



Systematic Review



Iodine Levels and Thyroid Hormones in Pregnant Women and Neonatal Outcomes: A Systematic Review

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ABSTRACT

Iodine plays a vital role in the synthesis of thyroid hormones, which are essential for fetal growth and brain development. During pregnancy, maternal iodine needs to increase. Both deficiency and excess can impair maternal thyroid function and lead to complications such as hypothyroxinemia, fetal growth restriction, or thyroid dysfunction in the mother or child.

Objectives: To assess the relationship between maternal iodine levels, thyroid function, and neonatal outcomes, and highlight the risks associated with both iodine deficiency and excess.

Methods: A systematic search was conducted in PubMed, Web of Science, Scopus, Springer, and MDPI for studies published from 2021 to 2025. Inclusion criteria involved studies assessing iodine status (Urinary Iodine Concentration (UIC) or Serum Iodine Concentration (SIC), maternal thyroid function (TSH, FT4, FT3), and neonatal outcomes. Articles were screened using PRISMA guidelines. The risk of bias was assessed using the Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool. Due to heterogeneity in methods and outcomes, results were narratively synthesized. **Results:** Ten studies were included. Iodine deficiency was consistently associated with low birth weight and disrupted thyroid hormone levels, while iodine excess particularly at levels ≥ 500 $\mu\text{g/L}$ was linked to transient neonatal hyperthyrotropinemia. Environmental exposures such as endocrine-disrupting chemicals also influence maternal thyroid function.

Conclusions: It was concluded that both iodine deficiency and excess pose risks to maternal and neonatal thyroid health. Routine monitoring and individualized supplementation based on regional dietary patterns and environmental exposures are recommended.

INTRODUCTION

Iodine is a critical micronutrient essential for the synthesis of thyroid hormones, which are vital for metabolic regulation, fetal growth, and neurological development [1]. During pregnancy, maternal iodine requirements increase significantly due to enhanced maternal thyroid hormone production, fetal thyroid development, and increased renal iodine clearance. Therefore, sufficient iodine intake is essential to maintain maternal thyroid health and ensure normal fetal development [2-4]. Iodine deficiency during pregnancy has been associated with a range of adverse

outcomes, including Maternal iodine deficiency can result in hypothyroxinemia, a condition characterized by low free thyroxine (FT4) levels despite normal TSH levels, which may impair fetal brain development, fetal growth restriction, and impaired neurodevelopment in children [5, 6]. In response to these risks, the World Health Organization (WHO) recommends an iodine intake of 250 $\mu\text{g/day}$ during pregnancy [7]. However, studies show that iodine intake varies across regions due to dietary habits, iodine fortification policies, and environmental factors. In iodine-



deficient regions, subclinical hypothyroidism is more prevalent in pregnant women, contributing to developmental risks for the fetus [8, 9]. While the risks of iodine deficiency are well-established, emerging evidence suggests that excess iodine intake may also be harmful [10]. High maternal iodine levels can disrupt thyroid homeostasis, potentially leading to maternal hyperthyroidism or neonatal hypothyroidism. Overconsumption from supplements or iodized salt can interfere with delicate maternal-fetal thyroid regulation. Thus, both insufficient and excessive iodine intake pose potential threats during pregnancy [11-13]. Despite the growing literature on this topic [14], there is still no global consensus on the optimal iodine concentration during pregnancy to ensure the best neonatal outcome. Previous reviews have focused primarily on iodine deficiency; however, the effects of iodine excess and the influence of environmental factors such as endocrine-disrupting chemicals (EDCs) remain underexplored [15]. This systematic review aims to comprehensively evaluate the association between maternal iodine intake, thyroid function, and neonatal outcomes by synthesizing findings from recent literature. It further seeks to clarify the impacts of both deficiency and excess iodine intake, emphasizing the need for individualized iodine assessment and supplementation strategies in pregnant populations. Despite extensive research on iodine and pregnancy, even after considerable studies of iodine use in pregnancy, there remains controversy regarding the best concentration of maternal iodine that results in the optimal outcome for the newborn. Some studies do emphasize the importance of iodine supplementation in the period of mild to moderate iodine deficiency, while others oppose the unconditional supplementation without prior evaluation of iodine status. Also, some recent studies of endocrine-disrupting chemicals (EDCs) exposure may view iodine metabolism during pregnancy in more complicated terms, which is already considered complex in the field of environmental health.

