



Clinical Biochemical Profile and Outcomes of Cerebral Venous Thrombosis in Puerperal and Nonpuerperal Presentation: A Prospective Observation Study from Northwest India

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ABSTRACT

Background: Cerebral venous thrombosis (CVT) is a rare but treatable cause of stroke, predominantly affecting younger individuals, particularly women during the puerperal period. Despite increased recognition through advanced imaging, clinical diagnosis remains challenging due to its diverse presentation and varying etiological factors.

Objective: To evaluate the clinical profile, etiological factors, treatment outcomes, and prognosis of CVT patients, with a focus on comparing puerperal and nonpuerperal cases in a tertiary care setting in Northwest India.

Materials and methods: This prospective observational study included 80 adult patients diagnosed with CVT via computed tomography venography (CTV) or magnetic resonance venography (MRV) over a 2-year period. Participants were categorized into male, puerperal female, and nonpuerperal female groups. Detailed clinical, laboratory, and radiological evaluations were performed. Modified Rankin Scale (mRS) was used to assess neurological outcomes. Statistical analyses were conducted using analysis of variance (ANOVA) and Chi-squared tests with significance at $p < 0.05$.

Results: Puerperal females were younger than other groups. Common symptoms included headache (85%), seizures (45%), and focal deficits (47.5%). Hyperhomocysteinemia (65%) and vitamin B12 deficiency (51.25%) were prevalent, particularly among males and nonpuerperal females. Anemia was significantly more common in females. No significant difference was noted in clinical outcomes across groups. Poor prognosis was associated with Glasgow Coma Scale (GCS) < 8 , focal deficits, and low vitamin B12 levels. In-hospital mortality was 6.25%; 97% of survivors had favorable outcomes (mRS < 3) at 3 months.

Conclusion: CVT in Northwest India affects a significant number of males and nonpuerperal females. Nutritional deficiencies, particularly vitamin B12 and anemia, play a crucial role. Early diagnosis and appropriate anticoagulation therapy are critical for favorable outcomes.

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INTRODUCTION

Cerebral venous thrombosis (CVT) is a rare cause of stroke, with an annual incidence of 2–4 per million, and accounts for 0.5–1% of strokes.¹ CVT is more prevalent among women aged 20–35 due to pregnancy, puerperium, and contraceptive use.^{2,3} Enhanced awareness and imaging have led to more frequent diagnoses, though clinical recognition remains difficult due to its wide presentation spectrum. CVT aligns with Virchow's triad—stasis, endothelial injury, and hypercoagulability. Risk factors include acquired (e.g., pregnancy, trauma, and cancer) and genetic (e.g., Factor V Leiden, protein C/S deficiency) causes.^{2,4} The superior sagittal sinus (72%) and lateral sinuses (70%) are most frequently affected,² often with multisinus involvement.⁵ Pregnancy and puerperium significantly increase thrombotic risk due to hypercoagulability and volume depletion.⁶ Up to 80% of CVT patients have identifiable risk factors,⁷ while 10–15% have

hereditary thrombophilia⁸; 20–30% remain idiopathic.²

Common symptoms include headache (~90%), focal deficits such as hemiparesis and aphasia, and sometimes isolated mental status changes—especially with deep venous thrombosis.^{5,9} Diagnosis relies on imaging: noncontrast computed tomography (CT) may show hyperdensity; contrast-enhanced CT can reveal the “empty delta” sign.^{8,10} Magnetic resonance imaging (MRI)/magnetic resonance venography (MRV) offers higher sensitivity, with evolving thrombus signals over time.¹¹ Computed tomography venography (CTV) and contrast MRV are used when plain MRV is inconclusive.^{2,12}

Coagulation profiles are important for unexplained or familial cases and must be timed appropriately.⁴ Historically diagnosed postmortem with high mortality (30–50%), modern diagnosis and treatment have reduced mortality to 5.5–18%, with 57–86% achieving full recovery. Poor outcomes are

linked to infancy, older age, coma, and deep venous involvement.^{3,7,13–15}

In India, particularly northwest regions, CVT incidence is uncertain due to lack of population-based studies. This study explores CVT cases from a tertiary hospital in Northwest India, comparing puerperal and nonpuerperal cases and evaluating clinical patterns, causes, outcomes, and treatment response.

