

Omega-3 and DHA Supplementation in Pregnancy: A Systematic Review of Its Role in Preventing Preeclampsia and Gestational Diabetes

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ABSTRACT

Background: Omega-3 fatty acids, such as docosahexaenoic acid (DHA), plays a crucial role in fetal development and pregnancy maintenance, potentially reducing the risk of complications like gestational diabetes mellitus (GDM) and preeclampsia. Supplementation of these fatty acids may improve pregnancy outcomes by promoting fetal growth, prolonging gestational age, and positively influencing neonatal birth weight. However, the clinical evidence supporting the role of omega-3 supplementation in preventing preeclampsia and GDM remains inconclusive. **Methods:** A preliminary database search identified over 100 relevant studies. Following a rigorous three-stage screening process, eight studies meeting the predefined inclusion criteria were selected for in-depth analysis. Each underwent a comprehensive critical assessment to examine the impact of Omega-3 and DHA supplementation on preventing preeclampsia and gestational diabetes. This systematic approach ensured that the analysis was based on high-quality data, aligned with the study's objectives, and provided meaningful insights. **Result:** The final selection comprised eight studies that met the inclusion criteria. A thorough evaluation of these studies allowed for an in-depth investigation of Omega-3 and DHA supplementation's role in preventing preeclampsia and gestational diabetes. This structured analysis reinforced the study's reliability, ensuring that conclusions were drawn from robust and credible evidence. **Conclusion:** DHA supplementation plays a crucial role in pregnancy, supporting placental function and maternal metabolic health. However, its preventive role in preventing preeclampsia and GDM remains uncertain. Future research should explore potential benefits and evidence-based guidelines.

Keywords: DHA supplementation, GDM, Omega-3, Preeclampsia

INTRODUCTION

The nutritional status of a mother before and during pregnancy plays a crucial role in maternal and fetal health, influencing morbidity, birth weight, and overall pregnancy outcomes. While traditional nutritional recommendations emphasize the consumption of essential proteins, vitamins, and minerals, recent research highlights the importance of long-chain omega-3 polyunsaturated fatty acids, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), in prenatal nutrition.¹ Since the human body cannot synthesize these essential fatty acids, they must be obtained through dietary sources or supplementation. DHA and EPA, predominantly found in fish oil, have gained increasing attention due to their role in fetal development and pregnancy maintenance.² Maternal DHA levels are particularly significant, as DHA is actively transported across the placenta to support fetal brain development, with transport rates peaking during the third trimester due to the fetus's rapid growth.³

Given the biological importance of DHA and EPA, numerous studies have explored their potential benefits in pregnancy, including their role in reducing the risk of complications such as gestational diabetes mellitus (GDM) and preeclampsia.^{4,5} Research suggests that omega-3 fatty acid supplementation may improve pregnancy outcomes by promoting fetal growth, prolonging gestational age, and positively influencing neonatal birth weight, height, and head circumference.^{2,5} However, despite growing interest, findings remain inconsistent. While some studies suggest that omega-3 supplementation has no significant effect on reducing the incidence of preeclampsia, others report protective benefits, highlighting the need for further investigation.^{6,7} Additionally, omega-3 fatty acids have been hypothesized to delay spontaneous labor due to their influence on prostaglandins, which regulate parturition and myometrial activity. Although several clinical trials have reported positive effects on fetal development and pregnancy duration, conflicting results and limited randomized controlled trials

(RCTs) make it challenging to draw definitive conclusions regarding the efficacy of omega-3 supplementation in preventing pregnancy complications.^{8,9}

Among the potential benefits of omega-3 fatty acids, their impact on preeclampsia remains a critical area of research. Preeclampsia, a hypertensive disorder affecting 5-10% of pregnancies and up to 20% of first-time pregnancies, is a leading cause of maternal and neonatal morbidity and accounts for over 40% of early preterm births requiring medical intervention.^{8,10} Emerging evidence suggests that omega-3 fatty acids may contribute to vascular health by increasing vascular permeability and promoting vasodilation, leading to reduced blood pressure and improved placental function.¹⁰ However, despite these promising mechanisms, the clinical evidence supporting the role of omega-3 supplementation in preventing preeclampsia and GDM remains inconclusive, necessitating further high-quality trials to establish definitive recommendations.

