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Analytical Study of Beneficial Effects of Magnesium Sulfate for the Neuroprotection in Pre-Term Babies in Tertiary Care Hospital Bahawalpur

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ABSTRACT

Neonatal morbidity and mortality are greatly influenced by preterm birth. Magnesium sulfate (MgSO4) has been suggested as a neuroprotective therapy to reduce the negative consequences on neurodevelopment in preterm infants. **Objective:** To investigate how MgSO4 works to reduce the incidence of cerebral palsy as well as other neurodevelopmental impairments in preterm infants. **Methods:** This quasi experimental study was conducted at Tertiary Care Hospital Bahawalpur in the Department of Obstetrics and Gynecology from September 30, 2022 to March 29, 2023. This research involved 312 preterm infants. The infants were divided to a group of treatment with MgSO4 or compared with a group without MgSO4 exposure. The incidence of intraventricular hemorrhage (IVH), need for mechanical ventilation, neonatal mortality, as well as cerebral palsy were also measured and compared between the groups using Chi-square and T-tests. **Results:** The administration of MgSO4, dramatically reduced the rate of IVH (6.4%, 16%, p = 0.007 respectively treatment and control group) and neonatal mortality (3.2%, 10.3%, p = .013). It did not significantly affect the need for mechanical ventilation.This proved to be effective in reducing cerebral palsy by 21.8 percentage points (4.5% vs 26.3%, p<0.001). **Conclusion:** MgSO4 administration antenatally greatly decreases the risks of IVH and neonatal mortality while decreasing the incidence of cerebral palsy in preterm infants, thereby resulting more to be a'gold standard' neuroprotective strategy in prenatal care.

INTRODUCTION

Preterm birth, defined as delivery prior to 37 weeks of gestation, remains a significant global health challenge, accounting for a considerable proportion of neonatal morbidity and mortality. It is closely associated with long-term neurodevelopmental impairments, including cerebral palsy (CP), cognitive deficits, and sensory dysfunction. These outcomes impose a profound burden on healthcare systems and families, particularly in low- and middle-income countries where neonatal intensive care resources are limited [1]. Among the strategies employed to mitigate these adverse outcomes, antenatal administration of magnesium sulfate ($MgSO_4$) has emerged as a widely recommended and evidence-based neuroprotective intervention for fetuses at risk of preterm birth [2]. Its protective role is primarily mediated through multiple biochemical and physiological mechanisms. These include blockade of N-methyl-D-aspartate (NMDA) receptors, antagonism of calcium influx into neurons, attenuation of oxidative stress, and modulation of excitatory neurotransmission all of which serve to prevent hypoxic-ischemic injury and stabilize the immature brain environment [3]. The efficacy of $MgSO_4$ in reducing the

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incidence of CP and enhancing survival without major neurological impairment has been consistently demonstrated. For example, Gupta et al., (2021) found that antenatal $MgSO_4$ significantly lowered the risk of cerebral palsy in preterm infants when administered before early delivery [4]. Similarly, Oddie in (2015) evaluated the use of antenatal magnesium sulfate for neuroprotection in preterm infants, highlighting its potential to reduce the risk of cerebral palsy. [5]. Hurrion in (2023) declared that the SuPreme Study outlined a protocol to investigate whether sulfate is the key neuroprotective component in antenatal magnesium sulfate therapy for very/extremely preterm infants [6]. These findings have reinforced guideline recommendations from bodies such as the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO), which advocate $MgSO_4$ use in women at risk of imminent preterm delivery before 34 weeks [7, 8]. Despite this, clinical implementation in low-resource settings remains inconsistent. The majority of existing studies have focused on high-income populations, with a lack of regional data from South Asia—particularly Pakistan—limiting the generalizability of these findings. Furthermore, the literature remains underdeveloped in terms of subgroup analysis based on maternal comorbidities, fetal sex, and gestational age [9, 10]. Emerging pharmacokinetic data suggest that treatment success depends on achieving adequate serum magnesium concentrations, balanced against potential risks such as neonatal electrolyte disturbances [11]. While adverse effects like transient hyperkalemia or hypocalcemia have been observed, they are usually self-limiting and manageable within neonatal care settings [12, 13]. Although the neuroprotective benefits of antenatal magnesium sulfate are well-established in high-income countries, there remains a significant gap in the literature from low- and middle-income regions, particularly South Asia. Current evidence is largely derived from Western populations with advanced neonatal intensive care systems, which may not reflect the realities of resource-constrained settings like Pakistan. Furthermore, there is limited data analyzing the stratified effects of $MgSO_4$ across different maternal comorbidities, fetal sexes, and degrees of prematurity factors that may influence outcomes but are often underreported. Given the high burden of preterm birth in Pakistan and the scarcity of local, context-specific evidence, this study was undertaken to evaluate the effectiveness of antenatal $MgSO_4$ for fetal neuroprotection in a tertiary care setting. By addressing this critical gap, the study aims to generate actionable insights tailored to the unique demographic, clinical, and infrastructural realities of developing countries. The findings of this study have the potential to inform national perinatal care guidelines, encourage standardized use of $MgSO_4$ for neuroprotection in preterm labor, and improve neonatal outcomes by preventing cerebral palsy and other severe neurological complications.

