

Clinico-radiological Profile of Posterior Reversible Encephalopathy Syndrome and Its Associated Risk Factors in PICU: A Single-center Experience from a Tertiary Care Hospital in Bhubaneswar, Odisha

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ABSTRACT

Objective: Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiographic entity of heterogeneous etiologies having similar clinical and neuroimaging features. Pediatric data are sparse, making early diagnosis challenging, which needs a high index of suspicion. So, we conducted this study to evaluate clinico-radiological features, associated risk factors, etiology, and outcome in children.

Materials and methods: This is a retrospective case series of patients, diagnosed as having PRES and followed up at a tertiary care hospital in Eastern India between September 2016 and December 2019.

Results: Among 16 patients with a median age of 9.5 years [interquartile range (IQR) 8–13.75] and a male preponderance (75%), common underlying diseases were post-streptococcal glomerulonephritis (56.3%) and renovascular hypertension (12.5%). Acute elevation of blood pressure was found in all patients ($n = 16$). The neurological symptom was seizure (87.5%), mental changes (68.75%), headache (43.8%), vomiting (31.3%), and visual disturbances (31.3%). The most common triggering factor was hypertension (100%), use of mycophenolate mofetil and prednisolone (12.5%), and hemodialysis (12.5%). Anemia was present in 15 (93.4%) patients at the time of admission. All showed abnormal neuroimaging with 55% having atypical involvement. The most common site was the parietal-occipital cortex (88%), frontal and temporal lobe (44% cases each), and the cerebellum (13%). Clinical recovery was followed by a radiological resolution in all survived except in one, who developed visual impairment.

Conclusion: Posterior reversible encephalopathy syndrome should be considered in the differential diagnosis of patients who present with acute neurological disturbances and underlying diseases such as renal disorders, vasculitis, malignancy, and use of immunosuppressant accompanied by hypertension. Early diagnosis and treatment of comorbid conditions are of paramount importance for the early reversal of the syndrome.

Keywords: Children, Hypertension, Neuroimaging, Posterior reversible encephalopathy syndrome.

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INTRODUCTION

The posterior reversible encephalopathy (PRES) was first reported in 1996 as an acute and reversible clinico-radiological condition characterized by vasogenic edema predominantly seen over the posterior part of the cerebral cortex.¹ Majority of PRES patients present with seizures, headaches, and mental changes. Visual impairment with or without focal neurological deficit may also occur. It is a clinico-radiographic syndrome of various etiologies, considered together due to similar neuroimaging findings and identical clinical scenarios. Though the majority of patients belong to the middle-aged age group (mean: 39–47 years) with female predominance, the mean age of presentation from multiple pediatric series with different etiology was found to be 11.6 years without any gender difference.² It has been increasingly reported in various childhood disorders like hypertensive emergencies, renal disorder, sepsis, lupus nephritis, sickle cell anemia disease, primary immunodeficiency, use of cytotoxic medications, and organ transplantation. Hypertension and renal diseases contribute to PRES in the majority of cases.³

There are two competing theories regarding the pathogenesis of PRES both of which disrupt the blood-brain barrier and fluid leakage into cerebral parenchyma, which need mention. According to the first hypothesis there occurs failure of cerebral autoregulation which is due to elevated or fluctuating blood pressure, causing fluid

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leakage from a blood vessel and vasogenic edema in addition to endothelial dysfunction. The second mechanism can be explained by the “toxic theory” where circulating toxins, pro-inflammatory

cytokines, and various drugs cause endothelial dysfunction leading to vasoconstriction of microvasculature, hypoperfusion, and edema formation, which is seen in 15 to 20% of patients with PRES.^{4,5} Preferential involvement of the posterior part of the cerebral cortex than the anterior part is due to poor innervation of the sympathetic nervous system.⁶ Diagnosis of PRES involves assessment of neurological symptoms in appropriate clinical settings and evaluation of brain imaging features by computed tomography (CT) scan and magnetic resonance imaging (MRI). Though the global incidence varies between 0.4 and 0.7%, pediatric studies are limited in Indian PICU.^{7,8} As there is a paucity of data in children with PRES and varied presentation as compared to adults. Therefore, the objective of this study to explore the clinical presentations, neuroimaging features, and risk factors of PRES in critically ill children.

