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Research Progress in Nursing Interventions for Isolated Maternal Hypothyroxinemia during Pregnancy

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Abstract

Isolated maternal hypothyroxinemia (IMH) is a common thyroid dysfunction during pregnancy. Its prevalence varies substantially according to iodine status, diagnostic criteria, and the use of pregnancy-specific reference ranges. IMH is closely associated with iodine imbalance, iron deficiency, advanced maternal age, parity, pre-pregnancy obesity, and other maternal characteristics. It has been linked to an increased risk of adverse pregnancy outcomes, including macrosomia, preterm birth, gestational diabetes mellitus, and hypertensive disorders of pregnancy, and may also affect offspring neurodevelopment. However, the optimal treatment strategy for IMH remains controversial, highlighting the growing importance of nursing interventions in clinical management. This review summarizes recent progress in nursing interventions for IMH, focusing on early screen and identification, health education and lifestyle management, medication-related nursing care, psychological support, postpartum care and follow-up, multidisciplinary collaboration and continuing care, and digital and intelligent nursing approaches. Current nursing strategies have gradually formed an integrated management model centered on nutritional intervention, particularly iodine and iron optimization. Nevertheless, important limitations remain, including inconsistent intervention standards and insufficient individualized care. This review aims to provide a theoretical basis for optimizing nursing protocols and improving maternal and neonatal health outcomes in pregnant women with IMH.

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Keywords

Isolated Maternal Hypothyroxinemia during Pregnancy, Nursing Intervention, Iodine Nutrition, Iron Deficiency

1. Introduction

Isolated maternal hypothyroxinemia (IMH), also referred to as isolated low thyroxine syndrome during pregnancy, is defined as a thyroid functional state in which pregnant women are negative for thyroid autoantibodies, have normal serum thyroid-stimulating hormone (TSH) levels, but show free thyroxine (FT4) concentrations below the lower limit of the pregnancy-specific reference range [1]. IMH is one of the common forms of thyroid dysfunction during pregnancy. Its reported prevalence varies widely because of differences in regional iodine status, diagnostic thresholds, and reference intervals, ranging from 0.2% to 31.0% across studies [2]. A recent meta-analysis reported a pooled prevalence of 2.1%, with higher rates observed in iodine-deficient countries and in studies that did not use pregnancy-specific reference ranges [3].

It should be noted that most reported links between IMH and adverse maternal or offspring outcomes are observational associations, and they should not be interpreted as direct evidence that treatment or nursing intervention necessarily prevents these outcomes. With the increasing implementation of thyroid function screening during pregnancy, the detection rate of IMH has gradually increased, and its potential impact on maternal and offspring health has received growing clinical attention. Evidence suggests that IMH is associated with adverse pregnancy outcomes such as macrosomia, preterm birth, gestational diabetes mellitus, and hypertensive disorders of pregnancy. It may also increase the risk of impaired intellectual development, autism spectrum disorder, attention-deficit/hyperactivity disorder, and other neurodevelopmental abnormalities in offspring [4]. At present, treatment strategies for IMH remain controversial. Under this circumstance, nursing intervention has become increasingly important. In recent years, researchers in China and abroad have conducted studies on nursing strategies for IMH and have proposed several targeted intervention approaches. However, clinical implementation is still limited by the lack of standardized intervention pathways and insufficient individualized care. This review summarizes the current research status of nursing interventions for IMH during pregnancy, with the aim of promoting early identification and intervention and reducing IMH-related adverse maternal and neonatal outcomes.

2. Main Etiologies of Isolated Maternal Hypothyroxinemia during Pregnancy

IMH is a multifactorial condition. Although its pathogenesis has not been fully clarified, accumulating evidence indicates that it is closely associated with iodine

abnormalities, iron deficiency, physiological adaptations during pregnancy, body weight and metabolic status, and maternal demographic characteristics. Among these, disturbances in iodine and iron nutrition are considered the two most important and clinically modifiable risk factors [5].