If proven effective within the local context, $MgSO_4$ administration could serve as a cost-effective, scalable intervention to reduce long-term disability and neonatal mortality in Pakistani healthcare settings.

METHODS

This quasi experimental was conducted at the Department of Obstetrics and Gynecology, Tertiary Care Hospital Bahawalpur, from September 30, 2022, to March 29, 2023. The primary objective was to evaluate the effectiveness of antenatal magnesium sulfate ($MgSO_4$) administration for fetal neuroprotection in women at risk of preterm delivery, with key neonatal outcomes including intraventricular hemorrhage (IVH), need for mechanical ventilation, neonatal mortality, and the incidence of cerebral palsy (CP). Based on the findings by Bansal and Desai who observed a reduction in IVH from 16% in the non-treated group to 8% in the $MgSO_4$-treated group, a total sample size of 312 participants (156 per group) was calculated to achieve a statistical power of 70% and an alpha of 0.10 [14]. Participants were recruited using a non-probability consecutive sampling technique. Women who met the eligibility criteria were divided into the treatment or control group using the lottery method. The study received ethical approval from the Ethical Committee of Combined Military Hospital Bahawalpur (Ref: EC-18-2022). Written informed consent was obtained from all participants after a thorough explanation of the study's aims, procedures, and potential risks. Confidentiality was strictly maintained. Inclusion criteria required participants to be pregnant women aged 18 to 45 years, with a gestational age between 26 weeks and 36 weeks + 6 days, confirmed by early ultrasound or reliable last menstrual period. Participants had to be at risk of imminent preterm delivery, defined by clinical evidence of spontaneous preterm labor (regular contractions and cervical dilation ≥3 cm), preterm premature rupture of membranes (PPROM), or medically indicated preterm delivery due to maternal or fetal complications such as preeclampsia or intrauterine growth restriction. Both singleton and twin pregnancies were included, provided the mother was hemodynamically stable and capable of receiving intravenous treatment. Exclusion criteria included known allergy or hypersensitivity to $MgSO_4$, severe renal dysfunction (serum creatinine >1.5 mg/dL or oliguria <30 mL/h), neuromuscular disorders such as myasthenia gravis, cardiac conduction abnormalities, recent $MgSO_4$ use for other obstetric indications, intrauterine fetal demise, and any major fetal congenital anomalies identified antenatally. Women with urgent medical or surgical conditions requiring immediate delivery were also excluded, as were those unable or unwilling to provide informed consent. Women in the

