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Original Research Article

Neurological complication of pregnancy: An experience from north east India

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ABSTRACT

Background: The neurology of pregnancy is usually of two types, those that are pregnancy-specific and those that worsen during pregnancy and the post-partum period. Almost 20% of maternal mortality can be attributed to neurological causes which warrants us to identify the red flag sign for early and proper intervention.

Materials and Methods: A retrospective study of three years duration in North East India. All demographic, clinical, and neurological findings, routine investigation, and neurological investigation were recorded. Further analysis was done to find out the most common neurological pathology in pregnancy and classify them into pregnancy-specific, incidental, and preexisting neurological conditions.

Results: A total number of 80 patients were included. The age ranged from 18 to 49 years with the maximum number of patients (forty-four) in the 20-30 age group. Guillain barre syndrome (GBS) seen in 21 patients (26%) which was the most common with maternal mortality and stillbirth. Eclampsia was seen in seventeen patients (21%) with three intra-uterine death and one maternal death noted. The other neurological disease was cerebral venous thrombosis (11%), seizure in isolation (six patients), and seizure with post-partum sepsis (five patients). Myelopathy was seen in four patients, carpal tunnel syndrome and cramps in six patients each, multiple sclerosis, tubercular meningitis (proven), thymoma-negative generalized myasthenia gravis, and arteriovenous malformation in one patient each.

Conclusion: An in-depth knowledge of the various neurological diseases during pregnancy helps us to recognize them early and provide proper approaches and management to reduce harm to maternal and child health.

1. Introduction

Almost any medical disorder occurring in a woman of childbearing age could complicate the period of pregnancy. There are, however, neurological disorders that are incidental, those that occur more commonly during pregnancy than at other times, or those that worsen or get exacerbated during this period.[1,2] Some of these diseases are mild not requiring attention but some present with acute neurological emergencies affecting maternal mortality rate.[3] Almost 20% of maternal mortality can be attributed to neurological causes, this alarms neurologists to give the necessary attention to 'red flag signs'.[2] Further, diagnosis and management of these patients cause a hurdle to a neurologist because of the varied adverse effects on the fetus. Management of pre-existing neurological disorders during epilepsy is also troublesome because of the various hormonal changes.[4] The neurology of pregnancy has been an area of interest and research as related to the care of neurological disorders in pregnancy and the outcome on the maternal and child health. With this in mind,

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we retrospectively studied all the different neurological disorders occurring during pregnancy and their outcome.

2. Materials and Methods

This was a retrospective study for three years from a tertiary referral center in Northeast India. After receiving the Institutional Ethical Committee approval, the observational study data was obtained.

All pregnant patients and those who presented in the post-partum period with any neurological symptoms were recruited in the study. Those patients with pre-co-morbid neurological conditions that worsen during their pregnancy period were also taken into consideration. These patients were recruited from both indoor and outdoor patients of the neurology and gynecology departments.

Demographic and clinical data were obtained. A detailed clinical history and general physical, gynecological, and neurological examination were done where positive findings were noted to understand the clinical semiology and neuro-axis involved. The routine blood investigation included a complete blood count, liver and kidney function test, thyroid profile, viral marker, and radiological investigation as and when needed. Neurological investigations like cerebrospinal fluid examination, electroencephalogram, nerve conduction studies, and neuroimaging were done according to the needs of the particular patient's clinical semiology. The patients were conservatively managed according to the diagnosis made and follow-up was done on OPD basis.

All data were obtained and recorded in an Excel sheet which included the demographic data, state of pregnancy and the gravida, clinical semiology, routine and neurological investigation, final diagnosis, and outcome of those patients.

These neurological complications or diseases which were made were further divided into those that are pregnancy-specific, incidental, and pre-existing neurological disorders worsening during pregnancy. Analysis of data was done to see the most common neurological complications occurring during pregnancy and post-partum period and their outcome concerning maternal and child health.

3. Results

A total number of 80 patients were included in the study over 3 years. The age ranged from 18 years to 49 years with the maximum number of patients (forty-four) in the 20-30 age group. The total no of patients <20 years of age was five in number similar to those >40 years of age. Most of them presented in the post-partum period(forty-seven) and third trimester(seventeen) while only three patients presented during active labor (Figure 1). Most of the patients were multi gravida (75%) with only twenty patients presented as primigravidae.

