

A STUDY OF CEREBRAL VENOUS THROMBOSIS IN PREGNANCY AND PUERPERIUM- A RETROSPECTIVE ANALYSIS

E. Premakumari¹, P. Sowkanthika²

¹Associate Professor, Department of Obstetrics and Gynaecology, Institute of Social Obstetrics and Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai, Tamilnadu, India.

²Final Year MBBS Student, Father Muller Medical College, Mangalore, Karnataka, India.

ABSTRACT

BACKGROUND

Cerebral venous thrombosis (CVT) is a neurological emergency caused due to thrombus formation in the cerebral veins or sinuses. CVT has a varied presentation and its ability to mimic other conditions makes diagnosis of CVT difficult.

Aims and Objectives:

1. To analyse pregnant and puerperal patients with cerebral venous thrombosis.
2. Identifying the possible risk factors, clinical presentations and prognosis of CVT in pregnant and puerperal women.

MATERIALS AND METHODS

Demographic and obstetric history, clinical features, management and prognostic details were retrospectively collected and recorded in a proforma. Results were expressed in terms of frequency. Chi-square test was used as the test of significance.

RESULTS

The observational study showed mean age to be 23.6 ± 3.90 years. Higher proportions of cases were from rural areas (60%), low socioeconomic status (66.7%), multipara (56.7%) and presented within 10 days postpartum (53.5%). Headache was present in all patients. Other symptoms included seizures (60%), altered level of consciousness (20%), visual disturbances (26.7%), papilloedema (53.3%), focal neurological deficits (10%) and cranial nerve palsy (3.3%). Superior sagittal sinus (63.3%) and transverse sinus (70%) were the most commonly involved sinuses. CT was normal in 26.7% of the cases, but magnetic resonance venogram showed positive signs even in CT negative cases. Recovery was good in 86.7% of the cases and ended in mortality in 13.3% of the cases.

CONCLUSION

Pregnant and puerperal women of 21 - 25 years of age were most commonly affected. Most of the cases presented within 10 days postpartum. Headache was the most frequently encountered symptom. Altered consciousness, cranial nerve involvement and headache of more than 24 hours of duration were associated with poor prognosis. CT was normal in 26.7% of the cases, but MRV was conclusive of CVT in these cases. Superior sagittal sinus and transverse sinus were the commonly affected venous channels. Involvement of superior sagittal sinus showed good prognosis, whereas involvement of deeper cortical veins showed poor prognosis. If adequate treatment is initiated before patient progresses to altered level of consciousness, almost complete recovery is possible.

KEY WORDS

Cerebral Venous Thrombosis (CVT), Pregnancy, Puerperium, Headache, Venous Sinus, CT, MRV, Heparin.

HOW TO CITE THIS ARTICLE: Premakumari E, Sowkanthika P. A study of cerebral venous thrombosis in pregnancy and puerperium- a retrospective analysis. J. Evolution Med. Dent. Sci. 2018;7(26):2994-2999, DOI: 10.14260/jemds/2018/674

BACKGROUND

Cerebral venous thrombosis (CVT) is a neurological emergency due to thrombus formation in the cerebral veins or sinuses. The incidence of CVT in pregnancy is significantly higher in developing countries (450 per 100,000 deliveries) as compared to developed countries (11.6 per 100,000 deliveries).¹ CVT may be due to septic or aseptic thrombi. In the current antibiotic era, increased number of cases with aseptic thrombus is seen. The cause of this aseptic thrombotic activity is primarily attributed to the hypercoagulable state of pregnancy.

This in turn is contributed by factors such as increase in level of certain clotting factors, decrease in level of protein C and S, and altered blood dynamics.² CVT has a varied presentation.

Its ability to mimic other conditions and its non-specific vague symptoms make diagnosis difficult. Imaging modalities like magnetic resonance venogram has improved the ease and certainty with which diagnosis is made.^{2,3} Nonetheless, it is important to identify the relevant clinical findings rapidly and initiate appropriate treatment. A delay is associated with poor outcome as compared to an effectively managed acute episode with almost complete recovery.¹

Aims and Objectives

1. To analyse pregnant and puerperal patients with cerebral venous thrombosis and
2. Identifying the possible risk factors, clinical presentations and prognosis of CVT in pregnant and puerperal women.

