Research Article

Effect of Magnesium Sulphate on Optic Nerve Sheath Diameter as an Indirect Measure of Intra-Cranial Pressure: A Case Study of Eclampsia Patients

Anum Zeb,[1] Sumera Zaib,[2] Zahra Safdar,[3] Uzma Zia,[4] Shirin Gul,[5] Rana Abid Ali,[6] Madeeha Rasheed[7]

[1]Department of Anesthesia and Intensive Care, Lahore General Hospital, Lahore, Pakistan; [2]Department of Obstetrics & Gynaecology, Lahore General Hospital, Lahore, Pakistan; [3-7]Department of Obstetrics & Gynaecology, Avicenna Medical & Dental College, Lahore, Pakistan

Abstract

Background: Eclampsia is associated with increased intracranial pressure (ICP). Magnesium sulphate ($MgSO_4$) is the usual treatment and is linked to a significant decrease in cerebral perfusion pressure (CPP) as well as the avoidance of brain injury. There are various invasive procedures which are still the gold standard for monitoring intracranial pressure (ICP), however, they are not always practical or easily available choices. Therefore, a non-invasive promising tool can be used to reflect variations in the intracranial pressure is optic nerve sheath diameter (ONSD) assessment using ultrasonography.

Objective: This study aims to measure changes in the Optic nerve sheath diameter in order to identify the impact of magnesium sulphate treatment; a proxy for elevated intracranial pressure in eclampsia patients.

Methods: In this pilot study the data was collected from sixty pregnant female patients with all signs and symptoms of eclampsia. The analysis of optic nerve sheath diameter was done using ultrasound prior to the start of magnesium sulphate treatment and then was measured after 01, 06 and 24 hours.

Results: The mean diameter of optic nerve sheath in women was high at baseline time point and they were presented with hypertension and disturbed vision. At one, six and twenty-four hours of taking magnesium sulphate, there was a statistically significant decrease in the mean optic nerve sheath diameter values. However, there is insignificant relationship between mean arterial pressure and optic nerve sheath diameter.

Conclusion: This study concludes that a high optic nerve sheath diameter value, indicative of elevated intracranial pressure, was present in the majority of study participants who were significantly eclamptic. This condition was significantly impacted by magnesium sulphate medication. Thus, ultrasound can be used as a convenient, affordable, point-of-care bedside technology to indirectly measure intracranial pressure in this high-risk group.

Received: 23-01-2024 | **1st Revision:** 25-06-2024 | **2nd Revision:** 07-08-2024 | **Accepted:** 17-11-2024

Corresponding Author | Dr. Zahra Safdar, Associate Professor, Department of Obstetrics & Gynaecology, Avicenna Medical & Dental College, Lahore **Email:** zsafdar2@gmail.com

Keywords | optic nerve sheath diameter, Magnesium sulphate therapy, Eclampsia, Intracranial Pressure

Production and Hosting by KEMU

https://doi.org/10.21649/akemu.v30i4.5615

2079-7192/

Introduction

Eclampsia is described as the occurrence of one or more tonic-clonic convulsions in pregnant women with hypertension disorders that are generalised and unrelated to other medical problems.[1] This illness is

well-known for causing one of the dangerous acute pregnancy issues, with a high chance of mortality and serious issues for both the mother and the unborn child. The incidence of eclampsia in developed nations is 1.6 to 10 per 10,000 deliveries.[2,3,4] There are reports that the rate of eclampsia in certain developing or low-resource nations is between 50 and 151 per 10,000 deliveries.[5] The disparities between industrialized and poor nations stem from inadequate access to healthcare, inappropriate and delayed prenatal care, protocols for surveillance and timely hospitalization and delivery, antihypertensive medication for women with severe preeclampsia to prevent stroke, pulmonary edema, congestive heart failure, and magnesium sulphate prophylaxis during the pre-partum period.[6] The early diagnosis is very important using various neurodiagnostic tests like cerebral angiography, magnetic resonance imaging (MRI), computed tomography (CT), and electroencephalography (EEG).[7] Even while invasive procedures are still the gold standard for monitoring intracranial pressure (ICP), they are not always a practical or easily available choice. Therefore, there is a need to assess this condition through non-invasive way.

