



Neurological Disorders Associated with Pregnancy: A Hospital Based Imaging Study of 57 Cases in North-East India

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Authors' contributions

This work was carried out in collaboration between all authors. Author DB designed the study, wrote the protocol and author PB performed the statistical analysis, wrote the first draft of the manuscript and author PRC managed the analyses of the study, managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To evaluate and characterize the Computed Tomography and Magnetic Resonance Imaging findings of the various neurological conditions of the central nervous system and pituitary gland that can occur during pregnancy and post partum period.

Place and Duration of Study: The study was carried out in the Department of Radiology, Gauhati Medical College and Hospital, Guwahati, from August 2012 to July 2013.

Methodology: A total of 57 patients of neurological disorders of the central nervous system and pituitary gland associated with pregnancy, who were referred to the Department for radiological evaluation and who had positive imaging findings were taken up for the study. CT scan was performed in those cases referred for imaging. For further evaluation, cases were referred to MRI

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or wherever possible, cases were directly referred for MRI. Contrast CT was avoided in most of the cases.

Results: Out of 57 patients, 54.39% patients were in age between 20 to 30 years. Headache was the most common presenting complaint (71.93%) in all the neurological disorders. Hypertensive encephalopathy (40.35%) was the most common neurological disorder followed by Cerebral Venous Thrombosis (17.54%). Infarct was the commoner complication of hypertensive encephalopathy accounting for 21.74% of cases. Magnetic resonance was able to detect infarct in 21.74% of cases compared to CT which could detect infarct in 13.04% of cases. P value 0.3534 and sensitivity 72%, 95% Confidence Interval 0.46 to 0.90 with negative predictive value 50% with 95% Confidence Interval 0.18 to 0.81.

Conclusion: Both CT and MRI can depict the characteristic imaging features of these neurological disorders in pregnancy as well as development of complications, hence leading to early and prompt diagnosis of these disorders and better management of these patients.

Keywords: Neurological disorder; pregnancy; computed tomography; magnetic resonance imaging.

ABBREVIATIONS

CI: Confidence Interval, TOF MRA: Time of Flight Magnetic Resonance Angiography, MRV: Magnetic Resonance Venography, TR: repetition time, TE: echo time, FLAIR: Fluid Attenuated Inversion Recovery, DWI: diffusion weighted image, SWI: Susceptibility Weighted Imaging, NECT: non enhanced computed tomography, ESR: erythrocyte sedimentation rate, ADC: Apparent diffusion coefficient.

1. INTRODUCTION

A variety of neurological disorders may be encountered during pregnancy and puerperium [1]. Diverse pathologic conditions affect the central nervous system and pituitary gland during pregnancy and the puerperium [2]. Some are specific to the physiologic process of reproduction (e.g., eclampsia, postpartum cerebral angiopathy, Sheehan syndrome, lymphocytic adenohypophysitis) [2]. Others are nonspecific but occur more often in pregnant women (eg, cerebral infarction, dural venous thrombosis, pituitary apoplexy) [2].

The primary neurological disorders studied in relation to pregnancy include eclampsia, strokes, epilepsy, benign intracranial hypertension, CNS tumours, Bell's palsy, obstetric pressure palsies, demyelinating diseases of the central or peripheral nervous system and neuromuscular junction disorders (myasthenia gravis) [1]. Neurological diseases may be incidental to pregnancy (e.g., meningitis) [1]. 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 [1].

Pregnancy can affect many neurological diseases, while certain neurological diseases or their treatments may have a significant negative effect on pregnancy, labour or delivery. Epilepsy, migraine and stroke are among the commonest neurological diseases which complicate pregnancy. Multiple sclerosis and myasthenia gravis are the two neurological disorders that specifically affect young women during their reproductive years [3].

Even when imaging changes are nonspecific, knowledge of those entities associated with pregnancy and awareness of the increased likelihood of certain diseases in pregnancy will allow a more informed differential diagnosis [2].

In accordance with an obstetric CVT (cerebral venous thrombosis) series symptoms of CVT appeared in the first 3 weeks after delivery in the majority of cases in the Indian series, women who had home deliveries and poor prenatal care were more often affected[14].

