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Omega-3, systemic inflammation and its importance in maternal and fetal health: a comprehensive approach in a literature review

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Omega 3, inflamación sistémica y su importancia en la salud materno-fetal: un enfoque integral en una revisión bibliográfica

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Abstract

Nutrition in a pregnant patient should meet the necessary requirements for the formation of the fetus and knowledge of it should be a key piece in the training of a health professional, foods rich in PUFA n-3 are mostly of marine origin and are essential for some physiological functions, supplementation with n-3 PUFA during pregnancy can offer benefits to the mother-child binomial. This article integrates the most recent research on omega-3 in pregnancy and evidences its action in some of the most known maternal and/or fetal pathologies.

KEY WORDS

Omega-3, eicosapentaenoic acid, docosahexaenoic acid, polyunsaturated acids, polyunsaturated acids

Resumen

La nutrición en una paciente embarazada debe cumplir los requisitos necesarios para la formación del feto y su conocimiento debe ser una pieza clave en la formación de un profesional de la salud, los alimentos ricos en PUFA n-3 son en su mayoría de origen marino y son esenciales para algunas funciones fisiológicas, la suplementación con PUFA n-3 durante el embarazo puede ofrecer beneficios al binomio madre-hijo. Este artículo integra las investigaciones más recientes sobre omega-3 en el embarazo y evidencia su acción en algunas de las patologías maternas y/o fetales más conocidas.

PALABRAS CLAVE

Omega-3, ácido eicosapentaenoico, ácido docosahexaenoico, ácidos poliinsaturados, ácidos poliinsaturados.

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Introduction

Knowledge of diet and nutrition in a pregnant patient is fundamental in medical practice, as insufficient intake of calories and/or micronutrients can lead to unfavorable pregnancy outcomes, such as low birth weight and intrauterine growth restriction, in addition to specific conditions depending on the element that is altered.[1] Recent studies have explained the role of omega-3 fatty acids in pregnancy, particularly in immunomodulation and neurodevelopment. The aim of this article was to integrate the most recent work on omega-3 during pregnancy and to demonstrate in anti-inflammatory, antioxidant, neurotransmitter, and membrane-generating action in some maternal and/or fetal pathologies. Furthermore, it aims to identify the need for additional supplementation of n-3 PUFA during pregnancy.

Table 1
Necessary requirements of polyunsaturated fatty acids with three double bonds or Omega 3 and Omega 6 according to age group

Estages of life	ALA	EPA	DHA	Omega 6
Newborn	0.5 g daily	There is no need	100 mg	4.4 g
Child	0.6-1 g daily	250 mg daily		10-12 g
Teenage	1-1.6 g	200-250 mg daily		12-16 g
Adult	1.1-1.6 g	250-500 mg daily		12-17 g
Pregnant women	1.4 g	dha: 450 mg daily + epa		13 g

Fuente: Trumbo P, 2002 (38); EFSA, 2010 (39).

Polyunsaturated Fatty Acids (PUFA), Nutrition, and Functions in Pregnancy

Among trienoic fatty acids (with three double bonds), commonly known in the literature as polyunsaturated fatty acids with three double bonds (n-3 PUFA) or omega-3, are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). These are considered essential during pregnancy as they cannot be synthesized independently.[2] The main polyunsaturated fatty acids with six double bonds (n-6 PUFA) or omega-6 in the diet are linoleic acid (LA) and arachidonic acid (AA).[3] Dietary guidelines for Americans advise that pregnant and lactating mothers consume 250 to 400 mg of n-3 PUFA daily,[4] similar to the 100 to 200 mg per day recommended by the European Food Safety Authority and the 200 mg per day recommended by the Food and Agriculture Organization of the United Nations (Table 1).[5]

Foods high in n-3 PUFA are especially those of marine origin, such as fatty fish (tuna, sardine, horse mackerel, salmon), shellfish and algae; however, their contribution of this essential nutrient is low, providing only 50 mg/day of DHA in the general population, which is far below the international recommendation of 200 to 500 mg/d.[6] DHA is found in the diet of individuals who consume fish oil, algae, cod oil, tuna, egg and in cold water fish such as salmon.[7] Other sources of n-3 PUFA fatty acids are seeds, from which oils are also derived, such as flaxseed oil and vegetable oils, which contain ALA but must go through a process to become EPA and DHA to be biologically useful. Butter is also a source; however, one study showed that high consumption of sunflower oil in pregnant women is concerning due to its lower oxidative stability, while high consumption of butter is beneficial due to its supply of conjugated linoleic acids Table 2.[8]

The absorption of n-3 PUFA (DHA) in pregnant women is influenced by various factors, starting with its source, whether through diet

Table 2
Plant and animal sources of the components of the polyunsaturated fatty acids with three double bonds or Omega 3