'Financial or Other Competing Interest': None.

Submission 15-05-2018, Peer Review 09-06-2018,

Acceptance 15-06-2018, Published 25-06-2018.

Corresponding Author:

Dr. E. Premakumari,

K-2, Paras Apartments,

Shanthi Colony, Jeevarathinam Nagar,

Adyar, Chennai-600020, Tamilnadu, India.

E-mail: drprema2016@gmail.com

DOI: 10.14260/jemds/2018/674



MATERIALS AND METHODS

Study Design

Retrospective descriptive study.

The present institution based observational study is a pilot study conducted in Coimbatore Medical College, Coimbatore during the period May - June 2015. In this retrospective descriptive study, 30 radiologically confirmed cases of CVT were randomly selected over a 5-year period from April 2010 to April 2015 and analysed. Radiological confirmation was through computed tomography (CT), Contrast Enhanced Computed Tomography (CECT) and magnetic resonance venogram (MRV). Patients above 18 years who were pregnant or in the puerperal period and confirmed to have aseptic CVT were included in the study. Patients less than 18 years of age, patients not pregnant or parturient woman at the time of presentation of complaints, patients known to have malignancy or CNS infection were excluded.

The medical records of the patients were collected, and the required data was recorded in a proforma. The proforma consisted of demographic details, clinical history, obstetric history, examination and investigation finding and course of treatment in the hospital and the outcome. History of co-morbid conditions like anaemia, pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), cardiovascular disorders, drug and contraceptive history and past history were recorded.

Statistical Analysis

The data collected were analysed statistically using SPSS version 21.0 software. All variables (demographic details, clinical presentations, radiological findings) were expressed in terms of frequencies n (%). Quantitative variables were also expressed as mean ± standard deviation. The variables were then assessed for their prognostic significance. Chi-square test/ Fisher's exact test was used as the test of significance. A p-value of < 0.05 was considered significant and p < 0.001 was considered highly significant.

RESULTS

The analysis of 30 radiologically confirmed patients with cerebral venous thrombosis has yielded the following results.

The mean age of the cases was 23.6 ± 3.90 years with a minimum age of 18 years and a maximum age of 35 years. 50% of the patients were in the age group of 21 - 25 years. Higher proportion of cases were from a rural set-up (60%), of a low socio-economic status (66.7%) (poor and below poverty line) and were booked cases in the antenatal period (70%). 56.7% of cases were multiparous women. 53.3% of women presented with complaints within 10 days postpartum. 33.3% of the patients had co-morbid conditions such as anaemia and gestational diabetes mellitus (GDM) in the antenatal period and 50% of the patients had pregnancy induced hypertension in the form of pre-eclampsia and gestational hypertension. However, none of the patients were identified to have cardiovascular disorders and none of the patients had history of intake of hormonal contraceptives. 73.3% of patients were delivered in health care setup which included primary health care centres, government hospital and tertiary care centres. 23.3% of the patients were delivered at home. 70% of the patients had undergone

vaginal delivery. Of the 30 cases admitted and treated with intravenous heparin (unfractionated) 86.7% of the patients showed good recovery with minimal deficits, whereas 13.3% of the patients deteriorated to show a bad prognosis which resulted in death. Of the patients who showed bad prognosis, 50% of them presented 20 - 30 days postpartum, 25% within 11 - 20 days postpartum and 25% within 10 days postpartum.