METHODS

Protocol

This study was meticulously conducted in full compliance with the PRISMA 2020 guidelines, ensuring methodological rigor and high research quality. By following these established protocols, the review upheld transparency, reproducibility, and scientific integrity. Every stage of the process, including comprehensive literature searches, precise data extraction, and systematic synthesis of findings, was carefully executed to minimize bias. This stringent methodology enhances the study's credibility and reliability, reinforcing its value in advancing evidence-based research.

Criteria for Eligibility

This study aims to evaluate the role of Omega-3 and DHA supplementation during pregnancy in preventing preeclampsia and gestational diabetes through a systematic review and synthesis of data from diverse studies. By identifying patterns and emerging trends in the existing literature, this research seeks to generate valuable insights that can inform more effective diagnostic approaches and

patient care strategies. The ultimate objective is to enhance understanding of the preventive potential of Omega-3 and DHA supplementation, contributing to improved clinical outcomes for pregnant individuals at risk of these conditions.

To ensure analytical rigor, the study applied strict inclusion and exclusion criteria. Only peer-reviewed articles published in English between 2014 and 2024 were included, with each study's authenticity verified through DOI validation. To maintain a focused and high-quality dataset, non-research materials such as reviews, editorials, and duplicate entries were excluded. This meticulous selection process enhances the reliability of the analysis by ensuring that the findings are derived from relevant and credible sources.

By employing a systematic and comprehensive methodology, the study ensures that its conclusions are supported by robust evidence. The anticipated findings aim to advance current knowledge on Omega-3 and DHA supplementation in pregnancy and its role in preventing preeclampsia and gestational diabetes, providing a foundation for improved clinical management. Ultimately, this research aspires to drive advancements in patient care and contribute to better maternal health outcomes.

Search Strategy

A comprehensive and systematic search strategy was implemented to identify relevant studies for this review, utilizing key terms such as "omega-3," "DHA supplementation," "pregnancy," "preeclampsia," and "gestational diabetes." To ensure thorough coverage of the topic, the search was conducted across three major academic databases—PubMed, SagePub, and ScienceDirect. This rigorous approach enabled the selection of diverse, high-quality sources, thereby strengthening the evidence base for analysis and enhancing the reliability and validity of the review's findings.

Table 1. Search Strategy

Database	Search Strategy	Hits
Pubmed	<i>("omega-3" OR "DHA supplementation" AND "pregnancy" AND</i>	26

	<i>"preeclampsia" AND "gestational diabetes")</i>	
Science Direct	<i>("omega-3" OR "DHA supplementation" AND "pregnancy" AND "preeclampsia" AND "gestational diabetes")</i>	63
Sagepub	<i>("omega-3" AND "DHA supplementation" AND "pregnancy" AND "preeclampsia" AND "gestational diabetes")</i>	18

Data retrieval

The authors conducted a meticulous preliminary review of each article, systematically evaluating titles and abstracts to determine their relevance before proceeding with a detailed analysis. Only studies that aligned with the research objectives and met the predetermined inclusion criteria were selected for further examination. This structured approach ensured the identification of consistent and meaningful patterns within the literature, maintaining a focused analysis on studies directly relevant to the research question.

To enhance uniformity and comparability, only full-text articles published in English were included in the review. A rigorous screening process was employed to verify that all selected studies adhered to the established inclusion criteria and effectively addressed the study's objectives. Articles that failed to meet these standards were excluded, ensuring a high-quality dataset that remained closely aligned with the research focus.

The evaluation process involved a comprehensive assessment of multiple factors, including study titles, authorship, publication dates, research locations, and methodologies. This thorough review ensured the inclusion of only the most relevant and reliable studies. By implementing a systematic and rigorous selection process, the authors strengthened the credibility of the findings, providing a robust foundation for drawing reliable, evidence-based conclusions.

Quality Assessment and Data Synthesis

The authors implemented a meticulous initial screening process, systematically reviewing the titles and abstracts of each article to identify studies

relevant for further analysis. Only those that met predefined relevance and quality criteria were selected for a comprehensive, in-depth evaluation. This rigorous approach ensured the inclusion of high-quality studies that directly aligned with the research objectives. By refining the selection process, the authors curated a dataset of contextually significant and methodologically robust studies. This strategy not only enhanced the precision and focus of the analysis but also strengthened the overall quality, relevance, and scientific rigor of the review.



