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Anum Irfan
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Soban Khan
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Zaid Waqar
Pakistan Institute of Medical Sciences, Islamabad

Sumaira Nabi
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Bushra Khalid
Pakistan Institute of Medical Sciences, Islamabad, Pakistan

See next page for additional authors

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Authors

Anum Irfan, Soban Khan, Zaid Waqar, Sumaira Nabi, Bushra Khalid, and Muhammad Tariq

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NEUROLOGICAL MANIFESTATIONS OF CEREBRAL VENOUS THROMBOSIS: EXPERIENCE FROM A TERTIARY CARE CENTER

Anum Irfan[1], Soban Khan[1], Zaid Waqar[1], Sumaira Nabi[1], Bushra Khalid[1], Muhammad Tariq[1]
[1].Pakistan Institute of Medical Sciences, Islamabad, Pakistan

Corresponding author:Zaid Waqar *Pakistan Institute of Medical Sciences, Islamabad, Pakistan* ***Email:*** *chikky789@gmail.com*

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ABSTRACT

Background and objective:

Cerebral venous thrombosis (CVT) is a common cause of cerebrovascular accident (stroke). CVT is caused due to blockage in blood flow either in cerebral veins or in dural sinuses. The objective of this study was to determine prevalence of various clinical and imaging characteristics in patients with cerebral venous thrombosis.

Methods:

A descriptive retrospective cross-sectional patient data was collected from November 2019 to February 2021. This study was conducted in Neurology Department in Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. This study contains patient medical histories of 60 patients who were admitted in two and a half year time. Monitoring for any seizure occurrence was carried out for all the patients included in this study. Patient medical histories were examined and CT, MRI and MRV Brain were performed.

Results:

Superior sagittal sinus was spotted as a hot spot location for CVT. Mean age calculated was 30 while more frequency was recorded in female patients.

Conclusion:

CVT is a condition with more prevalence in younger population with more affected females than males. Most common presentation of CVT is headache. Superior sagittal sinuses involved in majority of cases reported. Specificity of modalities used and neurological manifestations needs a validation through a larger cohort study.

Key words: Cerebral venous thrombosis, cerebral veins, dural sinus, seizures, dural sinus thrombosis, cortical vein thrombosis, hemorrhagic infarct.

INTRODUCTION

Cerebral venous thrombosis (CVT) is cerebrovascular condition. CVT is caused due to blockage in blood flow either in cerebral vein or in dural sinus. CVT was documented initially by a French researcher Ribes in 1825. At that time, it was diagnosed through autopsy of a 45-year male who presented headache and seizures.[1] Blood blockage in lateral sinuses and superior sagittal was reported in this patient. John Abercrombie reported puerperal CVT first case in 1828. It was reported in 24-years old woman who presented headache and seizures two weeks after delivery. Blood blockage in superior sagittal sinus and cortical vein was detected through autopsy.[2] Not much of CVT research was carried out in nineteenth century. In the last decade of twentieth century modalities of neuroimaging such as catheter cerebral angiography and computed tomography (CT) and magnetic resonance venography (MRV) were developed and then refined over time. After the arrival of new technology several international researches from single-center or multi-centers were published which helped us to understand the dynamics of CVT.[3–6]

Headache is the foremost and most prevalent symptom of CVT verified through various researches.[7-9] Approximately 60–90% of these cases complained for having severe headache.[7] Though, the location of the brain part involved and description of these headaches were enormously variable with no recognizable pattern.[8]

It affects approximately five people per million yearly and contributes for less than 1% of all strokes.[10,11] It affects more females in comparison with males, particularly females of age between 20 to 50. International Study on Cerebral Venous Thrombosis (ISCVT) published a multi-center study; It reported that 78% of CVT cases were less than age of 50.[4,10] Moreover, 74.5% of reported cases were of females.[4] This gender inconsistency in CVT prevalence could be because of oral contraceptive usage, puerperium, estrogen fluctuations and pregnancy. Silvis et al. published a meta-analysis in which they estimated the frequency of CVT risk factors. Approx. 71% of females taking oral contraceptives and 59% of pregnant/puerperium females were reported to have CVT.[12]