The present study is carried out to evaluate and characterize the CT (Computed Tomography) and MRI (Magnetic Resonance Imaging) findings of the various neurological conditions of the central nervous system and pituitary gland that can occur during pregnancy and post partum period.

2. MATERIALS AND METHODS

The study was a hospital based cross-sectional study, carried out in the Department of Radiology, Gauhati Medical College and Hospital, Guwahati, from August 2012 to July 2013. Clinically suspected cases of neurological disorders of the central nervous system and pituitary gland associated with pregnancy, who were referred to the Department for radiological evaluation and who had positive imaging findings were taken up for the study. Patients were mostly referred from the Department of Neurology, Obstetrics and Gynaecology, Endocrinology and Medicine with common presenting symptoms were headache, vomiting, seizures, altered sensorium, neurological deficits, visual disturbances and symptoms of pituitary hypo function. The present study was approved by the Institutional Ethics Review Committee of the Gauhati Medical College and Hospital, Guwahati.

All pregnant, postabortal and postpartum patients presenting with neurological manifestations of the central nervous system and pituitary gland associated with pregnancy were included. Also women presenting late after pregnancy but whose neurological manifestations are attributed or precipitated because of the pregnancy state were included. Patients presenting coincidentally at the time of pregnancy, postpartum and post-abortal period due to some other neurological disorders not directly related to pregnancy were excluded from the study.

Since most of these disorders occur in the 2nd, 3rd trimester and in the post partum period and also the risk of radiation hazard to the fetus is maximum in the 1st trimester, patients presenting in the 1st trimester were not included. Informed consent was taken from the patients following which radiological examination was done.

CT scan was performed in those cases which were referred for imaging. However, precaution was taken to avoid radiation hazard to the patient. Abdominal shield was used for all the patients. Any unnecessary radiation exposure was avoided and scans were strictly limited to the area of interest. Head CT was performed in an axial axis with a 15- to 20-degree angulation of the gantry to the cantho meatal line to decrease radiation to the eyes, defined as passing through the lateral canthus and middle of the external ear canal. For further evaluation, cases were referred to MRI or wherever possible, cases were directly referred for MRI. Routine MR

Sequences along with TOF MRA and MRV were done. Contrast CT was avoided in most of the cases.

The machine used for CT scan was Somatom dual slice CT machine (Siemens) and MX-16, 16 slice CT machine (Philips). A scanogram or topogram of the region of interest was taken and the CT scan protocol was planned on it in the console room. Eight- to 10-mm-thick sections were routinely obtained, but thinner slices with 1.5 to 3 mm thickness were necessary in evaluation of the orbits, pituitary gland, suprasellar and parasellar regions. In these situations, reformatted images in coronal and sagittal planes were useful. Bony algorithm was used in selected cases. Routinely 50 ml (and also dose calculated as per weight of the patient- 1 ml/kg body weight) of a non ionic iodinated contrast was used for CECT and 100ml of contrast for angiography was used.

The machine for MRI used was Siemens Tim Avanto 1.5 Tesla machine. Axial and sagittal spin-echo (SE) T1W (Repetition time i.e. TR, 450-600 msec; echo time i.e. TE, 15-20 msec) images; axial T2W (TR, 2000-3000 msec; TE, 80-100msec), FLAIR (Fluid Attenuated Inversion Recovery) images were obtained in all patients. A standard Gd DTPA-dimeglumine solution was injected IV in a dosage of 0.1 mmol/kg body weight. Gadopentate dimeglumine enhanced axial (SE) T1W (TR, 450-600 msec; TE, 15-20 msec) images were obtained in all patients. Sagittal and coronal postcontrast T1FF were taken in selected cases.

3. RESULTS AND DISCUSSION

3.1 Results

The selected patients were evaluated on the basis of detailed history, clinical and laboratory examination. Informed consent was taken from the patients. CT Scans were strictly limited to the area of interest and performed with abdominal shield. A total of 57 patients were included in the study.

