SPECIAL ARTICLE

Use of calcium during pregnancy: far beyond preeclampsia

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Abstract

Hypertensive disorders in pregnancy, particularly preeclampsia, represent a global public health issue and are the leading cause of maternal mortality in Brazil, accounting for 20% of maternal deaths. Despite advancements in prevention, disparities persist, especially in low- and middle-income countries, where calcium intake is often below recommended levels. This article reviews the evidence supporting calcium supplementation as an effective strategy for preventing preeclampsia, with benefits extending beyond blood pressure control. Systematic review data from the Cochrane Library highlight a reduction in preeclampsia, maternal morbidity, and preterm birth among women who supplement and have low calcium intake. However, recent debates have questioned the universality of this recommendation, suggesting supplementation only for high-risk pregnancies. These controversies arise from methodological limitations in sensitivity analyses and misinterpretations. Nevertheless, the World Health Organization guidelines advocate calcium supplementation of 1.5–2 g/day for pregnant women in regions with low calcium intake. This recommendation aligns with findings demonstrating improved maternal and neonatal outcomes, emphasizing the need for widespread implementation. Urgent national policies in Brazil are required to ensure equitable access to calcium, particularly given the high prevalence of preeclampsia and maternal mortality.

Key words *High-risk pregnancy, Calcium, Preeclampsia, Maternal mortality, Public health*

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Introduction

Hypertensive disorders in pregnancy (HDP) constitute a major public health concern both in Brazil and worldwide due to their significant impact on maternal and perinatal health. It encompasses a spectrum of disorders, including gestational hypertension, preeclampsia, eclampsia, and chronic hypertension with superimposed preeclampsia. The epidemiology of these conditions varies across different regions, influenced by socioeconomic, environmental, and healthcare access factors.[1]

Globally, hypertensive disorders are the second leading cause of maternal mortality, responsible for an estimated 14% of maternal deaths[2] particularly in low- and middle-income countries. The global prevalence of hypertensive disorders during pregnancy varies from 5% to 10% of all pregnancies.

Preeclampsia is the most common and severe form, affecting about 2% to 8% of pregnancies worldwide, translating to around 8.5 to 10 million cases per year.[1] From this total, about 10.0% progress to eclampsia, a life-threatening condition involving seizures and associated with a high risk of near miss and maternal mortality. Preeclampsia and eclampsia are significant contributors to maternal and perinatal morbidity and mortality worldwide.

In Brazil, hypertensive disorders of pregnancy are the leading cause of maternal mortality, accounting for approximately 20% of maternal deaths.[3] In the integrative review conducted by Guida and collaborators, which analyzed data from several studies, the pooled prevalence of preeclampsia in Brazil was estimated at 6.7%. The prevalence of eclampsia varied across studies, ranging from 1.7% to 6.2%.[4]

These findings highlight the significant burden of hypertensive disorders during pregnancy in Brazil. The high rate of hypertensive disorders in pregnancy is largely attributed to inadequate prenatal care, socioeconomic disparities, and the high prevalence of risk factors such as obesity, advanced maternal age, and pre-existing hypertension.

Considering the entire scenario described above, it is essential that all efforts are made to prevent preeclampsia and eclampsia, as well as to promote early diagnosis and appropriate treatment, which involves both the administration of magnesium sulfate and the timely termination of pregnancy, measures that have been proposed by various international and national guidelines over the past decade.[5-7]

Among the preventive measures recommended for all pregnant women are the promotion of a healthy lifestyle, pre-pregnancy weight control, avoiding excessive weight gain during pregnancy, physical exercise, and calcium supplementation in countries with low intake (less than 800 mg/day).[6-8]

Simultaneously, screening should be performed to identify pregnant women at high risk for preeclampsia, which can be done through strategies based on risk factors or through the algorithm with multiple markers proposed by the Fetal Medicine Foundation in 2013.[9] This algorithm allows for the calculation of risk between 11 weeks and 13 weeks and six days, using maternal history, mean arterial pressure, doppler velocimetry to calculate the pulsatility index (PI) of the uterine arteries, and the biomarkers Pregnancy-Associated Plasma Protein-A (PAPP-A) and Placental Growth Factor (PlGF)- although recent evidence has demonstrated that PAPP-A can be safely removed from the algorithm, with similar accuracy for predicting preeclampsia.[10]

