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A study on correlation between neuroimaging and maternal outcome in eclampsia

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ABSTRACT

Background: Hypertensive disorders remain among the most significant complications of pregnancy. Neurological complications of eclampsia are a major contributor to morbidity and mortality that is associated with eclampsia. Neuroimaging studies have revolutionized visualization of hypertensive encephalopathy aids in timely intervention and a favorable maternal and perinatal outcome. **Aims and Objectives:** (1) To study the spectrum of neuroimaging findings in patients with eclampsia. (2) To correlate these findings with the maternal outcome. **Materials and Methods:** A prospective observational study was undertaken in the Department of Obstetrics and Gynecology, Mysore Medical College and research institute Mysore, for 18 months. All the eclamptic mothers during the study were included in the study. They were studied in terms of neuroimaging and its correlation with maternal outcomes. **Results**: The incidence of eclampsia was 7.14% which is relatively high, attributed to the fact that being a tertiary care center many cases are referred. Higher incidence was seen in primigravida (72.4%) and lower maternal age of 18–20 years (48%). Cesarean section was indicated in 50% of deliveries indicating immediate action was necessary for better fetomaternal outcome. They presented with varied imminent symptoms such as headache in 20.4%, vomiting in 22.4%, and visual blurring in 22.4%. About 50% presented with altered sensorium. On non-contrast computed tomography brain, 64.3% (63) had normal findings, 17.3% (17) had posterior reversible encephalopathy syndrome (PRES) with a sensitivity of 68.42% and specificity of 85%, whereas on magnetic resonance imaging (MRI) brain, 36.26% had no abnormalities, 40.81% had PRES with a sensitivity of 86.84%, and specificity of 85%. About 58.6% had an uneventful maternal outcome. The others were hemolysis, elevated liver enzymes, and low platelet syndrome seen in 9.18% of patients, acute kidney injury in 6.12%, postpartum hemorrhage seen in 5.1%. The maternal mortality rate was 7.66%, the most common cause of death was intracranial hemorrhage. **Conclusion:** The common neuroimaging findings in eclampsia are cerebral edema, PRES, cerebral venous thrombosis, infarcts, hemorrhage, and hypertensive leukoencephalopathy. Although some abnormalities seen in neuroimaging studies are incidental and transient without chronic neurologic sequelae, both CT and MRI findings correlate with the clinical presentation and maternal outcome but MRI correlates better compared to CT and can be a better imaging modality in eclampsia patients and is indicated in all patients of eclampsia.

Key words: Eclampsia; Neuroimaging; Non-contrast computed tomography; Magnetic resonance imaging; Posterior reversible encephalopathy syndrome

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INTRODUCTION

Hypertensive disorders during pregnancy represent the primary cause of perinatal and maternal mortality and morbidity worldwide. Together with hemorrhage and infection, hypertension constitutes a lethal triad responsible for a significant portion of maternal morbidity and mortality.[1] Eclampsia is defined as the onset of convulsions or coma during pregnancy or post-partum in a patient who has signs and symptoms of preeclampsia.[1]

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The occurrence of eclampsia significantly elevates the risk for both the mother and the fetus. According to the World Health Organization, preeclampsia and eclampsia are responsible for causing no <16% of maternal deaths in developing nations.[2]

Eclampsia's prevalence ranges from 0.5% to 15%.[3] Apart from the early identification of preeclampsia, there are no dependable tests or symptoms for anticipating the onset of eclampsia. Hypertension is acknowledged as the primary diagnostic feature for eclampsia. However, in numerous cases, the initiation of preeclampsia is frequently subtle, with pathological changes commencing early in the disease's progression, and symptoms typically manifesting late. In 16% of the cases, hypertension may be absent.[4] Eclamptic patients usually present with generalized tonic–clonic seizures, the evaluation of which is mainly centered around the diagnosis of pre-eclampsia.[5] The central pathological process in eclampsia primarily affects the neurological organ system. Neurological complications are the foremost concern, contributing significantly to the high mortality in eclampsia. These neurological complications encompass seizures, cognitive impairment, visual field abnormalities, blurred vision, headaches, hemiparesis, coma, cortical blindness, and papilledema.[6,7]

