



## Original Article

# The Therapeutic Effect of Curcumin on Episiotomy Wound Healing: A Systematic Review and Meta-Analysis

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## Abstract

**Background:** Pain and infection after episiotomy are common challenges that hinder maternal recovery. Curcumin, with anti-inflammatory and antimicrobial properties, is a potential therapeutic agent, but its efficacy for episiotomy healing is unproven. This study aimed to systematically evaluate the effect of topical curcumin on episiotomy wound healing.

**Methods:** Databases including Google Scholar, PubMed, Cochrane, Web of Sciences, Scopus, Embase, ProQuest, SID, and Magiran were searched until March 11, 2025, using MeSH and Emtree keywords. Risk of bias was assessed with Cochrane RoB 1 and ROBINS-I tools. A random-effects meta-analysis calculated the mean difference (MD) with 95% CIs. Heterogeneity was quantified by the  $I^2$  statistic, and evidence certainty was assessed using the GRADE framework.

**Results:** The search retrieved 2531 articles; after removing duplicates and ineligible studies, four articles were included in the systematic review. Meta-analysis of three studies showed no statistically significant effect of curcumin on perineal wound healing compared to controls (MD = -1.02; 95% CI: -2.39 to 0.35,  $p = 0.14$ ), with substantial heterogeneity ( $I^2 = 83\%$ ,  $p = 0.003$ ). Evidence quality was very low.

**Conclusion:** Based on a limited number of studies, available evidence is of very low quality and does not demonstrate a statistically significant effect of curcumin on episiotomy wound healing. Due to the scarcity and low quality of evidence, firm conclusions cannot be drawn. This review underscores a critical evidence gap, highlighting the urgent need for high-quality randomized controlled trials.

### Implications for Nursing and Midwifery Preventive Care

- No reliable evidence supports topical curcumin for episiotomy healing.
- Focus on proven care: hygiene, pain management, infection detection.
- Critically evaluate natural remedies to ensure safe, evidence-based postpartum care.



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## Introduction

Episiotomy, a surgical incision of the perineum, is one of the most common procedures in obstetrics, with highly variable rates worldwide [1]. While intended to facilitate childbirth, the procedure is frequently associated with significant postpartum morbidity. Complications include acute perineal pain, oedema, infection, hematoma, and delayed wound healing, all of which can profoundly impair a new mother's quality of life [2,3]. This perineal trauma can interfere with mobility, urinary and fecal continence, the initiation of breastfeeding, and maternal-infant bonding. Prompt and effective wound healing is therefore a critical component of postpartum recovery [4].

Standard management for episiotomy wounds primarily focuses on preventive and symptomatic care, including proper hygiene and the use of non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief [5]. However, these approaches have limitations. NSAIDs can be associated with systemic side effects, and some patients may prefer to avoid pharmacological interventions while breastfeeding [6]. Furthermore, the proximity of the incision to the anus and vagina creates a high risk of infection, a complication that standard hygiene does not always prevent. This has led to a growing clinical and patient-driven interest in safe, effective, and accessible topical agents that can actively promote healing and reduce the risk of complications [7,8].

Curcumin, the primary bioactive compound in turmeric (*Curcuma longa*), has emerged as a promising therapeutic candidate. It possesses a strong biological plausibility for wound healing, underpinned by its well-documented anti-inflammatory, antioxidant, antimicrobial, and analgesic properties [9]. Preclinical research has shown that curcumin can accelerate wound repair by modulating inflammatory cytokines, promoting collagen synthesis, and stimulating fibroblast migration. These mechanisms directly target the key pathological processes of pain, inflammation, and infection that characterize complicated episiotomy healing [10-13].

Despite this compelling preclinical rationale and some positive results in other types of surgical wounds, the clinical efficacy of topical curcumin specifically for episiotomy care remains unclear. A few small clinical trials have been conducted, but their findings have not yet been systematically synthesized to provide a clear, evidence-based conclusion. This lack of a consolidated evidence base creates uncertainty for clinicians, nurses, and midwives who advise postpartum women.

## Objective

This systematic review and meta-analysis were conducted to evaluate the effect of topical curcumin application on the healing of episiotomy wounds in postpartum women. The primary objective of this systematic review was to evaluate the effect of topical curcumin application on the wound healing of episiotomy in postpartum women.

