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Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.ijogr.org

Original Research Article

A prospective observational study on posterior reversible encephalopathy syndrome in COVID-19 eclampsia patients in tertiary care hospital

Saikam Bhargavi[1,*], **V Janaki**[1]

[1]*Dept. of Obstetrics & Gynaecology, Gandhi Medical College, KNRUHS, Secunderabad, Telangana, India*

ARTICLE INFO

Article history:
Received 02-12-2021
Accepted 10-01-2022
Available online 20-05-2022

Keywords:
PRES
Eclampsia
COVID- 19

ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with neurological symptoms in one third of COVID-19 patients which is attributed to its hypercoagulable state or its neurotropism which is not yet defined. PRES (Posterior Reversible Encephalopathy Syndrome) is a rare clinico- neuro-radiological entity which can be associated with multiple clinical conditions and was observed frequently with preeclampsia and eclampsia patients. Neuro- imaging is important to diagnose PRES.

Materials and Methods: This study is a prospective observational study in COVID -19 positive eclampsia patients at Gandhi Hospital, Telangana during March 2021-august 2021.

Results: Among 55 COVID-19 positive eclampsia patients, 17 had PRES out of which 64.7% had antepartum eclampsia. Seven patients had severe COVID-19 disease out of which five patients required noninvasive ventilation and two patients required invasive ventilation. In my study, PRES was more common among primigravida, common age group 21-25 years. Mean SBP/DBP is 177±12 / 110±6 mm Hg respectively. Incidence of Thrombocytopenia is more in COVID-19 eclampsia patients. COVID -19 related complications are seen in 41.17% whereas eclampsia related maternal complications are seen in 29.4%. There was one maternal death and perinatal mortality was 17.64%.

Conclusions: COVID -19 positive eclampsia patients have more predilection to PRES. Diagnosis, treatment of eclampsia in COVID-19 should be evaluated and treated for PRES. Regular antenatal visits and regular bp monitoring can prevent eclampsia and its complications and can reduce maternal morbidity, mortality. Use of anticoagulants and corticosteroids may fasten the recovery rate.

1. Introduction

SARS-CoV-2 SS mRNA (30 kb) virus belongs to Beta corona family, a novel corona virus identified first in Wuhan, a city in Hubei Province of China. In addition to conventional respiratory complaints of flu, COVID-19 positive patients also exhibit neurological signs and symptoms which can result from direct viral invasion across cribriform plate of ethmoid bone close to olfactory bulb or hematogenous route or hypoxic, toxic or immune mediated injury.[1,2] The neuroinvasion potential is documented in most human coronaviruses (OC-43, 229E, MERS and SARS) and in some animal coronaviruses (porcine haemagglutinating encephalomyelitis coronavirus).[3] Neurological manifestations of COVID-19 include Anosmia, Ageusia, headache, insomnia, Epilepsy, stroke, rarely PRES, Guillian – Barre syndrome, Miller Fisher syndrome etc.[1,2,4]

Hinchey et al. in 1996 first described PRES, a clinico neuroradiological entity which is associated with acute cerebral endotheliopathy, consecutive disruption of the blood–brain barrier (BBB) resulting in vasogenic oedema

* *Corresponding author*.
E-mail address: bhargavi15312@gmail.com (S. Bhargavi).

https://doi.org/10.18231/j.ijogr.2022.046

due to abrupt rise of blood pressure in eclampsia.[5,6] The diagnosis is based on (1) at least 1 acute neurological symptoms (headache, visual disturbances, seizure, altered mental state etc); (2) CT/MRI with bilateral vasogenic oedema, cytotoxic oedema with PRES Patterns; and (3) with no other alternative diagnosis.[7]

Association between PRES and SARS-CoV-2 infection is not clear. Target receptor for SARS-CoV-2 is ACE2 receptor, which is expressed on several organs, endothelial cells. Entry of virus depends on interaction between spike protein, TMPRSS2, ACE2 receptor. Following virus entry, the expression and function of ACE 2 (ACE2) proteins are reduced, resulting in hypertension, endothelial inflammation that may induce PRES. The COVID related endothelitis[8] could explain the systemic impaired microcirculatory function in different vascular beds. In the brain, this endothelitis induce increased permeability of the BBB, leading to a brain oedema. Other classical causes of PRES in these patients could be ARDS, tocilizumab, sepsis and acute kidney injury requiring haemodialysis,[9] severe hypoxic pneumonia and treatment targeting SARS-CoV-2.