Computed tomography (CT) and magnetic resonance imaging (MRI) of the brain have revolutionized visualization of lesions in eclampsia and other organic conditions. CT is a rapid initial imaging tool preferred to MRI in some conditions, such as hemorrhage and space-occupying lesions, and complementary to MRI in others.[8]

Neuroimaging manifestations of eclampsia and preeclampsia often overlap, mainly presenting as posterior reversible encephalopathy syndrome (PRES) (Figure 1). PRES is a distinctive clinicoradiologic syndrome characterized by headaches, visual disturbances, and seizures with predominantly parieto-occipital vasogenic edema, occasionally with cytotoxic edema.[9]

Neuroimaging can also be very helpful in eclampsia patients who do not respond to conventional treatment with $MgSO_4$ magnesium sulfate) and antihypertensives. CT scan findings in eclampsia patients have found mainly transient cortical and subcortical white matter hypodensities which could be due to hypoxia or edema.[10] These lesions correspond to mainly watershed areas of circulation where anterior, middle, and posterior cerebral arteries meet. It is in this area where the earliest breakthrough in autoregulation occurs.[11]

Aims and objectives

1) To study the spectrum of neuroimaging findings in patients with eclampsia

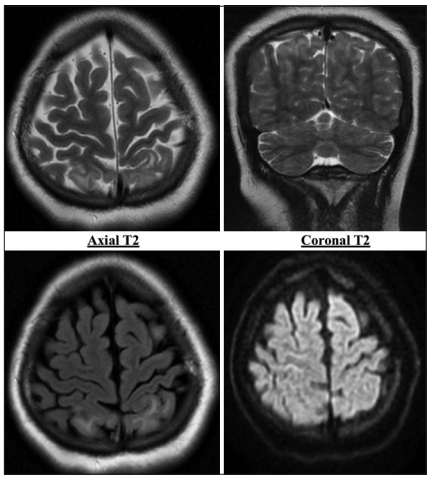

Figure 1: Axial T2 and FLAIR showing symmetrical hyperdensites in bilateral parietal lobes posterior reversible encephalopathy syndrome

2) To correlate the neuroimaging findings with various maternal outcome.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynecology, Mysore Medical College and Research, Mysore, Karnataka, India for a period of 10 months from March 2021 to August 2022.

Inclusion criteria

- All patients who presented with eclampsia or developed eclampsia during the hospital stay during the study period were included in the study.

Exclusion criteria

- Women whose gestational age was <20 weeks
- Those who were known epileptics or with a history of seizures due to neurological pathology were excluded from the study.

This study was conducted after obtaining clearance from the institutional ethical committee.

Data were collected using pre-designed pro forma. The patient was first stabilized for eclampsia as per hospital protocol following which they were subjected to both non-contrast CT (NCCT) brain and MRI brain.

All the data collected were entered into a Microsoft Excel worksheet and analyzed using the statistical software SPSS 20.0.

Ethical approval

The study was approved by the Institutional Ethics Committee.

RESULTS

A total number of 13707 women delivered during the defined period. Out of them, 1737 women were diagnosed to have hypertensive disorders of pregnancy, of which 98 women were diagnosed with cases of eclampsia making the incidence of eclampsia to be 7.14%/1000 deliveries.

Most of the patients 48% were under 20 years of age. Only 4% (n=4) of the patients were above the age of 30 years. Eclampsia was more common in primigravidae (72.4%) and in unbooked cases (63.26%) as shown in Table 1.

Majority of the cases presented as antepartum eclampsia (62.2%), eclampsia has occurred in all gestational age groups, majorly between 28 and 37 weeks (53.3%) as shown in Table 2. The definitive treatment of eclampsia is delivery. Eclampsia itself is not an indication of cesarean section, and the mode of delivery had no significant effect on the outcome of the eclamptic mother.

In our study, 58.68% (n=115) of study subjects had an uneventful outcome, and the remaining 41.32% (n=81) had various other maternal outcome as shown in Table 3.