Foods	Omega-3 component	Contribution
1 tablespoon (10 g) flax seed	ala	2.5 g
1 tablespoon (15 g) chia seed	ala	2.5 g
4 (28 g) walnuts	ala	1.5 g
1 tablespoon (14 g) linseed oil	ala	7.26 g
1 tablespoon (14 g) canola oil	ala	1.3 g
90 g spinach	ala	1.7 g
78 g broccoli	ala	0.1 g
130 g kale	ala	0.13 g
86 g of soy	ala	0.6 g
100 g salmon	EPA AND DHA	1.24 g of EPA, 0.59 g of DHA
100 g sardines	EPA AND DHA	0.50 g of EPA, 0.90 g of DHA
100 g tuna	EPA AND DHA	0.18 g of EPA, 0.16 g of DHA
100 g trout	EPA AND DHA	0.40 g of EPA, 0.44 g of DHA
1 cda (14 g) of cod liver oil	EPA AND DHA	0.93 g of EPA, 1.36 g of DHA
100 g octopus	EPA AND DHA	0.47 g of EPA, 0.26 g of DHA
100 g caviar	EPA AND DHA	0.6 g of EPA, 1.2 g of DHA
100 g crab	EPA AND DHA	0.32 g of EPA, 0.12 g of DHA
100 g clams	EPA AND DHA	0.25 g of EPA, 0.18 g of DHA
200-500 mg of algae (supplement)	DHA	100% DHA

Fuente: Calde PC, 2012 (40); Calder PC, 2017 (41).

or supplementation. Each of these affects absorption due to the individual metabolism of pregnant women, their digestion, and whether they have taken prenatal supplements. Similarly, factors such as alcohol consumption, physical activity, education level, advanced age, smoking, and dietary culture in the region can also play a role. In this regard, for patients with risk factors for dietary n-3 PUFA deficiency or low baseline levels, supplementation during pregnancy is recommended.[1,9,10] A study showed that dietary fatty acids stored in the mother's body reserves have a direct effect on the fatty acid status of the fetus and infant, as they are transferred to the fetus through the placenta during pregnancy and continue to be supplied through breast milk in the postnatal period.[8]

N-3 PUFAs are essential nutrients for physiological functions, such as oxygen transport, energy storage, and the biosynthesis of cell membranes.[11] Additionally, their role in immunomodulation is fundamental.[3] n-3 PUFAs, particularly EPA and DHA, have anti-inflammatory properties,[12] modulating cell signaling and antigen presentation.[13] Their consumption during pregnancy reduces the production of pro-inflammatory proteins such as IL-6, IL-8, TNF-alpha, and TLR4 in the placenta and adipose tissue through genomic mechanisms of downregulation. They attenuate the concentrations of prostaglandin F2 alpha, which is involved in the mechanism of preterm labor,[14] and reduce the levels of baseline and delivery-time serum C-reactive protein (CRP).[14-18] They regulate angiogenesis,[19] reduce the activity of peroxisome proliferator-activated receptors (PPARγ), and may modulate the expression of free fatty acid receptor 4 (FFAR4), which is expressed in the placenta and involved in insulin resistance. Regarding cellular immunity, diets rich in n-3 PUFA reduce the mitotic division of Th1 lymphocytes and increase the proliferation of Th2 lymphocytes, with immunomodulatory effects.[17] Additionally, n-3 PUFAs alone or in combination with vitamin E reduce oxidative stress, increase antioxidant capacity, and promote the release of nitric oxide.[17,18]

These anti-inflammatory, antioxidant, and even metabolic pathways have been proven in various recent studies to have beneficial effects on both the mother and the fetus, with supplementation or the maintenance of adequate baseline levels of n-3 PUFA. This includes benefits in fetal neurodevelopment and neuroprotection, reduced risk of hereditary allergies, positive effects on maternal health, reduced risk of preterm birth and preeclampsia, and aid in managing maternal obesity.

Neurodevelopment

PUFA, comprising 25 to 30 % of brain fatty acids, play a role in synaptic activity.[20] It is suggested that this process could promote neurogenesis, the development of dendrites and neuronal synapses, and the maturation of myelin in white matter.[21] Diets enriched with n-3 PUFA reduce pro-inflammatory placental reactions and prevent cytokine production in descendant microglial cells.[22] These macromolecules induce a downregulation of pro-inflammatory eicosanoids from n-6 PUFA, leading to a reduction in the inflammatory response in neonatal brain tissue, as well as promoting its development through adequate or supplementary intake of n-3 PUFA. Supplementing the maternal diet with these macronutrients reduces the prevalence of low neurocognitive scores at 18 months[21] and the higher the maternal intake of these macromolecules during the first trimester, the better the scores at ages 4 and 7.[23]

Nevins et al.[4] conducted a study evaluating n-3 PUFA supplementation during pregnancy and its effects, concluding that this intervention had slightly positive effects on children's cognitive development in areas such as language, visual, physical activity, academic performance, socio-emotional skills, memory, and a reduced risk of psychiatric conditions like ADD, ADHD, ASD, anxiety, or depression.[10,4] Christifano et al.[7] quantified the frequency of consumption of foods rich in DHA, choline, and other nutrients in 300 pregnant women, and measured its

relationship to neurodevelopment using biomagnetometry between weeks 32 and 36 of gestation. They found that the consumption of these foods and their nutrients, particularly DHA, had positive effects on neurodevelopment, fetal autonomic control, verbal intelligence, and behavior regulation.

