A study of neurological disorders in pregnancy and puerperium

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ABSTRACT

Background: Neurological diseases contribute to 20% of maternal deaths. The objective of this study was to find the prevalence of primary and secondary neurological disorders in pregnant and postpartum patients, to study their clinical features, feto-maternal outcome and diagnosis using radiological imaging.

Methods: This is a prospective cross-sectional study done over a period of 1 year. Pregnant and postpartum women with neurological disorders except eclampsia were enrolled. A total of 100 cases were analysed out of which 92 underwent radiological imaging to confirm diagnosis. Primary outcome in the form of prevalence of neurological disorders and secondary outcome in the form of maternal and foetal outcome was assessed.

Results: The prevalence of neurological disorders in pregnancy is 1150/100000 deliveries. 75 cases were classified as primary neurological disorders (prevalence of 862/100000) which included epilepsy, cerebrovascular accidents, CNS infections, neoplasm, neuropathies and miscellaneous. 25 cases were secondary neurological disorders (prevalence of 287/100000) which included hepatic and septic encephalopathy. Among primary disorders the prevalence of cerebrovascular accidents was found to be highest (33.3%) followed by epilepsy (32%) while that among secondary neurological disorder was of Hepatic encephalopathy (92%). Majority (68%) had recovery while 15% of women had residual deficit. There were 17 (17%) cases of maternal mortality.

Conclusions: Neurological disorders were significantly associated with poor feto-maternal outcome. Radiological imaging in the form of MRI is an excellent diagnostic tool for confirming diagnosis of neurological disorders.

Keywords: Cerebrovascular accident, Epilepsy, Neurological disorder

INTRODUCTION

A variety of neurological disorders may be encountered during pregnancy and puerperium. Management of pregnancy with neurological disease is highly challenging. Neurological diseases contribute to approximately 20% of maternal deaths.1 Neurological disorders in pregnancy can be primary or secondary. The primary neurological disorders studied in relation to pregnancy include Epilepsy, Cerebrovascular accidents, CNS infections, neoplastic diseases, neuropathies, demyelinating disorders etc.2 Secondary neurological disorders include metabolic encephalopathies secondary to hypoxia, ischaemia, hypoglycaemia, hepatic failure or azotemia.

Neurological disorders commonly manifest as headache, seizures, motor deficits, altered sensorium, visual deficits, aphasia, and cranial nerve palsies. According to WHO, headache emerged to be a very common neurological complaint during pregnancy.3 Epilepsy is the most common neurological disease that will be encountered by an obstetrician (1 in 200) followed by cerebrovascular accidents. Cerebrovascular accidents are further classified
into stroke - ischaemic and hemorrhagic, subarachnoid haemorrhage and cortical venous thrombosis (CVT).

The overall incidence of ischemic stroke during pregnancy is low (3.5-5 per 100,000 pregnancies in the developed world). Women 3–4 weeks' postpartum may develop an aseptic thrombosis of cerebral veins and sinuses.\(^4\) Mortality related to CVT is estimated at 9% and is primarily due to intra cerebral haemorrhage.\(^6\) Patients may present with neuropathies as bell’s palsy, Guillain Barre syndrome, meralgia paraesthetica and demyelinating disorders as multiple sclerosis.

Bell's palsy, or idiopathic palsy of the seventh cranial nerve, is seven times more prevalent than expected during the third trimester of pregnancy.\(^7\)

The advent of CT, MRI and MR venography has proved to be a boon for early diagnosis of pregnancy related neurological complications. There is minimal risk to the foetus. Early diagnosis of pregnancy with neurological complications will result in deciding appropriate treatment of neurological disease and termination of pregnancy at appropriate gestational age with better maternal and foetal outcome.

This study was conducted with the aim to determine the prevalence of total neurological disorders complicating pregnancy and puerperium and that of primary and secondary neurological disorders. Analysis of maternal and fetal outcome and co-relation with radiological imaging was done.

