MEDICAL CHANNEL

Original Article

SPECTRUM OF CEREBROVASCULAR COMPLICATIONS DURING PREGNANCY AND PUERPERIUM

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ABSTRACT

Objective: The purpose of this study was to analyze the clinicoradiological features of different cerebrovascular complications during late pregnancy and postpartum period.
Study design: Descriptive case series study
Place and duration: Department of Neurology, Jinnah Postgraduate Medical Centre (JPMC) Karachi, From 1st January 2011 to 31st December 2012.
Methods: Total of 77 patients were included in this study who were referred from gynaecology and obstetrics department of JPMC in last trimester of pregnancy and post partum period with signs and symptoms suggestive of cerebrovascular disorder (thunderclap headache, seizures, focal neurological deficits, visual symptoms and altered mental status). Statistical software SPSS version 16.0 was used for data analysis.
Results: 32 (41.6%) were in last trimester and 45 (58.4%) were in post partum period. Age ranged from 16-42 years with mean age of 28.6± 6.95 years. 35 (45.5%) patients had venous sinus thrombosis, 23 (29.9%) had eclampsia, 9 (11.7%) had ischemic cerebral infarction , 8 (10.4%) patients were diagnosed with reversible cerebral vasoconstriction syndrome (RCVS) while subarachnoid hemorrhage was diagnosed in two patients. Most common presentation was seizures, followed by focal neurological deficits, papilloedema, thunderclap headache and altered level of consciousness. Neuroimaging (CT brain/MRI/MRA/MRV brain) showed isolated superior sagittal sinus thrombosis in 16 patients (20.7 %), isolated lateral sinus thrombosis in 10 patients (13%) while 9 patients (11.7%) had thrombosis of superior sagittal and lateral sinus both. MRI findings consistent with PRLS were found in 16 (20.7%) patients. 4 (5%) patients had subarachnoid hemorrhage while findings consistent with RCVS were seen in 8 (10.4%) patients.
Conclusion: Many patients who are referred to tertiary care centers from primary and secondary care centers with the diagnosis of eclampsia turn out to have many other diagnostic possibilities besides eclampsia after proper clinical and radiological evaluation

Keywords: Cerebrovascular complications, pregnancy, postpartum period**Introduction:**

INTRODUCTION

Diverse pathologic conditions affect the central nervous system (CNS) during pregnancy and the puerperium. Cerebrovascular disorders in pregnancy and post partum period can be categorized into ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, eclamptic encephalopathy/ posterior reversible encephalopathy syndrome, postpartum cerebral angiopathy, and cerebral venous thrombosis. Due to several physiological changes in coagulation system, pregnancy and post partum period are considered to be pro thrombotic states.[1]

There is an increase in the relative risk and a small increase in the absolute risk of ischemic stroke and intracerebral hemorrhage during pregnancy.[2] As several causes of ischemic stroke in the young have been reported in pregnancy and the puerperium, in most cases it is quite difficult to decide whether pregnancy is coincidental or causative factor of cerebral infarction. There are several causes of stroke which are unique to pregnancy and the postpartum period, such as preeclampsia and eclampsia, amniotic fluid embolism, postpartum angiopathy and postpartum

cardiomyopathy.[3] Preeclampsia/eclampsia is one of the most common causes of both ischemic infarction and hemorrhagic stroke in pregnancy whereas cerebral venous thrombosis is rare, but occurs more commonly in association with pregnancy.[4] Several studies have found that around 50% cerebral venous sinus thrombosis (CVST) cases were associated with pregnancy.[2] Eclampsia is a leading cause of maternal death, with neurologic symptoms including headache, cortical blindness, coma, and convulsions.[5]

Posterior Reversible Leukoencephalopathy Syndrome (PRLS) is a distinct radiological entity and eclampsia is one of the commonest causes of PRLS. Symptoms may include headache, nausea, vomiting, altered mental status, seizures, stupor, and visual disturbances in varying combinations in individual patients . On Neuroimaging studies, edema has relatively symmetrical pattern, typically in the subcortical white matter and occasionally in the cortex of the occipital and parietal lobes. This syndrome is reversible when treatment is instituted early, but delayed diagnosis and treatment can result in neurological sequelae.[6]