MATERIALS AND METHODS

Medical records of PICU patients admitted from September 2016 to December 2019 were analyzed. The demographic profile and clinical data were collected using a predefined format following approval of the institutional research board.

The cases meeting the following three criteria⁹ as evaluated by a group of experts consisting of one neurologist, one neuroradiologist, and one pediatrician, were identified as PRES. 1. Presence of acute neurological manifestation in the form of headache, seizure, mental changes, visual disturbance, and/or focal neurological deficit. 2. Brain MRI showing fluid-attenuated inversion recovery (FLAIR) hyperintensities in B/L parietal-temporal-occipital area with relevant apparent diffusion coefficient (ADC) suggestive of vasogenic edema as detailed in methodology. 3. Reversibility of neurological changes as per clinical or neuroimaging assessment.

Data such as clinical presentations, underlying diseases, systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the time of onset of PRES, recent medication history, CT and MRI of the brain within 48 hours of the onset of encephalopathy and at follow-up, fundoscopic results, duration of neurological abnormality, length of PICU stay, and their outcome were collected. Hypertension was defined as elevated SBP \geq 95th centile and/or DBP \geq 95th centile for relevant age and sex categories.¹⁰ Brain MRI was performed in 1.5-T MRI system, GE Signa; GE Healthcare, Fairfield, CT, USA using T2W (T2-weighted), FLAIR T1W (T1-weighted) with or without gadolinium enhancement, diffusion-weighted imaging (DWI), ADC, and susceptible-weighted angiography (SWAN) technique. The neuroradiological changes were grouped into typical and atypical findings. Changes in subcortical white matter with T2W or FLAIR hyperintensity and FLAIR with no diffusion restriction in the posterior temporal-parietal-occipital regions were considered as typical findings. Significant involvement of frontal lobe, brainstem, basal ganglion, corpus callosum, cerebellum, and presence of hemorrhage, restricted diffusion were considered as atypical findings.¹¹⁻¹³ The patients were managed as per PICU protocol.

All the univariate and bivariate analysis was carried out using Statistical Package for Social Sciences (SPSS) version 23. Continuous data were described using measures of central tendency and dispersion. Categorical data were described using percentages. A two-tailed p value <0.05 was considered significant statistically.

RESULTS

One thousand nine hundred and twenty-five patients were admitted to the PICU during the study period, out of which 16 patients (male-75%) had PRES, making the annual burden of 0.25% among all PICU admissions. The mean age of PRES patients was 10.19 ± 3.79 years.

Table 1 summarizes demographic along with clinical data of identified PRES patients. The majority of patients had suffered from post-streptococcal glomerulonephritis (PSGN) (56.3%), followed by renovascular hypertension (12.5%). Among other causes of PRES, sepsis with acute kidney injury (AKI), nephrotic syndrome, pheochromocytoma, hypophosphatemic rickets, and atypical hemolytic uremic syndrome (aHUS) was found in one case each. All patients were presented with hypertension at the time of onset of PRES. Mean SBP, mean DBP, and mean arterial pressure (MAP) at the time of onset of PRES were 162.75 ± 23 , 108.88 ± 16.15 , and 127 ± 16 mm Hg, respectively.

Neurological symptoms were seen in all the patients. The commonest neurological symptom was seizure (generalized tonic-clonic-75%, partial-12.5%), mental changes (68.75%), headache (43.8%), vomiting (31.3%), and visual disturbances (31.3%) (Fig. 1). Out of five patients having visual disturbances, one had cortical blindness and another one had stage-2 retinopathy. The common triggering factors were hypertension (100%), use of mycophenolate mofetil and prednisolone (12.5%), hemodialysis (12.5%), and sepsis (6.25%). At the time of admission to PICU, anemia was present in all patients with PRES except one (Fig. 1), with median hemoglobin (Hb) level of 9.8 [inter quartile range (IQR): 1.72, range: 6.37-10.9] g/dL. Only one patient with aHUS received a blood transfusion before admission. Azotemia was found in seven (43.8%) patients and the majority of them had PSGN or Sepsis. Two patients (one aHUS and one nephrotic syndrome) received corticosteroids and mycophenolate mofetil during treatment.