Pregnant women considered at high risk for preeclampsia due to risk factors (one high-risk factor or two moderate-risk factors) or the algorithm (risk greater than 1:100 or 1:150, if biomarkers are not used) should receive low-dose aspirin (100-162 mg/day) for preeclampsia prevention.[6,7,9] Although the ideal dose of aspirin varies among different guidelines, its use is widely agreed upon for pregnant women with an increased risk of preeclampsia.[5,11] The effectiveness demonstrated in the Cochrane Systematic Review is modest (17.0%), but the landmark Aspirin for Evidence-Based Preeclampsia Prevention (ASPRE) Trial by the Fetal Medicine Foundation (FMF), published in 2017, showed a significant reduction in the risk of preterm preeclampsia , with an 82.0% reduction in early-onset preeclampsia (before 34 weeks), although no reduction was observed for term preeclampsia.[12]

Despite the importance of aspirin in the prevention of preeclampsia, one should not overlook the preventive measures that should be universally recommended, which can contribute to the overall reduction of preeclampsia risk, helping to prevent both early and late-onset preeclampsia. In this regard, the recommendation of calcium supplementation for all pregnant women in countries with low intake deserves special consideration, as proposed by the World Health Organization (WHO) in successive guidelines since 2011,[5] 2016,[13] and 2018.[14] It is important to emphasize that there is no recommendation to individually assess daily calcium intake or to measure calcium levels in pregnant women,[6,14] but rather to supplement calcium at a dose of 1.5 g-2 g/day of calcium carbonate or 2 g-4 g/day of calcium citrate.[7,14]

The Cochrane systematic review on calcium supplementation during pregnancy for the prevention of preeclampsia provides key insights into the benefits of this intervention. The review, which includes data from several randomized controlled trials, concludes that

calcium supplementation (especially in populations with low dietary calcium intake) significantly reduces the risk of preeclampsia, particularly for women at high risk of hypertensive disorders during pregnancy.[15]

The key findings of Cochrane review on calcium supplementation were[15]:

- Reduction in preeclampsia risk: the review found a moderate reduction in the risk of developing preeclampsia, with calcium supplementation lowering the relative risk by approximately 55.0%;
- Impact on severe outcomes: calcium supplementation also showed a significant reduction in the risk of severe hypertension, maternal death, and other serious outcomes related to hypertensive disorders;
- Population focuses: the benefits were most pronounced in women with low baseline calcium intake (<800 mg/day), making this intervention especially important in low- and middle-income countries where dietary calcium deficiency is prevalent;
- Doses: the recommended dose for calcium supplementation, according to the review, was 1.5 g to 2 g of calcium per day, in line with WHO guidelines.

Unfortunately, despite more than 13 years since the publication of the WHO guidelines for the prevention and treatment of preeclampsia, significant gaps have been identified in the poorest/developing countries (precisely those with the highest prevalence of preeclampsia/eclampsia) in following recommendations related to the use of aspirin and calcium.[5,13,14]

Despite clear evidence supporting the use of aspirin and calcium for the prevention of preeclampsia, there are significant global challenges in ensuring their widespread prescription, particularly in low- and middle-income countries. These challenges stem from several key issues:

1. Limited awareness: in many regions, healthcare providers may lack adequate training or awareness regarding updated guidelines for the prevention of preeclampsia. Despite organizations like the WHO recommending aspirin and calcium supplementation, knowledge gaps among frontline healthcare workers persist. In low-resource settings, these preventive measures are often underutilized due to insufficient dissemination of guidelines and educational materials.
2. Healthcare infrastructure: in low-income countries, the healthcare infrastructure may not support the routine implementation of preventive interventions. This includes inconsistent availability of prenatal care services, where opportunities for early risk assessment and intervention with aspirin and calcium are missed. Moreover, limited access to diagnostic tools for assessing high-risk pregnancies means that women who would benefit from these interventions are often not identified in time.
3. Supply chain and accessibility: even when guidelines recommend aspirin and calcium supplementation, ensuring the consistent availability of these medications can be problematic. In low-resource settings, there are often significant barriers to maintaining a reliable supply chain for these simple yet vital medications. Poor access to basic supplements in rural or underserved areas exacerbates this issue, contributing to the continued prevalence of preeclampsia and related complications.
4. Cultural and societal barriers: in some countries, cultural beliefs and practices may hinder adherence to medical recommendations, including the use of preventive medications like aspirin and calcium. Women may also face social barriers, such as lack of decision-making autonomy regarding their health, which limits their ability to seek preventive care or adhere to treatment.
5. Inconsistent guidelines and dosing uncertainty: while there is a consensus on the benefits of low-dose aspirin and calcium, different countries and medical societies recommend varying doses and timing for these interventions. For instance, the optimal dose of aspirin (ranging from 75 mg to 162 mg daily) can vary across guidelines, leading to confusion among healthcare providers regarding the best practice. Similarly, calcium supplementation is recommended at 1.5g to 2g/day by the WHO but ensuring accurate prescription and adherence in resource-poor settings is challenging.
6. Cost: although aspirin and calcium are relatively inexpensive, in low-income settings, the cost of even these simple interventions can be prohibitive for both healthcare systems and patients. This is particularly true when compounded by the additional cost of regular prenatal care visits, diagnostic tests, and the logistical challenges of delivering care in remote areas.
7. Regulatory and policy: some countries may lack national policies or protocols that prioritize

the widespread implementation of aspirin and calcium for preeclampsia prevention. Without strong policy frameworks and government support, preventive measures are less likely to be integrated into standard prenatal care practices, particularly in regions with limited healthcare resources.

Overcoming these barriers will require a multifaceted approach that includes better education and training for healthcare workers, stronger supply chains, clearer guidelines, and greater efforts to make preventive interventions accessible and affordable in resource-constrained settings. Collaborations between governments, international organizations, and healthcare providers are essential to address the inequities in preeclampsia prevention worldwide.[16]

In a previous study, conducted in Campina Grande (Paraíba), we were able to find that unfortunately, only 60.0% of pregnant women with preeclampsia and eclampsia admitted to our service had received some form of screening. Furthermore, 71.0% did not receive any preventive strategy, while among those who did, 41.3% receiving aspirin and 65.5% receiving calcium.[17]

However, and to our dismay, the WHO recommendation and those of all the most important guidelines for the prevention of preeclampsia, regarding calcium supplementation for all pregnant women in countries with low intake, have been the target of criticism by some professionals and groups of researchers. These critics have published, not original research articles, but in general only opinion pieces that are not evidence-based, challenging the current recommendations about calcium supplementation in pregnancy.[18,19] The authors claim that there is no evidence supporting calcium supplementation for all pregnant women, despite the substantial body of randomized clinical trials included in the Cochrane systematic review, whose findings we have summarized earlier in this text.[15]

The only attempt to add evidence to this debate was a recently published article by Wright *et al.*[19] This article conducted a sensitivity analysis of the Cochrane Systematic Review on calcium for the prevention of preeclampsia. Due to the high heterogeneity found for the preeclampsia outcome in this study, the authors question the validity of the Cochrane Systematic Review and present their own recommendation that calcium should be prescribed only for pregnant women at high risk of preeclampsia. We emphasize, however, that this was not an original article and does not, in any way, represent proof by the FMF that calcium should not be administered to pregnant women for the prevention of preeclampsia, as has been claimed and even presented at conferences and on social media.

Unfortunately, these criticisms have now reached Brazil, and we are concerned that they could undermine the still incipient but very promising efforts to expand the availability of calcium to pregnant women. The state of Rio de Janeiro standardized the supplementation of 1.5 g/day of calcium carbonate for all pregnant women in 2024,[20] an initiative that we wholeheartedly applaud. Braga *et al.*[21] published an article in Brazilian Journal of Gynecology and Obstetrics (RBGO) describing this strategy, which, in our view, should be implemented nationwide, given the erratic and unpredictable distribution of calcium carbonate across the states.

