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Reducing the Risk of Preterm Birth Through Maternal Nutrition Interventions

Prematurity, defined as birth at less than 37 weeks gestation, is a global burden and a leading cause of death in children under the age of 5 years. An estimated 13.4 million babies were born preterm (<37 weeks) in 2020 compared with 13.8 million in 2010 worldwide. Despite increasing health care setups reduction in global birth rates and substantial focus on routine health data systems, there has been no measurable change in preterm birth (PTB) rates over the last decade at global level.[1]

While most PTBs happen spontaneously, there are clinical conditions that can trigger early induction of labor and have been associated with PTB. Some of these conditions include:[2]

- Decidual hemorrhage caused by placental abruption
- Cervical insufficiency and uterine distention
- Maternal mood and distress that leading to increased prostaglandin production
- Extra- and intrauterine, and intra-amniotic infections
- Inflammation in the absence of infection
- Preterm premature rupture of membranes (PPROM)

Several risk modifiable and non-modifiable risk factors for PTB have also been identified.[3]

Figure 1: Modifiable and non-modifiable risk factors of PTB[3]

Modifiable	Non-modifiable
• Obesity*	• Previous PTB, C-section
• Low pre-pregnancy BMI*	• Uterine evacuation
• Poor gestational weight gain*	• Extremes in maternal age
• Suboptimal nutrition*	• Multiple pregnancies & use of assisted reproductive technologies
• Smoking	• Genetic factors, ethnicity
• Short inter-pregnancy interval	

**Can be addressed by nutritional solutions*

The role of nutrition in reducing PTB risk

Preventing deaths and complications from PTB starts with a healthy pregnancy. Nutritional solutions present a promising strategy to reduce the risk of PTB by addressing various risk factors such as inadequate nutrition, suboptimal body mass index, poor gestational weight gain, and gestational diabetes.[2]

Evidence links poor nutrition during preconception and pregnancy to an increased risk of PTB, while intervention studies highlight the potential roles for specific nutrients in reducing PTB risk and/or increasing the duration of gestation.[4]

Moreover, there is increasing evidence that infection and/or inflammation are the pathological process for which the molecular pathophysiology has been best defined and a causal link with PTB has been fairly well established. It is therefore of significant relevance to evaluate whether specific diet patterns and nutritional or bioactive interventions targeted to modulate inflammation can be efficacious in reducing the risk of PTB.[3]

A well-balanced diet during pregnancy is important to meet the increased needs for fetal growth and maternal health.[5]

Studies on Omega-3 LC-PUFA supplementation and reduction of PTB risk[6,7]

Studies on supplementation with Omega-3 long-chain polyunsaturated fatty acids (LC-PUFAs), particularly docosahexaenoic acid (DHA) and eicosapentaenoic (EPA), among women of childbearing age and during pregnancy can help protect from PTB and early PTB.[6-9]

Figure 2: Studies on Omega-3 LC-PUFA supplementation and reduction of PTB risk[6,7]

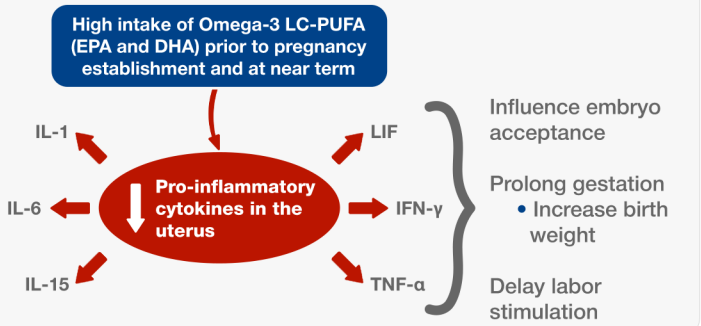
	Intervention	Outcome
ORIP (Omega-3 Fats to Reduce the Incidence of Prematurity) study[3,6]	900 mg/day of Omega-3 LCPUFA (DHA: EPA 8:1) before 20 weeks of gestation up to 34 weeks age of gestation	Reduced risk of preterm birth in compliant pregnant women
ADORE (Assessment of DHA on reducing early preterm birth)[7]	High dose DHA (1000mg) supplementation during pregnancy	Fewer early preterm birth particularly among those with low baseline omega-3 status

Higher intake of food rich in Omega-3 (LC-PUFAs) are also associated with longer gestations and improved perinatal outcomes.[8]

How Omega-3 LC-PUFAs help prevent PTB

It is hypothesized that Omega-3 LC-PUFAs reduce the risk of early onset labor or lengthen gestation via different actions that inhibits pro-inflammatory cytokines in the uterus.[9,10]

Proposed mechanism on how Omega-3 LC-PUFAs help reduce PTB risk[9]