Abnormal neuroimaging findings, including cerebral edema, infarction, and hemorrhage, are observed in hypertensive encephalopathy and eclampsia. Most clinicians agree that if a woman presents with hypertension, proteinuria, and convulsions; it is a clear case of eclampsia.[7,8] Even though hypertension is a defining feature of eclampsia, it may not be present in as many as 25% of cases. In addition to various manifestations of this severe pre-eclampsia, an increase in intra-cranial pressure (ICP) and neurological alterations are commonly observed.[9] It is critical to diagnose and treat brain edoema and elevated ICP as soon as possible.[10] The optic nerve is viewed as window into the central nervous system (CNS) because of its dural sheath covering. The space surrounds the optic nerve, interconnects openly with cerebral subarachnoid space (SAS). It has been seen that an increase in ONSD results in increase in the ICP.[11] A straightforward and useful ultrasonographic technique for identifying elevated ICP in individuals suffering from trauma or severe illness is bedside ultrasonography assessment of the ONSD.[12] This indirect relationship shows that change in ICP in eclampsia patients can be seen through measuring ONSD.[13] To identify patients with severe preeclampsia or eclampsia it is suggested that ONSD greater than 5.8 mm is used as the cutoff.[14]

As a treatment, literature guided that magnesium sulphate ($MgSO_4$) is a drug that is commonly used to pre vent eclampsia fits. In women with severe preeclampsia, the rate of seizures is 2.0% if magnesium sulphate is not given, but if given the rate of seizures decrease to 0.6%.[15] It stimulates the required chemicals at the neuromuscular junction and stabilizes the nerve axons as well. This standard preventative treatment for approaching eclampsia has been prophylaxis with $MgSO_4$, although its impact on ONSD in severely pre-eclamptic parturients has been least studied. Therefore, this study focuses on how eclampsia parturients with severe characteristics' ultrasonographically determined ONSD value changed after receiving MgSO4 medication for seizure prophylaxis. In simple terms, this study investigates the intravenous $MgSO_4$ effect on ultrasound measured ONSD as proxy of ICP in Eclampsia patients.

Methods

The study received ethical approval no. 00/24/23 from the ethical review board of Lahore General Hospital on 03/04/23. For every patient, written informed permission was acquired.

In this prospective observational study, sixty patients who met inclusion criteria which includes i) pregnancy and ii) severe symptoms of eclampsia as suggested in the literature were enrolled.[16] G-Power software was used to estimate sample size of 60 patients using 90% power of test with 95% confidence level, while considering the significant difference identified through t-test. This difference was based on baseline ONSD and after 1 hour of taking MgSO4 as mentioned in the literature.[17] Patients including in study are within age limit between 18-40 years, admitted in ICU and having singleton pregnancy. The patients excluded in study are those having glaucoma, cardiac diseases, chronic hypertension, cerebral disease, history of cranial or ocular procedures, and other eye pathologies. Furthermore, patients who received their $MgSO_4$ infusion prior to the initial ONSD reading were also excluded from study.

All eclampsia patients on $MgSO_4$ were admitted to the ICU for a minimum of 24 hours in accordance with the established practice mentioned in the literature[17] and institutional practice. Hourly assessments were made

of invasive blood pressure, along with constant monitoring of fluid intake and urine output. Every 12 hours, blood tests were conducted again to track liver transaminases, bilirubin, renal function, electrolytes, and complete blood count. For the prevention of eclampsia, 4 g of $MgSO_4$ was infused intravenously, followed by a 1 g/h infusion for 24 hours.

Ultrasound of eyes was performed in supine position using high frequency linear probe. Patients were asked to close both eyes and keeping thermal index less than 0.8, USG scan of both eyes was performed which showed 3 mm ONSD behind optic disc as a hypoechoic.

Demographic characteristics like age, parity, gestational age, BMI and symptoms of severe eclampsia like: headache, visual disturbance, optic nerve sheath diameter and serum magnesium level were observed as baseline before administration of $MgSO_4$ and at 1 hour, 6 hours, and 24 hours after finishing administration of loading dose of $MgSO_4$.

The data in the proforma was entered on SPSS version 25 and analyzed. Continuous data measured as mean ± SD using parameters like age, BMI, gestational age, ONSD and serum magnesium level were calculated with paired samples t-test and assessed with difference of means ONSD at various time points; baseline vs 1 hour, baseline vs 6 hours, baseline vs 24 hours. In this study, normality of quantitative data was also assessed through Saphrio-wilks test with p-value less than 0.05 as significant level.

