

Original Research Article

Incidence and clinical manifestations of posterior reversible encephalopathy syndrome (PRES) in patients with eclampsia. 2017-2021 data from a High Specialty Medical Unit, Mexico City

ABSTRACT

Aims: To identify the incidence of posterior reversible encephalopathy syndrome (PRES) on Tomography scan of the skull (CT) and/or Magnetic Resonance Imaging (MRI) and its clinical manifestations in patients with eclampsia.

Study design: Observational, cross-sectional, retrospective and descriptive study.

Place and Duration of Study: Patients with eclampsia admitted to the Intensive Care Unit (ICU) of a High Specialty Medical Unit (Hospital de Gineco-Obstetricia No. 3. Centro Médico Nacional "La Raza". Instituto Mexicano del Seguro Social) in Mexico City between 2017 to 2021.

Methodology: We studied a series of 25 cases with eclampsia admitted to the ICU. Their files were consulted to know the incidence of PRES on CT, MRI or both, as well as the signs and symptoms that accompanied the eclampsia. The data was analyzed with descriptive statistics using the statistical package SPSS version 20.

Results: Age 26.2 ± 7.13 years, parity (median) 1, gestational age 34.4 ± 5.05 weeks, comorbidities 12%, prepartum eclampsia 72% (n=18), intrapartum 4% (n=1) and postpartum 24% (n= 6). Imaging studies were performed only in 68% (n=17), the most used was CT (n=16). They found normal findings in 52.94%, PRES 29.41% (n=5), generalized edema 5.88%, Fisher class IV subarachnoid hemorrhage 5.88%, and parenchymal hemorrhage communicated to the IV ventricle 5.88%. The most frequent symptom was headache 40% and the most frequent sign was hyperreflexia 48%.

Conclusion: The incidence of PRES was 29.41%. CT was performed most frequently. The most frequent symptom was headache and the most frequent sign was hyperreflexia.

Keywords: Posterior reversible encephalopathy syndrome; Eclampsia; Computed tomography; Magnetic resonance imaging; Intensive Care in Obstetrics; High Risk Pregnancy.

1. INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) was first described in 1996 by Hinchey et al, [1] who reported on a series of 15 patients with neurological signs and symptoms that included headache, seizures, visual disturbances, and other focal neurological deficits accompanied by of images suggestive of cerebral edema predominantly in the posterior regions observed by computed tomography (CT) scan of the skull or by magnetic resonance imaging (MRI). The 15 reported cases included patients with hypertensive encephalopathy, eclampsia and patients undergoing immunosuppressive management. [1]

PRES has been reported in pediatric and adult patients with various diseases and with the administration of medications, immunosuppressive agents, and anticancer drugs. [2-4] Its pathogenesis is not fully understood; two theories have been proposed. The first is the theory of vasogenic edema due to hypertension and cerebral hyperperfusion in susceptible areas, and the second theory refers to endothelial dysfunction caused by circulating substances with a toxic effect. [3,5,6]

In eclampsia, the pathophysiological mechanisms are similar to those described for PRES and the neurological manifestations are similar. [5] Previous studies have found that the incidence of PRES in patients with preeclampsia and neurological findings and in women with eclampsia is very high. [7,8] In our country, research on the subject is scarce or non-existent. This scenario justified the realization of the present investigation. The objective of the research was to identify the incidence of PRES on CT scan and/or MRI and its clinical manifestations in patients with eclampsia.

2. MATERIAL AND METHODS

An observational, cross-sectional, retrospective and descriptive study was carried out in a series of cases consisting of 25 patients with eclampsia admitted to the Intensive Care Unit (ICU) of a High Specialty Medical Unit (Hospital de Gineco-Obstetricia No. 3. Centro Médico Nacional "La Raza". Instituto Mexicano del Seguro Social) in Mexico City between 2017 to 2021.

For the purposes of the investigation, the inclusion criteria were: patients with eclampsia of any age, parity, weeks of pregnancy, comorbidities, blood pressure, simultaneous complications with eclampsia such as HELLP syndrome, antepartum, intrapartum or postpartum presentation of eclampsia, technique of termination of pregnancy and with available clinical file. No cases were excluded or eliminated because the 25 patients met the inclusion criteria.

