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Beneficial Effect of Intravenous Magnesium Sulphate in Term Neonates with Perinatal Asphyxia

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ABSTRACT

Background: Hypoxic ischemic encephalopathy (HIE) is a significant contributor to neonatal morbidity and mortality. This study evaluated the clinical impact of intravenous magnesium sulphate in term neonates with HIE. **Methods:** A descriptive case series was conducted at the Department of Pediatrics, Jinnah Hospital Lahore, from March 1, 2025 to June 01, 2025. One hundred thirty-eight term neonates meeting diagnostic and severity criteria for HIE were enrolled. Severity was assessed using the Thomson score. All neonates received standard intensive care and intravenous magnesium sulphate at 250 mg/kg over 30 minutes on admission, with repeat doses at 24 and 48 hours. Outcomes were monitored over a 7-day period, including return to normal neurological status, seizure occurrence, establishment of suck feeding, and mortality. Data were analyzed using SPSS version 22. **Results:** The mean gestational age was 38.4 ± 1.1 weeks, with a mean birth weight of 2985 ± 355 grams. Of the 138 neonates, 82 (59.4%) were male and 56 (40.6%) were female; 44 (31.9%) had HIE grade I, 70 (50.7%) grade II, and 24 (17.4%) grade III. Following therapy, the mean Thomson score decreased from 13.1 ± 2.9 to 1.5 ± 1.2 by day 7. Return to normal neurological status was documented in 101 (73.2%) neonates. Seizure activity occurred in 36 (26.1%). The ability to establish effective suck feeding by day 7 was achieved in 110 (79.7%) neonates. Mortality within seven days was observed in 12 (8.7%) cases. **Conclusion:** The addition of intravenous magnesium sulphate to standard management was associated with substantial neurological recovery, improved feeding outcomes, and low short-term mortality in term neonates with HIE.

INTRODUCTION

Hypoxic ischemic encephalopathy (HIE) or perinatal asphyxia is a critical condition among neonates resulting from complex physiological, molecular and cellular changes occurring due to severe lack of supply of oxygen to brain leading to critical brain injury [1]. Neonates that suffer from hypoxic ischemic encephalopathy are highly prone to premature mortality and multiple serious life-long morbidities including seizures, impaired levels of consciousness, breathing disorders, hypotonia and long term chronic conditions like cerebral palsy, intellectual disability, mental retardation and epilepsy [2]. It is a fairly common condition with reported incidence of 6–10 newborns developing hypoxic ischemic encephalopathy per 1000 live full-term birth [3].

Multiple modes of interventions have been under investigation for the management of hypoxic ischemic encephalopathy (HIE) including melatonin, therapeutic hypothermia and magnesium sulphate. Although therapeutic hypothermia is a very useful intervention for the management of hypoxic ischemic encephalopathy, management of severe hypoxic ischemic encephalopathy results in increased costs, making it difficult to use as standard care for HIE in resource depleted and poor countries like Pakistan [4–6]. Similarly, melatonin is another intervention efficacy of which in reducing oxidative stress has been demonstrated in animal models but human trials including newborns are still lacking [7]. Use of intravenous magnesium sulphate has been reported to be particularly useful in recent times for the management of hypoxic ischemic encephalopathy [8]. However, there are also studies that have shown that the use of magnesium sulphate is not associated with significant improvement in the outcome of neonates suffering from hypoxic ischemic encephalopathy (HIE) [9,10].

A study reported that use of magnesium sulphate in addition to standard treatment, as compared to placebo, significantly improved the outcome of neonates with hypoxic ischemic encephalopathy with reported

occurrence of seizures [77.5% vs 82.5%, respectively], ability to suck feed [67.5% vs 40%, respectively; p = 0.004], return to normal neurological status at discharge [65% vs 37.5%] and mortality [25% vs 35%, respectively] [11]. On the other hand, a study reported that there was no statistically significant difference between addition of magnesium sulphate to standard therapy and placebo in terms of mortality [10% vs 10%, respectively; p = 1] and occurrence of seizures [17% vs 44%, respectively; p = 0.1] but use of magnesium sulphate was associated with significantly better outcome than placebo in terms of ability to suck feed [77% vs 37%, respectively; p = 0.02] [12].

Since results of previous studies regarding the role of intravenous magnesium sulphate among term neonates presenting with hypoxic ischemic encephalopathy are controversial. This makes it imperative to further research beneficial effects of this highly practical and cost effective mode of intervention to save precious lives to contribute in reduction of already high infant mortality rate in Pakistan and reduce the incidence of associated neurodevelopmental disabilities like cerebral palsy and mental retardation. This will be achieved by determining the outcomes of HIE in neonates treated with MgSO4 in addition to standard treatment.