Results

This ICU based study included a total of 60 patients who were recruited after careful observation on abovementioned criteria especially regarding Eclampsia. Average age of patients was 27.1 ± 5.3 years (range 20–40 years), and having a mean gestational age 33.5 ± 3.7 weeks. Patient's body mass index (BMI) was also measured and found that it was 28.5 ± 3.0 kg/m^2 (range 22.7–40.8 kg/m^2). All patients were presented with hypertension and 78% with visual disturbances. Further, the normality test; Shapiro–Wilk's test for normality was also used to test the normality of data which is basic assumption behind the paired samples t-test. These set of tests was performed at 5% level of significance. Paired samples t-test was used to assess the difference in ONSD caused by administration of $MgSO_4$. Based on time points six possible combinations were made and the presentation of these findings is mentioned in Table 1. Pair 1 means comparison between baseline ONSD and after 1 hour of taking MgSO4. This comparison shows that mean value of ONSD at baseline 0.651 that reduced to 0.623 after 1 hour of taking $MgSO_4$. The difference was 0.028 which was statistically significant at 5% level of significance as p-value is 0.000. Similar types of differences can be seen for other pairs as well. It showed that usage of $MgSO_4$ can continuously decrease the ONSD between 1, 6 and 24 hours. This decrease is statistically significant at each time point and visualized in Figure 1.

Additionally, simple linear regression analysis was also performed between ONDS and MAP for all time points; baseline, 1, 6 and 24 hours after taking $MgSO_4$.

Table 1: *Impact of MgSO4 on average ONSD at various time points*

		Mean	Std. Deviation	Mean Difference	Std. Error of Mean Difference	t-Statistic	P-value
Pair 1	Baseline	0.651	0.028	0.028	0.004	6.456	0.000
	After 1 Hour (taking $MgSO_4$)	0.623	0.022				
Pair 2	Baseline	0.651	0.028	0.113	0.005	21.441	0.000
	After 6 Hours (taking $MgSO_4$)	0.539	0.024				
Pair 3	Baseline	0.651	0.028	0.171	0.004	42.181	0.000
	After 24 Hours (taking $MgSO_4$)	0.480	0.016				
Pair 4	After 1 Hour (taking $MgSO_4$)	0.623	0.022	0.085	0.004	19.702	0.000
	After 6 Hours (taking $MgSO_4$)	0.539	0.024				
Pair 5	After 1 Hour (taking $MgSO_4$)	0.623	0.022	0.143	0.003	42.923	0.000
	After 24 Hours (taking $MgSO_4$)	0.480	0.016				
Pair 6	After 6 Hours (taking $MgSO_4$)	0.539	0.024	0.058	0.004	16.396	0.000
	After 24 Hours (taking $MgSO_4$)	0.480	0.016				

At all-time points it was observed that there was statistically insignificant relationship between MAP and ONSD. However, there was a continuous drop between this relationship and reflected in R2 at each time point 0.041, 0.032, 0.028 and 0.023, respectively (see Table 2).

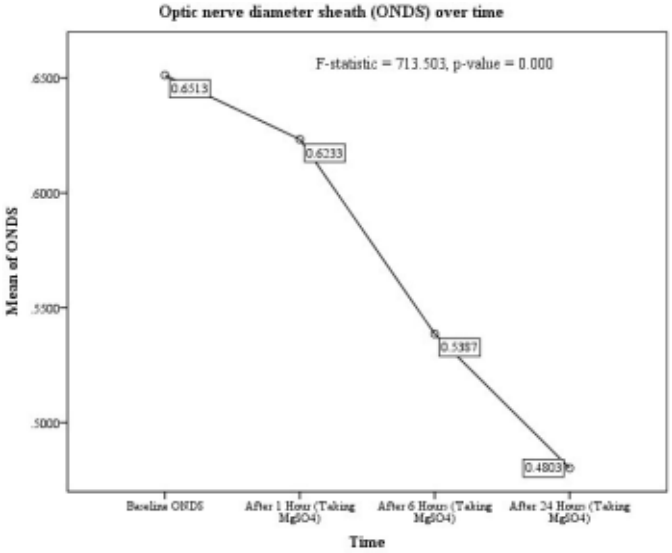

Figure 1: *Average level of ONDS overtime after taking Magnesium sulphate (MgSO4)*

