



The Analysis Study of Effect of Maternal Calcium Supplementation And Pediatric Health : A Comprehensive Systematic Review

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ABSTRACT

Background: Maternal calcium supplementation significantly impacts pediatric health, influencing growth and development. However, the effects on bone growth and mineralization remain inconsistent. Research in low habitual calcium intake populations shows sex-specific outcomes. Pregnancy-induced calcium supplementation has mixed outcomes, with increased mobilization during lactation and minimal impact on offspring growth. Further investigation is needed to improve pediatric health outcomes in diverse dietary calcium intakes. **Methods:** This systematic review was conducted in strict compliance with the PRISMA 2020 guidelines, ensuring methodological rigor and transparency. The review included only full-text articles published in English between 2013 and 2024, with a focus on high-quality sources. Editorials and review articles lacking a DOI were excluded to maintain the integrity and reliability of the dataset. An extensive literature search was performed using reputable databases, including ScienceDirect, PubMed, and SagePub, to identify studies relevant to the research objectives. **Result:** The initial database search yielded over 100 publications. Through a rigorous three-stage screening process, eight studies were carefully selected for inclusion based on their relevance and adherence to the established criteria. These selected studies underwent a thorough and critical analysis, offering a detailed evaluation of the impact of maternal calcium supplementation on pediatric health outcomes. **Conclusion:** Calcium supplementation is crucial for maternal and fetal health during pregnancy, reducing risks like gestational hypertension and pre-eclampsia. World Health Organization recommends 1500-2000 mg daily. Further research is needed to understand sex-specific growth patterns and IGF1-related pathways.

Keywords: calcium supplementation, maternal, pediatric health

INTRODUCTION

Childhood growth encompasses various dimensions, including linear growth (stature), bone accrual (width and mineral density), and the development of tissue compartments and organs (somatic growth). Adequate dietary calcium (Ca) intake is recognized as essential for healthy skeletal growth, yet the impact of calcium supplementation on bone growth and mineralization remains inconclusive. Many studies fail to demonstrate significant effects of supplementation, and those reporting positive outcomes often lack sufficient follow-up periods to evaluate the long-term sustainability of these effects.¹ A contributing factor may be that most trials are conducted in regions where average dietary calcium intake aligns with recommended levels.² Limited research exists on populations with habitually low calcium intakes, leaving gaps in understanding the influence of calcium supplementation at different developmental stages and its differential effects on skeletal and somatic growth between males and females.^{3,4}

Research in rural Gambia, where dietary calcium intakes are markedly low, provides valuable insights into these dynamics. A calcium supplementation trial involving pre-pubertal children with habitual calcium intakes of approximately 300 mg/day revealed sex-specific effects. Males who received calcium carbonate supplements for 12 months between the ages of 8 and 12 experienced an earlier pubertal growth spurt, resulting in greater height and bone development during mid-adolescence compared to the placebo group.^{4,5} However, long-term follow-up showed that these males ceased growing earlier and were significantly shorter (by 3.5 cm on average) at final height compared to their placebo counterparts.⁶ Additionally, initial gains in bone mineral content (BMC) and bone area (BA) associated with supplementation diminished over time.⁵⁻⁷ Interestingly, no similar effects were observed among female participants, underscoring the complexity and variability of calcium's impact on growth.

Another study focusing on maternal calcium supplementation during pregnancy further highlighted unexpected outcomes. Mothers receiving daily calcium carbonate supplements from 20 weeks of gestation to term mobilized more bone mineral during lactation compared to those on

placebo, resulting in lower bone mineral density (BMD) that persisted five years post-supplementation.^{8,9} Despite supplementation, there were no significant effects on offspring size at birth or during the first year postpartum.^{10,11} A subset analysis revealed a slower increase in whole-body BMC and BA among infants of supplemented mothers by 12 months.^{8,9,11} Notably, male infants were heavier at two weeks and longer at 52 weeks than females. By ages 8-12 years, boys and girls showed no differences in height, weight, or BMI, though girls had greater fat mass, spine BMC, and whole-body BMC, while boys exhibited higher lean mass, bone area, and hip BMC.¹² These findings suggest sex-specific growth patterns and underscore the nuanced effects of calcium supplementation on pediatric health.

