MICRONUTRIENTS IN PREGNANCY

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Abstract

Pregnancy is a very important stage in a woman’s life. From the period of preconception, to pregnancy states, including the post-pregnancy states, increased amount of macronutrients and micronutrients are required by the body; both for the health of the mother and for the growing foetus and infant. Maternal undernourishment at different stage of pregnancy has been linked with poor outcomes, together with augmented risk of maternal and infant death as well as low birth weight infants, preterm births, congenital anomalies and birth defects. In addition, gestational undernutrition has been a concern in rising the offspring’s vulnerability to chronic illness (i.e. type 2 diabetes, hypertension, coronary artery disease, and stroke) in adulthood, a phenomenon called Barker’s hypothesis. It has long been documented that sufficient iron is vital for best reproductive outcomes, including gestational cognitive development. Similarly, iodine and calcium have been known for their roles in development of the foetus/neonate. Zinc, copper, magnesium and selenium too have contribution towards maternal and offspring’s health. Folate sufficiency periconceptionally is known both by the observation of providing folic acid in antenatal iron/folic acid supplementation and by increasing figures of countries invigorating flours with folic acid. Other vitamins likely to be important include vitamins B12, D and A with the water-soluble vitamins usually not as much of expected to be a problem. This article highlights the importance of micronutrients in pregnancy and the impact of their deficiency and the status in India.

Keywords: Micronutrients, Pregnancy, Foetus, Nutrition.

Micronutrients

Micronutrients are nutritional components, frequently referred to as vitamins and minerals, which although only required by the body in little amounts, are very important to growth, illness prevention, and wellbeing. Micronutrients are not produced in the body and must be derived from diet. These substances enable the body to produce enzymes, hormones and other substances necessary for appropriate growth and development. Despite the fact that their every day requirement is small, the consequences of their absence are severe. Iodine, vitamin A and iron are mainly significant in global public health terms; their lack represents a major threat to the health and development of populations, particularly children and pregnant women in low-income countries. Micronutrients include dietary trace minerals in amounts generally less than 100 milligrams/day - in contrast to macrominerals which are necessary in more quanities. The microminerals or trace elements include iron, cobalt, chromium, copper, iodine, manganese, selenium, zinc and molybdenum. Micronutrients also include vitamins, which are organic compounds needed as nutrients in tiny amounts by an organism as well as phytochemicals.

Micronutrients in pregnancy

Pregnancy is associated with increased nutritional needs due to the physiologic changes of the woman and the metabolic demands of the embryo/fetus. Daily requirements for many micronutrients during pregnancy are higher to meet the physiologic changes and increased nutritional needs of pregnancy. Multiple micronutrient deficiencies commonly co-exist in pregnant women, especially in less developed nations.

Micronutrient deficiencies are a consequence of insufficient ingestion of meat, fruits and vegetables. Infections can also be a reason. Manifold micronutrient supplementations in pregnant women may be a promising strategy for reducing adverse pregnancy outcomes by way of enhanced maternal dietary and immune status. Good nutritional status prior to conception is also imperative for a good pregnancy. For example, folic acid supplementation during the periconceptional period (about one month earlier than and one month following conception) noticeably reduces the incidence of devastating birth defects called neural tube defects. Folic acid-iron supplementation is universally recommended during pregnancy. Deficiency of micronutrients at the time of pregnancy is very much associated to mortality and morbidity in the new born. Deficiencies of specific antioxidant actions related to the trace elements selenium, copper, zinc, and manganese can result in poor pregnancy outcomes, together with fetal development constraint, preeclampsia and the associated increased risk of diseases in adulthood, including cardiovascular ailment and type 2 diabetes.

Several systematic reviews of trials examining the effects of maternal multiple micronutrient supplementation have been conducted, but they have had limitations. The RDA (recommended dietary allowance), which is the average daily dietary intake level of a nutrient sufficient to

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meet the requirements of almost all (97.5%) healthy individuals in a specific life stage and gender group, should be used in the planning of diets for individuals (Table 1).