Table 2: *Simple Linear Regression between ONSD and MAP at Various time points*

Sr. No	Measurement	R-Square	F-statistic	P-value
1	Baseline	0.041	1.29	0.324
2	After 1 hour (taking $MgSO_4$)	0.032	0.85	0.798
3	After 6 hour (taking $MgSO_4$)	0.028	0.42	0.876
4	After 24 hour (taking $MgSO_4$)	0.023	0.03	0.902

Discussion

The elevated level of ICP in severe eclampsia are detected by highly sensitive, invasive monitoring techniques that needs specialised knowledge, tools, and protocols to handle difficulties, which are not easily accessible in developing country like Pakistan. Thus, it becomes crucial to investigate more noninvasive methods of ICP evaluation which is reflection of eclampsia. Numerous researchers including Kshirsagar et al.,[18], Weidner et al.,[19] and Müller et al.,[20] have become interested in ONSD measurements due to its ability to quickly quantify ICP at the bedside and their validation in identifying symptoms of eclampsia with close clinical and laboratory surveillance to identify impending eclampsia. Kshirsagar et al., studied different correlation with GCS and ONSD which in results in inverse relationship, patient with low GCS have higher ONSD. Kshirsagar et al., also observed that the ONSD examination using ultrasound has good sensitivity (86.42%) and specificity (64.29%), further investigations displayed strong relationship of ONSD of 5.0 mm with ICP greater than 20 mm Hg.[18] Weidner et al. showed use of an intraparenchymatic P-tel probe using which real-time measurements of intracranial pressure (ICP) in awake patients is possible and results showed ultrasonographic measurement of ONSD could predict elevated ICP in specific patient cohort.[19] Muller et al., reviewed studies for non-invasive intracranial pressure monitoring including MR-ICP, TCD, ONSD, Ocular Vessels, Tympanic membranes and dielectric properties. Since neurological symptoms are the characteristic of deteriorating pre-eclampsia, ONSD evaluated by ultrasonography has been the focus of current study as a surrogate marker of rising ICP in pregnant women. All parturients involved in the current study had baseline measurements of ONSD that were significantly higher than expected, this was in agreement with the previous work reported by Omran et al., where correlation of MgSO4 therapy with the ONSD as substitute to ICP were studied in patients with severe traumatic brain injury and preeclampsia/eclampsia,[17] Biswas et al., compared ONSD measurements with the maternal and neonatal outcomes at cut-offs values of 5.8 and 4.6 mm at which the neurological manifestations became obvious,[14] Bala et al., demonstrated the relationship among elevated ICP and ONSD in patients suffering from preeclampsia and eclampsia when they employed any ultrasound procedure.[14,21] The results of this study are also aligned with few other pilot studies of this domain which have executed their studies in pre-eclampsia patients.[22] However, the study of Assu, et al., considered patients who have severe features of pre-eclampsia.[23]

In this study the impact of MgSO4 on ONSD in eclamptic women by employing ocular sonography as a bedside technique used to detect an increase in the ICP and monitor the effect of MgSO4. Additionally, the study demonstrated that at all assessed time points, there was no association between the MAP and ONSD. The women who have severe eclampsia or hypertension in pregnancy should have weekly monitoring to observe neurological signs and symptoms decreased after taking $MgSO_4$, and both systolic and diastolic blood pressure was also decreased. Further, severe maternal morbidity was significantly reduced when a standardized treatment

plan using IV blood pressure medication and MgSO4 was used for sustained severe maternal blood pressure.[23] This decrease may have resulted from the delivery of hypertension drugs or from the vasodilatory and anti-hypertensive properties of magnesium. It is not possible to fully ascribe this drop to $MgSO_4$ treatment because this study was not intended to establish a definitive association between this magnesium therapy and neurological symptoms or patient vitals. There could be various interpretations about the mechanism and function of magnesium sulphate. Like it can acts as a central anticonvulsant, guarding the blood-brain barrier (BBB) to prevent the formation of cerebral edoema, or working as a vasodilator.[24] It can also work as a calcium antagonist in calcium channels in vascular smooth muscle both intracellularly and extracellularly. This causes a drop in intracellular calcium levels, which has a vasodilator effect.[15] For hypertension encephalopathy, a condition in which sudden increases in BP lead to increased BBB and cerebral edoema, a vasodilator, such magnesium sulphate, would be a counterintuitive treatment option.

