Maternal Iodine Levels and Their Impact on Breast Milk Iodine Concentration

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ABSTRACT

Adequate iodine intake during pregnancy and lactation is vital for thyroid hormone synthesis which is crucial for fetal and neonatal development, especially with exclusive breastfeeding. This review explores the link between maternal iodine levels and breast milk iodine concentration (BMIC), focusing on factors influencing maternal iodine and its impact on BMIC. This review synthesizes current findings on the determinants of maternal iodine status, including dietary intake, supplementation, and iodine metabolism, and their impact on BMIC underscores the necessity for healthcare providers to monitor and guide iodine intake in pregnant and lactating women. The findings advocate for targeted public health interventions and the implementation of robust guidelines to ensure adequate iodine nutrition.

Keywords: Breast milk iodine concentration (BMIC), fetal and neonatal development, iodine levels.

ABSTRAK

Asupan yodium yang memadai selama kehamilan dan menyusui sangat penting untuk sintesis hormon tiroid yang krusial bagi perkembangan janin dan bayi, terutama pada ASI eksklusif. Tinjauan ini mengeksplorasi hubungan antara kadar yodium ibu dan konsentrasi yodium dalam ASI (BMIC), serta faktor-faktor yang memengaruhinya. Tinjauan ini juga mensintesis temuan terkini tentang faktor penentu status yodium ibu termasuk asupan makanan, suplementasi, dan metabolisme yodium, serta dampaknya terhadap BMIC, yang menggarisbawahi perlunya pemantauan dan panduan asupan yodium oleh penyedia layanan kesehatan untuk wanita hamil dan menyusui. Temuan ini mendukung intervensi kesehatan masyarakat yang terarah dan penerapan pedoman yang kuat untuk memastikan nutrisi yodium yang memadai. **Ingrid Siahaan, Joshua Princeman Sinaga. Kadar Yodium Maternal dan Pengaruhnya terhadap Kadar Yodium ASI.**

Kata Kunci: Konsentrasi yodium dalam ASI (BMIC), perkembangan janin dan bayi, kadar yodium.

INTRODUCTION

Iodine is critical for thyroid hormone synthesis, which is essential in fetal and neonatal growth and mental development. During pregnancy, physiological changes result in a roughly 50% increase in iodine requirements, underscoring the importance of adequate iodine intake for maternal health and fetal development.[1] This increased demand supports the enhanced production and placental transfer of thyroid hormones necessary for fetal brain development and overall growth.[2] Adequate maternal iodine intake ensures normal thyroid hormone levels, essential for the fetus' neurological development and metabolic regulation.[3] Insufficient iodine during pregnancy can lead to maternal hypothyroidism and severe fetal developmental issues, including irreversible brain damage and intellectual disabilities.[4] However, excessive iodine intake can also disrupt maternal thyroid function, causing primary hypothyroidism and affecting iodide transfer to breast milk.[3]

A systematic review and meta-analysis revealed no significant association between maternal urinary iodine concentration (UIC) and adverse pregnancy outcomes in euthyroid pregnant women, indicating that UIC alone may not be sufficient for predicting pregnancy complications.[5] Research has shown that maternal UIC fluctuates during pregnancy and lactation, with median levels increasing in the third trimester and shortly after birth but potentially dropping to iodine-deficient levels one month postpartum.[6] Breast milk iodine concentration (BMIC) is a promising indicator of iodine status in lactating women, reflecting maternal iodine sufficiency. BMIC is also a valuable biomarker for assessing iodine intake in exclusively breastfed infants, providing a more sensitive and stable index for evaluating infant iodine nutrition compared to maternal UIC.[7-9]

This review aims to investigate the relationship between maternal iodine levels and breast milk iodine concentration and to identify factors influencing maternal iodine levels and their effects on breast milk.

