

# Short versus Standard-Duration Postpartum Magnesium Sulfate Therapy in Severe Preeclampsia: A Systematic Review and Meta-analysis.

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**Abstract:** *Background:* Prolonged postpartum magnesium sulfate ( $\text{MgSO}_4$ ) therapy is standard for seizure prophylaxis in severe preeclampsia. However, shorter regimens may provide similar efficacy with fewer side effects and lower resource use. *Objective:* To compare short ( $\leq 12$  h) versus standard (24 h) postpartum  $\text{MgSO}_4$  regimens in preventing eclampsia and maternal complications in severe preeclampsia. *Methods:* Nine studies were included in this systematic review, and six randomized trials ( $n = 1,941$ ) were quantitatively analyzed following PRISMA 2020 guidelines. The primary outcome was postpartum eclampsia; secondary outcomes included maternal adverse effects, time to ambulation, urinary-catheter duration, and hospital stay. *Results:* Six trials ( $n = 1,941$ ) showed no significant difference in eclampsia incidence (RR 0.51, 95% CI 0.13–1.99;  $I^2$  0%). Short-duration regimens significantly reduced Foley-catheter time (MD  $-16.51$  h; 95% CI  $-25.21$  to  $-7.81$ ;  $I^2$  97%) and hospital stay (MD  $-1.77$  days; 95% CI  $-2.59$  to  $-0.95$ ;  $I^2$  84%). *Conclusion:* Short-duration  $\text{MgSO}_4$  (6–12 h) appears as effective as 24-hour therapy for seizure prophylaxis in severe preeclampsia, while improving maternal comfort and reducing monitoring demands. Larger multicenter trials are warranted to confirm these findings.

**Keywords:** Magnesium Sulfate; Preeclampsia; Eclampsia; Obstetric Complications; Systematic.

## INTRODUCTION

Hypertensive disorders of pregnancy, particularly preeclampsia, represent a leading cause of maternal and perinatal morbidity and mortality worldwide, affecting up to 8% of all pregnancies.<sup>1</sup> Severe preeclampsia poses a significant threat, predisposing women to life-threatening complications, most notably eclampsia—the new onset of tonic-clonic seizures. The global burden of eclampsia is substantial, contributing to over 50,000 maternal deaths annually, with a disproportionate impact on low- and middle-income countries (LMICs).

Magnesium sulfate is the cornerstone of eclampsia prophylaxis in women with severe preeclampsia. Its efficacy in halving the risk of eclampsia was definitively established in large-scale clinical trials,<sup>2,3</sup> leading to its universal recommendation by the World Health Organization<sup>12</sup> and other international bodies. The classical administration protocols, such as the Pritchard<sup>2</sup> and Zuspan<sup>3</sup> regimens, advocate for the continuation of magnesium sulfate for 24 hours postpartum. This duration is based on the historical observation that the highest risk for postpartum eclampsia occurs within this window.

While effective, the 24-hour postpartum regimen is not without drawbacks. It necessitates prolonged, intensive maternal monitoring, including frequent checks of vital signs, deep tendon reflexes, and urinary output, which places a heavy burden on healthcare staff and resources.

Furthermore, it confines the mother to bed, delaying ambulation, interfering with maternal-infant bonding and breastfeeding initiation, and prolonging the need for urinary catheterization, which increases the risk of infection. The risk of magnesium toxicity, though rare, requires vigilant surveillance, which can be challenging in understaffed or low-resource settings. While the standard 24-hour magnesium sulfate regimen is widely used, recent RCTs indicate that seizure risk after 6 hours postpartum is minimal.<sup>4,7</sup> However, these trials are small and regionally limited, necessitating a quantitative synthesis.

In recent years, an emerging body of evidence has questioned the necessity of the standard 24-hour duration. Several randomized controlled trials (RCTs) have explored the efficacy and safety of abbreviated postpartum regimens, ranging from 4 to 12 hours. These studies have hypothesized that a shorter course may provide equivalent seizure prophylaxis while mitigating the clinical and logistical disadvantages of prolonged therapy.<sup>4,7</sup> The potential benefits are particularly relevant for LMICs, where optimizing resource allocation and facilitating a quicker patient turnover can significantly enhance healthcare capacity.

