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Original Article

Clinical Outcome of Cortical Venous Thrombosis in Stroke Patients at a Tertiary Care Hospital of Southern Punjab

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ABSTRACT

Objective: This study was determined to find out the clinical Outcome of Cortical Venous Thrombosis (CVT) in Stroke patients at a Tertiary Care Hospital of Southern Punjab.

Material & Methods: A total of 100 patients with cortical venous thrombosis were included in this descriptive case series study, which was conducted at Department of Neurology, Nishtar Hospital Multan. Outcome of patients in terms of partial recovery or complete recovery, any recurrence, any complication, indication for Surgery and any disability in terms of focal deficit, prolonged hospital stay and Mortality was followed.

Results: Our study included a total of 100 patients with cortical venous thrombosis (CVT), 35 (35%) were male and 65 (65%) were female patients with their mean age was 37.69 ± 16.52 years, ranging from 20 – 83 years (51.37 ± 17.44 in males versus 30.32 ± 10.15 years for females). Headache was noted in 80%, focal deficit in 57%, nerve palsy in 30%, coma in 22% and disability was noted in 35%. Partial recovery was noted in 65%, whereas complete recovery was noted in 35% while, complications were noted in 12 (12%) of these patients with CVT.

Conclusion: Cortical venous thrombosis was more prevalent in females in their younger age groups and it was associated with poor prognosis as high frequency of partial recovery was noted in our study.

Keywords: Cortical venous thrombosis, Stroke, headache, recovery, outcome.

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INTRODUCTION

Stroke is a significant cause of mortalities, disabilities and is associated with more than 5 million deaths annually.^{1,2} Of these deaths, estimated 66% of these occur in poor and middle income countries like Pakistan and hence has significant impact on the health economy of these countries due to loss in the productivity of adult

young population.³ It has also been observed that majority of stroke patients in these countries are younger than those from developed countries. World Health Organization (WHO) has estimated that stroke will be the second cause of death in this decade along with cardiovascular diseases in developing countries exhibiting 2 major subtypes; ischemic and hemorrhagic^{4,5} having different therapeutic techniques emphasizing towards role of diagnostic tools for optimal management of stroke patients. Thrombolytic or anti-platelet therapy is employed in ischemic stroke patients hemostatic therapy is required for the treatment of hemorrhagic stroke^{6,7} and these therapies should, ideally, be started immediately after onset of stroke symptoms to improve outcomes and prognosis.⁸ In addition, stroke patients in underdeveloped countries are 10 years younger than their western counterparts and hence the burden of sustained disability in survivors is greater.^{9,10} Ischemic Stroke accounts for 60 – 90% percent of all stroke cases in Pakistan, which occurs due to obstruction of certain blood vessels that supply blood to brain.¹¹

An ischemic stroke is of two types, that is, the arterial and venous variety commonly known as cortical venous Thrombosis. The available data suggested that cortical venous thrombosis (CVT) is uncommon. An annual incidence of CVT has been reported to be ranging from 0.2 to 1.6 approximately per 100, 000 individuals, being more prevalent in women. This higher proportion imbalance and burden of cortical venous Thrombosis (CVT) in females can be described in terms of pregnancy, use of oral contraceptive drugs and puerperium.¹² Sassi et al¹³ from Tunisia has reported 6.6% mortality in CVT and 87.5% had a good outcome while another study from Oman by Al – Hashmi et al¹⁴ has documented 68.5% complete recovery, 29.6 % partial recovery and mortality rate was 1.9%.

Upon comprehensive research, it was revealed that there is scarcity of local data on this topic to generate evidence based strategies in our

population. The current study aimed to generate useful baseline data based on our local population to ascertain the current magnitude of the problem. This will help to enhance prognosis and clinical outcome of these patients to reduce disease related morbidity and mortality.

MATERIAL & METHODS

Sample Size & Technique

A total of 100 newly diagnosed patients with cortical venous thrombosis were included in this descriptive case series study, which was conducted at Department of Neurology, Nishtar Hospital Multan from 1st January 2020 to 30 September 2020. The sample size was calculated with WHO sample size calculator for single proportion using mortality (p) = 6.6%.¹³ The Confidence interval was 95% and margin of error was 5. The calculated sample size was 95 which was rounded to 100 patients.

Inclusion Criteria

100 cases of Fire episode of cortical venous infarct were included.

Exclusion Criteria

Recurrent cases of cortical venous sinus thrombosis, patients with sepsis & metabolic abnormalities, patients with co morbidities like chronic renal failure, chronic liver disease and tumors were excluded from our study.