Computed tomography scan of the brain was done in 13 patients, out of which 92.3% had evidence of hypodense lesions, corresponding to areas of enhanced T2 and FLAIR signal on MRI of the brain (Fig. 2). All patients had abnormal MRI changes in the brain. Table 2 summarizes the radiological changes seen in brain MRI. The typical abnormality of T1 hypointense and T2/FLAIR hyperintense signal was noticed in all cases (100%), followed by hemorrhage in 12.5%, focal area of diffusion restriction on DWI with ADC in 33% (4/12), one patient had infarct in the cerebellar hemisphere. The most common site of lesion in the brain was bilateral parietal-occipital cortex (88%), followed by frontal (44%) lobe, temporal (44%) lobe, cerebellum (13%), corpus callosum (6%), and superior frontal sulcus (6%) (Fig. 3). These radiological changes were asymmetric in three cases and contrast enhancement was seen in one patient.

All patients were managed medically with antiedema measures (3% normal saline or mannitol), anticonvulsants, and antihypertensive drugs along with treatment of primary diseases. Antiepileptic drugs were used in 87.5% of cases (Table 1). Except for one, all patients (93.75%) responded to medical management resulting in the restoration of baseline mental status and nil neurological deficit at the time of discharge.

The median PICU stay was 5.5 days. There was a good correlation between maximum SBP at the onset of PRES and duration of PICU stay ($r = 0.611$). Only one patient (6.25%) with

Table 1: Summary of demographic and clinical data of PRES patients ($n = 16$)

<i>Variable</i>	<i>Observed value</i>
Age (in years)	
Mean (SD)	10.19 (3.79) (range: 4–17)
Median	9.5 (IQR: 6)
Sex	
Male, n (%)	12 (75)
Female, n (%)	4 (25)
Vitals	
Systolic blood pressure (mm Hg), mean (SD)	162.75 (23.07)
Diastolic blood pressure (mm Hg), mean (SD)	108.88 (16.15)
Mean arterial pressure (mm Hg), mean (SD)	126.83 (15.82)
Stage 1 hypertension, n (%)	2 (12.5)
Stage 2 hypertension, n (%)	14 (87.5)
Underlying conditions	
Post-streptococcal glomerulonephritis, n (%)	9 (56.3)
Renovascular hypertension, n (%)	2 (12.5)
Atypical hemolytic uremic syndrome (aHUS), n (%)	1 (6.3)
Hypophosphatemic rickets, n (%)	1 (6.3)
Nephrotic syndrome, n (%)	1 (6.3)
Pheochromocytoma, n (%)	1 (6.3)
Sepsis with acute kidney injury, n (%)	16 (100)
Precipitating factors	
Hypertension, n (%)	2 (12.5)
Immunosuppressive agents, n (%)	2 (12.5)
Hemodialysis, n (%)	7 (43.75)
Azotemia, n (%)	12 (92.3)
Initial neuroimaging	16 (100)
Abnormal CT (hypodense), n (%) ^a	8 (50)
Abnormal MRI, n (%)	5.5
Atypical MRI, n (%) ^b	
Median duration of PICU stay (days)	
Treatment for PRES	
Antihypertensive drugs $n = 16$ (100%)	2 (12.5)
Single drug, n (%)	4 (25.0)
Two drugs, n (%)	4 (25.0)
Three drugs, n (%)	5 (31.3)
Four drugs, n (%)	1 (6.3)
Six drugs, n (%)	
Antiepileptic drugs ($n = 14$)	2 (12.5)
Single drug, n (%)	7 (43.8)
Two drugs, n (%)	5 (31.3)
Three drugs, n (%)	
Recovery on MRI ^c	
Follow up at 2 weeks (partial resolution), n (%)	4 (100)
Follow up at ≥ 3 weeks complete resolution, n (%)	10 (100)
Disease outcome	
Recovery, n (%)	14 (87.5)
Recovery with visual impairment, n (%)	1 (6.25)
Death, n (%)	1 (6.25)

CT, computed tomography; MRI, magnetic resonance imaging

^aCT of three patients not done^bInvolvement of the brain other than parietal, occipital, and temporal lobes^cOne did not do the MRI and one died

PSGN and multiorgan failure died. A follow-up MRI brain could be performed in 14 patients, out of which 4 showed partial resolution at 2 weeks and the other 10 showed complete resolution at ≥ 3 weeks (f/u range 3–18 weeks). Median imaging follow-up duration was 6 weeks (IQR: 1 week). All had normal neurological status on follow-up examination, except one who had persistent visual impairment due to B/L occipital atrophy (Table 2). The underlying diseases did not influence the duration of radiologic or symptomatic resolution.