MATERNAL IODINE REQUIREMENTS AND METABOLISM

Iodine Requirements During Pregnancy and Lactation

Iodine deficiency during pregnancy can result in severe consequences, such as miscarriage, prematurity, stillbirth, and long-term cognitive impairments in offspring, including lower

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IQ and developmental delays.[4,10] WHO and various health authorities recommend a daily iodine intake of 250 μg for pregnant and lactating women to meet these increased needs.[2,10] Universal salt iodization has been a primary strategy to combat iodine deficiency globally, but it may not be sufficient for pregnant and lactating women, who often require additional supplementation.[2,11] The timing of iodine supplementation, whether preconception or early in pregnancy, is also crucial for maximizing its benefits on maternal thyroid function and offspring development.[4] Excessive iodine intake, however, should be avoided as it can adversely affect maternal and offspring thyroid function.[11] Research also indicates that iodine status can fluctuate significantly during the perinatal period, with maternal urinary iodine concentration (UIC) peaking shortly after birth and then declining, suggesting the need for ongoing monitoring and potential supplementation during lactation.[6]

Factors Influencing Maternal Iodine Levels

Maternal iodine status during pregnancy is influenced by various dietary factors, as evidenced by multiple studies.[12] A significant determinant is the intake of iodine-rich foods such as dairy products, fish, and eggs. Milk and dairy product intake were positively associated with urinary iodine-to-creatinine ratio (UI/Creat) in pregnant women across European cohorts, highlighting their importance in maintaining adequate iodine levels.[12] Fish and shellfish intake significantly influenced iodine status in some populations.[12] Despite mandatory fortification of bread with iodized salt in New Zealand, lactating women who did not consume iodine-rich foods or supplements were found to be iodine-deficient, underscoring the need for dietary vigilance.[13] The importance of nutritional supplements is also highlighted in the United States, where many pregnant women had iodine intakes below the estimated average requirement (EAR) from diet alone; supplementation improved their iodine status.[14] Longitudinal studies indicate that iodine status can fluctuate postpartum, and milk and iodine-containing supplements are crucial for maintaining adequate levels.[15] These findings emphasize that dietary intake, including consumption of iodine-rich foods and supplements, is a critical factor in maternal iodine status during pregnancy and lactation.[13,14]

Several factors, including supplementation, dietary intake, and regional iodine deficiency levels, influence maternal iodine status during pregnancy. Iodine is crucial for fetal brain development, and its deficiency can lead to adverse maternal and child health outcomes. Despite the success of salt iodization programs, many pregnant women worldwide still have insufficient iodine intake, a 2022 meta-analysis indicated that 53% of pregnant patients are affected.[16] A study in Portugal found that iodine supplementation initiated in preconception or the first trimester significantly increased urinary iodine concentration (UIC) but still fell short of WHO recommendations, highlighting the need for additional public health measures.[17] Similarly, in a European iodine-deficient region, iodine supplementation reduced severe iodine deficiency among pregnant women but still did not achieve the recommended UIC levels, suggesting that adjustments in dosage or timing, or universal salt iodization, may be necessary.[18] In New Zealand, despite government initiatives to fortify bread with iodized salt and subsidize iodine supplements for breastfeeding women, maternal iodine intake and status remained suboptimal, particularly among those not using iodine-containing supplements.[13] While iodine supplementation can improve maternal iodine status, its effectiveness varies based on regional iodine deficiency levels, dietary habits, and adherence to supplementation guidelines.[17]

Geographical location plays a significant role, as evidenced by the study in Zhejiang Province, China, where pregnant women in coastal regions had lower median urinary iodine concentrations (UIC) compared to those in the inland areas, likely due to lower consumption of iodized salt and varying iodine content in drinking water.[13,19] Environmental factors such as the iodine content in local water and food supplies also play a crucial role. In China, the iodine concentration in drinking water was low in coastal and inland regions, contributing to iodine deficiency among pregnant women and neonates.[20] This study underscores the multifaceted nature of iodine deficiency, influenced by regional, environmental, and individual factors among pregnant women.[20]

Metabolism of Iodine in the Maternal Body

Iodine metabolism undergoes significant changes during pregnancy to meet the increased demands for thyroid hormones, which are crucial for maternal health and fetal development. The daily iodine requirement for pregnant women rises to 250 μg, compared to 150 μg for nonpregnant women, to support the heightened production of thyroid hormones necessary for regulating metabolism, protein synthesis, and fetal neuronal maturation.[2] This increased demand begins in the first trimester and continues throughout pregnancy, necessitating a proportional increase in hormone production that depends directly on iodine availability.[21] Pregnant women often experience altered iodine turnover, with urinary iodine concentration (UIC) fluctuating significantly; for instance, UIC increases shortly after birth and then decreases within a month postpartum.[6]