## Methods

### Information Sources

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. A comprehensive literature search was performed to identify all relevant studies, regardless of publication status or language. We searched major international electronic databases, including PubMed, Scopus, Web of Science, the Cochrane Library, and Embase. Additional regional and grey literature databases (Google Scholar, ProQuest, SID, and Magiran) were also searched. The search was conducted from the inception of each database up to our final search date of March 11, 2025. Our search strategy combined Medical Subject Headings (MeSH), Emtree terms, and relevant free-text keywords. The full search strategy for PubMed is presented as an example. Similar search strategies, adapted for the syntax and controlled vocabulary of each database, were used for all other sources. To ensure a complete search, we also manually screened the reference lists of all included studies and any relevant previously published systematic reviews.

### Search Strategy

Our search strategy was developed based on the PICO (Population, Intervention, Comparison, Outcome) framework to ensure a comprehensive and relevant retrieval of literature. The strategy was constructed using a combination of MeSH terms, Emtree keywords, and free-text words.

- **Population (P):** Search terms for the population included keywords related to the perineum and episiotomy, such as "Episiotomy," "Perineum," "Perineal Wound," and "Genitalia." Both controlled vocabulary and text word searches

(e.g., perine\*) were used to maximize sensitivity.

- **Intervention (I):** Terms for the intervention focused on curcumin and its source, including "Curcumin," "Curcuma," "Turmeric," and "diferuloylmethane."

To ensure the highest possible sensitivity and to avoid prematurely excluding potentially relevant articles, no filters or keywords for the Comparison (C) or Outcome (O) components were applied in the search strategy. This is a standard methodological approach to broaden the initial search and rely on manual screening to identify studies with relevant comparators and outcomes. The full search strategy for PubMed is presented as an example, and similar, adapted strategies were used for all other databases. The full PubMed search string from the original text would follow here:

((("Perineum"[Mesh]) OR ("Genitalia"[Mesh]) OR (perine\*[Text Word]) OR (genit\*[Text Word]) OR ("Surgical Wound"[Mesh]) OR ("Episiotomy"[Mesh]) OR (Episiotom\*[Text Word])) AND ((nanocurc\*[Text Word]) OR ("Curcumin"[Mesh]) OR (mervis[Text Word]) OR (diferuloylmethane [Text Word]) OR (turmeric\*[Text Word]) OR ("Curcuma"[Mesh]) OR "turmeric extract" OR "curcum\*"[Text Word]))

After confirming the related studies in terms of title and content, their characteristics were recorded in a checklist. All steps of data extraction and evaluation were conducted independently by two researchers to avoid bias.

### Eligibility Criteria

Studies were selected for inclusion based on a predefined set of criteria structured around the PICO (Population, Intervention, Comparison, Outcome) framework.

**Population (P):** We included studies involving postpartum women (of any age or parity) who had undergone an episiotomy or sustained a second-degree perineal tear during childbirth.

**Intervention (I):** The intervention of interest was the topical application of curcumin in any formulation (e.g., cream, ointment, solution), dosage, or duration of treatment. The specific purpose of the intervention had to be the promotion of perineal wound healing.

**Comparison (C):** We included studies that compared the curcumin intervention to any of the following: a placebo (the vehicle without curcumin), no treatment, or routine/standard care (e.g., standard hygiene advice, povidone-iodine wash).

**Outcomes (O):** The primary outcome of interest was episiotomy wound healing. To be included, studies must have measured this outcome using a validated, quantitative assessment tool, such as the REEDA (Redness, Edema, Ecchymosis, Discharge, Approximation) scale. While pain is a clinically relevant outcome, it was not the primary focus of this review; however, if studies reported both, they were still eligible for inclusion based on their reporting of the wound healing outcome. **Types of Studies** We included randomized controlled trials (RCTs) and quasi-experimental studies. We chose to include quasi-experimental designs to ensure a comprehensive synthesis of all available interventional evidence, given the anticipated scarcity of high-quality RCTs in this field.