It is also suggested that the increased levels of cytokines (TNF-α, IFN-γ, IL-1) and inflammatory mediators in the course of the disease are responsible for cerebrovascular endothelial dysfunction and disruption of the blood-brain barrier.[1]

2. Aim

To study the maternal and perinatal outcome in COVID-19 positive eclampsia patients with PRES.

3. Materials and Methods

This is a prospective observational study conducted at GANDHI hospital, Secunderabad, a nodal centre for COVID-19 in Telangana and a tertiary care referral centre. This study was conducted on COVID -19 positive eclampsia patients during March 2021 to August 2021. This study was approved by Internal Institutional Ethics committee. All COVID-19 positive eclamptic women with neurological symptoms who had persistent headache, or visual disturbances even after 24 hours of magnesium sulphate (MgSo4) coverage who underwent neuro imaging study were included in this study.

Maternal outcomes expressed in terms of clinical presentations, associated maternal complications, need for mechanical ventilation, maternal mortality and neuro imaging to identify typical PRES changes and patients are being followed up after 4–6 weeks. The perinatal outcomes including birth weight, APGAR scores, NICU admissions and perinatal deaths were studied.

3.1. Inclusion criteria

All COVID-19 positive eclampsia patients with completed 20 weeks of gestational age or within 6 weeks of postpartum period.

3.2. Exclusion criteria

Patients with other causes of epilepsy/ neurological disorders.

3.3. Statistical methods

Number and percentages for the categorical variables. P value < 0.05 was considered as statistically significant. Statistical analyses were carried out using percentages, chi square values.

4. Results

A total of 471 covid-19 positive patients delivered from March 2021 to August 2021. Of these, 55 women were presented with eclampsia and 17 of them were PRES. Among 17 patients of PRES, Seven patients had severe COVID-19 disease out of which five patients required noninvasive ventilation and two patients required invasive ventilation. Out of 17 patients, 11(64.7%) had antepartum eclampsia, 6 (35.29%) had postpartum eclampsia. In our study Common age of the women at diagnosis of PRES was 21 – 25 years. Out of 17, 11 (64.7%) are of primigravida, 16(94.1%) are un-booked cases, 15 (88.2%) belong to low socio-economic status. Covid-19 related maternal complications are seen in 41.7% of cases. Eclampsia related maternal complications are seen in 29.4% of cases which increases with number of convulsions, convulsion to delivery interval and onset of convulsion to admission interval. There is one maternal death and 3 perinatal deaths, mostly due to prematurity. Most of them delivered term (11 out of 17). In the present study, 10 (58.8%) patients were delivered vaginally. The demographic and clinical characteristics are summarised in (Table 1).

1. Mean systolic and diastolic blood pressures were 177±12 and 110±6 mm Hg respectively.
2. The clinical features of PRES were summarised in Figure 1.

1. Among 17 Covid-19 positive eclampsia with PRES cases 15 patients had thrombocytopenia;41.1% of patients between 0.5 – 1 lakhs/mm^3.
2. Out of 17 women with PRES 5 (29.4%) had eclampsia related maternal complications like HELLP, AKI, DIC and pulmonary oedema, whereas 1 (5.8%) women required dialysis. There was 1 (5.8%) maternal death in the current study.

