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SERUM MAGNESIUM LEVELS AND OXIDATIVE STRESS MARKERS IN NEONATAL SEIZURES: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Neonatal seizures are a frequent neurological emergency with significant morbidity. Metabolic abnormalities, particularly hypomagnesemia, are important reversible causes. This study evaluated serum magnesium levels and oxidative stress in neonates with seizures and assessed their correlation. **Materials and Methods:** The present study was conducted to evaluate serum magnesium levels and oxidative stress markers in neonates presenting with seizures. A total of 100 neonates admitted to the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital were enrolled and systematically assessed using biochemical and clinical parameters. **Result:** Hypomagnesemia was common among neonates with seizures. Oxidative stress markers were elevated, particularly in neonates with low serum magnesium levels. A significant inverse correlation was observed between serum magnesium levels and oxidative stress parameters. **Conclusion:** Hypomagnesemia and increased oxidative stress frequently coexist in neonatal seizures and show a significant inverse relationship. Routine evaluation of serum magnesium may help identify a modifiable factor and improve seizure management in neonates.

INTRODUCTION

Neonatal seizures constitute one of the most common neurological emergencies in the newborn period and often indicate an underlying cerebral or systemic pathology. The reported incidence of neonatal seizures ranges from 1.5 to 3 per 1,000 live births, with a substantially higher burden among preterm and lowbirthweight infants.[1] The neonatal brain is uniquely vulnerable to seizures because of immature inhibitory pathways, predominance of excitatory neurotransmission, altered gammaaminobutyric acid activity, and limited antioxidant defense mechanisms, rendering it susceptible even to minor metabolic or hypoxic insults.[2] Clinica 1 manifestations are frequently subtle such as ocular deviation, apnea, lip smacking, or tonic posturing—making early diagnosis challenging and often leading to delayed intervention.[3]

Recent Indian studies published after 2023 have reported hypomagnesemia in nearly 28.9% of neonates presenting with seizures, a prevalence considerably higher than earlier estimates, with frequent coexistence of hypocalcemia and delayed seizure control when magnesium deficiency is overlooked.[4] Despite this, serum magnesium estimation is not routinely performed in many neonatal intensive-care units, especially in low- and middle-income countries.[5-7]

Magnesium is the second most abundant intracellular cation and a critical cofactor in numerous enzymatic reactions involved in energy metabolism, neuromuscular transmission, and cellular homeostasis.[8,9]

Experimental and clinical data support its anticonvulsant and neuroprotective properties, hig lighting magnesium as a potentially modifiable therapeutic factor in neonatal seizures.[10]

In addition to metabolic derangements, oxidative stress has emerged as a key mechanism in neonatal brain injury. Oxidative stress results from an imbalance between reactive oxygen species generation and antioxidant defenses, leading to lipid peroxidation, DNA damage, and mitochondrial dysfunction.[11] The neonatal brain is particularly susceptible due to high concentrations of polyunsaturated fatty acids and immature antioxidant systems. Seizure activity further

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increases metabolic demand and reactive oxygen species production, amplifying neuronal injury. Elevated lipid peroxidation markers and reduced antioxidant enzyme activity have been demonstrated in neonates with seizures.[6]

Magnesium deficiency and oxidative stress are closely interconnected. Hypomagnesemia promotes oxidative injury by impairing mitochondrial function, reducing antioxidant enzyme activity, and enhancing inflammatory responses, whereas adequate magnesium levels stabilize cell membranes and improve antioxidant capacity.[7] However, limited studies particularly from India have evaluated serum magnesium status in conjunction with oxidative stress markers in neonatal seizures.

MATERIALS AND METHODS

This Cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU) at Santosh Medical College & Hospital, Ghaziabad. The study included neonates presenting with seizures at the NICU during the study period.

Sample Size: A total of 100 neonates were included in the study.

After obtaining ethical approval from the institutional ethical committee, informed consent was obtained from the parents or guardians of the neonates enrolled in the study.

A 5 mL blood sample was collected from each neonate for biochemical analysis. The samples were stored under appropriate conditions until further analysis.

Biochemical Estimations

1. Serum Magnesium Level was estimated using a Magnesium Kit.
2. Oxidative Stress Level was assessed using the respective oxidative stress kit.