Table 1. RDA for Micronutrients during pregnancy

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Age</th>
<th>RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotin</td>
<td>14-50 years</td>
<td>30 µg/day (AI)</td>
</tr>
<tr>
<td>Folate</td>
<td>14-50 years</td>
<td>600 µg/day</td>
</tr>
<tr>
<td>Niacin</td>
<td>14-50 years</td>
<td>18 mg/day</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>14-50 years</td>
<td>6 mg/day (AI)</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>14-50 years</td>
<td>1.4 mg/day</td>
</tr>
<tr>
<td>Thiamin</td>
<td>14-50 years</td>
<td>1.4 mg/day</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>14-18 years</td>
<td>750 µg (2,500 IU)/day</td>
</tr>
<tr>
<td>Vitamin B₁</td>
<td>14-50 years</td>
<td>1.9 mg/day</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>14-50 years</td>
<td>2.6 µg/day</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>14-18 years</td>
<td>80 µg/day</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>14-50 years</td>
<td>15 µg (600 IU)/day</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>14-50 years</td>
<td>15 mg (22.5 IU)/day</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>14-18 years</td>
<td>75 µg/day (AI)</td>
</tr>
<tr>
<td>Calcium</td>
<td>14-18 years</td>
<td>1,300 mg/day</td>
</tr>
<tr>
<td>Chromium</td>
<td>14-18 years</td>
<td>29 µg/day (AI)</td>
</tr>
<tr>
<td>Copper</td>
<td>14-50 years</td>
<td>1 mg/day</td>
</tr>
<tr>
<td>Fluoride</td>
<td>14-50 years</td>
<td>3 mg/day (AI)</td>
</tr>
<tr>
<td>Iodine</td>
<td>14-50 years</td>
<td>220 µg/day</td>
</tr>
<tr>
<td>Iron</td>
<td>14-50 years</td>
<td>27 mg/day</td>
</tr>
<tr>
<td>Magnesium</td>
<td>14-18 years</td>
<td>400 mg/day</td>
</tr>
<tr>
<td>Manganese</td>
<td>14-50 years</td>
<td>2 mg/day (AI)</td>
</tr>
<tr>
<td>Molybdenum</td>
<td>14-50 years</td>
<td>50 µg/day</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>14-18 years</td>
<td>1,250 mg/day</td>
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<tr>
<td>Potassium</td>
<td>14-50 years</td>
<td>4,700 mg/day (AI)</td>
</tr>
<tr>
<td>Selenium</td>
<td>14-50 years</td>
<td>60 µg/day</td>
</tr>
<tr>
<td>Sodium</td>
<td>14-50 years</td>
<td>1,500 mg/day (AI)</td>
</tr>
<tr>
<td>Zinc</td>
<td>14-18 years</td>
<td>12 mg/day</td>
</tr>
<tr>
<td>Choline*</td>
<td>14-50 years</td>
<td>450 mg/day (AI)</td>
</tr>
</tbody>
</table>

AI = Adequate Intake
*Dietary Folate Equivalents,*

*NE, niacin equivalent: 1 mg NE = 60 mg tryptophan = 1 mg niacin
*Retinol Activity Equivalents, *Alpha-tocopherol
*Considered an essential nutrient, although not strictly a micronutrient

Various important micronutrients

**Vitamins**

Biotin (Vitamin B7 or Vitamin H)

Biotin is required as a cofactor for carboxylase enzymes and for attachment of biotin to molecules, such as proteins, for “biotinylatation”. Rapidly proliferating cells of the developing foetus require biotin for synthesis of indispensable carboxylase enzymes plus for histone biotinylatation. Thus, the biotin requirement is increased during pregnancy. At present, it is projected that at least 1/3 of women develop marginal biotin deficiency during pregnancy. Although the level of biotin depletion is not severe enough to cause diagnostic signs or symptoms, subclinical biotin deficiency has been shown to cause natal defects in several animal species. The potential risk for teratogenesis (abnormal growth of the embryo or foetus) due to biotin insufficiency makes it prudent to ensure adequate biotin intake preconceptionally and throughout pregnancy. Supplementation of biotin (at least 30 µg/day) in the form of a multivitamin that also contains at least 400 µg of folic acid can be a helpful step.

