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Original Research Article

Posterior reversible encephalopathy syndrome: a study of risk factors, presenting complaints, and magnetic resonance imaging findings from a tertiary care hospital in Pakistan

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ABSTRACT

Background: Posterior reversible encephalopathy syndrome (PRES) primarily occurs in the background of high blood pressure and manifests as symmetrical vasogenic edema involving the parieto-occipital lobes. This study aims to determine the risk factors, presenting complaints, and various typical and atypical radiological patterns of PRES in a larger single-center population.
Methods: This is a retrospective observational study of 81 patients with clinical and radiological diagnoses of PRES. Demographic data, concurrent medical illnesses, and presenting complaints were extracted from medical records. Areas of the brain involved and atypical imaging findings were studied on various MR imaging sequences.
Results: The most common risk factor was eclampsia (64.20%), followed by renal diseases (16.05%). All but eight cases occurred in the background of hypertension. The most frequent presenting complaint was seizure (79.01%). The most common radiological manifestation was bilaterally symmetrical vasogenic edema, with the parietal lobe (92.59%) and the occipital lobe (83.95%) primarily affected. Restricted diffusion was present in 23.46%, hemorrhage in 8.64%, and post-Gadolinium contrast enhancement in 2.47% of patients.
Conclusions: PRES has a diverse clinical and radiological presentation awareness about which among medical professionals is important for timely diagnosis and treatment.

Keywords: Eclampsia, Diffusion restriction, Hypertension, MR imaging, PRES, Radiological

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a rare neurological disorder primarily associated with conditions of high blood pressure, such as pre-eclampsia, eclampsia, and renal diseases.[1-3] Rapidly rising blood pressure is believed to impair the cerebral blood flow autoregulation mechanism, damaging the vascular endothelium and resulting in cortical and subcortical brain edema.[4] In addition to high blood pressure, factors such as chemotherapeutic drugs, organ transplantation, malignancy, and autoimmune disorders also occasionally predispose individuals to PRES.[2,3,5]

PRES is a clinical and radiological diagnosis. Clinically, it manifests as an acute or subacute onset of nonspecific symptoms such as headache, seizure, nausea, vomiting, mental status changes, visual disturbances, and focal neurological deficits.[1-3,5] Radiologically, it typically manifests as bilaterally symmetrical reversible vasogenic edema, predominantly affecting the parieto-occipital lobes. However, atypicality, which is defined by atypical areas involvement (the frontal and temporal lobes, basal

ganglia, cerebellum, deep gray matter, brain stem), unilaterality, diffusion restriction, post-contrast enhancement, and hemorrhage, is not uncommon, highlighting the variability in presentation.[3,6,7] All these make the diagnosis of PRES a bit challenging.

Given the reversibility of this syndrome, timely diagnosis and treatment are essential. Delays in diagnosis and treatment can result in significant neurological consequences, including death.[8] Literature shows limited studies on PRES in the Pakistani population.[9] It is therefore important to study this syndrome to fill the deficit in the available clinical and imaging data and thereby prevent delays in diagnosis and treatment. This study discusses the risk factors, presenting complaints and MR imaging features that were observed in individuals diagnosed with PRES in a tertiary care hospital in Pakistan.

METHODS

This is a retrospective observational study conducted at the radiology department of Nishtar hospital, Pakistan. The ethical approval was obtained from the institutional ethical review board of Nishtar medical Univesity (Ref. No. 7136/NMU, date: June 3, 2024). The study was conducted as per the Helsinki declaration of human rights.

Clinical records and MR images of patients who were referred to the radiology department from other departments of the hospital between January 2019 and March 2024 with signs and symptoms consistent with PRES were reviewed. The 81 patients who satisfied both the clinical and radiological criteria for PRES were included in the study. Those with clinical symptoms consistent with PRES but lacking either radiological evidence of PRES or follow-up improvement of clinical or radiological findings were excluded from the study. Demographic information, presenting complaints, concurrent medical illness, drug history and areas of brain involved on imaging were recorded. In addition, atypical imaging features like unilaterality, diffusion restriction, hemorrhage and post contrast enhancement were also recorded. The images were reviewed using picture archiving communication system (PACS) (Siemens AG, Munich, Germany) by senior radiologists to prevent inter-observer variability.