The blood samples were analyzed using the Calmagite Method (Coral Clinical Systems). In this method, magnesium in the serum reacts with Calmagite in an alkaline medium, forming a redcolored complex. The intensity of the color was directly proportional to the amount of magnesium in the sample. The method effectively eliminated interference from calcium and proteins through the addition of chelating agents and detergents.

Inclusion Criteria

1. Neonates presenting with seizures whose parents provided written consent for participation.
2. Seizures occurring within the first 4 weeks of life.
3. Neonates with seizures, whether born at the hospital or outborn.
4. Neonates presenting with at least one of the following clinical types of seizures:

- Subtle seizures
- Generalized tonic seizures
- Multifocal clonic seizures
- Focal seizures
- Myoclonic seizures

Exclusion Criteria:

1. Jitteriness in neonates.
2. Tetanic spasms in neonates.
3. Outborn neonates treated with anticonvulsants.
4. Infants of diabetic mothers.
5. Newborns with congenital anomalies such as hydrocephalus, Arnold-Chiari malformation, or Dandy-Walker malformation.

Sample Size Calculation:

The sample size was calculated using the following formula:

n= (Z2p(1 - p)) / E2

Where:

- n is the sample size needed,
- Z is the Z-score corresponding to the desired confidence level (1.96 for 95% confidence),
- p is the estimated prevalence rate,
- E is the margin of error.

Sample Size: 78 + 20% non-responder (16) = 94 ~ 100

Expected Outcome: The study expected to find increased cases of low serum magnesium levels and increased oxidative stress levels in neonates presenting with seizures.

Statistical Analysis: Data were entered and analyzed using SPSS version 27. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized as mean + standard deviation or median with interquartile range as appropriate. Associations between categorical variables were assessed using the chi-square test. Differences in mean values between two independent groups were analyzed using the independent Student's test. Pearson's cor relation coefficient was used to evaluate the relationship between serum magnesium levels and oxidative stress. Univariate logistic regression analysis was performed to identify potential predictors of elevated oxidative stress, followed by multivariate logistic regression to determine independent predictors after adjusting for confounding variables. Odds ratios with 95% confidence intervals were reported, and a p value of less than 0.05 was considered statistically significant.

RESULTS

Majority of neonates with seizures presented early in life. Most seizures occurred within the first 3 days of life (42%), followed by the 47 day age group (28%), indicating a clear predominance of early neonatal seizures. Fewer cases were observed beyond the first week of life, with only 12% presenting between 15to28 days. The mean age at presentation was 6.8 = 5.9days, while the median age was 5 days, reflecting a skew toward early onset. This pattern suggests that neonatal seizures predominantly occur during the immediate postnatal period.

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A male predominance among neonates with seizures. Males constituted 62% of the study population, while females accounted for 38%. This male preponderance is consistent with observations from previous neonatal seizure studies.

Nearly half of the neonates with seizures were low birth weight (<2.5 kg), accounting for 48 % of cases. The remaining 52% had a birth weight ≥2.5 kg. The mean birth weight was 2.46 + 0.51 kg, with a median of 2.5 kg, suggesting a borderline predominance of low birth weight neonates.

Type of Seizures Observed: [Table 1] shows that subtle seizures were the most common seizure type, accounting for 34% of cases. This was followed by generalized tonic seizures (26%) and multifocal clonic seizures (18%). Focal seizures and myoclonic seizures were less frequent, contributing 14% and 8 % respectively. The predominance of subtle seizures underscores the importance of careful clinical observation, as these seizures may be easily missed. Overall, the findings reflect the diverse seizure semiology seen in neonates.

Table 1: Type of Seizures Observed

Type of Seizure	Number (n)	Percentage (%)
Subtle seizures	34	34.0
Generalised tonic	26	26.0
Multifocal clonic	18	18.0
Focal seizures	14	14.0
Myoclonic seizures	8	8.0
Total	100	100.0

Serum Magnesium Levels in Neonates with Seizures: hypomagnesemia was present in nearly 1/3 (32%) of neonates with seizures, while the majority (68%) had normal serum magnesium levels. The mean serum magnesium level was 1.62 + 0.41 mg/dl, with a median value of 1.6 mg/dl, indicating values close to the lower normal range. The substantial proportion of hypomagnesemia highlights its potential role in neonatal seizure pathophysiology.

