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REVIEW ARTICLE

# Prevalence of Congenital Hypothyroidism in Iranian Neonates: A Systematic Review and Meta-Analysis

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## Abstract

**Background** Congenital hypothyroidism, characterized by insufficient thyroid hormone production at birth, significantly impacts neonatal growth and development. This deficiency can impair neonatal growth and development. This study aimed to estimate the prevalence of congenital hypothyroidism in Iranian neonates through a systematic review and meta-analysis.

**Methods** A systematic search was conducted in PubMed, Scopus, Web of Science, Science Direct, SID, and Magiran up to January 2025 to identify relevant studies. Manual searches of key review articles and primary studies were also performed. Only studies published in Persian or English were included. The Newcastle-Ottawa Scale checklist was used to assess the risk of bias in the selected studies. Data were analyzed using Comprehensive Meta-Analysis software (version 3).

**Results** Thirty-nine studies, comprising 3,124,702 neonates, were included in the analysis. The meta-analysis showed a congenital hypothyroidism prevalence of 2 per 1000 live births (95% CI: 0.002–0.003; $p < 0.05$). The prevalence was 3 per 1000 live births in both males (95% CI: 0.002–0.004; $p < 0.05$) and females (95% CI: 0.002–0.004; $p < 0.05$). No significant publication bias was observed ($p > 0.05$).

**Conclusion** The elevated prevalence of congenital hypothyroidism in Iran highlights the necessity for enhanced screening programs, early diagnostic protocols, intervention, and allocation of necessary resources are essential for the effective management of congenital hypothyroidism prevalence.

**Keywords** Congenital hypothyroidism, Infant, Iran, Meta-Analysis, Prevalence, Systematic review

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## 1 Introduction

Congenital hypothyroidism refers to a condition where the production of thyroid hormones, essential for normal growth and development, is insufficient at birth. This condition may result from various causes, including thyroid gland abnormalities, genetic mutations affecting hormone synthesis, or maternal factors such as iodine deficiency during pregnancy.[1, 2]

Congenital hypothyroidism can be classified into permanent and transient types, with permanent cases requiring lifelong thyroid hormone treatment to prevent developmental delays and other complications.[3, 4] The importance of early diagnosis and treatment of this condition cannot be overstated, as untreated congenital hypothyroidism can lead to severe intellectual disabilities and physical growth disorders. This condition is particularly significant because thyroid hormones play a crucial role in brain development during the early years of life. Insufficient hormone levels can disrupt neurodevelopmental processes, leading to long-term cognitive impairments.[5]

The impact of congenital hypothyroidism on infant health is profound and multifaceted. Untreated infants with congenital hypothyroidism typically present with symptoms such as poor feeding, lethargy, decreased muscle tone, and prolonged jaundice. Without timely diagnosis, these infants may develop serious complications, including growth retardation and developmental disorders.[6]

Thyroid hormones are crucial for brain development, particularly during the first few years of life when rapid neuronal development occurs. Therefore, untreated congenital hypothyroidism can lead to irreversible cognitive damage and developmental disorders. Furthermore, the long-term effects of congenital hypothyroidism extend beyond infancy into childhood and adulthood.[7]

Studies demonstrate that individuals diagnosed and treated at younger ages typically exhibit normal cognitive function and growth patterns. In contrast, those with delayed diagnosis or no treatment often require additional educational support services. This underscores the critical importance of early intervention in mitigating the adverse effects of congenital hypothyroidism.[8, 9]

The global prevalence of congenital hypothyroidism varies significantly due to factors including geographic location, dietary iodine intake, and differences in healthcare practices. Current estimates indicate that congenital hypothyroidism affects approximately one in 2,000 to 4,000 live births.[10] Regions with a prevalence of iodine deficiency, such as parts of Africa and Southeast Asia, typically exhibit higher rates due to insufficient maternal iodine levels during pregnancy. Conversely, countries with effective iodine supplementation programs generally report lower prevalence rates.[11]

In Iran, the reported prevalence of congenital hypothyroidism remains significantly higher than in many developed countries. Studies indicate an incidence of approximately one in 2,000 live births among Iranian neonates. This elevated rate may stem from multiple factors, including regional variations in dietary iodine intake and genetic predispositions. Despite public health initiatives to improve iodine nutrition, some regions continue to experience iodine deficiency, contributing to higher congenital hypothyroidism rates. In comparison, countries with effective neonatal screening programs typically report lower prevalence rates due to early diagnosis and intervention.[12]