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intervention group received a 4 g IV bolus of $MgSO_4$ administered over 20–30 minutes, followed by a 1 g/hour maintenance infusion for up to 12 hours or until delivery. The control group received a matched volume of normal saline placebo, administered in an identical manner. Both groups received standard obstetric and neonatal care throughout. Data collection was carried out using a structured and pre-tested proforma, including demographic details such as maternal age, gestational age at delivery, birth weight, and infant sex. Clinical outcomes were assessed based on standardized definitions. Cerebral palsy was diagnosed during follow-up visits using criteria established by the Surveillance of Cerebral Palsy in Europe (SCPE), which includes the presence of abnormal muscle tone, delayed developmental milestones, and persistent motor dysfunction at or after 6 months of age [15]. Intraventricular hemorrhage was diagnosed and graded using cranial ultrasonography based on the Papile classification system [16], and all scans were interpreted by neonatologists blinded to group assignment. Neonatal mortality was defined as death within the first 28 days of life, while the need for mechanical ventilation was recorded from NICU records and defined as the requirement for invasive respiratory support within the first 72 hours after birth. All data were analyzed using SPSS version 25.0. Descriptive statistics were computed for demographic variables. Categorical variables such as IVH, CP, mechanical ventilation, and mortality were analyzed using Chi-square tests, while continuous variables like birth weight and maternal age were assessed using independent-sample t-tests. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The descriptive statistics for the study population (n = 312) are as follows: The mean gestational age was 30.00 ± 1.95 weeks, and the average birth weight was 1500.26 ± 196.81 grams.The mean maternal age was 30.75 ± 4.76 years. These baseline characteristics provide a demographic overview of the preterm cohort enrolled in the study. The comparison of key neonatal outcomes between the magnesium sulfate ($MgSO_4$) treatment and control groups demonstrated a significant benefit of antenatal $MgSO_4$ administration in reducing several critical complications associated with preterm birth. A notable reduction in intraventricular hemorrhage (IVH) was observed in the treatment group (6.4%) compared to the control group (16.0%), with a statistically significant risk difference of 9.6% (95% CI: 2.7% to 16.5%), confirming a protective neurological effect. Similarly, the incidence of neonatal mortality was significantly lower in the $MgSO_4$ group (3.2%) versus controls (10.3%), corresponding to a risk difference of 7.1% (95% CI: 1.5% to 12.6%), indicating a meaningful improvement in survival among preterm neonates receiving neuroprotective therapy. The most pronounced benefit was seen in the reduction of cerebral palsy, where the treatment group had only 4.5% affected compared to 26.3% in the control group. This yielded a risk difference of 21.8% (95% CI: 14.2% to 29.4%), strongly supporting $MgSO_4$'s role in preventing long-term neuromotor impairment. In contrast, the need for mechanical ventilation was slightly higher in the treatment group (22.4%) than in controls (16.0%). This resulted in a negative risk difference of -6.4% (95% CI: -15.1% to 2.3%), suggesting that more neonates in the $MgSO_4$ group required respiratory support. However, this difference was not statistically significant (p = 0.151), and the confidence interval includes zero, indicating the observed increase may be due to chance rather than a treatment-related effect. Overall, the risk difference estimates and corresponding confidence intervals reinforce the conclusion that antenatal $MgSO_4$ confers substantial neuroprotective benefits particularly in reducing IVH, neonatal mortality, and cerebral palsy — with no conclusive evidence of harm in terms of respiratory outcomes. (Table 1).

Table 1: Comparison of Neonatal Outcomes between Treatment and Control Groups

Outcome	Group	Yes Frequency (%)	No Frequency (%)	p-Value	Risk Difference (%)	95% Confidence Interval
IVH	Treatment	10 (6.4%)	146 (93.6%)	0.007	9.6	2.7 to 16.5
	Control	25 (16.0%)	131 (84.0%)			
Mechanical Ventilation	Treatment	35 (22.4%)	121 (77.6%)	0.151	-6.4	-15.1 to 2.3
	Control	25 (16.0%)	131 (84.0%)			
Neonatal Mortality	Treatment	5 (3.2%)	151 (96.8%)	0.013	7.1	1.5 to 12.6
	Control	16 (10.3%)	140 (89.7%)			
Cerebral Palsy	Treatment	7 (4.5%)	149 (95.5%)	0.001	21.8	14.2 to 29.4
	Control	41 (26.3%)	115 (73.7%)			

Gender-based stratification of outcomes is detailed in Table 2.

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Table 2: Outcome Variables Stratified by Gender of Preterm Baby

Gender	Study Group	IVH Yes Frequency (%)	IVH No Frequency (%)	Total	P-value
Male	Treatment Group	4 (4.65%)	82 (95.35%)	86	0.018
Male	Control Group	12 (15.79%)	64 (84.21%)	76	
Female	Treatment Group	6 (8.57%)	64 (91.43%)	70	0.158
Female	Control Group	13 (16.25%)	67 (83.75%)	80	
Male	Treatment Group	14 (16.28%)	72 (83.72%)	86	0.932
Male	Control Group	12 (15.79%)	64 (84.21%)	76	
Female	Treatment Group	21 (30.00%)	49 (70.00%)	70	0.045
Female	Control Group	13 (16.25%)	67 (83.75%)	80	
Male	Treatment Group	3 (3.49%)	83 (96.51%)	86	0.043
Male	Control Group	9 (11.84%)	67 (88.16%)	76	-
Female	Treatment Group	2 (2.86%)	68 (97.14%)	70	0.129
Female	Control Group	7 (8.75%)	73 (91.25%)	80	-
Male	Treatment Group	3 (3.49%)	83 (96.51%)	86	0.000
Male	Control Group	25 (32.89%)	51 (67.11%)	76	-
Female	Treatment Group	4 (5.71%)	66 (94.29%)	70	0.010
Female	Control Group	16 (20.00%)	64 (80.00%)	80	-

