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Original Research Article

A Comprehensive Study on Atypical Posterior Reversible Encephalopathy Syndrome and Its Clinicoradiological Correlation in a Tertiary Care Centre Hospital, Trichy, Tamil Nadu

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Abstract:

Introduction: Posterior Reversible Encephalopathy Syndrome (PRES) is an acute-onset clinico-radiological syndrome characterized by headache, seizures, visual disturbances, altered sensorium, and distinctive neuroimaging findings. Although classically involving the parieto-occipital regions, PRES may affect atypical brain locations such as the frontal lobes, basal ganglia, and cerebellum, brainstem, and watershed zones. Recognition of these atypical presentations is crucial, as delayed diagnosis may result in irreversible neurological injury despite the potentially reversible nature of the syndrome. This study aimed to systematically evaluate atypical presentations of PRES, focusing on etiological factors, clinical manifestations, management strategies, and patient outcomes, to improve recognition and understanding of this under-recognized variant.

Materials and Methods: A prospective observational study was conducted over 24 months at a tertiary care teaching hospital. Among 218 patients diagnosed with PRES, 37 patients (16.97%) with atypical clinical and/or MRI features were included. Patients with involvement of uncommon brain regions or non-classical radiological patterns were selected. Detailed demographic data, clinical presentation, underlying etiologies, laboratory findings, neuroimaging characteristics, treatment details, and outcomes were systematically recorded and analyzed using appropriate statistical methods.

Results: The cohort showed a significant female predominance (64.86%), with a mean age of 32.8 years (range: 19–63 years). Pregnancy-related hypertensive disorders (pre-eclampsia/eclampsia) were the most common etiological factors (35.13%), followed by hypertension (24.32%) and sepsis (13.51%). Management strategies were similar to those for typical PRES, emphasizing blood pressure control, seizure management, treatment of underlying causes, and supportive care. Clinical outcomes were favorable, with complete recovery in 94.59% of patients. Mortality was 5.40% and was related to severe underlying systemic illness rather than PRES itself.

Conclusion: Atypical PRES constitutes a significant subset of PRES cases. Despite atypical radiological patterns, prognosis remains favorable with early diagnosis and prompt management, underscoring the importance of heightened clinical awareness.

Keywords: Posterior Reversible Encephalopathy Syndrome; Atypical PRES; Magnetic Resonance Imaging; Hypertension; Pre-eclampsia; Eclampsia; Seizures; Vasogenic Edema; Neuroimaging; Clinical Outcomes.

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Introduction

Posterior reversible encephalopathy syndrome (PRES), alternatively referred to as Reversible posterior leukoencephalopathy syndrome (RPLS), represents a clinico-radiological entity that has gained increasing recognition since its initial description by Hinchey and colleagues in 1996. This syndrome is characterized by an acute onset neurological disorder that typically manifests with a distinctive constellation of clinical symptoms and radiological features. While the condition is generally considered reversible with appropriate and timely management, it is crucial to recognize that complete reversibility is not guaranteed in all cases, and some patients may experience persistent neurological deficits or progression to irreversible complications such as cerebral infarction or hemorrhage. The clinical presentation of PRES is notably diverse and may include a wide spectrum of neurological symptoms. The most commonly reported presenting features include severe

headache, often described as sudden in onset and severe in intensity, particularly affecting the occipital region. Seizures represent another frequent manifestation, ranging from focal seizures to generalized tonic-clonic seizures. Visual disturbances constitute an important presenting feature, with patients reporting blurring of vision, visual field defects, cortical blindness, or visual hallucinations. Additionally, patients may experience vestibular symptoms such as vertigo or giddiness, altered levels of consciousness ranging from confusion to coma, and in some cases, focal neurological deficits such as hemiparesis or aphasia. The variability in clinical presentation often reflects the extent and location of cerebral involvement.[1]