Table 2: Serum Magnesium Levels in Neonates with Seizures

Serum Magnesium Status	Number (n)	Percentage (%)
Hypomagnesemia (<1.5 mg/dl)	32	32.0
Normal (≥1.5 mg/dl)	68	68.0
Total	100	100.0
Mean ± SD	1.62 ± 0.41 mg/dl	
Median (IQR)	1.6 (1.3–1.9) mg/dl	

Oxidative Stress Levels in Study Population: Table 10 shows that more than half of the neonates with seizures had elevated oxidative stress levels. Elevated oxidative stress was observed in 58% of the study population, while 42% had normal oxidative stress levels. This finding indicates that oxidative stress is a common biochemical abnormality among neonates presenting with seizures.

Table 3: Oxidative Stress Levels in Study Population

Oxidative Stress Level	Number (n)	Percentage (%)
Elevated	58	58.0
Normal	42	42.0
Total	100	100.0

Association Between Serum Magnesium Status and Oxidative Stress: A significant association between serum magnesium status and oxidative stress levels. A large majority of neonates with hypomagnesemia (81.3%) exhibited elevated oxidative stress compared to 47.1% among those with normal magnesium levels. This association was found to be statistically significant (χ^2= 15.9, p < 0.001).

Table 4: Association Between Serum Magnesium Status and Oxidative Stress

Serum Magnesium Status	Elevated Oxidative Stress n (%)	Normal Oxidative Stress n (%)	Total n (%)	Chi-square (χ^2)	P-value
Hypomagnesemia	26 (81.3)	6 (18.7)	32 (100)	15.9	<0.001
Normal Mg	32 (47.1)	36 (52.9)	68 (100)		
Total	58 (58.0)	42 (42.0)	100 (100)		

Correlation Between Serum Magnesium Level and Oxidative Stress: A moderate negative correlation between serum magnesium levels and oxidative stress (r =0.46). This correlation was statistically significant (p < 0.001), indicating that lower serum magnesium levels were associated with higher oxidative stress. The inverse relationship supports the hypothesis that magnesium deficiency

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may exacerbate oxidative stress. This finding strengthens the biological plausibility of magnesium's protective role in neonatal physiology.
Subtle seizures were more frequent among neonates with hypomagnesemia (58.8%) compared to those with normal magnesium levels (41.2%). Conversely, other seizure types were predominantly observed in neonates with normal magnesium levels (81.8%). The association was statistically significant (χ^2= 16.44, $p < 0.001$), indicating that hypomagnesemia is strongly linked with subtle seizure manifestations.

Serum Magnesium vs Hypocalcemia: A strong association between hypomagnesemia and hypocalcemia in neonates with seizures. Among neonates with hypocalcemia, 65% had hypomagnesemia, whereas only 10% of neonates without hypocalcemia had hypomagnesemia. This association was statistically significant (χ^2= 16.44, $p < 0.001$). These findings highlight the interrelationship between magnesium and calcium metabolism and emphasize the importance of assessing both electrolytes in neonatal seizures.

Table 5: Serum Magnesium vs Hypocalcemia

Serum Magnesium Status	Hypocalcemia n (%)	No Hypocalcemia n (%)	Total n (%)	Chi-square (χ^2)	P-value
Hypomagnesemia (<1.5 mg/dl)	26 (65.0)	6 (10.0)	32 (100)	16.44	<0.001
Normal Mg (≥1.5 mg/dl)	14 (35.0)	54 (90.0)	68 (100)		
Total	40 (40.0)	60 (60.0)	100 (100)		

Oxidative Stress Status vs Seizure Type: Elevated oxidative stress was markedly more common in neonates with subtle seizures (94.1 %) compared to those with other seizure types (39.4%). Normal oxidative stress levels were predominantly observed among neonates with other seizure types. The association was highly statistically significant (χ^2 = 27.57, $p < 0.001$). Highly significant association between serum magnesium status and seizure occurrence. Nearly half of the neonates with seizure onset had hypomagnesemia (48.3%), whereas hypomagnesemia was present in only 9.5% of neonates without seizures. This association was statistically significant (χ^2= 16.81, $p < 0.001$).

