Seizures	14 (14.0)
CVST present	15 (15.0)
CVST absent	85 (85.0)

Table II: Association of demographic and clinical characteristics with cerebral venous sinus thrombosis (n=100)

Variables	Total n	CVST Present n (%)	CVST Absent n (%)	p-value
Age group				0.386
18–30 years	32	6 (18.8)	26 (81.2)	
31–45 years	40	7 (17.5)	33 (82.5)	
46–60 years	28	2 (7.1)	26 (92.9)	
Gender				0.489
Male	38	4 (10.5)	34 (89.5)	
Female	62	11 (17.7)	51 (82.3)	
Residence				0.729
Urban	73	12 (16.4)	61 (83.6)	
Rural	27	3 (11.1)	24 (88.9)	
Headache severity				0.008*
Mild	18	0 (0.0)	18 (100.0)	
Moderate	43	4 (9.3)	39 (90.7)	
Severe	39	11 (28.2)	28 (71.8)	
Headache duration				0.276
Acute	28	2 (7.1)	26 (92.9)	
Subacute	55	11 (20.0)	44 (80.0)	
Chronic	17	2 (11.8)	15 (88.2)	
Nausea				0.144
Yes	46	10 (21.7)	36 (78.3)	
No	54	5 (9.3)	49 (90.7)	
Vomiting				0.106
Yes	38	9 (23.7)	29 (76.3)	
No	62	6 (9.7)	56 (90.3)	
Visual loss				0.021*
Yes	21	7 (33.3)	14 (66.7)	
No	79	8 (10.1)	71 (89.9)	
Loss of consciousness				0.020*
Yes	12	5 (41.7)	7 (58.3)	
No	88	10 (11.4)	78 (88.6)	
Loss of movement control				0.005*
Yes	10	5 (50.0)	5 (50.0)	
No	90	10 (11.1)	80 (88.9)	
Seizures				<0.001*

Yes	14	7 (50.0)	7 (50.0)	
No	86	8 (9.3)	78 (90.7)	

Table III: Radiological findings, treatment, and outcomes among patients with confirmed CVST (n=15)

Characteristics	Frequency n (%)
Location of thrombus	
Superior sagittal sinus	6 (40.0)
Transverse sinus	4 (26.7)
Sigmoid sinus	3(20.0)
Multiple/other sinuses	2(13.3)
Treatment initiated	
Anticoagulation	14(93.3)
Supportive/other	1(6.7)
Outcome at discharge	
Improved	12(80.0)
Static	2(13.3)
Worsened	1(6.7)

DISCUSSION

In the present study, 100 patients presenting with secondary headache were found to have cerebral venous sinus thrombosis in 15% of them. This means CVST is not a common diagnosis in the general population but was a significant diagnosis in a clinically selected headache population. Multicenter Indian registry data from the last few years have also pointed to the fact that CVST occurs in relatively young patients and is associated with a variety of features such as headache, vomiting, seizures, and altered consciousness [11]. Thus, the prevalence observed should not be viewed as an estimate of the prevalence in the population but as prevalence in patients preselected with red flag features, who were clinically indicated for neuroimaging.

Females were 62% of the study population and 73.3% of the CVST-positive cases. The current guidance acknowledges distinctive demographic and acquired risk factors for CVST and that its presentation can be variable, which can contribute to a low level of suspicion and delayed diagnosis [12]. Headache is a prominent symptom and can be accompanied by either a focal deficit or not, or by seizures or not, and by raised ICP or not [13]. We found that severe headache was significantly associated with CVST, but not the duration of headache. This helps give more focus to the severity of the headache and any neurological red flags. Reviews also emphasize CVST continuing to be a differential diagnosis for secondary headache as symptoms can be variable and nonspecific [14].

CVST was significantly associated with visual loss, loss of consciousness, motor impairment and seizures, and seizures had the highest association with CVST. Headache is reported as the most common symptom by imaging literature and focal neurologic manifestations and seizures as important presentations [15]. Most common site of involvement was the superior sagittal sinus followed by the transverse and sigmoid sinuses. Also, changes in CVST epidemiology have been demonstrated in contemporary literature, with the emergence of systemic prothrombotic conditions, such as the COVID-19 era [16].

This study's MRI confirmation aligns with the central role of neuroimaging in the diagnosis of CVST, when the clinical manifestations are not sufficiently specific [17]. CVST outcomes in COVID-19 hospitalizations also revealed that CVST may occur in unique high-risk settings and have atypical epidemiological characteristics [18]. The findings continue to support the idea that neurological presentation, as well as systemic thrombotic risk, should be taken into account.

93.3% of confirmed cases were given anticoagulation; 80% improved at discharge. Modern reviews focus on the importance of anticoagulation as the basis of therapy, and the changing etiologies and therapies for selected severe cases [19]. The predominance of female is also noteworthy as CVT during pregnancy has been linked to pregnancy, puerperium, dehydration, haematological abnormalities, autoimmune disease, and inherited thrombophilia [20].

The study evaluated clinically relevant population with suspected secondary headache with imaging confirmation and clinical, radiologic, treatment, and short-term outcome variables in single protocol.

Limitations of study: The small number of patients with the non-probability sampling, the single centre cross-sectional design, and selection of only those already chosen for MRI may have led to an overestimate of the prevalence. Thrombophilic, hormonal, pregnancy-related, infectious and drug-related risk factors were not systematically evaluated. Outcomes were only assessed at discharge.

RECOMMENDATIONS

Multi centre prospective studies should involve larger secondary-headache populations, standardized MR venography and detailed assessment of thrombotic risk-factors with longer follow-up. Prediction models

involving headache red flags, neurologic findings, risk factors should also be considered, especially in the emergency and outpatient neurology department in Pakistan.

CONCLUSION

CVST was diagnosed in 15% of the cases with a chief complaint of secondary headache. Important associated features were severe headache, visual loss, impaired consciousness, motor dysfunction and seizures. Timely diagnosis and treatment may be achieved with the use of neuroimaging if the diagnosis is suspected early.

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