MATERIALS AND METHODS

This descriptive case series was conducted in the Department of Pediatrics, Jinnah Hospital Lahore, from March 01, 2025 to June 01, 2025. The study was initiated following approval from the Institutional Review Board, and written informed consent was obtained from the parents or legal guardians of all enrolled neonates.

Eligible participants included term neonates, defined as infants born at a gestational age of 37 weeks or greater. Diagnosis of hypoxic ischemic encephalopathy (HIE) was established by a consultant pediatrician based on the requirement for neonatal resuscitation at birth and Apgar scores of ≤3 at one minute and ≤7 at five minutes [12]. Severity of HIE was graded using the Thomson score, which comprehensively assesses neurological function based on muscle tone, level of consciousness, seizure activity, posture, Moro and grasp reflexes, suck reflex, respiratory pattern, and fontanel tension. Scores for each domain range from 0 to 3, with total scores of 1–10 indicating grade I, 11–14 indicating grade II, and 15 or more indicating grade III HIE. Exclusion criteria included the presence of congenital malformations, maternal administration of general anesthesia, maternal receipt of magnesium sulphate or anticonvulsants, or failure to meet the operational definition of HIE.

All neonates received standard intensive care management. In addition, intravenous magnesium sulphate was administered at a dose of 250 mg/kg diluted in 10 ml of 10% dextrose, infused over 30 minutes, once daily on admission, and repeated at 24 and 48 hours. Clinical monitoring included regular assessment of pulse rate, respiratory rate, blood pressure, capillary refill time, and oxygen saturation before, during, and after each infusion. Baseline characteristics, including gestational age, gender, birth weight, mode of delivery, and initial Thomson score, were recorded at enrollment. The primary outcome was return to normal neurological status, defined as a reduction in Thomson score to zero on day 7 post-therapy. Secondary outcomes included occurrence of clinically observed seizures during the first seven days, ability to achieve effective oral feeding by day 7, and all-cause mortality during the 7-day study period. Outcome assessments were performed by a consultant pediatrician, and patient confidentiality was strictly maintained through assignment of anonymized study codes.

Data were analyzed using SPSS version 22. Quantitative variables, such as gestational age, birth weight, and Thomson scores, were summarized as mean and standard deviation. Qualitative variables, including gender, mode of delivery, HIE grade, and clinical outcomes, were presented as frequencies and percentages. Stratification was performed for gestational age, gender, birth weight, mode of delivery, and HIE grade to adjust for potential effect modifiers. The Chi-square test was used to compare categorical variables, and the Student t-test was used for continuous variables, with statistical significance set at a p-value of ≤0.05.

RESULTS

A total of 138 term neonates with hypoxic ischemic encephalopathy were enrolled in the study. The mean gestational age was 38.4 ± 1.1 weeks, and the mean birth weight was 2985 ± 355 grams. Of the total, 82 (59.4%) were male and 56 (40.6%) were female. Spontaneous vaginal delivery was observed in 84 neonates (60.9%), while 54 (39.1%) were delivered via cesarean section. The mean baseline Thomson score at admission was 13.1 ± 2.9. Distribution by HIE grade revealed that 44 (31.9%) were classified as grade I, 70 (50.7%) as grade II, and 24 (17.4%) as grade III.

Table 1

Baseline Characteristics of Study Population (n = 138)

Variable	Value/Category	Frequency (%) / Mean ± SD
Gestational age (weeks)	–	38.4 ± 1.1
Gender	Male	82 (59.4)
	Female	56 (40.6)
Birth weight (grams)	–	2985 ± 355
Mode of delivery	Spontaneous vaginal	84 (60.9)
	Cesarean section	54 (39.1)
Baseline Thomson score	–	13.1 ± 2.9
HIE Grade	I	44 (31.9)
	II	70 (50.7)
	III	24 (17.4)

Following intravenous magnesium sulphate therapy, there was a marked reduction in neurological impairment. By day 7, the mean Thomson score declined to 1.5 ± 1.2. A return to normal neurological status was documented in 101 neonates (73.2%). Seizure activity was noted in 36 (26.1%) patients during the observation period. The ability to establish effective suck feeding by day 7 was achieved in 110 (79.7%) neonates. Overall, mortality within the seven-day period was 12 (8.7%).