MATERIALS AND METHODS

This hospital-based, descriptive, prospective observational study was conducted at a tertiary care teaching hospital and research institute, from Northwest India. All patients aged ≥ 18 years diagnosed with CVT, confirmed via MRV or CTV, presenting over the 2-year study period were included. Patients < 18 years, those who left against medical advice before the outcome endpoint, or had incomplete data, were excluded.

The sample size was calculated at a 95% confidence level, assuming a seizure prevalence of 29.4% in CVT cases,¹⁶ requiring a minimum of 80 subjects at 10% allowable error. Ethical approval was obtained from the Institutional Ethics Committee prior to study initiation, and written informed consent was taken from all patients prior to inclusion in the study.

Participants were categorized into male and female groups, with the latter subdivided into puerperal (within 6 weeks postpartum)

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and nonpuerperal subgroups. A detailed history (lifestyle, comorbidities, and family history), physical examination, and relevant laboratory and imaging investigations were recorded on a structured proforma.

Investigations included routine blood tests [complete blood count (CBC), erythrocyte sedimentation Rate (ESR), electrolytes, glucose, liver function tests (LFTs), and renal function tests (RFTs)], human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), antinuclear antibody (ANA), venereal disease research laboratory (VDRL), folate, vitamin B12, homocysteine, antiphospholipid antibodies (APLA), electrocardiogram (ECG), chest X-ray, and MRV/CTV. Cerebrospinal fluid (CSF) analysis was done when clinically indicated. Neurological deficits or disability were assessed using mRS. "Best mRS" was recorded within the first 3 days of admission to avoid postictal bias. Only clinically discharged patients (fit for home care) were included in the outcome analysis.

Statistical analysis was performed using MedCalc v16.4. Continuous variables were analyzed using analysis of variance (ANOVA); categorical variables using Chi-square or Fisher's exact test. A p -value < 0.05 was considered statistically significant.

RESULTS

Puerperal females were relatively younger in age. Alcohol was used by 10/38 (26.32%)

male patients. History of oral contraceptive pill (OCP) use was given by 6/28 (21.43%) of the nonpuerperal females (Table 1). Headache (85%), seizure (45%), and focal deficit (47.5%) were the most common clinical features among patients with CVT. Papilledema was noticeable in 21 (26.3%) cases. No significant difference was seen in clinical presentation among male and female cases. No significant difference was seen in APLA positivity among male and female cases (Table 2). Mean hemoglobin level and hematocrit were significantly lower among females (both puerperal and nonpuerperal) as compared to males ($p < 0.001$). ESR was significantly higher among females (both puerperal and nonpuerperal). Homocysteine level was significantly higher in males (39.3%). No significant difference was seen in vitamin B12 and folate levels (Table 3). No significant difference was seen in mRS at admission, discharge, or 3 months between males, puerperal, and nonpuerperal females (Table 4). Glasgow Coma Scale (GCS) < 8 , presence of focal deficit, and lower vitamin B12 were significantly associated with poor prognosis at 3 months follow-up (Table 5).

DISCUSSION

This study was a prospective, single-center study done in a tertiary care hospital in Northwest India. A total of 80 patients were

included, and a detailed evaluation of all the patients was done, including demographic data, clinical features, radiological findings, and prothrombotic workup. To the best of our knowledge, this is the first study on CVT from Northwest India, particularly Rajasthan. Panagariya and Maru published a study from this region limited only to puerperal females and did not include other etiological or demographic features of CVT.¹⁷

Our study showed a large number of male (47.5%) and nonpuerperal female (35%) patients. A study conducted in the West (ISCVT trial) showed a female predominance with a 3:1 female-to-male ratio.⁸ However, Indian studies, including those by Pai et al., Christopher et al., and Khelaeni et al., reported higher male predominance, similar to our findings.^{18–20} This may be explained by cultural factors, differing risk profiles, and possibly genetic or environmental variations.