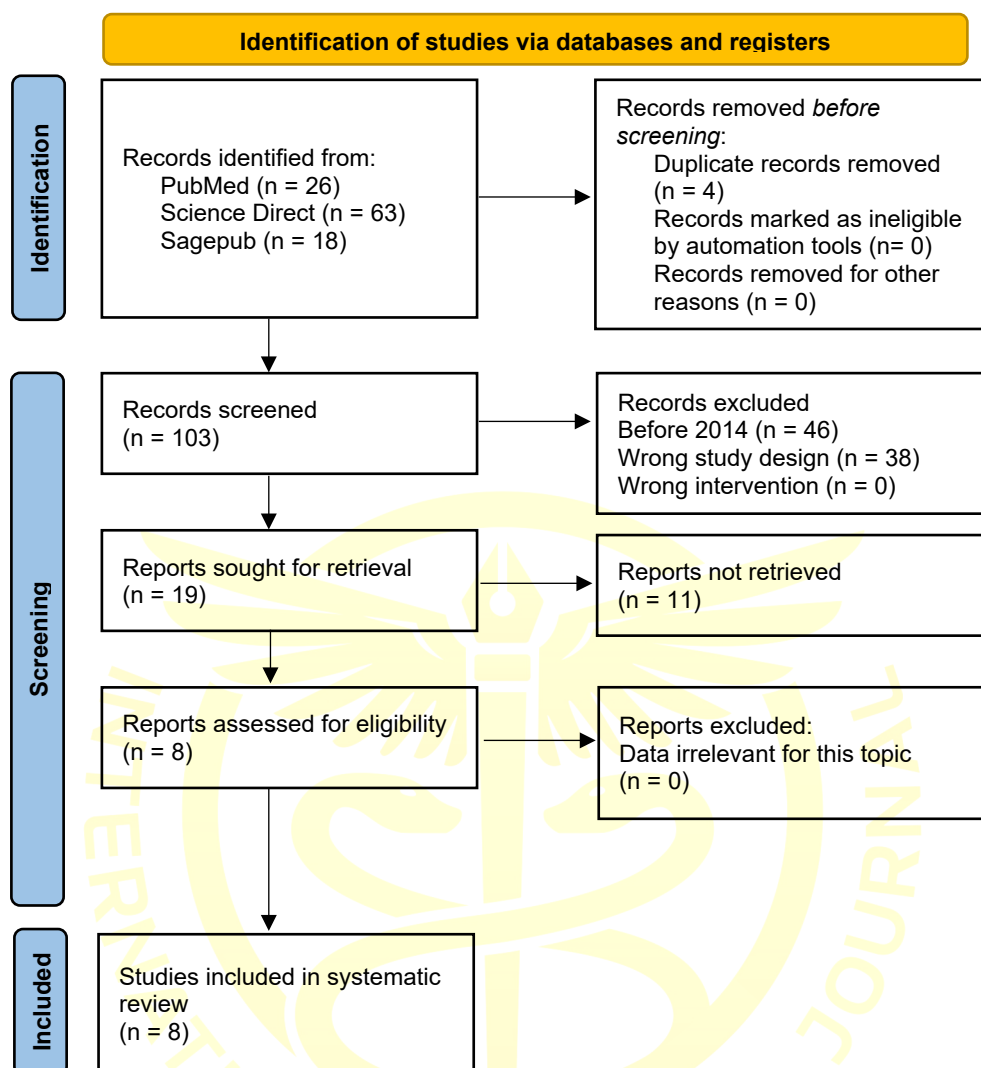


Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	(Burc hako v et al., 2017)	(Hubi nont et al., 2017)	(Deva rshi et al., 2019)	(Ghol ami et al., 2020)	(Serra et al., 2021)	(Jiang et al., 2023)	Amza et al., 2024)	(Cetin et al., 2024)
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?	No	No	No	Yes	No	No	No	No
3. Bias related to confounding factors								
Were participants included in any comparisons similar?	No	No	No	No	Yes	No	No	No
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?	No.	No.	No.	Yes.	Yes.	No.	No.	No.
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?	No	No	No	Yes	No	No	No	No
Were outcomes measured in a reliable way?	No	No	No	Yes	Yes	No	No	No
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?	No	No	No	Yes	No	No	No	No
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	No	No	No	Yes	Yes	No	No	No