The present study aims to explore these complexities further by systematically examining the effects of maternal calcium supplementation on pediatric health outcomes. By integrating findings from previous research and addressing the gaps in knowledge, this study seeks to deepen our understanding of calcium's role in early development and inform strategies for optimizing health outcomes in populations with varying dietary calcium intakes.

METHODS

Protocol

This study adhered strictly to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, ensuring methodological rigor and adherence to best practices. By following these established standards, the review process was designed to be transparent, reproducible, and scientifically sound. Key steps included comprehensive literature searches, meticulous data extraction, and a thorough synthesis of findings, all implemented to minimize bias and enhance the validity of the conclusions. This rigorous approach underscores the study's commitment to achieving the highest standards of research quality and credibility.

Criteria for Eligibility

This study investigates the impact of maternal calcium supplementation on pediatric health by systematically reviewing and synthesizing data from a wide range of studies. The research aims to identify patterns and emerging trends that can inform the development of more effective patient care strategies. By uncovering key insights from the academic literature, the study seeks to deepen understanding of how maternal calcium intake influences child health outcomes.

To ensure analytical rigor, strict inclusion and exclusion criteria were employed throughout the research process. Only peer-reviewed studies published in English between 2016 and 2024 were included, with each study's authenticity verified through its DOI. Non-research documents, such as reviews, editorials, and duplicate entries, were excluded to maintain the dataset's focus and integrity. This selective approach ensures that the analysis is grounded in high-quality, relevant studies, enhancing the reliability and credibility of the findings.

By adopting a meticulous and methodologically sound approach, the study guarantees the robustness and reliability of its data. The findings are expected to make meaningful contributions to clinical practice, particularly in understanding and optimizing the role of maternal calcium supplementation in improving pediatric health outcomes.

Search Strategy

The systematic review employed the keywords "maternal calcium," "supplementation," and "pediatric health" to guide the literature search. Studies were sourced from three reputable databases: PubMed, SagePub, and ScienceDirect, ensuring a comprehensive and diverse selection of relevant academic research.

Table 1. Search Strategy

<i>Database</i>	<i>Search Strategy</i>	<i>Hits</i>
Pubmed	<i>("maternal calcium" OR "supplementation" AND "pediatric health")</i>	39
Science	<i>("maternal calcium" AND "supplementation" AND "pediatric health")</i>	2

Direct		
Sagepub	<i>("maternal calcium" OR "supplementation" AND "pediatric health")</i>	168

Data retrieval

The authors conducted a meticulous preliminary review of each article, carefully evaluating titles and abstracts to determine their relevance before proceeding to a detailed analysis. Only studies that aligned with the research objectives and satisfied the predetermined inclusion criteria were selected for further examination. This systematic approach allowed the identification of consistent and meaningful patterns across the literature, ensuring that the final selection focused on studies directly pertinent to the research aims.

To ensure consistency, only full-text articles published in English were considered, providing uniformity in the language of the selected studies. A rigorous screening process verified that all included studies adhered to the established criteria and directly addressed the study's objectives. Articles failing to meet these standards were excluded, maintaining the focus and integrity of the dataset.

The evaluation process considered a range of critical factors, including study titles, authors, publication dates, research locations, and methodologies. This comprehensive and methodical approach ensured that only the most relevant and high-quality studies were incorporated, enhancing the reliability, validity, and overall rigor of the study's conclusions.

Quality Assessment and Data Synthesis

The authors carried out a meticulous initial screening by thoroughly reviewing the abstracts and titles of each article to identify studies relevant for further consideration. Only those that met the predefined relevance criteria progressed to an in-depth, comprehensive review. This rigorous and selective approach ensured a focused selection process, advancing only the most pertinent studies for detailed analysis. By refining the selection process, the authors were able to conduct a targeted and

nuanced assessment of the existing literature, ensuring that the selected studies were contextually significant and directly aligned with the study's objectives.