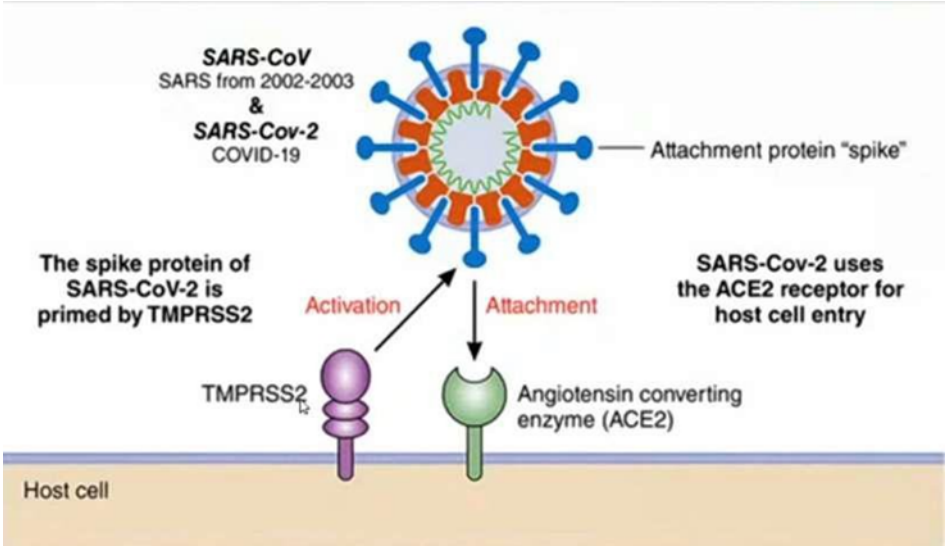

Diagram 1: a: Pathophysiology

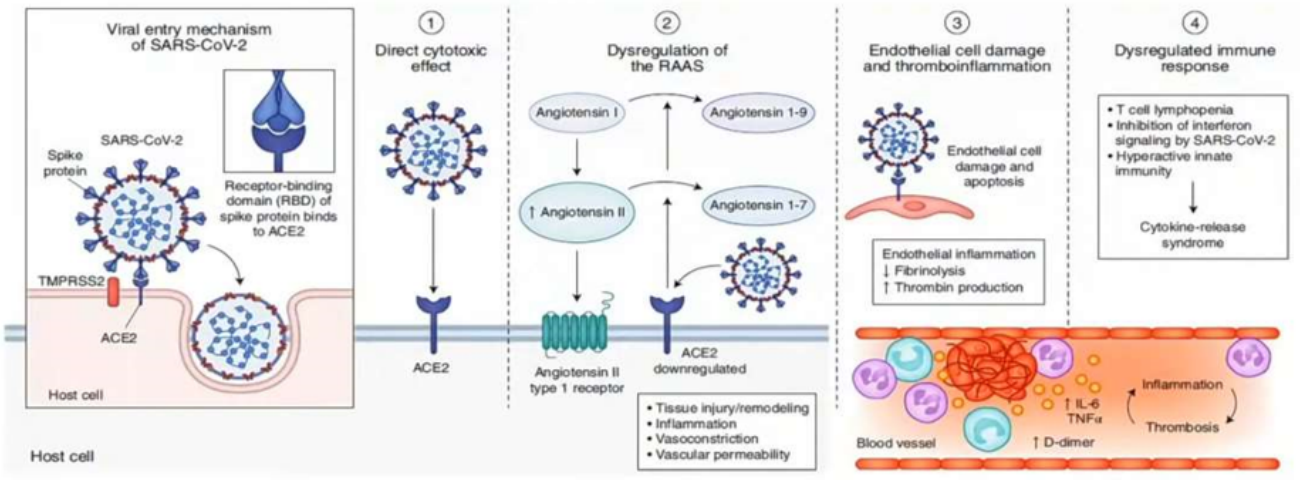

Diagram 2: b: Pathophysiology

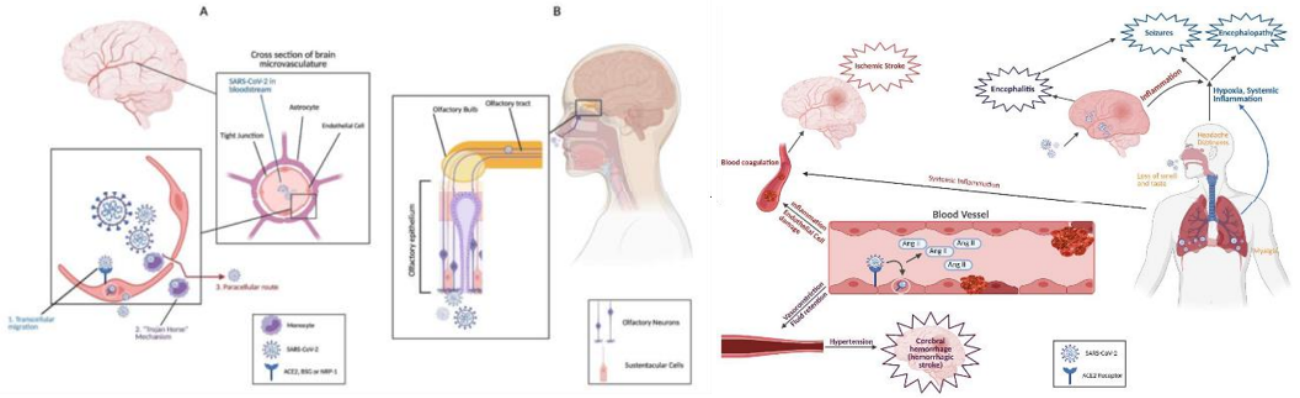

Diagram 3: c: Pathophysiology

Table 1:

Demographic / Clinical variables		No. of patients	Percentage
Age	19 - 20	1	6%
	21 - 25	12	71%
	>25	4	24%
Gravida / Parity	Primi Gravida	11	65%
	Multi Gravida	6	35%
Cases	Booked	1	6%
	Unbooked	16	94%
Socio economic status	Low	15	88%
	Middle	2	12%
Gestational age	Term	11	65%
	Preterm	6	35%
Type of eclampsia	Antepartum	11	65%
	Postpartum	6	35%
Associated complications	Covid related	7	41%
	Eclampsia related	5	29%
Mode of delivery	LSCS	7	41%
	Vaginal	10	59%
	Maternal	1	6%
	Perinatal	3	18%

Table 2:

Onset of convulsion to admission Interval	Eclampsia related maternal complications	
	Yes	No
< 6	1	11
> 6	4	1
Total	5	12

p value – 0.003, statistically significant.

Table 3:

No. of Convulsions	Eclampsia related maternal c omplications	
	Yes	No
≤ 2	1	10
3-5	4	2
Total	5	12

p value – 0.003, statistically significant.

Table 4:

Convulsion to delivery interval	Eclampsia related maternal complications	
	Yes	No
≤ 12	2	12
> 12	3	0
Total	5	12

p value – 0.003, statistically significant.

3. The site of lesions of PRES on MRI were summarized in Figure 2. 15 cases were reversible after 4-6 weeks, 1 had gliosis and 1 patient had intra cerebral haemorrhage.

1. Perinatal outcome: Birth weight of 47% babies: ≥ 2.5 kg, 41.1% are NICU admissions out of which 35.2% discharged healthy. Perinatal mortality was 17.64%.

5. Discussion

PRES is a rare complication of eclampsia and can also be associated with multiple clinical conditions like hypertensive encephalopathy, renal failure, auto immune disorders, and immunosuppressive drugs.[10] Uncommon clinical conditions include Acute intermittent porphyria, cryoglobulinemia, recently COVID-19. The pathophysiology behind PRES is not clearly understood and

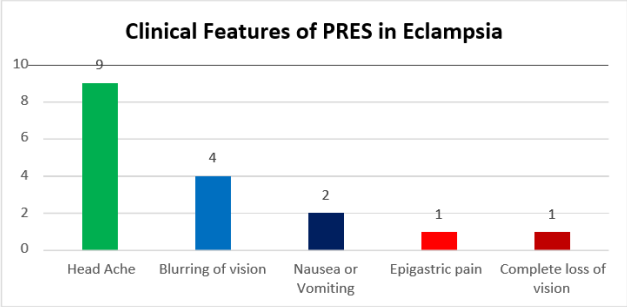

Fig. 1: Clinical features of PRES in eclampsia

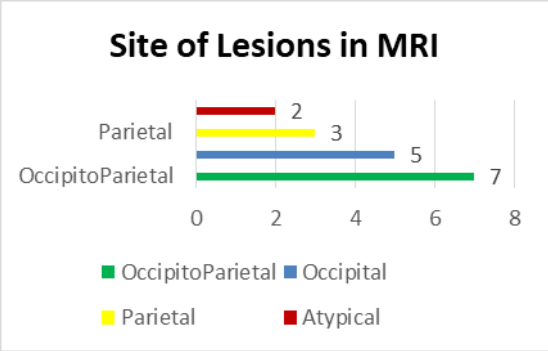

Fig. 2:

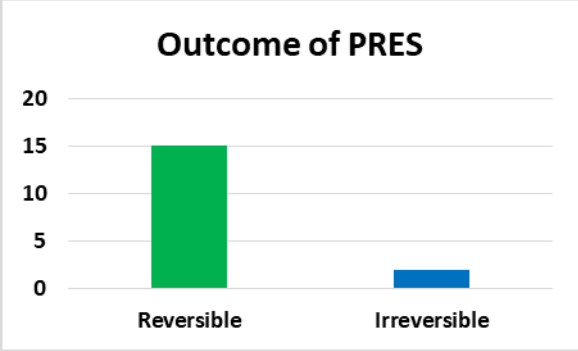

Fig. 3:

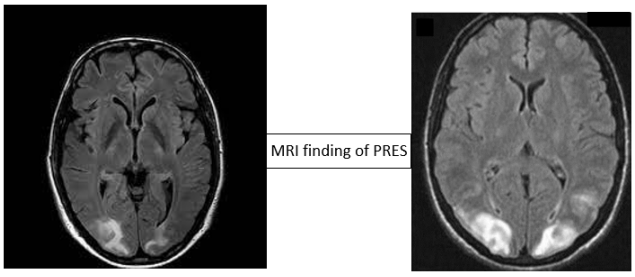

Fig. 4: Bilateral hyper intensities in occipital regions

shares the eclampsia pathophysiology.[11] Two mechanisms have been put forth, failure of auto regulation due to abrupt rise of B.P and endothelial dysfunction resulting in vasogenicoedema.[4,5]

The global incidence of PRES is unknown. Out of 253 eclampsia cases (Covid and Non-Covid), 17 (COVID positive) out of 50 PRES cases (covid and non covid) were COVID-19 positive with p value of 0.018, which is statistically significant. It implies that COVID -19 might be strongly associated with PRES in Eclampsia.

In present study, many were primigravida and common in age group 21-25 years as compared to Manavi PJ study[12] (average age is 21 years, many were primigravida).

In the present study we observed 64.7% and 35.2% of patients had PRES during antepartum and postpartum period respectively and is similar to Manavi PJ study.[12] According to Brewer J study[13] there was no significant difference between antepartum and postpartum PRES cases.

In the present study common presenting symptom of PRES was headache (52.9%) and blurring of vision (23.5%) which is similar to several studies.[6,10,13]

Most common site of lesions of PRES in MRI: Occipito Parietal (41.1%) > Occipital (29.4%) > Atypical (11.7%). All our patients had cerebral oedema compared to Zeeman GG study.[14] In the typical form, the abnormalities include bilateral symmetrical hyperintensities in subcortical white areas in occipitoparietal lobes. In the atypical forms, there can be unilateral or asymmetric pattern of involvement.[15]

According to the most accepted theory, an abrupt rise in blood pressure over a short period of time leads to a failure of normal auto regulatory mechanisms resulting in cerebral hyper perfusion, increased capillary pressure, vasodilatation, and therefore vasogenicedema especially in posterior circulation due to less sympathetic innervation and is usually reversible. So control of hypertension is the important component in PRES management. Labetalol is the drug of choice.[16]

Seizure control in eclamptic women and termination of pregnancy in antenatal eclampsia is the main step of the treatment and Mgso4 is the drug of choice. Magnesium decreases neuronal excitability, prevents endothelial damage by free radicals, or reduces cerebral perfusion pressure.[17,18] In CNS it may also protect the BBB (blood brain barrier) and therefore limit cerebral edema formation.

In the peripheral or cerebral vasculature, it acts as a vasodilator to decrease peripheral resistance.[13,17] 82.3% cases were controlled with MgSO4 alone in our study and 17.6% cases were treated with MgSO4 and Mannitol, where as Shobhabhomalgi study reported only 67% responded to MgSO4.

Corticosteroids can be used to treat hemolysis, elevation of liver enzymes and lowering platelet count that occurs in HELLP syndrome. Review of literature says corticosteroids reduce vasogenicedema.[19] Recent study

by Mayama et al. showed that patient who received antenatal steroid to enhance lung maturation or for HELLP management revealed faster recovery of CNS functions in eclamptic patients with PRES.[11,20] In our study effect of corticosteroids on recovery is not studied.

Out of 17 PRES cases, 15 cases were reversible after 4-6 weeks, 1 had gliosis and 1 patient had intra cerebral haemorrhage. Maternal mortality in our study was 5.8% and perinatal mortality was 17.6% as compared to 11% perinatal mortality rate in Manavi et al. study.[12]

6. Conclusion

Incidence of PRES in covid-19 eclamptic cases was high probably due to neurotropism, endothelial dysfunction or immune mediated or direct cell injury causing cerebral/vasogenic oedema which is precipitated by acute raise of blood pressure in eclampsia which results in disrupted auto regulation of brain which precipitates vasogenicedema especially in posterior circulation of brain. However, the association between SARS-CoV-2 and PRES is not clear. Regular antenatal checkups, early referral to tertiary care centre, regular B.P monitoring would prevent eclampsia and its related complications. Early diagnosis and Multidisciplinary approach in PRES management would prevent some of its devastating sequelae such as permanent visual loss or irreversible neurological deficit.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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Author biography

Saikam Bhargavi, Post Graduate https://orcid.org/0000-0001-7994-3906

V Janaki, Professor

Cite this article: Bhargavi S, Janaki V. A prospective observational study on posterior reversible encephalopathy syndrome in COVID-19 eclampsia patients in tertiary care hospital. *Indian J Obstet Gynecol Res* 2022;9(2):238-243.