Iodine is a critical micronutrient whose deficiency or excess during pregnancy can disrupt maternal thyroid function and adversely affect neonatal outcomes, including low birth weight and thyroid dysfunction. Despite extensive research, no global consensus exists on the optimal maternal iodine concentration for the best neonatal outcomes, and the risks of iodine excess alongside the influence of endocrine-disrupting chemicals (EDCs) remain underexplored. Prior reviews have focused predominantly on iodine deficiency and fetal neurodevelopment while neglecting the compounding role of environmental toxins and regional dietary variability. Therefore, this review aims to comprehensively evaluate the relationship between maternal iodine levels, thyroid

function, and neonatal outcomes, while advocating for individualized, region-specific supplementation strategies.

METHODS

This systematic review was conducted by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A structured search strategy was developed to identify studies evaluating maternal iodine levels and thyroid function about neonatal outcomes. Articles were retrieved from PubMed, Scopus, Web of Science, Springer Link, and MDPI, covering the period from January 2021 to February 2025. Both observational and interventional studies focusing on iodine status during pregnancy, maternal thyroid hormones, and infant health outcomes were considered. To maximize relevance and efficiency, the following keywords were used: "maternal iodine deficiency," "iodine levels," "thyroid function," "pregnant women," "neonatal outcomes," and the Me-SH term "Urinary Iodine Concentration (UIC)." Boolean operators AND and OR were applied to combine and refine searches. Additionally, the reference lists of included articles were screened to identify relevant studies not captured through database searches. Clear inclusion and exclusion criteria were defined to ensure relevance and quality. Inclusion Criteria: Studies published between 2021 and March 2025, peer-reviewed original research articles (excluding editorials, commentaries, and abstracts), studies assessing iodine levels in pregnant women via UIC or serum iodine concentration (SIC), studies evaluating maternal thyroid function (TSH, FT3, FT4, or thyroglobulin) and studies reporting neonatal outcomes (e.g., birth weight, preterm birth, stillbirth, neonatal thyroid function, or neurodevelopment). Exclusion Criteria: Studies not measuring iodine during pregnancy, studies on non-pregnant populations, articles with incomplete or unclear methodology for iodine measurement and case reports, reviews, meta-analyses, or animal studies. Two independent reviewers screened all titles and abstracts using the inclusion/exclusion criteria. Full texts of potentially eligible studies were then assessed. Discrepancies were resolved through discussion or by consulting a third reviewer. Extracted data included: author, year, study design, setting, sample size, gestational age at iodine assessment, iodine levels, measurement method, maternal thyroid parameters, neonatal outcomes, confounding variables, and key findings. The quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias Tool for interventional studies. Studies were scored on selection bias, comparability,

outcome assessment, and follow-up adequacy. Only studies with moderate to high methodological quality were included. Due to heterogeneity in study designs, iodine measurement methods, and outcomes, a narrative synthesis approach was adopted. Where applicable, studies were grouped by design or iodine assessment method to aid comparison. Special emphasis was placed on the relationship between iodine levels and maternal thyroid function and neonatal outcomes. Conflicting evidence, such as studies reporting no significant link between mild iodine deficiency and fetal outcomes, was noted and considered during synthesis (Figure 1).

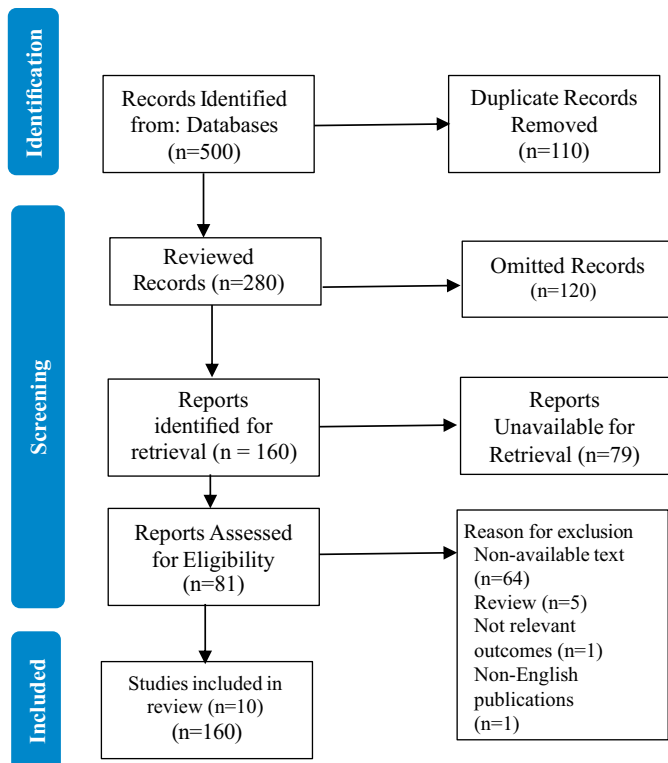


Figure 1: Selection Process of Studies Included in the Review

RESULTS

This systematic review includes ten studies that evaluated the relationship between maternal iodine intake, thyroid function, and neonatal outcomes. The studies varied in design, setting, and assessment methods, yet collectively they provide important insights into the dual risks of iodine deficiency and excess during pregnancy. Several studies emphasized the adverse effects of iodine deficiency on fetal development. For instance, Zha *et al.*, reported that lower urinary iodine concentration (UIC), adjusted by urinary creatinine, was significantly correlated with reduced maternal FT4 and increased TSH, contributing to a higher incidence of low birth weight (LBW) [16]. Similarly, Liu *et al.*, found that lower serum iodine levels in early pregnancy were associated with decreased birth weight and increased maternal thyroid dysfunction [17]. Fan *et al.*,