Data Collection

Prior Permission from Institutional ethical review committee was taken. Informed and written consent were taken and each Patient was evaluated as per written questionnaire. The demographic data including age, sex, residential address, marital Status, educational status & family income was obtained. Clinical data

including medical history, family history, history of oral Contraceptive use, presence of risk factors like Pregnancy, hyper-homocystinemia, infection, dehydration, presence of headache, seizure, any focal deficit and duration of Symptoms were obtained. Laboratory data in particular hypercoagulable states like Protein C&S deficiency, D-Dimers, PT, APTT, Antineutrophil Antibodies, Antiphospholipid Antibodies and cerebrospinal fluid (CSF) findings and involvement of venous sinuses on neuroimaging was obtained and evaluated.

Outcome of patients in terms of partial recovery or complete recovery, any recurrence, any complication, indication for Surgery and any disability in terms of focal deficit and prolonged hospital stay and mortality was followed.

Data Analysis

All data was entered and analyzed using SPSS v23.0. Frequencies and percentages were described for all of the following categorical variables. Effect modifiers such as gender and marital status was arranged by stratification. There was no bias due to randomization. The main outcome variables were as follows: outcome of treatment (partial recovery, complete recovery or expired), duration of stay in hospital, presence of any recurrence and Presence of any Disability. The dependent variables are as follows: socioeconomic class, pregnancy/ puerperium, presence of seizure and presence of coma.

Post-stratification chi-squared test was applied to assess any relationship between the frequency of different risk

Table 1: Stratification of the outcome with respect to gender.

Parameter		Outcome		P – value
		Partial Recovery (n =65)	Complete Recovery (n =35)	
Gender	Male (n = 35)	19	16	0.125
	Female (n = 65)	46	19	

Table 2: Stratification of the outcome with respect to the residential status.

Parameter		Outcome		P – value
		Partial Recovery (n =65)	Complete Recovery (n =35)	
Residential status	Rural (n = 53)	35	18	0.837
	Urban (n = 47)	30	17	

Table 3: Stratification of the outcome with respect to the socioeconomic status.

Parameter		Outcome		P – value
		Partial Recovery (n =65)	Complete Recovery (n =35)	
Socioeconomic status	Poor (n = 60)	39	21	0.999
	Middle Income (n = 40)	26	14	

Table 4: Stratification of the outcome with respect to marital status.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Marital status	Married (n = 94)	62	32	0.420
	Unmarried (n = 06)	03	03	

Table 5: Stratification of the outcome with respect to literacy.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Literacy	Illiterate (n = 57)	42	15	0.056
	Literate (n = 43)	23	20	

factors and the outcome variables p value less than 0.05 as a level of significance.

RESULTS

Our study included a total of 100 newly diagnosed patients with cortical venous thrombosis (CVT).

Age and Gender Distribution

35 (35%) were male and 65 (65%) were female patients with their mean age was 37.69 ± 16.52 years, ranging from 20 – 83 years (51.37 ± 17.44 in males versus 30.32 ± 10.15 years for females) as shown in Table 1.

Socioeconomic Status

Thirty five (35%) were from rural areas as shown in Table 2. 60% were poor and 40% were middle income as shown in Table 3.

Marital Status and Literacy

Ninety four (94%) were married as shown in Table 4. 57% were illiterate as shown in Table 5.

Clinical Features

26% had positive family history of stroke as shown in Table 6. 20% were in pro thrombotic condition as shown in Table 7. Use of oral contraceptive drugs was noted in 29% as shown in Table 8 and dehydration in 22% in Table 9.

Headache was noted in 80% as shown in Table 10. Focal deficit in 57% as shown in Table 11. Nerve palsy in 30% as shown in Table 12. Coma in 22% as shown in Table 13 and disability

Table 6: Stratification of the outcome with respect to family history.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Family History	Yes (n = 26)	17	09	0.999
	No (n = 74)	48	26	

Table 7: Stratification of the outcome with respect to Prothrombotic condition.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Prothrombotic condition	Yes (n = 20)	13	07	0.999
	No (n = 80)	52	28	

Table 8: Stratification of the outcome with respect to oral contraceptive.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Oral contraceptive	Yes (n = 29)	22	07	0.171
	No (n = 71)	43	28	

Table 9: Stratification of the outcome with respect to dehydration.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Dehydration	Yes (n = 22)	10	12	0.042
	No (n = 78)	55	23	

Table 10: Stratification of the outcome with respect to presence/absence of headache.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Headache	Yes (n = 80)	51	29	0.794
	No (n = 20)	14	06	

was noted in 35% as shown in Table 15.