Table 1: Maternal age distribution, parity status, and booking status among the study subjects

Age group (years)	Frequency (percentage)
18–20	47 (48)
21–25	28 (29)
26–30	19 (19)
31–35	4 (4)
Gravida	
Primigravida	71 (72.4)
Multigravida	27 (27.6)
Booking status	
Booked	36 (36.73)
Unbooked	62 (63.26)

Table 2: Types of eclampsia, gestational age at the onset of eclampsia (antepartum and intrapartum) and mode of delivery

Types of eclampsia	Frequency (percentage)
Antepartum	61 (62.2)
Intrapartum	15 (15.3)
Postpartum	22 (22.4)
Gestational age at the onset of eclampsia	**Frequency (percentage)**
<28 weeks	22 (14.6)
28–34 weeks	54 (36)
34–37 weeks	26 (17.3)
>37 weeks	48 (32)
Total	151 (100)
Mode of delivery	
Cesarean section	98 (50)
Full-term vaginal delivery	40 (20.4)
Preterm vaginal delivery	58 (29.59)

The various neuroimgaging findings in our study include PRES, edema, hemorrhage, infarcts, CVT as shown in Table 4 and the correlation between neuroimaging and maternal outcome is shown in Tables 5 and 6 with a significant $p<0.05$.

MRI has a better specificity (94.74%) and positive predictive value (94.29%) compared to NCCT as shown in the Table 7.

DISCUSSION

Eclampsia stands as a major contributor to maternal and fetal morbidity and mortality on a global scale, and its underlying causes remain poorly understood.

Despite significant progress in medical care and the widespread implementation of prenatal screening in recent years, eclampsia's global incidence and fatality rates persist at elevated levels, presenting a serious threat to the health of both mothers and their unborn children.

The global occurrence of eclampsia is 1 in 2000 pregnancies. In India, the reported incidence of eclampsia varies from 0.179% to 3.7%. In our study, the incidence of eclampsia was 7.14/1000 deliveries which is relatively high compared to both global and Indian incidence. Our

Table 3: Maternal outcome in the study subjects

Maternal outcome	Frequency (percentage)
HELLP syndrome	18 (9.1)
Acute kidney injury	12 (6.12)
Postpartum hemorrhage	10 (5.1)
Placental abruption	8 (4.08)
Blindness	6 (3.06)
Cerebrovascular accidents	5 (2.55)
Disseminated intravascular coagulation	4 (2.04)
Pulmonary edema	3 (1.53)

HELLP: Hemolysis, elevated liver enzymes, low platelet

Table 4: Neuroimaging findings in the study subjects

Neuroimaging	Frequency (percentage) NCCT brain	Frequency (percentage) MRI brain
No significant intracranial abnormality	63 (64.3)	37 (36.26)
PRES	17 (17.3)	40 (40.81)
Intracranial hemorrhage	8 (8.2)	8 (8.2)
Postictal edema	6 (6.1)	4 (4.1)
Infarcts	3 (3.06)	3 (3.06)
CVT	1 (1.0)	1 (1.0)
Total	(96) 100.0	92 (95.92)

NCCT: Non-contrast computed tomography, PRES: Posterior reversible encephalopathy syndrome, MRI: Magnetic resonance imaging, CVT: Cerebral venous thrombosis

Table 5: Correlation between NCCT brain and maternal outcome

NCCT brain	Maternal outcome		Total (%)	Chi-square	P-value
	Complications/mortality (%)	No complication (%)			
Positive	26 (26.5)	9 (9.2)	35 (35.7)	28.919	0.000 (<0.05)
Negative	12 (12.2)	51 (52)	63 (64.3)		
Total	38 (38.8)	60 (61.2)	98 (100)		

NCCT: Non-contrast computed tomography

Table 6: Correlation between MRI brain and maternal outcome

MRI brain	Maternal outcome		Total (%)	Fisher exact test P value
	Complications/mortality (%)	No complication (%)		
Positive	33 (33.7)	27 (27.6)	60 (61.2)	0.000 (<0.05)
Negative	5 (5.1)	33 (33.7)	38 (38.8)	
Total	38 (38.8)	60 (61.2)	98 (100)	