N-3 PUFA and its Relation to Ophthalmology

Adequate intake of PUFA seems to play a key role in the proper development of the fetal central nervous system, particularly vision. Omega-3 consumed by the mother during the third trimester and lactation plays an essential role.[24]. Premature infants with retinopathy are at risk of n-3 PUFA deficiency, especially DHA, due to its low content in parenteral nutrition solutions. These macronutrients form retinal membranes and accumulate in the neuroretina between intrauterine life and the first few weeks of life. Adding them to parenteral solutions could reduce oxygen-induced retinopathy by regulating prostanoid and TNF synthesis, further supporting the importance of n-3 PUFA use in both the mother during pregnancy and premature babies for the development of neural tissue.[25]

Maternal Mental Health

Reduced intake of n-3 PUFA has been associated with an increased risk of perinatal or postnatal depression. It is recognized that higher concentrations of these, especially EPA, during pregnancy reduce the prevalence of this disorder, and they also help reduce anxiety through a non-anti-inflammatory pathway.[10,15] Conversely, in a systematic review conducted by Rupanagunta et al.,[26] it was suggested that the relationship between low n-3 PUFA intake and depression occurs due to the restriction of pro-inflammatory mediators and through regulation of the synthesis, metabolism, and functions of serotonin neurotransmitters. Lastly, n-3 PUFA supplementation has shown greater benefit in preventing postpartum depression than in treating it.

Maternal Obesity and Gestational Diabetes

The use of n-3 PUFA has been associated with metabolic improvement in pregnant women, particularly those with gestational diabetes. This is reflected in the reduction of insulin resistance,[16,17,27] the decreased risk of cardiovascular disease in the mother,[17] the reversal of maternal atherosclerosis by increasing adiponectin and suppressing pro-inflammatory cytokines and nuclear factor kappa B protein,[16] and the reduction of fasting plasma glucose.[17,18]

Regarding lipid metabolism, n-3 PUFA supplementation lowers triglyceride levels, very low-density lipoproteins (VLDL), and low-density lipoproteins (LDL), increases the expression of the LDL receptor (LDLR), restores the function of lipoprotein lipase, hepatic triglyceride lipase, and lecithin-cholesterol acyltransferase, and raises HDL levels. This may explain the regression of atherosclerotic processes. Finally, it promotes a reversal process in aortic remodeling in the offspring of these patients .[17]

N-3 PUFA supplementation increases endogenous insulin production in pregnant women with a prior diagnosis of type 1 diabetes.[15] Additionally, DHA supplementation during pregnancy prevents the increase of insulin-like growth factor 2 (IGF-2), which has been linked to maternal obesity, significantly reducing it.[17,28] Lastly, it has been observed that the addition of 2 grams per day of n-3 PUFA for more than 25 weeks reduces inflammatory markers in maternal adipose and placental tissue in overweight or obese pregnant women.[18] These supplements also reduce the likelihood of macrosomia and obesity in the fetus, improve metabolism in fetal fluids, reduce insulin resistance, and limit neonatal body size growth.[17] However, a systematic review by Gao et al.,[18] found no significant impact on fetal macrosomia or neonatal hyperbilirubinemia, unlike the findings of Monthé-Drèze et al.,[27] which reported an increase in fat-free mass, fetal body mass, lean mass accumulation, improved fetal growth, and prolonged gestation.

Preterm Birth

Preterm birth is the expulsion or extraction of the fetus from the maternal body before 37 weeks of gestation, and it is the leading cause of neonatal mortality.[5,29] It is recognized that maintaining optimal basal levels of n-3 PUFA during pregnancy could help prevent this condition, as both DHA and EPA synthetically precede anti-inflammatory molecules formed via the COX, LOX and CYP pathways. They also inhibit the production of prostaglandin F2 alpha and prostaglandin E2 (PGE2), which mediate uterine contraction and cervical maturation. Additionally, they compete with arachidonic acid, inhibiting the production of pro-inflammatory eicosanoids, and increasing the synthesis of the anti-inflammatory leukotriene B5 and prostaglandin F3 instead of their pro-inflammatory analogs. This reduces or prevents the inflammatory cascade that leads to spontaneous labor.[30,31] Furthermore, n-3 PUFAs have antiarrhythmic effects on the myometrium, as EPA and DHA relax it, preventing the early onset of labor.[5,30]

