Neurological disorders during pregnancy and puerperium-still a significant cause of maternal morbidity and mortality in Rural India

C. S. Madkar[1,*], Garima Sinha[2], Shankar Burute[3], Mangal S. Puri[4], Pankaj Salvi[5]

[1,3,4]Professor, [2]Junior Resident, [5]Assistant Professor, Dept. of Obstetrics and Gynecology, Dr. D. Y. Patil Medical College, Pune, Maharashtra, India

***Corresponding Author:**
Email: drcsmadkar@gmail.com

Abstract

Introduction: A variety of neurological disorders may be encountered during pregnancy and puerperium. These disorders may be unrelated to the pregnant state (e.g., tuberculous meningitis) or peculiar to or more prevalent during pregnancy which are still a cause of significant maternal morbidity and mortality in rural India (e.g., eclampsia and cortical venous thrombosis).

Aim: To study the clinical profile of patients presenting with primary and secondary neurological disorders during pregnancy and puerperium and their outcome.

Materials and Methods: This study was carried out at the Mamata Medical College between january 2009 and december 2013. All antenatal patients, postabortal or postpartum period requiring neurological consultation were included in this study. Women with eclampsia were excluded.

Results: There were 75 women included in this study, with 45 cases of primary and 30 of secondary neurological disorders. The former included epilepsy,[21] CNS infections,[12] cerebrovascular disorders,[9] intra cranial tumour,[1] post traumatic paresis[1] and encephalomyelitis.[1] The latter included hepatic encephalopathy,[28] enteric encephalopathy[1] and polyneuropathy.[1] In patients of epilepsy, the seizures had an equal distribution in all the trimesters and post-partum period, they were mainly of generalized type (77.27%) and were controlled in the majority (90.9%). No fetal congenital malformations were seen. Tubercular meningitis,[8] pyogenic meningitis[3] and viral encephalitis[1] were the CNS infections encountered and pregnancy outcome was good in most cases. All cases of CVT presented in the postpartum period with fever and neurological signs following delivery. Among them 2 patients recovered completely, one patient had residual deficits, another had persistent seizures. We had one maternal death. HE affected patients mainly during the latter half of pregnancy or the post-partum period and was associated with 64.3% mortality.

Conclusion: The incidence of neurological disorders in pregnancy and puerperium was very high especially in our hospital since it is a tertiary care referral centre. Epilepsy and hepatic encephalopathy were the commonest primary and secondary neurological disorders respectively found in our study.

Keywords: Cerebrovascular disorders, CNS infections, Pregnancy, Seizures.

Introduction

A variety of neurological disorders may be encountered during pregnancy and puerperium. These disorders may be unrelated to the pregnant state (e.g., tuberculous meningitis) or peculiar to or more prevalent during pregnancy which are still a cause of significant maternal morbidity and mortality in rural India. (e.g., eclampsia and cortical venous sinus thrombosis). Pregnancy may affect the course of pre-existing neurological disorders such as epilepsy. A secondary neurological disorder (e.g., encephalopathy) can affect a pregnant patient with a non neurological medical disease. Neurological disorders may influence the management of otherwise uncomplicated obstetric cases necessitating a multi disciplinary team work involving physician and neurologist.

Aim

The present study was undertaken with an objective of finding the common primary and secondary neurological disorders in pregnant and postpartum patients and to study their clinical features and course in relation to pregnancy.

Materials and Methods

This study was conducted in Mamata Medical College during a period of 5 years extending from January 2009 to December 2013. All antenatal, post abortal and post partum patients (up to 6 weeks after the delivery) presenting with predominantly neurological signs and symptoms, requiring medical referral were included in the study. Patients with a pre-existing neurological disorder and Patients who develop a primary neurological disorder during the course of pregnancy or puerperium were included in our study. Patients with eclampsia managed exclusively in the obstetric unit were excluded. For all the patients, a detailed history and examination including obstetric examination; basic investigations like complete blood count, liver and renal function tests, serum electrolytes and Ultrasonogram were done. Radiological imaging (CT/MRI brain) was done in all 46 cases of primary neurological disorders. Other relevant investigations (e.g., EMG) were done according to the need. Wherever possible, a definitive diagnosis was established based upon standard diagnostic criteria for respective conditions. All patients were followed up for the outcome of the neurological

disorder as well as the pregnancy for a minimum period of 6 weeks following the delivery. Where applicable, the relation of outcome to various clinical parameters was statistically ascertained using the appropriate statistical method.