For instance, countries like the United States have implemented universal screening programs, enabling prompt diagnosis and management of affected neonates.[13] Neonatal screening programs play a vital role in the early detection of congenital hypothyroidism by identifying affected infants immediately after birth. These screenings are typically performed within the first few days postpartum through heel-prick blood samples measuring thyroid-stimulating hormone or thyroxine levels. Early identification enables prompt intervention with thyroid hormone replacement therapy, which is crucial for preventing severe consequences of untreated congenital hypothyroidism.[6]

Given the importance of estimating congenital hypothyroidism prevalence for healthcare systems and policy-making, this study aimed to determine the prevalence of congenital hypothyroidism in Iranian neonates. These findings will help inform the development of strategies for early diagnosis, intervention, and resource allocation. Accurate prevalence data enables health authorities to identify the scale of the problem in specific populations and implement targeted screening programs that can significantly prevent avoidable intellectual disabilities resulting from untreated congenital hypothyroidism.

Furthermore, understanding disease prevalence helps evaluate the effectiveness of existing public health initiatives and informs future policies aimed at improving maternal and child health outcomes. By incorporating these data into health planning, policymakers can ensure adequate allocation of resources for screening programs, healthcare provider training, and public awareness campaigns. This approach will ultimately improve health outcomes for affected neonates and reduce long-term healthcare costs associated with untreated conditions.

## 2 Methods

This study was conducted according to the PRISMA

checklist. Electronic databases including PubMed, Scopus, Web of Science, Science Direct, Scientific Information Database, and Magiran were systematically searched by two independent researchers up to January 2025 to identify relevant articles. To improve search sensitivity and identify additional evidence, a manual search was performed in other sources, key journals, and reference lists. Database-specific search strategies were developed for each electronic database. The search included articles published in Persian and English. The keywords used were "Congenital hypothyroidism", "Infant", "Iran", "Meta-Analysis", "Prevalence", "Systematic review".

EndNote version 8 was used to collect, organize, and screen the searched articles. Following comprehensive database searches and manual searches of other sources, two authors independently conducted the article screening process. Duplicate articles were first removed, and the remaining articles were screened based on title and abstract. Studies that failed to meet the inclusion criteria were excluded from the screening process. Subsequently, the full texts of eligible articles were reviewed. Disagreements between researchers were resolved through discussion with a third reviewer and consensus. The PubMed search strategy was as follows:

(((infants [MeSH Terms]) OR (infants [Title/Abstract]) OR (Neonate [MeSH Terms]) OR (Neonate [Title/Abstract]) OR (Newborn [Title/Abstract])) AND ((Congenital Hypothyroidism [MeSH Terms]) OR (Congenital Hypothyroidism [Title/Abstract])) AND (Iran [Title/Abstract]))

### Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) neonates with congenital hypothyroidism, (2) Observational studies (cross-sectional, cohort, and case-control), (3) Articles published in either Persian or English that reported the prevalence of congenital hypothyroidism in neonates, (4) Studies that used valid and standardized tools for assessing congenital hypothyroidism prevalence in neonates. In Iran's congenital hypothyroidism screening program, thyroid-stimulating hormone measurement was used as the primary diagnostic indicator, consistent with international guidelines, including those from WHO and the European Society for Pediatric Endocrinology. Heel-prick blood samples were collected three to five days postpartum, as this timeframe is optimal for screening due to stabilized TSH levels following initial physiological changes. The standard TSH cutoff in Iran was ≥ 5 mIU/L in the first week of life and ≥ 4 mIU/L after day 8, consistent with international standards for early congenital hypothyroidism detection. For TSH levels exceeding the cutoff, confirmatory tests - including free thyroxine and serum TSH measurements - were performed to differentiate permanent from transient hypothyroidism. Sampling utilized standard filter paper (Whatman 903), with TSH measurement performed using immunoassay methods (ELISA) or more advanced techniques (CLIA), ensuring high accuracy and sensitivity.

The exclusion criteria comprised: (1) letters to the editor, editorials, case reports, review articles, and studies with unavailable full texts, (2) Studies not using valid and standardized tools for assessing congenital hypothyroidism in neonates, (3) Studies where calculation of congenital hypothyroidism prevalence in neonates was not possible.

Two investigators independently extracted data using standardized Excel forms. The extracted data included author names, study location, publication year, study design, sample size, and prevalence of congenital hypothyroidism. For sex-specific analyses, only studies reporting stratified data (n = 17) were included, yielding a smaller sample than the overall analysis.

### Risk of Bias Assessment

The Newcastle-Ottawa Scale was used to assess the risk of bias in the included studies.[14] This scale evaluates observational studies across three domains: selection (including representativeness, sample size, non-respondents, and exposure determination), comparability, and outcome assessment. Studies were scored on a 9-point scale, with higher scores indicating lower risk of bias. Study quality was categorized as high (scores ≥ 7), moderate (scores 5-6), or low (scores ≤ 4).