2.1. Iodine Abnormalities

Iodine is an essential substrate for thyroid hormone synthesis, and iodine imbalance is considered the most common and important cause of IMH [6]. During pregnancy, the maternal glomerular filtration rate increases, urinary iodine excretion rises, and fetal iodine demand gradually increases. Consequently, maternal iodine requirements are significantly higher during pregnancy than before pregnancy [7]. In 2007, the World Health Organization recommended a daily iodine intake of 250 μg for pregnant women and established criteria for iodine nutrition assessment during pregnancy: urinary iodine concentration (UIC) <150 μg/L indicates iodine deficiency, 150 - 249 μg/L indicates adequate iodine nutrition, 250 - 499 μg/L indicates more-than-adequate iodine intake, and ≥500 μg/L indicates excessive iodine intake [5].

When iodine intake is insufficient, the substrate required for thyroid hormone synthesis becomes inadequate. Although the maternal thyroid gland is stimulated to compensate for the increased requirement for thyroid hormone during pregnancy, this compensatory mechanism may fail to meet the elevated physiological demand, ultimately leading to decreased FT4 with normal TSH levels, which is characteristic of IMH. In iodine-deficient regions, the prevalence of IMH is significantly increased. In a population-based study of pregnant women in Iran, Etemadi *et al.* reported that the prevalence of IMH reached 9.9% in mildly iodine-deficient areas, which was significantly higher than that in iodine-sufficient areas and represented the most common thyroid dysfunction during pregnancy [8].

Notably, excessive iodine intake may also increase the risk of IMH. In iodine-sufficient regions, excessive iodine intake during early pregnancy may inhibit thyroid hormone synthesis and release through the Wolff-Chaikoff effect, resulting in transient FT4 reduction and an increased risk of hypothyroxinemia [9]. A Chinese study showed that mild iodine deficiency was associated with an increased risk of gestational diabetes mellitus, while excessive iodine intake reduced maternal FT4 levels and was associated with a macrosomia rate of 12.42%, suggesting that iodine excess may adversely affect both thyroid function and pregnancy outcomes [10]. Therefore, women preparing for pregnancy and pregnant women should maintain appropriate iodine intake. Clinically, regular UIC monitoring may help guide dynamic adjustment of iodine supplementation and ensure that iodine nutrition remains within a sufficient and safe range.

2.2. Iron Deficiency

Iron deficiency is an independent and important cause of IMH [11]. Even under iodine-sufficient conditions, iron deficiency may still reduce maternal thyroid hor-

mone levels [12]. Iron participates in thyroid hormone synthesis and metabolism mainly because it serves as an essential cofactor for thyroid peroxidase (TPO). Iron deficiency may inhibit TPO activity, reduce thyroid hormone synthesis, and thereby contribute to hypothyroxinemia [7].

Several clinical studies have confirmed a significant association between iron deficiency and IMH. In a prospective cohort study of 596 thyroid peroxidase antibody (TPOAb)-negative women in early pregnancy, Rosario *et al.* reported that the incidence of IMH was significantly higher in the iron-deficient group. When FT4 was < 0.86 ng/dL, the incidence of IMH was 14.8% in iron-deficient women, markedly higher than the 3.9% observed in women without iron deficiency, indicating that iron deficiency is independently associated with IMH [13]. A systematic review by Parsaei *et al.*, which included 47 studies and 53,152 pregnant women, showed that FT4 levels were significantly lower in women with iron deficiency than in controls (10.7 pmol/L vs. 13.3 pmol/L), further supporting the inhibitory effect of iron deficiency on FT4 production during pregnancy [14]. Because pregnancy is characterized by plasma volume expansion and increased fetal and placental iron demand, iron deficiency is highly prevalent and represents an important target for the prevention and intervention of IMH.

2.3. Other Risk Factors

In addition to iodine and iron abnormalities, large epidemiological studies have shown that maternal demographic and constitutional factors are also independent risk factors for IMH. These include age, parity, place of residence, and pre-pregnancy body mass index (BMI), which may provide important information for high-risk screening and risk-stratified management.

