Higher DHA Intake on Birth Outcomes: Practical Pearls from Dr Susan Carlson

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This article presents the highlights of an interview conducted with international authority on foetal-maternal nutrition, Dr Susan Carlson, where she spoke about the implications of DHA in early preterm birth and infant outcomes, and the importance of pregnant women receiving adequate DHA for promoting infant health and development.

What is the role of DHA in pregnancy?

- Docosahexaenoic acid (DHA) is an omega-3 long-chain fatty acid that plays an essential role in infant growth and development – including the development of the brain, the nervous system, and visual acuity.[1]
- DHA is found in animal foods, with the richest sources from seafood.[2]
- Studies suggest that DHA supplementation contributes to longer duration of gestation, higher birth weight, and reduced early preterm birth.[3,4]
- The benefits of DHA on preterm birth were demonstrated in Dr Carlson's pivotal Phase 3 double-blind trial, KUDOS (Kansas University DHA Outcomes Study), which randomised 350 pregnant women to 600 mg/day of DHA, or placebo, from <20 weeks of gestation until birth.[3]
    - In KUDOS, women who received DHA delivered significantly fewer infants born at <34 weeks of gestation (i.e., early preterm birth; p=0.025) and a month shorter hospital stay for infants who underwent neonatal intensive care (p=0.026), compared to those on placebo.[3]

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What are the current recommendations for DHA intake in pregnant and lactating women?

- Current consensus guidelines, including international bodies such as the Food & Agriculture Organisation (FAO) of the United Nations, and the World Association of Perinatal Medicine (WAPM) recommend DHA intake of at least 200 mg per day and up to 1,000 mg per day during pregnancy and lactation.[5]
- US Dietary Guidelines encourage pregnant and lactating women to consume 1–3 servings of seafood per week, equating to around 200–300 mg of DHA per day.[5]

Who should be supplemented with DHA?

- Epidemiological studies have observed that women with lower baseline plasma omega-3 fatty acids during early pregnancy (including DHA), exhibited a significantly greater risk of early preterm birth when compared to women with higher plasma levels.[6,7]
- A secondary analysis of the Australian ORIP (Omega-3 to Reduce the Incidence of Prematurity) study associated low baseline status of omega-3 fatty acids (DHA and eicosapentaenoic acid [EPA]) and DHA with the risk of early preterm birth.[7]
    - Administration of omega-3 fatty acids in pregnant women with low baseline DHA status significantly reduced the risk of early preterm birth, with the study authors recommending the supplementation of omega-3 fatty acids in populations with low levels to prevent preterm birth.[7]
- No dose-response studies of DHA supplementation on pregnancy outcomes have been conducted, however, the most recent Cochrane Review suggests that the optimal dose of DHA supplementation for women with low DHA intake and low DHA status is likely to be between 500–1,000 mg.[8]

Are there any adverse effects with higher doses of DHA?

- In KUDOS, 600 mg/day of DHA was not associated with any safety concerns for both mothers and infants.[3]
- The Australian DOMInO (DHA to Optimize Mother Infant Outcome) trial that randomised women to 800 mg/day of DHA or placebo reported no differences in nose bleeds, vaginal blood loss, constipation, nausea, or vomiting between the two study groups.[4]
    - Significantly fewer infants of mothers in the DHA group were admitted for neonatal intensive care compared to infants in the placebo group.[4]
- The secondary analysis of ORIP also suggested that women entering pregnancy with high omega-3 status did not require additional DHA, and that taking a high dose combination of DHA and EPA (900 mg) may have slightly increased their risk of early preterm birth.[7]
    - While the results are controversial, it is best for women who already consume a 3-ounce (approx. 85 g) serving of seafood regularly, or who are taking a prenatal supplement with 200 mg DHA, not to further increase their DHA intake during pregnancy and lactation until the controversy is resolved by further studies.

When should women start DHA supplementation?