From a neuroanatomical perspective, PRES classically and predominantly affects the posterior regions of the cerebral hemispheres, particularly the parieto-occipital areas, which accounts for the syndrome's nomenclature. The predilection for posterior circulation territories is attributed to the relatively sparse sympathetic innervation of the vertebrobasilar circulation compared to the anterior circulation, making these regions more vulnerable to hypertension-induced endothelial dysfunction and vasogenic edema. However, accumulating clinical and radiological evidence has demonstrated that the distribution of lesions in PRES can extend well beyond these classical posterior territories. Atypical involvement may include the watershed zones located at the border between major vascular territories, the frontal lobes which may be affected in up to 30-40% of cases according to various series, the inferior temporal regions, the deep gray matter structures including the basal ganglia and thalami which show involvement in approximately 10-30% of cases, the cerebellum which demonstrates involvement in approximately 30-50% of cases, and the brainstem including the pons and medulla which may be affected in 10-30% of cases.[2] The presence of lesions in these atypical locations may significantly impact both the clinical presentation and the overall prognosis of the condition, with some studies suggesting that extensive or atypical involvement may be associated with worse outcomes.[11]

The pathophysiology of PRES remains incompletely understood, but two main theories have been proposed. The hyperperfusion theory suggests that severe hypertension exceeds the autoregulatory capacity of cerebral blood vessels, leading to breakthrough edema with disruption of the blood-brain barrier and resultant vasogenic edema. The alternative endothelial dysfunction theory proposes that various toxins, including immunosuppressive agents, cytokines in sepsis, or uremic toxins, cause direct endothelial injury leading to blood-brain barrier breakdown independent of blood pressure elevation. In reality, both mechanisms likely contribute to varying degrees depending on the underlying etiology, with hypertension playing a more prominent role in eclampsia-related PRES and endothelial dysfunction being more important in sepsis or drug-induced cases. Despite the growing recognition of PRES in the international medical literature, there remains a paucity of comprehensive studies specifically focusing on atypical presentations of this syndrome, particularly from the Indian subcontinent. Most published studies have concentrated on the classical presentation patterns with posterior-predominant involvement, and the atypical variants remain relatively under-recognized and understudied. This knowledge gap has significant clinical implications, as failure to recognize atypical presentations may lead to delayed diagnosis, inappropriate management decisions, potentially worse outcomes, and missed opportunities for prevention of irreversible complications. Furthermore, atypical presentations may be misdiagnosed as other neurological conditions such as posterior circulation stroke, viral encephalitis, demyelinating disorders, or primary CNS vasculitis, leading to unnecessary investigations and inappropriate treatments.

Given this context and the recognized need for more comprehensive data on atypical PRES presentations, the primary aim of this prospective observational study was to comprehensively evaluate the demographic characteristics, detailed clinicoradiological profile, underlying etiological factors, management approaches, and clinical outcomes of patients presenting with Atypical PRES at our tertiary care center. By systematically analyzing these atypical presentations, we aimed to enhance clinical awareness among healthcare providers, facilitate earlier and more accurate diagnosis, improve understanding of the prognostic implications of atypical involvement, and ultimately contribute to better patient outcomes through improved recognition and management of this challenging variant of PRES. Additionally, by documenting the experience from a major tertiary care center in South India, this study contributes valuable data to the growing body of literature on PRES from diverse geographic and ethnic populations.

Materials and Methods

This prospective observational study was conducted at Government KAPV Medical College and Hospital, Trichy, a tertiary care teaching hospital in Tamil Nadu, over a 24-month period from July 2022 to June 2024. The study aimed to evaluate the clinical profile, etiological factors, radiological patterns, management, and outcomes of patients with atypical Posterior Reversible Encephalopathy

Syndrome (PRES). Patients were recruited from general medicine, obstetrics, and neurology wards to ensure comprehensive case capture and minimize selection bias.

Patients were screened based on suggestive clinical features of PRES—such as headache, seizures, visual disturbances, altered sensorium, or focal neurological deficits—along with MRI findings of vasogenic edema in atypical locations (frontal lobes, anterior circulation, deep gray matter, cerebellum, brainstem, or asymmetric involvement). Classical posterior-predominant PRES cases were excluded. Of 218 PRES patients identified during the study period, 37 patients (16.97%) had atypical MRI patterns and were included for detailed analysis. Females constituted the majority both in the overall PRES cohort (61.93%) and in the atypical subgroup (64.86%).