DISCUSSION

Posterior reversible encephalopathy syndrome is a clinico-radiological syndrome presenting with headache, seizure, visual

disturbances, and altered mentation. Though hypertension is typically present at the onset of PRES, normal blood pressure has been reported.¹⁴ Considering the non-reversible nature of illness at times, the involvement of both white and gray matter beyond the posterior part of the brain makes the terminology “posterior reversible encephalopathy syndrome” a misnomer.¹⁵ Magnetic resonance imaging changes are not always restricted to the posterior hemisphere and sometimes in addition to or in isolation involve the frontal lobe, cerebellar hemisphere, basal ganglion, and brainstem.^{1,16} Similarly, it is not always reversible as evident by a persistent neurological deficit on long-term follow-up and in severe form can cause death.^{15,17,18}

The annual incidence of PRES in our study is 0.25% is slightly higher than other studies.^{7,8} Three-fourth of PRES patients are male in our study similar to a South Korean study.¹⁹ The usual clinical manifestation of PRES is headache, seizure, mental changes, nausea and vomiting, cortical blindness, and focal neurological deficit. Though seizure usually seen at the onset of neurologic symptoms, may develop later on and sometimes may be absent. Earlier it was believed that PRES is resulting from hypertension, renal disease, or immunosuppressive therapy, but its reporting in other clinical conditions, like eclampsia, HUS, nephrotic syndrome, pheochromocytoma, chemotherapy, vasculitis, intravenous globulin therapy, etc., has challenged the researchers.^{19–21} In this study, PSGN, renovascular hypertension, aHUS, nephrotic syndrome, hypophosphatemic rickets, and sepsis with AKI are associated with the development of PRES. Interestingly, one patient was diagnosed with intra-abdominal pheochromocytoma that has been reported earlier.²⁰ Dhakshayani et al. reported 14 children from South India, who presented with seizures (59%), headache (47%), altered sensorium (29%), vomiting (24%), and visual disturbances (12%).²²

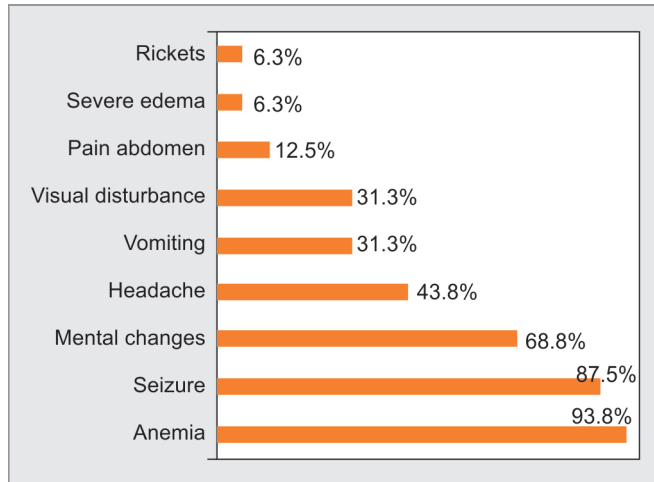
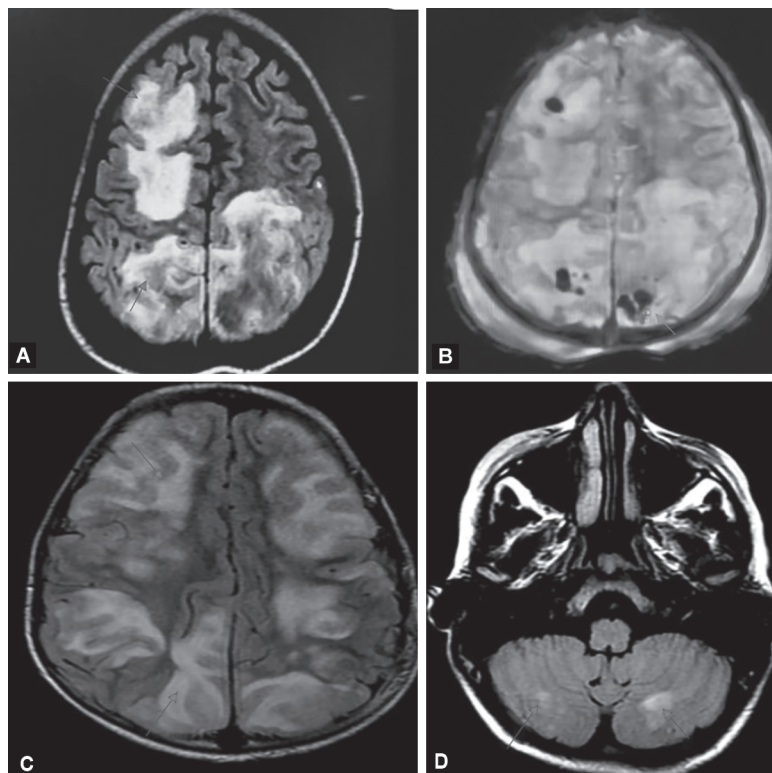