Table 6: Serum Magnesium vs Seizure Occurrence (Binary Outcome)

Serum Magnesium Status	Seizure Onset (Yes) n (%)	No Seizure (No) n (%)	Total n (%)	Chi-square (χ^2)	P-value
Hypomagnesemia (<1.5 mg/dl)	28 (48.3)	4 (9.5)	32 (100)	16.81	<0.001
Normal Mg (≥1.5 mg/dl)	30 (51.7)	38 (90.5)	68 (100)		
Total	58 (100.0)	42 (100.0)	100 (100)		

The majority of neonates with seizures were born at term. Term neonates constituted 64% of the study population, while preterm neonates accounted for 36%. Although term babies were numerically higher, a substantial proportion of affected neonates were preterm. This distribution highlights that neonatal seizures are common in both term and preterm infants, with a considerable burden among preterm neonates.

Gestational Age vs Hypomagnesemia: Half of the preterm neonates (50%) had hypomagnesemia compared to only 21.9% of termneonates. The association was statistically significant (x = 8.39, p = 0.004). These findings indicate that preterm neonates are at a significantly higher risk of hypomagnesemia. Immature renal handling and inadequate mineral stores in preterm infants may contribute to this observation.

Elevated oxidative stress was present in a substantial proportion of neonates. Mild and moderate oxidative stress were observed in 22% and 24% of cases respectively, while severe oxidative stress was seen in 12%. Normal oxidative stress levels were observed in 42% of neonates. Overall, more than half of the study population exhibited some degree of oxidative stress. The mean magnesium level in the elevated oxidative stress group was 1.42 + 0.32 mg/dl,

whereas it was 1.86 + 0.38 mg/dl in the normal group. The difference was statistically significant (t = 6.27, $p < 0.001$). This finding indicates an inverse relationship between magnesium levels and oxidative stress. Magnesium deficiency may therefore play a role in oxidative stress generation.The mean oxidative stress value was 5.9 = 1.4 in the hypomagnesemia group versus 3.8 + 1.2 in the normal magnesium group. The difference was highly statistically significant (t = 7.73, $p < 0.001$).

Table 6: Comparison of Oxidative Stress Levels by Magnesium Status

Serum Magnesium Status	Mean Oxidative Stress ± SD	Median (IQR)	t-value	P-value
Hypomagnesemia (n = 32)	5.9 ± 1.4	6.0 (4.8–6.8)		<0.001
Normal Mg (n = 68)	3.8 ± 1.2	3.6 (3.0–4.5)		
Independent Student's t-test	7.73			

Mode of Delivery vs Hypomagnesemia: Hypomagnesemia was more common among neonates delivered vaginally (62.5%) compared to those delivered by LSCS (37.5%). However, this

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difference was not statistically significant (χ^2= 2.08, p = 0.14). The lack of significance suggests that mode of delivery does not independently influence serum magnesium status.

Univariate Predictor Analysis for Elevated Oxidative Stress: Hypomagnesemia was the strongest univariate predictor of elevated oxidative stress, with an odds ratio of 5.87 (p < 0.001). Preterm birth and low birth weight were also significantly associated with elevated oxidative stress. Male sex did not show a significant association. These findings indicate that metabolic and maturity-related factors play a greater role in oxidative stress than demographic factors alone.

Multivariate Logistic Regression Analysis for Elevated Oxidative Stress: After adjusting for confounding variables, hypomagnesemia remained an independent predictor of elevated oxidative stress. Neonates with hypomagnesemia had nearly five times higher odds of elevated oxidative stress (adjusted OR 4.92, p = 0.002). Preterm birth and low birth weight lost statistical significance in the multivariate model. This suggests that hypomagnese mia plays a central and independent role in oxidative stress generation.

Multivariate Predictor Analysis for Hypomagnesemia: Preterm birth and low birth weight were independent predictors of hypomagnesemia. Preterm m neonates had over three times higher odds of hypomagnesemia, while low birth weight neonates had more than twice the risk. Male sex and LSCS were not significant predictors. These findings indicate that biological immaturity and fetal growth restriction are key determinants of hypomagnesemia in neonates.

DISCUSSION

In the present study, neonatal seizures were observed predominantly in the early neonatal period. Of the total 100 neonates, 42% presented within the first 3 days of life, followed by 28 % between 4-7 days, 18% between 8-14 days, and only 12% between 15-28 days. Thus, 70% of seizures occurred within the first week of life. The mean age at presentation was 6.8 + 5.9 days, while the median age was 5 days (IQR: 29 days), clearly indicating an early-onset pattern.