### Evidence Synthesis and Statistical Analysis

Data analysis was performed using Comprehensive Meta-Analysis software (version 3.0). Heterogeneity was assessed using Cochran's Q test and $I^2$ statistics, with $I^2 > 50\%$ and $p < 0.1$ indicating significant heterogeneity. Heterogeneity levels were classified as low ($I^2 < 25\%$), moderate ($I^2 = 25\text{-}75\%$), or high ($I^2 > 75\%$). A random-effects model was applied due to substantial observed heterogeneity. Publication bias was evaluated using Egger's test at a significance level of 0.05.

## 3 Results

The study screening, identification, and selection process is illustrated in Figure 1 using the PRISMA framework. The initial electronic database search identified 264 studies, of which 127 duplicate studies were excluded, leaving 137 studies for screening. Two researchers independently screened these studies by title and abstract. At this stage, 89 studies were excluded for not meeting the inclusion criteria, leaving 48 eligible studies for full-

text review. After full-text assessment against inclusion/exclusion criteria, nine additional studies were excluded. Ultimately, 39 studies (range: 15-52) comprising 3124702 neonates were included in the meta-analysis. Characteristics of included studies are presented in Table 1.

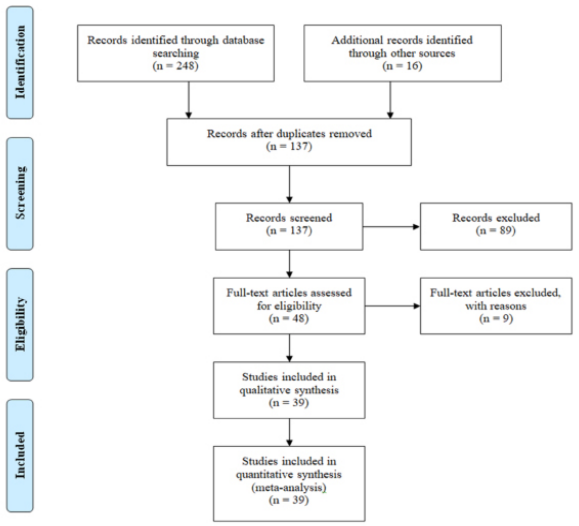


**Figure 1** Identification, screening, and selection process of included studies based on PRISMA structure

### Study Quality Assessment

The risk of bias in the included studies was assessed using the Newcastle-Ottawa Scale. The scores for included studies ranged from 6 to 7, with higher scores indicating lower risk of bias. The quality scores are presented in Table 2. Results indicated that 38.46% of studies (15 studies) were categorized as high quality (score = 7) and 61.54% (24 studies) as moderate quality (score = 6).

### Prevalence of Congenital Hypothyroidism in Neonates

Heterogeneity testing based on $I^2$ (98.19%) and significance level ($p < 0.05$) indicated substantial heterogeneity among studies, necessitating the use of a random-effects model. Thirty-nine studies (N=3,124,702 neonates) examined the prevalence of congenital hypothyroidism. The prevalence was 2 cases per 1000 live births (95% CI: 0.002-0.003, $p < 0.05$) (Figure 2).

### Prevalence of Congenital Hypothyroidism in Male Neonates

Heterogeneity testing based on $I^2$ (94.34%) and significance level ($p < 0.05$) indicated substantial heterogeneity, requiring the use of a random-effects model. Seventeen studies involving 276,910 male neonates examined the prevalence. The prevalence was 3 per 1000 live births (95% CI: 0.002-0.004, $p < 0.05$) (Figure 3).