Fig. 1: Distribution of sign and symptoms among PRES patients

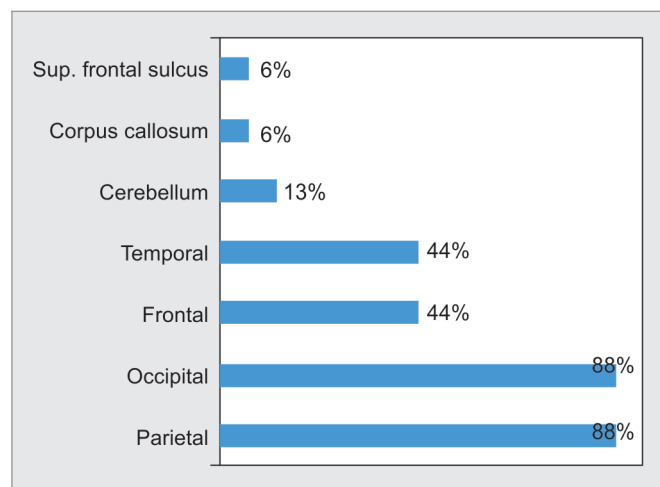


Figs 2A to D: (A) MRI of brain showing FLAIR high signal intensity over right frontal and bilateral parietal lobe in a 3-year-old female with sepsis and AKI; (B) Multiple foci of blooming (arrow) suggestive of hemorrhage on SWAN sequence of the same patient; (C and D) Axial FLAIR images showing hyperintensity in bilateral fronto-parietal-occipital lobes and in posterior inferior cerebellar hemispheres (red arrow)

Table 2: Neurological imaging and outcome in PRES patients

Case no.	Underlying disease	Brain CT	Initial MRI (typical)	Initial MRI (atypical)	Encephalopathy (yes/no)	PICU stay (days)	F/U MRI (in weeks)	Outcome
1	PSGN	Hypodense	Prt, Occ	Frt	Yes	3	Partial (2)	Recovery
2	PSGN	Hypodense	Tmp, Occ	Frt	Yes	3	Partial (2)	Recovery
3	NS	Hypodense	Tmp, Occ	Frt	Yes	10	Partial (2)	Visual impairment
4	aHUS	Not done	Prt, Occ	None	No	25	Total (12)	Recovery
5	PSGN	Hypodense	Prt, Occ	None	Yes	3	Total (6)	Recovery
6	PSGN	Normal	Prt, Occ	ADC (r)	No	9	Total (3)	Recovery
7	PSGN	Hypodense	Prt, Occ, Tmp	Frt (h) and ADC (r)	Yes	4	Total (12)	Recovery
8	RV-HPT	Not done	Prt, Occ	None	Yes	47	Total (6)	Recovery
9	PSGN	Hypodense	Prt, Occ	None	No	4	Total (18)	Recovery
10	RAS(lt)	Hypodense	Prt	None	No	7	Partial (2)	Recovery
11	PSGN	Hypodense	Prt, Occ, Tmp	None	Yes	10	Total (10)	Recovery
12	PSGN	Hypodense	Prt, Occ	None	No	5	Total (4)	Recovery
13	Sepsis + AKI	Hypodense	Prt	Frt with ADC (r)	Yes	15	Not done	Recovery
14	PCC	Hypodense	Prt, Occ, Tmp	Frt, CC	No	3	Total (12)	Recovery
15	h-Rickets	Hypodense	Prt, Occ, Tmp	Frt, Cbl	No	6	Total (6)	Recovery
16	PSGN+ AKI+MODS	Not done	Prt, Occ, Tmp	Frt, Cbl (i) Occ (h), ADC (r)	Yes	5	NA	Death