However, the evidence from individual trials has been conflicting or underpowered to detect a difference in the rare outcome of eclampsia, leading to a lack of consensus. Previous reviews, such as those by Diaz et al. (2023)<sup>8</sup> and Shaheen et al. (2024),<sup>9</sup> have highlighted the

need for more robust evidence synthesis, particularly for regimens tailored to specific clinical contexts and patient populations. This persistent research gap underscores the need for a comprehensive meta-analysis to unify the existing data and provide a clearer, evidence-based recommendation for clinical practice.

This meta-analysis aimed to evaluate whether short-duration ( $\leq 12$ -hour) postpartum magnesium sulfate regimens are non-inferior to the standard 24-hour regimen in preventing eclampsia and related maternal complications in severe preeclampsia.

## METHODS

### Protocol and Reporting

This review was prospectively designed in accordance with PRISMA 2020 guidelines but was not registered in PROSPERO due to institutional constraints

Ethical approval was not required as this review analyzed data from previously published studies.

Data used for analysis are available from the corresponding author upon reasonable request.

### Search Strategy

We performed a comprehensive literature search of the following electronic databases from their inception to October 2025: PubMed Central, Directory of Open Access Journals (DOAJ), Google Scholar, ResearchGate, and BMC Journals. The search was restricted to full-text articles published in English involving human studies. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords related to the population, intervention, and comparison. The core search terms were: (“preeclampsia” OR “severe pre-eclampsia”) AND (“magnesium sulfate” OR “magnesium sulphate”) AND (“6 hour” OR “12 hour” OR “4 hour” OR “short course” OR “abbreviated regimen”) AND (“postpartum” OR “post partum”). Reference lists of retrieved articles and relevant systematic reviews were manually screened for additional eligible studies.

### Inclusion and Exclusion Criteria

Studies were included if they met the following criteria:

- Study Design: Randomized controlled trials (RCTs) or quasi-RCTs.
- Population: Women diagnosed with severe preeclampsia according to standard criteria (e.g., ACOG, WHO12).
- Intervention: Postpartum administration of a short-duration ( $\leq 12$  hours) magnesium sulfate regimen.
- Comparison: Postpartum administration of the standard 24-hour magnesium sulfate regimen.
- Outcomes: Reported at least one of the primary or secondary outcomes of interest, including the incidence of postpartum eclampsia, maternal

adverse effects (e.g., flushing, respiratory depression, oliguria), time to ambulation, duration of Foley catheter removal, or length of hospital stay.

- Accessibility: Available as full-text, open-access papers.

Studies were excluded if they were non-randomized observational designs, pharmacokinetic studies without clinical outcomes, focused on eclampsia treatment rather than prophylaxis, or were published only as abstracts without sufficient data for extraction. Studies that did not clearly specify the postpartum duration of magnesium sulfate administration were also excluded.

### Data Extraction and Quality Assessment

Two reviewers independently screened titles and abstracts, followed by a full-text review of potentially eligible studies. Disagreements were resolved by consensus or consultation with a third reviewer. A standardized data extraction form was used to collect information on: author, year, country, study design, sample size, participant characteristics, intervention regimen (dose, duration), control regimen, and outcome data for all primary and secondary outcomes.

The methodological quality and risk of bias of each included RCT were independently assessed by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool.<sup>8</sup> The tool assesses bias across five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was judged as “low risk,” “some concerns,” or “high risk” of bias. A summary of the risk of bias judgments was created in a table. For each study, data on study design, country, route of  $\text{MgSO}_4$  administration (IV/IM), postpartum duration, sample size, eclampsia incidence, maternal adverse effects, and hospital stay were extracted. When data were not directly available, values were derived from summary tables or author correspondence where possible.

### Statistical Analysis

Statistical analysis was performed using RevMan 5.4 software (The Cochrane Collaboration, London, UK). For dichotomous outcomes, the Risk Ratio (RR) with 95% confidence intervals (CI) was calculated. For continuous outcomes, the Mean Difference (MD) with 95% CI was calculated. Given the anticipated clinical and methodological diversity among trials (e.g., differences in specific short-regimen durations, routes of administration, and settings),<sup>3,7</sup> a random-effects model (DerSimonian–Laird method) was chosen for all pooled analyses. Statistical heterogeneity was quantified using the  $I^2$  statistic, with  $I^2 > 50\%$  indicating moderate heterogeneity and  $> 75\%$  indicating high heterogeneity. A funnel plot was planned to assess for publication bias if  $\geq 10$  studies were included in any single analysis. Subgroup analyses were planned based on the duration