Variables	Number of Patients
Age	
• 20 years and below	8 (26.7%)
• 21-25 years	15 (50%)
• > 25 years	7 (23.3%)
Locality	
• Rural	18 (60%)
• Urban	12 (40%)
Socio-economic Status	
• High and upper high class	0 (0%)
• Lower middle and upper middle class	10 (33.3%)
• Poor and below poverty line	20 (66.7%)
Parity	
• Nullipara	1 (3.3%)
• Primi	12 (40%)
• Two	10 (33.3%)
• Three	5 (16.7%)
• Four	2 (6.7%)
Booking Status	
• Booked	21 (70%)
• Unbooked	9 (30%)
Period of Presentation of Symptoms	
• 1 st and 2 nd trimester	0 (0%)
• 3 rd trimester	1 (3.3%)
• 0-10 days postpartum	16 (53.3%)
• 11-20 days postpartum	10 (33.3%)
• 21-30 days postpartum	3 (10%)
Place of Delivery	
• Health care setup	22 (73.3%)
• Home	7 (23.3%)
• Not applicable	1 (3.3%)
Mode of Delivery	
• Vaginal	21 (70.0%)
• Lower segment caesarean section	8 (26.7%)
• Not applicable (antenatal)	1 (3.3%)
Co-morbid Conditions	
• Gestational diabetes mellitus	10 (33.3%)
• Pregnancy induced hypertension	16 (53.3%)
• Anaemia	0 (0%)
• Cardiovascular disorders	0 (0%)
• Others	
Outcome	
• Recovered	26 (86.7%)
• Death	4 (13.3%)

Table 1. Demography and Baseline Details of Participants

Variable	Sub-Categories	Number of Patients with Poor Outcome (Death)	Number of Patients with Good Outcome (Recovery)	P value
Age	20 and below	0	8	0.404
	21 - 25	3	12	
	Above 25	1	6	
Locality	Rural	3	15	0.511
	Urban	1	11	
Socio-economic Status	High and upper high class	0	0	0.448
	Lower and upper middle class	2	8	
	Poor and below poverty line	2	18	
Parity	Nullipara	0	1	0.785
	Primi	2	10	
	Two	2	8	
	Three	0	5	
	Four	0	2	
Booking Status	Unbooked	1	8	0.815
	Booked	3	18	
Period	1 st and 2 nd trimester	0	0	0.040
	3 rd trimester	0	1	
	0-10 days post-partum	1	15	
	11-20 days post-partum	1	9	
	21-30 days post-partum	2	1	
	3 rd trimester	0	1	
Place of Delivery	Health care set-up	3	19	0.923
	Home	1	6	
	Not applicable	0	1	
Mode of Delivery	Vaginal	3	18	0.916
	Lower segment caesarean section	1	7	
	None	0	1	

Table 2. Association of Demographic and Baseline Details with the Prognosis of the Disease

Analysis by Chi-square test showed a significant relationship between the outcome of disease and the period of presentation of complaints, $p = 0.040$. The later the symptoms presented, the lesser was the survival rate as observed in these limited cases. However, no significant association was obtained between the outcome of the disease and the other demographic or baseline variables (Table 2). No statistically significant association was found between anaemia, PIH and GDM and the outcome of the disease, $p > 0.05$ (Table 3).

Comorbid Condition	Number of Patients	Number of Patients with Bad Prognosis	Number of Patients with Good Prognosis	P value
PIH	16	2	14	0.886
Anaemia	10	1	9	0.704
GDM	10	2	2	0.448

Table 3. Association between the Comorbid Conditions and Disease Prognosis

All the patients presented with headache as a universal complaint, which was less than 24 hours duration in 77.3% of cases. Other symptoms encountered were seizures, both grand mal and partial seizures and visual disturbances in the form of blurring of vision, photophobia and diplopia. On examination, papilloedema bilaterally was found in 53.3% of cases, altered level of consciousness in the form of delirium, stupor and coma in 20% of cases, hemiparesis in 10% cases and 7th cranial nerve involvement in 3.3% of the cases (Table 4).