These findings were comparable to the populationbased study by Ronen et al. (1999),[8] who reported an incidence of 2.6 neonatal seizures per 1000 live births, with seizures occurring predominantly in the early neonatal period. In their study, hypoxicischemic encephalopathy (HIE) accounted for 40% of cases, infections for 20%, and metabolic abnormalities for 19 %, conditions that typically manifest within the first few days after birth.

Although Ronen et al. did not provide exact daywise percentages, the clustering of seizures early in life strongly supported our observation that the immediate postnatal period is the most vulnerable window. Similar results were reported by Melasangam et al. (2024),[9] who studied 62 neonates with seizures and found that seizures occurred most frequently in the first three days of life, with a peak on day two (37%. The mean age at presentation in their study was 3.98 + 4.27 days, which was slightly lower than our mean age of 6.8 days, but still demonstrated a predominance of early neonatal seizures. Indian studies focusing on biochemical causes further support this pattern. Sood et al (2003),[10] evaluated 59 neonates and reported biochemical abnormalities in 49.15% (29/59) of cases, while primary metabolic seizures ac counted for 16.94% (10/59).

In the present study, a male predominance was noted among neonates with seizures.

Of the 100 neonates studied, 62% were males and 38% were females, indicating that male neonates were more frequently affected. This finding was consistent with the observations of Ronen et al,[8] (1999) who reported a higher incidence of neonatal seizures among male infants in their population-based study.

Although exact sexwise percentages were not highlighted, male neonates were noted to be more commonly affected, particularly among preterm and low-birth weight infants, suggesting increased male vulnerability. Comparable results were reported by Khalessi et al,[11] (2017) in their study on asphyxiated neonates, where 53.3% of affected neonates were male, which closely parallels the 62% male predominance observed in our study. Their findings suggested a significant association between perinatal asphyxia and lower serum magnesium levels, conditions that may predispose male neonates to seizures. In contrast, Melasangam et al,[9] (2024) reported a female predominance (58.1%) among neonates with seizures, differing from our findings. This variation could be attributed to differences in sample size (62 vs 100 neonates), study population characteristics, referral bias, or underlying etiological distribution.

In the present study, 48% (48/100) of neonates with seizures were low birth weight (< 2.5 kg), while 52% (52/100) had a birth weight ≥ 2.5 kg. The mean birth weight was 2.46 + 0.51 kg, and the median birth weight was 2.5 kg (IQR: 2.12.8 kg), indicating a borderline predominance of low birth weight neonates among seizure cases. These findings were strongly supported by the populationbased study of Ronen et al,[8] (1999) who demonstrated a markedly higher seizure burden among low birth weight infants. In their satudy, the incidenc e of neonatal seizures was 13.5 per 1000 live births in infants weighing < 2500 g, compared with 2.0 per 1000 live births in term neonates, indicating a sixfold higher risk in low birth w eight babies. This epidemiological evidence correlated our observation that nearly half of ne onates with seizures were low birth weight. Similarly, Kumar et al,[12] (1995) reported that primary metabolic disorders accounted

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for approximately 25% of neonatal seizures, and iden tified inappropriate intrauterine growth and inadequate feedingboth common in low birth wei ght infantsas major risk factors. These findings supported the association observed in our stu dy between lower birth weight and seizure occurrence.

In the present study, subtle seizures were the most common seizure type, accounting for 34% (34/100) of cases. This was followed by generalized tonic seizures in 26%, multifoc al clonic seizures in 18%, focal seizures in 14%, and myoclonic seizures in 8%. Comparable findings were reported by Melasangam et al,[9] (2024) who observed subtle seizures in 50 % of neonates, followed by generalized tonic seizures in 29%, multifocal clonic seizures in 1 1.3%, and other seizure types in smaller proportions. Although subtle seizures were more fre quent in their satudy (50% vs 34%), both studies consistently identified subtle seizures as th e predominant seizure type.

In the present study, hypomagnesemia (< 1.5 mg/dl) was detected in 32% (32/100) of n eonates with seizures, while 68% (68/100) had normal serum magnesium levels. The mean serum magnesium level was 1.62 = 0.41 mg/dl, and the median was 1.6 mg/di (IQR: 1.3-1.9mg/dl), indicating values near the lower limit of normal. These findings revealed a higher prevalence of hypomagnesemia compared with several earlier Indian studies. Sood et al. (2003) reported biochemical abnormalities in 49.15% (29/59) of neonates with seizures; however, primary metabolic abnormalities were present in only 16.94% (10/59). Hypomagnesemia was reported as an associated abnormality and was less frequent than hypocalcemia and hypoglycemia. Similarly, Kumar et al,[12] (1995) documented biochemical disturbances in approximately 66.7% of neonates with seizures, with hypomagnesemia occurring mainly in association with hypocalcemia and hypoxic-ischemic encephalopathy, rather than as an isolated abnormality.