**Exclusion Criteria:** Studies were excluded if they met any of the following criteria:

- The intervention was oral curcumin.
- The curcumin was administered as part of a polyherbal formulation where its specific effect could not be isolated.
- The study did not report quantitative data on a validated wound healing scale.
- The study was an observational design (e.g., cohort, case-control) with no intervention.
- The article was a review, case report, letter to the editor, or conference abstract.

### Selection Process

Two review authors (MMo, RH) independently screened the titles and abstracts of all retrieved citations against the predefined eligibility criteria. The full texts of potentially relevant articles were then retrieved and assessed for final inclusion. To facilitate this process and manage citations, we used the systematic review management software Rayyan.ai. Any disagreements regarding study eligibility were resolved through discussion and consensus or, if necessary, by consulting two senior authors (FS, MMi). The results of the selection process are detailed in the PRISMA flow diagram.

## Data Collection Process

Data from the included studies were extracted independently by two review authors (MMo, RH) using a standardized data extraction form designed for this review, based on the Cochrane Handbook guidelines [14, 15]. The extracted information was then cross-checked for accuracy. A third author (FS) resolved any discrepancies. The form included fields for study characteristics (author, year, country, study design), participant details (sample size, baseline characteristics), intervention specifics (formulation, dose, duration), comparison group, outcome measures, and results relevant to the primary outcome.

## Study Risk of Bias Assessment

The methodological quality and risk of bias of the included studies were assessed independently by two review authors (MMo, RH), with disagreements resolved by a third author (FS). We used specific, validated tools for this assessment. For RCTs, we used the Cochrane Risk of Bias 1 (RoB 1) tool. For the non-randomized quasi-experimental study, we used the Risk of Bias in Non-randomized Studies - of Interventions (ROBINS-I) tool.

## Effect Measures and Data Synthesis

For continuous outcomes measured on the same scale (i.e., the REEDA scale), we calculated the mean difference (MD) with a 95% confidence interval (CI) as the primary effect measure.

The meta-analysis was performed using a random-effects model in RevMan (Version 5.3). This model was chosen a priori because we anticipated significant clinical and methodological heterogeneity between studies, given the expected variations in curcumin formulations, control groups, and study populations.

We assessed statistical heterogeneity using the Chi-squared test (with  $p < 0.10$  indicating significance) and quantified its magnitude using the  $I^2$  statistic. The  $I^2$  statistic describes the percentage of total variation across studies that is due to heterogeneity rather than chance. We interpreted  $I^2$  values of <40% as potentially low, 30-60% as moderate, and >75% as considerable heterogeneity.

We conducted a pre-planned subgroup analysis based on the curcumin formulation (cream vs. solution) to investigate this as a potential source of heterogeneity. We did not perform a meta-regression due to the very small number of included studies ( $n=3$  in the meta-analysis), which would make such an analysis underpowered and the results unreliable.

## Certainty of Evidence and Publication Bias

The overall certainty of the body of evidence for the primary outcome was assessed independently by two review authors using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. We evaluated the evidence based on five domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty was rated as high, moderate, low, or very low.

An assessment of publication bias (e.g., via funnel plot analysis) was planned but was not conducted. According to Cochrane guidelines, such methods are not reliable and should not be used when there are fewer than 10 studies included in the meta-analysis, as was the case here.

## Outcome Measures

The improvement of perineal healing in all included studies was evaluated through the REEDA scale. It has five domains: Redness, Edema, Ecchymosis, Discharge, and Approximation. Each domain contains 0-3 points; the overall score is from 0 to 15.

## Results

### Study selection

The comprehensive database search yielded a total of 2531 citations prior to the removal of duplicates. The search was led by a methodologically robust query in PubMed, which retrieved 366 citations. Similar searches adapted for other major databases, including Scopus, Web of Science, and the Cochrane Library, along with other regional sources, identified the remaining citations. After removing 672 duplicate records, 1859 unique citations remained for screening. Of these, 1841 articles were excluded during the title and abstract screening phase because they were not relevant to the review's objective. This left 18 articles for full-text eligibility assessment.

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Following the full-text review, a further 14 studies were excluded. This process resulted in four studies that met all eligibility criteria and were included in the systematic review. Of these four studies, one randomized trial, Vardanjani et al. (2012), was deemed ineligible for the meta-analysis because it reported the primary outcome using the median and interquartile range. Therefore, three studies were included in the final quantitative synthesis (meta-analysis). The entire selection process is detailed in the PRISMA flow diagram (Figure 1).