Clinical Features	Number of Patients
Headache	
• < 24 hours duration	22 (77.3%)
• > 24 hours duration	8 (26.7%)
Seizures	
• Grand mal seizures	13 (43.3%)
• Partial seizures	5 (16.7%)
Visual disturbances	8 (26.7%)
Altered level of consciousness	6 (20%)
Papilloedema	16 (53.3%)

Focal Neurological Deficits <ul style="list-style-type: none"> • Hemiparesis 	3 (10%)
Cranial Nerve Palsies <ul style="list-style-type: none"> • 7th cranial nerve 	1 (3.3%)

Table 4. Clinical Features of CVT associated with Pregnancy

Analysis by Chi-square test showed significant association between disease outcome and cranial nerve involvement $p= 0.10$ and headache $p= 0.019$. Headache of > 24-hour duration and cranial nerve involvement had poor prognosis. Chi-square analysis showed a highly significant association between disturbed consciousness and poor disease outcome, $p= 0.000$ (Table 5).

Symptoms and Signs	Presence of Symptoms	Number of Patients with Poor Outcome (Died)	Number of Patients with Good Outcome (Recovery)	P value
Headache	< 24 hours duration	1	21	0.019
	> 24 hours duration	3	5	
Seizures	Grand mal	3	10	0.212
	Partial	1	4	
Visual disturbances	Present	0	8	0.195
Papilloedema	Present	1	15	0.222
Focal neurological deficits	Present	1	2	0.283
Altered level of consciousness	Present	4	2	0.000
Cranial nerve palsy	Present	1	0	0.010

Table 5. Association between Clinical Findings and Prognosis of the Disease

Radiological imaging by CT and CECT showed a normal film in 26.7% of the patients. 50% of the patients showed venous infarcts which showed statistically significant good prognosis, $p=0.032$. 30% of the CT reports were positive for empty delta sign which did not show significant association with the prognosis, $p=0.160$. A combination of both delta sign and infarcts were also observed in some cases.

Imaging by MRV showed involvement of superior sagittal sinus in 21 (70%) of the cases, transverse sinus in 19 (63.3%) of the cases, sigmoid sinus in 16 (53.3%) of the cases and deeper veins in 1 (3.3%) of the case including cases with multiple sinus involvement. Chi-square analysis shows a statistically significant good prognosis associated with involvement of superior sagittal sinus $p= 0.035$ and sigmoid sinus $p= 0.022$ in contrast to involvement of deeper cortical veins which were indicative of a statistically significant poor prognosis $p=0.010$ (Table 6).

Sl. No.	Venous System Involved	Number of Patients with Involvement	Number of Patients Died	Number of Patients with Good Prognosis	P value
1	Sigmoid sinus	16	0	16	0.022
2	Superior sagittal sinus	21	1	20	0.035
3	Transverse sinus	19	3	16	0.603
4	Deep cortical vein	1	1	0	0.010

Table 6. Association between Venous System Involvement and Prognosis of the Disease

DISCUSSION

Cerebral venous thrombosis is a pathological condition due to clot formation in the vascular lumen resulting from an imbalance in the Virchow’s triad. The blood clot formed in the vascular channel obstructs the normal blood flow to the organs causing ischaemia.⁴ The brain is an organ with elaborate network of vascular channels that provide collateral supply in the very initial stage of vessel block. The

clinical picture of CVT becomes evident when the alternative pathway becomes insufficient to meet the demands.⁵ A high degree of suspicion is required to identify this neurological emergency, failing which the chance of recovery falls.

CVT in pregnancy and puerperium can be septic or aseptic. Aseptic CVT can be a direct result of hypercoagulability caused by increased clotting factors (I, VII, VIII, X), decreased levels of protein C and S, decreased fibrinolysis or a combination of multiple factors.⁶ The physiological state of pregnancy and puerperium in addition to factors such as intake of hormonal contraceptive pills,⁷ immobilisation after delivery, inadequate intake of water make women at a higher risk of developing CVT. The hypercoagulable state of pregnancy behaves as a double-edged sword with a protective role against post-partum haemorrhage as well as a negative role in the causation of CVT.⁸ Furthermore, the uterine contractions facilitate dislodgement of the formed clot and its movement along a retrograde route via vertebral veins.⁹