All the patients were sent from other hospitals for specialized care. Their records were consulted, the diagnosis of eclampsia was confirmed according to the recommendations of the American College of Obstetricians and Gynecologists (ACOG) of the United States of America published in the year 2020. [9] In addition, the neurological manifestations (symptoms and signs) that accompanied the eclampsia were recorded and the brain imaging studies (CT scan, MRI) were consulted with the description of the findings. No patient had a history of preeclampsia, eclampsia, HELLP syndrome, or neurological diseases (trauma, epilepsy, brain tumors) or chronic conditions that may compromise brain function. Prior to the study, approval was obtained from the Local Health Research and Ethics Committees of the host hospital (Registration: R-2022-3504-014). Descriptive statistical measures (mean,

median, standard deviation and range) were used for data analysis using the statistical package SPSS version 20.

3. RESULTS AND DISCUSSION

During the period from 2017 to 2021, a total of 1,952 patients were admitted to the ICU to receive critical care, 25 patients with eclampsia were found. Thus, the overall incidence of eclampsia cases in the ICU was 1.28% (median 5 cases per year).

General Data

The mean age was 26.2 ± 7.13 years with a range of 22 years (limits 15 to 37). The median parity was 1 with a range of 4 (limits 1 to 5) and the mean gestational age was 34.4 ± 5.05 weeks with a range of 19 weeks (limits 21 to 40). It was found that 22 patients (88%) had no associated morbidities while 3 patients (12%) had only one comorbidity less than one-year evolution (1 case with type 2 diabetes mellitus with good control, 1 case with arterial hypertension, 1 case with arterial hypertension and compensated primary hypothyroidism). It was found that in 18 patients (72%) eclampsia occurred in the antepartum period, 1 case in the intrapartum period (4%) and 6 cases (24%) in the postpartum period. In 12% (3 cases) eclampsia was accompanied by HELLP syndrome. For termination of pregnancy, all cases underwent cesarean section. There were no cases of maternal death.

Neurological manifestations

Symptoms were headache (n=10), confusion (n=3), lethargy (n=3) and blurred vision (n=2), nausea (n=1), vomiting (n=1), phosphenes (n=1) and transient blindness (n=1). Neurological signs were hyperreflexia (n=12), superficial coma (n=2), and clonus (n=1). Thus, headache was the most frequent neurological symptom in 40% (10/25 cases) and the most frequent sign was hyperreflexia in 48% (12/25 cases).

Imaging studies

It was found that in 32% (8 cases) imaging studies were not performed, 64% (16 cases) were studied with CT scan and 4% (1 case) MRI was performed after a CT scan. Thus, only 17 patients underwent imaging studies, normal data were reported in 52.94% (9 cases) and structural alterations in 47.06% (8 cases). Abnormal findings included 5 cases with data compatible with PRES (CT scan 4 cases, MRI 1 case) and 3 cases with different diagnoses. Thus, the incidence of PRES in our case series was 29.41% (5/17 cases) **Table 1** When the findings of the 17 patients with CT scan and MRI were ordered to analyze their distribution, it was found that the most frequent were normal data followed by lesions compatible with PRES. **Figure 1** and **Figure 2**

Table 1. Findings in 17 patients with eclampsia who underwent brain imaging studies.

Type of study	Findings
---------------	----------

Skull CT scan 94.12%, n=16	Normal structures n=9 Structural alterations n=7 Data compatible with PRES n=4 Generalized edema n=1 Fisher class IV subarachnoid hemorrhage n=1 Parenchymal hemorrhage with communication to the IV ventricle n=1
Skull CT scan with MRI 5.88%, n=1	CT without focal or diffuse lesions 4 days later: MRI: diffuse hyperintensity in T2 and T2 in the right occipital subcortical white matter suggestive of vasogenic edema compatible with PRES.

CT = Computed Tomography; MRI = Magnetic Resonance Imaging; PRES = Posterior Reversible Encephalopathy Syndrome.