A systematic review found that n-3 PUFA can reduce early preterm birth (before 34 weeks of gestation) compared to no treatment or placebo.[29] In the systematic review by Serra et al.,[5] a 27 % reduction in the risk of early preterm birth was observed in pregnant women who took n-3 PUFA supplements, along with a decrease in overall preterm birth rates, especially among women with low basal levels of n-3 PUFA.[32] In ISFALL statement number 7,[30] it was found that pregnant patients treated with n-3 PUFA had a 35 % lower chance of early preterm birth and a 12 % lower chance of preterm birth, along with an average increase of 71 grams in newborn weight. Furthermore, in a multicenter study,[14] pregnant patients who had consumed n-3 PUFA at least once showed lower concentrations of prostaglandin F2 alpha. In the study by Gustafson et al.,[33] where neurocognitive and sensory responses of newborns from DHA-supplemented mothers were analyzed, these results were further supported in relation to early preterm birth.

Preeclampsia

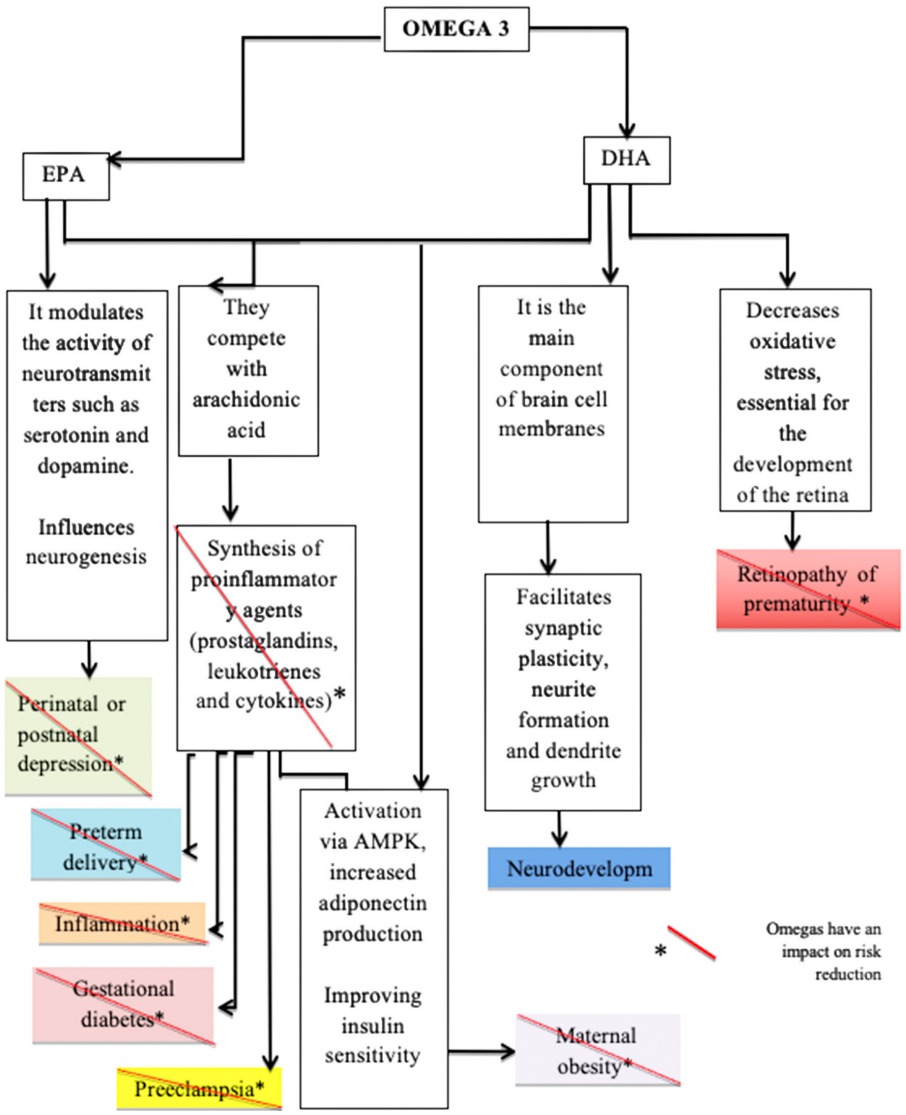
Supplementing the diets of pregnant patients with n-3 PUFAs can prevent the development of preeclampsia, thanks to the downregulation that these molecules exert on the expression of angiogenic transcription factors.[17,34] Additionally, synthetic derivatives of n-3 PUFAs have potent vasodilatory effects, which enhances this outcome.35 This is supported by the case-control study conducted by Li et al.,[36] which suggested that higher intake of EPA and DHA is associated with a lower risk of developing preeclampsia during pregnancy. Furthermore, a systematic review and meta-analysis by Bakouei et al.[2] concluded that the addition of these components to maternal diets reduces the incidence of preeclampsia in low-risk women. Additionally, with a 1 % increase in basal serum levels of n-3 PUFAs during mid-pregnancy, there is a 24 % lower likelihood of developing pregnancy-induced hypertension.