**METHODS**

This was a hospital based prospective cross-sectional study done in the Department of Obstetrics and Gynaecology and Department of Neurology at King George Medical University, Lucknow for a duration of 1 yr. This was a pilot study that included all the cases presenting with neurological disorders in pregnancy and puerperium (107) during the study period.

**Inclusion criterion**

Pregnant and postpartum women with: Signs and symptoms suggestive of neurological disease.

Primary neurological disorders that includes epilepsy, CNS infections, cerebrovascular. Disorders (cerebral venous thrombosis, Ischaemic stroke & haemorrhage), CNS neoplasms, etc. Secondary neurological disorders like metabolic encephalopathies.

**Exclusion criterion**

Women not compliant for follow up. Women unwilling to participate. Women diagnosed with eclampsia. Women in whom MRI is contraindicated as those with claustrophobia, prosthetic cardiac valves, etc.

For all subjects written and informed consent was taken. A special proforma was filled for all patients which included history, general examination, neurological examination and obstetric examination. Expert opinion by neurologist was taken for all patients. Routine blood investigations (hemogram, LFT, KFT, electrolytes) relevant radiological imaging CT/MRI brain, MRA/MRV brain, MRI spinal cord and other specific investigations as NCV/EEG/EMG according to merits of individual conditions were done.

Patients were then classified as those with primary and secondary neurological disorders and outcome was assessed as primary and secondary outcome. The primary outcomes analysed included prevalence of total neurological disorders, primary and secondary neurological disorders in pregnancy and puerperium. The secondary outcomes were assessed as pertaining to the foetus as abortion, preterm or term delivery, livebirth or stillbirth and maternal outcome in the form of complete recovery, residual deficit or mortality.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD. Statistical formula used was chi square test and level of significance was determined.

**RESULTS**

A total 107 patients presented with neurological complaints of which 100 patients were analysed as 7 patients could not be followed. Majority of the cases were unbooked (84), of age group 25-30 years (61%), multiparous (58%) and belonged to lower socioeconomic status (63%).75 (75%) were classified as with primary neurological disorders whereas remaining 25 (25%) had secondary neurological disorders. The total no of deliveries in the hospital during study period was 8691. The prevalence of neurological disorders primary and secondary per 1 lakh deliveries with percentage is shown in Table 1.

**Table 1: Distribution of patients according to type of neurological disorder.**

| Type of Neurological disorder | No. of cases | Percentage | Prevalence/100,000 |
|------------------------------|--------------|------------|-------------------|
| Primary Neurological disorder | 75           | 75         | 862               |
| Secondary Neurological disorder | 25           | 25         | 287               |
| Total                        | 100          | 100        | 1150              |

The most common clinical presentation in patients was seizure with associated symptoms as altered
consciousness or motor deficit (49%) followed by altered consciousness (32%) and headache (30%) (Table 2).

Table 2: Distribution of patients according to clinical presentation.

| Clinical Features                          | No. of cases | Percentage |
|-------------------------------------------|--------------|------------|
| Seizures alone or h/o seizure             | 22           | 22         |
| Altered Consciousness                     | 32           | 32         |
| Seizure and altered consciousness         | 09           | 09         |
| Seizure with altered consciousness with motor deficit | 18           | 18         |
| Motor weakness with altered consciousness | 10           | 10         |
| Headache                                  | 30           | 30         |
| Motor Weakness                            | 20           | 20         |
| Visual Symptoms                           | 20           | 20         |
| Aphasia                                   | 08           | 08         |
| Facial Nerve Palsy                        | 12           | 12         |

Table 3: Distribution of patients according to type of primary (75) and secondary neurological disorder (n=25).