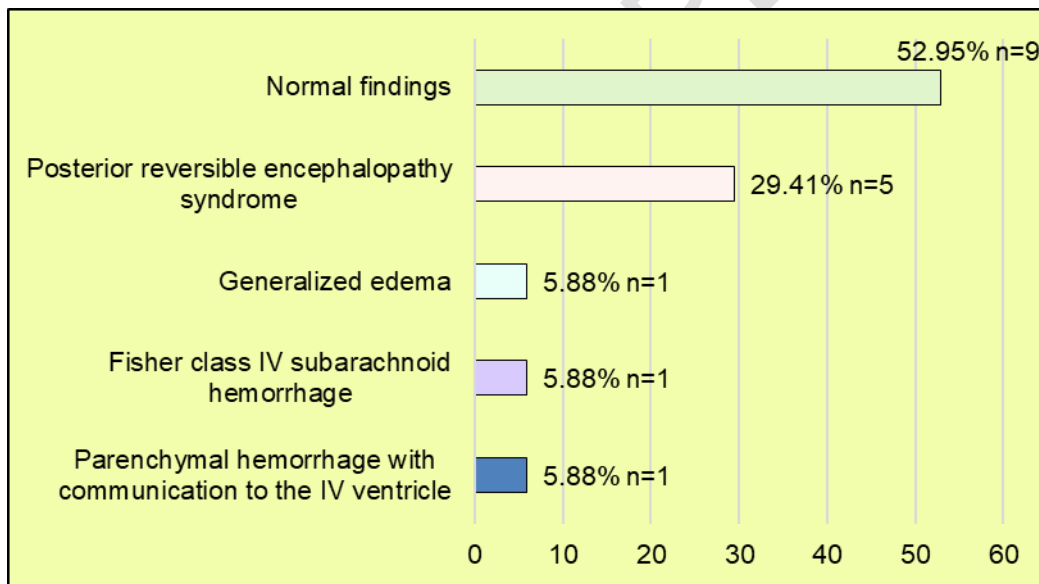
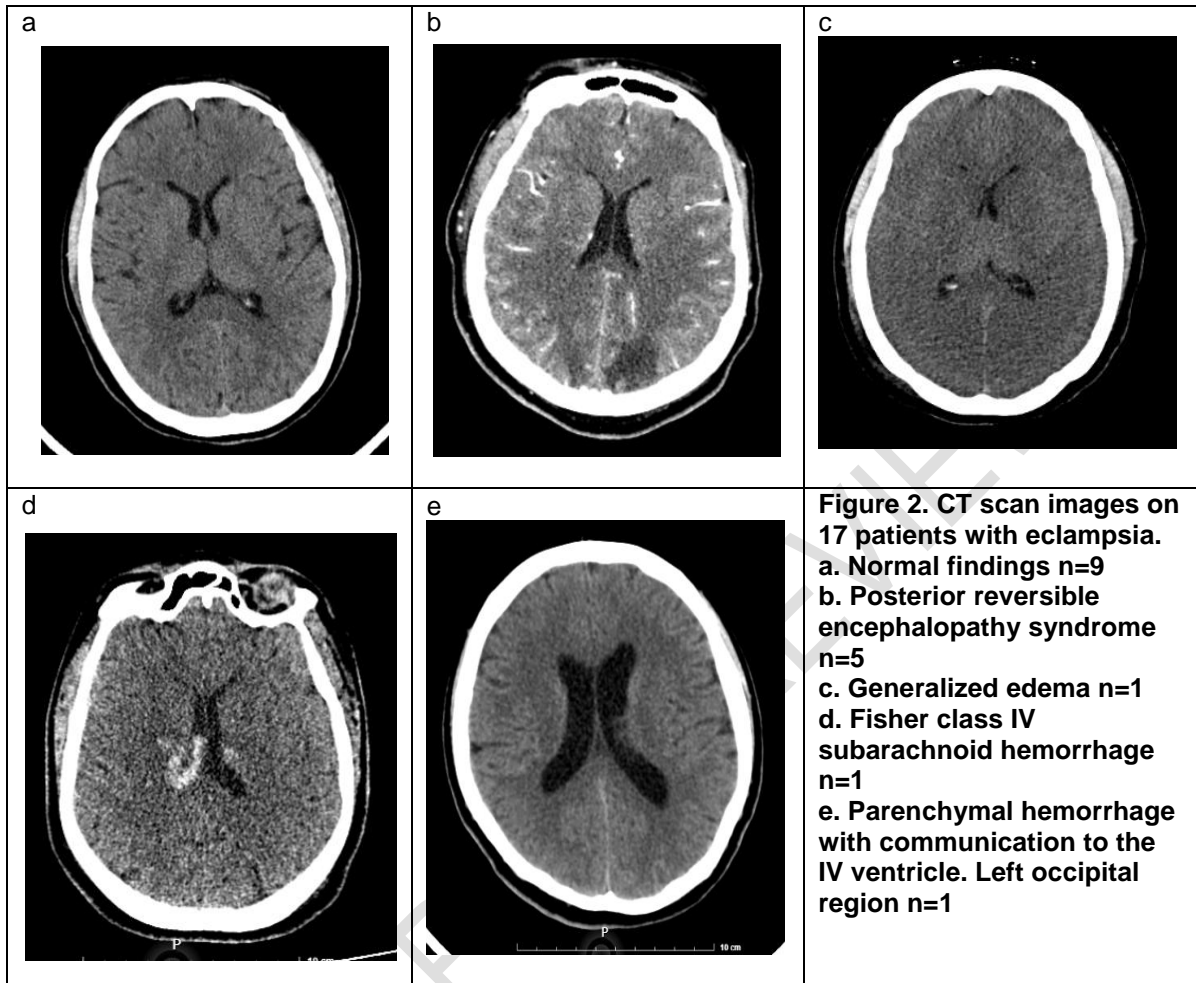