Expert Recommendations

The following are recommendations developed by a group of experts for risk reduction of PTB and early PTB:[10,11]

- ☑ **Women of childbearing age should obtain a supply of at least 250 mg/day of DHA+EPA from diet or supplements**
- ☑ **During pregnancy, they should receive an additional ≥ 100 to 200 mg/day of DHA**
- ☑ **Women with low DHA intake and/or low DHA blood levels should receive approximately 600 to 1,000 mg/day DHA + EPA respectively, or DHA alone**
- ☑ **This additional supply should preferably begin in the second trimester of pregnancy (not later than approximately 20 weeks' gestation) and continue until approximately 37 weeks' gestation or until childbirth if before 37 weeks' gestation**

Multiple micronutrient supplementation and PTB prevention

Micronutrient deficiencies are exacerbated during pregnancy due to increased requirements of the growing fetus, placenta and maternal tissues. The inability to fulfill the increased demands results in potentially adverse effects on the mother and the fetus.[6]

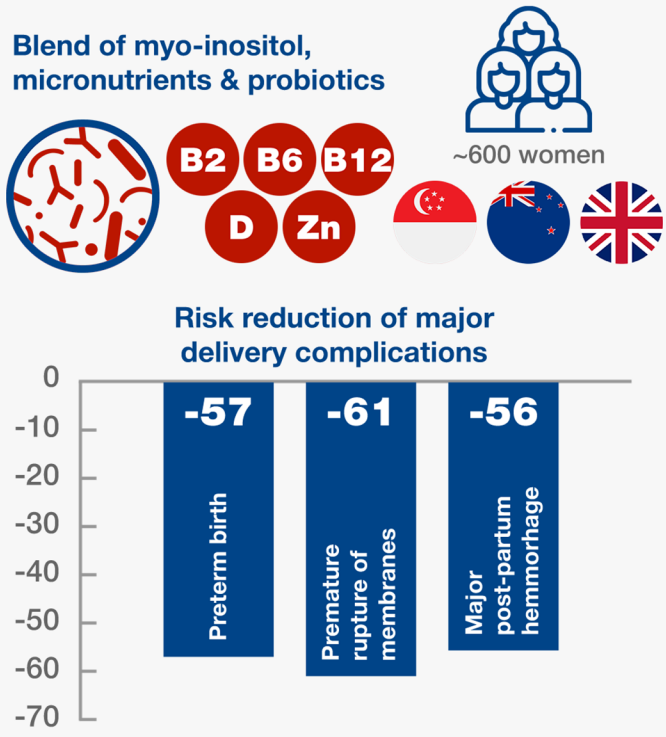
Studies show that pregnant women who received multiple-micronutrient supplementation (MMS) had fewer babies that were born too small (weighing less than 2500 g), fewer babies who were smaller in size than normal for their gestational age, and fewer births that occurred before week 37 of pregnancy.[12]

Micronutrient deficiencies are highly prevalent among women of reproductive age, especially in low- and middle-income countries. These deficiencies contribute significantly to adverse pregnancy outcomes, including PTB. Recent studies show that MMS provides 6 to 8% risk reduction for PTB, and 13 to 19% for PTBs, compared to iron and folic acid alone. The risk reduction in PTB was found to be 16% for underweight and anemic women, and 14% among adolescents who receive MMS.[13]

Better preconception metabolic and nutritional health are hypothesized to promote gestational normoglycemia and reduce PTB. The Nutritional Intervention Preconception and During Pregnancy to Maintain Healthy Glucose Metabolism and Offspring Health (NiPPeR) trial demonstrated that a supplement containing myo-inositol, probiotics, and micronutrients reduced PTB.[14]

The study also highlighted reduced risks of PPROM and major postpartum hemorrhage among the intervention group. Potential mechanisms for a preventive effect on PPROM-associated PTBs in the study may include anti-inflammatory effects of myo-inositol and contribution from the potential synergistic effect of micronutrients, including zinc and vitamin D.[3,14]

Results of the NiPPeR clinical trial



Maternal micronutrient insufficiency during preconception or in early pregnancy are common in the general population and thought to influence the risk of adverse pregnancy outcomes. Therefore, starting supplementation before conception may collectively result in optimal maternal and fetal health benefits.[14]

PTB remains a global concern with significant impact on families, offspring, and society, including heightened risks of morbidity, mortality, and economic strain. Thus, preventing PTB should be a priority for healthcare providers. A key challenge is the need for global efforts to develop clinical recommendations that are easy to implement for clinicians. Primary prevention of PTB is essential, with nutritional approaches offering promising alternatives. Strategies to lower PTB risk include a well-balanced diet incorporating diverse food groups, alongside supplementation with multiple micronutrients and high doses of Omega-3 LC-PUFAs.

References

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