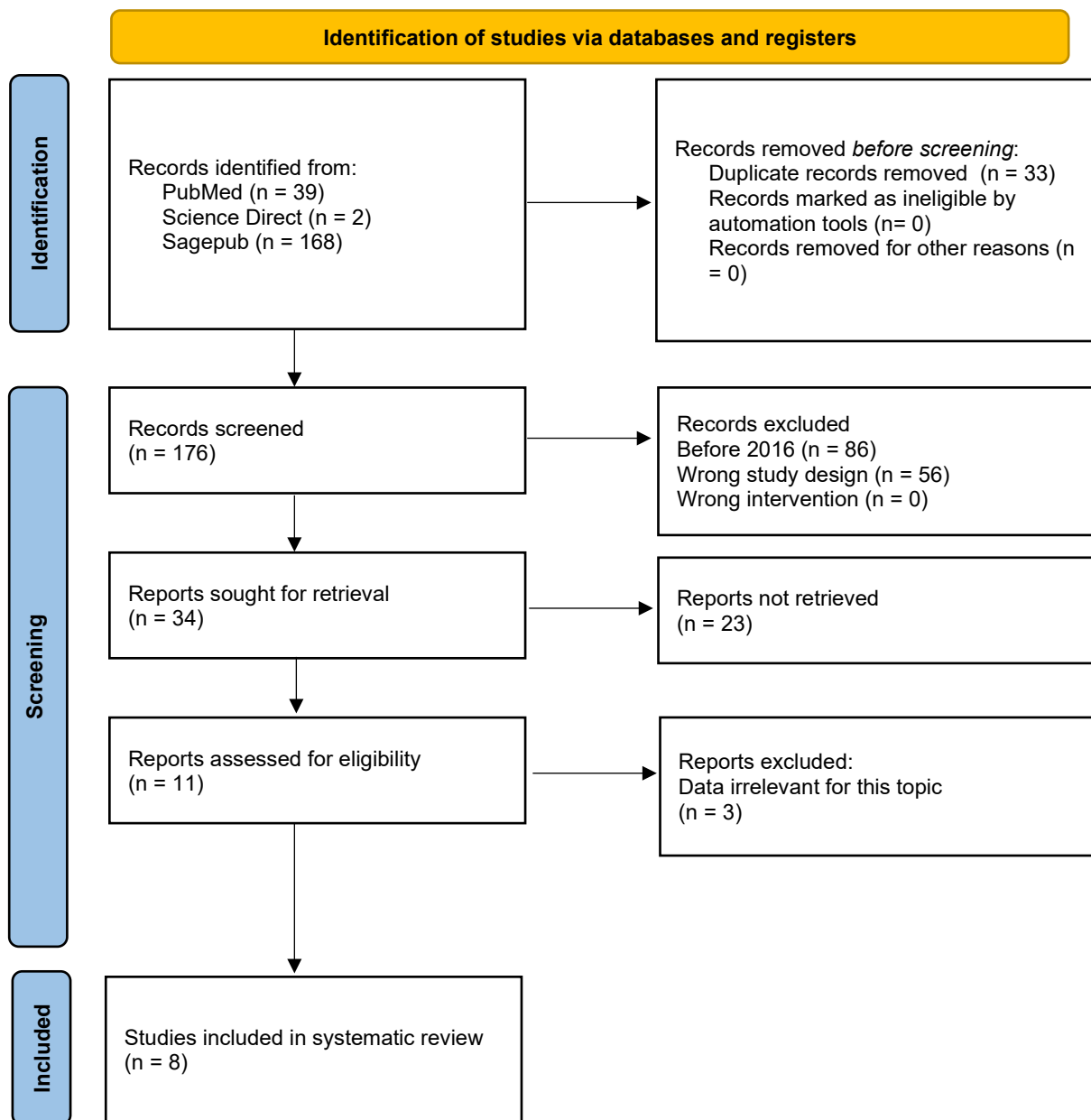


Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	(Gold berg et al., 2013)	(Jarjo u et al., 2013)	(Jams hidi et al., 2015)	(War d et al., 2017)	(Prentic e et al., 2019)	(Korh enen et al., 2022)	(Tihto nen et al., 2022)	(Prenti e et al., 2023)
1. Bias related to temporal precedence								
Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation								
Was there a control group?	Yes	No	No	Yes	Yes	No	No	Yes
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	Yes	No	No	Yes	Yes	No	No	Yes
4. Bias related to administration of intervention/exposure								
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.	Yes.
5. Bias related to assessment, detection, and measurement of the outcome								
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	No	No	No	No	No	No	No	No
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

