

# Omega 3 and Preterm Birth

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Preterm birth (PTB) is a major cause of neonatal death and long-term consequences for the newborn. There is not enough available evidence that supports the conclusion that omega 3 supplementation during pregnancy reduces the risk of PTB and ePTB.

omega 3 supplementation

preterm birth

## 1. Introduction

Preterm birth (PTB), defined as birth <37 weeks of gestational age (GA), has been estimated to affect one in nine infants worldwide and represents the most significant cause of neonatal death <sup>[1]</sup>. Likewise, early PTB (ePTB, birth <34 weeks of GA) also represents a high risk of heart failure, infections and neonatal mortality <sup>[2]</sup>. Additionally, women who give birth before 37 weeks of GA have an increased risk of preterm deliveries in their second pregnancies <sup>[3]</sup>. Many strategies have been used to reduce the risk of PTB, particularly, the use of progesterone and cervical cerclage, which have limitations such as cost, availability and safety <sup>[4]</sup>. One strategy focused on the prevention of PTB is the administration of long-chain polyunsaturated fatty acids (LCPUFA) during pregnancy, which is accessible and cheap and has minimal side effects.

Omega 3 LCPUFA, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential in metabolic and physiological processes during embryonic and fetal development <sup>[5]</sup>. Although higher intakes of DHA and EPA's have been recommended worldwide, Dietary Reference Intakes (DRIs) have not been established. The Institute of Medicine (IOM) recommends that the intake of EPA and DHA contributes to 10 percent of the total omega 3 fatty acid intake (160 mg per day approximately) <sup>[6]</sup>. In the case of the Food and Agriculture Organization (FAO), the recommendation is an intake of 200 mg/day of DHA during pregnancy <sup>[7]</sup>.

Lower plasma levels of omega 3 LCPUFAs during pregnancy have been associated with detrimental perinatal outcomes, such as preterm delivery <sup>[8]</sup> and preeclampsia <sup>[9]</sup>. However, until now, there is no consensus on whether omega 3 supplementation during pregnancy reduces the risk of prenatal complications. A significant number of studies have been carried out to address this topic, including randomized controlled trials (RCTs) and meta-analyses. Some of them have shown a significant association between the consumption of fish or DHA supplements in pregnancy and decreased PTB incidence <sup>[10][11][12]</sup>, but others have failed to demonstrate this association <sup>[13]</sup>. In 2010, Makrides et al. conducted an RCT to evaluate the impact of DHA supplementation during pregnancy on maternal depression and concluded that the consumption of DHA was associated with a decrease in the incidence of ePTB compared to the control group <sup>[14]</sup>. However, this outcome was secondary, and the analyses

were not adjusted for multiplicity, limiting the confidence in the results. Olsen et al. showed in an RCT that fish oil does not prevent PTB in Chinese women; however, it is important to consider that supplementation started at midgestation [15]. Among the mechanisms suggested to explain the effect of omega 3 on PTB are the production of eicosanoids involved in the parturition process [16] and their role in the inflammatory pathway, including an increase in resolving R3 production [17][18]. Besides its tocolytic properties, omega 3 may also have an effect on the electrical activity of the myometrium during the pre-labor period, demonstrating an antiarrhythmic effect that could explain the role of omega 3 in the prevention of PTB [19].

## 2. Supplementation of Omega 3 during Pregnancy and the Risk of Preterm Birth

Preterm delivery is a leading cause of neonatal and childhood mortality and is associated with cognitive deficiencies and increased risk of cardio-metabolic diseases in adult life [20][21]. LC-PUFA are involved in optimum fetoplacental growth and development through their function associated with oxidative stress, angiogenesis and inflammation [22]. The consumption of oily fish and DHA supplements during pregnancy has been associated with maternal and infant benefits, including decreased maternal blood pressure [23] and infant neurodevelopment and growth [24]. Previous studies have explored the relationship between omega 3 intake during pregnancy and timing of delivery or preterm risk; however, the results are still inconsistent. Meanwhile, some clinical trials reported an increase in gestational length after DHA and fish oil supplement interventions [25], and others reported no effect in the incidence of ePTB [26] and PTB [15]. A previous meta-analysis also analyzed the effect of omega 3 supplementation on PTB rates; in 2015, Saccone and Berghella reported no effect of omega 3 with only two RCTs analyzed [27]. However, in 2016, Kar et al., following the analyses of nine studies, did find a positive effect of omega 3 supplementation on the prevention of PTB [28]. Besides including a greater number of studies, compared with Kar and Colleagues, our work provides an update of RCTs published until June 2020 as well as the analyses of secondary outcomes, such as preeclampsia, IUGR and fetal and neonatal death.