Among male preterm infants, $MgSO_4$ treatment was associated with significant reductions in IVH (4.65% vs. 15.79%, $p = 0.018$), neonatal mortality (3.49% vs. 11.84%, $p = 0.043$), and cerebral palsy (3.49% vs. 32.89%, $p < 0.001$). No significant difference was observed in mechanical ventilation need ($p = 0.932$). Among female infants, a significant reduction in cerebral palsy was also observed in the treatment group (5.71% vs. 20.00%, $p = 0.010$). However, the requirement for mechanical ventilation was significantly higher in treated females (30.00% vs. 16.25%, $p = 0.045$). This observation, although statistically significant, warrants cautious interpretation due to the narrow margin of significance. IVH and neonatal mortality rates in female infants did not differ significantly between groups ($p = 0.158$ and $p = 0.129$, respectively). Outcomes stratified by maternal health conditions are shown in Table 3. A statistically significant reduction in IVH was observed in neonates born to mothers with diabetes mellitus (4.17% vs. 26.09%, $p = 0.035$). While neonates of mothers with no disease also showed lower IVH rates in the $MgSO_4$ group (6.96% vs. 14.68%), the difference was not statistically significant ($p = 0.062$). No meaningful differences were found in mechanical ventilation need across maternal subgroups: no disease ($p = 0.430$), diabetes ($p = 0.477$), or preeclampsia ($p = 0.175$). Neonatal mortality also did not differ significantly by maternal health status, although the "no disease" group trended toward lower mortality in the treatment arm ($p = 0.061$). Significant reductions in cerebral palsy were seen among neonates of mothers with no disease ($p < 0.001$) and those with preeclampsia ($p = 0.014$), indicating subgroup-specific neuroprotective effects of $MgSO_4$.

Table 3: Outcome Variables Stratified By Maternal Health Conditions

Maternal Health Condition	Study Group	IVH Yes Frequency (%)	IVH No Frequency (%)	Total	P-value
No Disease	Treatment Group	8 (6.96%)	107 (93.04%)	115	0.062
	Control Group	16 (14.68%)	93 (85.32%)	109	
Diabetes Mellitus	Treatment Group	1 (4.17%)	23 (95.83%)	24	0.035
	Control Group	6 (26.09%)	17 (73.91%)	23	
Preeclampsia	Treatment Group	1 (5.88%)	16 (94.12%)	17	0.482
	Control Group	3 (12.50%)	21 (87.50%)	24	
No Disease	Treatment Group	26 (22.61%)	89 (77.39%)	115	0.430
	Control Group	20 (18.35%)	89 (81.65%)	109	
Diabetes Mellitus	Treatment Group	5 (20.83%)	19 (79.17%)	24	0.477
	Control Group	3 (13.04%)	20 (86.96%)	23	
Preeclampsia	Treatment Group	4 (23.53%)	13 (76.47%)	17	0.175
	Control Group	2 (8.33%)	22 (91.67%)	24	
No Disease	Treatment Group	3 (2.61%)	112 (97.39%)	115	0.061
	Control Group	9 (8.26%)	100 (91.74%)	109	
Diabetes Mellitus	Treatment Group	1 (4.17%)	23 (95.83%)	24	0.276
	Control Group	3 (13.04%)	20 (86.96%)	23	

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Preeclampsia	Treatment Group	1 (5.88%)	16 (94.12%)	17	0.299
	Control Group	4 (16.67%)	20 (83.33%)	24	
No Disease	Treatment Group	5 (4.35%)	110 (95.65%)	115	0.000
	Control Group	29 (26.61%)	80 (73.39%)	109	
Diabetes Mellitus	Treatment Group	2 (8.33%)	22 (91.67%)	24	0.197
	Control Group	5 (21.74%)	18 (78.26%)	23	
Preeclampsia	Treatment Group	0 (0%)	17 (100%)	17	0.014
	Control Group	7 (29.17%)	17 (70.83%)	24	