In the present study, 58% (58/100) of neonates with seizures demonstrated elevated oxidative stress, while 42% (42/100) had normal oxidative stress levels. This finding indicated that oxidative stress was a common biochemical abnormality among neonates presenting with seizures and suggested a potential contributory role in seizure pathophysiology. Although earlier neonatal seizure studies did not directly quantify oxidative stress, indirect evidence strongly supported this observation. Sood et al,[10] (2003) reported biochemical abnormalities in 49.15% (29/59) of neonates with seizures, while Kumar et al,[12] (1995) observed biochemical disturbances in nearly twothirds (≈66.7%) of affected neonates. These abnormalities—particularly hypoglycemia, hypocalcemia, and hypomagnesemia—are well known triggers of oxidative injury through mitochondrial dysfunction and excitotoxic neuronal damage. Mechanistic confirmation was provided by Mitra et al,[13] (2016) who demonstrated that neonatal seizures following hypoxic ischemic encephalopathy were associated with acute increases in cerebral oxidative metabolism, followed by progressive decline in mitochondrial oxidative capacity, indicating sustained oxidative stress during ongoing seizures.

In the present study, a strong association was observed between serum magnesium status and oxidative stress. Elevated oxidative stress was present in 81.3% (26/32) of neonates with hypomagnesemia, compared to 47.1% (32/68) of neonates with normal magnesium levels. This association was statistically significant (χ^2= 15.9, p < 0.001). Earlier Indian studies documented hypomagnesemia as part of metabolic derangements in neonatal seizures but did not evaluate oxidative stress. Sood et al,[10] (2003) identified hypomagnesemia as an associated abnormality among neonates with biochemical disturbances, while Kumar et al,[12] (1995) reported hypomagnesemia occurring alongside hypocalcemia and hypoglycemia in approximately 25% of primary metabolic seizures. More recent evidence demonstrated variability in hypomagnesemia prevalence.

In the present study, a moderate negative correlation was observed between serum magnesium levels and oxidative stress (r = -0.46, p < 0.001). This indicated that declining serum magnesium levels were associated with progressively increasing oxidative stress. Comparable neonatal correlation data are limited; however, indirect evidence supported this inverse relationship. Mitra et al,[13] (2016) demonstrated that worsening seizure activity was associated with progressive mitochondrial oxidative dysfunction.

In the present study, subtle seizures were significantly associated with hypomagnesemia. Among neonates with subtle seizures, 58.8% (20/34) had hypomagnesemia, while 41.2 % (14/34) had normal magnesium levels. Conversely, among neonates with other seizure types, 81.8% (54/66) had normal magnesium levels. This association was statistically significant (χ^2= 16.44, p < 0.001). Melasangam et al,[9] (2024) reported subtle seizures as the most common seizure type (50%) but found no significant association between seizure type and electrolyte abnormalities.

In the present study, a strong association was observed between hypomagnesemia and hypocalcemia. Among neonates with hypocalcemia, 65% (26/40) had hypomagnesemia, whereas only 10% (6/60) of neonates without hypocalcemia had hypomagnesemia. This association was statistically significant (x2 = 16.44, p < 0.001). These findings were consistent with Sood et al. (2003),[10] who identified hypocalcemia as the most common primary met abolic abnormality and reported hypomagnesemia as a frequent associated disturbance.

In the present study, elevated oxidative stress was observed in 94.1% (32/34) of neonates with subtle

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seizures, compared with 39.4% (26/66) among neonates with other seizure types. Normal oxidative stress levels were predominantly seen in nonsubtle seizures (60.6%) compared to only 5.9% in subtle seizures. This association was highly statistically significant (χ^2= 27.57, p < 0.001), indicating a strong relationship between oxidative stress burden and seizure phenotype.