A nationwide cross-sectional study conducted by Etemadi *et al.* in Iran showed that, after adjustment for iodine status and thyroid autoantibody levels, pregnant women aged ≥30 years had a 1.6-fold higher risk of IMH than younger women (OR = 1.6, 95% CI: 1.0 - 2.5) [8]. Similarly, a large cross-sectional study by Liu *et al.*, including 54,586 singleton pregnant women, demonstrated that age ≥35 years (OR = 1.30, 95% CI: 1.20 - 1.40), non-local residence, multiparity (≥2 pregnancies, OR = 1.11), pre-pregnancy overweight or obesity, and iron deficiency were all independent risk factors for IMH. These findings suggest that maternal age, residence, parity, BMI, and iron status should be incorporated into comprehensive IMH risk assessment [15].

Recent evidence has further clarified the role of obesity in the development and progression of IMH. In a 2025 retrospective cohort study including 11,478 pregnant women, Zhang *et al.* found that women with pre-pregnancy obesity (BMI ≥30 kg/m^2) had a 6.96-fold higher risk of IMH than women with normal body weight (95% CI: 4.58 - 10.58). In addition, obesity and IMH showed a significant synergistic effect on the risk of large-for-gestational-age infants in late pregnancy. When both conditions coexisted, the risk of macrosomia increased to 7.60 times that of women with normal pre-pregnancy weight and normal thyroid function

(95% CI: 5.26 - 10.97) [16].

Overall, maternal age ≥30 - 35 years, multiparity, rural or non-local residence, pre-pregnancy overweight or obesity, and iron deficiency are independent risk factors for IMH. Identification of these factors may facilitate the development of early warning models for high-risk populations and provide a basis for early screening, stratified management, and individualized nursing intervention.

3. Current Status of Nursing Interventions for Isolated Maternal Hypothyroxinemia during Pregnancy

3.1. Early Screening and Identification

Early screening and identification are the foundation of nursing intervention for IMH and are essential for reducing adverse maternal and neonatal outcomes. At present, international and Chinese guidelines differ in their recommendations for thyroid function screening during pregnancy. The central controversy lies in whether universal screening or targeted screening of high-risk populations should be adopted.

The 2025 Royal College of Obstetricians and Gynaecologists (RCOG) guideline on the management of thyroid disorders in pregnancy does not recommend universal thyroid function screening for all pregnant women and instead supports screening only among subgroups with specific risk factors [17]. In contrast, the 2022 Chinese Guideline for the Prevention and Management of Thyroid Diseases During Pregnancy and the Perinatal Period recommends that all women should undergo thyroid disease screening in early pregnancy, preferably before 12 weeks of gestation, regardless of whether preconception thyroid screening was normal. The recommended screening indicators should include at least serum TSH, FT4, and TPOAb [4].

Liu *et al.* found that age ≥ 35 years, non-local residence, multiparity, pre-pregnancy overweight or obesity, and iron deficiency were independent risk factors for IMH [15]. Zhou *et al.* developed a nomogram for predicting adverse pregnancy outcomes based on a cohort of 1,254 pregnant women with IMH. Embedding such risk prediction models into obstetric outpatient systems may enable automatic identification of high-risk patients and real-time clinical reminders, thereby reducing missed screening and delayed diagnosis [18]. Therefore, nursing staff should focus on identifying women at high risk of thyroid dysfunction, reminding them to complete timely screening, improving screening adherence, and promoting early detection, early assessment, and early intervention.

In clinical practice, nurses may follow a simple workflow for IMH management. At the first prenatal contact, nurses should assess gestational age, thyroid screening results, thyroid antibody status, iodine intake, iron status, dietary pattern, pre-pregnancy BMI, parity, residence, previous thyroid disease, and family history of thyroid disorders. During follow-up, key items include repeated thyroid function tests when indicated, UIC or dietary iodine exposure, ferritin or hemoglobin levels, adherence to nutritional supplementation, symptoms of thyroid dysfunction,

psychological distress, and fetal growth-related findings. Referral to endocrinology should be considered when FT4 remains persistently low, TSH becomes abnormal, thyroid autoantibodies are positive, goiter or thyroid nodules are present, severe iodine excess or deficiency is suspected, LT4 therapy is being considered, or abnormal thyroid function persists after delivery.