### Study Characteristics

The four included studies were published between 2008 and 2021. Three were conducted in Iran and one in Indonesia. A summary of the characteristics of the included studies is presented in Table 1.

Three of the studies were double-blind randomized controlled trials (RCTs), while the study by Mutia et al. (2021) [16] was quasi-experimental. A total of 272 postpartum women were included across the four studies, with sample sizes ranging from 30 to 120 participants. The interventions varied across the studies. Two RCTs investigated a curcumin cream applied twice daily for 10 days. The quasi-experimental study by Mutia et al. (2021) [16] evaluated a curcumin solution, with participants analyzed in different groups based on the duration of application. The RCT by Vardanjani et al. (2012) [17] used a curcumin solution applied three times a day for 10 days. The comparator groups included a placebo cream, conventional medical care, and a povidone-iodine solution. The primary outcome in all studies was perineal wound healing, assessed using the REEDA scale.

### Design of Study

The participants were divided into three groups in two studies [16, 18] and into two groups in other studies [17, 19]. Control groups received a placebo [18, 19], povidone-iodine solution [17], and routine medical care after delivery [16].

### Number of Samples

A number of 272 people were included in the review; it ranged from 30 people in one study [16] to 120 in another [17].

### Study Location

Three studies have been conducted in Iran [18, 19] and one in Indonesia [16].

### Participants

Participants were postpartum women who had given birth to their first or second child on the day of sampling at 37-42 weeks of pregnancy by vaginal delivery with episiotomy or second-degree tear. Exclusion criteria were a history of chronic diseases such as diabetes, anemia, and kidney disease, specific medication history, and postpartum complications such as hemorrhage and perineal hematoma.

### Types of Interventions

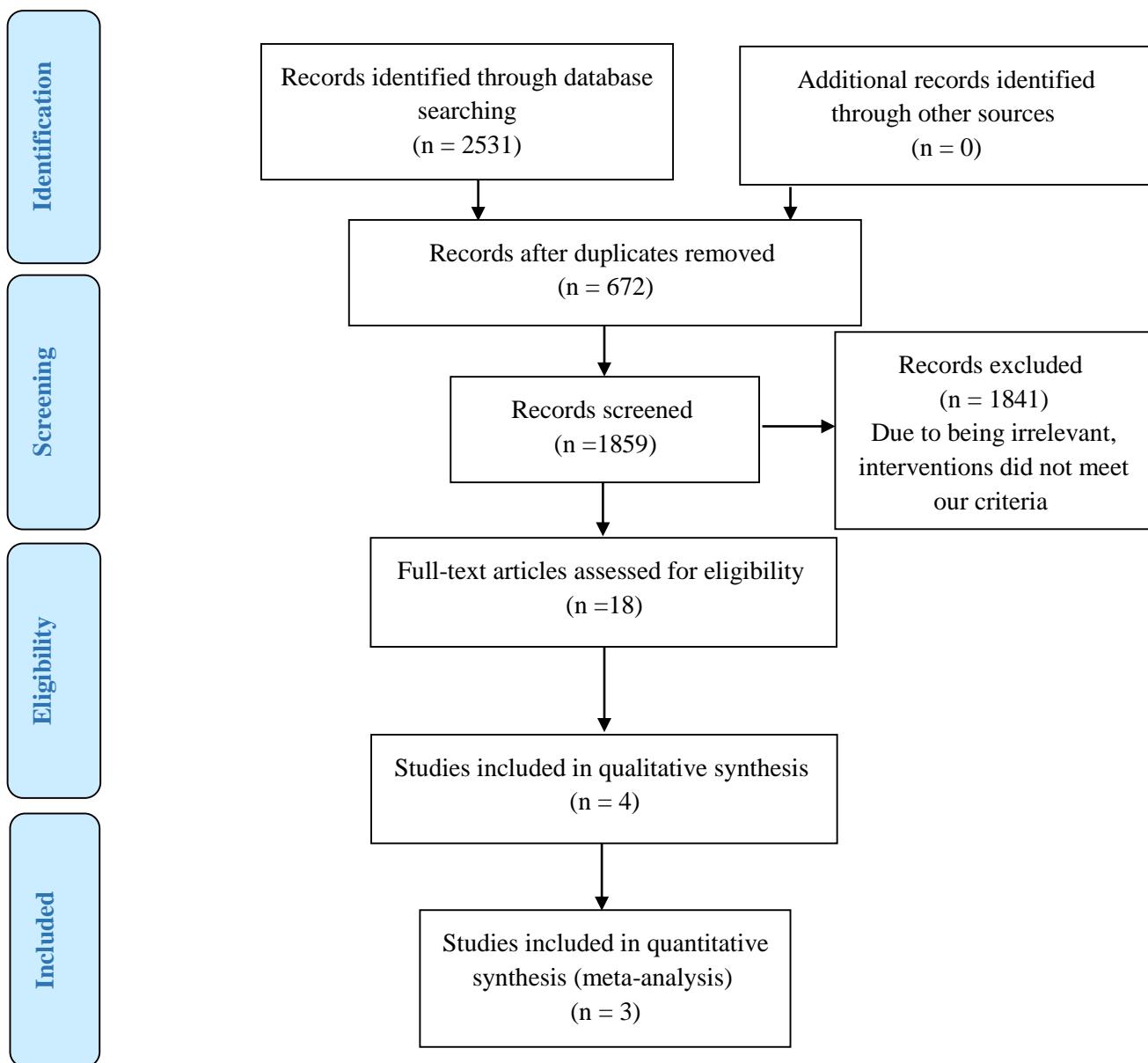
In two studies, the participants used curcumin ointment twice daily from the first day after delivery for ten days [18, 19]. In one study, the participants used a 10% curcumin solution twice daily to wash the sutures [16]; in another, they used it three times daily [17].