RESULT

The investigation commenced with a systematic search across reputable academic databases, including ScienceDirect, PubMed, and SagePub, to identify relevant studies for the review. A rigorous three-stage screening process was implemented to filter and select the most pertinent research, ultimately narrowing the selection to eight studies that met the predefined inclusion criteria. These studies underwent a comprehensive analysis, with key topics meticulously extracted for in-depth evaluation. To enhance clarity and ensure effective presentation, the findings are concisely summarized in Table 3, providing a well-structured overview of the analyzed data.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result
Burchakov et al.¹¹ (2017)	Russia	Review	-	Preeclampsia, a pregnancy disorder characterized by hypertension and proteinuria, is linked to low intake of omega-3 long-chain polyunsaturated fatty acids (LCPUFA). However, recent research suggests that trials should consider factors like fetus gender, smoking's impact on preeclampsia prevalence, and the potential for high LCPUFA doses to promote the disorder, highlighting the need for future research.
Hubinont et al.¹² (2017)	Belgium	Review	-	DHA supplementation has been linked to reduced maternal concentrations, which can increase the risk of gestational diabetes, preeclampsia, postpartum depression, preterm labor, and IUGR. While some studies suggest improved outcomes, the efficacy of preventive DHA supplementation remains uncertain. Despite these

				concerns, DHA is a safe and effective supplement with few side effects, especially in patients with low dietary intake.
Devarshi et al.¹³ (2019)	USA	Review	-	Pregnancy and preeclampsia, both conditions characterized by gestational diabetes mellitus (GDM), can significantly impact the intake of docosahexaenoic fatty acid (DHA), a crucial nutrient for fetal and infant neurodevelopment, highlighting the need for increased DHA intake.
Gholami et al.¹⁴ (2020)	Iran	Case Control	339 participants	Pregnancy outcomes, including preeclampsia, eclampsia, preterm labor, gestational diabetes, and weight, showed a significant difference in gestational age between two study groups. However, no significant difference was found in preterm birth, preeclampsia, eclampsia, IUGR, and GDM. Fish oil supplements increased pregnancy age but did not decrease these outcomes.
Serra et al.¹⁵ (2021)	Chile	Systematic Review	37 studies	During pregnancy, omega 3 supplementations have been found to reduce the risk of preterm birth (PTB) and early preterm birth (ePTB) by 11% and 27%, respectively. However, sensitivity analyses showed no significant difference, suggesting further research is needed to determine the impact of these

				supplementations on fetal outcomes.
Jiang et al.¹⁶ (2023)	China	Review	-	During pregnancy, DHA intake is recommended due to its neurological, visual, and cognitive effects. Research suggests that DHA supplementation may prevent and treat pregnancy complications, but the specific mechanism remains unclear. The impact of DHA intake on pregnancy complications and offspring neurodevelopment is limited, with the exception of preterm birth and gestational diabetes mellitus.
Amza et al.¹⁷ (2024)	Romania	Review	-	During pregnancy, DHA and EPA supplementation have associated effects on neurological development, improving language, memory, attention, and sleep patterns. These effects are also associated with maternal intake during breastfeeding. Pregnant women should consume 250 mg/day of DHA and EPA daily to reduce preterm birth risk.
Cetin et al.¹⁸ (2024)	Italy	Review	-	Pregnancy is a critical time for obtaining docosahexaenoic acid, a crucial omega-3 fatty acid, according to strong evidence from randomized clinical trials. Women should consume at least 250 mg/d of docosahexaenoic acid from

				diet or supplements, with an additional intake of 600-1000 mg/d during pregnancy.
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DISCUSSION

Hypertensive disorders during pregnancy, particularly preeclampsia, pose significant threats to maternal and fetal health, with incidence rates rising globally. While pharmacological treatments are available, severe cases often necessitate cesarean delivery as the only viable intervention.¹⁹ Emerging evidence suggests that inadequate omega-3 fatty acid intake may be associated with an increased risk of preeclampsia, as these essential fatty acids play a crucial role not only in the later stages of pregnancy but also in early implantation and placentation. However, clinical trials evaluating DHA supplementation for preeclampsia prevention have yielded inconsistent results. The DOMInO (DHA to Optimize Mother Infant Outcome) trial, which involved 2,399 pregnant women who received 800 mg/day of DHA from before 21 weeks of gestation until birth, found no significant reduction in the risk of preeclampsia or gestational diabetes mellitus.^{11,20} Likewise, a systematic review by Horvath et al. concluded that there is insufficient evidence to support omega-3 supplementation for reducing intrauterine growth restriction or hypertensive disorders in high-risk pregnancies.⁸ These findings highlight the complexity of omega-3 fatty acid interactions in pregnancy and emphasize the need for more targeted, well-designed clinical trials to assess their precise role in maternal and fetal health.