Headache was the most common presenting complaint (71.93%) in all the neurological disorders. It was found that most of the patients presented during the 3rd trimester (45.6%) closely followed by post partum period (40.35%). 5.26% of patients were of Sheehan's syndrome presented after post partum period, specifically after an average duration of 5 years after pregnancy.

3.1.1 Hypertensive encephalopathy

86.96% cases of hypertensive encephalopathy presented during the 3rd trimester. None of the cases detected in the post partum period possibly because eclampsia resolved after delivery.

Infarct was the commoner complication of hypertensive encephalopathy accounting for 21.74% of cases. MR was able to detect infarct in 21.74% of cases compared to CT which could detect infarct in 13.04% of cases. $P = 0.3534$ and sensitivity 72%, 95% CI 0.46 to 0.90 with negative predictive value 50% with 95% CI 0.18 to 0.81. Hemorrhage was present in 4.35% of cases and was detected by both CT and MR.

Among 5 cases of hypertensive encephalopathy with infarct (21.74%), two showed hemorrhagic transformation in MR (8.69%) compared to CT which could detect hemorrhagic transformation in one case (4.35%). Arterial narrowing was found in 2 cases by TOF (Time of Flight) MR which accounted for 8.69%. CT angiography was not done to avoid radiation hazard.

3.1.2 Cerebral venous thrombosis

60%, 30% and 10% of cases of cerebral venous thrombosis presented during the 1st, 2nd and 3rd weeks of delivery respectively.

Infarct is the commonest complication of cerebral venous thrombosis. All the cases in the present study were associated with venous infarcts. Compared to MR which detected infarcts in all the cases, NECT could detect infarcts in 60% of cases. In 70% of cases, there was hemorrhagic transformation of infarcts as detected by SWI (Susceptibility Weighted Imaging) sequence. However CT could detect hemorrhagic transformation in 50% of cases. MRI can detect infarct and hemorrhagic transformation in more number of cases than CT ($P = 0.5646$ with specificity 58%, 95% CI 0.58 to 0.85 and positive predictive value 54%, 95% CI 0.23 to 0.83, accuracy 0.9).

All the infarcts associated with cerebral venous thrombosis were venous infarcts. Of these infarcts, 80% were detected in the sub-acute stage and 20% in the acute stage.

3.1.3 Border zone infarcts

In the present study there were 4 cases (7.02%) of border zone infarct. All the cases were internal

border zone infarcts. Of these 75% were confined to Anterior Communicating Artery-Middle Communicating Artery distribution and 25% was confined to Middle Communicating Artery-Posterior Communicating Artery territory.

3.1.4 Sheehan's syndrome

In the present study, there were 3 cases of Sheehan's syndrome accounting for 5.26% of cases and all of these patients revealed empty sella on evaluation with MR. All of these cases presented after 5 years of delivery.

3.1.5 Post partum cerebral angiopathy

Two cases of post partum cerebral angiopathy were found in the present study. There was involvement of the cortical branches of Middle Communicating Artery, Anterior Communicating Artery and Posterior Communicating Artery in the form of multifocal narrowing in both cases.

3.1.6 Meningioma

In the present study, two (3.51%) cases were meningioma. One of them was a diagnosed case who showed increase in size of the meningioma during 2nd trimester. The other case presented during 3rd trimester, in whom on evaluation with NECT and further with MR, a falcine meningioma was detected

3.1.7 Lymphocytic hypophysitis and pituitary adenoma

In the present study, there were one case of lymphocytic hypophysitis and pituitary macroadenoma, each constituting 1.75% of cases respectively. Pituitary macroadenoma was already a previously diagnosed case who presented with headache and visual disturbance during 2nd trimester. So the patient was directly evaluated with MR which revealed increase in size of the adenoma along with presence of areas of necrosis and hemorrhage. There was one case of lymphocytic hypophysitis which on MR evaluation showed diffusely enlarged moderately enhancing pituitary without any focal lesion, presence of T2 parasellar hypointensity, thickened infundibulum. These features were absent in pituitary adenoma.

3.2 Discussion

In the present study maximum numbers of patients (54.39%) were from 21-30 years age group (Table 1).