MRI: Magnetic resonance imaging

Table 7: Comparison between NCCT brain and MRI brain

NCCT brain	MRI brain		Total
	Positive	Negative	
Positive	33 (33.7)	2 (2)	35 (35.7)
Negative	27 (27.6)	36 (36.7)	63 (64.3)
Total	60 (61.2)	38 (38.8)	98 (100)
Statistic	**Value**	**95% confidence interval**	
Sensitivity	55	41.61%=67.88%	
Specificity	94.74	82.25%=99.36%	
Positive predictive value	94.29	80.77%=98.48%	
Negative predictive value	57.14	49.95%=64.04%	
Accuracy	70.41	60.34%=79.21%	

NCCT: Non-contrast computed tomography, MRI: Magnetic resonance imaging

Table 8: Comparison of maternal outcome with similar studies

Maternal outcome	Our study	Sunita et al.[14]	Ndaboine et al.[15]	Pannu et al.[16]
AKI	6.12% (12)	2% (2)	7.8% (6)	12% (10)
PPH	5.10% (10)	6% (6)	0%	9.6% (8)
HELLP syndrome	9.18% (18)	7% (7)	38.1% (29)	13.2% (11)
Placental abruption	4.09% (8)	2% (2)	11.8% (9)	-
Pulmonary edema	2.04% (4)	-	-	14.5% (12)
DIC	2.04% (4)	3% (3)	2.6% (2)	2.4% (2)
Blindness	3.06% (6)			3.3% (3)
CVA	3.06% (6)	2% (2)	6.5%	2.4% (2)

HELLP: Hemolysis, elevated liver enzymes, low platelet, AKI: Acute kidney injury

incidence is comparable to a similar study in Rajasthan by Agarwal and Gautam.[12]

As most of the population in our study group is from a rural background and a low socioeconomic status, the age at marriage is early compared to the urban population. Hence, the age at first conception is also early. The mean age in our study population was 22.57. About 48% of women between the age group of 18–20 years. This result correlates with the Ugran and Donimath,[13] where the mean age was 23.89 years. Comparison between maternal outcomes of various similar studies are quoted in Table 8.

Disruption of the blood–brain barrier occurs due to both the hypertension-induced capillary damage and the immune-mediated endothelial dysfunction. This leads to extravasations of red cells and plasma proteins into perivascular space causing cerebral edema. Cerebral vasospasm, produced by a combination of reaction to hypertension, prostaglandin deficiency, defects in the NOS gene (coding for nitric oxide synthase), and endothelial damage, play an important role, producing ischemia and infarction in the brain tissue. The impaired blood coagulation system and the abnormalities and deficiency of platelets predispose to intracranial bleeds.

Thus, a varied picture of cerebral pathology showing evidence of cerebral edema, microinfarcts, cortical petechiae, and pericapillary hemorrhages is observed in the brains of patients with pre-eclampsia or eclampsia, which clinically manifest as headache, visual disturbances, confusion, and seizures. Characteristic lesion locations are the parietal and occipital lobes, followed by the frontal lobes, the inferior temporal occipital junction, and the cerebellum.

Neuroimaging within a short time after seizure in eclamptics may yield more abnormalities, presumably due to the transient nature of lesions. The most common lesions detected on CT in eclampsia are focal areas of cerebral edema in the subcortical white matter of parietal and occipital areas.

In this study, 35.7% (n=35) had positive NCCT brain findings, 65% of the patients did not have any significant

Table 9: Comparison of neuroimaging findings with similar studies

CT findings	Our study	Ugran and Donimath[13]	Brouh et al.[17]	Jindal et al.[18]
PRES	17.3% (17)	27% (27)	7.7% (3)	75% (9)
Intracranial Hemorrhage	8% (8)	1% (1)	2.5% (1)	8.3% (1)
Postictal edema	6% (6)	-	23% (9)	-
Infarcts	3% (3)	14% (14)	25.6% (10)	8.3% (1)
Cerebral venous thrombosis	1% (1)	23% (23)	-	-
No abnormality	63% (62)	48% (48)	51.2% (20)	8.3% (1)
Hypertensive leucoencephalopathy	-	5% (5)		-