- Women should consider consuming 1–2 servings of seafood and eggs each week, even if they are not planning to get pregnant, for the other known health-promoting benefits of DHA such as maintaining cardiovascular and cognitive well-being, and for reducing inflammation.[9]
    - Seafood and eggs are also excellent sources of many other nutrients important for foetal development.
- Women (including lactating mothers) who do not consume seafood or eggs routinely can consider regular DHA supplementation.
- In KUDOS, where DHA was associated with significantly fewer early preterm deliveries, supplementation began in women who were at <20 weeks gestation (mean 14.4 weeks).[3]
- DHA consumed by the mother can be stored in fat tissues in the body and are preferentially mobilised to the foetus during pregnancy.[2,9,10]

Is there a link between DHA supplementation compliance and rate of preterm birth?

- Pooled data from clinical trials, including data from KUDOS, suggest that better DHA compliance is significantly associated with better birth outcomes, i.e., lower probability of early preterm birth (<34 weeks gestation), very low birth weight (<1,500 g) and low birth weight (<2,500 g).[11]
    - A significant correlation was found between maternal age and education level with DHA supplementation compliance.[11]

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Does prenatal DHA supplementation provide benefits to an infant's development?

- 171 children of mothers from the KUDOS trial were followed: At 5 years, children who became overweight or obese and whose mothers received DHA 600 mg/day had, on average, 3.94 and 4.97 mmHg lower systolic and diastolic blood pressure, compared to overweight or obese children of mothers who received placebo.[12]
    - It is hypothesised that DHA *in utero* contributes to the developmental programming that protects against the "second hit" of childhood overweight and obesity.[12]
    - Both groups in KUDOS received DHA during infancy.[12]
- In KUDOS, DHA supplementation provided favourable effects on cognition: Infants of mothers who received 600 mg/day of DHA could maintain high levels of sustained attention (SA) during their first year, whereas SA for infants from the placebo group decreased.[13]
    - Long term effects on cognition were also associated with higher maternal DHA at the end of the study but confounded by the fact that more educated mothers were also more compliant with capsule intake.[14]
    - Maternal supplementation in KUDOS also resulted in long term effects on childhood behavioural and brain responses during performance on an inhibitory task.[15]
- In another study in Kansas, supplementation with 600 mg/day of DHA during the 2nd and 3rd trimesters of pregnancy resulted in better foetal cardiac autonomic control, with infants of mothers in the DHA group exhibiting reduced heart rate and improved heart rate variability measures, compared to infants whose mothers received placebo.[16]
    - This suggests that infants exposed to sufficient DHA *in utero* have an adaptive advantage through early programming of the autonomic nervous system.[16]

Is higher intake of DHA associated with any benefits to maternal health?

- There is little data on the benefits of prenatal DHA intake on maternal health, though the literature associates low DHA levels with age-related cognitive decline and neurodegenerative conditions, such as Alzheimer's disease.[17]

Who are at risk for low DHA levels?

- Those at risk for low DHA levels are generally consuming a diet low in seafood and eggs or not taking a daily supplement that includes DHA, or DHA and EPA (e.g., fish oil).
- An Australian study observed that women of childbearing age who were obese had significantly lower levels of serum DHA compared with women of healthy weight, despite similar dietary DHA intake.[18]
- A study on twin pregnancies revealed that daily supplementation with fish oil (comprising 900 mg of DHA) reduced the incidence of early preterm birth compared to controls.[19]
    - Physicians caring for women with twin pregnancies should consider recommending higher dose supplementation with omega-3 fatty acids.

Women should consider consuming 1–2 servings of seafood and eggs each week, even if they are not planning to get pregnant, for the other known health-promoting benefits of DHA such as maintaining cardiovascular and cognitive well-being, and for reducing inflammation.

Any clinical tips for healthcare providers during their daily practice?

- Healthcare professionals can devise a checklist that asks patients about seafood and egg intake to gauge the amount of DHA they are consuming and determine whether to suggest DHA supplementation.
- Patients can be referred to dietitians to have their DHA intake assessed, which can be helpful as different species of fish can contain varying amounts of DHA.

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