The present study correlated with multiple reports of reversible T2 hyper intense white matter lesions (Tables 3 and 4) with predominance in the posterior circulation where there were less vasomotor sympathetic innervations. The predilection for the posterior circulation and watershed zones was believed to be related to its sparse vasomotor sympathetic innervations [4,5]. Yasuhara et al. [6] also found symmetrical high signal intensity lesions in bilateral parieto-occipital lobes on T2 WI MRI in cases of hypertensive encephalopathy. Zak et al. [2] found CT which demonstrated transitory posterior areas of patchy low attenuation, MR imaging is superior to CT in imaging patients with eclamptic encephalopathy (Fig. 1).

The present study correlated with the study done by Loureiro and co-workers [7] who found that 25% of women with eclampsia had areas of cerebral infarction. Preeclampsia and eclampsia were present in 24-47% of ischemic strokes [8] and 14-44% of intracranial haemorrhages [9,10]. In their studies conducted by Trommer et al. [11] and Duncan et al. [12] angiographic findings of diffuse or focal vasospasm were seen in patients of hypertensive encephalopathy who had developed infarct (Fig. 2).

In the present study, cerebral venous thrombosis accounted for 17.54% of cases (Table. 2). According to Lamy et al. [13] the pregnant and puerperal state accounted for 5 to 20% of all cerebral venous thrombosis in occidental countries; this proportion may reach 60% in developing countries (Fig. 3).

In the present study 60% of cases of cerebral venous thrombosis presented in the 1st week post partum. In accordance with a study done by Dibakdsib et al. [14] symptoms of cerebral venous thrombosis appeared in the first 3 weeks

after delivery in the majority of cases in the Indian series, women who had home deliveries and poor prenatal care were more often affected (Fig. 3).

Ferro et al. [15] also found cerebral venous thrombosis with involvement of the following vessels in decreasing frequency: The superior sagittal sinus (62%), left and right transverse sinus (respectively 44.7% and 41.2%), straight sinus (18%), cortical veins (17.1%), deep venous system (10.9%), cavernous sinus (1.3%), and cerebellar veins (0.3%) (Table 5).

In the present study, frontal and parietal regions were the commonest site of infarcts (Table 6). According to Rodallec et al. [16], Linn et al. [17] on unenhanced CT direct visualization of thrombosis in dural sinus may give a dense clot sign and approximately one third of cerebral venous thrombosis demonstrated direct signs of hyperdense dural sinus.

In the present study, MRI compared to CT could better detect venous sinus thrombosis as well as the brain parenchymal abnormalities like infarction and hemorrhagic transformation of infarcts (Tables 5 and 6). According to Bousser et al. [18], Biukobza et al. [19], MRI is more sensitive for the detection of cerebral venous thrombosis than CT at each stage for detection of thrombus in a venous sinus.

Neudecker et al. [20] in his study also found that cerebral angiography demonstrated multifocal segmental vasoconstriction involving the medium and small sized cerebral arteries, which resolved spontaneously over weeks (Table 7). Konstantinopoulos et al. [21] found infarcts, hemorrhage or both and usually occurred within 1st week following a normal pregnancy and uncomplicated delivery.

Table 1. Showing age distribution of neurological disorders associated with pregnancy cases

Age group (In Yrs)	No. of cases	Percentage of cases
≤ 20	15	26.31%
20 ≤ 30	31	54.39%
30 ≤ 40	9	15.79%
40 ≤ 50	2	3.51%
Total	57	100
Mean	14.25	25
S.D	±12.366	±21.696
S.E.M	±6.183	±10.848

(S.D is standard deviation and S.E.M is standard error of mean)