To our surprise, however, a group of Brazilian authors promptly published a Letter to the Editor in the same RBGO, questioning this important initiative. At the same time, they suggested that all pregnant women should be screened using the Fetal Medicine Foundation algorithm at 12 weeks, with subsequent administration of aspirin at a dose of 150 mg/day, based on the findings of the ASPRE Trial.[22]

We understand that this controversy reflects ongoing international discussions about the use of calcium to prevent preeclampsia. These discussions are not new but have intensified in recent months following the publication of a study on two clinical trials conducted by the WHO in India and Tanzania, published in the New England Journal of Medicine (NEJM) in January of this year. In these trials, involving 11,000 participants in each country, a low daily dose of calcium (500 mg) was found to be non-inferior to a high dose (1.5 g) for preventing preeclampsia. Nevertheless, non-inferiority was only demonstrated for preterm birth in India, but not in Tanzania.[23]

Magee and Dadelszen[18] shortly thereafter published a letter to the Editor for the NEJM stating that the results of the two calcium clinical trials were invalid. They contended that comparing high and low doses of calcium was illogical, given their belief in calcium's general ineffectiveness, thus making the trial's outcome obvious. However, they considered as an argument only the effect of calcium on preeclampsia found in the Cochrane Systematic Review, disregarding the clinically relevant effects on maternal death and severe maternal morbidity and even the outcome of prematurity itself, which proved to be different, and more frequent in 500 mg/day calcium group in Tanzania. In the same issue of NEJM, Wright and Nicolaides make similar claims, citing their own study in which they perform the sensitivity analysis of the Cochrane Systematic Review, and asserting uncertainty about whether high-dose calcium actually reduces the risk of preeclampsia.[19]

We regret that such discussions have reached the point of constituting true "Calcium Wars", the term we have coined for this intense debate about whether or not to

supplement calcium for all pregnant women in countries with low calcium intake. However, on the other hand, we are convinced that our common interest, the well-being of the mother-baby binomial, with a focus on preventing maternal and neonatal morbidity and mortality, should be placed above possible disagreements, as it is possible to reach a consensus in the development of public policies for calcium supplementation in pregnancy.

We would like to make our own comments. Brazil is a country with a high frequency of preeclampsia (PE) and eclampsia, as demonstrated in the integrative review by Guida *et al*.[4] Hypertension is the main cause of maternal death in the country (20.0%), which results in more than 200 deaths from hypertension per year.[3] In addition to these serious problems, we are a country considered to have low calcium intake (below 800mg/day), according to data from Brazilian Institute of Geography and Statistics (IBGE – Portuguese acronym).[24] According to all the recommendations of the most important guidelines, including the WHO, International Society for the Study of Hypertension in Pregnancy (ISSHP), and Brazilian Network of Studies on Hypertension in Pregnancy (RBEHG – Portuguese acronym), all Brazilian pregnant women should, therefore, receive calcium for the prevention of preeclampsia.

We highlight that this WHO recommendation is based on the highly reliable Cochrane Systematic Review on calcium, which we mentioned earlier. This review includes a robust set of randomized clinical trials that demonstrated calcium's effectiveness, particularly in populations with low dietary calcium intake, in reducing the risk of preeclampsia and its complications. The latest version of this Review was published in 2018 by Hofmeyr *et al*.[15]

Indeed, a renowned and truly distinguished Brazilian, Professor Álvaro Atallah, is one of the collaborators and was the lead author of the first version published in 2000.[25] This is an exceptionally well-crafted Systematic Review that indicates the quality of the evidence for each outcome, but also transparently highlights heterogeneity (not a novel discovery made by Wright *et al.*[19]). Furthermore, it explicitly addresses limitations of the evidence, without hiding the negative findings in terms of lack of effect or effect unlikely to be caused by calcium.[25]

The Cochrane Systematic Review was exhaustively evaluated in the process of developing the WHO guidelines, as it was about reviewing previous recommendations from 2011 and 2016 pertinent to calcium supplementation to prevent preeclampsia. Through a structured process, the Guideline Development Group (GDG) reviewed the balance between desirable and undesirable effects and the overall certainty of supporting evidence, stakeholder values and preferences, resource requirements and cost-effectiveness, acceptability, viability and equity.[5]