A clot in veins forms because of fluctuations in prothrombotic and thrombolytic factors. Subsequently blood circulation within the cerebral veins and cerebral sinuses causes a back flow increasing capillary pressure and venous pressure.[13] High blood pressures together with this backflow causes breakage of blood-brain barrier and reduction in cerebral overflow, which in return leads to either intra cerebral hemorrhage or localized cerebral ischemia/edema.[13,14] Cerebral veins could be categorized into two areas: cerebral veins and dural venous sinuses. Venous sinuses have a major role in veins drainage and cerebrospinal fluid (CSF) absorption through Pacchionian granulations.[15] Consequently, clotting in sinus region could result in CSF absorption dysfunction and intracranial hypertension.[15] Most reported locations involved in CVT are lateral sinuses and superior sagittal sinus. In ISCVT report, 62% of CVT cases reported were in the superior sagittal sinus, with 44.7% in left lateral sinuses and 41.2% in right lateral sinuses.[4] Blood clotting in cortical vein could cause injury of brain parenchyma cells. Injury of parenchymal cells after blockage of veins depends on the size of clot, pressure of the capillary, breakage of blood-brain barrier and figures of robust collaterals.[16] Parenchymal injuries happen in approximately 50–60% cases of CVT, and unexpectedly, research on animal models proposes parenchymal injuries could also happen in blockage of dural venous sinuses.[16,17]

CVT widespread clinical presentation is headache. Second most prevalent is seizures, in which approx. 80% of acute symptomatic seizures happening before CVT diagnosis.[18] More details about its clinical presentation depends on the structural locations of the clotting and affected parenchymal cells of brain. Patients suffering from dural venous sinus blockage lacking hemorrhage usually presents as intracranial hypertension syndrome symptoms including decreased visual acuity, papilledema, and headache. A clotting of deep venous system causes mental status conditions, coma, or diffuse encephalopathy. Cases with cavernous sinus blood clot shows with proptosis, orbital pain, ophthalmoplegia, or chemosis.[11] Mainstay treatment opportunities are heparin or low molecular weight heparin (LMWH) along with connection with warfarin or direct acting oral anticoagulants.[10] Patients who do not improve when treated with mentioned medications were referred for decompressive craniectomy or endovascular treatment.[10,19]

The present study was conducted to assess neurological manifestations of CVT and gender wise distribution in Pakistani population.

METHODS

Study design: Descriptive, retrospective cross-sectional study.

Place and duration of study: This study was conducted in Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan and contains patient data from November 2019 to February 2021.

Sample size: Sixty patients of CVT were admitted in the period.

Sampling technique: Non-probability consecutive sampling.

Data collection: This study contains records of 60 patients which were admitted with CVT in two and a half year time. Monitoring for any seizures occurrence was carried out for all the patients included in this study. Patient medical histories were examined. Age of patient, gender of patients, their clinical diagnosis, demographics, CT, MRI and MR venography (MRV) results and duration and findings of monitoring were listed.

Data analysis: The data was analyzed using SPSS version 25.0

Ethical considerations: This study was approved by the Ethics Review Committee of Pakistan Institute of Medical Sciences.

RESULTS

All of the 60 patients admitted in the study underwent monitoring for CVT during admission time. When patients were listed according to their gender, 12 patients were male while 48 patients were female. Figure 1 is illustrating the gender wise distribution of patients included in the study.

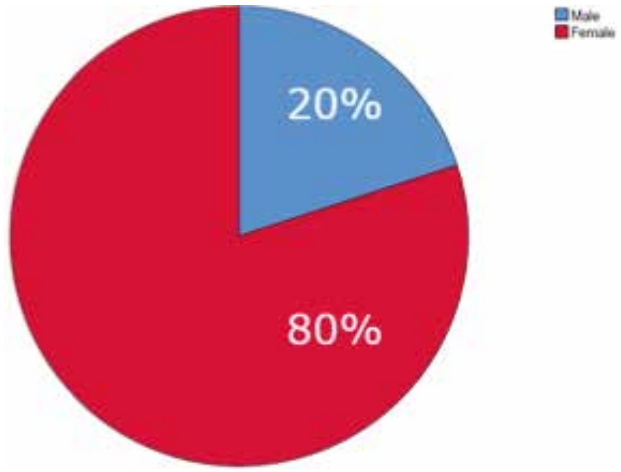
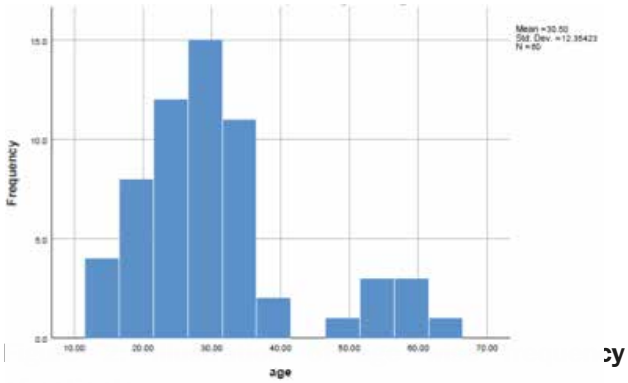