Results

Out of the 75 patients presented during pregnancy or puerperium with neurological disorders during the study period, 45 cases were of primary neurological disorders and 30 cases were of secondary neurological disorders. The distribution of various disorders is given in Table1. The details of patients presenting with Epilepsy are shown in Table 2. Out of 21 patients, 10 had no abnormality on radiological imaging and 9 were diagnosed to have granuloma. Other findings on CECT/ MRI brain included lacunar infarct[1] and a combination of haemorrhage, infarct and granuloma in three different regions.[1] Seizures were controlled in 20 cases (90.9%) on one or more anti-epileptic drugs including phenytoin, carbamazepine and sodium valproate. Among the 16 patients with epilepsy during pregnancy: 10 had uncomplicated deliveries, three patients presenting in status epilepticus underwent MTP due to teratogenic risk, one had a spontaneous abortion at 20 weeks and one had a term still-birth. This patient was admitted with status epilepticus and a still born baby,she was induced with prostaglandins – misoprostol vaginally every 3rd hourly for 3 such doses and delivered a dead male baby. She was intubated since she did not regain consciousness in between convulsions .she was treated with anti epileptic drugs through out the labour. She also had uncontrolled hypertension during labour and nitro glycerine drip was started. Later she was diagnosed to have intra cranial bleed on CT scan and was on ventilator support for 5 days. Patient was on conservative support and she recovered completely. Gross congenital malformations were not seen in any neonate. Out of the 12 patients with CNS infections, there were eight cases of tubercular meningitis (five out of them were already on treatment with anti tuberculous drugs for less than a month duration), three cases of acute pyogenic meningitis and one case of viral encephalitis. All eight patients presented during the postpartum period, while the rest presented during pregnancy. Clinical features included fever, headache, altered sensorium,[12] seizures,[2] focal neurological deficits[3] and evidence of extra-neural involvement.[6] Laboratory findings were consistent with disease presentations. Two patients of pyogenic meningitis recovered completely, while one developed focal neurological deficit and expired. Seven patients with Tuberculous Meningitis improved on ATT with steroids, whereas one patient developed a concurrent sub dural empyema and expired. The patient with viral encephalitis had residual psychiatric disturbance. Out of the five pregnant patients, one patient of Tuberculous Meningitis underwent MTP in the first trimester. Rest of the patients had normal deliveries.Out of 9 cases of cerebro vascular disorders, 5 were of CVT, all of them presented within the first two weeks after their delivery. Clinical features included fever,[5] headache,[3] generalized seizures,[4] altered sensorium,[4] focal neurological deficits[4] and features of pre-eclampsia.[1] All cases showed anaemia, leucocytosis and sterile blood cultures. USG revealed retained products of conception in one patient. Venous sinus thrombosis was seen on MRI brain in three cases and three patients had haemorrhagic infarcts. All patients were treated with anti-coagulants. Two patients recovered completely, one had residual neurological deficit; seizures persisted in one and one expired in spite of our best efforts. The patient who expired was 12 weeks pregnant presented with headache for one week and drowsiness for two days. Computed tomography of the brain revealed intra cranial hematomas. Decompressive craniectomy was done to relieve the increased intracranial pressure. Magnetic resonance angiography and cerebral angiography were subsequently performed, both demonstrating thrombosis of the left transverse sinus. Treatment of sinus thrombosis with administration of anticoagulants, such as heparin and mannitol for reducing raised intracranial tension was done. Inspite of these effective measures we could not save the patient. Three patients presented with arterial infarctions: one had rheumatic heart disease; she presented on the tenth postpartum day with left hemiparesis was found to have infarcts. Two patients presented on the eighth post partum day-one had aphasia and right hemiparesis and the other presented with bilateral cerebellar signs. The former was found to have multiple infarcts in the internal capsule, basal ganglia, mid-brain and cerebellum, while the latter had bilateral cerebellar infarcts on neuro imaging. All three were treated with anti-coagulants and had residual neuro deficits.