Imaging technique

The brain MRI of each patient was done using a Toshiba Vantage Titan 1.5 Tesla MRI scanner with a dedicated head coil. The sequences used were T1-weighted axial and sagittal, T2-weighted axial and sagittal, fluid attenuated inversion recovery (FLAIR) axial, diffusion-weighted (DWI), apparent diffusion coefficient (ADC) map and T1 post contrast (when necessary). Sometimes T2*- weighted image, gradient echo (GRE) image, MR arteriography (MRA) and MR venography (MRV) were obtained as well.

Areas of the brain involved and signal intensity changes were identified on T2-weighted, FLAIR, and diffusion weighted images. On T1 and T2*-weighted images, hemorrhagic changes were identified, and on T1-weighted post-contrast images, if they were available, gadolinium enhancement was detected.

Statistical analysis

The statistical analyses were carried out using the SPSS software version 26.0 (SPSS, Chicago, IL, USA). Results for continuous variables are reported as means ± standard deviations, while categorical variables are presented as number and proportion. Categorical variables were compared using a Fisher exact test or Chi-square test, as appropriate. A $p<0.05$ indicated significance.

RESULTS

This study consisted of 81 patients, of whom 76 (93.82%) were females and 5 (6.17%) were males. The mean age was 25.01±10.61 (range, 7-70 years). Largest subsets of patients were found in the 18-30 age groups (n=50, 61.73%) (Figure 1). The most frequent presenting complaints were seizures (n=64, 79.01%) and headaches (n=44, 54.32%). Visual disturbances and altered mental status were present in 28 (34.57%) and 17 (20.99%) patients, respectively (Table 1).

Table 1: frequency distribution of presenting complaints among HDPs-associated and other risk factors associated PRES.

Presenting complaints	N, (%)	Causes of PRES		P value
		HDPs, (n=59)	Others, (n=22)	
Seizure	64 (79.01)	52 (88.14)	12 (54.55)	0.002
Headache	44 (54.32)	35 (59.32)	9 (40.91)	0.139
Visual disturbances	28 (34.57)	27 (45.76)	1 (4.55)	0.001
Altered mental status	17 (20.99)	7 (11.86)	10 (45.45)	0.002

*Seizure and visual disturbances were significantly more common among HDPs-associated PRES while altered mental status was significantly more common among other risk factors associated PRES.

In the majority of cases, PRES occurred in association with hypertensive disorders of pregnancy (HDPs), with eclampsia (n=52, 64.20%) being the most common. Renal diseases were the second-most frequently encountered risk factor seen in 13 (16.05%) patients (Table 2).

All the patients except 4 had bilaterally symmetrical vasogenic edema (Figure 2). The most common area of the brain involved was the parietal lobe (n=75, 92.59%), followed by the occipital lobe (n=68, 83.95%), the frontal lobe (n=32, 39.51%), and the temporal lobe (n=17, 20.99%) (Figure 3). Capsuloganglionic area was involved in 13 (16.05%) patients, of whom 5 had basal ganglia involvement, 4 had thalamus involvement, and 4 had whole of the capsuloganglionic area involvement. On DW images, there was evidence of restricted diffusion in 19 (23.46%) patients. Hemorrhage was evident in 7 (8.64%) patients, and post-Gadolinium contrast enhancement was observed in 2 (2.47%) patients (Figure 4).

Table 2: Frequency of risk factors encountered in patients diagnosed with PRES, (n=81).

Risk factors	N (%)
HDPs	
Eclampsia	52 (64.20)
Pre-eclampsia	6 (7.41)
HELLP	1 (1.23)
Renal diseases	
CKD	5 (6.17)
Nephrotic syndrome	4 (4.94)
SGN	3 (3.70)
HUS	1 (1.23)
SLE	3 (3.70)
chemotherapy	2 (2.47)
APS	1 (1.23)
ALL	1 (1.23)
Epilepsy	1 (1.23)
Anti-tuberculosis therapy	1 (1.23)

*PRES, Posterior reversible encephalopathy syndrome; HDPs, hypertensive disorders of pregnancy; HELLP, hemolysis, elevated liver enzymes and low platelets; CKD, chronic kidney disease; SGN, streptococcal glomerulonephritis; HUS, hemolytic uremic syndrome; SLE, systemic lupus erythematosus; APS, antiphospholipid syndrome; ALL, acute lymphoblastic leukemia