These results imply that patients have reduced values of ONSD, indicative of decreased level of ICP, because their neurological symptoms have improved after starting $MgSO_4$ medication. However, we must handle these high-risk patients with extreme vigilance, both before and after the delivery. Ocular sonography can be a helpful bedside technique during this time to aid the management of ICP in this high-risk pregnant population by noninvasively monitoring it.

As per our literature survey, there is no such study/ research reported in Pakistan with relationship of $MgSO_4$ dosage with ONSD as substitute of ICP in pregnant patient suffering from pre-eclamsia/ severe eclampsia. In observing the main focus is on strict inclusion criteria, strict observation and hourly invasive assessments. The use of $MgSO_4$ was reported by Dhandapani et al. for traumatic brain injury which results in decrease in intraoperative brain swelling and improved neurological output in the control group.[17,24,25]

The limitations of current study/research include that the negative correlation between drop in ONDS and MAP is due to cofounding effect of antihypertensive drugs and its withhold to patients (control group). Anesthesia dose effect on the ONSD measurement in patients need further estimation.

Conclusion

This study is designed to investigate the impact of $MgSO_4$ on ONSD in eclamptic women by employing ocular sonography as a bedside technique. This Pakistani study showed that in individuals with eclampsia, ONSD might be utilized to identify the presence of ICP and can track the effects of MgSO4 in eclampsia patients. Additionally, the study demonstrated that at all assessed time points, there was no association between the MAP and ONSD.

Ethical Approval: The Institutional Review Board, Postgraduate Medical Institute, Lahore, Ameer-ud-din Medical College, Lahore General Hospital, Lahore approved this study vide letter No Ref No. 00/24/23.

Conflict of Interest: The authors declare no conflict of interest.

Funding Source: None

Authors' Contribution:

AZ: Conception & design, drafting of article

SZ: Conception & design, final approval of the version to be published

ZS: Drafting of article, final approval of the version to be published

UZ: Acquisition of data, critical revision of the article

SG: Acquisition of data

RAA: Analysis & interpretation of data

MR: Analysis & interpretation of data

References

1. Chhabra S, Kumar N, Tejane H. Awareness of eclampsia among rural tribal women of reproductive age. Int. J. Gynecol. Obstet. 2024; 165 (2): 756-763. doi: 10. 1002/ ijgo.15320.
2. Leonard SA, Carmichael SL, Main EK, Lyell DJ, Abrams B. Risk of severe maternal morbidity in relation to prepregnancy body mass index: Roles of maternal co-morbidities and caesarean birth. Paediatr. Perinat. Epidemiol. 2020;34(4):460-468. doi: 10.1111/ppe. 12555.
3. Wang L, Di J, Wang Q, Zhang H, Zhao W, Shi X, et. al. Heat exposure induced risks of preterm birth mediated by maternal hypertension. Nat. Med. 2024; 30(7): 1974-1981. doi: 10.1038/s41591-024-03002-w.