One patient presenting at 10 weeks of pregnancy with right hemiparesis and right seventh nerve palsy was found to have a left basal ganglia bleed due to ruptured intra cranial aneurysm on neuro imaging. She underwent Medical Termination of Pregnancy (MTP) and was referred for neurosurgical intervention. The patients with intra cranial tumour and acute disseminated encephalomyelitis succumbed to their illnesses, while the one with traumatic quadriparesis was successfully operated upon and delivered a healthy baby by forceps extraction. In cases of HE, specific etiology could not be proved in most cases due to derranged coagulation profile. Sixteen patients presented in the second trimester, seven in the third trimester and five in the postpartum period. Clinical features included fever,[23] altered sensorium,[28] jaundice,[28] seizures[1] and oliguria.[5] Fourteen patients (50%) had Grade IV HE and a Glasgow Coma Score of 3. Liver span could not be localized in 10 cases. Leucocytosis was present in 24 cases. LFT, coagulation

profile, renal Function Tests and electrolytes were derranged in all the cases. Out of 28 patients, 18 (64.3%) died, of which 7 died in the antenatal period, 9 post abortal and two following normal vaginal delivery. Ten patients (35.7%) recovered completely: two after spontaneous abortions, one after a still-birth, three after delivering healthy babies and four with foetuses in situ. Statistically significant associations were seen between mortality and the grade of he, Glasgow Coma Score at presentation, liver span on examination, value of serum bilirubin and retained foetus.

Table 1: Etiology of neurological disorders

Neurological disorder		Number of cases	Percentage
1.	Primary neurological disorders	45	60%
a.	Epilepsy	21	28%
b.	CNS infections	12	16%
c.	Cerebro vascular disorders	9	12%
d.	Traumatic, quadriparesis	1	1.3%
e.	Acute disseminated encephalomyelitis	1	1.3%
2.	Secondary neurological disorders	30	40%
a.	Hepatic encephalopathy	28	37.3%
b.	Enteric encephalopathy	1	1.3%
c.	Critical illness polyneuropathy	1	1.3%

Table 2: Comparitive studies

Condition	To et al (n=161) (%)	Janaki et al (n=97) (%)	Agarwal (n=87) (%)	Srinivasan et al (n=68) (%)	Present study (n=75) (%)
Epilepsy	102 (63.3)	30 (30. 9)	5 (5.7)	17 (23.5)	21 (28.0)
Cerebro vascular disorders	7 (4.3)	48 (49.5)	72 (82.7)	41 (60.3)	9 (12.0)
CNS infection	-	4 (4.1)	5 (5.7)	3 (4.4)	12 (16.0)
CNS tumors	12 (7.5)	7 (7.2)	1 (1.1)	16 (23.5)	1 (1.3)
Eclampsia	19 (11.8)	Not included	Not included	Not included	Not included
Demyelinating disease	4 (2.5)	1 (1.03)	1 (1.1)	3 (4.4)	1 (1.3)
Peripheral neuropathies	12 (7.5)	1 (1.03)	2 (2.3)	1 (1.5)	1 (1.3)
Metabolic encephalopathies	Not included	Not included	Not included	Not included	28 (37.3)
Cord affections	-	-	-	5 (7.4)	1 (1.3)
Incidence of primary neurological Disorders	326 per 100,000 deliveries	Not included	Not included	Not included	353 per 100,000 deliveries

