Peripartum neurological emergencies in a Critical Care Unit

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ABSTRACT

الأهداف: حالات الطوارئ العصبية هي إحدى الدواعي المهمة لدخول وحدات العناية الحرجة أثناء الحمل والنفاس. درسنا في هذا البحث الأسباب المختلفة الكامنة وراء حالات كهذه أدخلت بصورة متتابعة خلال سنة كاملة.

الطريقة: دراسة متسلسلة تضمنت مجموعة من النساء، ادخلن في حالة تدهور حاد في الوعي سواء صحب ذلك نوبات صرع أو نقوص عصبية أم لا، على أن تكون هذه الأعراض قد حصلت أثناء الحمل والنفاس. خلال الفترة من ايلول2005 إلى اب2006 تم إدخال ثلاثين مريضة تنطبق عليها هذه الشروط في وحدة العناية الحرجة في مستشفى ابن سينا التعليمي في الموصل شمال العراق. تمت دراسة هؤلاء النسوة سريريا وخضعن للفحوصات المختبرية الهادفة إلى تحديد سبب أعراضهن المرضية، وقد تضمن ذلك إجراء فحص الدماغ بواسطة المفراس أو المغنام (مع تلوين الأوردة).

النتائج: وجد أن الصرع الولادي هو المسبب لثلثي الحالات التي تمت دراستها (20مريضة)، بينما شخص الثلث الباقي كما يلي : تخثر الأوردة الدماغية (7مريضات)، جلطة دماغية متعلقة بالولادة (حالة واحدة)، نزف داخل المخ (حالة واحدة)، تشحم الكبد الحاد أثناء الحمل (حالة واحدة). أربعة من النساء اللواتي شخصت حالتهن على أنها تخثر الأوردة الدماغية كن مصابات بتسمم الحمل . كان للتصوير الطبي (وبالأخص المغام وتلوين الأوردة المغامي) الفضل في تحديد التشخيص النهائي في تكثر الحالات . وجد أن الصرع الولادي اكثر حدوثا عند المريضات اللواتي كن في (او اتممن) حملهن الأول، بينما كان تخثر الأوردة العماغية اكثر العشري متعلق بحالات الصرع الولادي أكثر من تخثر الأوردة الدماغية اكثر القشري متعلق بحالات الصرع الولادي أكثر من تخثر الأوردة الدماغية حدوث العمى (و 0.01) .

خاتمة: الأعراض العصبية الحادة في فترة الحمل والنفاس تمثل مجموعة مختلفة من الحالات المرضية وتتطلب تحليلا سريريا متأنيا مع الإسراع في الحصول على تصوير للدماغ وخاصة المغنام. يجب أن تتضمن الفحوصات إجراء تلوين الأوردة المغنامي عندما يكون تخثر الأوردة الدماغية في الحسبان.

Objectives: To assess the proportion of eclampsia among patients admitted to the critical care unit (CCU) with an acute neurological emergency in the peripartum period, and careful clinical, laboratory, and radiological evaluation of non-eclampsia cases responsible for such presentation.

Methods: A case series study that included women with acute deterioration of consciousness, with or without convulsions or neurological deficits, during pregnancy or puerperium, received in the CCU of Ibn Sina Teaching Hospital in Mosul, Iraq, from September 1st 2005 to August 31st 2006. A total of 30 women were included. They received careful clinical, radiological, and laboratory evaluation in an attempt to identify the cause of their presentation.

Results: Eclampsia was found to be responsible for two thirds of cases (20 patients). The remaining one third was diagnosed as cerebral venous thrombosis (CVT) (7 patients), peripartum cerebral infarction (one patient), intracerebral hemorrhage (one patient), and acute fatty liver of pregnancy (one patient). Four of the women with CVT had preeclampsia during pregnancy. Imaging studies, particularly MRI and MR venography, provided the final diagnosis in most cases. Eclampsia was found more common in women presenting during their first pregnancy, while CVT was more common in multiparous women (p=0.0001). Cortical blindness was significantly associated with eclampsia instead of CVT (p=0.01).

Conclusion: Acute neurological symptoms in the peripartum period represent a diverse group of conditions, requiring careful clinical evaluation and early access to imaging studies.