Figure 1. Distribution of Computerized Tomography scan and Magnetic Resonance Imaging findings performed on 17 patients with eclampsia.



Since the first publication in 1996 by Hinchey cols, [1] the presence of PRES has been reported in various types of diseases and in patients with a wide range of incidence. [2-4] The evidence indicates that it is more of a clinical-radiological syndrome. During subsequent years and up to the present time the risk factors and the clinical environment of patients who may develop it or who already suffer from it have been identified. [2-5,10]

The pathophysiology of PRES is not fully understood. Despite the complexity of the pathophysiological mechanisms, common findings have been identified: vasogenic edema and endothelial dysfunction in characteristic brain territories. [2-4] Preeclampsia/eclampsia, the most common group of hypertensive states complicating human pregnancy, share key mechanisms of the complex pathophysiology of PRES. [5] It is noteworthy that in the pioneering work by Hinchey cols, [1] patients with preeclampsia and eclampsia were included in the study group, this situation led to the suspicion of an association.

The incidence of PRES in this special group of patients has been studied intentionally in recent years. In 2016, Mayama et al. [7] published the results of a study. The authors conducted a series of 39 patients, 13 patients with eclampsia and 26 cases with preeclampsia and neurological symptoms treated at a University Hospital in Japan to

determine the incidence of PRES by interpreting the MRI and MRI angiography studies of the patients. They found that the incidence of PRES was 92.30% (12 cases) in women with eclampsia and 19.2% (5 cases) in patients with preeclampsia and neurological symptoms. On the other hand, in 2021 Mai et al. [8] reported the characteristics of brain edema by MRI in 126 patients with preeclampsia and 24 with eclampsia studied in a Chinese Hospital from September 2012 to March 2020. They found that the incidence of PRES in eclampsia was 87.50% (21 cases) and in preeclampsia 46.03% (58 cases) ($p=0.001$). We studied a series of 25 patients with eclampsia who underwent brain imaging studies on only 17 of them. We found that the incidence of PRES on CT scan and MRI was 29.41% (5/17 cases), a figure much lower than the reported by Mayama et al. [7] in Japan 2016 and Mai et al. [8] in China 2021. **Figure 3**