Outcome and Recovery

Partial recovery was noted in 65%, whereas complete recovery was noted in 35%. Parameters like dehydration ($p = 0.042$), nerve palsy ($p = 0.043$), coma ($p = 0.022$), complications ($p = 0.007$) and disability ($p = 0.001$) showed a significant association with partial recovery as shown in the Tables 9 and 12-15. While, distribution of outcome has been given in each table 1 to 15. Complications were noted in 12 (12%) of these patients with CVT as shown in Table 14.

Table 11: Stratification of the outcome with respect to presence/absence of focal deficit.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Focal deficit	Yes (n = 57)	33	24	0.095
	No (n = 43)	32	11	

Table 12: Stratification of the outcome with respect to presence/absence of nerve palsy.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Nerve palsy	Yes (n = 30)	24	06	0.043
	No (n = 70)	41	29	

Table 13: Stratification of the outcome with respect to presence/absence of coma.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Coma	Yes (n = 22)	19	03	0.022
	No (n = 78)	46	32	

Table 14: Stratification of the outcome with respect to complication.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Complications	Yes (n = 12)	12	00	0.007
	No (n = 88)	53	35	

Table 15: Stratification of the outcome with respect to presence/absence of disability.

Parameter		Outcome		P – value
		Partial Recovery (n = 65)	Complete Recovery (n = 35)	
Disability	Yes (n = 35)	32	03	0.001
	No (n = 65)	33	32	

DISCUSSION

Cortical venous thrombosis (CVT) is regarded as uncommon neurovascular disorder presenting with a high degree of variation in clinical presentation, diverse etiologies & disease course and may lead to late diagnosis due to less burden of the disease and incongruous presentation with its incidence being reported around 5 million per year.^{15,16} Incidence of CVT is increasing day by day due to advancement of diagnostic modalities (such as CT and MRI) all over the world and new cases are being reported regularly showing upward trends in disease burden.^{17,18} Early diagnosis is crucial for the prognosis of the disease which leads to the early recovery, return to work, physical activities and productivity of the patient.¹⁵⁻¹⁸ We performed this study in 100 newly diagnosed patients of the CVT to ascertain the outcome of the CVT in these patients.

Our study included a total of 100 newly diagnosed patients with cortical venous thrombosis (CVT), 35 (35%) were male and 65 (65%) were female patients. A study conducted by Wasay et al¹⁹ from Karachi has also reported high female gender preponderance with 60% female patients. A study conducted in different parts of the world by Khealani et al²⁰ has also reported 53% CVT patients were females. Devasagayam et al²¹ also reported 52% female patients with CVT from Australia, similar to our results. Coutinho et al²² from Netherland has also reported 72% female gender preponderance in CVT patients. Mehndiratta et al²³ from India has also reported 66% CVT female patients' preponderance.

Mean age of our patients was 37.69 ± 16.52 years, ranging from 20 – 83 years. A study conducted by Wasay et al¹⁹ from Karachi has also reported 37 years as the mean age in CVT patients. A study conducted in different parts of the world by Khealani et al²⁰ has also reported 35.76 ± 13.15 years as the mean age of the CVT patients showing similar results and also reported

that female CVT patients were significantly younger than male patients. Devasagayam et al²¹ from Australia reported 49 years mean age, which is slightly higher which indicates that CVT is more prevalent in our population in younger ages. Similar to our results, another study conducted by Coutinho et al²² from Netherland has also reported 41 years as median age. Mehndiratta et al²³ from India has reported 41.5 years as a mean age among male CVT patients compared with 27.75 years as a mean age for female CVT patients, showing similar trends of disease burden in young females as that of our results.

Thirty five (35%) were from rural areas, 60 % were poor and 40% were middle income. Ninety four (94%) were married, 57% were illiterate, 26% had positive family history of stroke, 20% were in prothrombin condition, use of oral contraceptive drugs was noted in 29% and dehydration in 22%. A study conducted by Wasay et al¹⁹ from Karachi has also reported similar results. Devasagayam et al²¹ from Australia reported 31% use of oral contraceptive drugs in CVT patients, similar to our findings. Coutinho et al²² from Netherland has also reported 52% use of oral contraceptive drugs.

Headache was noted in 80%, focal deficit in 57%, nerve palsy in 30%, coma in 22% and disability was noted in 35%. A study conducted by Wasay et al¹⁹ from Karachi has also reported 68% headache, coma in 19% and 23% neurological deficit, similar to our results. A study conducted in different parts of the world by Khealani et al²⁰ has also reported 81% headache, 45% focal deficit and 37% coma.