**Folic acid**

Folate is required for amino acid as well as nucleic acid (DNA and RNA) metabolism. Adequate folate status is critical to embryonic in addition to foetal growth-developmental stages marked by increased cell division. In particular, folate is needed for closure of the neural tube early in pregnancy, and periconceptional supplementation with folic acid has been shown to dramatically reduce the incidence of neural tube defects (NTDs). Because these birth defects occur between 21 to 27 days after conception, time and again before a lot of women make out their pregnancy, it is recommended that all women capable of becoming pregnant receive supplemental folate. A recent systematic meta-analysis of five trials, including 6,105 women, found that periconceptional vitamin H supplementation, only or with additional micronutrients, was associated with a 72% lower risk of NTDs. The US Preventive Services Task Force recommends a daily basis supplement of 400-800 µg of folic acid for all women planning or capable of pregnancy. A number of countries have programs of compulsory folic acid fortification to help reduce the incidence of NTDs. Additionally, folic acid supplementation in the form of an everyday multivitamin may be more effective in reducing NTDs than when used alone. Doses of greater than 1 mg/day of folic acid are used pharmacologically to treat hyperhomocysteinemia along with averting recurrence of NTDs. Women who have had a previous NTD-affected pregnancy may be advised to consume up to 4 mg/day (4,000 µg/day) of folic acid if they are planning a pregnancy. Inadequate folate status may also be associated with further
birth defects, like cleft lip, cleft palate, and limb malformations, but the support for these results is not as obvious or regular as the support for NTDs. Impaired folic acid condition at the time of pregnancy could also be linked with other adverse pregnancy outcomes. Elevated blood homocysteine levels, measured as a marker of functional folic acid shortage, have been associated with increased risk of preeclampsia, premature delivery, low birth weight, very low birth weight (<1,500 grams), NTDs, and stillbirth. In the developing world, the incidence of megaloblastic anaemia is considerably higher—approximately 25% of women with anaemia during pregnancy. It can occur due to deficiency of Folate or Vitamin B12. Thus, it is reasonable to maintain folic acid supplementation all through pregnancy, even subsequent to closure of the neural tube, in order to decrease the risk of other potential problems during pregnancy.

**Riboflavin (Vitamin B2)**

Vitamin B2 is a constituent of flavoenzymes concerned in energy metabolism, and antioxidant functions. The Food and Nutrition Board of the Institute of Medicine recommends that all pregnant women take 1.4 mg of vitamin B2 every day. Vitamin B2 deficit has been connected to preeclampsia. Even though the exact causes of preeclampsia are not recognized, reduced intracellular levels of flavoenzymes could result in mitochondrial dysfunction, augment oxidative stress, and get in the way with nitric oxide release and consequently blood vessel dilation.

**Vitamin A**

Sufficient maternal vitamin A level is vital for a healthy pregnancy. Forms of vitamin A, known as retinoids, are implicated in the control of gene expression, cell proliferation and differentiation, growth and development, vision, and immunity. The retinoids, retinol and retinoic acid, are essential for embryonic and foetal development; for instance, retinoic acid role in forming the heart, eyes, ears, and limbs. Vitamin A deficiency during pregnancy has been connected to weakened immunity, increased susceptibility to infection, and increased risk of maternal morbidity and mortality. Vitamin A deficiency may exacerbate iron-deficiency anaemia, which is relatively common during pregnancy, because co-supplementation with vitamin A and iron appears to relieve anaemia more effectively than either micronutrient supplement alone.

Even though usual embryonic and foetal growth necessitate sufficient maternal vitamin A intake, consumption of excess preformed vitamin A during pregnancy has been proven to result in birth defects. Pregnant women must avoid multivitamin or prenatal supplements that have greater than 1,500 μg (5,000 IU) of vitamin A. Moreover, pharmacological use of retinoids by pregnant women results in serious birth defects; thus, tretinoin, isotretinoin and other retinoids should not be used at the time of pregnancy or when there is a likelihood of becoming pregnant.

**Vitamin B6**

Vitamin B6 has diverse roles in the body, including nervous system function, red blood cell formation and function, steroid hormone role, nucleic acid synthesis, and niacin formation. The RDA for vitamin B6 during pregnancy is 1.9 mg/day. Supplementation with high-dose vitamin B6 may help mitigate nausea and vomiting in pregnancy (commonly called “morning sickness”). Outcomes of 2 double-blind, placebo-controlled trials that used 25 mg of pyridoxine every eight hours for 3 days or 10 mg of pyridoxine every 8 hours for 5 days suggest that vitamin B6 may be beneficial in alleviating morning sickness. All studies establish a small but considerable reduction in nausea or vomiting in pregnant women.

