REVIEW ARTICLE

Association of Maternal Thyroid Function with Iron, Vitamin B12, and Folic Acid Status in Pregnancy

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ABSTRACT

Pregnancy is a physiological condition and induces complex hormonal and immunological changes that modify normal thyroid physiology. It has a profound impact on the thyroid gland and thyroid function. Pregnant women are often iron deficient, and iron deficiency has adverse effects on thyroid metabolism. Therefore, evaluation of thyroid function during pregnancy in association with iron, vitamin B12 and folic acid should be interpreted according to these changes in different trimesters during pregnancy. Impaired maternal thyroid function during pregnancy may cause neuro developmental delays in the offspring. It has been shown in recent studies that iron deficiency in mothers predicts increased levels of TSH and decreased levels of the thyroid hormone thyroxin (T4) in pregnancy.

Keywords: pregnant women, thyroid hormone, thyroid stimulating hormone, iron status, iron deficiency.

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INTRODUCTION

Pregnancy is a physiological condition and usually has no effect on general health of a pregnant woman. However pregnancy results in hormonal, hemodynamic and haematological changes. These physiological changes need to be viewed as normal adaptations determined by nature. Increased total blood volume and haemostatic changes help to combat the hazards of haemorrhage at delivery.[1] In iron deficient women this inability to expand plasma volume may mask a decrease in haemoglobin concentration.[2] The healthy non pregnant women lowest haemoglobin level is 12g/dl. As per WHO the haemoglobin should be maintain at or more than 11g/dl, and should not be decreased less than 10g/dl in the 2nd trimester.[3] Hypothyroidism during pregnancy affects both mother and child. Child born to nutritionally compromised mothers will show poor intellectual development in future. During pregnancy synthesis of thyroid hormone as well as iodine requirement will be increased more than 50%.[4] Hypothyroidism is the most common pregnancy-related thyroid disorder, affecting 3–5% of all pregnant women. Pregnant women are often iron deficient, and iron deficiency has adverse effects on thyroid metabolism. Impaired maternal thyroid function during pregnancy may cause neuro developmental delays in the offspring. Iron deficiency and iron deficiency anaemia (IDA) have been universally recognized as the commonest forms of malnutrition occurring in the world. These affect approximately 2 billion people, 80% of whom live in the developing world.[5] However, its distribution is not uniform throughout the world. Southeast Asia has the highest levels at 79%. The Indian subcontinent alone contains nearly half the world's anaemic women.[6] The Indian Council of Medical Research, estimated the prevalence of anaemia among pregnant women to be 88%.[7] In one of the studies conducted on a large population, it was estimated that 87% of the Indian pregnant women are anaemic.[8] Iron deficiency anemia during early pregnancy has been linked to low birth weight, premature birth, and negative effects on children's neuropsychological development.[9] Iodine deficiency is also a common nutrient deficiency, globally affecting approximately 2 billion individuals, out of which approximately 50-60% of the population are women who suffers from impaired thyroid function even in developed European countries.[10] The impaired thyroid function may cause extra burden during pregnancy, leading

to a serious risk of mental retardation, low birth weight, increased infant mortality, as well as increased risk of health complications later in life such as metabolic syndrome and type-2 diabetes. It has recently shown that iron deficiency in mothers predicts increased levels of TSH and decreased levels of the thyroid hormone thyroxin (T4) in pregnancy.[11] However there was no previous study to assess the thyroid function, iron status in different trimesters of pregnancy and its correlation.

Folic Acid

It is a water soluble vitamin, Folic acid plays an important role in growth, synthesis of nucleic acids, amino acids and essential for cell division.[12] Folic acid is very important for development of the foetal brain, skull and spine, during the first four weeks of pregnancy. During pregnancy the RBC formation and rate of cell division increases as well as it enlarges size of the uterus, increasing maternal blood volume, placenta develops and the embryo is converted in to foetus.[13] Folate is transferred from the mother to the growing foetus.[14] The RDA for women of childbearing age is 400 µg/day of folic acid according to the Institute of Medicine.[15] These recommendations are based on the amount of dietary folate equivalents needed to maintain normal red blood cells. In addition to this dietary recommendation, all women who may become pregnant should take a multivitamin containing 400 µg/day of folic acid to reduce the risk of neural tube defects except for few countries like Newzealand where the recommendation is 800 µg/day for at least four weeks prior to conception and for 12 weeks after conceiving to reduce the risk of neural tube defects.[16] Folate intake from food is not associated with any health risk. The risk of toxicity from folic acid intake from supplements and/or fortified foods is also low.[17] It is a water soluble vitamin, so any excess intake is usually lost in the urine and recommendations are that anyone taking such medications should consult with a medical doctor before taking a folic acid supplement.