3.2. Health Education and Lifestyle Intervention

Health education is a core component of non-pharmacological management for IMH. It helps improve disease awareness, strengthen self-management capacity, and enhance adherence to treatment and nursing interventions. Standardized health education can guide pregnant women in developing a balanced diet and healthy lifestyle, thereby improving the nutritional environment required for thyroid hormone synthesis, reducing the risk of IMH, and improving maternal and neonatal outcomes [19].

Iodine is indispensable for thyroid hormone synthesis, and iodine imbalance during pregnancy is closely related to IMH. The 2025 RCOG guideline recommends that women planning pregnancy, pregnant women, and breastfeeding women should maintain a daily iodine intake of 200 - 250 μg, while avoiding sustained iodine intake above 500 μg/day [20]. Excessive iodine intake may lead to maternal and fetal thyroid dysfunction [17] and increase the risk of adverse outcomes such as macrosomia [21].

Regarding iron nutrition, nursing staff should provide targeted dietary guidance. Pregnant women should be encouraged to consume heme iron-rich foods with high bioavailability, such as animal liver and red meat, together with fresh fruits and vegetables rich in vitamin C to promote iron conversion and absorption. Evidence shows that nutrition education during pregnancy can significantly improve adherence to iron–folic acid supplementation, increase hemoglobin levels, and reduce the risk of iron-deficiency anemia during pregnancy [22]. In addition, the International Federation of Gynecology and Obstetrics (FIGO) recommended in 2025 that, in regions with a high prevalence of multiple micronutrient deficiencies, iron-containing multiple micronutrient supplements should be prioritized over iron-folic acid alone [23]. This approach may help correct nutritional imbalance more comprehensively during pregnancy. Nursing staff should provide individualized supplementation recommendations based on pre-pregnancy BMI, dietary structure, iron stores, and overall nutritional status, thereby optimizing nutritional intervention and improving thyroid function and pregnancy outcomes.

3.3. Medication-Related Nursing Care

Levothyroxine (LT4) is the first-line medication for thyroid dysfunction during pregnancy. However, whether pregnant women with IMH should routinely receive LT4 therapy remains controversial, and no unified consensus has been reached among clinical guidelines or related studies [24] [25]. This makes medi-

cation-related nursing care an important but challenging part of IMH management.

Current guideline recommendations reflect this uncertainty. The RCOG guideline does not provide a specific treatment recommendation for IMH, while the Chinese Guideline for the Prevention and Management of Thyroid Diseases during Pregnancy and the Perinatal Period neither recommends nor opposes routine LT4 therapy in early pregnancy. Rather than advocating universal medication, the Chinese guideline emphasizes etiological assessment and correction of modifiable factors, including iron deficiency, iodine deficiency, and iodine excess [4] [17]. These differences are largely related to inconsistent IMH definitions, variation in pregnancy-specific FT4 reference ranges and assay methods, the predominance of observational evidence, and the limited randomized evidence supporting clear treatment benefit.

A retrospective study by Liu *et al.* further suggested that early initiation of LT4 treatment may be beneficial in selected patients. In pregnant women with IMH who started LT4 treatment at ≤13 + 6 weeks of gestation, FT4 and high-density lipoprotein cholesterol levels increased significantly, while TSH, total cholesterol, triglycerides, and low-density lipoprotein cholesterol levels decreased significantly. The risks of spontaneous abortion, gestational diabetes mellitus, and macrosomia were also reduced. However, when LT4 treatment was initiated at 14 - 20 weeks of gestation, no significant improvement was observed in thyroid function indicators or pregnancy outcomes. These findings suggest that, if LT4 treatment is considered for IMH, earlier initiation may be associated with better clinical benefits [26].

For nursing practice, the key point is not to promote routine LT4 use for all women with IMH, but to support individualized decision-making. Nurses should assist physicians in assessing gestational age, thyroid function, antibody status, iodine and iron status, and pregnancy risk factors. When LT4 is prescribed, nurses should provide medication education, remind patients to take LT4 separately from iron, calcium, or prenatal supplements, monitor adherence, and encourage timely thyroid function reassessment. For women managed without LT4, nurses should emphasize nutritional correction, follow-up testing, and early referral if FT4 remains persistently low or TSH becomes abnormal.