Hypersensitivity in Pediatric Age

There is a correlation between high consumption of foods rich in n-3 PUFAs (such as fish) during pregnancy and its protective effect against the development of allergies in offspring. This is due to its role in protecting against allergic sensitization and supporting immune system development, reducing inflammatory responses. It has been shown that pregnant women with allergies who receive daily n-3 PUFA from week 25 of pregnancy give birth to babies with a lower risk of food allergies during the first two years of life.[13] This is supported by a meta-analysis conducted by Huynh et al.,[38] which suggested that maternal supplementation with n-3 PUFA during pregnancy and lactation is associated with lower risks of egg and peanut allergies during the first three years of life. Additionally, a study by Gardner et al.[12] found that children of mothers who consumed higher amounts of EPA and DHA during pregnancy had a slight

protection against atopic dermatitis, associated with the anti-inflammatory actions of both compounds Scheme 1.

Scheme 1
Interaction of Omega 3 and its components with different pathologies



Source: Own elaboration based on 40, 42, 43-49.

Conclusion

Omega-3 fatty acid supplementation during pregnancy can offer significant benefits depending on factors such as baseline omega-3 levels, socioeconomic status, and maternal habits. These fatty acids are essential for immunomodulation, antioxidation, and fetal neuronal development, especially in pregnant women with low omega-3 levels. They may help prevent postpartum depression and anxiety, as well as reduce the risk of allergic diseases in childhood, particularly in those with a family history of allergies. Additionally, they provide protection against gestational hypertension, preeclampsia, obesity, and gestational diabetes, while improving lipid profiles and insulin sensitivity. However, further studies are needed to confirm these benefits and their long-term impact on the mother-child pair.

Conflict of interests

The authors declare no conflict of interests.

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References

1. Chunda-Liyoka C, Lubeya MK, Imakando M, Kisling S, Majid S, Willis MS, et al. Healthy pregnancies and essential fats: focus group discussions with Zambian women on dietary need and acceptability of a novel RUSF containing fish oil DHA [Internet]. BMC Pregnancy Childbirth. 2020; 20(1): 93. Disponible en: http://dx.doi.org/10.1186/s12884-020-2783-8
2. Bakouei F, Delavar MA, Mashayekh-Amiri S, Esmailzadeh S, Taheri Z. Efficacy of n-3 fatty acids supplementation on the prevention of pregnancy induced-hypertension or preeclampsia: A systematic review and meta-analysis. Taiwan J Obstet Gynecol [Internet]. 2020; 59(1): 8–15. Disponible en: http://dx.doi.org/10.1016/j.tjog.2019.11.002

