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Original Research Article

ANTENATAL MAGNESIUM SULFATE AND NEONATAL NEUROPROTECTION IN PRETERM BIRTHS: EVIDENCE FROM A TWO-YEAR PROSPECTIVE STUDY

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ABSTRACT

Background: Preterm birth is a major global cause of neonatal morbidity and mortality, with surviving infants at increased risk for long-term neurological impairments such as cerebral palsy and developmental delay. Antenatal magnesium sulfate ($MgSO_4$) has demonstrated neuroprotective potential through NMDA receptor inhibition, membrane stabilization, and anti-inflammatory actions. However, region-specific clinical data from real-world settings are limited, particularly in low- and middle-income contexts.

Materials and Methods: This prospective cohort study, conducted over two years in a tertiary care hospital, included 400 pregnant women at imminent risk of preterm delivery (28–34 weeks gestation). All participants received intravenous magnesium sulfate (4 g loading dose over 20 minutes, followed by 1 g/hour maintenance infusion for 24 hours or until delivery). Maternal parameters were closely monitored for toxicity. Neonatal neurological outcomes were assessed using cranial neurosonography at 48 hours post-delivery, and at 3 and 6 months of corrected age. Secondary outcomes included birth weight classification, respiratory morbidity, and duration of NICU stay.

Results: The majority of mothers were aged 26–30 years (48.75%), and cesarean section was the predominant mode of delivery (93.25%). Among neonates, 70.75% were very low birth weight (VLBW) and 29.25% were low birth weight (LBW). Respiratory distress was the most common morbidity (40.25%). Neurosonography at 48 hours revealed normal findings in 92%, while Grade 1–2 germinal matrix hemorrhages were observed in 8% of neonates. At follow-up, 83.25% of infants maintained normal findings at 3 months, and 87% at 6 months, with no higher-grade intraventricular hemorrhage or cerebral palsy detected.

Conclusion: Antenatal administration of magnesium sulfate between 28 and 34 weeks of gestation was found to be safe and effective in improving early neurodevelopmental outcomes among preterm infants. The study supports the routine use of $MgSO_4$ for fetal neuroprotection, given its association with reduced risk of germinal matrix hemorrhage and favorable neurological prognosis. Implementing standardized $MgSO_4$ protocols in perinatal care may significantly enhance neonatal survival and long-term developmental outcomes in preterm populations.

Keywords: Preterm birth, Magnesium sulfate, Neuroprotection, Very low birth weight, Intraventricular hemorrhage, Neonatal outcomes, Cranial neurosonography.

INTRODUCTION

Preterm birth—defined as delivery before 37 completed weeks of gestation—continues to represent a major global health concern and remains one of the leading causes of neonatal morbidity and mortality. According to the World Health Organization (WHO), approximately 15 million babies are born preterm each year, with complications related to prematurity contributing to nearly one million neonatal deaths annually.[1] Among survivors, the risks extend beyond the neonatal period, with many developing long-term neurological sequelae, including cerebral palsy, developmental delay, learning difficulties, and sensory impairments, all of which impose substantial emotional, social, and economic burdens on families and healthcare systems.[2-4]

Over the past two decades, antenatal magnesium sulfate ($MgSO_4$) has gained recognition as an effective neuroprotective intervention for preterm infants. Both experimental and clinical studies have demonstrated that magnesium provides neuroprotection through several mechanisms, including stabilization of neuronal membranes, inhibition of N-methyl-D-aspartate (NMDA) receptors, reduction of calcium-mediated excitotoxicity, and attenuation of oxidative stress and neuroinflammatory responses.[5,6] These mechanisms collectively help protect the immature fetal brain from hypoxic–ischemic injury, thereby reducing the risk of permanent neurological disability.