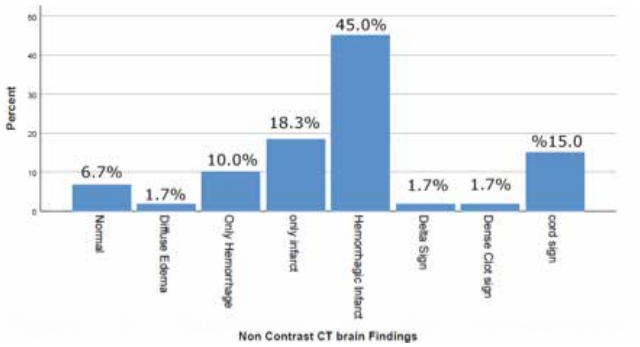
Figure 1: Illustration of the gender distribution in patients

When patient data was distributed according to their age, mean age calculated was 30 years and highest number of patients were present in age between 25 to 30 years. Figure 2 is illustrating the age wise frequency of patients included in the study.



of patients

When patient data was distributed on the bases of non-contrast CT brain imaging, hemorrhagic infarct was visualized in highest number of CT (27 cases). In 11 cases, CT depicted infarct while cord sign was visible in 9 cases. Other CT showed normal (4 cases), hemorrhage (6 cases), diffuse edema (1 case), delta sign (1 case) and dense clot sign (1 case) in imaging. Figure 3 is illustrating the non-contrast CT findings in patients included in the study.



CT findings

When patient data was distributed on the basis of brain MRI, unilateral hemorrhagic infarct was visualized in highest number cases (26). In 10 cases, MRI depicted unilateral infarct while in 8 cases, MRI was normal. Other MRI showed unilateral hemorrhage(7 cases), bilateral hemorrhagic infarct (4 cases), bilateral infarct (3 case), diffuse edema (1 case) and evidence of clot (1 case) in results. Figure 4 is illustrating the MRI brain findings in patients included in the study.

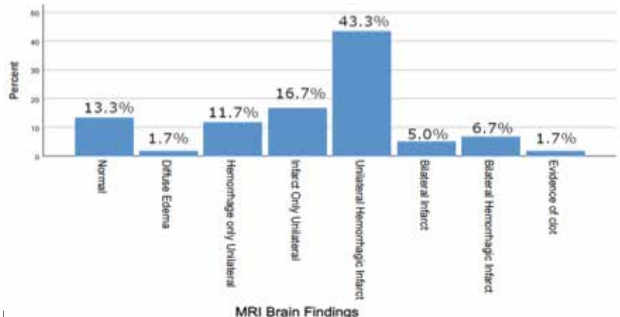


Figure 4: Illustration of MRI brain findings

When MRV was carried out for the patients included in the study, superior sagittal sinus involvement was recorded in the highest number of cases (22.0%). Second most involved location was right transverse sinus (16.8%). Third most involved location recorded was left transverse sinus (15.0%). Other location whose involvement was recorded in MRV results were right sigmoid sinus (12.7%), left sigmoid sinus (12.1%), right internal jugular vein (6.4%), left internal jugular vein (4.6%), Galen's vein (1.7%), straight sinus (4.0%), inferior sagittal sinus (2.9%) and cortical vein (1.7%).

Details about location and its involvement in CVT are given in Table 1.

Table 1: Data about location and its involvement in CVT

		Responses	
		N	Percent
MRV Brain Findings[a]	Right Transverse sinus involvemenet	29	16.8%
	Left Transverse sinus involvemenet	26	15.0%
	Right sigmoid sinus involvemenet	22	12.7%
	Left sigmoid sinus involvemenet	21	12.1%
	Right Internal Jugular Vein Involvement	11	6.4%
	Left interal jugular vein involvement	8	4.6%
	Superior sagittal sinus involvement	38	22.0%
	Galen's vein involvement	3	1.7%
	Straight Sinus Involvement	7	4.0%
	Inferior sagittal sinus involvement	5	2.9%
	Cortical vein involvement	3	1.7%
Total		173	100.0%

When MRV data was divided on bases of patient gender included in the study, left transverse sinus (58.3%), superior sagittal sinus (58.3%) and right transverse sinus (50.0%) involvement was recorded in most of the male patients. Superior sagittal sinus (64.6%), right transverse sinus (47.9%) and left transverse sinus (39.6%) involvement was recorded in most of the female patients. Details about location and its involvement in CVT on the bases of gender are given in Table 2.