**Vitamin B12**

Adequate vitamin B12 status during pregnancy is critical for DNA methylation. Inadequate dietary intake of vitamin B12 causes elevated homocysteine levels, which have been associated with adverse pregnancy outcomes, including preeclampsia, premature delivery, low birth weight (<2,500 grams), very low birth weight (<1,500 grams), neural tube defects (NTDs), and stillbirth. Moreover, low serum levels of vitamin B12 during pregnancy have been directly linked to an increased risk for NTDs, and there is some concern that folic acid supplementation during pregnancy may mask the clinical diagnosis of vitamin B12 deficiency. After iron deficiency anaemia, megaloblastic anaemia is the second most prevalent cause of anaemia in India. For these reasons, adequate vitamin B12 intake during pregnancy (RDA=2.6 μg/day) is important. Because vitamin B12 is found only in foods of animal origin, vegans and lacto-ovo vegetarians are prone to suffer from vitamin B12 deficiency, making its supplementation even more important in countries like India.

**Vitamin C, D, E and K**

Low Vitamin D levels are associated with poor foetal and infant skeletal growth and mineralization and poor infant tooth mineralization.

Oxidative stress produced by free radicals has been involved in many studies in the etiology of preeclampsia. Because ascorbic acid and vitamin E hinder free radical production, a double-blind randomized trial was conducted in 283 women who had either a prior record of pregnancy issues or an unusual ultrasound. The supplement provided 1000 mg ascorbic acid in addition to 400 IU vitamin E on a daily basis from week 16-22 of pregnancy, and resulted in a 76% reduction in preeclampsia as well as a 21% decrease in indicators of endothelial activation and placental dysfunction.
Minerals

Iron

Iron is needed for a number of biological functions, but during pregnancy, it is generally needed to support growth and development of the foetus and placenta and to gather the increased demand for red blood cells to transport oxygen. The recommended dietary allowance is 27 mg/day for pregnant women of each and every age in contrast to 15-18 mg for nonpregnant women. The World Health Organization evaluates that the global occurrence of anaemia among pregnant women is 42%; iron deficiency is the primary cause of anaemia during pregnancy. 18 Iron-deficiency anaemia causes an estimated 115,000 maternal deaths each year, and severe iron shortage at the time of pregnancy has been linked to increased risk of low birth weight infants (<2,500 grams), premature delivery and perinatal mortality. However, evidence that iron-deficiency anaemia is a causal factor in poor pregnancy outcomes is still lacking.

Zinc

Zinc is an indispensable element of more than 200 metalloenzymes participating in carbohydrate and protein metabolism, nucleic acid synthesis, antioxidant role (through Cu/Zn SOD), and other vital functions such as cellular division and differentiation, making it necessary for productive embryogenesis. It was estimated in 2002 by the World Health Organization that suboptimal zinc nutrition affected nearly half the world’s population. 19 During pregnancy, zinc is also used to help the foetus to develop the brain as well as to be a support to the mother in labour. Alteration in zinc homeostasis possibly will have disturbing effects on pregnancy result, together with prolonged labour, foetal growth restriction, embryonic or foetal death. 20 Zinc deficiency has been associated with preeclampsia since the 1980s including adolescent pregnancies. 21 It is imperative to note that supplemental levels of iron (38-65 mg/day of elemental iron), but not dietary levels of iron, may decrease zinc absorption.

Magnesium

Sufficient consumption of the mineral is required for balanced embryonic and foetal development. Maternal magnesium deficiency has been linked to premature labour as well as implicated in the pathogenesis of Sudden Infant Death Syndrome (SIDS). 22 Magnesium is thought to alleviate cerebral blood vessel spasm, increasing blood flow to the brain and hence has a unique role in management of eclampsia and preeclampsia.