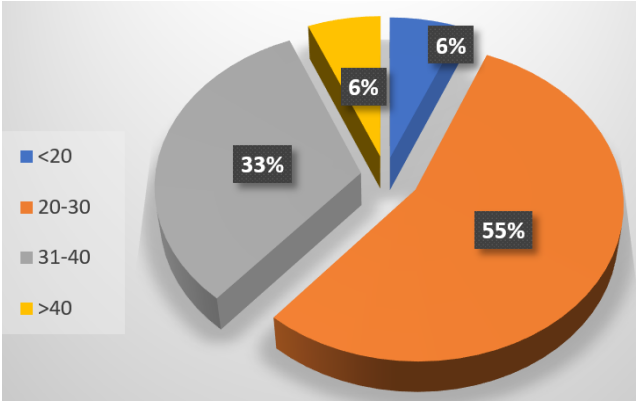

Figure 1: Age wise distribution of the patients

The benign neurological disorders seen in our cohort were carpal tunnel syndrome and cramps in six patients each. The most common neurological disorder seen was Guillain barre syndrome (GBS) seen in 21 patients (26%) Among the GBS patients fifteen were of AIDP variant, four AMAN, one AMSAN, and recurrent AIDP was seen in one patient with subsequent pregnancy. Post-partum sepsis associated with GBS was seen in 3 patients with maternal mortality in one patient and stillbirth in one patient. Eclampsia was seen in seventeen patients (21%), out of which three intra-uterine deaths and one maternal death were seen among these patients. An abnormal MRI was seen in ten patients reported as PRES (Figure 4).

The other neurological disease was cerebral venous thrombosis (11%), with thrombosis in the superior sagittal sinus in 5, transverse sinus in 3, and sigmoid sinus in 1 patient (Figure 5). Seizure in isolation in six patients and seizure with post-partum sepsis in five patients. Among the seizures in isolation, four patients were old neurology patients with neurocysticercosis in two patients and idiopathic in two patients. These patients had an increased frequency of seizure for which optimization of medication was done. Two patients developed seizures during pregnancy whose etiology remained unknown. One intrauterine death was reported among the seizure with sepsis patients. Myelopathy was seen in four patients whose diagnosis was made in two patients tuberculosis (Pott's spine) and neuromyelitis optica spectrum disorder (NMSOD) who had recurrent attacks. The other two patients remain undiagnosed due to constraining in investigation. The other neurological disorder seen as multiple sclerosis, tubercular meningitis (proven), thymoma-negative generalized myasthenia gravis, and arteriovenous malformation in one patient each. We had one patient who presented with hypoxic brain injury after the caesarian section as a complication (Figure 2). These neurological disorders were divided into pregnancy-related, incidental, or preexisting neurological disorders that worsen

during pregnancy are depicted in Table 1.

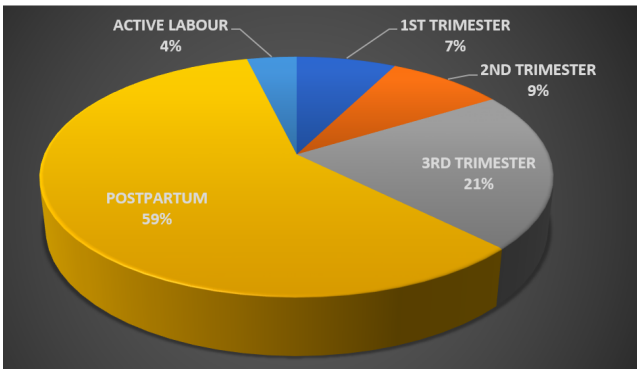

Figure 2: The stages of pregnancy at the time of their neurological complication

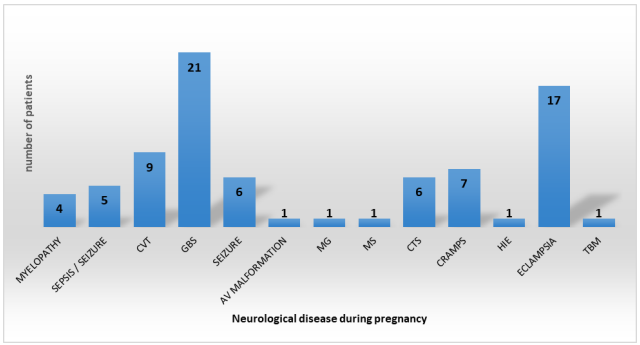

Figure 3: The spectrum of neurological complication during pregnancy

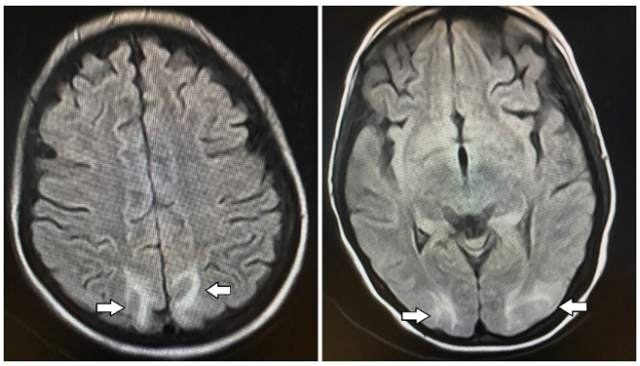

Figure 4: Axial FLAIR image showing hyperintense signal in bilateral parietal and occipital lobes representing vasogenic oedema consistent with Posterior Reversible Encephalopathy Syndrome (PRES)

There were two maternal deaths (2.5%) and five intrauterine deaths (6.2%), sequalae in the form of paraparesis, seizure, and encephalopathy were seen in ten patients (12.5%). Complete recovery was seen in 60 patients (75%) and no follow-up in eight patients (Table 2).