Table 2

Primary Clinical Outcomes at Day 7 Post-Therapy (n = 138)

Outcome	Frequency (%) / Mean ± SD
Day 7 Thomson score	1.5 ± 1.2
Return to normal neurological status	101 (73.2)

Seizures during observation	36 (26.1)
Ability to suck feed (Day 7)	110 (79.7)
Mortality (within 7 days)	12 (8.7)

Stratified analysis by grade of hypoxic ischemic encephalopathy revealed significant differences across all major outcomes ($p < 0.001$ for each, Chi-square test). Neonates with HIE grade I demonstrated the highest rates of neurological recovery (95.5%) and ability to suck feed (95.5%), with minimal incidence of seizures (6.8%) and no mortality. Among those with HIE grade II, 75.7% achieved normal neurological status, and 85.7% established suck feeding; seizures were observed in 25.7%, and mortality occurred in 3 patients (4.3%). Outcomes were poorest in HIE grade III, where only 29.2% returned to normal neurological status and 33.3% established suck feeding, while seizures occurred in 62.5% and mortality in 37.5% of cases.

Table 3

Outcomes Stratified by Grade of HIE (n = 138)

Outcome	HIE I (n=44)	HIE II (n=70)	HIE III (n=24)	p-value (χ^2)
Return to normal neurological status (%)	42 (95.5)	53 (75.7)	7 (29.2)	<0.001
Seizures (%)	3 (6.8)	18 (25.7)	15 (62.5)	<0.001
Suck feeding at Day 7 (%)	42 (95.5)	60 (85.7)	8 (33.3)	<0.001
Mortality (%)	0 (0)	3 (4.3)	9 (37.5)	<0.001

DISCUSSION

The present study provides robust evidence supporting the beneficial role of intravenous magnesium sulphate in improving short-term neurological and feeding outcomes among term neonates with hypoxic ischemic encephalopathy (HIE). Analysis of 138 neonates demonstrated a high proportion of neurological recovery, early establishment of effective feeding, and low short-term mortality, with pronounced differences observed across HIE severity grades.

A key finding in this study was the return to normal neurological status by day 7 in 73.2% of neonates. This outcome is consistent with the prospective data from Ichiba et al., where 73.3% of neonates achieved normal neurodevelopmental outcomes at 18 months following magnesium sulphate administration, despite the inclusion of only severe cases and a longer-term assessment [13]. Furthermore, Sajid et al. reported significant neurological improvement in 75.8% of neonates in the magnesium group, in contrast to 45.4% in the placebo group, at the time of discharge [6]. The similarity in recovery rates across these studies strengthens the evidence that magnesium sulphate facilitates meaningful early neurological improvement.

Savitha and Rajprakash further documented neurological recovery within four days in 84% of neonates receiving magnesium compared to 53% in the standard care group [14]. Ahmed et al. observed improvement in 82.35% of the magnesium group, confirming that rapid neurological normalization is a consistent finding when magnesium sulphate is administered early in HI [15]. In stratified analysis, the current study also revealed that early and complete neurological recovery was closely related to HIE severity: 95.5% in grade I, 75.7% in grade II, but only 29.2% in grade III. This trend mirrors the observations of Pius et al., where favorable neurological outcomes were more prevalent in less severe cases and when magnesium was given within the initial hours after birth [16].

The incidence of seizures in this cohort was 26.1% overall, but increased substantially in grade III HIE (62.5%). These findings are in line with previous randomized studies, such as that by Savitha and Rajprakash, who reported seizure control with a single anticonvulsant in 96% of the magnesium group versus 74% in controls, as well as a shorter mean duration of seizures (1.52 ± 0.65 days versus 2.29 ± 1.56 days, $p = 0.026$) [14]. Ahmed et al. also observed improved seizure control in the magnesium group (86.27% vs. 72.55%), although the difference did not reach statistical significance [15].

The occurrence of seizures was lowest among neonates with mild HIE, as also seen in the prospective pilot study by Pius et al., where magnesium administration, particularly within 6 hours of life, was associated with earlier restoration of neurological reflexes and resolution of encephalopathy [16]. The lower rate of seizures in mild and moderate HIE, alongside more rapid neurological recovery, further underscores the neuroprotective potential of magnesium when given promptly.