The mean age of patients in our study was 34 years, which is in accordance with Indian data.^{20,21} Puerperal CVT was noted in 17.5% of patients with a mean age of 27.85 years, younger than the overall cohort, due to the early age of marriage and childbirth in this region.

Hyperhomocysteinemia was found in 65% of patients, which is much higher than in Western and Indian studies.^{17,22,23} In our study, 51.25% of patients had vitamin B12 deficiency, which likely contributes to this

Table 1: Demographics

Parameters	Male (N = 38)	Puerperal females (N = 14)	Nonpuerperal females (N = 28)	p-value	p-value		
					A vs B	A vs C	B vs C
Age	34.79 ± 14.45	24.29 ± 2.95	38.04 ± 12.47	0.005	0.002	0.262	0.010
Alcohol	10 (26.32%)	0	0	0.002	0.046	0.004	NA
OCPs		0	6 (21.43%)				
Gravid							
Nulli		0	3 (10.71%)				
Primi		5 (35.71%)	2 (7.14%)				0.042
Multi		9 (64.29%)	23 (82.14%)				

A, males; B, puerperal females; C, nonpuerperal females

Table 2: Clinical profile

Parameters	Male (N = 38)	Puerperal females (N = 14)	Nonpuerperal females (N = 28)	Total	p-value
Headache	33 (86.8%)	13 (92.9%)	22 (78.6%)	68 (85%)	0.430
Seizure	17 (44.7%)	5 (35.7%)	14 (50%)	36 (45%)	0.680
Focal deficit	18 (47.4%)	6 (42.9%)	14 (50%)	38 (47.5%)	0.908
Altered sensorium	7 (18.4%)	1 (7.1%)	4 (14.3%)	12 (15%)	0.595
Idiopathic intracranial hypertension (IIH)-like presentation	2 (5.3%)	2 (14.3%)	1 (3.6%)	5 (6.3%)	0.377
Papilledema	11 (28.9%)	4 (28.6%)	6 (21.4%)	21 (26.3%)	0.772
APLA positive	4 (10.53%)	0	3 (10.71%)	7 (8.8%)	0.443

Table 3: Laboratory profile and hospital stay among CVT patients

Parameters	Male (N = 38)	Puerperal females (N = 14)	Nonpuerperal females (N = 28)	p-value
Hemoglobin	14.1 ± 2.46	10.58 ± 2.25	10.89 ± 2.72	<0.001
Hematocrit	42.59 ± 5.76	34.44 ± 7.28	35.71 ± 7.71	<0.001
ESR	20.5 ± 13.03	44.57 ± 30.4	45.75 ± 31.53	<0.001
Body mass index (BMI)	23.1 ± 1.54	22.81 ± 1.06	25.53 ± 4.03	<0.001
Homocysteine	39.3 ± 32.28	11.16 ± 4.49	18.97 ± 10.15	<0.001
Vitamin B12	252.33 ± 134.24	266.92 ± 45.65	233.65 ± 70.52	0.064
Folate	4.02 ± 2.06	3.95 ± 1.48	4.96 ± 2.6	0.185
Hospital stay (days)	12.35 ± 11.02	10.07 ± 6.08	10.63 ± 5.13	0.608

Table 4: Comparison of mRS among different groups

		Group						Total		p-value
		Male		Puerperal		Nonpuerperal		No.		
		No.	%	No.	%	No.	%			
mRS at admission	<3	22	57.89	9	64.29	20	71.43	51	63.75	0.527
	≥3	16	42.11	5	35.71	8	28.57	29	36.25	
mRS at discharge	<3	32	84.21	13	92.86	23	82.14	68	85.00	0.645
	≥3	6	15.79	1	7.14	5	17.86	12	15.00	
mRS at 3 months	<3	29	93.55	13	100.0	24	100.0	66	97.06	0.292
	≥3	2	6.45	0	0.00	0	0.00	2	2.94	