RESULTS

The investigation commenced with a systematic search across reputable databases, including ScienceDirect, PubMed, and SagePub, to gather relevant studies for the review. A rigorous three-stage screening process was implemented to identify and filter the most pertinent studies, resulting in the selection of eight papers that met the established inclusion criteria. These studies underwent a comprehensive analysis, with key themes and topics identified for in-depth exploration. To enhance clarity and effectively present the findings, a concise summary of the analyzed data is provided in Table 3, offering a clear and streamlined overview of the results.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result
Goldberg et al.¹¹ (2013)	USA	RCT	525 participants	A study involving 525 women with varying blood pressure levels found no significant effect of calcium supplementation on BP, pregnancy weight gain, postpartum weight, or infant weight, length, or other measures of growth. The study also found no significant effect of supplementation on pregnancy weight gain, weight postpartum, or infant weight, but the comparability of the original randomly assigned groups may have been compromised.
Jarjou et al.⁹ (2013)	Gambia	Cohort	58 participants	A study of 58 women found that the mean time from L52 to F52 was 4.9 years for NPNL and 5.0 years for F52. The calcium group had a lower SA-BMC at L52, but no significant changes were observed in either group. The lower SA-BMC in the calcium group persisted at both NPNL and F52.
Jamshidi et al.¹³ (2015)	Iran	Systematic Review	7 studies	This review of four randomized trials and three observational studies found that higher maternal calcium intake during pregnancy can reduce offspring's systolic blood pressure, particularly in older children (1-9 years), and significantly reduce the incidence of elevated blood pressure in 7-year-olds.

Ward et al.¹² (2017)	United Kingdom	RCT	447 participants	A study of 447 children found significant sex-supplement interactions in anthropometric and bone outcomes. Females receiving calcium were shorter, lighter, and had smaller bones and less bone mineral than those receiving a placebo. Males in the calcium group had greater mid-upper arm circumference, fat mass, and bone mineral content.
Prentice et al.¹⁴ (2019)	United Kingdom	RCT	526 participants	Boys had lower levels of IGF1, IGFBP3, leptin, and insulin compared to girls. IGF1 was higher in M-Ca than M-P but lower in F-Ca than F-P. Similar sex-supplement interactions were observed for IGFBP3 and IGF1-adjusted-for-IGFBP3, but group differences were smaller. No significant supplement effects were found on other biochemical indices.
Korhonen et al.¹⁵ (2022)	Finland	Systematic Review	31 studies	The impact of prenatal calcium supplementation on offspring growth, metabolic, and neurodevelopmental outcomes is unclear due to conflicting or insufficient data, high attrition bias risk, and limited RCT data, which do not provide sufficient evidence to conclude its influence beyond the newborn period.
Tihtonen et al.¹⁶ (2022)	Finland	Systematic Review	7 studies	Calcium supplementation did not show any advantage on maternal BMD post-delivery, during breastfeeding, or on offspring BMD, even with low dietary calcium intake. The results were not influenced by calcium dose or vitamin D administration. The impact of calcium supplementation on maternal and offspring bone health remains unknown.
Prentice et al.¹⁷ (2024)	Gambia	RCT	523 participants	A trial involving 523 singleton infants and 491 children showed differences in systolic blood pressure and height curves between pregnancy supplement groups in females and males. F-Ca had lower systolic blood pressure and peak

				height velocity than F-P at all ages. No significant pregnancy supplement effects were observed.
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DISCUSSION