The phenomenon of reversible cerebral vasoconstriction syndrome (RCVS) has been associated with several conditions including pregnancy and puerperium ("postpartum angiopathy"), thunderclap headache, and use of vasoconstrictor medications. Patients with cerebral vasoconstriction typically present with sudden, severe, and recurrent ("thunderclap") headaches and can develop stroke and also cortical subarachnoid hemorrhage.[7] The most common cause of subarachnoid hemorrhage during pregnancy or the postpartum period is aneurysmal rupture or bleeding from a vascular malformation.[8,9,10]

MATERIAL AND METHOD

This was a descriptive case series study conducted at the department of Neurology, Jinnah Postgraduate Medical centre (JPMC), Karachi, from 1st January 2011 to 31st December 2012. All referred patients from gynecology and obstetrics department of JPMC in last trimester of pregnancy and post partum period with acute neurological symptoms like thunderclap headaches ,seizures, altered mental status and focal neurological deficits were included for further evaluation and diagnostic workup. We specifically screened these patients for underlying pregnancy linked conditions like cerebral venous sinus thrombosis, eclamptic encephalopathy and Reversible cerebral vasoconstriction syndrome (RCVS).

Permission was taken from the Ethical committee of JPMC. Informed Consent was taken from patient or her informant and purpose of study was explained. Detailed history and physical examination were carried out in all the patients with special reference to signs of increased intracranial pressure and meningeal irritation .Patients were carefully examined for any motor, sensory or visual field deficit to look for underlying focal cerebral insult.

CBC, ESR, BUN, creatinine, random blood sugar, liver function tests, Serum Electrolytes, coagulation profile, serum calcium & phosphate and urine analysis were done in all the patients. ANA, C Reactive proteins, Antiphospholipd antibodies ,CSF analysis and beta HCG were carried out in selected patients, whenever required.

Non enhanced CT scan was done in all patients. 1.5 Tesla MRI is available in our institute, so MRI, MRV and MRA studies were performed in all these patients.T1, T2, FLAIR and diffusion weighted Images (DWI) images were obtained routinely in all these patients.

After thorough evaluation, patients with meningitis, viral encephalitis, thrombotic thrombocytopenic purpura and connective tissue disorders were excluded from the study. Patients with past history of epilepsy, trauma, tumor, stroke, diabetes, essential hypertension and ischemic heart disease were also not included in this study.

Finally patients with following pregnancy linked conditions were further studied for variable

STATISTICAL ANALYSIS:

Statistical software SPSS version 16.0 was used for data analysis. In the results were given number and percentages for qualitative variables (age group, diagnosis, symptoms and MRI/MRA/MRV findings and mean ± standard deviation for quantitative variable (age).

RESULTS

Table 1 shows general characteristics of 77 patients who were included in this study with different neurological manifestations in last trimester of pregnancy or post partum period. 32 (41.6%) of them were in last trimester and 45 (58.4%) were in post partum period. Age ranged from 16-42 years with mean age of 28.6± 6.95. Equal no of patients (31/77) were found between 20-29 and 30-39 years of age groups (Table. 1)

Table 1 also shows frequency distribution of different diagnostic categories. 35 /77(45.5%) patients had venous sinus thrombosis, among whom 23 (65.7%) were post partum and 12 (34.2%) were in last trimester of pregnancy. 23/77 (29.9%) had eclampsia among whom 13 (56.5%) were in post partum period and 10 (43.4%) in last trimester of pregnancy. 9/77 (11.7%) had ischemic cerebral infarction, among whom 3 (33.3%) were in post partum period and 6 (66.6%) were in last trimester. 8/77 (10.4%) patients were diagnosed with reversible cerebral vasoconstriction syndrome (RCVS), 5 (62.5%) of whom were in post partum period and 3(37.5%) in last trimester.. Subarachnoid hemorrhage (SAH) was diagnosed in 2/77 patients (2.6%); one was in last trimester (50%) and one in post partum period(50%).

Table 2 depicts symptomatic profile of all the patients as per underlying diagnoses. Seizures and focal neurological deficit were found to be present in 43% and 34% of cases of cerebral venous sinus thrombosis respectively . Focal deficits were primarily venous infarctions with or without hemorrhagic component in non-arterial distribution corresponding to underlying pattern of sinus or cortical venous involvement. . Papilloedema was most frequently found in 11/35 (31.4%) of patients with cerebral venous sinus thrombosis followed by 5/23(21.7%) of patients with eclamptic encephalopathy.