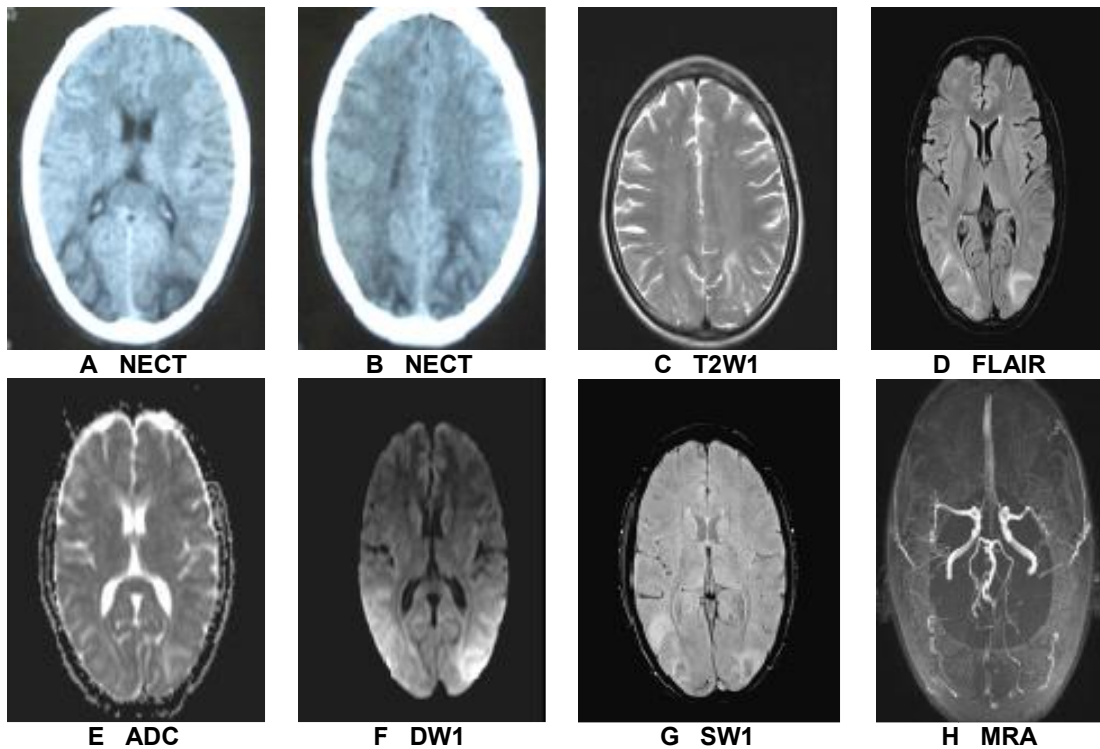


Fig. 1. A 27 year pregnant patient presented during the 3rd trimester with headache, visual disturbance and seizures. BP was 150/100 mm Hg. Bilaterally symmetrical white matter hypodensity in NECT (A, B) and T2 FLAIR (C, D) hyperintensity in parieto-occipital lobes. No diffusion restriction on DWI (E, F) and susceptibility artifacts in SWI (G). TOF MRA (H). Diagnosis is Hypertensive Encephalopathy

Table 2. Showing number of cases of various types of neurological disorders associated with pregnancy

Neurological disorders	No. of cases	Percentage of cases
Hypertensive encephalopathy	23	40.35%
Cerebral venous thrombosis	10	17.54%
Border zone infarcts	4	7.02%
Sheehan's syndrome	3	5.26%
Post partum cerebral angiopathy	2	3.51%
Pituitary adenoma	1	1.75%
Lymphocytic hypophysitis	1	1.75%
Meningioma	2	3.51%
Intra cranial hypertension (Unknown Cause)	6	10.52%
Infarct (Unknown Cause)	5	8.77%
Other tumours	0	-

Nakata et al. [22] found that T2 hypointensity in the parasellar region was present in cases of lymphocytic hypophysitis and was useful in differentiating from a pituitary adenoma. Caturegli et al. [23] reported that parasellar fibrosis was common (47% of 267 cases of lymphocytic hypophysitis) giving rise to T2 parasellar hypointensity (Fig. 5).

Anterior pituitary atrophy in cases of Sheehan's syndrome was also found by Zak et al. [2] in his study (Fig. 4). Lusic et al. [24] in their study also found that pregnancy appeared to enhance the growth of meningioma.