Iodine metabolism also undergoes significant changes during the breastfeeding period, reflecting the body's adaptation to meet the increased iodine demands for both the mother and the infant. Studies have shown that the iodine content in the urine, milk, and blood of lactating mothers and their offspring increases with higher dietary iodine intake, with the most substantial changes observed in urinary iodine, followed by milk and blood iodine levels.[22] During lactation, the urinary iodine concentration (UIC) in mothers typically increases shortly after birth but may decrease to levels suggesting iodine deficiency or near deficiency by one month postpartum. Breast milk iodine concentration (BMIC) is a reliable indicator of maternal iodine status, with studies indicating that BMIC decreases from 17.6 μg/100 gram on the fourth postpartum day to 13.5 μg/100 gram by the 32nd day.[6]

In cases of severe iodine deficiency, lactating mothers and their infants can develop hypothyroidism, characterized by decreased serum thyroxine (TT4) and increased thyrotropin (TSH) levels, along with histological changes in the thyroid gland. Conversely, due to compensatory mechanisms, mild iodine deficiency and iodine excess do not significantly affect thyroid function.[23] Overall, while lactating women may experience fluctuations in iodine metabolism, maintaining adequate iodine intake is essential to ensure sufficient iodine levels in breast milk and support the thyroid health of both mother and child.[20]

Assessment Method for Maternal Iodine Level

Maternal iodine levels can be assessed using various methods, including urinary iodine concentration (UIC), serum measurements, surveys or questionnaires, and breast milk iodine concentration (BMIC). UIC is a standard method that reflects recent iodine intake and assesses iodine status in pregnant and lactating women. Studies have shown that UIC can indicate iodine sufficiency or deficiency, with median UIC values during lactation ranging from 110.0 μg/L to 125 μg/L in different populations.[7,21] However, UIC alone may not always provide a complete picture, as it can vary significantly due to hydration status and other factors.[25]

Serum measurements, including thyroid-stimulating hormone (TSH) levels, can also be used, although their correlation with iodine status is less direct. For example, neonatal TSH levels have been used to infer maternal iodine status, but this method requires further validation.[21] Surveys and food frequency questionnaires (FFQs) are valuable for assessing dietary iodine intake, which is crucial for understanding potential iodine deficiency. These tools have been used to correlate nutritional habits, such as the consumption of iodized salt and dairy products, with iodine status.[7,25,26]

BMIC is emerging as a reliable biomarker for assessing iodine status in lactating women, as it directly reflects the iodine available to the breastfeeding infant. Studies have demonstrated significant correlations between BMIC and UIC and dietary iodine intake, suggesting that BMIC is a sensitive and stable indicator of iodine nutrition.[25,26]

IODINE TRANSFER FROM MATERNAL STORES TO BREASTMILK

Mechanisms of Iodine Transfer to Breastmilk

Transfer of iodine into breast milk is a complex process involving several mechanisms and regulatory factors. The primary transporter responsible for iodine uptake in the lactating mammary gland is the sodium/iodide symporter (NIS), which is also crucial for iodine transport in the thyroid gland. NIS expression in mammary alveolar cells begins mid-pregnancy and significantly increases during lactation, driven by developmental signals and breast suckling post-delivery. The regulation of NIS is influenced by various hormones, including oxytocin, prolactin, and insulin, which enhance its functional expression and iodine secretion into milk.[27]

Additionally, the mammary gland contains another iodide transporter, pendrin, which is essential for iodide accumulation in milk. Prolactin stimulates pendrin expression, further facilitating iodide uptake into milk.[24] The concentration of iodine in breast milk positively correlates with maternal iodine intake, as demonstrated in studies where higher dietary iodine led to increased milk iodine levels.[28] However, the mammary gland's ability to compensate for iodine deficiency or excess is limited, as evidenced by altered expressions of NIS, DPAGT1, and VCP in response to varying iodine levels.[28] In summary, transferring iodine into breast milk is a multifaceted process regulated by specific transporters, hormonal influences, maternal iodine intake, and other possible external factors critical in ensuring adequate iodine levels for the developing infant.