Table 2: Data about location and its involvement in CVT on the bases of gender

			gender		
			Male	Female	Total
MRV Brain Findings[a]	Right Transverse sinus involvemenet	Count	6	23	29
		% within gender	50.0%	47.9%	
	Left Transverse sinus involvemenet	Count	7	19	26
		% within gender	58.3%	39.6%	
	Right sigmoid sinus involvemenet	Count	5	17	22
		% within gender	41.7%	35.4%	
	Left sigmoid sinus involvemenet	Count	7	14	21
		% within gender	58.3%	29.2%	
	Right Internal Jugular Vein Involvement	Count	3	8	11
		% within gender	25.0%	16.7%	
	Left interal jugular vein involvement	Count	3	5	8
		% within gender	25.0%	10.4%	
	Superior sagittal sinus involvement	Count	7	31	38
		% within gender	58.3%	64.6%	
	Galen's vein involvement	Count	2	1	3
		% within gender	16.7%	2.1%	
	Straight Sinus Involvement	Count	2	5	7
		% within gender	16.7%	10.4%	
	Inferior sagittal sinus involvement	Count	2	3	5
		% within gender	16.7%	6.3%	
	Cortical vein involvement	Count	0	3	3
		% within gender	0.0%	6.3%	
Total		Count	12	48	60

Table 3, 4 and 5 present the details of headache, seizures, papilledema and Glasgow Coma Scale (GCS) in the study population.

Table 3: Percentage of our patients who reported headache and seizures respectively

Headache

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	60	100.0	100.0	100.0

Seizures

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	34	56.7	56.7	56.7
	No	26	43.3	43.3	100.0
	Total	60	100.0	100.0	

Table 4: Different percentages of papilledema reported in our study

Papilledema

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Absent	32	53.3	53.3	53.3
	Grade 1	9	15.0	15.0	68.3
	Grade 2	10	16.7	16.7	85.0
	Grade 3	4	6.7	6.7	91.7
	Grade 4	5	8.3	8.3	100.0
	Total	60	100.0	100.0	

Table 5: Glasgow coma scale grouped percentages

Glasgow coma scale

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	13-15	43	71.7	71.7	71.7
	9-12	15	25.0	25.0	96.7
	3-8	2	3.3	3.3	100.0
	Total	60	100.0	100.0	

DISCUSSION

CVT is a vital contributing factor of stroke in adult patients (mean age = 33 years) (two-third prevalence in females). It is majorly caused due to partial blockage or complete occlusion of the cerebral venous sinuses or blockage of cortical veins. It often remains undiagnosed or is diagnosed late as it could imitate different serious neurological ailments and could be diagnosed only via exquisite and timely imaging of brain.

Present study includes 60 adult individuals suffering from CVT, their clinical diagnosis and neuroimaging were recorded and analyzed. Our study co-relates with Neetu et al. research in which females constituted two third of the cases.[20] Mean age in our study was recorded as 30 years. Our study co-relates with an Indian study by Narayan et al., in which 428 successive CVT patients were registered 8 years of duration. Mean age was recorded as 31.3 years for CVT patients.[21]

All individuals included in this study went through brain imaging. Modalities used were CT head, MRI and MRV brain. In brain CT and MRI, hemorrhagic infract was recorded in most of the cases. IN MRV, superior sagittal sinus and transverse sinus (both right and left) were recorded in most of the cases. In a study including UAE and Pakistani patients of CVT, Khealani et al.,reported that 66% of cases had infarctions and 37 (34%) out of these had hemorrhagic infract. In 54 of the cases (50%), only single type sinus was observed which was superior sagittal sinus. It was subsequently followed by transverse sinuses and sigmoid sinuses. [22]

In our study population headache was reported in all (100%) patients at some point in disease course and was the most common manifestation followed by seizures as the second most common manifestation. Similar findings were reported in other studies with headache and seizures being the two most common manifestations.[23,24] All of the female cases reported in our study population presented in association with obstetric / gynecological risk factors i.e., either use of OCP, fertility treatment, or pregnancy/postpartum. This high percentage of obstetric/ gynecological complications is mirroring other studies .[24]

There were various limitations in this study. Firstly, number of cases included are inadequate for the true prediction of several clinical features percentages and risk factors associated with CVT. Secondly, all cases included were from single health care faculty. Lastly, even though the specificity of modalities used and their sensitivity appears to be pretty fare but still it is a necessity that its validation should be checked in a larger cohort.

CONCLUSION

CVT is a condition with more prevalence in younger population with more affected females than males. Most common presentation of CVT is headache followed by seizures. Superior sagittal sinus is involved in majority of cases reported. Specificity of modalities used and neurological manifestations needs a validation through a larger cohort study.

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Authors' contribution:
Anum Irfan; Design, data collection, data analysis manuscript writing
Soban Khan; Design, data collection, manuscript writing
Zaid Waqar; Concept, data collection, manuscript revision
Sumaira Nabi; Concept, design, manuscript revision
Bushra Khalid; Design, data collection, manuscript writing
Muhammad Tariq; Concept, data collection, manuscript writing