In the current study, majority of the cases were in the post-partum period as against the study conducted by Liang Z (2017) in China, where more number of cases were in the antenatal period as to puerperium (122/100,000 versus 80/100,000 cases).¹ However, the results were consistent with the study conducted in India by Saroja AO (3 antenatal versus 66 postnatal cases of CVT).¹⁰ This could be suggestive of a possible geographical variation. In the location of the present study the tropic climate, excessive sweating and inadequate intake of water (superstitious beliefs) result in dehydration. Immobilisation worsens the situation. Moreover, there is a gross under-reporting of cases in developing countries and delay in the seeking of health care due to lack of awareness.

In our study, more number of cases with CVT were seen in the group delivered vaginally. This may be due to the perineal and pelvic structure injury sustained during labour. Secondly, Valsalva manoeuvre that occurs in patients with labour raises the intra-abdominal and intra-thoracic pressure. The large and bulky uterus compresses the

abdominal veins. Both these factors result in increased intravenous pressure. Valsalva retinopathy is a condition where the Valsalva manoeuvre causes intraocular haemorrhage.¹¹ Similarly, the raised intravenous pressure in the cerebral veins during the Valsalva manoeuvre of labour could probably injure the cerebral veins also and cause thrombus formation (arising de novo). However, more clinical and analytical studies are required to give a definite conclusion.

In the present study, 33.3% cases of CVT had anaemia. The association between anaemia and CVT was explained by Coutinho J et al (2015) who suggested that iron deficiency anaemia could result in thrombocytosis as a causal relationship.¹² 53.3% of the patients among those studied were diagnosed to have PIH. Exaggerated hypercoagulable state of pregnancy, intravascular volume depletion due to oedema, generalised endothelial injury and dysfunction favour thrombus formation.^{13,14} 33.3% of the cases had GDM.

The clinical presentation recorded in the current study was restricted to headache, grand mal and partial seizures, blurring of vision, diplopia, photophobia, altered level of consciousness, hemiparesis, papilloedema and facial nerve involvement. However, only headache showed statistical significance. Cranial nerve involvement and disturbed consciousness showed a statistically significant association with the prognosis of the disease. This limited number of symptoms encountered is most likely due to the smaller number of cases analysed. In an observational study conducted by Bansal, Gupta and Prakash (1980) with 138 cases of CVT, a spectrum of additional symptoms including fever, paraesthesia, vertigo, limb pain, excessive salivation, motor aphasia and 6th cranial nerve involvement was also noted. These findings were attributed to raised intracranial tension, haemorrhagic meningeal irritation and active thrombotic process.¹⁵ In the current study, the superior sagittal sinus and transverse sinus were the two commonly involved venous channels which is consistent with the reports of Liang Z.¹

In the 30 patients studied, the treatment given was targeted at thrombolysis using unfractionated heparin (UFH) which showed good outcome. However, the treatment protocol has undergone improvisation and low molecular weight heparin (LMWH) is preferred over UFH. Though both unfractionated and low molecular weight heparin do not cross the placental barrier, LMWH is preferred in acute episodes. In patients with previous episodes of CVT, LMWH is recommended prophylactically in pregnancy and puerperium. Symptomatic treatment with antiepileptic has been recommended to prevent recurrence. Recent advances are being directed towards surgical management such as decompressive surgeries in acute cases and supratentorial lesions.¹⁶ Further studies are required to analyse the efficacy of the current treatment.

CONCLUSION

Pregnant and puerperal women of 21-25 years of age were most commonly affected. Most of the cases presented within 10 days postpartum. Headache was the most frequently encountered symptom. Altered consciousness, cranial nerve involvement and headache of more than 24 hours of duration were associated with poor prognosis. CT was normal in 26.7% of the cases, but MRV was conclusive of CVT in these

cases. Superior sagittal sinus and transverse sinus were the commonly affected venous channels. Involvement of superior sagittal sinus showed good prognosis, whereas involvement of deeper cortical veins showed poor prognosis. If adequate treatment is initiated before patient progresses to altered level of consciousness, almost complete recovery is possible.