Discussion

A variety of neurologic conditions can affect women during pregnancy and puerperium.[1,2] The primary neurological disorders studied in relation to pregnancy include eclampsia, stroke, epilepsy, benign intra cranial hypertension, CNS tumours, Bell's palsy, obstetric pressure palsies, demyelinating diseases of the central/peripheral nervous system and neuro muscular junction disorders (myasthenia gravis). Neurological diseases may be incidental to pregnancy (e.g., meningitis). Patients may also present with secondary neurological disorders such as metabolic encephalopathies secondary to hypoxia-ischaemia, hypoglycemia, hepatic failure, azotemia, hypercalcemia and nervous system disorders secondary to nutritional deficiencies and endocrine dysfunction. The studies carried out by Thomas et al and Agarwal et al so far have included only primary neurological disorders[3-6] and their incidence during pregnancy has not been studied systematically in most studies. The incidence of primary neurological disorders in this study was comparable to that in a study done by Cheung RT from Hong Kong. Computed tomography and magnetic resonance imaging have opened new vistas for the diagnosis, classification, and management of many neurological disorders as observed by Dineen and

colleagues in 2005.[7] Chalela and associates in 2007 found that MR imaging is superior for detecting acute ischemia and acute and chronic hemorrhage, and therefore, is preferable for stroke evaluation[8]. In our study we could diagnose almost all the intra cranial catastropes with the help of CT and MRI .Analysis of various studies shows a wide variation in the occurrence of epilepsy. In the current study, the timing of seizures in relation to pregnancy showed an almost uniform distribution across the trimesters and the postpartum period, whereas in other studies[9,10] done by Knight et al and Jacob et al ,the seizure frequency was found to be least during the third trimester and postpartum period. Most seizures in this study were encountered in the peri partum period and were attributable to noncompliance, physical exhaustion or metabolic derrangements. The distribution of type of seizures (generalized vs. partial) was similar to study[11] conducted by Schmidt D et al in New York. However, a significantly greater number of patients presented with status epilepticus in this study in comparison to other studies (31.8% vs. 0.53 to 5.3%), which can be explained by: delayed presentation of patients to the hospital after the onset of seizures, non compliance, and discontinuation of Anti-epileptic drugs. A higher proportion of patients had seizure occurrence for the first time during pregnancy as compared to study done by Devinsky et al. Out of nine patients who were on Anti Epileptic Drugs, three had stopped medication due to the fear of adverse effects. Seizures occurring in the other three patients despite adequate compliance lends credence to the fact that seizure frequency may change during pregnancy in the absence of alterations in the doses of AED due to changes in AED protein binding or clearance[12]. The Centers for Disease Control and Prevention reported that the prevalence of epilepsy in adults in 2005 was 1.65 percent, it was also found by Kobau and colleagues in 2008[13]. Brodie and Dichter in 1996 and also Yer by in 1994 observed in their study 1.1 million American women of childbearing age were affected with epilepsy, and seizure disorders complicate 1 in 200 pregnancies[14].In a recent community-based, prospective study from Finland, Viinikainen and co-workers in 2006 reported that epilepsy either was better controlled or showed no change in 83 percent of pregnant women[15]. Meador and co-workers in 2006 also reported an 81-percent seizure-free rate in pregnancy for 333 women enrolled in multicenter observational studies[16]. From the Australian Registry, Vajda and colleagues in 2008 reported that the risk of seizures during pregnancy was decreased by 50 to 70 percent if the year before was seizure free[17]. In our study the incidence of epilepsy was 28% which is comparable to study done by Janaki et al. There was no incidence of gross congenital malformations, unlike other studies where it varied between four and 12%.
A higher occurrence of cerebro vascular disorders in the previous Indian studies was noted in comparison to the present study. The difference is due to less cases of CVT (6.6%) as compared to these studies where CVT accounted for 35-65% of the cases. CVT has an exceptionally high incidence in India, attributable to a combination of dehydration, infection, and the traditional fat-rich diet fed to postpartum women causing a hyper coagulable state[18]. However, the lower incidence in this study could be explained by the increased awareness among patients and their families, with better facilities for asepsis during delivery as compared to the other studies, which were carried out around few decades back. All cases presented with classical clinical features, similar to those studies[19-21] done by Deshpande,Srinivasan and Tang. Anaemia, a predisposing factor for CVT, was uniformly present. All cases were treated with anti-coagulants according to accepted treatment strategies. No patient had residual motor paralysis, but 20% mortality was seen. Mortality rate in cases of CVT was ~28% in these studies. Current mortality rates are estimated to be as low as 5.5% with anti-coagulation. The incidence rates for ischemic strokes associated with pregnancy or puerperium vary in literature from five to 210 (23 in our study) per 100,000 deliveries[22]. The incidence of arterial thrombosis in most studies varied between 8 and 64% of the total cases, which is higher than in the present study (3.8%). Residual paralysis as seen in this study, is a common sequlae of ischemic arterial occlusion. Intracranial haemorrhage constituted from 2 to 7% of the total cases of neurological disorders in most studies (1.3% in our study). From a Swedish study of 1207 epileptic women, Pilo and colleagues during the year 2006 reported a 1.5-fold increased incidence of cesarean delivery, preeclampsia, and postpartum hemorrhage. They also found that lateral or superior sagittal venous sinus thrombosis usually occurs in the puerperium, and often in association with pre-eclampsia, sepsis, or thrombophilias. It is more common in patients with inherited thrombophilias, lupus anticoagulant, or antiphospholipid antibodies.[23] In our study we had patients with pre - eclampsia and thrombophilias who presented with cerebral venous sinus thrombosis and were managed effectively. Wasay and colleagues in 2008 also observed that headache was the most common presenting symptom, neurological deficits were also common, and up to a third of patients had convulsions.[24] In the 28 women described by Martin and associates in 2005, half of them died and most survivors had permanent disabilities. They underscored the importance of proper management for gestational hypertension—especially systolic hypertension—to prevent cerebrovascular pathology[25].In the present study we have diagnosed early and treated patients with hypertensive disorders in time ,thus we could prevent maternal morbidity and mortality. Rupture of a cerebral aneurysm or angioma or bleeding from a vascular malformation occurs in 1 in