| Type of Primary/secondary Neurological disorder | No. of cases | Percentage | Prevalence / 100,000 |
|------------------------------------------------|--------------|------------|----------------------|
| Epilepsy                                      | 24           | 32.0       | 276                  |
| Vascular                                      | 25           | 33.3       | 287                  |
| CNS Infection                                 | 11           | 14.7       | 126                  |
| Space Occupying Lesion                        | 09           | 12.0       | 103                  |
| Neuropathy                                    | 02           | 2.7        | 23                   |
| Miscellaneous                                 | 04           | 5.3        | 34                   |
| Total                                         | 75           | 100        | 862                  |
| Hepatic encephalopathy                        | 23           | 32.0       | 264                  |
| Septic encephalopathy                         | 02           | 8.0        | 23                   |
| Total                                         | 25           | 100        | 287                  |

Table 4: Case Distribution according to imaging modality.

| Investigation | Total Number | Primary Neurological disorder (n=75) | Secondary Neurological disorder (n=25) |
|---------------|--------------|-------------------------------------|---------------------------------------|
|               | Result       | No. | %    | No. | %    |
| MRI & MRA & MRV | 80           | 66  | 88.0 | 14  | 56.0 |
| CT             | 12           | 07  | 9.3  | 05  | 20.0 |
| Not Done       | 8            | 02  | 2.7  | 06  | 24.0 |

Table 5: Diagnosis and co-relation of neurological disease with neuro-imaging.

| Clinical feature                          | MRI and MRA and MRV n=66 | Result | N   | CT N=7 | Result | n   |
|-------------------------------------------|---------------------------|--------|-----|--------|--------|-----|
| Seizure alone or h/o seizure              | 22                        |        |     |        |        |     |
|                                           | MRI                       |        |     |        |        |     |
|                                           | 11                        |        |     |        |        |     |
|                                           | NAD                       | 08     |     |        |        |     |
|                                           | glioma                    | 01     |     |        |        |     |
|                                           | Diffuse cell atrophy      | 01     |     |        |        |     |
|                                           | Epidermoid tumour         | 01     |     |        |        |     |
|                                           |                            |        |     |        |        |     |
| Altered consciousness                     | 09                        |        |     |        |        |     |
|                                           | Tubercular meningitis     | 04     |     |        |        |     |
|                                           | Encephalopathy            | 02     |     |        |        |     |
|                                           | Diffuse cell atrophy      | 01     |     |        |        |     |
|                                           | Calcified granuloma       | 01     |     |        |        |     |
|                                           | Colloid cyst              | 01     |     |        |        |     |
|                                           |                            |        |     |        |        |     |
| Seizure with altered consciousness       | 07                        |        |     |        |        |     |
|                                           | Tubercular meningitis     | 02     |     |        |        |     |
|                                           | Glioma                    | 02     |     |        |        |     |
|                                           | Encephalopathy            | 01     |     |        |        |     |
|                                           | Central pontine myelinolysis | 01   |     |        |        |     |
|                                           | Inflammatory granuloma    | 01     |     |        |        |     |
|                                           |                            |        |     |        |        |     |
| Seizure with altered consciousness with motor weakness | 18                        |        |     |        |        |     |
|                                           | Ischaemic stroke          | 10     |     |        |        |     |
|                                           | Cortical venous thrombosis | 03   |     |        |        |     |
|                                           | Tubercular meningitis     | 02     |     |        |        |     |
|                                           | Glioma                    | 02     |     |        |        |     |
|                                           | Paravertebral neoplasm    | 01     |     |        |        |     |

Continued.
Among different primary neurological disorders, vascular disorders were most common (33.3%) followed by Epilepsy (32%) while hepatic encephalopathy was the most common secondary neurological disorder (Table 3).

**Role of radiological imaging**

MRI with MRA with MRV was done in 66 (88%) cases of primary neurological disorders while CT scan was done in 7 cases (9.3%).

The diagnosis of epilepsy (22), ischemic stroke (11), hemorrhagic stroke (8), subarachnoid haemorrhage (1), TBM (6), encephalopathy (3), CNS neoplasm (9) and miscellaneous was thereby made (Table 4 and 5).

