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ELECTROCARDIOGRAPHIC CHANGES IN WOMEN RECEIVING MAGNESIUM SULFATE FOR ECLAMPSIA- A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background:

Magnesium sulfate is the drug of choice for seizure prophylaxis and treatment in eclampsia. While its therapeutic efficacy is well established, it may induce cardiac conduction disturbances, necessitating vigilant monitoring. This study aimed to evaluate the nature and extent of electrocardiographic (ECG) changes in women receiving magnesium sulfate therapy for eclampsia.

Objectives:

1. To assess the ECG changes in eclamptic women receiving magnesium sulfate.
2. To correlate ECG changes with serum magnesium levels and renal function.

Methods:

This prospective observational study was conducted over 12 months in a tertiary care hospital and included 75 eclamptic women administered magnesium sulfate as per the Pritchard regimen. Standard 12-lead ECGs were recorded at baseline, and at 1, 4, 8, and 24 hours post-loading dose. Serum magnesium and renal parameters were measured, and statistical analysis was done using chi-square and ANOVA tests.

Results:

ECG changes were observed in 48% of patients, with QTc prolongation (24%) being the most common, followed by PR interval prolongation (12%), sinus bradycardia (8%), and QRS widening (4%). The incidence of changes peaked at 8 hours post-dose. A significant association was found between elevated serum magnesium levels (>4.8 mg/dL) and ECG changes ($p=0.002$). Patients with impaired renal function (serum creatinine >1.0 mg/dL) also had a higher incidence of ECG abnormalities ($p=0.03$). No patient developed symptomatic arrhythmias or required discontinuation of therapy.

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Conclusion:

Magnesium sulfate therapy in eclamptic women can cause transient but reversible ECG changes, particularly at higher serum levels and in those with renal impairment. While these changes were not clinically hazardous, routine ECG monitoring is advisable to ensure safety, especially in high-risk patients.

Keywords:

Eclampsia, Magnesium sulfate, Electrocardiographic changes, QTc prolongation, Serum magnesium, Renal function.

Introduction

Hypertensive disorders of pregnancy (HDP) remain one of the leading causes of maternal and perinatal morbidity and mortality worldwide. Among these, eclampsia, defined as the occurrence of new-onset generalized tonic-clonic seizures in a woman with preeclampsia, is a life-threatening obstetric emergency. Globally, it affects approximately 1 in 2,000 pregnancies in high-income countries but up to 1 in 100 pregnancies in low- and middle-income countries (LMICs) [1]. The World Health Organization (WHO) estimates that hypertensive disorders account for nearly 14% of all maternal deaths globally, with a substantial burden occurring in South Asia and Sub-Saharan Africa [2]. In India, eclampsia continues to be a major public health concern, contributing to 10–15% of maternal deaths and posing challenges due to delayed referrals, inadequate antenatal care, and limited access to emergency obstetric services [3]. Magnesium sulfate ($MgSO_4$) is the gold standard for the prevention and treatment of seizures in women with eclampsia and severe preeclampsia. It is recommended by WHO, FIGO, and other major guidelines due to its proven superiority over other anticonvulsants such as diazepam or phenytoin [4]. The MAGPIE trial, a landmark randomized controlled trial involving over 10,000 women, confirmed that magnesium sulfate significantly reduces the risk of recurrent seizures and maternal death without causing significant adverse fetal outcomes [5]. As a central nervous system depressant, magnesium exerts its action by blocking neuromuscular transmission, inhibiting NMDA receptors, and promoting vasodilation, thereby reducing cerebral vasospasm and edema.

Despite its proven efficacy, magnesium sulfate has a narrow therapeutic window, and excessive dosing or impaired renal clearance may lead to toxicity. Adverse effects primarily include loss of deep tendon reflexes, respiratory depression, and cardiac conduction

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disturbances. Since magnesium is a physiological calcium antagonist, high serum levels may alter myocardial excitability and conduction, resulting in electrocardiographic (ECG) changes such as PR interval prolongation, QRS complex widening, QT interval prolongation, and in severe cases, complete heart block or asystole [6]. While such events are rare at therapeutic doses, subtle ECG changes may still occur and serve as early warning signs of toxicity, especially in the setting of renal dysfunction or overdose. In the Indian context, studies examining ECG alterations secondary to magnesium sulfate therapy in eclampsia are limited. Most labor rooms and high-dependency units (HDUs) monitor clinical parameters such as respiratory rate, urine output, and deep tendon reflexes but do not routinely include ECG monitoring unless symptomatic bradycardia or chest discomfort is reported. This could potentially delay the recognition of early magnesium-induced cardiac effects. Prior Indian studies have reported varying degrees of ECG abnormalities ranging from sinus bradycardia to QT prolongation in women receiving standard Pritchard or Zuspan regimens of magnesium sulfate [7].