Grading of Recommendations Assessment, Development and Evaluation (GRADE) tables were prepared for several important outcomes, not only preeclampsia, but also preeclampsia with severe features, prematurity and the composite outcome of maternal death plus severe maternal morbidity.[5] In the interpretation of the Guideline Development Group (GDG), the joint findings of this important review favor the use of calcium and are sufficient to make the recommendation to supplement calcium to pregnant women in low-intake countries. This is the group that most benefited from the use of calcium, with no demonstrable effect on pregnant women in rich countries with high calcium intake.[14]

And which Cochrane Systematic Review findings deserve special attention and relevance? First, the reduction of preeclampsia and high blood pressure during pregnancy, with a reduction in preeclampsia of around 64.0% for women with low calcium diets and 78.0% in pregnant women at high risk for preeclampsia. Critics of calcium intake argue that this evidence is of low quality, hampered by the heterogeneity of studies and the effect of small studies that increase the positive effect of calcium.

However, in that same review it was demonstrated that, in addition to preeclampsia, calcium reduced (albeit modestly) the composite outcome of "death or severe maternal morbidity" (RR=0.80; 95%CI=0.66-0.98). There was no problem of heterogeneity found in this outcome, which was considered by both the authors of Cochrane Systematic Review and the WHO GDG to be high quality evidence. Furthermore, although the evidence is considered to be of low quality, calcium reduced prematurity. This reduction was more pronounced amongst women at higher risk of developing preeclampsia (55.0%).[14]

The study by Wright *et al*.[19] published in British Journal of Obstetrics and Gynaecology (BJOG) this year, which has been cited and disseminated at conferences (and on social media) as evidence that calcium is ineffective. Regrettably, this study conducted a sensitivity analysis of the Cochrane Systematic Review solely for the preeclampsia outcome, while other crucial outcomes received no consideration. We express our concern regarding the dissemination of this study as "the study that demonstrated that calcium does not prevent preeclampsia". We reiterate that this was merely a sensitivity analysis, not an original study, and failed to consider the effects of calcium on death and severe maternal morbidity, the latter considered high-quality evidence by Cochrane and the WHO.

Discussions concerning the differences between the Cochrane Systematic Review and major calcium studies have become highly polarized. It is important to note that the large study of the United States, the Calcium for Preeclampsia Prevention (CPEP), published in 1997 and

often cited as evidence that calcium "does not work", was conducted in a country with a high calcium intake.[26] Notwithstanding, a later study with 8,324 participants, approximately twice as many CPEP participants, was conducted by the WHO. Although this study did not find a reduction in preeclampsia risk, it did observe reductions in severe forms and complications.[27] Specifically, it reported a 32% reduction in eclampsia, a 29% reduction in gestational hypertension, and there was a reduction in maternal death and severe maternal morbidity (20.0%), in addition to neonatal mortality (30.0%).

On the other hand, we must consider the various mechanisms of action that make calcium a compelling candidate for preventing preeclampsia. They include reduction of parathyroid release and intracellular calcium and reduction of smooth muscle contractility, indirect effect on smooth muscle function by increasing magnesium levels, amelioration of uteroplacental blood flow (it lowers the resistance index in uterine and umbilical arteries), in the second half of pregnancy appears to reduce blood pressure directly, rather than preventing the endothelial damage associated with preeclampsia.[15]

Furthermore, recent studies have demonstrated calcium's antioxidant and anti-inflammatory actions, including a reduction in inflammatory cytokines. This makes calcium a promising agent not only for the prevention of early-onset preeclampsia but also late-onset preeclampsia, which is strongly associated with obesity, inflammation and metabolic syndrome.[28]

We highlight that although there is good quality evidence corroborating the use of aspirin in pregnancy,[13,29] we should not limit prevention strategies solely to aspirin, as it has been shown to prevent only early-onset preeclampsia and not late-onset disease.[12] It should also be considered that despite the optimistic data from the ASPRE Trial, which found an 82.0% reduction in the risk of early-onset preeclampsia, the effect of aspirin in the Cochrane Systematic Review is merely modest (17.0%),[29] and we certainly cannot be against the idea of associating interventions with different mechanisms of action and whose interaction is not dangerous, but may even have a positive effect, as can occur with exercise and aspirin.