The present study found that 79.7% of neonates achieved effective suck feeding by day 7. This rate is highly comparable to previous trials: Sajid et al. reported 75.7% in the magnesium group, significantly higher than 39.4% in the placebo group [6]. Akram et al. found a similar benefit, with the appearance of a good sucking reflex in 75% of magnesium-treated neonates compared to 45% in controls [17]. Ahmed et al. also reported a higher proportion of neonates establishing oral feeding in the magnesium group (82.35% vs. 64.71%, $p = 0.043$), as did Savitha and Rajprakash (91.4% vs. 65.6%, $p = 0.009$) [14,15].

The consistency of these findings across different settings and study designs highlights the role of magnesium sulphate in facilitating early feeding recovery, which has important implications for neurodevelopment and hospital discharge planning. This advantage was most prominent among neonates with milder forms of HIE, with 95.5% of grade I and 85.7% of grade II neonates in the current cohort achieving this outcome. In severe HIE (grade III), feeding recovery was significantly reduced, reflecting the established association between neurological injury severity and feeding dysfunction [18].

Short-term mortality in this study was 8.7%, with a marked increase in mortality among neonates with grade III HIE (37.5%). This figure is lower than those reported by Ichiba et al. (6.7%), Ahmed et al. (7.84%), and Rasheed et al. (7.8% in the magnesium group), but considerably below the rates observed in historical or untreated cohorts (up to 25%) [13,15,19]. Rasheed et al. specifically documented a significant reduction in mortality with early magnesium administration compared to those not receiving the intervention (7.8% vs. 23.6%, $p = 0.003$) [19].

Conversely, Riaz et al. observed a non-significantly higher frequency of adverse outcomes (including mortality) in the magnesium group compared to phenobarbital (9 vs. 3 patients), but the difference did not achieve statistical significance ($p = 0.122$), and subgroup analysis revealed some advantages for magnesium in higher birth weight infants [20]. Akram et al. also found no significant

difference in mortality rates between the magnesium and control groups (15.0% vs. 7.5%, p = 0.2885) [17]. These variable results may reflect differences in study populations, the timing of intervention, and severity of asphyxia.

Despite this, the overall evidence suggests a favorable trend toward reduced mortality with magnesium sulphate, particularly when used early and in moderate HIE, as echoed in the survival analyses of Rasheed et al. and in the present study's low overall and stratified mortality [19].

Across all referenced studies, intravenous magnesium sulphate was consistently reported as safe and well tolerated, with no significant treatment-related complications or physiologic disturbances. Ichiba et al. found no cases of hypotension or abnormal laboratory indices attributable to magnesium administration, even in ventilated neonates [13]. Akram et al. similarly reported no adverse effects in their randomized trial, while Savitha and Rajprakash noted no difference in adverse event rates between the magnesium and comparison groups [14,17]. The current study observed no infusion-related complications, further supporting the safety profile of magnesium in neonatal neuroprotection.

The collective evidence, including the present results, strongly supports the use of intravenous magnesium sulphate as an effective adjunct in the management of term neonates with HIE, especially for early neurological recovery, improved seizure control, enhanced feeding outcomes, and potentially reduced short-term mortality. Notably, the benefit appears most pronounced in neonates with mild to moderate HIE and when magnesium is administered early in the postnatal period.

Several limitations require consideration. First, the observational duration was limited to seven days; thus, long-term neurodevelopmental outcomes, including cognitive and motor sequelae, could not be evaluated. While other studies provided longer follow-up, most other referenced studies, including the present one, focused on short-term clinical endpoints. Second, the absence of a parallel control group in the current study prevents direct assessment of treatment effect size; however, the outcomes align closely with those reported in contemporary randomized and controlled studies. Third, severity stratification revealed diminished efficacy in grade III HIE, a consistent trend across published data and emphasizing the critical importance of early intervention and accurate severity grading.

CONCLUSION

Intravenous magnesium sulphate, when administered alongside standard care, was associated with meaningful improvement in neurological recovery and feeding ability among term neonates with hypoxic ischemic encephalopathy. The findings indicate a favorable safety profile and suggest that magnesium sulphate may support better short-term outcomes in this population. The benefits were most notable in neonates with less severe forms of encephalopathy, supporting its use as an accessible adjunctive therapy, particularly where resources for advanced neuroprotective interventions are limited.

Authors' Contribution

K.S. was responsible for study conception, data collection, and drafting the manuscript. **A.A.** provided supervision, critical revision, and final approval of the manuscript. **N.M.** assisted in data analysis and interpretation of findings. A.T. contributed to literature review and methodology development. **M.I.J.** participated in data acquisition and patient monitoring. **M.A & M.I.U.** supported statistical analysis and manuscript editing. All authors reviewed and approved the final version of the manuscript.

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