We conclude that omega 3 supplementation during pregnancy does not reduce the risk of PTB and ePTB. Although preliminary results showed that omega 3 supplementation reduced the risk of PTB and ePTB by 11% and 27%, respectively, after sensitivity analyses were performed and only low risk of bias studies were analyzed, the significance of the effect of omega 3 on PTB and ePTB risk disappears. Concerning the effect of omega 3 supplementation on other perinatal outcomes, such as preeclampsia, IUGR risk and fetal and neonatal death, no differences were found in this study. These results suggest that among the studies analyzed, there is not enough evidence suggesting that omega 3 supplementation during pregnancy decreases the risk of PTB and other perinatal complications.

The form of omega 3 supplementation in the analyzed trials differed and included capsules; liquid fish oil; and enriched food products, such as eggs high in DHA and bars containing DHA. The intake of 600 mg of DHA/day as capsules or bars has shown an increased length of pregnancy by 2.9 days [12] and 4.0–4.5 days [29]; meanwhile, the ingestion of 137 mg of DHA from high-DHA eggs showed a gestation increase of 6 days [25]. It can be hypothesized that food-based DHA (i.e., DHA-rich eggs) might have a more pronounced impact on pregnancy

lengths as omega 3 bioavailability is higher when DHA is consumed in a high-fat food matrix [30]. The administration of omega 3 as DHA and EPA by itself or in combination with other nutrients should also be considered at the moment of describing the effect of omega 3 on fetal and maternal outcomes. In this review, considering the number of studies, it was not possible to differentiate between different doses and different components of supplementations. Similarly, nutritional status and omega 3 deficiency should also be considered. Lower levels of plasma EPA and DHA showed a 10-fold increased risk of ePTB compared to the higher plasma levels [8], demonstrating a potential benefit of the supplementation effect during deficiency.

Timing and length of supplementation are important factors determining the effect of omega 3 on preterm delivery risk. Considering the mechanism of action of omega 3 associated with inflammation and electrical activity of myometrium, it can be expected that acute (short-term) and chronic (throughout the pregnancy) supplementation have different effects on outcomes related to preterm delivery. The time of administration, the gestational week when the supplementation started and if the treatment continued through the whole pregnancy or not are characteristics that have to be considered in future studies. The potential adverse effects of omega 3 supplementation are not discussed in this review; however, post-term partition or bleeding have been associated with high omega 3 doses (>2.7 g/day) [31].

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## References

1. Blencowe, H.; Cousens, S.; Oestergaard, M.Z.; Chou, D.; Moller, A.B.; Narwal, R.; Adler, A.; Vera Garcia, C.; Rohde, S.; Say, L.; et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: A systematic analysis and implications. *Lancet* 2012, 379, 2162–2172.
2. Blencowe, H.; Cousens, S.; Chou, D.; Oestergaard, M.; Say, L.; Moller, A.B.; Kinney, M.; Lawn, J. Born Too Soon: The global epidemiology of 15 million preterm births Understanding the data Preterm birth—What is it? Defining preterm birth. *Reprod. Health* 2013, 10, 1–13.
3. Adams, M.M.; Elam-Evans, L.D.; Wilson, H.G.; Gilbertz, D.A. Rates of and Factors Associated with Recurrence of Preterm Delivery. *Obstet. Gynecol. Surv.* 2000, 55, 534–536.
4. Spong, C.Y. Prediction and Prevention of Recurrent Spontaneous Preterm Birth. *Obstet. Gynecol.* 2007, 110, 405–415.
5. Carlson, S.E.; Colombo, J. Docosahexaenoic Acid and Arachidonic Acid Nutrition in Early Development. *Adv. Pediatr.* 2016, 63, 453–471.
6. Institute of Medicine. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids*; Institute of Medicine: Washington, DC, USA, 2005; ISBN 030908525X.