The diagnosis of secondary neurological disorder was confirmed by exclusion of focal pathology in 14 (56%) cases with MRI and 6 (20%) cases by CT scan and on the basis of biochemical investigations as serum bilirubin levels and liver function tests.

Diagnosis of 6 cases of tubercular meningitis was confirmed by CSF analysis and 2 case of GBS by nerve conduction velocity.

The presentation of both primary and secondary neurological disorders was found to be more common in pregnancy than puerperium (86% vs 14%). 87.5% cases of epilepsy, 85% cases of stroke, 90.9% cases of CNS infections and 100% cases of CNS neoplasm presented antenatally.

Cortical Venous Thrombosis was the only primary neurological disorder where significantly higher no. of subjects presented in the postpartum period (80% vs 20% p < 0.001). Among secondary neurological disorders, all cases of septic encephalopathy and 73.9 % cases of HE presented in antenatal period.

**Maternal outcome**

The total no. of maternal deaths during study period were 328. So neurological disorders contributed to 5.4% of maternal deaths. Total no. of live births during this period were 7767. Therefore, maternal mortality ratio due to neurological disorders was 218 per 100000 live births (Table 6).

| Clinical feature                              | MRI and MRA and MRV n=66 | Result                           | N | CT N=7 | Result                           | n |
|-----------------------------------------------|--------------------------|---------------------------------|---|--------|---------------------------------|---|
| Motor weakness with altered consciousness     | 10                       | Hemorrhagic stroke              | 03|        | Neurocystic encephalitis        | 02|
|                                               |                          | Cortical venous thrombosis      | 02|        |                                 |   |
|                                               |                          | GBS                             | 02|        |                                 |   |
|                                               |                          | Ischaemic stroke                | 01|        |                                 |   |
|                                               |                          | Subarachnoid hemorrhage         | 01|        |                                 |   |
|                                               |                          | Neurocystercerosis              | 01|        |                                 |   |

Table 6: Case distribution on the basis of maternal outcome (n=100).

| Maternal Outcome                              | No. of cases | Percentage |
|-----------------------------------------------|--------------|------------|
| Recovery                                      | 68           | 68         |
| Residual Deficit                              | 15           | 15         |
| Mortality                                     | 17           | 17         |
| MMR in pregnancy with neurological disease    | 100          | 218/100000 |

The rate of recovery was highest in cases of epilepsy (100%) and lowest in cerebrovascular accidents (77.7%). It was 43.5% in cases of hepatic encephalopathy. Statistically, a significant difference in recovery rate within primary neurological disorders (p<0.001) and between primary and secondary neurological disorders was observed (p=0.010) (Figure 1).

Figure 1: Case distribution according to maternal outcome among primary neurological disorders.

Morbidity in terms of residual deficit was highest in patients with stroke (45%) and Cortical Venous Thrombosis (40%). No residual deficit was seen in cases with epilepsy and HE. Statistically, a significant difference in morbidity within primary neurological disorder (p=0.005) and between primary and secondary neurological disorders was observed (p=0.015) (Figure 1).

Mortality rate was highest in cases of CVT (20%) amongst primary neurological disorders. No maternal
deaths were seen in cases of Epilepsy and CNS neoplasm. Maternal deaths were 56.7% in cases with HE. Overall mortality rate in primary disorders was 5.56%. In secondary disorders, mortality rate was 52%. Mortality rate in secondary disorders was significantly higher as compared to that in primary disorder group (p<0.001) (Figure 1).

**Fetal outcome**

Still birth rate was 22.22% in primary neurological and 62.5% in secondary neurological disorders. A significant difference in the stillbirth rate was observed between primary and secondary neurological disorders (p<0.001) (Table 7). Low birth weight rate was 58.33% in primary neurological and 87.5% in secondary neurological disorders. Preterm births in patients with HE was 81.8%. Preterm rate was 41.67% in primary and 79.17% in secondary neurological disorders. A significant difference in preterm birth rate was observed between primary and secondary neurological disorders (p=0.001) (Table 8).