added that maternal serum iodine concentrations influenced neonatal TSH levels, suggesting that maternal thyroid hormone fluctuations directly affect fetal thyroid regulation [1]. These studies underline that iodine deficiency, even in mild to moderate forms, can impact fetal growth through disruption of maternal thyroid homeostasis. Study showed that exposure to phthalates endocrine-disrupting chemicals—may exacerbate thyroid hormone dysregulation in iodine-deficient regions. This highlights the potential influence of environmental toxins in altering thyroid function beyond iodine intake alone. Ovadia *et al.*, also reported that inadequate iodine intake was linked to isolated hypothyroxinemia and a higher risk of large-for-gestational-age (LGA) neonates, adding complexity to the narrative that both deficiency and excess can result in poor outcomes [18]. Conversely, studies such as Mathews *et al.*, and Rao *et al.*, discussed the effects of excessive iodine intake [19, 20]. In both studies, high maternal iodine exposure specifically UIC levels ≥ 500 $\mu\text{g/L}$ during the third trimester was associated with transient neonatal hyperthyrotropinemia. Although this condition normalized by 12 weeks postpartum, it highlights that excessive iodine can temporarily disrupt neonatal thyroid homeostasis. However, not all findings were consistent. Purdue-Smithe *et al.*, found no significant association between maternal iodine levels and the risk of stillbirth, suggesting that mild to moderate iodine deficiency may not always lead to adverse pregnancy outcomes [21]. The overall evidence demonstrates that both insufficient and excessive iodine intake during pregnancy can adversely affect neonatal outcomes primarily through altered thyroid function. Bonell *et al.*, concluded that both low and high maternal iodine levels were linked to decreased birth weight and length [22]. These outcomes emphasize the need for precise, region-specific monitoring of iodine intake in pregnant populations to prevent either extreme (Table 1).

Table 1: Summary of Included Studies on Maternal Iodine Status, Thyroid Function, and Neonatal Outcomes

References	Study Design	Sample Size	Gestational Age (Weeks)	Iodine Levels (µg/L)	Thyroid Function (TSH, FT4, FT3)	Thyroid Dysfunction Prevalence (%)	Neonatal Outcomes	Confounders Adjusted	Key Findings
[16]	Observational Cohort	212	The second half of pregnancy	Group 1: <106.96; Group 2: 106.96–259.08; Group 3: >259.08	FT4↓, TSH↑	Not specified	Low birth weight	Not specified	Lower iodine levels linked to lower FT4, higher TSH; risk of LBW
[17]	Longitudinal Cohort	1,000	Early pregnancy	Median SIC: 60.3	FT4↓, TSH↑	Not specified	Lower birth weight	Age, BMI, education, parity, GWG	Low SIC linked to thyroid dysfunction and LBW
[1]	Prospective Cohort	559	All trimesters	Median SIC: 79.6	FT3↓, FT4↓, TSH↑	Not specified	Neonatal TSH levels	Age, gestational week, thyroid disorders	SIC influences maternal and neonatal thyroid hormones
[23]	Cross-Sectional	835	Not specified	Not directly measured	Altered thyroid hormones due to phthalates	Not specified	Birth weight changes	Age, education, smoking, SES	Pollution + iodine deficiency impact thyroid function and birth weight
[18]	Prospective Cohort	118	All trimesters	Median Tg: 16.5	Isolated hypothyroxinemia	OR = 3.4 (95% CI: 1.2–9.9)	LGA risk	Not specified	Iodine deficiency linked to hypothyroxinemia and LGA
[19]	Prospective Cohort	57	Not specified	Measured post-HSG	Neonatal TSH↑, FT4↓	No primary hypothyroidism	Altered thyroid markers	Not specified	High maternal iodine → altered neonatal thyroid levels
[24]	Prospective Cohort	202	Not specified	Dietary + UIC	Tg↑, Ft4 measured	Not specified	LGA	Age, BMI, parity, smoking	Tg >13 µg/L linked to LGA births (HR = 3.4)
[20]	Prospective Observational	400	Term neonates (≥37 wks)	UIC ≥500 µg/L	Neonatal TSH at birth, follow-up FT3/FT4	TSH ≥11 mIU/L in 12.2%	Transient hyperthyrotropinemia	Not specified	Excess iodine linked to temporary thyroid dysfunction in neonates
[21]	Nested Case-Control	448 (199 cases, 249 controls)	10–14 weeks	Q1: 0.1–6.5; Q2–3: 6.7–38.3; Q4: 38.3–228.3	Tg, TSH measured	Not specified	Stillbirth	Age, BMI, SES, smoking	No link between iodine and stillbirth in mildly deficient settings
[22]	Prospective Cohort	Not specified	Not specified	UIC	TSH, FT4	Not specified	BW, length, HC, Apgar	Age, BMI, smoking, education	Both low and high iodine are linked to poor birth outcomes