All included patients underwent standardized evaluation comprising detailed clinical history, neurological examination, assessment of comorbidities, obstetric and medication history, and comprehensive laboratory investigations.

Neuroimaging with MRI brain using standardized sequences (T1, T2, FLAIR, DWI/ADC, GRE/SWI, and MRA/MRV when indicated) formed the diagnostic cornerstone. EEG was performed in all patients to evaluate seizures, cerebral dysfunction, and exclude non-convulsive status epilepticus.

Management focused on treating the underlying etiology with careful blood pressure control, seizure management, modification or withdrawal of offending drugs, treatment of associated systemic conditions, and supportive care. Obstetric patients received magnesium sulfate as indicated. Outcomes assessed included neurological recovery, in-hospital mortality, duration of hospital and ICU stay, complications, and recurrence. Statistical analysis used descriptive and comparative methods, with a p-value <0.05 considered significant. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all participants.

Results and Interpretation

Study Population and Demographics: During the 24-month study period (July 2022–June 2024), 218 patients were diagnosed with Posterior Re-versible Encephalopathy Syndrome (PRES) across general medicine, obstetrics, and neurology departments. Of these, 37 patients (16.97%) demonstrated atypical clinicoradiological features and were included for detailed analysis, a proportion consistent with published literature (15–20%). A significant female predominance was observed in the atypical PRES cohort, with 24 females (64.86%) and 13 males (35.14%), yielding a female-to-male ratio of 1.85:1. This distribution parallels that reported in typi-cal PRES and is largely attributable to pregnancy-related hypertensive disorders and autoimmune conditions. The mean age at presentation was 32.8 years (range: 19–63 years). Younger age predominance was noted, mainly due to the high number of obstetric cases, highlighting the socioeconomic impact of PRES affecting individuals in their productive years.

Table 1: Demographic Distribution of Study Population

Category	Males	Females
Total PRES patients admitted (n=218)	83 (38.07%)	135 (61.93%)
Atypical PRES patients (n=37)	13 (35.14%)	24 (64.86%)
Proportion of atypical PRES	37/218 (16.97%)	

Clinical Presentation: Atypical PRES exhibited heterogeneous clinical manifestations. Headache was the most frequent presenting symptom, reported in 16 patients (43.24%), followed by seizures in 7 patients (18.91%), and predominantly generalized tonic–clonic seizures. Visual disturbances and altered sensorium were each observed in 4 patients (10.8%), while vomiting occurred in 3 patients (8.1%). Focal neurological deficits were uncommon; hemiparesis was noted in one pa-tient (2.7%). Rare presentations included dysarthria and neck pain. The variability in symptoms correlated with involvement of atypical brain regions.

Table 2: Initial Clinical Presentation of Atypical PRES

Symptoms	Total & Percentage	Male	Female
Headache	16 (43.24%)	5 (13.51%)	11 (29.72%)
Seizures	7 (18.91%)	2 (5.40%)	5 (13.51%)
Altered sensorium	4 (10.8%)	2 (5.40%)	2 (5.40%)
Visual impairment	4 (10.8%)	2 (5.40%)	2 (5.40%)
Vomiting	3 (8.1%)	1 (2.7%)	2 (5.40%)
Hemiparesis	1 (2.7%)	1 (2.7%)	0
Others (dysarthria, neck pain)	2 (5.40%)	0	2 (5.40%)

Etiological Factors: The most common etiological factor was pregnancy-related hypertension (pre-eclampsia/eclampsia), ac-counting for 13 cases (35.13%), all in females. Hypertension (chronic or emergency) was the most frequent non-obstetric cause (9 cases; 24.32%). Other identified causes included sepsis (13.51%), autoimmune dis-orders (8.1%), chemotherapeutic drugs (8.1%), chronic kidney disease (5.40%), and rare causes such as carotid stenting and high-altitude exposure.