**Table 7: Case distribution on the basis of foetal outcome (n=96).**

| Fetal Outcome | No. of cases | Percentage |
|---------------|--------------|------------|
| Live          | 65           | 67.7       |
| Stillbirth    | 31           | 32.3       |

**Table 8: Case distribution on the basis of period of gestation (n=96).**

| Fetal outcome | No. of cases | Percentage |
|---------------|--------------|------------|
| Preterm       | 49           | 51.0       |
| Term          | 47           | 49.0       |

**DISCUSSION**

The prevalence of primary neurological disorders in the present study is more than the studies by Gupta et al and To et al that is 862 vs 353 and 326 respectively.²,⁸ This may be because the study is carried out in a tertiary care hospital which caters to a population of more than 20 crore and has nearby states as Bihar and is also a referral centre for Emergency obstetric care. Most of the studies carried out so far have been done in Department of Neurology as by Janaki et al, Agarwal et al and Srinivasan et al which included only primary neurological disorders.⁹,¹¹ except two studies by To et al. (1994) and S Gupta et al (2004-2005) which were done in department of Obstetrics and Gynaecology. The studies carried out so far do not give an account of secondary neurological disorders except for the study by Gupta et al.²

This study had headache as the third commonest symptom which is similar to study by WHO.³ In this study CNS tumours were found to be 12% while cerebrovascular accidents were 33.3%. This is higher than the study by Gupta et al (1% and 9%) but is comparable to studies by Janaki et al (7% and 48%); Agarwal et al (1% and 72%) and Srinivasan et al (16 % and 41%).⁹,¹¹ Among the cerebrovascular accidents the incidence of hemorrhagic stroke in the present study is 80.5 per 100000 deliveries and that of ischaemic stroke is 126. This is higher in comparison to the study by Liang, Chang in which the incidence of hemorrhagic and
ischaemic stroke was 4.3 and 4.6 per 100000 deliveries respectively.12

MRI was diagnostic investigation in all cases of primary neurological disorders while diagnosis of secondary neurological disorders was made by exclusion of any focal pathology by radiological imaging. This is consistent with the study done by Dr. Subhashree Chandrasekara et al who used MRI in antenatal period and CT/ MRI in postnatal period.13 Cortical venous thrombosis presented in puerperium in 80% cases in this study which is consistent with the study by Jeng JS, Tang SC in which 73% cases of CVT occurred in the puerperium.14

In the present study 68% subjects had complete recovery, residual deficit was associated with 15% subjects and maternal mortality rate was 17%. This is consistent with the study by Berg CJ et al (20% vs 17%).1 Subjects with cerebrovascular accidents had the worst prognosis with residual deficit in 44% of the cases. In the study by Agarwal et al and Dias MS Sekhar et al mortality rate in cases of CVT was 28% which is comparable to our study (20%).10 In a study Liang et al mortality rate due to cerebrovascular accidents was 17.8% which is comparable to our study (17.6 vs 17.8%).12 In the present study, the mortality rate in subjects with HE was 56.7% which is lower than the study by S Gupta et al (56.7% vs 64.3%).2

CONCLUSION

This study throws light on the fact that neurological disorders contribute significantly to maternal morbidity and mortality. Routine antenatal care for all pregnant patients for early diagnosis and timely referral to tertiary care hospitals is needed for optimal outcome. The symptom of headache should be taken with caution and it requires elaborate history, examination and investigation to make early diagnosis of primary neurological disorder to decrease maternal and perinatal morbidity and mortality. MRI with MRA with MRV proved to be the most beneficial diagnostic tool in this study and should be recommended for early diagnosis of the disorder and thus decide its management. The diagnosis of diseases such as epilepsy, cerebrovascular accident, tubercular meningitis, encephalopathy, glioma, neurocysticercosis, central pontine myelinolysis etc can be confirmed using this modality. This study gives an insight to the prevalence and presenting symptoms of neurological disorders followed by their diagnosis and outcome for mother and baby.