3. Mohd Fauzy NK, Haris MS, Ibrahim A, Muhd Helmi MA, Harith S. Beneficial outcomes of omega-6 and omega-3 polyunsaturated fatty acids on malnourished children: A scoping review. Malays J Med Health Sci [Internet]. 2023; 19(6): 285–96. Disponible en: http://dx.doi.org/10.47836/mjmhs.19.6.38
4. Nevins JEH, Donovan SM, Snetselaar L, Dewey KG, Novotny R, Stang J, et al. Omega-3 fatty acid dietary supplements consumed during pregnancy and lactation and child neurodevelopment: A systematic review. J Nutr [Internet]. 2021; 151(11): 3483–94. Disponible en: http://dx.doi.org/10.1093/jn/nxab238
5. Serra R, Peñailillo R, Monteiro LJ, Monckeberg M, Peña M, Moyano L, et al. Supplementation of omega 3 during pregnancy and the risk of preterm birth: A systematic review and meta-analysis. Nutrients [Internet]. 2021; 13(5): 1704. Disponible en: http://dx.doi.org/10.3390/nu13051704
6. Puca D, Estay P, Valenzuela C, Muñoz Y. Effect of omega-3 supplementation during pregnancy and lactation on the fatty acid composition of breast milk in the first months of life: a narrative review. Nutr Hosp [Internet]. 2021; 38(4): 848–70. Disponible en: http://dx.doi.org/10.20960/nh.03486
7. Christifano DN, Chollet-Hinton L, Hoyer D, Schmidt A, Gustafson KM. Intake of eggs, choline, lutein, zeaxanthin, and DHA during pregnancy and their relationship to fetal neurodevelopment. Nutr Neurosci [Internet]. 2023; 26(8): 749–55. Disponible en: http://dx.doi.org/10.1080/1028415X.2022.2088944
8. Broś-Konopielko M, Białek A, Oleszczuk-Modzelewska L, Zaleśkiewicz B, Różańska-Walędziak A, Czajkowski K. Nutritional, anthropometric and sociodemographic factors affecting fatty acids profile of pregnant women's serum at labour-chemometric studies. Nutrients [Internet]. 2021; 13(9): 2948. Disponible en: http://dx.doi.org/10.3390/nu13092948
9. Nikolajeva K, Aizbalte O, Piskurjova A, Rezgale R, Cauce V, Začs D, et al. Fatty acid composition of a maternal diet and erythrocyte phospholipid status in Latvian pregnant women. Medicina (Kaunas) [Internet]. 2023; 59(9). Disponible en: http://dx.doi.org/10.3390/medicina59091514
10. Masot O, Ochoa Herrera JJ, Paraíso Pueyo E, Roca J, Miranda J, Lavedán A. The impact of docosahexaenoic acid on maternal mental health: scoping review. Nutr Hosp [Internet]. 2023; 40(4): 848–57. Disponible en: http://dx.doi.org/10.20960/nh.04523
11. Ishihara T, Yoshida M, Arita M. Omega-3 fatty acid-derived mediators that control inflammation and tissue homeostasis. Int Immunol [Internet]. 2019; 31(9): 559–67. Disponible en: http://dx.doi.org/10.1093/intimm/dxz001
12. Gardner KG, Gebretsadik T, Hartman TJ, Rosa MJ, Tylavsky FA, Adgent MA, et al. Prenatal omega-3 and omega-6 polyunsaturated fatty acids and childhood atopic dermatitis. J Allergy Clin Immunol Pract [Internet]. 2020; 8(3): 937–44. Disponible en: http://dx.doi.org/10.1016/j.jaip.2019.09.031
13. Feketea G, Kostara M, Bumbacea RS, Vassilopoulou E, Tsabouri S. Vitamin D and omega-3 (fatty acid) supplementation in pregnancy for the primary prevention of food allergy in children-literature review. Children (Basel) [Internet]. 2023; 10(3). Disponible en: http://dx.doi.org/10.3390/children10030468
14. Sley EG, Rosen EM, van 't Erve TJ, Sathyanarayana S, Barrett ES, Nguyen RHN, et al. Omega-3 fatty acid supplement use and oxidative stress levels in pregnancy. PLoS One [Internet]. 2020; 15(10): e0240244. Disponible en: http://dx.doi.org/10.1371/journal.pone.0240244
15. Rees G, Brough L, Orsatti GM, Lodge A, Walker S. Do micronutrient and omega-3 fatty acid supplements affect human maternal immunity du-

