

# Micronutrients and DHA during Pregnancy

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First randomized trial of multiple micronutrients and DHA in pregnant women during second and third trimester.

Supplementation complemented dietary intake and increased maternal DHA.

Vitamin D levels increased with supplementation but decreased in controls.

Results are clinically relevant as DHA is vital for fetal neurodevelopment.

Keywords: Micronutrients ; DHA ; vitamin D ; pregnancy

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## 1. Introduction

During pregnancy, an adequate maternal dietary intake is essential to meet the increased nutritional demands required to maintain metabolism and support fetal development <sup>[1]</sup>. Micronutrients such as folic acid and other B vitamins, vitamin D, vitamin C, calcium, copper, magnesium, iodine, selenium, zinc, and iron all have vital roles throughout all stages of pregnancy <sup>[2][3][4]</sup>. Poor dietary intake or deficiencies in both micro- and macronutrients can have adverse effects on pregnancy outcomes and neonatal health <sup>[5]</sup>, including an increased risk of neural tube defects, preeclampsia, miscarriage, and low birth weight <sup>[6][7]</sup>. Many women are at risk of insufficient nutrient intake in industrialized as well as developing countries <sup>[8][9][10]</sup>. Therefore, micronutrient supplementation is frequently recommended during pregnancy to help improve pregnancy outcomes in the mother and child <sup>[11][12]</sup>. International guidelines (i.e., from the World Health Organization) currently recommend supplementation of iron and folic acid (0.4 mg/day) during pregnancy for the purpose of improving pregnancy outcomes and for reducing the risk of neural tube defects and maternal anemia in pregnancy <sup>[13]</sup>. Recently, there have been extensive scientific and medical discussions around the need to include vitamin D as a standard nutrient to be supplemented during pregnancy, due to low intake. Vitamin D regulates calcium and phosphate body stores and is therefore critical for bone health <sup>[14]</sup>. Furthermore, low concentrations of blood vitamin D in pregnant women have been associated with pregnancy complications <sup>[15][16]</sup>.

In addition to micronutrients, a balanced macronutrient intake is recommended. In particular, the long-chain polyunsaturated fatty acids (LCPUFAs) found at high concentrations within the brain and central nervous system are essential for the development of the fetal brain <sup>[17]</sup>. Docosahexaenoic acid (DHA)—representing the largest proportion of LCPUFAs in the brain and retina—plays a key role during the pre- and early postnatal period <sup>[17][18][19][20]</sup>. After the first trimester, when the neural tube has closed and grey matter begins to form <sup>[21]</sup>, DHA begins to rapidly accumulate in the brain <sup>[18][22]</sup>; accumulation continues for up to two years <sup>[23][24]</sup>.

## 2. Development

However, the human body is not efficient at producing essential LCPUFAs <sup>[22]</sup>, and maternal concentrations decrease over the course of gestation <sup>[25]</sup>. Of note, the levels of DHA available to the fetus during pregnancy are governed by the diet of the mother <sup>[17][26][27][28]</sup>. Studies suggest that consumption of a diet rich in omega-3 LCPUFAs including DHA may have a reduced risk of common pregnancy complications such as intrauterine growth restriction, preeclampsia, and preterm deliveries <sup>[29][30][31]</sup>. Supplementation with DHA can also increase the expression of fatty acid transport proteins, thus increasing transport through the placenta and improving the fatty acid status of both the mother and child <sup>[32][33]</sup>.

Meta-analyses have demonstrated that there are clinical benefits associated with prenatal multiple micronutrient <sup>[34]</sup> and LCPUFA supplementation <sup>[35]</sup> during pregnancy. However, there is limited data on the effects of prenatal supplementation in industrialized countries, particularly when used in combination. Clinical guidelines for pregnant women tend to focus on single nutrients for supplementation <sup>[36][37]</sup>. Given the interest in the potential beneficial effects of supplementation with micronutrients and DHA during pregnancy, we carried out a randomized trial to evaluate the effects of multiple

micronutrients plus DHA supplementation during the second and third trimesters of pregnancy on maternal biomarkers compared with no supplementation in the control group in an industrialized country. The primary variable, i.e., the concentration of DHA (weight percent of total fatty acids (*w*% TFA)) in maternal red blood cells (RBC), was considered indicative of LCPUFA status. Secondary explorative variables were other biomarkers of fatty acid and oxidative status, vitamin D, and anthropometric parameters of infants at delivery. We included vitamin D status as a secondary endpoint to investigate whether vitamin D supplementation is needed to maintain adequate status, and whether the levels of vitamin D in the supplement would be sufficient to maintain an adequate status. We hypothesized that supplementation might help to improve maternal DHA and vitamin D status in a healthy population of pregnant women, whereas dietary intake would be insufficient to meet the increased needs during pregnancy.

### 3. Conclusions

Supplementation with MMS plus DHA in pregnant women can complement dietary intake and significantly improve maternal DHA and vitamin D status. This finding is important in light of the essential roles of DHA in the developing brain of the fetus, in visual development, and in immunomodulation.

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