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Acute neurological emergencies in the form of coma, neurological dysfunction, or convulsion are common in the peripartum period,¹⁻³ and are important causes for admission to the Critical Care Units (CCU).^{1,3,4} Eclampsia is the major pregnancy related cause of such presentation,^{1,2,4-6} but many

other acute neurological conditions can occur during pregnancy and puerperium and may mimic eclampsia.^{1,7} Stroke, ischemic or hemorrhagic, is thought to be more common during this period,^{2,8-10} and is the second leading cause of death in women in developed countries.11,12 Cerebral venous thrombosis (CVT) is also an important pregnancy related acute neurological disorder, which is more common in the developing world,^{1,13} and is difficult to diagnose without brain imaging.^{1,14} Pregnant ladies are also at higher risk of subarachnoid hemorrhage, worsening of primary epilepsy, acute fatty liver of pregnancy (AFLP) and acute intermittent porphyria, among others.¹⁻³ They all present with acute deterioration of conscious level, commonly with convulsions. The aim of this study is to assess the proportion of eclampsia among patients admitted to the CCU with an acute neurological emergency in the peripartum period, the characteristics of these patients, and the results of their imaging studies. It also aims at careful clinical, laboratory, and radiological evaluation of non-eclampsia cases responsible for such presentation.

Methods. The study included women with acute deterioration of conscious level with or without convulsions or focal neurological signs, who were admitted to the CCU in Ibn Sina Teaching Hospital in Mosul, Iraq. The study included only patients in who the condition occurred during pregnancy or puerperium up to 6 weeks postpartum. Patients without disturbance of consciousness were excluded. A total of 30 patients fulfilling these criteria were collected during the period from September 1st 2005 to August 31st 2006, most were first referred from the nearby Al-Batool Maternity Hospital for suspected eclampsia. The patients were clinically evaluated with a special consideration of their parity, the timing of the event (ante or postpartum), the level of consciousness, and the presence of convulsions, focal neurological signs, papilledema, or signs of meningeal irritation. Detailed systemic examination was also performed including frequent blood pressure checking. All patients were repeatedly assessed for basic laboratory tests that included blood glucose, serum urea, creatinine, electrolytes, transaminases, and alkaline phosphatase. Complete blood count and general urine examination were also obtained. Investigations such as activated partial thromboplastin time (APTT), prothrombin time, serum albumin, hepatitis serology, chest radiograph, and echocardiography were carried out when indicated. The diagnosis of preeclampsia and eclampsia was based on the classification of hypertensive disorders during pregnancy that has been recommended by the American College of Obstetricians and Gynecologists and endorsed by the National Institute of Health Working Group on High Blood

Pressure.¹⁵ According to this classification, preeclampsia is defined as maternal hypertension and proteinuria and/or pathologic edema. Eclampsia is the occurrence of convulsions precipitated by hypertensive disease of pregnancy. Thirteen out of 30 patients had a brain spiral CT scan (43.3%), 2 of them subsequently received brain MR and MR venography (MRV) to exclude cerebral sinus thrombosis. The MRI (including MRV) was the initial brain imaging performed for another 16 patients (53.3%). Only one patient with deep jaundice (who was proved later to have AFLP) did not receive any form of brain imaging. The radiology team in Ibn Sina and Al Salam Teaching Hospitals in Mosul reported on the CT and MRI scans. We also studied the main line of treatment, the duration of stay in the CCU, the in-hospital mortality, and the presence of any residual neurological dysfunction on discharge. All patients received the standard of care for their illness, and they did not receive any new medication or were subjected to unnecessary investigations. Ethical approval was obtained from the local review board, and informed patient consent was obtained.

Data were analyzed applying 2 proportions test, using MINITAB release 13.20. A *p*-value <0.05 was considered statistically, with 95% confidence interval.