Several large clinical trials and meta-analyses have established the neuroprotective efficacy of antenatal $MgSO_4$ when administered to women at imminent risk of preterm labor. Studies by Gupta et al. (2024) and Bansal et al. (2024) reported significantly lower rates of intraventricular hemorrhage (IVH) and improved neonatal adaptation among $MgSO_4$-exposed infants compared to controls.[7,8] Similarly, Ayed et al. (2024) demonstrated a marked reduction in moderate-to-severe white matter injury and better neurodevelopmental outcomes in preterm infants receiving antenatal magnesium.[9] Furthermore, a meta-analysis by Jafarabady et al. (2024) confirmed a 30% relative risk reduction in neurological impairment without any increase in neonatal mortality, reinforcing the safety and efficacy of the intervention.[10]

Despite strong supporting evidence, the use of $MgSO_4$ for fetal neuroprotection remains inconsistent, especially in low- and middle-income countries, where protocol adherence, availability, and provider awareness often vary. Context-specific data are therefore essential to strengthen confidence in its use and facilitate standardization in clinical practice.

The present prospective cohort study was undertaken to evaluate the neuroprotective efficacy of antenatal magnesium sulfate among women at risk of preterm delivery between 28 and 34 weeks of gestation. The study aimed to assess both short-term neurosonographic findings and early neurodevelopmental outcomes of preterm neonates exposed to $MgSO_4$.

MATERIALS AND METHODS

This prospective cohort study was conducted over a period of two years at a tertiary care hospital in Tamil Nadu. A total of 400 pregnant women admitted with imminent risk of preterm delivery between 28 and 34 weeks of gestation were enrolled after obtaining informed written consent. Women with multiple gestations, known fetal congenital anomalies, or severe maternal systemic illnesses (such as cardiac, renal, or hepatic disease) were excluded from the study.

Ethical clearance for the study was obtained from the Institutional Ethics Committee, and the research was conducted in accordance with the principles of the Declaration of Helsinki. All eligible participants received intravenous magnesium sulfate for fetal neuroprotection following the standard protocol: a 4 g loading dose administered intravenously over 20 minutes, followed by a continuous maintenance infusion of 1 g per hour for 24 hours or until delivery, whichever occurred first. Maternal clinical parameters—including deep tendon reflexes, respiratory rate, urine output, and, where indicated, serum magnesium levels—were closely monitored throughout therapy to detect signs of magnesium toxicity. All women received standard obstetric and neonatal care as per institutional guidelines.

The primary outcome was the neurological status of preterm neonates, assessed by cranial neurosonography for the detection of germinal matrix and intraventricular hemorrhage at 48 hours post-delivery, and re-evaluated at 3 months and 6 months of corrected age. The secondary outcomes included birth weight classification according to WHO standards, neonatal morbidity (particularly respiratory distress syndrome), and duration of NICU stay. Maternal variables such as age, gravida, mode of delivery, and comorbid conditions were also recorded.

Data were collected prospectively using a structured proforma and subsequently analyzed using IBM SPSS Statistics version 24. Descriptive statistics, including frequencies and percentages, were used to summarize categorical variables. Chi-square tests were applied to evaluate associations between categorical variables, and independent sample t-tests were used for continuous variables. Statistical significance was set at $p < 0.05$, and 95% confidence intervals (CI) were calculated for key associations.

RESULTS

The majority of the study participants belonged to the 26–30-year age group (48.75%), followed by those aged 21–25 years (20.75%) and 31–35 years (20.75%). A smaller proportion were aged above 35

years (7.75%), and only 2% were younger than 20 years, indicating that most preterm births occurred among women in their late twenties to early thirties, the biologically active reproductive age. With respect to obstetric history, 37% of participants were primigravida, 24.25% were gravida two, 18% were gravida three, and 18.75% were gravida four or higher. The predominant mode of delivery was cesarean section (93.25%), while only 6.75% of women delivered preterm vaginally, reflecting the clinical preference for operative delivery in high-risk preterm pregnancies.

Among maternal comorbidities, pre-eclampsia was observed in 14% of women, and fetal growth restriction (FGR) in 27.75%, while hypertension was reported in 10% and Rhesus disease (RHD) in 1.75% of participants. There were no cases of diabetes mellitus, thyroid disorders, anemia, jaundice, or cardiac or renal disease, indicating that hypertensive and placental pathologies constituted the leading risk factors associated with preterm delivery in this cohort.