Table 3: Underlying Etiological Causes of Atypical PRES

Etiology	Total & Percentage	Male	Female
Pre-eclampsia / Eclampsia	13 (35.13%)	0	13 (35.13%)
Hypertension	9 (24.32%)	5 (13.51%)	4 (10.8%)
Sepsis	5 (13.51%)	3 (8.1%)	2 (5.40%)
Autoimmune disorders	3 (8.1%)	1 (2.7%)	2 (5.40%)
Chemotherapeutic drugs	3 (8.1%)	2 (5.40%)	1 (2.7%)
Chronic kidney disease	2 (5.40%)	1 (2.7%)	1 (2.7%)
Recent carotid stenting	1 (2.7%)	1 (2.7%)	0
High altitude exposure	1 (2.7%)	0	1 (2.7%)

Clinical Outcomes: Clinical outcomes were predominantly favorable**.** Complete neurological recovery was observed in 35 patients (94.59%)**.** Two patients (5.40%) died due to severe underlying systemic illness (sepsis with cardiac failure and advanced chronic kidney disease), rather than direct neurological complications of PRES.

Table 4: Clinical Outcomes

Outcome	Total & Percentage	Male	Female
Recovery	35 (94.59%)	11 (84.61%)	24 (100%)
Death	2 (5.40%)	2 (15.38%)	0

Imaging Findings

MRI confirmed the diagnosis in all patients. Typical PRES signal characteristics were observed, with T2/FLAIR hyperintensities representing vasogenic edema and facilitated diffusion on DWI/ADC.

Among atypical patterns, cerebellar involvement was most common (35.29%), followed by thalamic (21.62%) and brainstem (18.91%) involvement. Frontal lobes, basal ganglia, and anterior circulation territories were less frequently affected. These imaging patterns align with previously reported atypical PRES distributions.

Discussion

Posterior Reversible Encephalopathy Syndrome (PRES) was first described comprehensively by Hinchey and colleagues in 1996, though cases fitting this description had been reported in medical literature prior to this landmark publication. Since its initial description, PRES has gained increasing recognition as an important clinico-radiological syndrome that can complicate a diverse array of underlying medical conditions. The syndrome is characterized by a constellation of neurological symptoms including headache, seizures, visual disturbances, and altered mental status, in combination with distinctive neuroimaging findings showing vasogenic edema predominantly affecting the posterior circulation territories. While the condition has traditionally been described as affecting primarily the posterior regions of the brain, accumulating evidence over the past two decades has demonstrated that PRES can involve various other brain regions, leading to the recognition of atypical PRES presentations.[1,3] The present study adds to the growing body of literature on atypical PRES by providing comprehensive data from a tertiary care center in South India, representing one of the few studies specifically focused on atypical presentations from the Indian subcontinent. Our findings demonstrate that atypical PRES, while less common than typical presentations, represents a significant proportion (16.97%) of all PRES cases. The demographic characteristics of our atypical PRES cohort, including female predominance and mean age in the fourth decade, are consistent with previously reported series of both typical and atypical PRES.[4,5,6]

The etiological spectrum observed in our study reflects both universal risk factors for PRES and region-specific patterns related to the patient population characteristics. In the present series, the most common etiologies were eclampsia/pre-eclampsia (35.13%) and hypertension (24.32%). In a recently published series from India by Goyal and Jeswani, the commonest cause of PRES was also eclampsia (36.4%), with chronic kidney disease and hypertension each accounting for 22.7% of cases.[10] Similar results have been reported in other studies from different geographic regions, though with some variations in the relative frequencies.[3]

The predominance of eclampsia/pre-eclampsia in our series is likely related to the demographic characteristics of our catchment population and the

substantial obstetric referrals to our institution. The high burden of pregnancy-related PRES in India and other developing countries may reflect factors including inadequate antenatal care in some populations, late presentation to medical facilities, and high prevalence of risk factors such as hypertension.[7,8]