Limitations of the Study

The current study was a pilot study with less number of cases. More studies with large number of participants are required for conclusive results. Also, the coagulation profile could not be assessed to rule out thrombophilia.

Recommendations

- Prophylactic anticoagulant therapy should be given in all the puerperal women with anaemia, PIH, diabetes mellitus and previous thromboembolic episodes.
- The efficacy of the current treatment methods over the conventional unfractionated heparin should be evaluated.

REFERENCES

- [1] Liang ZW, Gao WL, Feng LM. Clinical characteristics and prognosis of cerebral venous thrombosis in Chinese women during pregnancy and puerperium. *Scientific Reports* 2017;7:43866.
- [2] Kakade AS, Kulkarni YS. Cerebral venous thrombosis in pregnancy. *Bombay Hospital Journal* 2011;53(Special Issue):414-9.
- [3] Karthikeyan D, Vijay S, Kumar T, et al. Cerebral venous thrombosis-spectrum of CT findings. *Ijri.org*. 2018. [cited 10 April 2018]. <http://www.ijri.org/text.asp?2004/14/2/129/28567>
- [4] Stam J. Thrombosis of the cerebral veins and sinuses. *New England Journal of Medicine* 2005;352(17):1791-8. <http://www.nejm.org/doi/full/10.1056/NEJMra042354>
- [5] Allroggen H, Abbott RJ. Cerebral venous sinus thrombosis. *Postgraduate Medical Journal* 2000;76(891):12-5. <http://pmj.bmj.com/content/76/891/12>
- [6] Ferro JM, Lopes MG, Rosas MJ, et al. Long-term prognosis of cerebral vein and dural sinus thrombosis: results of the VENOPORT study. *Cerebrovascular Diseases* 2002;13(4):272-8.
- [7] Buccino G, Scoditti U, Pini M, et al. Low-oestrogen oral contraceptives as a major risk factor for cerebral venous and sinus thrombosis: evidence from a clinical series. *Ital J Neurol Sci* 1999;20(4):231-5.
- [8] Raj O, Rupasinghe M. Postpartum cortical venous thrombosis: an unusual presentation of post-dural puncture headache. *Journal of Obstetric Anaesthesia and Critical Care* 2016;6(2):95-7.
- [9] Batson OV. The function of the vertebral veins and their role in the spread of metastases. *Annals of Surgery* 1940;112(1):138-49.
- [10] Saroja AO, Tapsi C, Naik KR. Cerebral venous thrombosis in women from Indian subcontinent. *Journal of the Scientific Society* 2017;44(1):20-5.

- [11] Klein A, O'Neal A, Scifres C, et al. Neurological illness in pregnancy: principles and practice. 1st edn. John Wiley & Sons 2016.
- [12] Coutinho JM, Zuurbier SM, Gaartman AE, et al. Association between anaemia and cerebral venous thrombosis. *Stroke* 2015;46(10):2735-40.
- [13] Gallery ED, Hunyor SN, Gyory AZ. Plasma volume contraction: a significant factor in both pregnancy-associated hypertension (pre-eclampsia) and chronic hypertension in pregnancy. *Q J Med* 1979;48(192):593-602.
- [14] Kupfermanc M]. Thrombophilia and pregnancy. *Current Pharmaceutical Design* 2005;11(6):735-48. <https://rbej.biomedcentral.com/articles/10.1186/1477-7827-1-111>.
- [15] Bansal B, Gupta RR, Prakash C. Stroke during pregnancy and puerperium in young females below the age of 40 years as a result of cerebral venous/venous sinus thrombosis. *Japanese Heart Journal* 1980;21(2):171-83.
- [16] Ferro JM, Marie-Germaine B, Canhão P, et al. European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – endorsed by the European Academy of Neurology. *European Stroke Journal* 2017;2(3):195-221. <http://journals.sagepub.com/doi/full/10.1177/2396987317719364>.