Among patients with eclamptic encephalopathy, seizures activity was the most commonly reported symptom in 20/23 (87%) cases followed by coma in 6/23 (26%) and focal neurological deficits in 5/23 (21%) of the cases. (Table.2)

Although majority of the patients with cerebral vasoconstriction syndrome (RCVS) reported headache at the time of presentation but thunderclap headache was reported in 50% of the case. (Table.2)

There were 9/77 patients who were found to have ischemic infarction but did not meet our inclusion criteria for cerebral venous sinus thrombosis, eclamptic encephalopathy or reversible cerebral vasoconstriction syndrome(Table 2). Two of them had valvular heart disease while one was found to have arterial dissection. However underlying cause could not be discovered in remaining cases of ischemic infarction.

Table 3 depicts radiological features of different pregnancy linked complications in this study. Neuroimaging (CT brain/MRI/MRA/MRV brain) showed cerebral venous sinus thrombosis (CVST) in 35 patients among whom 16 patients had isolated superior sagittal sinus thrombosis (SSST), 10 patients had isolated lateral sinus thrombosis

TABLE 1:
GENERAL CHARACTERISTICS AND DIAGNOSIS IN POST PARTUM PERIOD AND LAST TRIMESTER

Variables	Total		Post-Partum Period		Last trimester	
	No.	%	No.	%	No.	%
Number of patients	77		45	(58.4%)	32(41.6%)	
Age						
Under 20	11	14.3	5	45.4	6	54.5
20-29	31	40.3	18	58	13	41.9
30-39	31	40.3	20	64.5	11	35.4
40 & above	4	5.2	2	50	2	50
Diagnosis						
Venous Sinus Thrombosis (VST)	35	45.5	23	65.7	12	34.2
Eclampsia	23	29.9	13	56.5	10	43.4
Cerebral Infarction	9	11.7	3	33.3	6	66.6
Reversible Cereberal Vasoconstriction Syndrome (RCVD)	8	10.4	5	62.5	3	37.5
Subarachnoid Hemorrhage (SAH)	2	2.6	1	50	1	5o
Symptoms						
Seizures	39	50.6	26	66.6	13	33.3
Focal neurological deficit	30	39.0	17	56.6	13	43.3
Papilloedema	19	24.7	12	63	7	37
Thunderclap Headache	12	15.6	8	66.6	4	33.3
Coma	12	15.6	8	66.6	4	33.3
MRI/MRV/MRA						
Superior Sagittal Sinus Thrombosis (SSST)	16	20.7	6	37.5	10	62.5
Lateral Sinus Thrombosis (LST)	10	13	8	80	2	20
Combined superior sagittal sinus and lateral thrombosis	9	11.7	7	77.7	2	22.22
Posterior reversible Leuukoencephalopathy Syndrome (PRLS)	16	20.7	9	56.2	7	43.7
Reversible Cereberal Vasoconstriction Syndrome (RCVD)	8	10.3	5	62.5	3	37.5
Subarachnoid Hemorrhage SAH/ cSAH	4	5.2	2	50	2	50

(LST) and 9 patients had thrombosis of superior sagittal and lateral sinus both (Table 3). MRI findings consistent with Posterior reversible leukoencephalopathy syndrome (PRLS) were found in 16 patients .This syndrome was exclusively found in patients with eclamptic encephalopathy. 11 patients had cerebral infarction. Nine out of them had ischemic cerebral infarction with no evidence of CVST, RCVS, or Eclampsia. While one each had infarction due to reversible cerebral vasoconstriction syndrome and eclamptic encephalopathy .

Findings consistent with RCVS were reported in 8/77(10.4%) of total patients .Isolated subarachnoid hemorrhage was reported in 2 cases whereas cortical subarachnoid hemorrhage was also discovered in two patients with reversible cerebral vasoconstriction syndrome (Table 3).