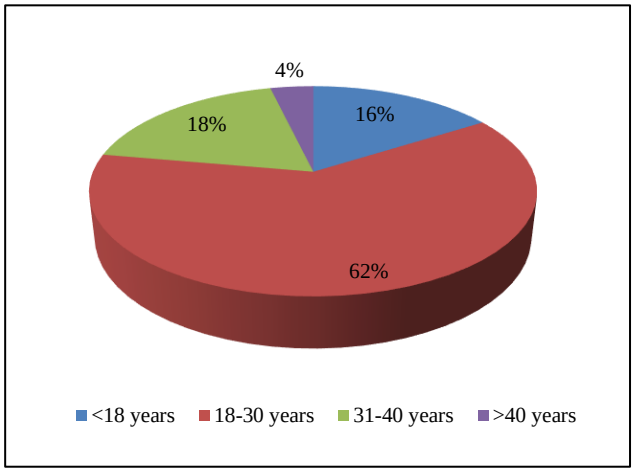

Figure 1: Age distribution of individuals diagnosed with PRES.

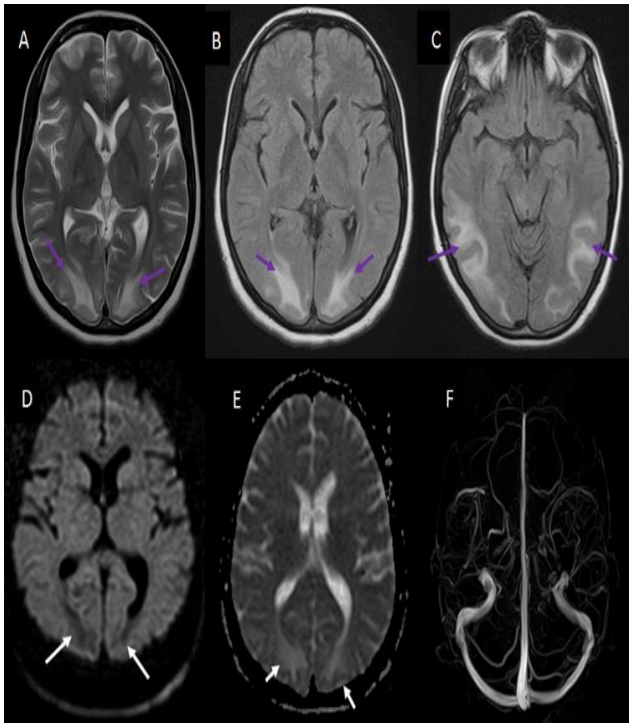

Figure 2 (A-F): A 32-year-old female presented with headache and seizure on the second day of post-cesarean delivery. MR imaging showed typical features of PRES: Axial T2W (A), axial FLAIR (B), axial FLAIR (C), axial DWI (D), axial ADC (E) and MRV (F).

Bilateral symmetrical hyperintense signals extending from bilateral occipital regions into temporal regions (purple arrows) showing no diffusion restriction (white arrows) along with normal MR venogram.

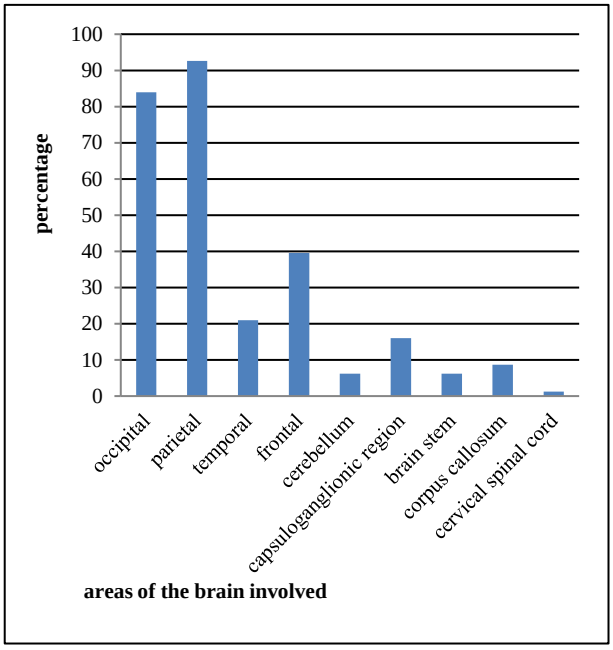

Figure 3: Frequency distribution of the areas of the brain involved in individuals diagnosed with PRES, (n=81).