### Risk of Bias in Studies

Randomization was low-risk in 2 studies [17, 18] in which the participants were randomly assigned to the intervention and control groups; it was high-risk in one study [19].

Concealment of allocation had a low risk of bias in two studies [17, 18] through computer-generated random number tables; it had a high risk of bias in another study in which participants were allocated to the study groups one in between [19]. Blinding (personnel, participants, and outcome assessment) was low-risk in the studies [18, 19]. Two studies were at low risk of attrition bias [17, 18] since reasons were reported and balanced across groups; it was considered an Unclear Risk in one study [19]. All studies were at low risk of selective reporting bias as all results were stated (Figure 2).

According to ROBINS-I, Mutia's study was at a serious Risk of Bias due to the lack of investigation of confounding factors and Bias in measurement of outcomes (Table 2).



**Figure 1.** Flow diagram of the systematic literature search

### Results of Individual Studies

In the study conducted by Golmakani et al., the mean (SD) of the REEDA score was significantly lower in the curcumin group [2.09 (1.59)] compared to the control group [4.10 (1.77)] ( $P = 0.001$ ) at the 10th day after delivery.

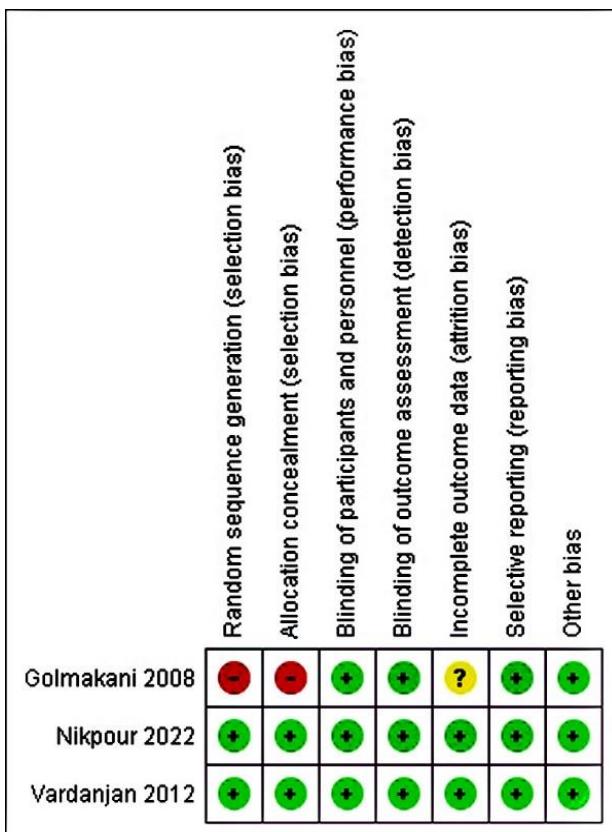
In the study conducted by Nikpour et al., there was no statistically significant difference between the mean (SD) of the REEDA score in the intervention [1.63 (1.27)] and control [1.83 (1.10)] groups ( $P > 0.05$ ) at the 10th day after delivery. In the study conducted by Mutia et al., the overall REEDA score