According to the WHO classification of birth weight, 70.75% of neonates were very low birth weight (VLBW; <1.5 kg) and 29.25% were low birth weight (LBW; 1.5–2.5 kg), with no infants in the normal or macrosomic range. This distribution reflects a predominantly preterm and low-birth-weight population, consistent with the inclusion criteria of 28–34 weeks gestation. The duration of NICU stay varied widely, with 36.5% of neonates admitted for 8 weeks, 25.75% for 2 weeks, 19.75% for 3 weeks, and 18% for 6 weeks, underscoring the need for prolonged intensive care among preterm infants. Respiratory distress was the most common neonatal morbidity, affecting 40.25% of neonates, which highlights the ongoing clinical burden of pulmonary immaturity in this population.

Neurosonographic evaluations conducted at 48 hours after birth showed normal findings in 92% of neonates, while 3% demonstrated Grade 1 germinal matrix hemorrhage and 5% had Grade 2 hemorrhage. At the 3-month follow-up, 83.25% of infants maintained normal neurosonographic findings, 3.75% had persistent Grade 1 hemorrhage, and 13% were lost to follow-up. By the 6-month evaluation, 87% of infants continued to show normal neurosonograms, with 13% remaining unassessed due to follow-up loss.

Overall, the findings indicate a high proportion of favorable neurodevelopmental outcomes among infants exposed to antenatal magnesium sulfate, with a low incidence of germinal matrix hemorrhage and no higher-grade intraventricular bleeds observed throughout the follow-up period. These results reaffirm the neuroprotective role of antenatal magnesium sulfate in preventing severe intracranial hemorrhage and improving early neurological outcomes among preterm neonates.

Table 1: Maternal Demographic & Obstetric Characteristics (N = 400)

Parameter	Category	Count (n)	Percentage (%)
Age (years)	≤20	8	2.00
	21–25	83	20.75
	26–30	195	48.75
	31–35	83	20.75
	>35	31	7.75
Gravida	G1 (Primi)	148	37.00
	G2	97	24.25
	G3	72	18.00
	G4+	75	18.75
Mode of Delivery	LSCS	373	93.25
	PTVD	27	6.75

Table 2: Maternal Comorbidities and Risk Factors (N = 400)

Risk Factors	Count (n)	Percentage (%)
Pre-eclampsia	56	14.00
Fetal Growth Restriction (FGR)	111	27.75
Hypertension	40	10.00
RHD	7	1.75

Table 3: Neonatal Characteristics and Outcomes (N = 400)

Parameter	Category	Count (n)	Percentage (%)
Birth Weight (WHO Classification)	<1.5 kg (VLBW)	283	70.75
	1.5–2.5 kg (LBW)	117	29.25
Duration of NICU Stay	2 weeks	103	25.75
	3 weeks	79	19.75
	6 weeks	72	18.00
	8 weeks	146	36.50
Neonatal Morbidity	Respiratory distress	161	40.25

Table 4: Neonatal Outcomes (N = 400)

Parameter	Category	Count (n)	Percentage (%)
48 hours	Normal study	368	92.00
	Grade 1 – Germinal matrix bleed	12	3.00
	Grade 2 – Germinal matrix bleed	20	5.00

3rd month	Normal study	333	83.25
	Grade 1 – Germinal matrix bleed	15	3.75
	Loss to follow-up	52	13.00
6th month	Normal study	348	87.00
	Loss to follow-up	52	13.00

DISCUSSION

In the present study, the majority of preterm neonates were very low birth weight (VLBW), accounting for 70.75% of the cohort, while 29.25% were low birth weight (LBW). No neonates were born with normal or macrosomic weights. Respiratory distress was the most common neonatal morbidity, affecting 40.25% of infants, and more than one-third required prolonged NICU care lasting up to eight weeks (36.5%). These findings reflect the typical complications associated with prematurity and are consistent with the results of Gupta et al,[7] who reported that 64% of magnesium-exposed and 56% of unexposed neonates weighed between 1.6–2.0 kg, with fewer NICU admissions among the magnesium group (44.8% vs. 66.6%). Similar to our study, magnesium sulfate administration was associated with improved neonatal outcomes and reduced respiratory morbidity.