Iodine

Iodine requirement become greater by >45% at the time of pregnancy. Adequate intake of iodine is needed for maternal thyroid hormone production, and thyroid hormone is needed for myelination of the central nervous system and is thus essential for normal foetal brain development. 23 Iodine deficiency disorders (IDD) constitute the single largest cause of preventable brain damage worldwide. Majority of consequences of IDD are invisible and irreversible but at the same time these are preventable. Maternal iodine deficiency has been associated with increased incidence of miscarriage, stillbirth, and birth abnormalities. Extreme iodine deficiency during pregnancy can result in congenital hypothyroidism and neurocognitive deficits in the offspring. 24 A severe form of congenital hypothyroidism may lead to a condition that is occasionally referred to as cretinism and produces permanent mental retardation. Even mild forms of maternal iodine deficiency possibly will have unfavorable effects on cognitive maturity in the offspring, and iodine deficiency is now accepted as the main universal reason for avoidable brain damage in the world. 25 There are many studies which have reported a decrease of IQ points in children born to mothers living in iodine deficient regions of world untreated in pregnancy compared to supplemented mothers also living in severely iodine deficient regions. A meta-analysis of 18 studies concluded that maternal iodine deficiency lowered offspring IQ score by 13.5 points. 26 There is strong evidence that iodine supplementation improves fetal outcomes with severe iodine deficiency. 27 Thus, adequate intake of the mineral throughout pregnancy is critical. According to public health experts, iodization of salt may be the world’s simplest and most cost-effective measure available to improve health.

Recommendations from various International bodies:

International Federation of Gynecology and Obstetrics (FIGO)-2015 states that that even with use of iodized salt and eating seafood 2-3 days per week, a woman’s daily iodine intake would be approximately half the amount recently recommended during pregnancy and lactation28.

Organisations like American Academy of Pediatrics recommends that all the pregnant and breast-feeding women should seek out prenatal supplements that contain iodine. American Thyroid Association & Endocrine Society-2011 guidelines recommends that all the women attempting to conceive and pregnant women take a prenatal vitamin containing 150mcg of iodine while IOM (Institution of medicine) recommends daily iodine intake of 220 mcg during pregnancy and 290 mcg during lactation; and the WHO recommends27 iodine intake of 250 mcg for both pregnant and lactating women.

Chromium

Chromium is identified to improve the effect of insulin; as a result, several studies have investigated the utility of chromium supplementation for the management of plasma glucose levels in type 2 diabetes. However, its use in
gestational diabetes is not well studied and more RCTs are needed.

Others

Copper is an essential cofactor for a number of enzymes involved in metabolic reactions, blood vessel formation, oxygen carrying, and antioxidant protection, including catalase, superoxide dismutase (SOD) and cytochrome oxidase. Copper is essential for embryonic development. Maternal dietary deficiency can result in both temporary outcomes, together with early embryonic fatality and gross structural abnormalities, and long-term consequences such as increased risk of cardiovascular disease and reduced fertilization rates.

Selenium and manganese are antioxidant trace elements important for various body functions although at present sensitive biomarkers of exposure and nutritional status are not available other than some estimates from blood concentrations.

Indian Scenario

In India malnutrition has been called 'The Silent Emergency'. The burden of reproductive and child health nutrition is greater than any other country, with 1.8 million deaths among children under 5 years and 68,000 deaths among mothers, and 52 million children who are stunted in the year 2008. According to the National Family Health Survey carried out in 2005-06, 58% of Indian pregnant women are anaemic. Concurrent deficiencies of micronutrients are well documented among young pregnant women and young children and are a result of poor quality diets, high fertility rates, repeated pregnancies, short interpregnancy intervals, increased physiological needs, as well as inadequate health systems with poor capacity and adolescent pregnancies and some traditional dietary practices. Although iron deficiency is highly common, there is often at least one other deficiency that co-exists. Pregnant women in India have coexisting deficiencies of zinc, iron, copper, iodine, magnesium, folate, and vitamin A along with a deficit in the intake of protein and fats. Deficiency of vitamin B12 is also considered to be highly prevalent in India and the metabolic signs of vitamin B12 deficiency have been reported in 75% of adult men and women from urban areas of West India.

Hence, micronutrient supplementation in pregnancy is an issue which needs to be taken care of at the grass root levels to prevent the epidemic of malnutrition in our country. In this aspect, in a country like ours, where basic health care services are not so effective, pregnancy provides an important platform to identify and treat women with micronutrient deficiencies.

References