Partial recovery was noted in 65%, whereas complete recovery was noted in 35% and complications were noted in 12 (12%) of these patients with CVT. A study conducted in different parts of the world by Khealani et al²⁰ has reported 6% mortality and 40% partial recovery while in our study there was no mortality while 65% CVT patients had partial recovery. Devasagayam et al²¹

from Australia reported 12% mortality, however, there was no mortality in our study.

In our study, various underlying factors such as dehydration ($p = 0.042$), nerve palsy ($p = 0.043$), coma ($p = 0.022$), complications ($p = 0.007$) and disability ($p = 0.001$) showed a significant association with partial recovery. Khealani et al²⁰ has reported coma and functional status to be predictors of poor outcomes on univariate analysis, similar to our results while Khealani et al²⁰ also reported coma was an independent predictor of mortality in these patients. However there was no mortality in our study cases. Similar results have been reported by Kalita et al³ from India.

CONCLUSION

Cortical venous thrombosis was more prevalent in females in their younger age groups and it was associated with poor prognosis as high frequency of partial recovery was noted in our study. Partial recovery was significantly associated with literacy, dehydration, nerve palsy, coma, complications and disability.

Limitation

This study conducted on a limited number of sample size and thus further studies are required for evaluation.

REFERENCES

1. Maali L, Khan S, Qeadan F, Ismail M, Ramaswamy D, Hedna VS. Cerebral venous thrombosis: continental disparities. *Neurol Sci.* 2017; 38 (11): 1963-1968. Doi: 10.1007/s10072-017-3082-7.
2. Goyal G, Charan A, Singh R. Clinical Presentation, Neuroimaging Findings, and Predictors of Brain Parenchymal Lesions in Cerebral Vein and Dural Sinus Thrombosis: A Retrospective Study. *Ann Indian Acad Neurol.* 2018; 21 (3): 203-208. Doi: 10.4103/aian.AIAN_470_17.
3. Kalita J, Singh VK, Jain N, Misra UK, Kumar S. Cerebral Venous Sinus Thrombosis Score and its Correlation with Clinical and MRI Findings. *J Stroke Cerebrovasc Dis.* 2019; 28 (11): 104324. Doi: 10.1016/j.jstrokecerebrovasdis.2019.104324.
4. Wang Y, Meng R, Duan J, Liu G, Chen J, Li S, Ji X. Nephrotic Syndrome May Be One of the Important Etiologies of Cerebral Venous Sinus Thrombosis. *J Stroke Cerebrovasc Dis.* 2016; 25 (10): 2415-22. Doi: 10.1016/j.jstrokecerebrovasdis.2016.06.013.
5. Gunes HN, Cokal BG, Guler SK, Yoldas TK, Malkan UY, Demircan CS, Yon MI, Yoldas Z, Gunes G, Haznedaroglu IC. Clinical associations, biological risk factors and outcomes of cerebral venous sinus thrombosis. *J Int Med Res.* 2016; 44 (6): 1454-1461. Doi: 10.1177/0300060516664807.
6. Lee DJ, Ahmadpour A, Binyamin T, Dahlin BC, Shahlaie K, Waldau B. Management and outcome of spontaneous cerebral venous sinus thrombosis in a 5-year consecutive single-institution cohort. *J Neurointerv Surg.* 2017; 9 (1): 34-38. Doi: 10.1136/neurintsurg-2015-012237.
7. Jankowitz BT, Bodily LM, Jumaa M, Syed ZF, Jovin TG. Manual aspiration thrombectomy for cerebral venous sinus thrombosis. *J Neurointerv Surg.* 2013; 5 (6): 534-8. Doi: 10.1136/neurintsurg-2012-010476.
8. Adachi H, Mineharu Y, Ishikawa T, Imamura H, Yamamoto S, Todo K, Yamagami H, Sakai N. Stenting for acute cerebral venous sinus thrombosis in the superior sagittal sinus. *Interv Neuroradiol.* 2015; 21 (6): 719-23. Doi: 10.1177/1591019915609120.
9. Zhang S, Hu Y, Li Z, Huang D, Zhang M, Wang C, Wang Z. Endovascular treatment for hemorrhagic cerebral venous sinus thrombosis: experience with 9 cases for 3 years. *Am J Transl Res.* 2018; 10 (6): 1611-1619.
10. Wang Y, Zhao C, Huang D, Sun B, Wang Z. Stent retriever thrombectomy combined with long-term local thrombolysis for severe hemorrhagic cerebral venous sinus thrombosis. *Exp Ther Med.* 2020; 20 (5): 66. Doi: 10.3892/etm.2020.9194.
11. Ilyas A, Chen CJ, Raper DM, Ding D, Buell T, Mastorakos P, Liu KC. Endovascular mechanical thrombectomy for cerebral venous sinus thrombosis: a systematic review. *J Neurointerv Surg.* 2017; 9 (11): 1086-1092.
12. Cabral de Andrade G, Lesczynsky A, Clímico VM, Pereira ER, Marcelino PO, Franco A, De Almeida