PRES: Posterior reversible encephalopathy syndrome

intracranial abnormality detected on a CT scan. The cause for normal findings might be due to the temporal relationship of the scan to the seizure. The most common abnormal finding is PRES accounts for 17.3% followed by intracerebral bleed in 8.2% (n=8), post-ictal edema was seen in 6.1% (n=6) patients, infarcts were seen in 3.06% and cerebral venous thrombosis (CVT) was seen in one patient. The most common neurological presentation was altered sensorium in 50% of the patients. In PRES with hypertension, the myogenic cerebral autoregulation effect decreased depending on elevated blood pressure. The neurogenic autoregulatory mechanism takes over the regulation of cerebral perfusion, becomes more sensitive to elevation in blood pressure, and leads to vasogenic edema. In PRES, apart from hypertensive pathogenesis, a direct endothelial injury which might cause a surge in permeability of blood-brain barrier also plays a key role in its pathogenesis. Comparison of neuroimaging findings with other similar studies are shown in Table 9.

In our study, MRI had a better sensitivity (86.84%) compared to the sensitivity of CT (68%). Our results are comparable to a prospective observational study conducted in Safdarjang Hospital, New Delhi, India to compare CT and MRI findings of eclampsia patients with respect to neurological signs and symptoms. It was reported that MRI was found to be correlating more than CT with the neurological presentation and had 90% sensitivity and 100%, respectively.[18]

Despite the availability of intensive care units and advanced technology, some women still die from eclampsia. A common cause of death in eclampsia is central nervous system pathology such as intracerebral hemorrhage or massive cerebral edema. It is obvious that improving our understanding of the neuropathophysiology of eclamptic seizures is imperative to appropriate management and reduction of morbidity and mortality.

Morbidity and mortality observed in patients of eclampsia in our study are similar to that observed in studies from other regions of our country and other developing countries. Case fatality rate observed in our study, i.e., 4.08% is comparable to studies from Eastern India (4.4%).[19] It is significantly lower in studies from Tanzania (7.89%)[20] and Benin (10.7%).[15] However, the case fatality rate is much higher than reported from developed countries. (0.5% to 1.8%).

Limitations of the study

In a few cases there was a delay in obtaining the CT/MRI due to certain patient factors. This delay could have caused false negative neuroimaging results in such patients.

CONCLUSION

Neurological complications of eclampsia are a major contributor to morbidity and mortality that is associated with eclampsia. Cranial CT and MRI of the brain have revolutionized the visualization of lesions in hypertensive encephalopathy. The spectrum of findings obtained on neuroimaging was cerebral edema, PRES, intracerebral hemorrhage, CVT, acute and chronic infarcts, and periventricular leukomalacia.[21]

Although some abnormalities seen in neuroimaging studies are incidental and transient without chronic neurologic sequelae, MRI correlates better with the clinical presentation and maternal outcome compared to CT and can be a better imaging modality in eclampsia patients.[22]

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REFERENCES

1. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al. Hypertensive disorders. In: Williams Obstetric. 26th ed. New York: McGraw-Hill Education; 2022. p. 1777-1892.
2. Health E. Balancing the Scales: Expanding Treatment for Pregnant Women with Life-Threatening Hypertensive Conditions in Developing Countries. A Report on Barriers and Solutions to Treat Preeclampsia and Eclampsia. Washington, D.C.: Engender Health; 2007.
3. Mahela S, Sarma HD, Mech T and Talukdar B. Computed tomography of brain in eclampsia and its clinical correlation. New Indian J Obgyn. 2021;8(1):14-18.