3.4. Psychological Nursing Care

Although psychological nursing has rarely been examined as an independent intervention in IMH populations, studies in pregnant women with other thyroid dysfunctions provide useful clues for clinical practice. Pregnant women with IMH may have specific psychological needs because of limited disease awareness and concerns about the potential effects of thyroid dysfunction on fetal and offspring health. Psychological nursing care has therefore become an indispensable component of multidimensional IMH management.

Based on the Ma'anshan Birth Cohort, Li *et al.* found that the coexistence of

IMH and pregnancy-related anxiety was associated with a higher risk of anxiety/depression and internalizing behavioral problems in preschool children. IMH and pregnancy-related anxiety may exert a synergistic effect on offspring internalizing and externalizing problems [27]. These findings suggest that psychological care should be implemented on the basis of careful assessment of maternal psychological status and should not be separated from nutritional intervention and disease education.

At present, psychological nursing studies specifically targeting IMH remain limited. Most available evidence comes from populations with overt hypothyroidism, subclinical hypothyroidism, or gestational diabetes mellitus complicated by subclinical hypothyroidism. Nevertheless, these findings provide useful references for psychological nursing in IMH. Nursing based on the information–knowledge–attitude–practice (IKAP) model combined with positive psychological intervention has been shown to improve disease control and illness perception in pregnant women with hypothyroidism [28]. This model promotes the transformation of information into knowledge, knowledge into health beliefs, and beliefs into active health behaviors, thereby reducing anxiety caused by uncertainty and inadequate disease understanding.

Group prenatal care has also shown positive effects on psychological status. In pregnant women with gestational diabetes mellitus complicated by subclinical hypothyroidism, the intervention group had significantly lower scores on the Self-Rating Depression Scale (SDS; 20.54 ± 2.88) and Self-Rating Anxiety Scale (SAS; 22.63 ± 3.01) than the control group (31.27 ± 3.14 and 33.24 ± 3.30, respectively). The complication rate was also lower in the intervention group. By organizing pregnant women with similar clinical backgrounds into fixed groups for antenatal examination, interactive health education, and experience sharing, group care can reduce pregnancy-related stress, relieve anxiety, and improve social support [29]. In addition, midwife-led group antenatal health management has been shown to improve childbirth confidence in pregnant women with hypothyroidism [30]. Peer-support psychological nursing can improve well-being and social support among women with hypothyroidism during pregnancy and reduce adverse pregnancy outcomes and postpartum depression [31]. Therefore, psychological nursing for IMH should adopt a multi-level intervention strategy and contribute to a biopsychosocial model of care.

3.5. Postpartum Care and Follow-Up

Postpartum management of IMH has not been well studied as a separate clinical issue, but follow-up remains necessary, especially for women with persistent low FT4, thyroid autoantibody positivity, or suspected iodine or iron imbalance. Recent guidelines and consensus statements also recommend reassessing thyroid function during the postpartum period in women who experienced thyroid dysfunction during pregnancy.

The 2025 RCOG guideline recommends that all women who receive manage-

ment for thyroid dysfunction during pregnancy should have thyroid function reassessed during the postpartum recovery period, with medication adjusted as needed [17]. Women with complex disease or persistent abnormal indicators should be referred by obstetricians to endocrinologists for ongoing follow-up, so as to avoid missed diagnosis, delayed management, or disease progression.

In clinical practice, individualized postpartum follow-up should be implemented according to the underlying cause of IMH. For women with transient IMH caused by iron deficiency or iodine deficiency, thyroid function may return to normal after postpartum correction of nutritional imbalance and removal of the causative factor. For women with persistent hypothyroxinemia or positive thyroid autoantibodies, thyroid function should be rechecked at 6 weeks postpartum to identify early signs of postpartum thyroiditis and avoid unnecessary long-term LT4 therapy [32]. The 2025 edition of the global management standards for thyroid diseases during pregnancy and postpartum, formulated by the American Thyroid Association, has updated the postpartum diagnosis tools and expanded the risk assessment framework, thereby providing more flexibility in the testing period and individualized medication adjustments. This offers precise guidance based on the latest clinical evidence for future postpartum monitoring and long-term stratified follow-up of IMH.