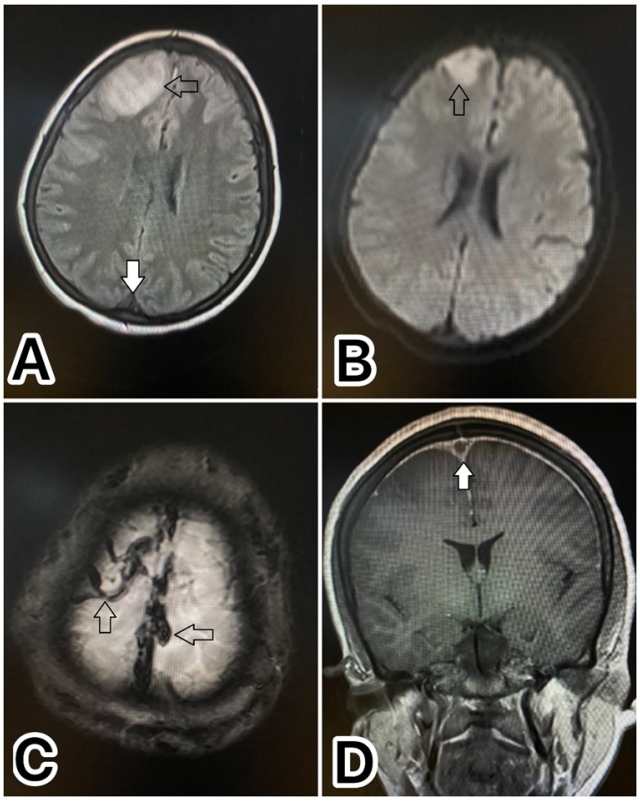

Figure 5: A): Showing absence of flow void in the superior sagittal sinus (White arrow) and a hyperintense lesion in the right frontal lobe (Black arrow) that shows restriction on DWI axial image; **B**): Axial image; **C**): Shows blooming in the superior sagittal sinus and right cortical veins (Black arrows) on GRE sequence. Post contrast coronal image; **D**): Shows a triangular filling defect outlined by contrast (empty delta sign) within the superior sagittal sinus. Findings are consistent with cerebral venous thrombosis of superior sagittal sinus and right cortical veins with venous infarct involving right frontal lobe

Table 1: Age distribution of patients

Age Distribution	
Age Group	**Number of Patients**
<20	5
20-30	44
31-40	26
>40	5
Pregnancy Status	
Primigravidae	20
Multigravidae	60

Table 2: Classification of neurological complications of pregnancy

Pregnancy-specific neurological disorder	Eclampsia
	Cerebral venous thrombosis
	Postpartum sepsis/seizure
	Gulli and Barre syndrome
	Carpal tunnel syndrome
	Cramps
Incidental neurological disorder	NMSOD and Pott's spine
	Tubercular meningitis
	Multiple sclerosis
	Hypoxic brain injury (post-cesarean section)
	Seizure
Preexisting neurological disorder	Seizure disorder
	AV malformation
	Myasthenia gravis

NMSOD: Neuromyelitis optica spectrum disease; AV: Arterio-venous

Table 3: Outcome of neurological complication of pregnancy

Outcome	No of patients	Aetiology
Intrauterine death	5	GBS with sepsis
		Seizure disorder
		Eclampsia
		Press with help syndrome
Maternal death	2	Post partum sepsis/GBS
		Eclampsia
Sequalae	10	Myelopathy -NMSOD
		Myelopathy -Pott's spine
		GBS-AMSAN/AMAN
		Seizure-eclampsia
		CVT
		HIE
Full recovery	60	
No follow-up	8	

GBS: Gullian barre syndrome; CVT: Cortical venous thrombosis HIE: Hypoxic-ischemic encephalopathy

4. Discussion

A pregnant lady undergoes a variety of physiological changes which include hormonal changes, hyperdynamic circulation, changes in the connective tissues, and a hypercoagulable state due to increased production of procoagulant factors and fibrinogen.[5] Pharmacokinetic of drugs also altered during pregnancy due to alterations in renal clearance and liver metabolism.[6] A knowledge of all this is important to understand the neurology of pregnancy. Few benign disorders like carpal tunnel syndrome and cramps usually resolve by themselves after delivery of the child. One study from North India reported musculoskeletal pain as the most common symptom followed by carpal tunnel syndrome.[1] Benign disorder is less reported in the present study as most of the cases were recruited from the emergency department.