A 2023 Systematic Review by Chen and Sun, published in the journal Medicine,[30] demonstrated that low-dose aspirin combined with calcium supplementation was more effective than aspirin alone in preventing preeclampsia (an 80.0% reduction). This combination reduced the risk of preterm birth and postpartum hemorrhage, and promoted fetal growth. The authors concluded that this combination (aspirin and calcium) holds clinical value and should be considered for high-risk pregnant women.

Finally, in addition to all these studies, a new Cochrane Review was published in November 2024, evaluating the effects of calcium supplementation during pregnancy on maternal and neonatal outcomes, excluding its use in the prevention of preeclampsia and hypertension. The analysis included 19 studies with 16,625 participants, with moderate to high quality and low risk of bias.[31] Their key findings were:

- For preterm birth: calcium supplementation with doses exceeding 1000 mg/day reduced the risk of preterm birth (before 37 weeks) by 24% (RR= 0.76; 95%CI=0.60-0.97).
- For extremely preterm birth and low birth weight: no significant impact was observed on these outcomes.
- No relevant differences in adverse effects were found between the supplemented and non-supplemented groups.

Integration with the previously discussed Cochrane review, which demonstrated benefits in preventing preeclampsia, gestational hypertension, and reducing maternal morbidity and mortality, suggests that calcium supplementation may indeed have a favorable effect on reducing preterm births, particularly in populations with low calcium intake. These benefits may be linked to both the prevention of preeclampsia and potential effects on reducing uterine contractility. Future studies are needed to clarify the mechanisms involved, however, in summary, calcium supplementation is beneficial for preventing preeclampsia and reducing preterm births in at-risk populations but has a limited impact on other neonatal outcomes.

It is challenging to extrapolate to Brazil recommendations and conjectures from researchers in countries with high calcium consumption and low preeclampsia incidence, especially given their long-established low Maternal Mortality Ratios (MMR). In contrast, Brazil faces a high frequency of preeclampsia and an MMR that has remained stagnant for many years (with the exception of a sharp increase exceeding 110 per 100,000 live births during the COVID-19). The "Bonfire of Vanities" cannot burn the need to prevent preeclampsia to reduce maternal morbidity and mortality.

In short, at this point, considering the brilliant response by Hofmeyr *et al.*[32] to the article by Wright *et al.*,[19] – in which it was reiterated that s of calcium's effects extended beyond merely reducing preeclampsia to including a reduction in maternal death and severe maternal morbidity – we paraphrase their recommendation to demand moderation in this "calcium war" (the term in quotation marks is ours). We urge caution so that attacks on the "meta-analytic calcium bathwater", despite the authors

agreeing that this water appears to be cloudy, do not lead to throwing the baby out with the bathwater. Because yes, the effects of calcium certainly go far beyond preeclampsia!

The universal adoption of calcium supplementation policies in countries with low calcium intake is not only evidence-based but also essential for advancing maternal health equity on a global scale. Accordingly, we extend our deepest and most sincere congratulations to Professor Braga for his exemplary initiative at the Rio de Janeiro SHD, which reflects an unwavering commitment to maternal health.

We underscore the importance of incorporating the WHO and RBEHG recommendations into the national guidelines for prenatal care and the management of hypertension during pregnancy. Such a measure would not only broaden the reach of the best practices implemented in Rio de Janeiro but also foster a positive impact nationwide.

Ensuring the effective distribution and widespread availability of calcium through Primary Health Care is critical to guaranteeing that all pregnant women in Brazil have access to this essential resource. The Ministry of Health has a pivotal role to play and must dedicate all necessary efforts to transform this proposal into a tangible reality, benefiting thousands of women and their babies across the country.

Final Considerations

Hypertensive disorders in pregnancy (HDP) represent a significant public health challenge in Brazil, demanding effective preventive strategies. Universal calcium supplementation, as recommended by the WHO and supported by scientific evidence, has proven effective in reducing preeclampsia, gestational hypertension, and maternal morbidity.