75,000 pregnancies. This incidence does not differ from that in the general non - obstetrical population, but the mortality rate during pregnancy is reported to be as high as 35 percent by Dias and Sekhar in 1990.[26] There were also case-control studies from Japan and New Zealand which showed that nulligravidity significantly increased the risk of sub- arachnoid hemorrhage done by Mhurchu and co-workers in 2001 and Okamoto and colleagues in 2001.[27] About one in 10,000 pregnancies is reported to be complicated by the rupture of an intracranial aneurysm,[28] roughly the same as in our study. However, this patient presented in the first trimester, though aneurysmal rupture is more likely in the second and third trimesters. CNS infections showed a higher incidence in the present study than in others. TBM usually presents with classical manifestations during pregnancy, commonly between the 5th and 7th months or in the postpartum period. Most patients improve with treatment,[29] as in our study. The only patient with a CNS tumour (glioma) presented in the post partum period, which is relatively rare. Usually there is an increase in the size of the tumour during pregnancy due to hormonal changes and amelioration of symptoms in the postpartum period. She in pregnancy may be related to a wide variety of acute and chronic liver diseases, out of which Hepatitis E virus infection is an important cause in India.[30,31] Acute fatty liver of pregnancy generally presents after the 30th week of pregnancy. Fulminant viral hepatitis leading to hepatic encephalopathy may be seen in any trimester. All patients presented with jaundice and altered sensorium of less than 10 days duration, in accordance with the definition of fulminant hepatic failure. Leucocytosis was observed in most of our cases. In a recent study done by Kumar et al from Delhi, mortality of he was upto 85.7%. In our study, the overall mortality from he was 64.3%. The factors determining outcome in patients with he have been highlighted in the results. Hurley and colleagues in 1991 reported that one third of affected pregnant women with Guillain – Barre syndrome, ultimately required ventilatory support, and the overall mortality rate was 13 percent.[32] Treatment of acute GBS in pregnancy is with either high-dose immunoglobulin or plasmapheresis.

Conclusion

To conclude, epilepsy and hepatic encephalopathy emerge as the predominant neurological disorders during pregnancy and puerperium with a substantial contribution by cerebro vascular diseases and CNS infections. Effects of these conditions and their treatments on pregnancy and the effects of pregnancy on the course of these disorders should be kept in mind while dealing with these conditions in pregnancy. Appropriate management, preferably under the combined care of neurologists, obstetricians and neurosurgeons, is required to optimize maternal and foetal outcomes.

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