ring pregnancy? A scoping review. Nutrients [Internet]. 2022; 14(2): 367. Disponible en: http://dx.doi.org/10.3390/nu14020367
16. Liu W, Gao M, Yang S, Sun C, Bi Y, Li Y, et al. Effects of omega-3 supplementation on glucose and lipid metabolism in patients with gestational diabetes: A meta-analysis of randomized controlled trials. J Diabetes Complications [Internet]. 2023; 37(4): 108451. Disponible en: http://dx.doi.org/10.1016/j.jdiacomp.2023.108451
17. Elshani B, Kotori V, Daci A. Role of omega-3 polyunsaturated fatty acids in gestational diabetes, maternal and fetal insights: current use and future directions. J Matern Fetal Neonatal Med [Internet]. 2021; 34(1): 124–36. Disponible en: http://dx.doi.org/10.1080/14767058.2019.1593361
18. Gao L, Lin L, Shan N, Ren C-Y, Long X, Sun Y-H, et al. The impact of omega-3 fatty acid supplementation on glycemic control in patients with gestational diabetes: a systematic review and meta-analysis of randomized controlled studies. J Matern Fetal Neonatal Med [Internet]. 2020; 33(10): 1767–73. Disponible en: http://dx.doi.org/10.1080/14767058.2018.1526916
19. Godhamgaonkar AA, Wadhwani NS, Joshi SR. Exploring the role of LC-PUFA metabolism in pregnancy complications. Prostaglandins Leukot Essent Fatty Acids [Internet]. 2020; 163(102203): 102203. Disponible en: http://dx.doi.org/10.1016/j.plefa.2020.102203
20. Moltu SJ, Nordvik T, Rossholt ME, Wendel K, Chawla M, Server A, et al. Arachidonic and docosahexaenoic acid supplementation and brain maturation in preterm infants; a double blind RCT. Clin Nutr [Internet]. 2024; 43(1): 176–86. Disponible en: http://dx.doi.org/10.1016/j.clnu.2023.11.037
21. Mohammadzadeh P, Rosenberg JB, Vinding R, Møllegaard Jepsen JR, Lindberg U, Følsgaard N, et al. Effects of prenatal nutrient supplementation and early life exposures on neurodevelopment at age 10: a randomised controlled trial - the COPSYCH study protocol. BMJ Open [Internet]. 2022; 12(2): e047706. Disponible en: http://dx.doi.org/10.1136/bmjopen-2020-047706
22. Chumak, T., Lecuyer, M. J., Nilsson, A. K., Faustino, J., Ardalan, M., Svedin, P., Sjöbom, U., Ek, J., Obenaus, A., Vexler, Z. S., & Mallard, C. Maternal n-3 Polyunsaturated Fatty Acid Enriched Diet Commands Fatty Acid Composition in Postnatal Brain and Protects from Neonatal Arterial Focal Stroke. Translational stroke research. 2022; 13(3): 449–461. Disponible en: https://doi.org/10.1007/s12975-021-00947-9
23. Tahaei H, Gignac F, Pinar A, Fernandez-Barrés S, Romaguera D, Vioque J, et al. Omega-3 fatty acid intake during pregnancy and child neuropsychological development: A multi-centre population-based birth cohort study in Spain. Nutrients [Internet]. 2022; 14(3): 518. Disponible en: http://dx.doi.org/10.3390/nu14030518
24. Martínez R. M. Lípidos y desarrollo cerebral: importancia del ácido docosahexanoico (DHA) en el niño sano y en el enfermo con síndrome de Zellweger. Pediatrika. 2002; 22: 275-288.
25. Daruich A, Bremond-Gignac D, Behar-Cohen F, Kermorvant E. Rétinopathie du prématuré: de la prévention au traitement. Med Sci (Paris) [Internet]. 2020;36(10):900–7. [citado el 07 de octubre de 2024]. Disponible en: http://dx.doi.org/10.1051/medsci/2020163
26. Rupanagunta GP, Nandave M, Rawat D, Upadhyay J, Rashid S, Ansari MN. Postpartum depression: aetiology, pathogenesis and the role of nutrients and dietary supplements in prevention and management. Saudi Pharm J [Internet]. 2023; 31(7): 1274–93. Disponible en: http://dx.doi.org/10.1016/j.jsps.2023.05.008

27. Monthé-Drèze C, Sen S, Hauguel-de Mouzon S, Catalano PM. Effect of omega-3 supplementation in pregnant women with obesity on newborn body composition, growth and length of gestation: A randomized controlled pilot study. Nutrients [Internet]. 2021; 13(2): 578. Disponible en: http://dx.doi.org/10.3390/nu13020578
28. Castro JJ, Umana-Perez A, Castaño-Moreno E, Casanello P, Ronco AM. DHA supplementation during pregnancy in women with obesity normalizes IGF2R levels in the placenta of male newborns. Int J Endocrinol [Internet]. 2023; 2023: 1–10. Disponible en: http://dx.doi.org/10.1155/2023/1515033
29. Care A, Nevitt SJ, Medley N, Donegan S, Good L, Hampson L, et al. Interventions to prevent spontaneous preterm birth in women with singleton pregnancy who are at high risk: systematic review and network meta-analysis. BMJ [Internet]. 2022; 376: e064547. Disponible en: http://dx.doi.org/10.1136/bmj-2021-064547
30. Best KP, Gibson RA, Makrides M. ISSFAL statement number 7 - Omega-3 fatty acids during pregnancy to reduce preterm birth. Prostaglandins Leukot Essent Fatty Acids [Internet]. 2022; 186(102495): 102495. Disponible en: http://dx.doi.org/10.1016/j.plefa.2022.102495
31. Cetin I, Carlson SE, Burden C, da Fonseca EB, di Renzo GC, Hadjipanayis A, et al. Omega-3 fatty acid supply in pregnancy for risk reduction of preterm and early preterm birth. Am J Obstet Gynecol MFM [Internet]. 2024; 6(2): 101251. Disponible en: http://dx.doi.org/10.1016/j.ajogmf.2023.101251
32. Yelland LN, Sullivan TR, Gibson RA, Simmonds LA, Thakkar SK, Huang F, et al. Identifying women who may benefit from higher dose omega-3 supplementation during pregnancy to reduce their risk of prematurity: exploratory analyses from the ORIP trial. BMJ Open [Internet]. 2023; 13(4): e070220. Disponible en: http://dx.doi.org/10.1136/bmjopen-2022-070220
33. Gustafson KM, Liao K, Mathis NB, Shaddy DJ, Kerling EH, Christifano DN, et al. Prenatal docosahexaenoic acid supplementation has long-term effects on childhood behavioral and brain responses during performance on an inhibitory task: Prenatal DHA and childhood inhibitory performance. Nutr Neurosci [Internet]. 2022; 25(1): 80–90. Disponible en: http://dx.doi.org/10.1080/1028415X.2020.1712535
34. Kasture V, Sundrani D, Dalvi S, Swamy M, Kale A, Joshi S. Maternal omega-3 fatty acids and vitamin E improve placental angiogenesis in late-onset but not early-onset preeclampsia. Mol Cell Biochem [Internet]. 2019; 461(1–2): 159–70. Disponible en: http://dx.doi.org/10.1007/s11010-019-03599-4
35. Liu Y, Zu L, Cai W, Cheng Q, Hua T, Peng L, et al. Metabolomics revealed decreased level of omega-3 PUFA-derived protective eicosanoids in pregnant women with pre-eclampsia. Clin Exp Pharmacol Physiol [Internet]. 2019; 46(8): 705–10. Disponible en: http://dx.doi.org/10.1111/1440-1681.13095
36. Li S-N, Liu Y-H, Luo Z-Y, Cui Y-F, Cao Y, Fu W-J, et al. The association between dietary fatty acid intake and the risk of developing preeclampsia: a matched case-control study. Sci Rep [Internet]. 2021; 11(1): 4048. Disponible en: http://dx.doi.org/10.1038/s41598-021-83674-3
37. Huynh LBP, Nguyen NN, Fan H-Y, Huang S-Y, Huang C-H, Chen Y-C. Maternal omega-3 supplementation during pregnancy, but not childhood supplementation, reduces the risk of food allergy diseases in offspring. J Allergy Clin Immunol Pract [Internet]. 2023; 11(9): 2862-2871.e8. Disponible en: http://dx.doi.org/10.1016/j.jaip.2023.06.005