Table 5: Factors associated with poor prognosis at 3-month follow-up

Variable	Good prognosis mRS <3 (N = 73)	Poor prognosis mRS ≥3 (N = 7)	p-value
GCS <8	3 (4.1%)	3 (42.9%)	0.003
GCS ≥8	70 (95.9%)	4 (57.1%)	
Focal deficit	31 (42.5%)	7 (100%)	0.012
Vitamin B12 level	269.1 ± 199.1	169.9 ± 16.89	0.028

high prevalence. Vitamin B12 deficiency was found exclusively in males and nonpuerperal females, possibly due to antenatal B12 supplementation in pregnant females. An inverse relationship between vitamin B12 and homocysteine levels was found, supporting the role of nutritional deficiency in thrombosis risk.^{24,25}

Antiphospholipid antibodies was positive in 8.75% of patients, consistent with other studies.^{17,22,26} Anemia was found in 43.75% of patients and in 64.29% of female patients. The high incidence of anemia, particularly in females, is a modifiable risk factor for CVT and should be addressed through nutritional and public health interventions.

Among males, alcohol intake was the second most common risk factor after hyperhomocysteinemia and was not reported in any female patients. This is consistent with the cultural pattern of alcohol consumption in the region. OCP intake was reported in 20% of females, similar to other Indian studies,^{20,27} and lower than Western studies.⁸ No significant seasonal variation was found, though most cases presented in summer

and monsoon seasons, possibly due to dehydration or other climatic factors.²⁸

Headache was the most common presenting symptom, followed by seizures and focal deficits, aligning with prior studies.^{17,20,22} Papilledema was present in 25% of patients, indicating that its absence should not exclude the diagnosis. Neuroimaging showed that the superior sagittal sinus, transverse sinus, and sigmoid sinus were the most commonly involved sinuses, consistent with other studies.¹⁷ Hemorrhagic infarcts were found in 21.25% of patients.

Most patients received anticoagulation, including those with hemorrhagic infarcts, following standard recommendations.¹⁷ Decompressive craniectomy was done in five patients; two of them died. The relatively high mortality in these cases emphasizes the importance of early recognition of increased intracranial pressure and prompt neurosurgical intervention.

The in-hospital mortality was 6.25%, which is comparable with other studies.^{17,20,21} On follow-up, 97% of patients had an mRS <3, indicating a good outcome. Poor outcome

was associated with low GCS at admission and focal neurological deficits, as supported by earlier studies.²⁹

In conclusion, our study provides valuable insights into the demographic and etiological profile of CVT in Northwest India. Male and nonpuerperal female patients represent a significant burden of the disease. Hyperhomocysteinemia, vitamin B12 deficiency, and anemia were common, especially in males and nonpuerperal females. Early diagnosis, appropriate anticoagulation, and identification of poor prognostic indicators are key to improving outcomes.

CONCLUSION

Cerebral venous thrombosis is a treatable cause of stroke with a generally favorable prognosis. Our study highlights its higher incidence in males and nonpuerperal populations, with hyperhomocysteinemia and vitamin B12 deficiency as key risk factors, along with anemia, oral contraceptive use, and alcoholism. The most common symptoms were headache, seizures, focal deficits, and

altered sensorium, with papilledema being the most frequent sign. Poor outcomes were linked to focal deficits and low GCS scores at admission. Anticoagulation therapy, even with hemorrhagic infarction, is recommended. Early imaging and screening for hyperhomocysteinemia and vitamin B12 deficiency are essential for diagnosis and treatment. This study, the first broad hospital-based analysis from Rajasthan, underscores regional variations in CVT's pathophysiology and presentation.

KEY MESSAGE

Cerebral venous thrombosis, increasingly recognized in both puerperal and nonpuerperal patients, often presents with reversible risk factors such as vitamin B12 deficiency and anemia, underscoring the importance of early diagnosis and targeted treatment for favorable outcomes.

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