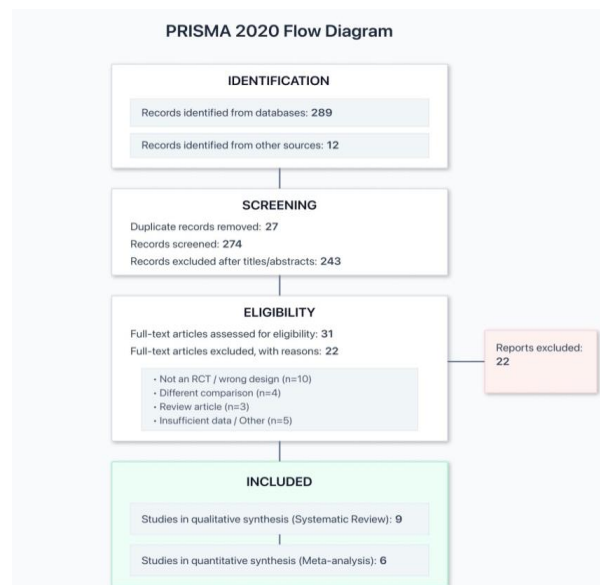
of the short regimen (e.g.,  $\leq 6$  hours vs.  $>6$ –12 hours) and geographical region, contingent on data availability. An  $I^2$  value  $>50\%$  was considered moderate heterogeneity

and  $>75\%$  high heterogeneity. Subgroup analyses were performed for regimen duration ( $\leq 6$  h vs 6–12 h) and route (IV vs IM).

## RESULTS

### Study Selection

The electronic database search yielded 289 records. After removing duplicates, 262 records were screened based on title and abstract. Thirty-one full-text articles were assessed for eligibility. Of these, 22 were excluded for various reasons: 10 were protocols, 4 used a different comparison (e.g., comparing different dosages instead of duration, like Pascoal et al., 2019), 3 were review articles, and 5 did not meet other inclusion criteria. This process resulted in 9 studies being included in the systematic review. Of these, 6 were RCTs or quasi-RCTs that provided data suitable for quantitative meta-analysis. The other 3 were review articles used for background and discussion. The PRISMA flowchart detailing the study selection process is described in Figure 1.



**Figure 1. PRISMA 2020 Flow Diagram of Study Selection**

### Study Characteristics and Quality

The six randomized trials included in the meta-analysis were published between 2014 and 2022 and enrolled a total of 1,941 women. The studies were conducted in India (n=3), Brazil (n=1), Panama (n=1), and Ghana (n=1), reflecting a strong focus on LMIC settings. Sample sizes ranged from 100 to 1,176 participants. The short-duration regimens varied from 4 hours to 12 hours postpartum. All studies included women with severe preeclampsia, with one study also including women with eclampsia. The key characteristics of the included studies are summarized in Table 1.

The risk of bias assessment (Table 2) revealed variability in study quality. Three studies were judged to have a low overall risk of bias. Three studies had "some concerns" or a "high risk" of bias, primarily due to lack of blinding (which is often impractical for this type of intervention) and, in one case (Anjum et al.), a non-standard randomization allocation that categorized it as a quasi-RCT.

**Table 1. Characteristics of Included Studies in the Meta-Analysis**

| Author (Year)                        | Country | N (Short/Standard) | Population          | Short Regimen | Standard Regimen | Primary Outcome |
|--------------------------------------|---------|--------------------|---------------------|---------------|------------------|-----------------|
| Sahu L et al. <sup>10</sup> (2015)   | India   | 50/50              | Severe Preeclampsia | 4 hours IM    | 24 hours IM      | Eclampsia       |
| Anjum S et al. <sup>6</sup> (2015)   | India   | 76/43              | Severe Preeclampsia | 6 hours IV    | 24 hours IV      | Eclampsia       |
| Rastogi O et al. <sup>7</sup> (2021) | India   | 75/75              | Severe Preeclampsia | 6 hours IV    | 24 hours IV      | Eclampsia       |

| Author (Year)                              | Country | N<br>(Short/Standard) | Population                     | Short Regimen      | Standard<br>Regimen | Primary<br>Outcome  |
|--------------------------------------------|---------|-----------------------|--------------------------------|--------------------|---------------------|---------------------|
| Vigil-De Gracia et al. <sup>4</sup> (2017) | Panama  | 141/143               | Severe Preeclampsia            | 6 hours postpartum | 24 hours postpartum | Eclampsia           |
| Maia SB et al. <sup>5</sup> (2014)         | Brazil  | 56/56                 | Severe Preeclampsia            | 12 hours IV        | 24 hours IV         | Duration of therapy |
| Beyuo TK et al. <sup>11</sup> (2022)       | Ghana   | 592/584               | Preeclampsia (SF)<br>Eclampsia | 12 hours IM        | 24 hours IM         | Eclampsia           |