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## Working Proforma

| Particulars       |          |
|-------------------|----------|
| Name              |          |
| Age               |          |
| Handedness RT LT  |          |
| Address           |          |
| Phone no          |          |
| Religion          |          |
| Occupation        |          |
| Diet Veg          |          |
| Non Veg           |          |
| Education         |          |
| Date of admission |          |
| Date of discharge |          |
| Date of expiry    |          |
| Chief complaints  |          |
| Headache          |          |
| Altered consciousness |          |
| Visual disturbance |          |
| Seizures          |          |
| Antepartum 1\(^{st}\), 2\(^{nd}\), 3\(^{rd}\) |          |
| Intrapartum       |          |
| Postpartum within 24 hrs | >24 hrs | >48hrs |
| Frequency         |          |
| Duration          |          |
| Type of seizures  | GCTS, Focal Seizures |          |
| Last episode of seizure |          |
| Motor complaint   |          |
| Weakness in upper limb left right |          |
| Weakness in lower limb left right |          |
| Sensory complaint |          |
| H/o suggestive of cranial nerve involvement |          |
| Bladder/bowel complaints |          |
| **PAST H/O**      |          |
| Seizure disorder  |          |
| Hypertension      |          |
| Diabetes mellitus |          |
| Stroke            |          |
| Ischaemic heart disease |          |
| Pregnancy induced hypertension |          |
| **Family history**|          |
| Diabetes mellitus |          |
| Hypertension      |          |
| Stroke            |          |
| Ischaemic heart disease |          |
| Seizure disorder  |          |
| **Obstetric history** |          |
| Gravida/parity    |          |
| Gestational age at the time of presentation |          |
| Gestational age at the time of delivery |          |
| **Treatment history** |          |
| Antihypertensive medication |          |
| Antiepileptic medication |          |
| Others            |          |
| Physical examination |
|----------------------|
| **General examination** |
| PR                  |
| B.P.                |
| RR                  |
| TEMP                |
| WT                  |
| HT                  |
| BMI                 |
| Pallor              |
| Icterus             |
| Cyanosis            |
| Edema               |
| Lymphadenopathy     |
| Clubbing            |
| **CNS examination** |
| GCS                 |
| Level of consciousness |
| Orientation         |
| Speech              |
| Cranial nerves      |
| **Motor system**    |
| RT. UL LT.UL. RT.LL LT.LL |
| Nutrition           |
| Tone                |
| Power               |
| Involuntary movements |
| Coordination        |
| **Reflexes**        |
| Biceps              |
| Triceps             |
| Supinator           |
| Knee                |
| Ankle               |
| Plantar             |
| **Sensory system**  |
| Pain/touch /temperature |
| Joint position /vibration |
| Cortical sensation  |
| Signs of meningeal irritation |
| **CVS examination** |
| Respiratory system examination |
| GI examination      |
| **Outcome of pregnancy** |
| Abortion            |
| Term delivery       |
| Preterm delivery    |
| IUD                 |
| **Mode of delivery** |
| Vaginal             |
| C-section           |
| **BABY**            |
| LIVE/IUD/could not be revived |
| Birth WT          |
|------------------|
| APGAR/IPPR +O2   |
| Any birth defect |

**Outcome of neurological disorder**

- Recovery
- Residual defect
- Persisting seizure
- Death

**Investigations**

- Hb
- Hct
- MCV
- TLC
- DLC
- PC
- Blood urea
- S creatinine
- Urine protein
- S.uric acid
- S.bilirubin
- SGOT
- SGPT
- SALP
- Total Protein
- S. LDH
- S. Sodium
- S. potassium
- S. calcium
- S. magnesium
- CT/MRI/EEG

**Others**