7. Food and Agriculture Organization FAO. Fats and Fatty Acids in Human Nutrition. Proceedings of the Joint FAO/WHO Expert Consultation; FAO: Rome, Italy, 2008; Volume 55.
8. Olsen, S.F.; Halldorsson, T.I.; Thorne-Lyman, A.L.; Strøm, M.; Gørtz, S.; Granstrøm, C.; Nielsen, P.H.; Wohlfahrt, J.; Lykke, J.A.; Langhoff-Roos, J.; et al. Plasma Concentrations of Long Chain N-3 Fatty Acids in Early and Mid-Pregnancy and Risk of Early Preterm Birth. *EBioMedicine* 2018, 35, 325–333.
9. Wadhvani, N.; Patil, V.; Pisal, H.; Joshi, A.; Mehendale, S.; Gupte, S.; Wagh, G.; Joshi, S. Altered maternal proportions of long chain polyunsaturated fatty acids and their transport leads to disturbed fetal stores in preeclampsia. *Prostaglandins Leukot. Essent. Fat. Acids* 2014, 91, 21–30.
10. Olsen, S.F.; Secher, N.J.; Tabor, A.; Weber, T.; Walker, J.J.; Gluud, C. Randomised clinical trials of fish oil supplementation in high risk pregnancies. *BJOG Int. J. Obstet. Gynaecol.* 2000, 107, 382–395.
11. Borod, E.; Atkinson, R.; Barclay, W.R.; Carlson, S.E. Effects of third trimester consumption of eggs high in docosahexaenoic acid on docosahexaenoic acid status and pregnancy. *Lipids* 1999, 34, 1999.
12. Carlson, S.E.; Colombo, J.; Gajewski, B.J.; Gustafson, K.M.; Mundy, D.; Yeast, J.; Georgieff, M.K.; Markley, L.A.; Kerling, E.H.; Shaddy, D.J. DHA supplementation and pregnancy outcomes. *Am. J. Clin. Nutr.* 2013, 97, 808–815.
13. Harper, M.; Thom, E.; Klebanoff, M.A.; Thorp, J.; Sorokin, Y.; Varner, M.W.; Wapner, R.J.; Caritis, S.N.; Iams, J.D.; Carpenter, M.W.; et al. Omega-3 fatty acid supplementation to prevent recurrent preterm birth: A randomized controlled trial. *Obstet. Gynecol.* 2010, 115, 234–242.
14. Makrides, M.; Gibson, R.A.; McPhee, A.J.; Yelland, L.; Quinlivan, J.; Ryan, P. DOMInO Investigative Team, and the Effect of DHA Supplementation during Pregnancy on Maternal Depression and Neurodevelopment of Young Children. *JAMA* 2010, 304, 1675.
15. Olsen, S.F.; Halldorsson, T.I.; Li, M.; Strøm, M.; Mao, Y.; Che, Y.; Wang, Y.; Duan, F.; Olsen, J.; Zhou, W. Examining the Effect of Fish Oil Supplementation in Chinese Pregnant Women on Gestation Duration and Risk of Preterm Delivery. *J. Nutr.* 2019, 149, 1942–1951.
16. Mosaad, E.; Peiris, H.N.; Holland, O.; Morean Garcia, I.; Mitchell, M.D. The Role(s) of Eicosanoids and Exosomes in Human Parturition. *Front. Physiol.* 2020, 11, 594313.
17. Ishihara, T.; Yoshida, M.; Arita, M. Omega-3 fatty acid-derived mediators that control inflammation and tissue homeostasis. *Int. Immunol.* 2019, 31, 559–567.
18. Yamashita, A.; Kawana, K.; Tomio, K.; Taguchi, A.; Isobe, Y.; Iwamoto, R.; Masuda, K.; Furuya, H.; Nagamatsu, T.; Nagasaka, K.; et al. Increased tissue levels of omega-3 polyunsaturated fatty acids prevents pathological preterm birth. *Sci. Rep.* 2013, 3, 1–7.