Table 3. Number of cases of hypertensive encephalopathy with white matter edema shown by CT and MR (magnetic resonance)

Radiological investigation	White matter edema according to symmetry			
	Bilaterally symmetrical		Asymmetrical	
	No. of cases	Percentage of cases (out of 23 cases)	No. of cases	Percentage of cases (out of 23 cases)
CT scan	17	73.91%	6	26.1%
MRI	20	86.96%	3	13.04%

Symmetrical white matter edema was detected in 73.91% cases by CT and 86.96% cases by MR with P = 0.0322, considered moderately significant with sensitivity 74% [95% CI (Confidence Interval) 0.64 to 0.82] with accuracy 0.9.

Table 4. Distribution of location of white matter edema in hypertensive encephalopathy

Location	No. of cases (in CT)	Percentage of cases (in CT & out of 23 cases)	No. of cases (in MR)	Percentage of cases (in MR & out of 23 cases)
Parietal	22	95.65%	22	95.65%
Occipital	14	60.87%	16	69.56%
Frontal	11	47.83%	14	60.87%
Temporal	1	4.35%	3	13.04%
Cerebellum	0	-	0	-
Corona radiata	3	13.04%	3	13.04%
Capsuloganglionic	2	8.69%	2	8.69%

Table 5. Distribution of cases of cerebral venous thrombosis according to the sinuses involved

Location	No. of cases (NECT)	Percentage of cases (NECT)	No. of cases (MR)	Percentage of cases (MR)
Sagittal sinus	5	50%	8	80%
Transverse sinus	0	-	6	60%
Sigmoid sinus	1	10%	3	30%
Straight sinus	1	10%	1	10%
Deep veins	-	-	-	-

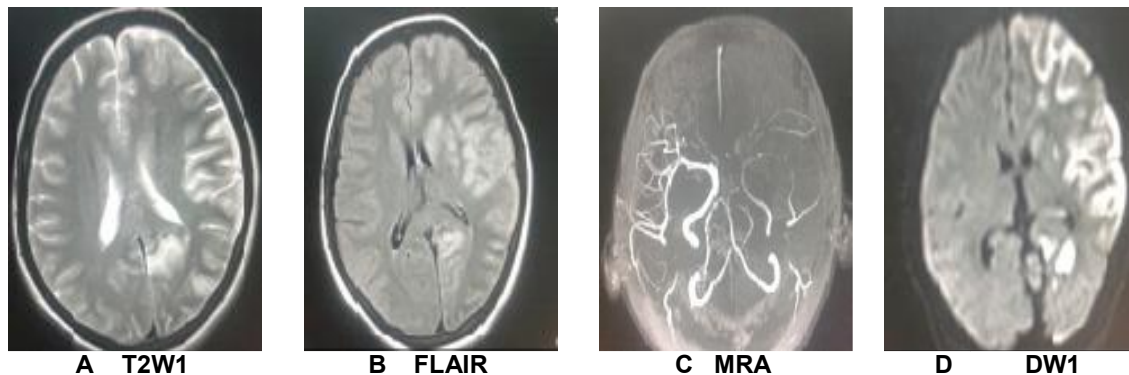


Fig. 2. A 21 yr old pregnant patient presented during 3rd trimester with history of headache, vomiting, seizures and right sided weakness. BP was 170/110 mm Hg. MRI brain revealed presence of T2 (A) and FLAIR (B) hyper intensities in left fronto-parietal lobe and occipital lobe along with evidence of diffusion restriction (D) and arterial narrowing (C) involving left middle communicating artery, anterior communicating artery and their cortical branches. Diagnosis: Hypertensive encephalopathy with arterial narrowing and infarcts