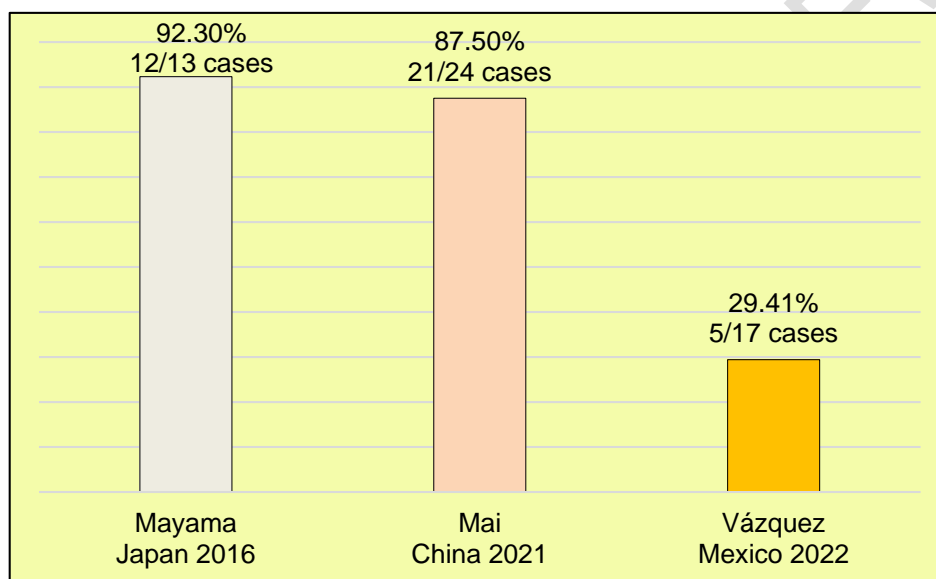


Figure 3. Frequency of Posterior Reversible Encephalopathy Syndrome in series of patients with eclampsia.

The difference in the incidence of PRES in our series of cases and the previously reported series may be a consequence of various factors that have already been identified in previous investigations. [11] The comorbidities of the patients, the gestational stage in which the eclampsia manifests itself, the duration and severity of the clinical manifestations prior to the eclampsia or after it, the timely comprehensive management and care of the patients in a center with experience or in a highly specialized hospital with available imaging studies may be determining factors. [2,4,5,6,10-12]

The characteristics of the study protocol of the patients in our series should also be considered. It was found that in 32% (8 cases) no imaging studies were performed, 64% (16 cases) had a CT scan and only 4% (1 case) MRI was performed. The medical decision not to perform imaging studies on all patients with eclampsia can be considered a deviation in clinical practice. **The performance of CT scan and not MRI as the most popular study is due to the availability of the types of image from the limited economic resources of the host**

hospital and not to the preference of the medical team. This topic is relevant around the world and not only in Mexico.

The predominance of CT scan over MRI may have limited the identification of PRES because it has been described that when the initial CT scan findings are interpreted as normal, MRI can discover structural lesions because it has higher resolution. This was the situation of a patient in our series. **Table 1** In addition, in cases where the first CT scan shows a lesion, MRI can show more lesions. [12] These characteristics make MRI the method of choice for the diagnosis of PRES. [6,10,13]

The inexperience or misinformation of the radiologist in the interpretation of the images is another factor that must be considered. Previous literature has documented that the presence of cerebral vasogenic edema in varying degrees is not the only finding compatible with PRES, other rare alterations can also be found such as the presence of microbleeds, macrobleeds, unilateral PRES, presence of edema in central structures, areas of ischemia and non-traumatic subarachnoid hemorrhage. [6,10,12,13] In our series, a patient with generalized edema, a patient with Fisher class iv subarachnoid hemorrhage, and a case with parenchymal hemorrhage communicated to the IV ventricle were reported, which leaves doubt as to whether or not it was PRES variants. In the worst case, the incidence of PRES would have increased to 47.05% (8/17 cases), a figure not yet comparable with reports from other series. [7,8]

The long-term sequelae of PRES in preeclampsia/eclampsia and other related conditions have been poorly described. Postma et al. [14] reviewed the topic in patients with preeclampsia/eclampsia in 2014. For the prevention of long-term sequelae, they recommend early recognition, adequate treatment, and supportive follow-up after the acute event. This may be particularly true for the patients in our series with hemorrhagic-type complications.

The results of the research are consistent with the recommendation to use imaging studies, MRI and not CT scan, for the diagnosis and treatment of all patients with eclampsia, regardless of whether PRES syndrome is suspected or not. Similarly, the recommendation can be applied to the clinical follow-up of eclampsia and early differential diagnosis and management.

We consider that the main strength of the research was having promptly identified the incidence of PRES on CT scan and/or MRI and the clinical manifestations in patients with eclampsia. The description of the deviations regarding the imaging studies that the international literature recommends to document PRES in eclampsia is an additional strength because it highlights an issue that needs an improvement plan.

The research has weaknesses that are inherent in its design due to the fact that it was a small series of cases with an observational, cross-sectional, and descriptive study with results subject to retrospective analysis.

4. CONCLUSIONS

The frequency of PRES in 17 patients with eclampsia who underwent imaging studies was 29.41% (5 cases). CT scan was the most frequently performed study. All patients had accompanying clinical manifestations, the most frequent symptom was headache and the most frequent sign was hyperreflexia.

CONSENT

Due to the fact that it was an observational, cross-sectional, retrospective and descriptive study that consisted of reviewing the clinical files and brain imaging studies of patients who had already been permanently discharged from the hospital, the Local Health Research Committee and the Local Ethics Committee of the host hospital authorized the investigation to be carried out without informed consent (Registration: R-2022-3504-014).