IRON

Anemia is defined as low hemoglobin or hematocrit, Anemia during pregnancy continues to be a common clinical problem with high rate prevalence in many developing countries.[18] Iron deficiency anemia is the commonest anemia in developed or developing countries, mainly reproductive women are suffering in iron deficiency anemia due to menstruation (heavy blood loss). In pregnancy the amount of iron requirement in increased, expanding plasma volume, red cell mass that allows growth of fetus. Women in their reproductive years often have a dietary iron intake that is too low to offset losses from menstruation and the increased iron requirement for reproduction during pregnancy iron is required (3– 4 mg/d).[19]

Vitamin B12

Vitamin B12 maintains constant folate metabolism which is essential for cell multiplication, especially in the rapidly dividing placental and fetal tissues. The fetus uses the available amount of vitamin B12 for biochemical reactions, but is not able to synthesize vitamin B12.[20] From the first to the third trimester of pregnancy there is a gradual decline in the serum concentration of vitamin B12 due to hormonal changes, alterations in the concentration of vitamin B12 binding proteins , hemodilution, and placental transport of vitamin B12 to the fetus. The lowest concentration of vitamin B12 is seen at 9th month of pregnancy or before delivery and again it increases to reach a normal level after birth.[21] A vitamin B12 deficiency is seen worldwide lately but not all patients with a deficiency develop symptoms. Hematological signs of vitamin B12 deficiency mainly occur in very severe deficiency. Globally the data clearly shown that megaloblastic anemia does not accompany the level of vitamin B12 deficiency that is so prevalent in developing countries. Vitamin B12 status during pregnancy is critical since maternal vitamin B12 deficiency can affect the pregnancy outcome for both mother and the offspring. For women who want to get pregnant, a vitamin B12 deficiency means an increased risk of developing intra-uterine growth retardation, preeclampsia, and preterm labor.[22]

Breastfeeding and Vitamin B12

A vitamin B12 deficiency can affect health of the infant, due to lack of vitamin B12 in breast milk.[23] Infants who are exclusively breastfed by mothers who have a low dietary intake of vitamin B12 such as vegetarians are therefore at risk for developing vitamin B12 deficiency possibly influencing cognitive and psychomotor development. A severe vitamin B12 deficiency in the infant can cause megaloblastic anemia, neurological symptoms, failure to thrive, apathy, anorexia and irritability.[24] At a later age developmental regression, like impaired growth, poor school performance, gross motor function and other adaptive skills has been suggested to be a consequence of a poor maternal vitamin B12 status during pregnancy.[25]

DISCUSSION

Pregnant women are high risk group for iron deficiency. Maternal iron deficiency and especially iron deficiency anemia may be associated with detrimental effects on maternal and infant function and particularly with a higher risk of delivery of low birth weight neonate and preterm delivery. Pregnant women are often iron deficient, and iron deficiency has adverse effects on thyroid metabolism. Impaired maternal thyroid function during pregnancy may cause neuro-developmental delays in the offspring. During the second and third trimester, pregnant women are highly vulnerable to iron deficiency (ID) anemia because their increased iron needs are rarely met by dietary sources.[26] In developed countries, the prevalence of anemia and Iron Deficiency during pregnancy range from 6–28% and 24–44%, respectively. In industrialized countries, the majority of women are anemic in the second half of pregnancy.[27] Requirements for thyroid hormone during pregnancy also sharply increase to maintain maternal euthyroidism and transfer thyroid hormone to the fetus. To support this, the iodine requirement in pregnancy increases from 150–250g/d, making maternal thyroid function particularly vulnerable in regions of marginal iodine intake. ID has multiple adverse effects on thyroid metabolism. It decreases circulating thyroid hormone concentrations, likely through impairment of the heme-dependent thyroid peroxidase (TPO) enzyme.[28] ID blunts the efficacy of iodine prophylaxis and iron repletion improves the efficacy of iodized salt in goitrous children with ID. Two prospective studies, using two different measures of impaired thyroid function in pregnancy (an increased TSH in the second trimester and hypothyroxinemia at 12 wk gestation) reported that even mild maternal thyroid dysfunction may impair neurodevelopment in the offspring. Iron deficiency anemia and iron deficiency in pregnancy is a main important preventable cause of maternal and perinatal morbidity and mortality. Iron deficiency is most prevalent in only single micro-nutrient deficiency affecting around 50% of the world population. Among the most affected by this malady are pregnant women due to added iron requirements during pregnancy. This is primarily because the amount of dietary iron absorbed is often too small to meet the increased demand during pregnancy. Interest in thyroid dysfunction complicating pregnancy has increased greatly during the past decade. This increased interest has been largely fueled by two reports in 1999 that suggested offspring of women with variously defined hypothyroidism identified during pregnancy, to include overt and subclinical disease, are at increased risk of impaired neurodevelopment.[29] There have also been reports linking subclinical hypothyroidism with an increased risk for preterm birth. As a result, several national endocrine authorities have recommended routine screening for hypothyroidism during pregnancy. Ferritin is an iron storage protein found in almost all of the body tissues. In individuals, serum ferritin levels correlate well with body iron storage. Serum ferritin measurements have been widely used in clinical medicine as a diagnostic test for iron storage diseases or as a marker of some neoplastic diseases.[30]

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