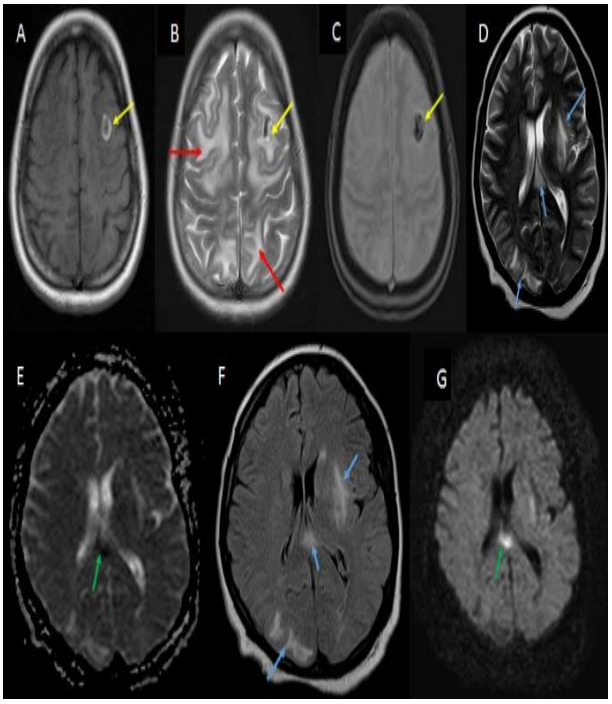

Figure 4 (A-G): (I) A 35-year-old female presented with headache and seizure on the third day of post-spontaneous vaginal delivery. MR imaging showed atypical features of PRES: Axial T1W (A), axial T2W (B) and axial T2* (C). (II) A 25-year-old female presented with headache, seizure, and visual disturbances on the second day of post spontaneous vaginal delivery. MR imaging showed atypical features of PRES: axial T2W (D), axial DWI (E), axial FLAIR (F) and axial ADC (G).

(I) showing T2 and FLAIR hyperintense signals in bilateral fronto-parietal regions (red arrows) with an internal focus of hemorrhage in the left frontal region (yellow arrows) that shows blooming artifact on T2*. (II) showing hyperintense signals in the right occipital region, left lentiform nucleus and genu of corpus callosum (blue arrows) with genu of corpus callosum showing diffusion restriction on DWI and ADC (green arrows).

DISCUSSION

In 1996, Hinchey et al was the first to describe PRES in a group of 15 patients presenting with headaches, seizures, visual disturbances, altered mental status, and focal neurological deficits.[10] Even after more than two decades, a limited amount of clinical and radiological data is available in the literature about this syndrome. It is likely due to underreporting of the cases because of misdiagnosis and lack of awareness among clinicians. However, in recent years, due to increasing awareness among clinicians and the advancement in imaging techniques, various clinical and radiological pictures of this syndrome have emerged. In this study, we discuss the risk factors, complaints, and MR imaging findings of individuals diagnosed with PRES in a tertiary care hospital, which, to the best of our knowledge, is the second study on PRES with a large sample size from Pakistan.

The majority of PRES patients are young to middle-aged individuals, with a mean age of 39-47. However, cases have been documented across all age groups, including neonates, children, and old age, underscoring its broad demographic reach.[2,11-13] There is a marked female predominance, the reason behind which remains unknown and warrants further investigation as it may establish some of the possible causes of this syndrome. The mean age in our study was 25.01±10.61, which is lower than the previous studies. This is likely due to the more HDPs associated PRES cases in our study, as seen in other HDPs associated PRES studies.[6,14] The female predominance in our study is consistent with the previous studies.