The atypical imaging findings in our cohort, with cerebellar involvement in 35.29%, thalamic involvement in 21.62%, and brainstem involvement in 18.91%, are consistent with patterns reported in the literature on atypical PRES. Several mechanisms may explain the involvement of these atypical locations. The cerebellum, despite being part of the posterior fossa, has relatively sparse sympathetic innervation similar to the posterior cerebral hemispheres, making it vulnerable to the same pathophysiological processes. Thalamic and basal ganglia involvement may result from watershed vulnerability at the border zones between deep and superficial perforating arteries. Brainstem involvement, while less common, may occur through similar mechanisms and is often associated with more severe presentations.[1,2,9]

The outcome of PRES is primarily determined by the underlying etiology, the promptness of diagnosis and treatment initiation, and the presence of complications such as hemorrhage or ischemic injury. Death has been reported in 15-19% of PRES cases in various studies.[10] In a retrospective study by Hinduja and colleagues, 36% of 100 PRES patients had poor neurological outcome at the time of hospital discharge, defined as modified Rankin Scale score between 2 and 6.[11] Singer and colleagues reported a 19% mortality rate in their cohort of cancer patients with PRES.[17] In our series, the mortality rate was 5.40%, which is lower than many reported series. This favorable outcome may be attributed to several factors including the high proportion of eclampsia cases which generally have good prognosis with appropriate management, prompt diagnosis facilitated by increased clinical awareness, aggressive management in critical care settings, and the relatively young age of our patient population. The two deaths in our series occurred in patients with severe underlying conditions (sepsis with cardiac failure and advanced CKD), emphasizing that outcomes are heavily influenced by the severity of the underlying disease process.

An important finding of our study is that the presence of atypical radiological features does not appear to significantly worsen the prognosis compared to typical PRES, provided that diagnosis is established early and appropriate management is initiated promptly. The overall recovery rate of 94.59% in our atypical PRES cohort is comparable to or better than recovery rates reported for typical PRES in many series. This suggests that with heightened clinical suspicion and awareness of atypical presentations, outcomes can be optimized even when the radiological distribution deviates from classical patterns.

Conclusion

Atypical Posterior Reversible Encephalopathy Syndrome represents an under-recognized yet clinically significant variant of PRES that requires heightened clinical awareness for timely diagnosis and optimal management. Our current study emphasizes the critical importance of recognizing atypical PRES early through strong clinical suspicion combined with careful evaluation of MRI findings demonstrating vasogenic edema in atypical brain regions including the cerebellum, thalamus, brainstem, frontal lobes, and other non-posterior locations.

The fundamental principle underlying the management of PRES is that the condition can be reversed promptly if recognized early and appropriate interventions are initiated without delay. Therefore, identifying and understanding uncommon presentations of PRES, such as those with atypical radiological distributions, is of paramount importance for clinicians across multiple specialties including neurology, critical care medicine, obstetrics, nephrology, and oncology. The clinical outcome in atypical PRES is generally favorable and does not differ significantly from typical PRES presentations, with our study demonstrating a 94.59% recovery rate. Importantly, no significant increase in morbidity or mortality was noted in atypical PRES cases when diagnosis is established early and management is initiated promptly.

The management approach for atypical PRES does not differ substantially from that of typical PRES and is mainly focused on identifying and treating the underlying or predisposing factors.

This includes aggressive blood pressure control in hypertensive cases, delivery and magnesium sulfate therapy in eclampsia cases, treatment of sepsis with appropriate antimicrobials, discontinuation of offending medications in drug-induced cases, management of renal dysfunction, and immunosuppressive therapy modification in autoimmune conditions. Clinical improvement may be noted within a period of 2-3 weeks in most cases, though patients with severe underlying conditions such as advanced chronic kidney disease or severe sepsis may require prolonged intensive care and have more guarded prognoses.

In conclusion, strong clinical suspicion for PRES even in the presence of atypical clinical features, combined with early and comprehensive MRI brain imaging to identify lesions in uncommon brain regions, are the key factors in successfully

identifying this uncommon but important presentation of PRES. Increased awareness among clinicians regarding the diverse clinical presentations and radiological patterns of PRES, including atypical variants, is essential for reducing diagnostic delays, preventing misdiagnosis, and ultimately improving patient outcomes through timely and appropriate therapeutic interventions.[14,15,16]

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