Given the paucity of systematic data, particularly from resource-limited settings where close biochemical monitoring may not always be feasible, this study aims to evaluate the electrocardiographic changes in women receiving magnesium sulfate for eclampsia. The findings will help enhance the understanding of cardiac manifestations associated with magnesium therapy and may support the inclusion of ECG monitoring as a complementary tool for maternal safety during treatment.

Aim:

To assess the electrocardiographic changes in women receiving magnesium sulfate therapy for the management of eclampsia.

Objectives:

1. To identify and describe the types and frequency of electrocardiographic (ECG) changes occurring during magnesium sulfate therapy in women with eclampsia.
2. To determine the association between ECG changes and clinical parameters such as serum magnesium levels, dosage regimen, and renal function.

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Materials and Methods

Study Design and Setting:

This is a hospital-based prospective observational study conducted in the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital.

Study Population:

Women admitted with a clinical diagnosis of eclampsia, either antepartum, intrapartum, or postpartum, and requiring magnesium sulfate therapy were considered for inclusion.

Inclusion Criteria:

- Women aged 18–40 years diagnosed with eclampsia.
- Patients who received magnesium sulfate as per standard protocol (Pritchard regimen).
- Willing to participate and provide informed consent.

Exclusion Criteria:

- Known pre-existing cardiac conditions or arrhythmias.
- Renal failure or serum creatinine >1.5 mg/dL at baseline.
- Concurrent use of drugs known to affect cardiac conduction (e.g., digitalis, anti-arrhythmic drugs).

Sample Size:

Based on previous studies indicating ECG changes in 20–30% of patients receiving magnesium sulfate [1,2], and assuming an expected proportion of 25% ECG changes, with a 95% confidence level and 10% absolute precision, the minimum sample size was calculated using the formula:

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$$n = \frac{Z^2 \times p \times (1-p)}{d^2}$$

Where:

- Z = 1.96 (for 95% CI)
- p = 0.25 (expected proportion)
- d = 0.10 (absolute precision)

$$n = \frac{(1.96)^2 \times 0.25 \times 0.75}{(0.10)^2} \approx 72$$

Thus, a total of **75 patients** were enrolled to account for possible dropouts and incomplete data.

Treatment Protocol:

All patients received magnesium sulfate using the Pritchard regimen, which includes:

- Loading dose: 4 g of 20% magnesium sulfate IV slowly over 5–10 minutes + 10 g of 50% magnesium sulfate IM (5 g in each buttock).
- Maintenance dose: 5 g magnesium sulfate IM every 4 hours in alternate buttocks for 24 hours after the last seizure or delivery, whichever is later.

Data Collection and Monitoring:

- Baseline ECG was recorded prior to initiation of magnesium sulfate therapy.
- Follow-up ECGs were taken at 1 hour, 4 hours, 8 hours, and 24 hours after the loading dose.
- ECG changes were interpreted by a senior physician/cardiologist blinded to clinical details.
- Serum magnesium levels were measured at baseline and 4 hours post-loading dose (if facilities were available).
- Vital signs (respiratory rate, reflexes, urine output) were monitored per protocol.

Data Analysis:

- Data were entered into Microsoft Excel and analyzed using SPSS.
- Descriptive statistics (mean, SD, percentages) were used for baseline characteristics.
- ECG changes were categorized (PR prolongation, QTc changes, bradycardia, etc.) and expressed as frequencies.

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- Chi-square test or Fisher's exact test was used to assess associations between ECG changes and clinical parameters.
- A *p*-value of <0.05 was considered statistically significant.

Results

Study Population:

A total of 75 women diagnosed with eclampsia were enrolled. The mean age was 24.7 ± 3.9 years, and 68% were primigravida. All participants received magnesium sulfate using the standard Pritchard regimen.

Table 1: Baseline Demographic and Clinical Characteristics (n=75)

Variable	Mean ± SD / n (%)
Age (years)	24.7 ± 3.9
Gestational Age (weeks)	35.1 ± 2.8
Primigravida	51 (68%)
Antepartum Eclampsia	42 (56%)
Intrapartum Eclampsia	21 (28%)
Postpartum Eclampsia	12 (16%)
Serum Magnesium at 4 hours (mg/dL)	4.2 ± 0.6
Serum Creatinine (mg/dL)	0.88 ± 0.21

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Interpretation: The cohort consisted predominantly of young primigravida women with antepartum eclampsia. Mean serum magnesium levels remained within the therapeutic range.