was reported in three groups of 0, 1-5, and 6-15 as numbers (percentage); there was a statistically significant difference between the curcumin and control groups ( $P = 0.001$ ).

In the study conducted by Vardanjani et al., there was a statistically significant difference in terms of the Median (Interquartile Range) of the REEDA score between the curcumin [0 (0.1)] and control [1 (1.2)] groups ( $P < 0.001$ ) at the 10th day after delivery.

**Table 1.** Characteristics of Included Studies

First author	Date of Pub.	Country	Type of Clinical trial	Participants	Intervention group	Comparison group	Duration of follow up	Outcomes	Outcome Measurement	Results
Golmakani et al.	2008	Iran	Double-Blind Randomized Clinical	17-35 years old postpartum mothers with episiotomy	Curcumin cream twice daily for 10 successive days after birth	placebo cream twice daily for 10 successive days after birth	10 days	Episiotomy wound healing	Episiotomy wound healing was evaluated based on REEDA scale	Curcumin cream was effective in healing episiotomy wound
Nikpour et al.	2019	Iran	Double-Blind Randomized Clinical	17-35 years old postpartum mothers with episiotomy	Curcumin cream twice daily for 10 successive days after birth	placebo cream twice daily for 10 successive days after birth	10 days	Episiotomy wound healing	Episiotomy wound healing was evaluated based on REEDA scale	No significant difference was found between groups
Mutia et al.	2021	Indonesia	Quasi-experimental	Postpartum mothers with grade II perineal wounds	Conventional medicine	Curcumin solution applied twice daily; outcomes were analyzed across different duration-of-use groups.	7 days	Perineal wounds healing	Perineal wound healing was evaluated based on REEDA scale	Curcumin solution decreased the total REEDA score
Vardanjani et al.	2012	Iran	Double-Blind Randomized Clinical	Postpartum mothers with episiotomy	Povidone-iodine three times a day for 10 days	Curcumin Solution three times a day for 10 days	10 days	Perineal wounds healing	Perineal wound healing was evaluated based on REEDA scale	Perineal wound healing was evaluated based on REEDA scale



**Figure 2.** Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across included studies.

**Table 2.** Risk of Bias in a Quasi-Experimental Trial according to ROBINS-I

Author	Mutia et al. (2021)
Bias due to confounding	Serious*
Bias in the selection of participants	Low Risk
Bias in the classification of interventions	Low Risk
Bias due to deviations from the intended interventions	Low
Bias due to missing data	Low
Bias in the measurement of outcomes	Serious
Bias in the selection of reported results	Low
Overall	Serious

\*Serious: Serious risk of bias (the study has some important problems)

## Results of Syntheses

Meta-analysis was conducted with three studies [16, 18, 19]. Sub-group analysis was used due to the difference in the method of using Curcumin in Mutia et al.'s study; the result showed no significant difference in the healing process of the perineal wound between the curcumin and control groups ( $MD=-1.02$ ; 95% CI: -2.39 to 0.35) (Figure 3).

## Certainty of Evidence

According to the GRADE system, we found very low-quality evidence comparing curcumin ointment with the placebo group on the healing process of the perineal wound; it was low-quality when comparing curcumin solution with routine medical care. Thus, the results were considered with very low certainty (Table 3).

## Discussion

### Principal Finding in the Context of Limited Evidence

This systematic review and meta-analysis found insufficient and very low-certainty evidence to either support or refute the efficacy of topical curcumin for improving episiotomy wound healing. The pooled estimate from three small studies showed no statistically significant difference between curcumin and control interventions ( $MD=-1.02$ ; 95% CI: -2.39 to 0.35). However, this result must be interpreted with extreme caution. The primary finding of this review is not the statistical outcome itself, but the profound lack of robust clinical evidence in this area, which precludes any firm clinical conclusions.