Results. Thirty patients with acute peripartum neurological emergency were studied. Their ages ranged from 15-35 years, with a mean of 24.38 ± 5.693. Eclampsia was diagnosed in 20 out of 30 patients (66.7%). The remaining 10 patients had CVT [7 patients (23.3%)], peripartum cerebral infarction [one patient (3.3%)], intracerebral hemorrhage [one patient (3.3%)], and AFLP [one patient (3.3%)]. Four out of 7 patients with CVT had preeclampsia during pregnancy. The clinical characteristics of patients with eclampsia are summarized in Table 1. Hemolysis, elevated liver enzymes, and low platelet count (HELLP) complicated 4 patients (20%), while disseminated intravascular coagulation developed in one (5%) patient. Four patients (20%) had renal impairment and one (5%) developed severe left ventricular failure and pulmonary edema. Spiral CT scan of the brain was carried out in 11 eclamptic patients, while MRI and MRV were performed in the other 9 patients. CT scan was normal in 4 of the 11 patients (36.4%), while the other 7 (63.6%) showed low attenuation areas that involved the occipital cortex, and variably extended to the temporoparietal region. Small foci of hemorrhage were also present in one of these patients. High signal intensity lesions on T₂ weighted images were detected in all the 9 patients who underwent MRI examination of the brain, with the same distribution seen on CT scan. The patients received standard treatment care, including successful use of magnesium sulphate to control the convulsions.

Characteristics	Eclampsia (N=20) n (%)	Cerebral venous thrombosis (N=7) n (%)	P-value
Age (years) Mean ± SD Range	23.47 ± 5.32 15-35	25.83 ± 7.679 17-35	NS
<i>Parity</i> Primigravida Multigravida	17 (85) 3 (15)	1 (14.3) 6 (85.7)	0.0001
<i>Timing</i> Antepartum Multigravida	12 (60) 8 (40)	3 (42.9) 4 (57.1)	NS
<i>Clinical presentation</i> Convulsions Papilledema Cortical blindness Hemiparesis	20 (100) 4 (20) 5 (25) 1 (5)	$\begin{array}{ccc} 7 \ (100) \\ 2 \ \ (28.6) \\ 0 \ \ \ (0) \\ 1 \ \ (14.3) \end{array}$	NS NS 0.01 NS
Stay in the Critical Care Unit (average in days)	5.2	7	

Table 1 - Comparison between the clinical characteristics of patients with eclampsia and cerebral venous thrombosis.

On average, patients with eclampsia stayed (5.2 days) in the CCU. None of them died, and only one of them was discharged with persistent hemiparesis. The others showed uneventful recovery. Table 1 summarizes the clinical characteristics of patients with CVT. Severe headache preceded the deterioration of consciousness in 4 patients (57.1%). The diagnosis was confirmed by MRI and MRV in all the 7 patients (Figure 1). A prior CT scan was carried out in 2 patients, and was normal in one, and showed a small infarction in the occipital lobe on the other. Management of these patients had included routine administration of unfractionated heparin through intravenous infusion. All the patients were discharged with full recovery after an average of 7 days stay in the CCU. When comparing eclampsia and CVT patients, primigravida (p=0.0001), and cortical blindness (p=0.01) were significantly associated with the diagnosis of eclampsia (Table 1). The remaining 3 patients were as follows: 1. A 30-year-old multiparous woman who developed severe headache at the third trimester of pregnancy, followed by deep coma, repeated convulsions, and right hemiplegia. Her brain CT scan showed a big left intracerebral hemorrhage. She was discharged fully conscious, but with persistent hemiparesis. 2. A 26-year-old primigravida with drowsiness and convulsions 2 days after delivery, without preexistent maternal hypertension, or preeclampsia. Her CT scan showed left frontoparietal infarction. She was discharged well after 6 days stayed in the CCU. 3. A 24-year-old multiparous woman who developed jaundice and disturbed consciousness late in pregnancy,



Figure 1 - Magnetic resonance imaging and MR venography (MRV) of the brain of a 30-year-old multiparous woman who developed repeated convulsions and coma during the third trimester of her pregnancy, revealing patchy infarction in the white matter and subcortical areas of both hemispheres. Partial missing of right transverse sinus is shown in MRV, consistent with cerebral venous thrombosis.

and was admitted postpartum with deep coma. Acute hepatic encephalopathy complicating fatty liver of pregnancy (AFLP) was diagnosed after excluding viral hepatitis. She was however, discharged well after 18 days of stay in the CCU. Follow up visits showed complete neurological recovery.