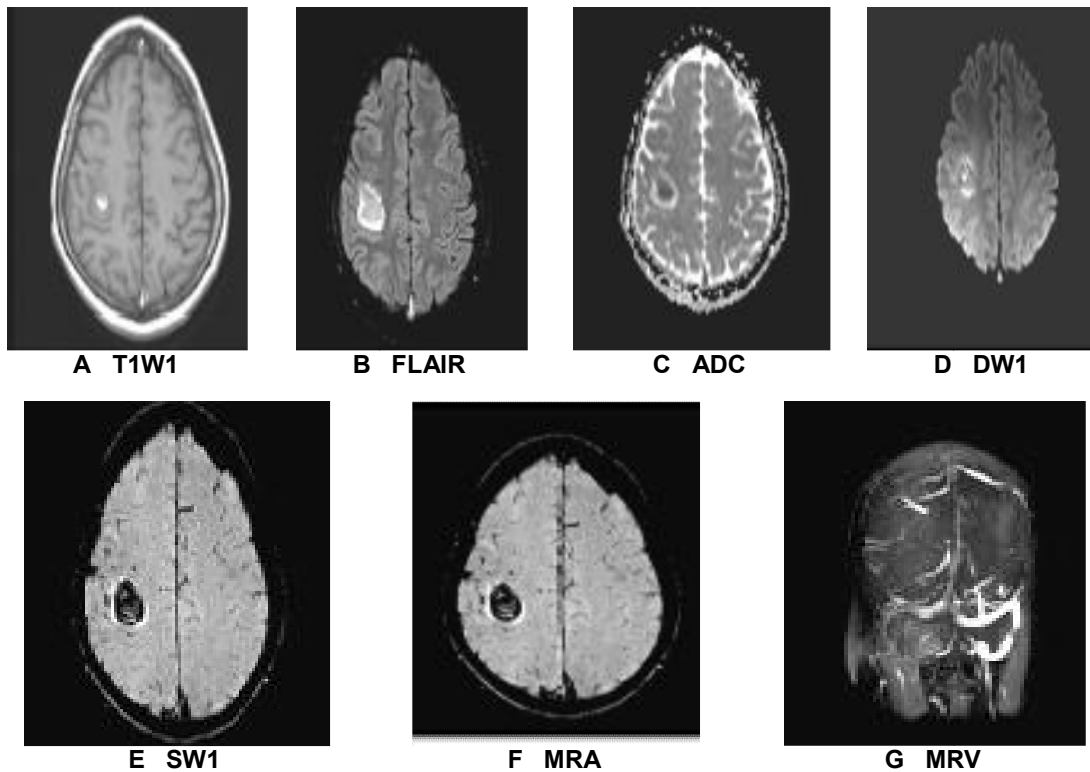


Fig. 3. A 32 yrs old, 14 days post partum patient presented with headache, altered sensorium and weakness of limbs. ESR was raised, Hb was low. MRI showed filling defect involving right transverse, sigmoid sinus and superior sagittal sinus (A, B, C, D, F, G). Infarct is seen in right parietal lobe with hemorrhagic transformation (E). Diagnosis: Cerebral venous thrombosis with infarct showing hemorrhagic transformation

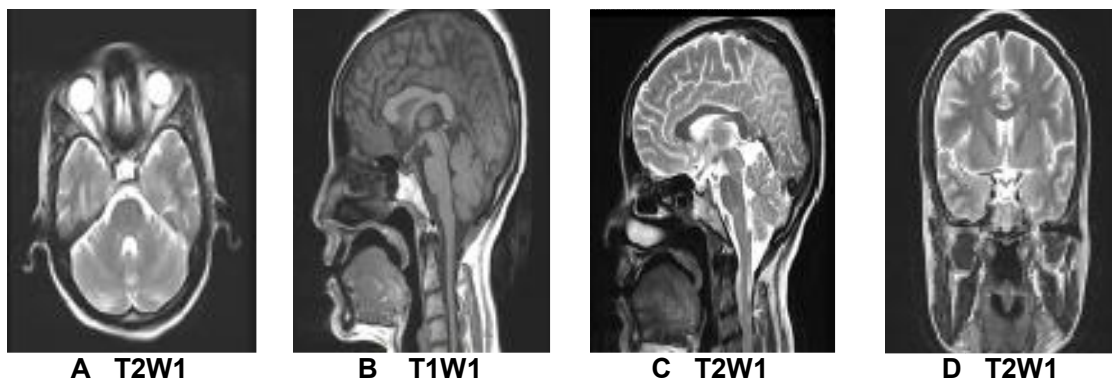


Fig. 4. A 42 year old female patient presented with lethargy, malaise, history of lactational failure and amenorrhoea following her last delivery 8 yrs back. There was history of post partum hemorrhage. Serum TSH, T3,T4, cortisol and gonadotrophins was low. T1 and T2 WI revealed presence of empty sella with herniation of the suprasellar cistern into the pituitary fossa (A, B, C D). Diagnosis: Sheehan's syndrome

James et al. [25] in his study found that eclampsia was the commonest cause of ischemic stroke accounting for 47% of all cases. The other common causes were cerebral venous thrombosis, postpartum cerebral angiopathy,

post partum hemorrhage, inherited protein S deficiency and disseminated intravascular coagulation associated with amniotic fluid embolism (Table 8).