DISCUSSION

This study investigated the neuroprotective role of antenatal magnesium sulfate ($MgSO_4$) in preterm infants and revealed significant improvements in several key neonatal outcomes.Notably, $MgSO_4$ administration was associated with a significant reduction in intraventricular hemorrhage (IVH) (6.4% vs. 16.0%, p = 0.007), neonatal mortality (3.2% vs. 10.3%, p = 0.013), and cerebral palsy (4.5% vs. 26.3%, p < 0.001).The strongest effect was observed in reducing cerebral palsy, with a 21.8% absolute risk reduction (95% CI: 14.2% to 29.4%).While the need for mechanical ventilation was slightly higher in the treatment group (22.4% vs. 16.0%), the difference was not statistically significant (p = 0.151). Gender-based stratification showed more pronounced benefits in male infants, while female infants exhibited a higher rate of mechanical ventilation following treatment.Subgroup analysis by maternal comorbidities confirmed the neuroprotective effect of $MgSO_4$ in reducing cerebral palsy among neonates of mothers with no disease and preeclampsia, and in lowering IVH in infants of diabetic mothers. Our findings are consistent with those of Bansal and Desai (2021), who reported a decrease in IVH incidence from 16% in untreated infants to 8% in those receiving $MgSO_4$ [14].Cans C in (2000) presented data from European cerebral palsy (CP) registries, improving surveillance and understanding of CP prevalence and patterns across Europe [15].Papile LA *et al.*, identified the incidence and grading of subependymal and intraventricular hemorrhage in very low birth weight infants, forming the basis for the Papile classification [16]. Chollat C *et al.*, reviewed bridges translational research and clinical practice, discussing the mechanisms and evidence supporting magnesium sulfate's neuroprotective role in preterm infants [17].Monteagudo BF *et al.*, evaluated the neuroprotective impact of antenatal magnesium sulfate in preterm infants after implementing a standardized administration protocol in a tertiary hospital [18].The pronounced reduction in cerebral palsy observed in our study parallels the findings of Crowther *et al.*, who confirmed $MgSO_4$'s effectiveness in lowering cerebral palsy risk through meta-analysis [19].The robust neuroprotective effect we observed supports its inclusion in preterm labor protocols.Interestingly, our study identified gender-specific differences, particularly a higher incidence of mechanical ventilation in treated female neonates.This echoes the hypothesis presented by McLeod *et al.*, who suggested that male and female fetuses may respond differently to $MgSO_4$ due to neurobiological and hormonal factors [20].Such differential responses merit further investigation. Subgroup findings in our study also support those of Burhouse *et al.*, who emphasized the feasibility and success of integrating $MgSO_4$ protocols in diverse clinical settings, including those with maternal comorbidities [21].The reduction in cerebral palsy among neonates of mothers with preeclampsia in our study further affirms $MgSO_4$'s protective role across risk profiles. Safety remains a crucial aspect of $MgSO_4$ use.Our study did not report any treatment-related complications, aligning with prior literature indicating minimal maternal or neonatal side effects when $MgSO_4$ is administered with proper monitoring [14].Moreover, as noted by Ayed *et al.*, timing is critical, with administration ideally occurring 4–6 hours prior to delivery for optimal neuroprotection [22]. While our study did not analyze timing in depth, we adhered to this recommended window in most cases.In summary, our findings reinforce the evidence supporting $MgSO_4$ as a safe and effective neuroprotective intervention in preterm infants.Its use significantly reduces IVH, neonatal mortality, and cerebral palsy, especially in specific subgroups.These results advocate for the broader implementation of $MgSO_4$ protocols, particularly in resource-limited settings, and emphasize the need for further studies to optimize dosage, timing, and subgroup-specific effects.

CONCLUSIONS

This study demonstrated that antenatal administration of magnesium sulfate significantly reduces the incidence of intraventricular hemorrhage, neonatal mortality, and cerebral palsy in preterm infants. The treatment was especially effective in male neonates and in those born to mothers without comorbidities or with preeclampsia. No significant impact was found on the need for mechanical ventilation. These findings support the inclusion of $MgSO_4$ in clinical protocols for neuroprotection in preterm deliveries.

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Authors Contribution

Conceptualization: SB
Methodology: VA, SM
Formal analysis: SU
Writing, review and editing: RS, SZC, VA, SM
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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