Given the high incidence of HDP and low dietary calcium intake in the country, universal supplementation policies, such as the one adopted in Rio de Janeiro, should be expanded nationwide. It is essential for the Ministry of Health to implement these recommendations, ensuring proper training for healthcare professionals and equitable access to supplements, thereby contributing to the reduction of maternal mortality in Brazil.

Authors' contribution

Amorim MMR, Albuquerque MA, Neves LFM, Cunha ACC, Bernardo BC and Katz L: participated in the conception, planning, analysis, interpretation and writing of the work. All authors approved the final version of the article and declared no conflicts of interest.

Data Availability

The entire data set supporting the results of this study has been published in the article itself.

References

1. Fu R, Li Y, Li X, Jiang W. Hypertensive Disorders in Pregnancy: Global Burden From 1990 to 2019, Current Research Hotspots and Emerging Trends. Curr Probl Cardiol. 2023 Dec; 48 (12): 101982.
2. 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): e323-33.
3. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Boletim Epidemiológico Vol.52 N° 29. Brasília (DF): Ministério da Saúde. Agosto; 2021. [*Internet*]. [access in 2024 Out 10]. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2021/boletim_epidemiologico_svs_29.pdf/view
4. Guida JPS, Andrade BG, Pissinatti LGF, Rodrigues BF, Hartman CA, Costa ML. Prevalence of preeclampsia in Brazil: an integrative review. Rev Bras Ginecol Obstet. 2022 Jul; 44 (7): 686-91.
5. World Health Organization (WHO). WHO recommendations for prevention and treatment of preeclampsia and eclampsia. Geneva: WHO; 2011. [access in 2024 Out 10]. Available from: https://www.who.int/publications/i/item/9789241548335
6. Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, *et al*. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens. 2022 Mar; 27: 148-69.
7. Centro de Referência em Saúde da Mulher. (2023). Protocolo de manejo da hipertensão gestacional e pré-eclâmpsia. [access in 2024 Out 10]. Available from: https://rbehg.com.br/wp-content/uploads/2023/04/PROTOCOLO-2023.pdf
8. FEBRASGO. Predição e prevenção da pré-eclâmpsia. Femina. 2023; 51 (1). [access in 2024 Out 10]. Available from: https://www.febrasgo.org.br/media/k2/attachments/Femina-01-2023-WEB.pdf
9. Poon LC, Nicolaides KH. First-trimester maternal factors and biomarker screening for preeclampsia. Prenatal Diag. 2014; 34: 618-27.

10. O'Gorman N, Wright D, Syngelaki A, Akolekar R, Wright A, Poon LC, *et al*. H. (2023). Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation. Am J Obstet Gynecol. 2016 Jan; 214 (1): 103.e1-e12.

11. National Institute for Health and Care Excellence (NICE). Hypertension in pregnancy: diagnosis and management (NICE guideline [NG133]). [*Internet*]. 2023. [access in 2024 Out 10]. Available from: https://www.nice.org.uk/guidance/ng133

12. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, Paco Matallana C, *et al*. Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. N Engl J Med. 2017 Aug 17; 377 (7): 613-22.

13. World Health Organization (WHO). WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: WHO; 2016. [access in 2024 Out 10]. Available from: https://www.who.int/publications/i/item/9789241549912

14. World Health Organization (WHO). WHO recommendation: Calcium supplementation during pregnancy for prevention of preeclampsia and its complications. Geneva: WHO; 2018. [access in 2024 Out 10]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535812/

15. Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2018; 10: CD001059.

16. Unitaid. (2024). Unitaid launches report on tools and interventions for diagnosis and management of preeclampsia, a major driver of maternal mortality. [*Internet*]. [access in 2024 Out 10]. Available from: https://unitaid.org/news-blog/unitaid-launches-report-on-tools-and-interventions-for-diagnosis-and-management-of-pre-eclampsia-a-major-driver-of-maternal-mortality/

17. Amorim M, Araújo I. Screening and prevention of preeclampsia in patients with preeclampsia and eclampsia admitted to a maternity school in Campina Grande-PB. 21st World Congress in Fetal Medicine. Lisboa, Portugal. Abstracts, 2024. [access in 2024 Out 10]. Available from: https://www.fetalmedicine.org/abstracts/2024/var/pdf/abstracts/2024/06787.pdf

18. Magee LA, Dadelszen PV. Two Randomized Trials of Low-Dose Calcium Supplementation in Pregnancy. New Engl J Med. 2024 Abr; 390 (16): 1535-7.