- DF. Cerebral venous sinuses thrombosis in both transverse sinus and torcula: Multistep endovascular treatment and stenting. *Interv Neuroradiol.* 2017; 23 (1): 84-89. Doi: 10.1177/1591019916674917.
13. Sassi SB, Touati N, Baccouche H, Drissi C, Romdhane NB, Hentati F. Cerebral Venous Thrombosis: A Tunisian Monocenter Study on 160 Patients. *Clin Appl Thromb Hemost.* 2017; 23 (8): 1005-1009. Doi: 10.1177/1076029616665168.
14. Al Hashmi K, Al Wahaibi K, Al-Khabori M, Al Lamki S. Characteristics and Outcomes of Patients with Cerebral Venous Sinus Thrombosis. *Oman Med J.* 2019; 34 (5): 434-437. Doi: 10.5001/omj.2019.79.
15. Bushnaq SA, Qeadan F, Thacker T, Abbas M, Carlson AP. High-Risk Features of Delayed Clinical Progression in Cerebral Venous Thrombosis: A Proposed Prediction Score for Early Intervention. *Interv Neurol.* 2018; 7 (6): 297-307. Doi:10.1159/000487960
16. Siddiqui FM, Weber MW, Dandapat S, Scaife S, Buhnerkempe M, Ortega-Gutierrez S, Aksan N, Elias A, Coutinho JM. Endovascular Thrombolysis or Thrombectomy for Cerebral Venous Thrombosis: Study of Nationwide Inpatient Sample 2004-2014. *J Stroke Cerebrovasc Dis.* 2019; 28 (6): 1440-47. Doi: 10.1016/j.jstrokecerebrovasdis.2019.03.025.
17. Nasr DM, Brinjikji W, Cloft HJ, Saposnik G, Rabinstein AA. Mortality in cerebral venous thrombosis: results from the national inpatient sample database. *Cerebrovasc Dis.* 2013; 35 (1): 40-4. Doi: 10.1159/000343653.
18. Korathanakhun P, Sathirapanya P, Geater SL, Petpichetchian W. Predictors of hospital outcome in patients with cerebral venous thrombosis. *J Stroke Cerebrovasc Dis.* 2014; 23 (10): 2725-2729. Doi: 10.1016/j.jstrokecerebrovasdis.2014.06.020.
19. Wasay M, Kojan S, Dai AI, Bobustuc G, Sheikh Z. Headache in cerebral venous thrombosis: incidence, pattern and location in 200 consecutive patients. *J Headache Pain.* 2010; 11: 137-39.
20. Khealani BA, Wasay M, Saadah M, Sultana E, Mustafa S, Khan FS, Kamal AK. Cerebral venous thrombosis: a descriptive multicenter study of patients in Pakistan and Middle East. *Stroke*, 2008; 39(10):2707-11. Doi: 10.1161/STROKEAHA.107.512814.
21. Devasagayam S, Wyatt B, Leyden J, Kleinig T. Cerebral Venous Sinus Thrombosis Incidence Is Higher Than Previously Thought: A Retrospective Population-Based Study. *Stroke*, 2016; 47 (9): 2180-2.
22. Coutinho JM, Zuurbier SM, Aramideh M, Stam J. The incidence of cerebral venous thrombosis: a cross-sectional study. *Stroke*, 2012; 43 (12): 3375-7. Doi: 10.1161/STROKEAHA.112.671453.
23. Mehndiratta M, Garg S, Gurnani M. Cerebral venous thrombosis – clinical presentations. *J Pak Med Assoc.* 2006; 56 (11): 513-5.

Additional Information

Disclosures: Authors report no conflict of interest.

Ethical Review Board Approval: The study was conformed to the ethical review board requirements.

Human Subjects: Consent was obtained by all patients/participants in this study.

Conflicts of Interest:

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Sohaib Hassan	1. Study design and methodology & Data collection and calculation, Paper writing.
2.	Ashraf Mahmood	2. Paper writing, referencing, data calculations.
3.	Ahsan Numan	3. Analysis of data and quality insurer.
4.	Asif Mughal Senior	4. Analysis of data and interpretation of results etc.
5.	Samra Majeed	5. Literature review and manuscript writing.