The most common neurological emergency that a pregnant patient presents with is a seizure, whose etiology may be an eclamptic seizure, secondary to stroke or CVT sepsis dyselectrolytemia or organ failure, idiopathic or a preexisting epilepsy patient. The incidence of epilepsy in pregnancy is 3-5 per 1000 births.[7] In those patients where seizure started during pregnancy, importance is given to the diagnostic procedure and medication, especially during the first trimester.[6] In those patients with pre-existing epilepsy patient, counseling and choice of anti-epileptic pre-pregnancy period and alteration of the dose during pregnancy is important. A total of nine months of seizure-free period is usually recommended before pregnancy to prevent recurrence.[4] We reported seizures in all eclampsia patients (17 patients), post-partum sepsis associated with seizure in five patients, four patients with CVT, two isolated seizures of pregnancy, one tubercular meningitis patient, and four patients with preexisting epilepsy conditions.

Guillain barre syndrome is a disease that affects the peripheral nerve causing an ascending paralysis with areflexia. It is not more common during pregnancy but is reported more during the first 14 days post-partum. The course of pregnancy is not affected although pre-term labour is known to occur.[8] The management of GBS is almost similar to the normal population.[9] GBS has frequently been reported as case report [10]but our cohort had the maximum number of patients having GBS seen in 21 patients (26%). All variants including AIDP (15 patients), AMAN (4 patients) AMSAN, and recurrent AIDP were seen in one patient each. Most of our patients presented during the post-partum period (76%). Such a huge number of GBS during pregnancy is a requisite for a need of research in this area.

Hypertension in women during pregnancy is common, it accounts for almost 12% maternal mortality rate.[10] Pre-eclampsia or mild eclamptic seizure can be managed by experienced gynecologists with anti-hypertensive drugs and magnesium sulfate.[11] Fulminant presentations like eclampsia crisis,[12] persistent seizures, coma, HELLP syndrome, and severe eclampsia usually require a multidisciplinary approach. The maternal mortality rate is as high as 15% among eclampsia patients especially in developing countries due to lack of resources and illiteracy.[13] Our present cohort reported eclampsia in seventeen patients (21%) with HELLP syndrome in two patients. There were three intra-uterine death and one maternal death was seen among these patients which is almost similar to other studies reported.[2] We had abnormal MRI brain suggestive of PRESS in ten patients although the

classical clinical presentation was seen only in two patients.

Although hemorrhagic stroke is common in pregnancy and is usually associated with poor outcomes,[12] CVST forms a different platform of stroke in pregnancy. This particular disease has a gender prediction occurring more in females but the pregnancy and the immediate post-partum period adds increased risk to cerebral venous thrombosis.[14] We hereby report 9 patients on CVST whose clinical presentation was seizure (3 patients), neuro-deficit (2 patients), and secondary headache in 4 patients. Thrombosis in superior sagittal sinus in 5, transverse sinus in 3 and sigmoid sinus in 1 patient in neuroimaging.

Myelopathy in pregnancy especially NMSOD has received special importance because of the increased relapse rates and a higher risk of disability during this period.[15] One single center studied thirty-four AQP4 antibody-positive NMOSD pregnant patients and concluded that pregnancy can induce the onset or relapse of attacks with special consideration to the treatment part due to risks of adverse effects to the fetus.[16] In the present cohort we had four myelopathy patients with one patient being diagnosed as NMO.

A change in the immunological status during pregnancy can make them prone to infection. One series has reported up to 44% of tubercular meningitis among the neurological complications during pregnancy.[2] Our cohort also reports two patients with tuberculosis one with TBM and the other with Pott's spine.

Another disorder that usually aggravates during pregnancy is myasthenia gravis, multiple sclerosis, and pituitary apoplexy. All these conditions need proper assessment and management to reduce harm to foetus. Our patient of generalised myasthenia gravis was diagnosed during her early post-partum period and responded to a combination of pyridostigmine and immunosuppressant.

5. Conclusion

A failure to identify the red flag symptoms associated with various neurological pathologies during pregnancy would lead to a delay in the correct therapeutic approach leading to increased mortality and morbidity. For those with pre-existing neurological disease, prior knowledge helps the neurologist to counsel and treatment regime plan to reduce harm to the fetus and avoid relapse in the mother.

6. Limitations

The present study being retrospective has a lot of research restrictions, active case recruitment would include a variety of benign pathologies in pregnancy. The increased number of GBS patients warrants active research into etiopathogenesis during pregnancy and the postpartum period.

7. Sources of Funding

None.

8. Conflict of Interest

None.

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