PRES is associated with multiple factors, including hypertension, HDPs [eclampsia, pre-eclampsia, and hemolysis, elevated liver enzymes and low platelets (HELLP)], renal diseases, autoimmune diseases, chemotherapeutic agents, and malignancy. Studies have reported hypertension in 20-65% of cases.[15] In our study, hypertension was present in 72 (88.89%) patients, which is higher than the previous studies. Hypertension primarily occurred in the form of HDPs. Hypertension secondary to renal diseases was present in 13 (16.05%) patients. These were mostly pediatric patients with streptococcal glomerulonephritis (SGN), nephrotic syndrome, hemolytic uremic syndrome (HUS), and chronic kidney disease (CKD). Other studies have also shown that hypertensive crises due to underlying renal disorders are the most common cause of PRES in the pediatric population.[11,16] Although hypertension was the most common risk factor in the current study, nevertheless, 9 (11.11%) patients still developed PRES in the absence of hypertension. The risk factors in these patients were autoimmune diseases, malignancy, epilepsy, and drugs. Interestingly, 1 patient in our study developed PRES following anti-tuberculosis treatment, a rare risk factor with few cases reported.[17,18]

PRES typically manifests with a constellation of neurological symptoms, seizures (74-87%) and altered mental status (28–94%) being the most common, followed by headaches (50%) and visual disturbances (39%).[2,5] The most frequent symptoms in our study were seizures (79.01%), followed by headaches (54.32%) and visual disturbances (34.57%). Altered mental status was observed in 20.99% of patients, which is lower than what has been observed in other studies. This is again likely due to the more HDPs associated PRES cases in our study. The frequency of altered mental status in HDPs associated cases was 7 (11.86%), which was significantly (p=0.002) lower than the frequency (n=10, 45.45%) observed in non-HDPs associated cases. A similar lower incidence of altered mental status was observed in HDPs associated PRES patients compared to non-HDPs associated PRES patients in a study by Liman et al.[19]

MR imaging is considered a key imaging modality for the diagnosis and characterization of PRES. It typically

shows bilaterally symmetrical cortical and subcortical hyperintense signal abnormalities on T2-weighted and FLAIR sequences. However, in rare instances, asymmetrical or unilateral involvement can occur.[20,21] In the current study, unilateral involvement was detected in 4 patients, of whom 2 had right occipital lobe, 1 had left occipital lobe, and 1 had right parieto-occipital lobe involvement. The most commonly involved areas are the occipital lobe and parietal lobe, which in the current study were present in 83.95% and 92.59% of patients, respectively. Involvement of other areas, including the frontal and temporal lobes, basal ganglia, cerebellum, brain stem, and splenium, is not uncommon.[3,6,7] However, predominant involvement of deep gray matters, including the basal ganglia, brain stem, and thalamus, with sparing of cortical and subcortical areas is uncommon and has been observed in fewer studies and case reports. [22,23] In our study, we found no such isolated central variation (PRES). Interestingly we had 1 patient with cervical spinal cord involvement, an extremely rare form of PRES termed as PRES-SCI (PRES spinal cord involvement). [24]

Diffusion restriction, which indicates the development of cytotoxic edema, was encountered in 19 (23.46%) patients. This is concordant with the studies by McKinney et al and Li et al.[25,26] Literature has shown the incidence of hemorrhage in PRES in 15-19.4% of cases.[2,27] However, in our study, hemorrhage was detected in only 7 (8.64%) patients, all of whom had intracerebral haemorrhage. This is again due to the more HDPs associated PRES cases in our study. Hefzy et al found a similar lower incidence rate (5.5%) of hemorrhage in eclampsia-associated PRES.[28] Post-contrast enhancement rate ranges from 23.1% to 43.7% in the literature.[26,29] In our study it was observed in only 2 (2.47%) patients. The reason behind this is that in most cases of PRES, given a typical imaging finding, a contrast study wasn't performed.

Our study has some limitations. Firstly, a repeat MRI to prove the reversibility of the syndrome wasn't performed in every patient whose clinical symptoms had improved. Secondly, most of the cases in our study were associated with HDPs (pre-eclampsia, eclampsia), which might not have unveiled the true face of PRES in the general population. Thirdly, contrast study wasn't performed in every patient, making the determined frequency of post-contrast enhancement unsure.

CONCLUSION

PRES presents with acute or sub-acute neurological symptoms, including seizures, headaches, altered mental status, and visual disturbances. A typical imaging finding involving symmetrical parieto-occipital lobes in the background of high blood pressure is diagnostic. However, clinicians and radiologists must be aware of the diverse clinical manifestations and multiplicity of imaging patterns, including atypical area involvement, asymmetrical involvement, restricted diffusion, hemorrhagic changes, and post-contrast enhancement, to prevent misdiagnosis.

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