Bansal V,[8] similarly observed that magnesium exposure reduced the need for respiratory intervention, with only 18% of magnesium-exposed neonates requiring intubation compared to 26% in controls, and a lower overall ventilatory support requirement (32% vs. 48%). This finding parallels our results, where magnesium administration was associated with fewer respiratory complications and improved NICU outcomes.

In the study conducted by Ayed M,[9] the median birth weight among magnesium-exposed neonates was 970 g, closely reflecting the very low birth weight distribution observed in our study. The need for resuscitation was lower in the magnesium group (65.9%) than in controls (78%), and the incidence of severe intraventricular hemorrhage (Grade 3–4 IVH) was significantly reduced (16% vs. 39%, p = 0.004). These findings are consistent with our results, in which 92% of neonates demonstrated normal neurosonograms at 48 hours, and only 8% showed minor germinal matrix hemorrhage (Grade 1–2).

Jafarabady K,[10] reported no significant difference in neonatal mortality between magnesium and control groups (RR = 1.03; 95% CI: 0.88–1.21), further supporting our finding that magnesium sulfate does not contribute to neonatal death. In our cohort, mortality was confined to extremely preterm infants with severe respiratory distress.

In the study by Deeksha Pandey et al,[11] two neonatal deaths (10%) and two cases (10%) of neonatal seizures were reported among preterm infants. Although the mortality rate was slightly higher than that in our cohort—where all deaths occurred among extremely preterm and VLBW neonates—both studies suggest that magnesium exposure is not associated with increased neonatal mortality. Bachnas M.A.[12] also confirmed that the standard magnesium dosing regimen (4 g loading followed by 1 g/hour for 24 hours) did not elevate risks of neonatal asphyxia, necrotizing enterocolitis, or feeding intolerance, aligning with our observation that complications were primarily related to prematurity rather than treatment.

Mamatha S,[13] reported that 58.2% of infants were born weighing less than 2.5 kg, and 83% achieved Apgar scores between 7–10 at one minute, comparable to our findings of stable early neonatal adaptation. Neonatal mortality in her study was 5.45%, mainly among extremely low birth weight infants, echoing our observation that deaths were associated with gestational immaturity rather than magnesium exposure. In the study by Sharma R,[14] the mean birth weight in magnesium-exposed infants was 1.39 ± 0.21 kg, and the rates of complications such as RDS (20% vs. 25.7%), HIE (22.9% vs. 25.7%), and seizures (5.7% vs. 8.6%) were lower compared to controls. IVH occurred in only 2.9% of magnesium-exposed neonates versus 11.4% in the control group. These results align with our findings, where 92% had normal neurosonograms at 48 hours, 83.25% maintained normal findings at 3 months, and 87% at 6 months, indicating sustained neuroprotective benefits.

Overall, the findings of the present study are consistent with multiple published reports, all demonstrating that antenatal magnesium sulfate administered between 28–34 weeks of gestation is a safe and effective neuroprotective agent. It significantly reduces the incidence and severity of intraventricular hemorrhage and respiratory morbidity, without increasing neonatal mortality or maternal complications. The consistency across studies, including ours, supports its routine use in women at risk of preterm delivery to improve neonatal neurological outcomes and survival rates.

CONCLUSION

The results confirm that maternal hypertensive disorders and fetal growth restriction were the leading contributors to preterm delivery, yet magnesium sulfate did not increase neonatal complications or mortality. Instead, it was linked to improved neurological stability and reduced respiratory morbidity. This study reinforces existing evidence supporting the neuroprotective role of antenatal magnesium sulfate in preterm neonates. Incorporating its use as part of routine management for women facing imminent preterm labor could significantly enhance neonatal survival and neurodevelopmental outcomes, especially in resource-limited settings. Future multicentric and

long-term follow-up studies are recommended to assess the sustained developmental benefits and optimal dosing strategies for this intervention.