19. Wright D, Wright A, Magee LA, Von Dadelszen P, Nicolaides KH. Calcium supplementation for the prevention of preeclampsia: Challenging the evidence from meta-analyses. BJOG. 2024 Oct; 131 (11): 1524-9.

20. Secretaria Estadual da Saúde do Rio de Janeiro. Subsecretaria de Vigilância e Atenção Primária à Saúde. Nota Técnica 74239170 de 19 de setembro de 2022. Suplementação de Cálcio na Gestação. Rio de Janeiro (RJ): Secretaria Estadual da Saúde; 2022. [access in 2024 Out 10]. Available from: http://www.cib.rj.gov.br/arquivos-para-baixar/boletins-cib/2722-contextualizacaonota-tecnica/file.html

21. Braga A, Marinho PS, Nakamura-Pereira M, Peraçoli JC, Mello C. Prediction and secondary prevention of preeclampsia from the perspective of public health management – the initiative of the State of Rio de Janeiro [Editorial]. Rev Bras Ginecol Obstet. 2024 May; 46: e-rbgoedt3.

22. Rezende KBC, Barmpas DS, Werner H, Rolnik DL, Costa FS, Poon L, *et al*. Comment on: Prediction and secondary prevention of preeclampsia from the perspective of public health management – the initiative of the State of Rio de Janeiro. Rev Bras Ginecol Obstetr. 2024; 46: e-rbgo80.

23. Dwarkanath P, Muhihi A, Sudfeld CR, Wylie BJ, Wang M, Perumal N, *et al*. Two Randomized Trials of Low-Dose Calcium Supplementation in Pregnancy. N Engl J Med. 2024 Jan 11; 390 (2): 143-53.

24. Instituto Brasileiro de Geografia e Estatística (IBGE). Pesquisa de Orçamentos Familiares: 2008-2009 / IBGE, Coordenação de Trabalho e Rendimento. Rio de Janeiro: IBGE; 2010. [access in 2024 Out 10]. Available from:https://www.ibge.gov.br/estatisticas/multidominio/genero/9050-pesquisa-de-orcamentos-familiares.html

25. Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2002; 1: CD001059.

26. Levine RJ, Hauth JC, Curet LB, Sibai BM, Catalano PM, Morris CD, *et al*. Trial of calcium to prevent preeclampsia. N Engl J Med. 1997 Jul 10; 337 (2): 69-76.

27. Villar J, Abdel-Aleem H, Merialdi M, Mathai M, Ali MM, Zavaleta N, *et al*; World Health Organization Calcium Supplementation for the Prevention of Preeclampsia Trial Group. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. Am J Obstet Gynecol. 2006 Mar; 194 (3): 639-49.

28. Brito Pitilin E, Marafon F, Bonadiman BSR, Pelazza BB, Pillat MM, Lara JD, *et al*. Effects of calcium supplementation on changes in the IL2, IL4, IL6, IL10 axes and oxidative stress in pregnant women at risk for preeclampsia. BMC Pregnancy Childbirth. 2024 Jan; 24 (1): 71.

29. Duley L, Meher S, Hunter KE, Seidler AL, Askie LM. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev. 2019; 10: CD004659.

30. Chen W-Y, Sun S-F. Clinical efficacy of low-dose aspirin combined with calcium in preventing preeclampsia: A systematic review and meta-analysis. Medicine. 2023; 102 (34): e34620.

31. Kongwattanakul K, Duangkum C, Ngamjarus C, Lumbiganon P, Cuthbert A, Weeks J, *et al*. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database Syst Rev. 2024 Nov; 11: CD007079.

32. Hofmeyr GJ, Atallah AN, Torloni MR. Evidence for calcium supplementation in pregnancy: More than preeclampsia. BJOG. 2024 Dec; 131 (13): 1898-9.

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