3.6. Multidisciplinary Collaboration and Continuing Care

Although IMH-specific evidence remains limited, multidisciplinary care is particularly suitable for IMH because its management often requires simultaneous attention to thyroid function, iodine and iron nutrition, pregnancy outcomes, and psychological status. A multidisciplinary nursing model has gradually been introduced into the clinical management of IMH. By integrating medical and nursing resources from different specialties, this model strengthens communication and collaboration among nurses and other healthcare professionals and provides systematic, comprehensive, and integrated care for pregnant women.

Han *et al.* proposed a six-in-one cooperative nursing model that integrates obstetrics, endocrinology, neonatology, psychology, nutrition, and community nursing. This model defines the responsibilities and collaboration procedures of each discipline and establishes a seamless management pathway from pregnancy screening and intervention to postpartum follow-up, thereby improving the quality of perinatal nursing care [33]. Multidisciplinary collaboration and continuing care can help establish a patient-centered, life-cycle health management model for women with IMH, and provide continuous and comprehensive nursing services.

3.7. Digital and Intelligent Nursing

With the rapid development of mobile internet, artificial intelligence, and wearable devices, digital and intelligent nursing has gradually been incorporated into the full-cycle management of IMH. Digital nursing has not yet been fully validated in IMH-specific cohorts, but its functions—such as follow-up reminders, nutri-

tion recording, medication alerts, and remote monitoring—match several key needs in IMH management. A narrative review on postpartum thyroid dysfunction suggested that telemedicine has potential value in individualized care for thyroid dysfunction [34].

Mahdavi *et al.* developed a mobile self-management application for pregnant women with hypothyroidism. The application included nine functional modules, such as medication reminders, follow-up reminders, and nutrition records. When combined with indicators such as UIC and ferritin, such tools may be used to provide individualized dietary recommendations [35]. Overdijkink *et al.* reported that mobile health technology-based lifestyle and medical intervention applications are feasible and acceptable in pregnancy health management. Through individualized education, remote monitoring, and intelligent reminders, these applications may improve adherence to interventions and increase medication adherence among pregnant women with chronic diseases by 20% - 30% [36].

Although digital and intelligent nursing has considerable potential, it still faces several challenges, including insufficient clinical validation, variation in patient acceptance, and lack of unified standards. With continued development of digital health technologies, digital and intelligent nursing is expected to become an important breakthrough in optimizing full-cycle IMH management and improving maternal and neonatal outcomes.

4. Limitations

Several limitations should be acknowledged. First, the definition of IMH varies across studies, particularly with regard to FT4 cut-off values, gestational age at diagnosis, antibody status, and the use of pregnancy-specific reference ranges. Second, FT4 reference intervals differ substantially according to assay methods, population characteristics, iodine status, and laboratory standards, which may affect the comparability of prevalence estimates and intervention thresholds [37]. Third, direct evidence on nursing interventions specifically designed for IMH remains limited, and many current recommendations are extrapolated from studies of overt hypothyroidism, subclinical hypothyroidism, gestational diabetes with thyroid dysfunction, or general pregnancy care. Therefore, future research should prioritize well-designed prospective studies and nurse-led intervention trials focused specifically on IMH [38].

5. Summary and Perspectives

IMH is a common thyroid dysfunction during pregnancy and an important target for perinatal prevention and management. It is primarily associated with iodine imbalance and iron deficiency, while also being influenced by maternal age, prepregnancy obesity, parity, and other demographic and constitutional factors. IMH is closely related to adverse pregnancy outcomes and may also affect long-term neurodevelopment in offspring.

Current nursing interventions for IMH mainly focus on screening and identi-

fication, health education, medication-related nursing care, psychological support, and postpartum follow-up. An integrated nursing strategy centered on iodine and iron nutritional intervention has gradually emerged. However, standardized nursing pathways and high-quality evidence remain insufficient. Future studies should strengthen the integration of multidisciplinary collaboration and continuing care, explore nurse-led full-cycle health management models for IMH, and improve continuous care pathways covering preconception, pregnancy, and the postpartum period. High-quality clinical studies are needed to validate the effectiveness of these interventions. Ultimately, IMH nursing practice should move toward standardization, individualization, and precision, thereby protecting maternal physical and mental health and improving long-term developmental outcomes in offspring.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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