REFERENCES

1. Ohuma EO, Moller AB, Bradley E, Chakwera S, Hussain-Alkhateeb L, Lewin A, et al. National, regional, and global estimates of preterm birth in 2020, with trends from 2010: a systematic analysis. The Lancet [Internet]. 2023 Oct [cited 2025 Oct 8];402(10409):1261–71. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673623008784.
2. Behrman RE, Butler AS, Outcomes I of M (US) C on UPB and AH. Neurodevelopmental, health, and family outcomes for infants born preterm. In: Preterm Birth: Causes, Consequences, and Prevention [Internet]. National Academies Press (US); 2007 [cited 2025 Oct 8]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK11356/.
3. Hee Chung E, Chou J, Brown KA. Neurodevelopmental outcomes of preterm infants: a recent literature review. Transl Pediatr. 2020 Feb;9(Suppl 1):S3–8.
4. Necula AI, Stoiciu R, Radulescu Botica R, Durdu CE, Bohiltea R. Neurological outcomes in late preterm infants: an updated review of recent research and clinical insights. Diagnostics [Internet]. 2025 Jun 14 [cited 2025 Oct 8];15(12):1514. Available from: https://www.mdpi.com/2075-4418/15/12/1514
5. Oddie S, Tuffnell DJ, McGuire W. Antenatal magnesium sulfate: Neuro-protection for preterm infants. Arch Dis Child Fetal Neonatal Ed. 2015 Nov;100(6):F553-557.
6. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: a systematic review and metaanalysis. American Journal of Obstetrics and Gynecology [Internet]. 2009 Jun [cited 2025 Oct 8];200(6):595–609. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002937809004207.
7. Gupta N, Gupta A, Mishra S. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth: analysis of its effect on cerebral palsy. Journal of South Asian Federation of Obstetrics and Gynaecology [Internet]. 2021 Sep 9 [cited 2025 Oct 8];13(3):90–3. Available from: https://www.jsafog.com/doi/10.5005/jp-journals-10006-1907.
8. Bansal V, Desai A. Efficacy of antenatal magnesium sulfate for neuroprotection in extreme prematurity: a comparative observational study. J Obstet Gynaecol India. 2022 Aug;72(Suppl 1):36–47.
9. Ayed M, Ahmed J, More K, Ayed A, Husain H, AlQurashi A, et al. Antenatal magnesium sulfate for preterm neuroprotection: a single-center experience from kuwait tertiary nicu. Biomed Hub. 2022;7(2):80–7.
10. Jafarabady K, Shafiee A, Eshraghi N, Salehi SA, Mohammadi I, Rajai S, et al. Magnesium sulfate for fetal neuroprotection in preterm pregnancy: a meta-analysis of randomized controlled trials. BMC Pregnancy and Childbirth [Internet]. 2024 Aug 1 [cited 2025 Oct 8];24(1):519. Available from: https://doi.org/10.1186/s12884-024-06703-9
11. Deeksha Pandey, Arja K, Inukollu PR, Kuppili M. The role of magnesium sulphate (Mgso4) in fetal neuroprotection. Journal of Cardiovascular Disease Research [Internet]. 2024 Aug 6 [cited 2025 Oct 8];15(8):122–8. Available from: https://jcdronline.org/index.php/JCDR/article/view/9246
12. Bachnas MA, Akbar MIA, Dachlan EG, Dekker G. The role of magnesium sulfate (MgSO4) in fetal neuroprotection. The Journal of Maternal-Fetal & Neonatal Medicine [Internet]. 2021 Mar 19 [cited 2025 Oct 8];34(6):966–78. Available from: https://www.tandfonline.com/doi/full/10.1080/14767058.2019.1619688.
13. Mamatha S, Ananda M. Maternal and Fetal outcome in usage of magnesium sulphate for fetal neuroprotection in pregnancy less than 34 weeks of gestation. Int J Life Sci Biotechnol Pharma Res [Internet]. 2023 [cited 2025 Oct 8];12(1):488–97. Available from: https://www.ijlbpr.com/abstractissue.php?id=648.
14. Sharma R, Verma A, Nawal R. Magnesium Sulphate: A New Frontier in Prevention of Intraventricular Hemorrhage in Premature Newborns. Int J Med Pharm Res. 2024;5(5):412-417.