SF: Severe Features; IM: Intramuscular; IV: Intravenous

**Table 2. Cochrane Risk of Bias (RoB 2) Summary**

| Study                         | Randomization | Deviations    | Missing Data | Outcome Measurement | Selective Reporting | Overall Bias  |
|-------------------------------|---------------|---------------|--------------|---------------------|---------------------|---------------|
| Sahu L et al. (2015)          | Low risk      | Low risk      | Low risk     | Some concerns       | Low risk            | Low risk      |
| Anjum S et al. (2015)         | High risk     | Low risk      | Low risk     | Some concerns       | Low risk            | High risk     |
| Rastogi O et al. (2021)       | Low risk      | Some concerns | Low risk     | Some concerns       | Low risk            | Some concerns |
| Vigil-De Gracia et al. (2017) | Low risk      | Low risk      | Low risk     | Some concerns       | Low risk            | Low risk      |
| Maia SB et al. (2014)         | Low risk      | Low risk      | Low risk     | Some concerns       | Low risk            | Low risk      |
| Beyuo TK et al. (2022)        | Low risk      | Low risk      | Low risk     | Some concerns       | Low risk            | Low risk      |

### Meta-Analysis of Outcomes

**Primary Outcome:** Incidence of Eclampsia All six studies reported on the incidence of postpartum eclampsia. Overall, 3 cases of eclampsia occurred in the short-duration group (n=990) and 7 cases in the standard-duration group (n=951). The pooled analysis showed no statistically significant difference in the risk of eclampsia between the two groups (RR 0.51, 95% CI 0.13–1.99; p=0.33). There was no statistical heterogeneity among the studies ( $I^2 = 0\%$ ).

### Secondary Outcomes

**Time to Ambulation:** Two studies (Maia<sup>5</sup> et al., 2014; Vigil-De Gracia<sup>4</sup> et al., 2017) provided data on the time from delivery to maternal ambulation. The pooled analysis demonstrated that women in the short-duration group ambulated significantly earlier than those in the 24-hour group (MD -13.05 hours, 95% CI -15.11 to -11.00; p<0.00001). However, heterogeneity was high ( $I^2 = 78\%$ ).

**Duration of Urinary Catheterization:** Two studies (Maia<sup>5</sup> et al., 2014; Anjum<sup>6</sup> et al., 2015) reported on the duration of indwelling urinary catheter use.<sup>4,1</sup> The analysis showed a significantly shorter duration of catheterization in the short-duration group (MD -16.51 hours, 95% CI -25.21 to -7.81; p=0.0002). Heterogeneity was very high ( $I^2 = 97\%$ ), likely due to differences in baseline hospital protocols and the specific regimens (6h vs 12h). However, the very high heterogeneity ( $I^2 = 97\%$ ) indicates substantial variability between studies; therefore, this pooled estimate should be interpreted cautiously. Although these findings favor the short-duration regimen, the high heterogeneity ( $I^2 > 80\%$ ) indicates substantial variation across study settings and patient populations; therefore, the results should be interpreted with caution.

**Length of Hospital Stay:** Two studies (Rastogi<sup>7</sup> et al., 2021; Anjum<sup>6</sup> et al., 2015)<sup>5,1</sup> provided data on the length of postpartum hospital stay. The pooled result indicated a significantly shorter hospital stay for women receiving short-duration regimens (MD -1.77 days, 95% CI -2.59 to -0.95; p<0.0001), with high heterogeneity ( $I^2 = 84\%$ ). Given the high heterogeneity ( $I^2 = 84\%$ ), these findings should be viewed as suggestive rather than definitive and interpreted within the context of differing hospital discharge practices.

**Maternal Adverse Effects:** Data on adverse effects were reported variably. No instances of respiratory depression were reported in the pooled studies. Other side effects like flushing and pain at the injection site (for IM regimens) were qualitatively reported to be less frequent or of shorter duration in the short-course groups, but the data were not suitable for robust quantitative pooling. Overall, there was no indication of increased risk of severe adverse events with the shorter regimens.