NS, nephrotic syndrome; PSGN, post-streptococcal glomerulonephritis; aHUS, atypical hemolytic uremic syndrome; RV-HPT, renovascular hypertension; RAS(lt), renal artery stenosis (left); AKI, acute kidney injury; MODS, multiorgan dysfunction syndrome; Prt, parietal; Occ, occipital; Tmp, temporal; Frt, frontal, CC, corpus callosum; Cbl, cerebellum; ADC(r), apparent diffusion coefficient (restriction); h-Rickets, hypophosphatemic rickets, PCC, pheochromocytoma; Cbl(i), cerebellum infarction; Occ(h), occipital hemorrhage

**Fig. 3:** Brain involvement as per MRI scan of PRES patients

The common presenting symptoms in this study patient are seizure (87.5%), altered sensorium (68.75%), headache (43.8%), vomiting (31.3%), visual disturbance (31.3%), and abdominal pain (12.5%), which is different from previous studies.^{21,23}

There are multiple risk factors for PRES such as hypertension, anemia, immunosuppressive agents, renal dysfunction, infection/sepsis, eclampsia, dialysis, and dyselectrolytemia, which have been identified in the literature.^{8,24,25} Chen et al. in a systematic review found hypertension in 58 to 100% of patients with PRES.^{19,21} All patients in this study had hypertension at the time of presentation of illness, unlike one adult study where the author found normal blood pressure in 40% of their sepsis patients associated with PRES.¹² But one study from India found 82% of their children are hypertensive.²² In this study, one patient with sepsis subsequently developed hypertension due to AKI and hyperreninemia.

Renal failure associated with PRES was found in up to 55% of cases.⁶ But its role in PRES as an independent risk factor is still unknown. In this case series, azotemia was observed in 43.8% of the PICU population, all have primary renal disorders. Posterior reversible encephalopathy syndrome is frequently observed in patients with sepsis or during treatment with immunosuppressive or cytotoxic medication, which causes endothelial dysfunction contributing to raised blood pressure and release of inflammatory cytokines, resulting in vascular permeability and edema.^{4,26} In this study, two patients received oral steroid and mycophenolate mofetil (aHUS and nephrotic syndrome), which has been reported in lupus nephritis patients before.¹⁷ In a series of 14 patients in Taiwan, Chen et al. have found two of their patients had undergone hemodialysis before the onset of PRES, which is similar to this study finding.²¹

Although anemia has been rarely reported to be associated with PRES, 93.75% of patients in this study had chronic nutritional anemia similar to one small case series, where the author had observed mild to moderate degree of anemia in all of their patients at the time of admission to PICU except one having sickle cell disease and ulcerative colitis who received a blood transfusion before the onset of PRES, but recovered completely after exchange transfusion.⁸ None of our patients had received a blood transfusion. Despite the absence of a plausible explanation for a cause-effect, authors have proposed anemia induced hypoxic and non-hypoxic cerebral vascular injury may have significance to PRES, where the inducible nitric oxide synthase plays a major role by amplifying the effect of shear stress due to hemodilution, resulting in vasogenic edema, which was seen in an animal model.²⁷ We have not investigated to know the association of anemia and PRES in our study due to the high incidence of anemia in our locality. In a study by Behera and Bulliyya in our locality, the prevalence of anemia was found to be 62%.²⁸