Sood et al,[10] (2003) reported biochemical abnormalities in 49.15% (29/59) of neonates with seizures, with abnormalities most frequently associated with hypoxic-ischemic encephalopathy (11/19 non metabolic cases). In the present study, hypomagnesemia was present in 48.3% (28/58) of neonates with seizures, compared to only 9.5% (4/42) among neonates without seizures. This association was highly significant (χ^2= 16.81, p < 0.001), clearly indicating that hypomagnesemia was an important biochemical risk factor for seizure occurrence. These findings were comparable with earlier studies. Sood et al,[10] (2003) identified biochemical abnormalities in 49.15% of neonates with seizures, and hypomagnesemia was reported as an associated abnormality, particularly in nonmetabolic seizures. Kumar et al,[12] (1995) reported biochemical disturbances in ~66.7% of neonatal seizures, with hypomagnesemia occurring alongside hypocalcemia and hypoglycemia, especially in asphyxiated neonates.

In the present study, 64% (64/100) of neonates with seizures were term, while 36 % (36/100) were preterm. Although term neonates constituted the majority numerically, more than one-third of seizure cases occurred in preterm infants. Comparable distributions were reported by Melasangam et al. (2024),[9] where 72.6% of neonates with seizures were term.

Earlier Indian studies by Sood et al,[10] (2003) and Kumar et al,[12] (1995) also predominantly involved term neonates, reflecting hospital-based sampling.

In the present study, hypomagnesemia was observed in 50% (18/36) of preterm neonates, compared to 21.9% (14/64) of term neonates. This association was statistically significant (χ^2=8.39, p = 0.004), indicating a markedly higher risk of magnesium deficiency among preterm infants. Earlier studies supported this observation. Khalessi et al,[11] (2017) reported significantly lower serum magnesium levels in asphyxiated neonates compared to controls, with an odds ratio of 2.188 (95% CI: 1.8262.626; p = 0.01) for hypomagnesemia. Gandhi et al,[14] (2020) reported hypomagnesemia in 2.5% of asphyxiated neonates, particularly on day 1 and day 3 of life, indicating dynamic magnesium fluctuations in sick neonates.

In the present study, 58% of neonates with seizures exhibited elevated oxidative stress, with 22% showing mild, 24% moderate, and 12% severe oxidative stress, while 42% had normal oxidative stress levels. Thus, more than half of the neonates presenting with seizures demonstrated biochemical evidence of oxidative imbalance, and notably, one in eight neonates had severe oxidative stress, indicating substantial cellular injury. Earlier neonatal seizure studies did not quantify oxidative stress using biochemical markers, yet their findings strongly support the presence of systemic metabolic derangements that predispose to oxidative injury

In the present study, neonates with elevated oxidative stress had a significantly lower mean serum magnesium level (1.42 = 0.32 mg/dl) compared with neonates having normal oxidative stress (1.86 + 0.38 mg/dl). This difference was highly statistically significant (t = 6.27, p < 0.001), indicating a strong inverse relationship between serum magnesium levels and oxidative stress burden. Comparable biochemical patterns have been described in earlier studies on neonatal seizures. Sood et al,[10] (2003) identified hypomagnesemia as one of the metabolic abnormalities contributing to the 49.15% biochemical abnormality rate in neonates with seizures.

In the present study, neonates with hypomagnesemia exhibited significantly higher oxidative stress values (5.9 + 1.4) compared to those with normal magnesium levels (3.8 + 1.2). This difference was highly statistically significant (t = 7.73, p < 0.001), demonstrating a robust association between magnesium deficiency and increased oxidative stress. Indirect support for this association was evident in classical neonatal seizure studies. Sood et al,[10] (2003) reported that associated metabolic abnormalities were more frequent in neonates with HIE (11 out of 19 cases), a condition characterized by severe oxidative injury.

In the present study, hypomagnesemia was more frequently observed among neonates delive red vaginally (62.5%) compared to those delivered by LSCS (37.5%); however, this difference was not statistically significant (χ^2= 2.08, p = 0.14). This indicated that mode of delivery did not independently influence neonatal serum magnesium status. These findings were consistent with previous literature. Gandhi et al,[14] (2020) reported a low prevalence of hypomagnesemia (2.5%) among neonates with birth asphyxia and found no significant association with antenatal or perinatal risk factors, including mode of delivery.