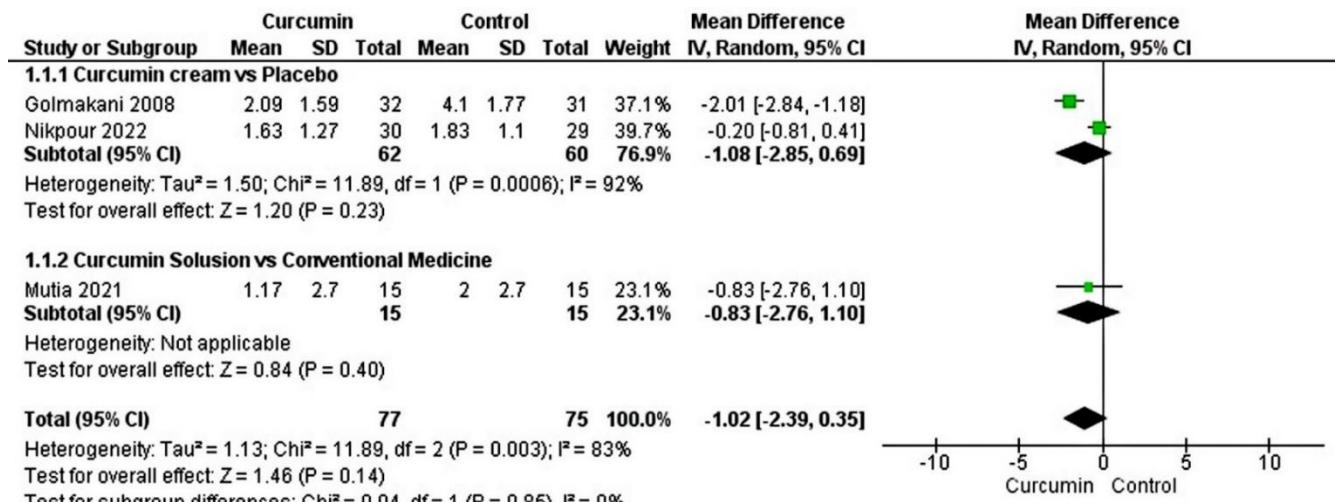
### Critical Interpretation of Heterogeneous Findings

The meta-analysis was hampered by substantial clinical and statistical heterogeneity ( $I^2 = 83\%$ ), which complicates the interpretation of the pooled result. A critical examination of the included studies reveals several sources for this inconsistency. Firstly, the interventions themselves varied significantly; two studies used a curcumin cream formulation against a placebo, while another used a

curcumin solution against "conventional medicine". The physicochemical properties of the delivery vehicle (cream versus aqueous solution) are known to dramatically influence the release, skin penetration, and local bioavailability of active compounds, which could fundamentally alter the therapeutic effect.

Secondly, the choice of comparator groups differed, ranging from inert placebos to routine medical care, which is poorly defined and variable. This makes it impossible to ascertain if curcumin is ineffective or

simply not superior to current, undefined standards of care. The fourth study, a randomized controlled trial by Vardanjani et al. [17], which was excluded from the meta-analysis due to its data reporting format, compared a curcumin solution to povidone-iodine, an active antiseptic agent. Comparing curcumin to an inert placebo and to an active antiseptic are two fundamentally different clinical questions, and pooling such studies would be inappropriate.



**Figure 3.** Forest Plot of the Meta-Analysis Comparing the Effect of Topical Curcumin versus Control on Episiotomy Wound Healing (REEDA Scale).

**Table 3.** Quality Assessment of Included Studies according Grade Approach

Comparison	No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	MD† (95% CI•)	Certainty
Curcumin cream vs. placebo	2	Randomized trials	Low risk	Very serious inconsistency*	No serious indirectness	Serious imprecision**	Undetected	-1.08 (-2.85, 0.69)	Very low $\oplus\ominus\ominus\ominus$
Curcumin solution vs. conventional medicine	1	Quasi-experimental	Serious risk of bias	No inconsistency	No serious indirectness	Serious imprecision**	Undetected	-0.50 (-1.58, 0.58)	Low $\oplus\oplus\ominus\ominus$

\*Substantial Heterogeneity  $I^2 > 70\%$ , \*\* Total number of participants is less, † Mean difference, • Confidence Interval

### Comparison with Findings from Other Wound Healing Studies

The inconclusive findings of our review for episiotomy wounds align with the broader landscape

of clinical research on topical curcumin, which is characterized by a significant gap between promising preclinical data and inconsistent clinical outcomes. A systematic review by Akbik et al.