The typical MRI findings in PRES is cerebral edema involving the subcortical white matter of the B/L parieto-occipital region. In this study, many atypical findings such as hemorrhage, infarction, cortical lesions, significant anterior involvement, and asymmetry have been found (Fig. 2). T2-weighted high signal intensity image can occur in other regions involving the frontal lobe, basal ganglion, cerebellum, corpus callosum, thalamus, and brain stem.²¹ In this study, frontal lobe involvement is common among the atypical presentations, which is consistent with other studies.²³ An acute severe hypertension-induced brain hemorrhage can occur as a complication in PRES patients even without any coagulopathy, which is also reported in 12.5% of patients in this study.²³ Diffusion-weighted MRI is more commonly preferred in the diagnosis of PRES due to its higher specificity and sensitivity and in addition, it can easily differentiate between vasogenic edema and cytotoxic edema in PRES patients, which can be used to monitor the development of ischemia in PRES patients.¹⁸ Therefore, patient outcome correlates well with the findings of both T2W and DWI MRI changes in the brain.²⁹ Non-reversibility of the PRES changes is signaled by high DWI signal intensity along with normal or low ADC values, indicating underlying cerebral infarction. One-fourth of our patients showed focal restricted diffusion on MRI, only one developed infarction. Contrast enhancement in T2W abnormality areas is not a typical finding in PRES, which is seen in only one of our patients.¹⁸ In this case series, there is no correlation between the distribution of specific imaging findings in the brain and the underlying clinical conditions (typical MRI: PSGN 4, aHUS 1, renovascular 2 atypical MRI: PSGN 4, AKI 2, NS 1, rickets 1, pheochromocytoma 1) as well as stages of hypertension similar to previous studies.^{20,30}

It is not clear when to advise for repeat MRI of the brain to record neuroradiological recovery. In this study, all of our patients were advised for the periodical follow-up. All seven patients with typical initial MRI findings and 7/9 (80%) patients with atypical MRI brain recovered well clinically with a resolution of signs and symptoms within 48 to 72 hours of treatment. But out of two patients with initial atypical brain MRI, one on follow-up had visual impairment (2 weeks) and another died due to multiorgan failure. As there was no uniformity in follow-up in our study, it is difficult to establish a correlation between atypical MRI changes in the brain and time for radiological resolution. Among four patients (one typical and three atypical), who showed incomplete resolution at 2 weeks, further serial imaging was not possible due to financial issues. In a series by Lee et al., out of 38 patients they studied, 4 patients showing incomplete resolution at 3 to 7 days, took weeks to years for complete resolution.¹¹

Posterior reversible encephalopathy syndrome should be treated efficiently to avoid permanent brain damage.¹¹ There is no specific treatment, but supportive treatment is the mainstay of therapy which includes control of raised intracranial pressure, hypertension, and seizure, discontinuation of offending drugs, and treatment of primary disease. No randomized control trial has been undertaken to assess the therapeutic intervention.⁶ All the patients in this study received antihypertensive drugs as in other studies.²¹ Despite the absence of any consensus guideline regarding the long-term use of antiepileptic drugs for seizure after PRES, Legriël et al. in their study recommended it for 3 to 6 months for uncomplicated cases within occasional cases for at least 12 months for patients having a recurrent seizure and abnormal electroencephalography (EEG) on follow-up.³¹

Though most of the patients in PRES recover, the mortality was about 3 to 6% in a series, which followed patients for about 1 to 3 months, similar to this study where only one patient (6.5%) died during treatment due to malignant PRES and multiorgan failure.^{30,31}

LIMITATION

The retrospective study design and a small number of cases limited this study to evaluate all possible risk factors associated with PRES. So, a multicentric prospective study for the active surveillance of various risk factors associated with PRES is highly warranted in the future. This PICU-based study may not be comparable to PRES in general pediatric populations. There was non-uniformity in follow-up of patients as far as time duration from discharge is concerned, which may affect the comparison of neuroradiological findings from patient to patient. But we believe this study is the largest cohort of study in the pediatric intensive unit in Eastern India to the best of our knowledge.

CONCLUSION

The study highlights that PRES is being recognized more frequently in children than before. Other than hypertension and renal disorders which are the most common risk factors, the role of anemia in PRES needs further evaluation in a large multicentric prospective study. Atypical imaging pattern is not uncommon, which sometimes makes it difficult in excluding PRES. Complete recovery from this illness is not always anticipated and hence early diagnosis and prompt treatment are highly desirable in an appropriate clinical setting to prevent morbidity and mortality.

CLINICAL SIGNIFICANCE

Early suspicion, diagnosis, and management of PRES are crucial for better outcomes for patients. Although blood transfusion is a known risk factor in anemic children with hemoglobinopathy, the majority of our patients had associated nutritional anemia.

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