Discussion. Over one year, 30 women were admitted to the CCU with coma and convulsions in the peripartum period. Most of them were first referred as eclampsia. This diagnosis was confirmed in two thirds (20 patients), but an alternative diagnosis was ultimately made in the other third. Although the diagnosis of preeclampsia and eclampsia is generally easy, the diagnosis may prove difficult in the presence of focal neurological deficits, prolonged coma or atypical eclampsia.¹⁶Various neurological disorders may resemble eclampsia, and their clinical differentiation may be quit challenging. The differential diagnoses should include cerebrovascular accidents (strokes), hypertensive encephalopathy, epilepsy, previously undiagnosed brain tumour, metastatic gestational trophoblastic disease, metabolic disorders (hypoglycemia and hyponatremia), thrombotic thrombocytopenic purpura, and CVT. In addition, in some patients gestational hypertension and preeclampsia may develop in association with these disorders, further contributing to the diagnostic difficulty.¹⁷

In this study, CVT has emerged as the second most important diagnosis after eclampsia. It was the cause of coma in 7 out of 30 patients, 4 of them with an

antenatal diagnosis of preeclampsia. This finding calls for careful consideration of this disease, which has variable presentation and non specific clinical picture.¹⁴⁻¹⁸ It also pays attention to the fact that eclampsia is not the only cause of coma and convulsions in a patient with preeclampsia. In fact, maternal hypertension was shown to increase the risk CVT by an odds ratio of 1.9.¹⁹ When patients with eclampsia were compared with those having CVT, certain differences in clinical presentation were noticed. Most eclampsia patients were primigravida [17 (85%)], compared with 1 (14.3%) patients with CVT (p=0.0001). No direct comparison has been previously carried out, but it is well known that preeclampsia is more common in the first pregnancy,²⁰ while increasing maternal age is an important risk factor for the development of CVT.¹⁹ Although classically described to present in the postpartum period, patients with CVT in our study did not differ significantly from patients with eclampsia regarding the timing of the event, where neurological symptoms started in the postpartum period in 4 (57.4%) of patient with CVT, and in 8 (40%) of eclampsia cases. Among recent studies, postpartum eclampsia has similarly ranged from 11-44%.²¹⁻²⁴

Cortical blindness was found a useful indicator of eclampsia instead of CVT, where it developed in 5 (25%) of these cases, but in no woman with CVT (p=0.01). However, hemiparesis was more common in CVT patients than in eclampsia [1 (14.9%) versus 1 (5%)], but the difference did not reach statistical significance. This pattern of neurological complications is explained by the site of the lesion in the 2 disorders. In eclampsia, the predominant occipital involvement (as shown by the imaging studies) is responsible for the cortical blindness, while thrombosis of the superior sagittal sinus (the most commonly involved sinus in CVT)¹⁴ causes adjacent venous infarction presenting as hemiparesis. Cortical blindness was similarly noticed to be the most important focal neurological symptom of eclampsia developing in 19-32% of cases in other studies.^{21,23,24} Papilledema was present in a similar proportion of patients in both groups. However, in our study, papilledema was detected in a larger proportion of patients with eclampsia than other authors noticed (2.6-6%).^{25,26} This can be explained by the fact that our cohort included more severe cases with coma and prominent MRI findings.²⁷ However, most studies of CVT found higher percentage of papilledema (40-44%),^{18,28,29} but these studies included patients with more chronic presentations, and the development of papilledema was shown to correlate with the duration of the disease.29