https://doi.org/10.21276/obgyn.2021.8.1.4

4. Katz VL, Farmer R and Kuller JA. Preeclampsia into eclampsia: Toward a new paradigm. Am J Obstet Gynecol. 2020;182(6):1389-1396.
   https://doi.org/10.1067/mob.2000.106178
5. Sailaja B, Cooly V, Sailcheemala B, and Sailaja S. A study on risk factors, maternal and foetal outcome in cases of preeclampsia and eclampsia at a tertiary care hospital of South India. Int J Reprod Contracept Obstet Gynecol. 2018;7(1):266-271.
   https://doi.org/10.18203/2320-1770.ijrcog20175859
6. Wilkerson RG and Ogunbodede AC. Hypertensive disorders of pregnancy. Emerg Med Clin North Am. 2019;37(2):301-316.
   https://doi.org/10.1016/j.emc.2019.01.008
7. Gasnier R. Eclampsia: An overview clinical presentation, diagnosis and management. MOJ Womens Health. 2016;3(2):182-187.
   https://doi.org/10.15406/mojwh.2016.03.00061
8. Sardesai S, Dabade R, Deshmukh S, Patil P, Pawar S and Patil A. Posterior reversible encephalopathy syndrome (PRES): Evolving the mystery of eclampsia! J Obstet Gynaecol India. 2019;69(4):334-338.
   https://doi.org/10.1007/s13224-019-01214-6
9. Garg RK, Kumar N and Malhotra HS. Posterior reversible encephalopathy syndrome in eclampsia. Neurol India. 2018;66(5):1316-1323.
   https://doi.org/10.4103/0028-3886.241364
10. Lanska DJ and Kryscio RJ. Peripartum stroke and intracranial venous thrombosis in the national hospital discharge survey. Obstet Gynecol. 1997;89(3):413-418.
    https://doi.org/10.1016/S0029-7844(96)00516-9
11. Millez J, Dahoun A and Boudraa M. Computed tomography of the brain in eclampsia. Obstet Gynecol. 1990;75(6):975-980.
12. Agarwal M and Gautam A. Study of fetomaternal outcome in eclampsia. Int J Reprod Contracept Obstet Gynecol. 2020;9(10):4155-4159.
    https://doi.org/10.18203/2320-1770.ijrcog20204305
13. Ugran SM and Donimath KV. Correlation between neuroimaging (CT scan) and neurological presentation in antepartum and postpartum eclampsia. Int J Reprod Contracept Obstet Gynecol. 2016;5(2):419-424.
    https://doi.org/10.18203/2320-1770.ijrcog20160382
14. Sunita TH, Desai RM, Hon N, Shinde KJ and Hashmi SI. Eclampsia in a teaching hospital: Incidence, clinical profile and response to magnesium sulphate by zuspan's regimen. IOSR J Dent Med Sci. 2013;4(2):1-5.
15. Ndaboine EM, Kihunrwa A, Rumanyika R, Im HB and Massinde AN. Maternal and perinatal outcomes among eclamptic patients admitted to bugando medical centre, Mwanza, Tanzania. Afr J Reprod Health. 2012;16(1):35-41.
16. Pannu D, Das B, Hazari P and Shilpa. Maternal and perinatal outcome in eclampsia and factors affecting the outcome: A study in North Indian population. Int J Reprod Contracept Obstet Gynecol. 2014;3(2):347-351.
17. Brouh Y, Jean KK, Ouattara A, Tétchi Y, Pete Y, Koffi N, et al. Brain lesions in eclampsia: A series of 39 cases admitted in an intensive care unit. Indian J Crit Care Med. 2016;20(3):178-181.
    https://doi.org/10.4103/0972-5229.178183.
18. Jindal MA, Gaikwad HS, Hasija BD and Vani K. Comparison of neuroimaging by CT and MRI and correlation with neurological presentation in eclampsia. Int J Reprod Contracept Obstet Gynecol. 2013;2(1):83-87.
19. Singh S and Behera AK. Eclampsia in Eastern India: Incidence, demographic profile and response to three different anticonvulsant regimes of magnesium sulphate. Internet J Gynecol Obstet. 2011;15(2):1-8.
20. Onuh SO and Aisien AO. Maternal and fetal outcome in eclamptic patients in Benin city, Nigeria. J Obstet Gynaecol. 2004;24(7):765-768.
    https://doi.org/10.1080/01443610400009451
21. Lal AK, Gao W and Hibbard JU. Eclampsia: Maternal and neonatal outcomes. Pregnancy Hypertens. 2013;3(3):186-190.
    https://doi.org/10.1016/j.preghy.2013.04.013
22. Zwart JJ, Richters A, Ory F, de Vries JI, Bloemenkamp KW and Roosmalen J. Eclampsia in the Netherlands. Obstet Gynecol. 2008;112(24):820-827.
    https://doi.org/10.1097/AOG.0b013e3181875eb3

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MK- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, statistical analysis and interpretation, manuscript preparation and submission of the article; **SVD-** Coordination and manuscript revision

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