(2014) [20] on curcumin's role in skin regeneration found that while animal studies were overwhelmingly positive, the human clinical evidence was sparse and methodologically weak, a conclusion that our review strongly reinforces in the specific context of perineal care. This highlights a persistent challenge in translating curcumin's biological activity into tangible clinical benefits.

The overall non-significant result of our meta-analysis must be interpreted with caution, as it likely reflects the limitations of the interventions studied rather than a true lack of efficacy for curcumin itself. The substantial heterogeneity observed across the included trials suggests that outcomes are highly sensitive to the specifics of the intervention. The critical, rate-limiting factor for curcumin's clinical success is the formulation of the delivery vehicle. A comprehensive 2019 review by Fereydouni et al. [21] in the Journal of Cellular Physiology provides the definitive explanation for this.

The authors detail how advanced formulations, such as electrospun nanofibers, are specifically designed to overcome curcumin's primary limitations of poor stability and low bioavailability, thereby enabling a sustained therapeutic release directly at the wound site. The simple cream and aqueous solution formulations used in the trials included in our meta-analysis are unlikely to possess these advanced delivery characteristics. Therefore, the inconclusive findings of our review are not surprising; they are likely a direct reflection of the varying and probably suboptimal drug delivery in the primary studies. This aligns perfectly with the conclusion of another review by Mohanty and Sahoo (2017) [22], suggesting that future clinical research on curcumin for episiotomy healing will only be meaningful if it utilizes advanced, optimized formulations designed to ensure adequate local bioavailability.

The primary strength of this review lies in its rigorous and transparent methodology, including a pre-registered PROSPERO protocol, a comprehensive search across eight databases without time or language restrictions, and the use of standardized Cochrane and GRADE methodologies for bias assessment and evidence synthesis.

However, the review is profoundly limited by the quantity and quality of the available primary studies, which is the central finding. The inclusion of only four studies (three in the meta-analysis) with a total of 272 participants provides a very fragile evidence base.

Furthermore, the risk of bias varied, with one quasi-experimental study rated as having a "serious" risk of bias, further reducing our confidence in the findings. The high heterogeneity, as discussed, makes any pooled estimate unreliable. Finally, due to the small number of included studies (<10), a meaningful assessment of publication bias via funnel plot analysis was not possible, leaving this potential bias unexplored.

## Conclusion

While curcumin possesses a plausible biological mechanism for promoting wound healing, this systematic review reveals that the current clinical evidence for its use on episiotomy wounds is insufficient and of very low quality. The available studies are too few, too small, and too heterogeneous to allow for any meaningful conclusions about its efficacy.

Therefore, the routine use of topical curcumin for episiotomy care cannot be supported. This review highlights a clear need for high-quality, methodologically sound RCTs to determine if this widely available natural compound has a role in improving outcomes for postpartum women.

## Registration and Protocol

The review was registered in Prospero, ID: CRD42021269055. The review protocol can be accessed through the <https://www.crd.york.ac.uk/prospero/>.

## Ethical Considerations

This study is a systematic review and meta-analysis of previously published literature. As all data were obtained from publicly available, anonymized sources, and the study did not involve any direct interaction with human participants, institutional review board approval was not required.

### Acknowledgments

N/A

### Conflict of Interest

The authors declare that they have no competing interests

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### Authors' Contributions

Montazeri M. contributed to conceptualization, methodology, formal analysis, data curation, and original draft writing. Hasanzadeh R. participated in methodology, investigation, and data curation. Shabani F. was involved in conceptualization, validation, supervision, and manuscript review. Mirghafourvand M. contributed to validation, supervision, and manuscript review. All authors reviewed and approved the final manuscript.

### Artificial Intelligence Utilization

N/A

### Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on request.

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