DISCUSSION

The findings of this systematic review highlight the critical role of maternal iodine status in determining neonatal health outcomes. Both Zha *et al.*, and Liu *et al.*, reported significant associations between iodine deficiency and low birth weight, consistent with earlier literature linking inadequate maternal iodine to poor fetal growth and adverse pregnancy outcomes [16, 17]. These results were supported by evidence that iodine deficiency may lead to maternal hypothyroxinemia, which impairs fetal brain and physical development. However, this view is not universally held; for example, researchers found no significant relationship between mild iodine deficiency and stillbirth, illustrating a key controversy in the field it was according to the previous systemic reviews [25-27]. A review by Nazeri *et al.*, emphasized the association between iodine intake and birth weight but noted a lack of consistent evidence linking mild iodine deficiency to neurocognitive impairments in children [28]. This discrepancy underscores the need for well-designed longitudinal studies that examine both immediate and long-term consequences of maternal iodine intake [29]. While iodine deficiency is widely recognized, this review also draws attention to the potential risks of iodine excess. Mathews *et al.*, and Rao *et al.*, identified high maternal iodine intake (UIC \geq 500 μ g/L) as a trigger for transient neonatal hyperthyrotropinemia [19, 20]. These findings align with previous work by Nazarpour *et al.*, who warned that excessive fetal exposure to iodine may impair thyroid function regulation [7]. Although some studies suggest that neonatal thyroid disturbances may normalize postnatally, others caution that maternal overconsumption of iodine can increase the likelihood of persistent hypothyroidism in neonates [30, 31]. This inconsistency supports the need for individualized monitoring of iodine intake during pregnancy. Beyond direct iodine intake, environmental and dietary factors also influence maternal thyroid function. Zha *et al.*, reported that phthalate exposure negatively affects iodine metabolism and maternal thyroid hormone levels [1]. Similar findings were echoed in other environmental health studies, which emphasize the vulnerability of iodine metabolism to endocrine-disrupting chemicals (EDCs) [32, 33]. Additionally, many studies highlighted the influence of dietary iodine intake on maternal thyroglobulin levels and neonatal growth, aligning with evidence that food-based iodine alone is often insufficient to meet pregnancy demands [34, 35]. In summary, this review supports prior research linking iodine status with neonatal outcomes, while also expanding on the dual risks of both deficiency and excess. Unlike earlier reviews that focused primarily on fetal neurodevelopment, this study incorporates additional outcomes such as birth weight and thyroid regulation, along with environmental interactions. Furthermore, while previous reviews have supported universal iodine supplementation policies, our findings emphasize the need

for tailored strategies that account for regional dietary habits, environmental exposures, and individual maternal risk factors.

This review is limited by significant heterogeneity across included studies in terms of study designs, iodine measurement methods, sample sizes, and outcome definitions, which precluded meta-analytic pooling and may affect the generalizability of findings. Additionally, most studies did not adequately adjust for confounding variables such as dietary patterns, socioeconomic status, and environmental exposures, introducing potential bias. Future research should prioritize well-designed, large-scale prospective cohort studies that establish region-specific iodine intake thresholds, evaluate long-term neurodevelopmental outcomes in offspring, and systematically investigate the combined effects of iodine status and endocrine-disrupting chemical exposure during pregnancy.

CONCLUSIONS

It was concluded that this systematic review highlights the importance of iodine status in maternal health and pregnancy outcomes. Both deficient and excess iodine levels can lead to thyroid complications and difficulties in neonatal health. The results suggest that routine monitoring of maternal iodine status and personalized supplementation based on regional needs should be prioritized. Future research should focus on establishing region-specific iodine intake thresholds and evaluating long-term outcomes through prospective cohort studies.

Authors' Contribution

Conceptualization: SA

Methodology: MI, MIK

Formal analysis: OK, AI, UF

Writing And Drafting: SA, MI, MIK, OK, AI, UF

Review and editing: SA, MI, MIK, OK, AI, UF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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