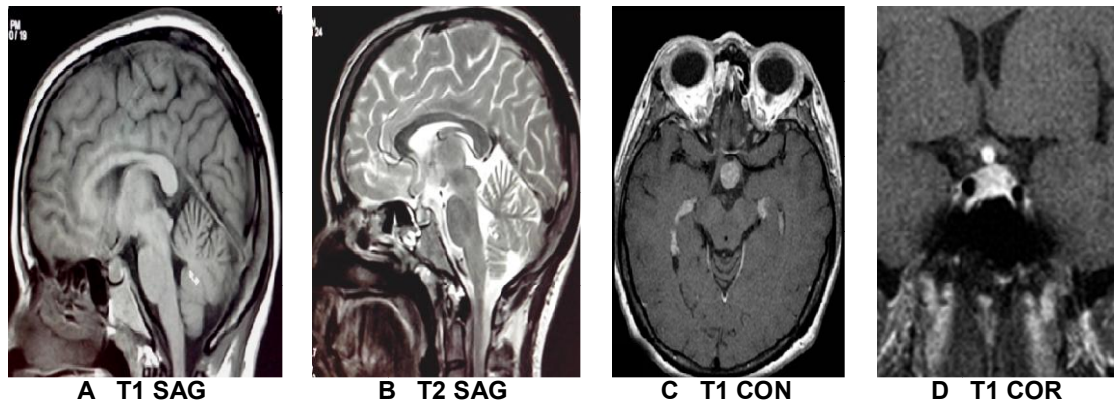


Fig. 5. A 25 yr old female patient in the post partum period presented with headache, visual disturbance and malaise. MR was done which showed diffusely enlarged moderately enhancing pituitary gland with bulky infundibulum. No focal lesion within pituitary was seen (A, B, C, D). Diagnosis: Lymphocytic hypophysitis

Table 6. Distribution of cases of cerebral venous thrombosis according to location of infarct

Location	No. of cases (CT)	Percentage of cases (CT)	No. of cases (MR)	Percentage of cases (MR)
Frontal	6	60%	9	90%
Occipital	1	10%	3	30%
Parietal	6	60%	9	90%
Temporal	1	10%	2	20%
Cerebellum	1	10%	2	20%
Corona radiata	-	-	-	-
Capsuloganglionic	-	-	-	-

Table 7. Table showing detection of the imaging characteristics of post partum cerebral angiopathy by CT & MRI

Imaging characteristics of post partum cerebral angiopathy	CT	MR
Vasogenic edema	Present	Present
Infarct	Absent	Present
Hematoma	Present	Present
Vessel involvement	Contrast not done	Cortical branches

Table 8. Distribution of infarcts according to cause

Cause of infarct	No. of cases	Percentage of cases (%)
Cerebral venous thrombosis	10	40
Hypertensive encephalopathy	5	20
Border zone infarcts	4	16
Post partum cerebral angiopathy	1	4
Unknown	5	20
Total	25	100
Mean	5	20
S.D	±3.240	±12.961
S.E.M	±1.449	±5.797

(S.D is standard deviation and S.E.M is standard error of mean)

4. CONCLUSION

Though pregnancy is a natural phenomenon, various central nervous system and pituitary disorders can arise during the course of pregnancy and post partum period. Failing to diagnose these disorders at the earliest can lead to life threatening complications. Both CT and MRI can depict the characteristic imaging features of these disorders as well as development of complications, hence leading to early and prompt diagnosis of these disorders and better management of these patients. It is imperative that the radiologist be familiar with these entities so that patients can be evaluated rapidly and efficiently.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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