ETHICAL APPROVAL

The Local Health Research Committee and the Local Ethics Committee of the host hospital authorized the investigation (Registration: R-2022-3504-014).

REFERENCES

1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A et al. A Reversible posterior leukoencephalopathy syndrome. *N Engl J Medicine*. 1996;334(8):494-500.
<https://www.nejm.org/doi/pdf/10.1056/NEJM19960223340803?articleTools=true>
2. Hinduja A. Posterior reversible encephalopathy syndrome: clinical features and outcome. *Frontiers in Neurology*. 2020;11:article 71
file:///C:/Users/WINDOWS_10/Downloads/fneur-11-00071.pdf
3. Marra A, Vargas M, Striano P, Del Guercio L, Buonanno P, Servillo, G. Posterior reversible encephalopathy syndrome: the endothelial hypotheses. *Medical Hypotheses*. 2014;82:619-622.
<https://www.iris.unina.it/retrieve/handle/11588/666356/105507/1-s2.0-S0306987714000929-main.pdf>
4. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. *Mayo Clin Proc*. 2010;85(5):427-432.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2861971/pdf/mayoclinproc_85_5_004.pdf
5. Cooray SD, Edmonds SM, Tong S, Samarasekera SP, Whitehead CL. Characterization of symptoms immediately preceding eclampsia. *Obstet Gynecol*. 2011;118(5):995–999.
<https://pubmed.ncbi.nlm.nih.gov/22015866/>
6. Fischer M, Schmutzhard E. 2017. Posterior reversible encephalopathy syndrome. *J Neurol*. 2017;264(8):1608-1616.
<https://link.springer.com/content/pdf/10.1007/s00415-016-8377-8.pdf>
7. Mayama M, Uno K, Tano S, Yoshihara M, Ukai M, Kishigami Y, et al. Incidence of posterior reversible encephalopathy syndrome in eclamptic and patients with preeclampsia with neurological symptoms. *AJOG*. 2016;215(2):P239 E1-239 E5
[https://www.ajog.org/article/S0002-9378\(16\)00339-2/pdfSummary](https://www.ajog.org/article/S0002-9378(16)00339-2/pdfSummary)
8. Mai H, Liang Z, Chen Z, Liu Z, Xu Y, Chen X, et al. MRI characteristics of brain edema in preeclampsia/eclampsia patients with posterior reversible encephalopathy syndrome. *BMC*

Pregnancy Childbirth. 2021;21(1):669.

<https://bmcpregnancychildbirth.biomedcentral.com/track/pdf/10.1186/s12884-021-04145-1.pdf>

9. Gestational Hypertension and Preeclampsia: ACOG Practice Bulletin, Number 222.

Obstet Gynecol. 2020;135(6):e237-e260.

https://journals.lww.com/greenjournal/Abstract/2020/06000/Gestational_Hypertension_and_Preeclampsia__ACOG.46.aspx

10. Parasher A, Jhamb R. Posterior reversible encephalopathy syndrome (PRES): presentation, diagnosis and treatment. Postgrad Med J. 2020;96(1140):623-628.

<https://pubmed.ncbi.nlm.nih.gov/32467104/>

11. Chen Z, Zhang G, Lerner A, Wang AH, Gao B, Liu J, et al. Risk factors for poor outcome in posterior reversible encephalopathy syndrome: systematic review and meta-analysis.

Quant Imaging Med Surg. 2018;8(4):421-432.

<https://qims.amegroups.com/article/view/19564/19540>

12. Neill TA. Reversible posterior leukoencephalopathy syndrome. UpToDate 2022.

<https://www.uptodate.com/contents/reversible-posterior-leukoencephalopathy-syndrome>

13. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR. 2007;28(7):1320-1327.

<http://www.ajnr.org/content/ajnr/28/7/1320.full.pdf>

14. Postma I, Slager S, Kremer HPH, de Groot JC, Zeeman GG. Long-term consequences of the posterior reversible encephalopathy syndrome in eclampsia and preeclampsia: a review of the obstetric and nonobstetric literature. Obstet Gynecol Surv. 2014;69(5):287-300.

https://journals.lww.com/obgynsurvey/Abstract/2014/05000/Long_term_Consequences_of_the_Posterior_Reversible.17.aspx