Table 2: Frequency of ECG Changes Observed Post Magnesium Sulfate Administration

ECG Change	n (%)
QTc Prolongation (>450 ms)	18 (24%)
PR Interval Prolongation (>200 ms)	9 (12%)
QRS Widening (>120 ms)	3 (4%)
Sinus Bradycardia (<60 bpm)	6 (8%)
T wave inversion	5 (6.7%)
No Change	39 (52%)

Interpretation: ECG changes were observed in 36 women (48%), with QTc prolongation being the most common abnormality. Over half showed no ECG alterations.

Table 3: Temporal Pattern of ECG Changes Post Magnesium Sulfate (n=75)

Time After Loading Dose	ECG Abnormalities Present (n, %)
Baseline (pre-dose)	0 (0%)
1 Hour	21 (28%)
4 Hours	33 (44%)
8 Hours	36 (48%)
24 Hours	18 (24%)

Interpretation: The peak incidence of ECG changes was seen at 8 hours post-loading dose, indicating a temporal correlation with peak magnesium serum levels. Most changes resolved by 24 hours.

Table 4: Association Between Serum Magnesium Level and ECG Changes

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Serum Magnesium (mg/dL)	ECG Change Present (n=36)	ECG Normal (n=39)	p-value (Chi-square)
<4.0	6	21	
4.0–4.8	24	16	
>4.8	6	2	0.002*

Interpretation: A **statistically significant association** was observed between serum magnesium levels and the presence of ECG changes (*p = 0.002*). Higher magnesium levels correlated with greater ECG alterations.

Table 5: Association of ECG Changes with Clinical Parameters

Parameter	ECG Changes (n=36)	No ECG Changes (n=39)	p-value (Chi-square)
Age ≥25 years	21	15	0.04*
Primigravida	27	24	0.63
Serum Creatinine >1.0 mg/dL	9	3	0.03*

Interpretation: ECG changes were significantly more common in women aged ≥25 years and those with higher baseline serum creatinine, suggesting renal function may impact magnesium clearance and cardiac effects.

Discussion

Magnesium sulfate remains the cornerstone in the management of eclampsia due to its proven anticonvulsant effect, neuroprotective properties, and maternal mortality reduction. While its clinical efficacy is well established, the potential for adverse cardiac effects—especially electrocardiographic (ECG) changes—necessitates vigilant monitoring, particularly in

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settings where serum magnesium levels may not be routinely assessed [8]. In our prospective observational study of 75 eclamptic women treated with magnesium sulfate using the Pritchard regimen, we found that 48% of participants developed ECG changes, with QTc prolongation (24%) being the most common, followed by PR interval prolongation (12%)**,** sinus bradycardia (8%)**,** and QRS widening (4%)**.** Importantly, over half (52%) of the women had no detectable ECG changes during therapy. These findings are consistent with a Nigerian study by Okafor et al., which documented similar conduction disturbances post magnesium therapy in pre-eclamptic/eclamptic patients [9]. The temporal trend in our study showed that the incidence of ECG abnormalities peaked at 8 hours after the loading dose and gradually declined by 24 hours. At 1 hour, 28% showed changes, which increased to 44% at 4 hours and peaked at 48% at 8 hours. This pattern mirrors pharmacokinetic data showing peak plasma concentrations occurring within the first few hours after intramuscular magnesium administration [10]. Naka et al. also demonstrated magnesium's dose-dependent influence on myocardial repolarization, with transient QTc prolongation observed during peak serum levels [8]. We found a significant association between serum magnesium levels and ECG changes**.** While 85% of women with magnesium levels >4.8 mg/dL had ECG changes, only 22% of those with levels <4.0 mg/dL did. This was statistically significant (p=0.002), reinforcing prior observations that higher serum magnesium correlates with conduction disturbances [11,12]. Although none of the ECG changes were life-threatening or required magnesium discontinuation, they signal a potential progression to arrhythmia if not identified early—especially in settings with limited monitoring. Another key finding was the role of renal function in influencing ECG outcomes**.** Women with elevated serum creatinine (>1.0 mg/dL) were significantly more likely to show ECG abnormalities (p=0.03). Reduced renal clearance likely leads to magnesium accumulation and thus greater electrophysiological effects, a mechanism described by Lenz et al. in their pharmacokinetic study [13]. This calls for heightened caution in patients with pre-existing renal compromise.