Calcium intake during pregnancy remains suboptimal in many low- and middle-income countries compared to international recommendations, posing significant risks to maternal and fetal health. Calcium is critical for fetal skeletal development and broader health outcomes, including maternal health. While physiological adaptations help to ensure calcium sufficiency during increased requirements, inadequate intake is linked to heightened risks of gestational hypertension, pre-eclampsia, and impaired fetal growth.^{18,19} In response, the World Health Organization (WHO) recommends calcium supplementation at 1500–2000 mg per day for pregnant women in populations with low dietary calcium intake, aiming to reduce pre-eclampsia risks and associated complications. Despite this, there is limited understanding of how supplementation influences long-term maternal and offspring health, particularly in regions with severe calcium deficits.¹⁷

Systematic reviews and meta-analyses affirm the benefits of calcium supplementation in pregnancy, particularly for populations with dietary calcium intakes below 900 mg/day.²⁰ Supplementation has been shown to mitigate pre-eclampsia risk and improve pregnancy outcomes, with lower doses (<1000 mg/day) proving as effective as higher doses in preventing complications.²⁰ However, long-term follow-ups of maternal and offspring health remain scarce. Two notable trials—one in Argentina and another in the United States—examined maternal calcium supplementation (2000 mg/day) and reported lower systolic blood pressure (SBP) in offspring aged 2 to 9 years. The reductions, particularly pronounced among overweight children, highlight the potential for calcium supplementation to influence early-life cardiovascular outcomes.^{21,22}

Unique insights come from a trial in rural Gambia, where maternal calcium intake averages 300–400 mg/day. This study supplemented women with 1500 mg/day of calcium from 20 weeks of gestation until delivery and followed maternal and offspring outcomes over several years.^{10,11} Short-

term impacts on maternal blood pressure and fetal growth were negligible. However, unexpected long-term effects emerged, including greater lactational bone mineral mobilization among supplemented mothers compared to the placebo group, with partial skeletal restitution even five years postpartum.⁹ For offspring, maternal calcium supplementation significantly influenced growth trajectories. Female offspring exhibited slower growth and delayed development, whereas male offspring demonstrated accelerated growth patterns.¹² These findings underscore the sex-specific impacts of maternal calcium intake on childhood growth and bone development.

Further analysis of the Gambian cohort revealed that maternal calcium supplementation had enduring effects on offspring blood pressure and growth, differing markedly by sex. Female offspring of supplemented mothers consistently exhibited SBP reductions of 2 mmHg throughout childhood and adolescence compared to the placebo group, aligning with results from Argentinian and U.S. trials.^{23,24} Such decreases, while modest, are significant for populations with high rates of adult hypertension and stroke, such as rural Gambia.^{25,26} Conversely, female offspring displayed altered growth patterns, characterized by a prolonged growth spurt and lower peak height velocity, potentially resulting in long-term societal and health consequences. Male offspring, by contrast, exhibited no significant differences in blood pressure or anthropometry, underscoring distinct sexual dimorphism in response to maternal calcium supplementation.

The observed sex-specific outcomes may be linked to fetal programming effects on the growth hormone-insulin-like growth factor-1 (IGF1) axis. Maternal calcium intake has been associated with IGF1 alterations in human and animal studies, suggesting potential mechanisms influencing offspring growth trajectories and cardiovascular health.^{27,28} While sex differences in responses to maternal diet and micronutrient supplementation have been documented in various contexts, such as maternal famine and tobacco exposure, the mechanisms remain poorly understood.^{3,29} These findings from the Gambian cohort highlight the need for further research into the long-term effects of calcium supplementation during pregnancy, particularly the interplay of sex-specific growth patterns, IGF1-related pathways, and broader health outcomes. Exploring these dynamics may inform strategies to optimize maternal nutrition and improve pediatric health in resource-limited settings.

CONCLUSION

Calcium supplementation is crucial for maternal and fetal health during pregnancy, as it reduces risks like gestational hypertension and pre-eclampsia. The World Health Organization recommends 1500-2000 mg per day. However, understanding its long-term effects, particularly in regions with severe calcium deficits, is limited. Further research is needed to understand sex-specific growth patterns and IGF1-related pathways.

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