Variability in Iodine Concentration in Breastmilk

Several factors, including maternal iodine status, stage of lactation, time of day, and maternal diet or supplementation, influence the variability of iodine concentration in breast milk (BMIC). Studies have shown that BMIC can vary significantly among individuals and within the same individual over 24 hours. BMIC follows a "V" shaped curve throughout the day, with lower concentrations observed between 08:00 and 12:00 and higher concentrations from 20:00 to 04:00 **(Figure)**. This diurnal variation suggests that the timing of the breast milk sample collection is crucial for accurate iodine status assessment.[29]

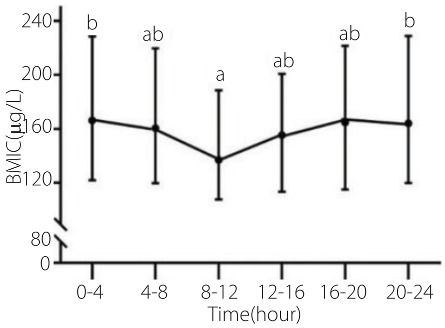

Figure. Circadian rhythm of breast milk iodine concentration (BMIC, μg/L) over 24 h in 30 lactating women.[29]

The BMIC measurement method is also critical, and the ammonia dilution method using inductively coupled plasma mass spectrometry (ICP-MS) has been validated as accurate and reliable for this purpose.[30] BMIC has been proposed as a promising biomarker for iodine status assessment in lactating women and infants, with studies indicating that it correlates well with urinary iodine concentration (UIC).[7] However, there are discrepancies, as some studies have found that BMIC can be adequate even when UIC suggests iodine insufficiency, highlighting the need for multiple biomarkers to assess iodine status comprehensively.[25]

Maternal iodine intake from diet and supplements plays a significant role in determining BMIC. Women who consume dairy products and multivitamins tend to have higher BMIC, while those who do not are at increased risk of lower BMIC.[25] Additionally, the type of diet followed by lactating mothers, such as vegan or vegetarian diets, can negatively impact BMIC, with vegans and vegetarians often having lower BMIC compared to omnivores.[31]

The stage of lactation also affects BMIC, studies indicated that BMIC is generally higher in the first week postpartum and can vary as lactation progresses.[7] Maternal urinary iodine concentration (UIC) and 24-hour urinary iodine excretion (24-h UIE) are correlated with BMIC, making them valuable biomarkers for assessing iodine status in lactating women.[9] However, UIC alone may not be sufficient, as BMIC, UIC/creatinine ratio, and 24-hour UIE provide a more comprehensive picture.[25] BMIC is a dynamic indicator influenced by a complex interplay of dietary intake, supplementation, timing, and individual physiological factors.

CONCLUSION

This literature review demonstrates a direct positive correlation between maternal iodine levels and iodine concentration in breast milk. The consequences of iodine deficiency in breastfeeding mothers can be severe, potentially leading to inadequate iodine transfer to the exclusive breastfeeding infant, which may impair cognitive and physical development. This review highlights several key findings: First, maternal iodine


status is influenced by dietary intake, supplementation, and the efficiency of iodine metabolism during pregnancy and lactation. Second, accurate assessment methods for maternal iodine levels and breast milk iodine concentration are essential for identifying iodine deficiencies or excesses. Third, both urinary iodine concentration (UIC) and breast milk iodine concentration (BMIC) are essential biomarkers for assessing iodine status in pregnant and lactating women. BMIC offers a more stable and reliable indicator of infant iodine nutrition. However, BMIC varies depending on the time of day, stage of lactation, maternal diet, and supplementation, highlighting the importance of considering these factors when assessing iodine status.

Future research should focus on several key areas. First, developing standardized protocols for measuring BMIC will ensure consistency and accuracy across studies. Second, conducting long-term studies is crucial for monitoring the effects of maternal iodine supplementation on neonatal health outcomes over time. Third, investigating the effectiveness of different iodine supplementation programs in various regions, particularly in areas with severe iodine deficiency, will provide valuable insights. Lastly, exploring the potential adverse effects of excessive iodine intake on maternal thyroid function and neonatal health is essential for a comprehensive understanding of iodine's impact.

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