At the cellular level, DHA has been shown to play a critical role in placental development and function. In vitro studies using trophoblastic cell cultures demonstrated that DHA promotes cell proliferation and enhances angiogenesis—marked by increased tube formation and upregulation of the vascular endothelial growth factor (VEGF) gene, a key regulator of placental vascularization.²¹ Additionally, DHA exerts anti-inflammatory effects and reduces oxidative stress, both of which are essential for optimal placental function and fetal development.²²

These biological mechanisms suggest a potential role for DHA in supporting a healthy pregnancy; however, translating these cellular benefits into clinically meaningful outcomes remains a challenge. A meta-analysis in 2020 suggested that DHA and EPA supplementation in the second half of pregnancy may provide a protective effect against preeclampsia in low-risk pregnancies. However, no significant benefits were observed in high-risk pregnancies, when supplementation was limited to DHA alone, or when initiated in the first half of pregnancy.²³ This suggests that the efficacy of omega-3 supplementation may be influenced by factors such as maternal risk profile, the specific combination of fatty acids administered, and the timing of supplementation.

In the context of gestational diabetes mellitus (GDM), impaired placental transport of DHA is a major concern, as it can lead to reduced cord blood DHA levels, potentially affecting neonatal neurodevelopment.²⁴ Some studies indicate that DHA supplementation does not significantly improve fetal DHA status in GDM pregnancies, highlighting the need to focus on optimizing placental DHA transfer. Strategies such as improving maternal glycemic control through diet, exercise, or medication may help restore DHA transport and mitigate its adverse effects on fetal development.^{25,26} Additionally, DHA has been implicated in upregulating FATP1 and FATP4 expression through the PPAR- γ pathway, which may enhance placental fatty acid transport. While standard DHA supplementation (600 mg/day) has shown limited effects on fetal DHA levels, higher doses may be more effective.²⁵ Previous studies have demonstrated the safety of n-3 PUFA doses up to 2.4 g/day in overweight children with metabolic syndrome, suggesting that future research should evaluate the efficacy and safety of higher DHA doses in GDM pregnancies.^{27,28} Although DHA supplementation does not appear to prevent GDM onset in healthy pregnancies, it may have therapeutic benefits for those already diagnosed. Clinical studies indicate that DHA-rich cod liver oil can lower blood glucose, lipid levels, and inflammatory markers in GDM patients,²⁹ while combined supplementation with vitamin D has shown beneficial effects on insulin-related parameters.³⁰ Given these findings, DHA may serve as an important adjunct

in GDM management, and large-scale clinical trials are needed to determine its full therapeutic potential in improving maternal and neonatal outcomes.

These findings underscore the importance of considering individual risk factors, supplementation timing, and the combined effects of DHA and EPA rather than DHA alone when evaluating omega-3 supplementation during pregnancy. The inconsistencies in clinical outcomes suggest that a one-size-fits-all approach may not be appropriate, and further large-scale, randomized controlled trials are essential to establish definitive guidelines. Understanding the intricate interactions between omega-3 fatty acids, maternal metabolic health, and fetal development will be critical in optimizing prenatal nutritional strategies to enhance both maternal and neonatal well-being.

CONCLUSION

Omega-3 fatty acids, particularly DHA, play a crucial role in pregnancy by supporting placental function, fetal neurodevelopment, and maternal metabolic health. However, current evidence on their effectiveness in preventing pregnancy complications such as preeclampsia and gestational diabetes mellitus (GDM) remains inconclusive. While DHA supplementation has demonstrated beneficial effects on placental angiogenesis, inflammation reduction, and fatty acid transport mechanisms, translating these cellular benefits into clinical outcomes has proven challenging. Studies suggest that DHA may offer therapeutic advantages in GDM management, improving glycemic control and lipid profiles, but its preventive role remains uncertain. Similarly, omega-3 supplementation may reduce preeclampsia risk in low-risk pregnancies when initiated in the second half of gestation, yet no significant benefits have been observed in high-risk groups. The discrepancies in findings highlight the complexity of DHA metabolism during pregnancy and the need for individualized approaches based on maternal risk factors, supplementation timing, and the specific combination of DHA and EPA. Future large-scale, randomized controlled trials should explore the potential benefits of higher DHA doses, evaluate its impact on maternal and neonatal outcomes, and establish evidence-based guidelines for omega-3 supplementation in pregnancy. A more

nuanced understanding of omega-3 fatty acids in maternal-fetal health will be critical in optimizing prenatal nutritional strategies to enhance both maternal and neonatal well-being.

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