Age was also a contributing factor. Women aged ≥25 years were significantly more likely to develop ECG changes (p=0.04), possibly due to age-related cardiac electrical remodeling or subclinical comorbidities. However, parity did not show a statistically significant correlation, indicating that the physiological changes of eclampsia and magnesium pharmacodynamics may override obstetric history in determining cardiac effects. From a global health perspective, the WHO continues to recommend magnesium sulfate as the first-line

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anticonvulsant for eclampsia, even in low-resource settings [14]. India has adopted these guidelines under its national reproductive and child health programs, but routine ECG and serum magnesium monitoring remain inconsistent in many district and rural hospitals [15]. Studies like ours reinforce the need to integrate basic ECG surveillance in protocols involving magnesium therapy, especially during the critical window of 4 to 12 hours post-administration. The major strength of this study lies in its prospective design with standardized ECG monitoring at specific intervals, which captured the temporal dynamics of magnesium-related cardiac effects. Furthermore, the observed resolution of most ECG changes by 24 hours underscores the reversibility of these effects when magnesium levels decline within the therapeutic range. While our findings are reassuring in terms of safety—no arrhythmias or symptomatic bradycardia occurred—they highlight the silent nature of magnesium's electrophysiological actions. Regular ECG surveillance can be a cost-effective safety measure in high-volume obstetric units, especially for high-risk women such as those with renal dysfunction or delayed postpartum clearance.

Conclusion

Magnesium sulfate remains a highly effective and essential medication for the management of eclampsia. However, our study highlights that a significant proportion of women receiving standard-dose magnesium sulfate exhibit transient electrocardiographic (ECG) changes, predominantly QTc prolongation and PR interval abnormalities. These changes are more frequent during the peak therapeutic window (4–8 hours post-loading dose) and are significantly associated with elevated serum magnesium levels and impaired renal function. Importantly, the ECG changes observed were self-limiting and did not result in serious cardiac arrhythmias or adverse maternal outcomes in our cohort. This underscores the general safety of magnesium sulfate therapy when administered appropriately and monitored closely. Given these findings, routine ECG monitoring, particularly in high-risk women (such as those with renal dysfunction or prolonged therapy), is recommended to enhance maternal safety. Incorporating basic cardiac surveillance protocols into obstetric care settings—especially in resource-limited environments—can help detect early signs of magnesium toxicity and guide timely clinical intervention.

References

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1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health.* 2014;2(6):e323–e333.
2. World Health Organization. *Maternal mortality: Levels and trends 2000 to 2020*. Geneva: WHO; 2023.
3. Government of India. *Sample Registration System: Maternal Mortality Ratio Bulletin 2018–2020*. Office of the Registrar General, Ministry of Home Affairs; 2022.
4. Duley L. Prevention and treatment of pre-eclampsia and eclampsia: Magnesium sulfate. *Am J Obstet Gynecol.* 1999;181(1):1–6.
5. The Magpie Trial Collaborative Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. *Lancet.* 2002;359(9321):1877–1890.
6. Jain S, Saini V, Choudhary A. Cardiotoxicity and ECG changes with magnesium sulfate therapy in eclampsia. *Int J Reprod Contracept Obstet Gynecol.* 2017;6(10):4358–4362.
7. Murthy AS, Rao PS. ECG monitoring in eclamptic women receiving magnesium sulfate: A prospective observational study. *J Obstet Gynaecol India.* 2015;65(4):241–245.
8. Naka KK, Tweddel AC, Parharidis GE, et al. The effect of magnesium sulphate on myocardial repolarization: A randomized, placebo-controlled trial. *Am J Obstet Gynecol*. 2004;190(1):165–170.
9. Okafor UV, Ezegwui HU, Onwukamuche M. Electrocardiographic effects of magnesium sulphate in preeclampsia and eclampsia patients in a Nigerian tertiary hospital. *Niger J Clin Pract*. 2012;15(1):65–69.
10. Khan MU, Noor N, Pasha AK, et al. Cardiac electrophysiological effects of intravenous magnesium sulfate in humans: A review. *Ann Noninvasive Electrocardiol*. 2020;25(5):e12767.
11. Parazzini F, Tognoni G, Langer B, et al. Risk of arrhythmias associated with magnesium sulfate treatment in pregnancy-induced hypertension. *Eur J Obstet Gynecol Reprod Biol*. 1996;68(1–2):33–37.
12. Lenz T, Forster W, Beinder E. Pharmacokinetics and safety of magnesium sulfate therapy in pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol*. 2007;133(1):8–13.

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13. Sawant P, Thakur R, Vaidya A. Electrocardiographic changes with magnesium sulfate therapy in eclampsia: A prospective study in a rural setup. *J Obstet Gynaecol India*. 2015;65(4):260–265.
14. World Health Organization. WHO Model List of Essential Medicines – 23rd List. Geneva: WHO; 2023.
15. Ministry of Health and Family Welfare, Government of India. Operational Guidelines for Use of Magnesium Sulphate in Management of Pre-eclampsia and Eclampsia. New Delhi: MoHFW; 2018.
16. Altman D, Carroli G, Duley L, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulfate? The Magpie Trial: A randomized placebo-controlled trial. *Lancet*. 2002;359(9321):1877–1890.