4. Macedo TCC, Montagna E, Trevisan CM, Zaia V, de Oliveira R, Barbosa CP, et al. Prevalence of preeclampsia and eclampsia in adolescent pregnancy: A systematic review and meta-analysis of 291,247 adolescents worldwide since 1969. Eur. J. Obstet. Gynecol. Reprod. Biol. 2020; 248(1): 177-86. https://doi.org/10.1016/j. ejogrb. 2020.03.043.
5. Vousden N, Lawley E. Incidence of eclampsia and related complications across 10 low- and middle-resource geographical regions: Secondary analysis of a cluster randomised controlled trial. PLoS Med. 2019; 16(3): 1-15. https://doi.org/10.1371/journal.pmed.1002775
6. Wang L, Zhang C, Di L, Wang Q, Ren M, Huang A, et. al. Increased risk of preterm birth due to heat exposure during pregnancy: Exploring the mechanism of fetal physiology. Sci. Total Environ. 2024; 931(1): 172730. doi:10.1016/j.scitotenv.2024.172730.
7. Fishel Bartal M, Sibai BM. Eclampsia in the 21st century. Am. J. Obstet. Gynecol. 2022; 226(2): 1237-53.
8. Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia. Lancet (London, England). 2021;398(10297): 341-54.
9. Tejaswi MS, Kanthi MJ, Vinya P, Bhaskaran R. Urine Calcium-Creatinine Ratio in Prediction of Pre-eclampsia. J. Obstet. Gynaecol. India. 2023;73(1):51-56. doi: 10. 1007/s13224-022-01712-0.
10. Simenc GB, Ambrozic J, Prokselj K, Tul N, Cvijic M, Mirkovic T, et al. Ocular ultrasonography for diagnosing increased intracranial pressure in patients with severe preeclampsia. Int. J. Obstet. Anesth. 2018;36(1):49-55.
11. Hanafi MG, Verki MM, Parei SN. Ultrasonic Assessment of Optic Nerve Sheath to Detect Increased Intracranial Pressure. J Med Ultrasound. 2019;27(2):69-74. doi:10.4103/JMU.JMU-54-18.
12. Kim S-E, Hong EP, Kim HC, Lee SU, Jeon JP. Ultrasonographic optic nerve sheath diameter to detect increased intracranial pressure in adults: a meta-analysis. Acta Radiol. 2019;60(2):221-9.
13. Evensen KB, Eide PK. Measuring intracranial pressure by invasive, less invasive or non-invasive means: limitations and avenues for improvement. Fluids Barriers CNS. 2020;17(1):1-33. doi:10.1186/s12987-020-00195-3.
14. Biswas J, Khatun N. Optic nerve sheath diameter measurements using ultrasonography to diagnose raised intracranial pressure in preeclampsia: an observational study. J. Turk. Ger. Gynecol. Assoc. 2023;24(1):5-11.
15. Liu Y, Li D, Wang Y, Qi H, Wen L. Impact of Gestational Diabetes and Hypertension Disorders of Pregnancy on Neonatal Outcomes in Twin Pregnancies Based on Chorionicity. J Clin Med. 2023;12(3):1-10. doi:10.3390/jcm12031096.
16. Tang S, Liu Y, Gu Y, Yang Q, Wang Q. Effects of electronic screen exposure time on hypertensive disorders in pregnancy: a retrospective cohort study. BMC public health. 2024;24(1):1-8. https://doi.org/10.1186/s12889-024- 18793-3.
17. Omran AS, El Ansari T, Riad W. Effect of magnesium sulphate on the intracranial pressure of preeclampsia patients using ultrasound-guided optic nerve sheath diameter: A pilot study. Saudi J. Anaesth. 2021; 15(1): 14-8.
18. Kshirsagar SJ, Pande AH, Naik SV, Yadav A, Sakhala RM, Salve SM, et al. Bedside ultrasonographic evaluation of optic nerve sheath diameter for monitoring of intracranial pressure in traumatic brain injury patients: a cross sectional study in level II trauma care center in India. Acute Crit. Care. 2024;39(1):155-61.
19. Weidner N, Kretschmann J, Bomberg H, Antes S, Leonhardt S. Real-Time Evaluation of Optic Nerve Sheath Diameter (ONSD) in Awake, Spontaneously Breathing Patients. J. Clin. Med. 2021;10(16):1-9. doi:10.3390/jcm10163549.
20. Müller SJ, Henkes E, Gounis MJ, Felber S, Ganslandt O, Henkes H. Non-Invasive Intracranial Pressure Monitoring. J. Clin. Med. 2023;12(6): 1-27. 9. https://doi.org/10.3390/jcm12062209.
21. Bala R, Banerjee A, Taxak S, Kumar R. Optic Nerve Sheath Diameter Measured Using Ocular Sonography is Raised in Patients With Eclampsia. Int. J. Obstet. Anesth. 2019;9(2): 65-69. doi: 10.4103/joacc. JOACC - 1-19
22. Assu SM, Bhatia N. Sonographic Optic Nerve Sheath Diameter Following Seizure Prophylaxis in Pre-Eclamptic Parturients With Severe Features: A Prospective, Observational Study. J. Ultrasound Med. 2021;40(11):2451-7.
23. Shields LE, Wiesner S, Klein C, Pelletreau B, Hedriana HL. Early standardized treatment of critical blood pressure elevations is associated with a reduction in eclampsia and severe maternal morbidity. Am. J. Obstet. Gynecol. 2017; 216(4):415. 1-5.
24. Bakrania BA, George EM, Granger JP. Animal models of preeclampsia: investigating pathophysiology and therapeutic targets. Am. J. Obstet. Gynecol. 2022; 226 (2):973-87.
25. Dhandapani S, Aditya G, S V, Sharma B, Ak M. Randomized controlled trial of magnesium sulphate in severe closed traumatic brain injury. Indian J. Neurotrauma. 2008; 5 (1): 27-33. https://doi.org/10.1016/S0973-0508 (08)80025-1.