19. Olsen, S.F.; Secher, N.J.; Björnsson, S.; Weber, T.; Atke, A. The potential benefits of using fish oil in relation to preterm labor: The case for a randomized controlled trial? *Acta Obstet. Gynecol. Scand.* 2003, 82, 978–982.
20. Linsell, L.; Johnson, S.; Wolke, D.; O'Reilly, H.; Morris, J.K.; Kurinczuk, J.J.; Marlow, N. Cognitive trajectories from infancy to early adulthood following birth before 26 weeks of gestation: A prospective, population-based cohort study. *Arch. Dis. Child.* 2018, 103, 363–370.
21. Liu, L.; Johnson, H.L.; Cousens, S.; Perin, J.; Scott, S.; Lawn, J.E.; Rudan, I.; Campbell, H.; Cibulskis, R.; Li, M.; et al. Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. *Lancet* 2012, 379, 2151–2161.
22. Godhamgaonkar, A.A.; Wadhvani, N.S.; Joshi, S.R. Exploring the role of LC-PUFA metabolism in pregnancy complications. *Prostaglandins Leukot. Essent. Fat. Acids* 2020, 163, 102203.
23. Lalooha, F. Evaluation of the effect of omega-3 supplements in the prevention of preeclampsia among high risk women. *Afr. J. Pharm. Pharmacol.* 2012, 6, 2580–2583.
24. Ostadrahimi, A.; Salehi-Pourmehr, H.; Mohammad-Alizadeh-Charandabi, S.; Heidarabady, S.; Farshbaf-Khalili, A. The effect of perinatal fish oil supplementation on neurodevelopment and growth of infants: A randomized controlled trial. *Eur. J. Nutr.* 2017, 57, 2387–2397.
25. Smuts, C.M.; Huang, M.; Mundy, D.; Plasse, T.; Major, S.; Carlson, S.E. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. *Obstet. Gynecol.* 2003, 101, 469–479.
26. Makrides, M.; Best, K.; Yelland, L.; McPhee, A.; Zhou, S.; Quinlivan, J.; Dodd, J.; Atkinson, E.; Safa, H.; van Dam, J.; et al. A Randomized Trial of Prenatal n-3 Fatty Acid Supplementation and Preterm Delivery. *N. Engl. J. Med.* 2019, 381, 1035–1045.
27. Saccone, G.; Berghella, V. Omega-3 supplementation to prevent recurrent preterm birth: A systematic review and metaanalysis of randomized controlled trials. *Am. J. Obstet. Gynecol.* 2015, 213, 135–140.
28. Kar, S.; Wong, M.; Rogozinska, E.; Thangaratnam, S. Effects of omega-3 fatty acids in prevention of early preterm delivery: A systematic review and meta-analysis of randomized studies. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 2016, 198, 40–46.
29. Harris, M.A.; Reece, M.S.; McGregor, J.A.; Wilson, J.W.; Burke, S.M.; Wheeler, M.; Anderson, J.E.; Auld, G.W.; French, J.I.; Allen, K.G.D. The Effect of Omega-3 Docosahexaenoic Acid Supplementation on Gestational Length: Randomized Trial of Supplementation Compared to Nutrition Education for Increasing n-3 Intake from Foods. *Biomed Res. Int.* 2015, 2015, 1–8.
30. Cholewski, M.; Tomczykowa, M.; Tomczyk, M. A Comprehensive Review of Chemistry, Sources and Bioavailability of Omega-3 Fatty Acids. *Nutrients* 2018, 10, 1662.

31. von Schacky, C. Omega-3 Fatty Acids in Pregnancy—The Case for a Target Omega-3 Index. *Nutrients* 2020, 12, 898.

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