38. Trumbo P, Schlicker S, Yates AA, Poos M. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. J Am Diet Assoc [Internet]. 2002; 102(11): 1621–30. Disponible en: http://dx.doi.org/10.1016/s0002-8223(02)90346-9
39. EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA). Scientific Opinion on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. EFSA J [Internet]. 2010; 8(3). Disponible en: http://dx.doi.org/10.2903/j.efsa.2010.1461
40. Calder PC. Mechanisms of action of (n-3) fatty acids. J Nutr [Internet]. 2012; 142(3): 592S-599S. Disponible en: http://dx.doi.org/10.3945/jn.111.155259
41. Calder, PC. Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochemical Society Transactions. 2017; 45(5): 1105–1115. [citado el 14 de octubre de 2024]. Disponible en: https://doi.org/10.1042/BST20160474
42. Innis SM. Dietary (n-3) fatty acids and brain development. J Nutr [Internet]. 2007; 137(4): 855–9. Disponible en: http://dx.doi.org/10.1093/jn/137.4.855
43. SanGiovanni JP, Chew EY. The role of omega-3 long-chain polyunsaturated fatty acids in health and disease of the retina. Prog Retin Eye Res [Internet]. 2005; 24(1): 87–138. Disponible en: http://dx.doi.org/10.1016/j.preteyeres.2004.06.002
44. Freeman MP, Hibbeln JR, Wisner KL, Davis JM, Mischoulon D, Peet M, et al. Omega-3 fatty acids: evidence basis for treatment and future research in psychiatry. J Clin Psychiatry [Internet]. 2006; 67(12): 1954–67. Disponible en: http://dx.doi.org/10.4088/jcp.v67n1217
45. Burger KS, Stice E. Neural responsivity during soft drink intake, anticipation, and advertisement exposure in habitually consuming youth: Neural Response to Soft Drinks. Obesity (Silver Spring) [Internet]. 2014; 22(2): 441–50. Disponible en: http://dx.doi.org/10.1002/oby.20563
46. Khan D, Ahmed SA. Epigenetic regulation of non-lymphoid cells by Bisphenol A, a model endocrine disrupter: Potential implications for immunoregulation. Front Endocrinol (Lausanne) [Internet]. 2015; 6: 91. Disponible en: http://dx.doi.org/10.3389/fendo.2015.00091
47. Carlson SE, Colombo J, Gajewski BJ, Gustafson KM, Mundy D, Yeast J, et al. DHA supplementation and pregnancy outcomes. Am J Clin Nutr [Internet]. 2013; 97(4): 808–15. Disponible en: http://dx.doi.org/10.3945/ajcn.112.050021
48. Crofts JF, Lenguerrand E, Bentham GL, Tawfik S, Claireaux HA, Odd D, et al. Prevention of brachial plexus injury-12 years of shoulder dystocia training: an interrupted time-series study. BJOG [Internet]. 2016; 123(1): 111–8. Disponible en: http://dx.doi.org/10.1111/1471-0528.13302