DISCUSSION:

Pregnant and postpartum patients with new onset neurological

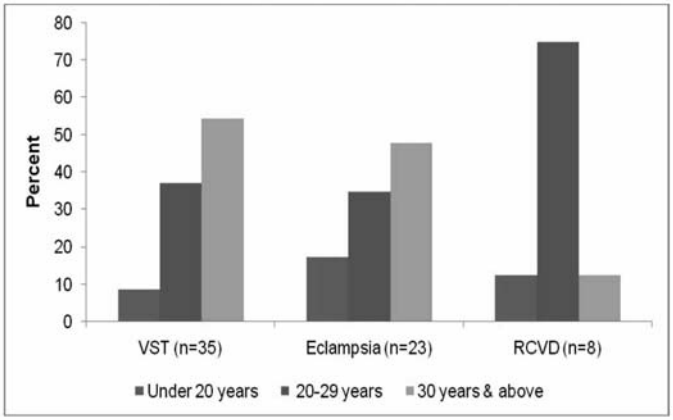
TABLE 2:
SYMPTOMS ACCORDING TO DIAGNOSIS

Symptom profile	Diagnosis				
	VST	Eclampsia	Cerebral Infarction	RCVD	SAH
	n = 35	n = 23	n = 9	n = 8	n = 2
Seizures	15 (42.8%)	20 (87%)	1 (11.1%)	3 (37.5%)	-
Focal neurological deficit	12 (34.3%)	5 (21%)	9 (100%)	3 (50 %)	2 (100%)
Papilloedema	11 (31.4%)	5 (21.7%)	-	2 (25.0%)	1 (50.0%)
Thunderclap Headache	3 (8.6%)	2 (8.7%)	1 (11.1%)	4 (50.0%)	2 (100%)
Coma	3 (8.6%)	6 (26.1%)	-	2 (25.0%)	1 (50%)

TABLE 3:
DIAGNOSIS CORRELATES WITH MRI FINDINGS

MRI / MRA / MRV	Diagnosis				
	Venous Sinus Thrombosis (VST)	Reversible Cerebral Vasoconstriction Syndrome (RCVD)	Subarachnoid Hemorrhage (SAH)	Cerebral Infarction	Eclampsia
Lateral Sinus Thrombosis (LST)	10	0	0	0	0
Superior Saggital Sinus Thrombosis (SSST)	16	0	0	0	0
SSST + LST	9	0	0	0	0
Subarachnoid Hemorrhage (SAH)	0	2	2	0	0
Stroke (Infarction/hemorrhage)	12 (hemorragic)	1/3	0	9	1/4
Posterior Reversible Leukoencephalopathy Syndrome (PRLS)	0	0	0	0	16

FIGURE 1:
DIAGNOSIS ACCORDING TO AGE (YEARS)



VST = Venous Sinus Thrombosis, RCVD = Reversible Cerebral Vasoconstriction Syndrome

symptoms need thorough diagnostic evaluation to rule out diverse pathological conditions that affect the CNS during pregnancy and puerperium like cerebralvenous sinus thrombosis ,eclampsia, subarachnoid hemorrhage and cerebral infarction etc.[11]

Cerebral venous sinus thrombosis is leading cause of acute neurological symptoms in pregnant women during last trimester and postpartum period. This condition is believed to be more common in developing countries because of high frequency of poor nutrition, infections and dehydration.[12]

Majority of patients with CVST in our study were between 20 and 40 years of age. 17/35(48%) of them were between 30 and 39 years of age while 13/35(37%) were between 20 and 29 years of age(Fig 1) . However, in a series of 138 patients from India, 112(81.2%) were under 30 years of age .[13] CVST occurs more frequently in postpartum period compared to last trimester. This ratio is reported to be 2-3:1 from European countries while much higher ratios have been reported from India and Mexico.[14, 15] We observed similar pattern of twice frequent occurrence of cerebral venous sinus thrombosis in our patients during puerperium compared to last trimester.

Among different acute neurological symptoms in patients with CVST, seizures were the most commonly reported (42.8%) reason for referral to our unit. This proportion was comparable to study by Masuhr et al 16 on 194 patients with CVT where seizures were reported in 44% of cases.

Papilloedema with characteristic blurred disc margins was seen in 11/35 (31.4%) of CVST patients. In a recent review by G Guenther et al 17, this sign was found in one third of cases.

34% of patients with CVST in our series were observed to have focal motor and/or sensory deficit with stroke like presentation. During stay in ward, we found such deficits to be of permanent nature in few cases only while majority made good recovery with few sequelae. This finding did not correspond to respectively 69% and 52% incidence of stroke in patients with CVST reported by Masuhr e et al in 2006 and Ferro et al in 2004.[14,16] We believe that nonspecific selection of cases (including pregnancy and non pregnancy linked) in these studies may be responsible for significant difference in proportion of cases with stroke in these studies.