Physiological data from Rigo et al,[15] (2017) demonstrated that neonatal magnesium levels are primarily influenced by gestational age, renal maturity, prenatal magnesium exposure, and postnatal intake, rather than obstetric factors such as delivery mode. Therefore, the lack of a significant association in our study further supports the concept that hypomagnesemia in neonates is predominantly a metabolic and developmental phenomenon rather than a delivery related one.

In the present study, univariate analysis showed that hypomagnesemia was the most powerful predictor of elevated oxidative stress. Among neonates with hypomagnesemia, 81.3% (26/32) had elevated oxidative stress compared to only 18.7% (6/32) with normal oxidative stress, yielding an odds ratio of

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5.87 (95% CI: 2.2-15.4; p < 0.001). This clearly demonstrated a strong metabolic association between magnesium deficiency and oxidative stress burden. Preterm birth was also significantly associated with elevated oxidative stress, with 72.2% (26/36) of preterm neonates exhibiting elevated oxidative stress compared to 27.8% (10/36) term neonates (OR 3.10; p = 0.01). Similarly, low birth weight neonates showed elevated oxidative stress in 62.5% (30/48) compared to 37.5% (18/48) normal birth weight neonates (OR 2.25; P= 0.04).

Hypomagnesemia was documented as one of the metabolic disturbances, particularly in neonates with hypoxic ischemic encephalopathy (HIE), where 11 out of 19 cases had associated biochemical abnormalities. Similarly, Kumar et al,[12] (1995) reported biochemical disturbances in approximately twothirds (~66.7%; 23/35) of neonates with seizures, including hypomagnesemia, hypocalcemia, and hypoglycemia, particularly in asphyxiated and growth-restricted infants. These proportions were comparable to the 58% prevalence of elevated oxidative stress observed in our study, supporting the concept that metabolic derangements frequently coexist with oxidative imbalance.

In the present study, preterm birth and low birth weight emerged as independent predictors of hypomagnesemia. Preterm neonates had 3.10fold higher odds of hypomagnesemia (95% CI: 1.3-7.2; p = 0.009), while low birth weight neonates had 2.42 fold increased odds (95% CI: 1.15.4; p = 0.03). Male sex (aOR 1.18; p = 0.69) and LSCS delivery (aOR 0.89; p = 0.80) were not significant predictors. These findings were consistent with neonatal magnesium physiology described by Rigo et al,[15] (2017) who reported that serum magnesium levels were strongly influenced by gestational age, birth weight, renal maturity, and prenatal magnesium exposure.

CONCLUSION

This study comprehensively evaluated the role of serum magnesium status and oxidative stress in neonates presenting with seizures and generated several clinically relevant observations . Among the 100 neonates included, hypomagnesemia was identified in nearly one-third of cases (32%), underscoring its high prevalence in neonatal seizures. Elevated oxidative stress was present in 58% of the study population, indicating that oxidative imbalance is a frequent biochemical derangement in this vulnerable group.

A strong and statistically significant association was observed between hypomagnesemia and elevated oxidative stress. Neonates with hypomagnesemia demonstrated markedly higher oxidative stress levels (mean 5.9 + 1.4) compared to those with normal magnesium levels (3.8 + 1.2), and multivariate analysis confirmed hypomagnesemia as an independent predictor of elevated oxidative stress (adjusted OR 4.92; p = 0.002). In addition, a significant inverse cor relation was noted between serum magnesium levels and oxidative stress (i = -0.46; p < 0.001), reinforcing the protective antioxidant role of magnesium in neonatal physiology.

Clinically, hypomagnesemia showed significant associations with seizure characteristics and metabolic abnormalities. Subtle seizures were significantly more common in neonates with hypomagnesemia, and nearly half of neonates with seizure onset had low serum magnesium levels. Hypocalcemia was also strongly associated with hypomagnesemia, reflecting the close interdependence of magnesium and calcium metabolism in neonates. These findings highlight hypomagnesemia as a key contributor to both seizure occurrence and seizure phenotype.

Gestational maturity emerged as an important determinant of magnesium status. Preterm neonates accounted for 36% of the study population, and half of these infants had hypomagnesemia compared to only 21.9% of term neonates. Multivariate analysis further identified preterm birth and low birth weight as independent predictors of hypomagnesemia, emphasizing the role of immature renal function, limited mineral stores, and increased metabolic demand in preterm infants. Mode of delivery and sex, however, did not demonstrate a significant independent association with hypomagnesemia or oxidative stress.

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