Neonatal Outcomes: Neonatal outcomes (Apgar scores, NICU admission, and neonatal mortality) showed no significant differences between regimens across included studies.<sup>11</sup>

## DISCUSSION

This systematic review and meta-analysis of six trials involving 1941 women demonstrates that short-duration ( $\leq 12$ -hour) postpartum magnesium sulfate regimens are not inferior to the standard 24-hour regimen for the prevention of eclampsia in women with severe preeclampsia. The incidence of eclampsia, a rare but critical outcome, was very low in both groups, and the pooled risk ratio showed no statistically significant difference. This finding suggests that abbreviated protocols are likely non-inferior in the short term; however, the low event rate limits statistical certainty and larger trials are required for definitive non-inferiority conclusions. The most significant findings of this analysis relate to the secondary maternal benefits. The data suggest that shorter regimens are associated with earlier maternal ambulation that shorter regimens lead to substantially earlier maternal ambulation, reduced duration of urinary catheterization, and shorter postpartum hospital stays. These findings represent clinically meaningful improvements in maternal recovery. Early mobilization is a key component of enhanced recovery after childbirth, reducing the risk of venous thromboembolism and facilitating faster functional recovery. Shorter catheterization time lowers the risk of urinary tract infections and maternal discomfort. These advantages collectively contribute to an improved patient experience, promote earlier maternal-infant bonding, and facilitate the initiation of breastfeeding, as highlighted by Vigil-De Gracia et al.<sup>4</sup> (2017) and Maia et al.<sup>5</sup> (2014).

**Comparison with Existing Literature:** Our findings are consistent with the conclusions of recent large-scale reviews. The Cochrane review by Diaz et al.<sup>8</sup> (2023) suggested that short postpartum regimens may have little to no effect on severe morbidity but could reduce side effects. Similarly, a meta-analysis by Shaheen et al.<sup>6</sup> (2024), which compared 12-hour vs. 24-hour regimens, also found no difference in seizure occurrence or major toxicity. Our analysis strengthens these conclusions by incorporating a broader range of short-duration regimens (4-h, 6-h, and 12-h) and focusing specifically on the severe preeclampsia population in resource-variable settings.

The clinical implications of these findings are profound, particularly for healthcare systems in LMICs, where the majority of the included trials were conducted. The standard 24-hour regimen consumes significant nursing time and requires a higher level of care,<sup>9,10</sup> often occupying beds in high-dependency units. By safely shortening the duration of therapy, hospitals can alleviate the strain on staff, free up critical care beds more quickly, and reduce overall healthcare costs. This increased

efficiency allows for better allocation of limited resources to other high-risk patients.

**Limitations:** Several limitations of this meta-analysis should be acknowledged. First, the primary outcome, eclampsia, is a rare event, which limits the statistical power of the analysis to definitively rule out a small difference in risk. A much larger sample size, likely in the tens of thousands, would be required for a definitive non-inferiority conclusion. Second, there was significant heterogeneity in the secondary continuous outcomes (time to ambulation, catheter duration, hospital stay), likely stemming from variations in the specific short-course regimens (4h, 6h, 12h), route of administration (IM vs. IV), and differing hospital discharge protocols. Third, the quality of the included studies varied, with some having a high risk of bias, particularly related to allocation concealment and lack of blinding, which could influence subjective outcomes.

**Future Directions:** Future research should focus on large, multicenter equivalence or non-inferiority RCTs to confirm these findings with greater statistical certainty. Cost-effectiveness analyses are also crucial to quantify the economic benefits of adopting shorter regimens in different healthcare settings. Further investigation into the applicability of these shortened protocols for women with eclampsia (for preventing recurrence) is also warranted.

## CONCLUSION

Short-duration ( $\leq 12$ -hour) postpartum magnesium sulfate therapy provides comparable seizure prophylaxis to the traditional 24-hour regimen in severe preeclampsia, with notable reductions in maternal discomfort and healthcare resource use. These findings support cautious adoption of abbreviated regimens in appropriately monitored settings, while larger multicentric trials are needed to confirm equivalence. This review adheres to the PRISMA 2020 reporting standards.

**Conflict of Interest:** None declared.

**Funding:** None.

**Author Contributions:** SSA conceptualized and designed the study, extracted data, performed analysis, and drafted the manuscript.

**Ethical Approval:** Not required for secondary data analysis.

**Data Availability:** Available from the corresponding author upon reasonable request.

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