Despite the importance of careful clinical evaluation, it was the imaging studies that provided the final diagnosis in most of our cases. This was especially true in cases of CVT, where the diagnosis was confirmed by MRV in all of them. The MRV is well established as the imaging modality of choice in the diagnosis of this disease,^{30,31} replacing the more invasive traditional catheter angiogram.¹⁴ The CT was negative or inconclusive in the 2 patients who received this imaging prior to MRI and MRV. When CT scan is used, confidant diagnosis is made in 20-30% of cases of CVT only (by showing empty delta sign).^{14,32,33} Imaging is not routinely required in every patient with eclampsia, but is indicated in severe cases with prolonged coma and neurological dysfunction.¹⁶ All the 9 MRI studies and the majority of CT scans were positive in women with eclampsia. The changes are consistent with the changes of reversible posterior leukoencephalopathy syndrome (RPLS), which has been described to represent transient subcortical vasogenic edema without infarction.³⁴ These changes predominate in the occipital and occipitoparietal region. Reversible posterior leukoencephalopathy syndrome has also been described in other cases of hypertensive encephalopathy, and in patients receiving cytotoxic and immunosuppressive drugs.^{34,35} Although the pathogenesis is not completely understood, it seems to be related to breakdown of autoregulation and endothelial dysfunction rather than to the degree of elevation of blood pressure.²⁷ Autoregulation of cerebral blood flow maintains mean cerebral blood pressure at 60 and 150 mm Hg. Cerebral autoregulation depends on 2 mechanisms: myogenic and neurogenic. The neurogenic component is controlled by sympathetic innervation which, predominates in the anterior circulation.²⁷ The precise alteration in cerebral blood flow in eclampsia is not exactly known. However, 2 theories have been proposed: forced dilatation and vasospasm.¹⁶ In forced dilatation theory, the upper limit of autoregulation is exceeded by the rapid and severe rise of blood pressure with consequent forced overdistention of the cerebral vasculature decreasing the effect of the myogenic mechanism, allowing local hyperfusion with consequent vasogenic and interstitial edema. The posterior circulation which lacks effective sympathetic innervation suffers most, resulting in predominant involvement of the occipital region of the brain. According to the vasospasm theory; cerebral overregulation occurs in response to acute severe hypertension with resultant ischemia, cytotoxic edema, and infarction.¹⁶ In case of eclampsia without hypertension (16% of cases), direct endothelial cell dysfunction, with increased blood brain barrier permeability, is thought to be responsible for the pathogenesis of RPLS in these patients.^{27,34} The RPLS has been described in up to 93-100% of women with eclampsia.^{16,36,37} Concurrent foci of infarction, some not reversible on subsequent imaging have been described in 11-22% of patients in several studies.^{36,37} No such

finding has been noticed in our patients, however, one woman was discharged with persistent hemiparesis, but she did not undergo follow up imaging to confirm this possibility.

Physiological changes during pregnancy and the puerperium is thought to increase the risk of stroke even without eclampsia.^{9,38,39} There is a higher incidence of stroke (both ischemic and hemorrhagic) in women than in men between the ages of 15-35 years, pregnancy associated strokes may be partly responsible for the increased incidence.9 Two of our patients with coma and convulsions were diagnosed with peripartum stroke (one ischemic and the other hemorrhagic). In one woman, deterioration of consciousness, and convulsions was proved to be caused by AFLP. The diagnosis of this disease is not always easy, as AFLP shares features with many other common disorders during pregnancy including eclampsia, especially when jaundice is absent.⁴⁰ Ten out of 22 cases of a recent study from Tunisia were non-icteric on presentation.⁴⁰ The mortality rate is around 30%^{40,41} and delayed diagnosis is associated with poor result.⁴⁰

It is the standard in our hospital to admit women with acute peripartum neurological symptoms and signs to the CCU. This unit is especially designed to provide continuous monitoring of vital signs, oxygen saturation, and ECG. The staff working in the CCU includes physicians with special interest and experience in intensive care, and an anesthesiologist to provide support in case ventilatory therapy is required. The women were received after pregnancy had been terminated in the maternity hospital. Nursing care of unconscious patients was provided. Measures to maintain patent airways and adequate oxygenation with prevention of aspiration were particularly ensured during convulsions. Intravenous (IV) diazepam was used, followed by phenytoin in resistant cases. Moreover, patients with eclampsia received a loading dose of magnesium sulphate (6 gm over 20-30 min.), followed by a maintenance of 2 gm/hour as a continuous IV infusion.^{16,42} The systolic blood pressure was kept below 155 mmHg and the diastolic below 105.16,43 Hydralazine was the most commonly used parental antihypertensive drug. This was followed by oral antihypertensive therapy. Women with CVT received an intravenous infusion of unfractionated heparin at a dose sufficient to keep APTT 1.8-2 times the control, followed by 3 months of warfarin therapy.^{14,44}

With the above therapy, none of our patients died. The mortality rate of these critically ill women is not however, high. In a study from Singapore, the maternal mortality of obstetric admissions to the intensive therapy unit was 1.3% (but they included non-neurological cases as well).⁴ The mortality rate of CVT in modern medical practice ranks between 5.5-18%.^{13,18,29} However, the mortality was zero in a recent wide US survey, similar to the results of our study.¹⁹

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