MRI and MRV were extremely helpful in making final diagnosis of cerebral venous sinus thrombosis. The two most frequent sites of thrombosis are the superior sagittal sinus, affected in 62% to 80% of cases, and the lateral sinus involved in 38% to 86% of cases.14, 18 We found Isolated superior sagittal sinus involvement in 16/35(45.7%) patients followed by isolated transverse sinus in 10/35(28.7%) patients and combined superior sagittal plus transverse sinuses in 9/35 patients in descending order of frequency in our series of patients.

Eclampsia was the second most common cause of acute neurological symptoms in our series of patients. Seizures are the hallmark of eclampsia and these were reported in 20/23 (87%) of our eclamptic patients. These were usually generalized tonic clonic in nature.

Stroke occurred in five of our twenty three eclamptic patients. Four out of five patients had an intracerebral hemorrhage while one was reported to have cerebral infarction. Four out of these five cases were reported in postpartum period. In Taiwan, 7 out of 19 (37%) eclamptic women with peripartum stroke had intracerebral hemorrhage.19 Similarly in a detailed series of 27 women with eclampsia and subsequent stroke, 25(89%) had hemorrhagic and 2(12%) had ischemic stroke.[20]

An association between posterior reversible leukoencephalopathy syndrome and eclampsia was first described in 3 of his 15 patients by Hinchey et al in 1996. [21] In a study done by Brewer et al, 46 out of 47 (97.9%) eclamptic patients were found to have PRLS on neuroimaging .[22] In an study in Pakistan including 12 patients of PRLS, 10 (83.3%) patients had eclampsia.[23] . We found this syndrome in 16 out of our 23 (70%) eclamptic patients as well. Because DWI and ADC sequences were available with us, we were able to make confidential distinction between cytotoxic insult (infarction) and vasogenic edema of posterior reversible encephalopathy syndrome in our series of patients.

There were small number of patients with various patterns of ischemic and hemorrhagic stroke (ICH/cSAH) in our study who were not preeclamptic and had no evidence of cortical vein or dural sinus thrombosis on MRI AND MRV studies. However MRA studies in these patients revealed multifocal constriction of cerebral arteries especially around circle of Willis. They were total eight in number. 3 out of 8 had ICH (37%), 2 of them had cSAH (25%) and 1(12%) was found to have cerebral infarction. Our rate for ICH is comparable to the 35% seen in a recent large, prospectively collected series of patients with RCVS which included 12 with post partum angiopathy [24]

CLINICO-RADIOLOGICAL VARIABLES.

(1) Patients with established diagnosis of preeclampsia who developed seizures, any focal neurological deficit (motor,sensory or visual) or depressed consciousness (GCS<10) were labeled as having eclamptic encephalopathy.

(2) Patients with imaging evidence of cerebral vasoconstriction with at least 2 narrowings per artery on 2 different arteries, assessed by MRA, CT angiography (CTA) and/or Transfemoral angiography were labeled as having reversible cerebral vasoconstriction syndrome.

(3) Diagnosis of CVST was base upon association of negative(non visualization of the entire sinus or its part at MR venography) and positive signs(definite spontaneous hyperintense signal on MRI T1 and T2 images with filling defect on contrast studies in corresponding sinuses) with or without parenchymal lesions.

(4) Any patient with imaging evidence of ischemic infarction without clinico radiological proof of eclamptic encephalopathy, reversible cerebral vasoconstriction syndrome or cerebral venous sinus thrombosis was labeled as having cerebral infarction in this study.

CONCLUSION:

After conducted this study it was observed that many patients who are referred to tertiary care centers from primary and secondary care centers with the diagnosis of eclampsia turn out to have many other diagnostic possibilities besides eclampsia after proper clinical and radiological evaluation. Timely diagnosis and management is necessary to prevent morbidity and mortality associated with pregnancy related cerebrovascular disorders.

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Authorship:

Author 1 (Dr. Khalid Sher) and 3 (Dr. Shahnaz) contributed to:

1) Conception and design of study
2) Acquisition of data
3) Analysis and interpretation of data;
4) Drafting the article
5) Revising it critically for important intellectual content; and
6) Final approval of the version to be published.

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2) Analysis and interpretation of data;
3) Drafting the article
4) Revising it critically for important intellectual content; and
5) Final approval of the version to be published.