**Table 1** Characteristics of studies included in the systematic review and meta-analysis

| Author | Year | Province | Sample Size | CH* Prevalence (per 1000 neonates) | Study Design | N O S * * Score |
|---|---|---|---|---|---|---|
| Mohtasham | 2024 | Gilan | 26,738 | 4.2 | Cross-sectional | 6 |
| Koohshouri | 2022 | Chaharmahal-Bakhtiari | 128,650 | 5 | Cross-sectional | 6 |
| Habib | 2021 | Fars | 294,214 | 1.3 | Cross-sectional | 7 |
| Soodejani | 2020 | Chaharmahal-Bakhtiari | 54,486 | 2 | Cross-sectional | 7 |
| Zamani | 2019 | Lorestan | 13,741 | 6.1 | Cross-sectional | 6 |
| Hemmati | 2019 | Fars | 389,101 | 3.2 | Cross-sectional | 6 |
| Amiri | 2019 | Kerman | 4,998 | 4.7 | Cross-sectional | 7 |
| Deliri | 2019 | Ilam | 106,900 | 6.2 | Cross-sectional | 7 |
| Hemmati | 2018 | Isfahan | 320,886 | 1.1 | Cross-sectional | 7 |
| Pikani | 2018 | Razavi Khorasan | 4,484 | 6.2 | Cross-sectional | 6 |
| Beheshti | 2018 | Mazandaran | 269,088 | 4.1 | Cross-sectional | 6 |
| Mirzarahimi | 2017 | Ardabil | 158,624 | 3.1 | Cross-sectional | 6 |
| Mobaraki | 2016 | West Azerbaijan | 17,074 | 6.0 | Cross-sectional | 6 |
| Shojaeifar | 2016 | Yazd | 51,973 | 3.3 | Cross-sectional | 6 |
| Keshavarzian | 2016 | Khuzestan | 11,941 | 16 | Cross-sectional | 7 |
| Ghasemi | 2015 | Tehran | 464,648 | 4.3 | Cross-sectional | 7 |
| Mahmoudi | 2015 | Golestan | 45,360 | 1 | Cross-sectional | 7 |
| Nasehi | 2014 | Mazandaran | 37,117 | 4.1 | Cross-sectional | 6 |
| Haghshanas | 2014 | Mazandaran | 10,573 | 6.2 | Cross-sectional | 6 |
| Siami | 2013 | Mazandaran | 139,111 | 2 | Cross-sectional | 6 |
| Valizadeh | 2013 | Zanjan | 18,008 | 1.1 | Cross-sectional | 6 |

**Table 1** (continued)

| | | | | | | |
|---|---|---|---|---|---|---|
| Karimi | 2013 | Razavi Khorasan | 2,500 | 2.1 | Cross-sectional | 6 |
| Khasi | 2013 | Kermanshah | 33,826 | 7.1 | Cross-sectional | 6 |
| Karamizadeh | 2012 | Fars | 63,031 | 6.0 | Cross-sectional | 7 |
| Mohammadi | 2012 | Kerman | 11,550 | 4 | Cross-sectional | 7 |
| Namakin | 2012 | South Khorasan | 38,987 | 8.1 | Cross-sectional | 6 |
| Shadkam | 2012 | Yazd | 13,022 | 4.3 | Cross-sectional | 6 |
| Zeinalizadeh | 2011 | East Azerbaijan | 62,459 | 5.1 | Cross-sectional | 6 |
| Akhi | 2011 | Mazandaran | 45,218 | 6.1 | Cross-sectional | 6 |
| Ghaderi | 2011 | Kermanshah | 68,587 | 8.0 | Cross-sectional | 6 |
| Aminzadeh | 2010 | Ahvaz | 35,655 | 3.2 | Cross-sectional | 7 |
| Dorreh | 2010 | Markazi | 26,658 | 3.3 | Cross-sectional | 7 |
| Nouri | 2008 | Yazd | 11,418 | 9.3 | Cross-sectional | 7 |
| Saffari | 2008 | Qazvin | 33,488 | 2.2 | Cross-sectional | 7 |
| Eftekhari | 2008 | Kerman | 3,000 | 1 | Cross-sectional | 6 |
| Neili | 2005 | Kurdistan | 50,539 | 4.3 | Cross-sectional | 6 |
| Hashemipour | 2004 | Isfahan | 20,000 | 7.2 | Cross-sectional | 6 |
| Kalantari | 2004 | Gilan | 3,000 | 6.0 | Cross-sectional | 6 |
| Ordookhani | 2004 | Tehran | 35,067 | 8.0 | Cross-sectional | 7 |

*CH = Congenital Hypothyroidism; **NOS = Newcastle-Ottawa Scale

**Table 2** Quality assessment of included studies using the Newcastle-Ottawa checklist

| Author | Choices | | | | Comparability | Outcome | | Total Score |
|---|---|---|---|---|---|---|---|---|
| | Case Representation | Sample Size | Non-response Rate | Screening Tool Determination | | Outcome Assessment | Statistical Test | |
| Mohtasham | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Koohshouri | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Habib | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Soodjani | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Zamani | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Hemmati | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Amiri | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Deliri | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Hemmati | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Pikani | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Beheshti | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Mirzarahimi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Mobaraki | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Shojaeifar | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Keshavarzian | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Ghasemi | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Mahmoudi | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Nasehi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Haghshanas | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Siami | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Valizadeh | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Karimi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |

**Table 2** (continued)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Khasi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Karamizadeh | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Mohammadi | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Namakin | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Shadkam | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Zeinalizadeh | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Akhi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Ghaderi | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Aminzadeh | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Dorreh | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Nouri | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Safari | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |
| Eftekhari | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Neili | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Hashemipour | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Kalantari | 1 | 1 | 1 | 1 | - | 1 | 1 | 6 |
| Ordookhani | 1 | 1 | 1 | 2 | - | 1 | 1 | 7 |

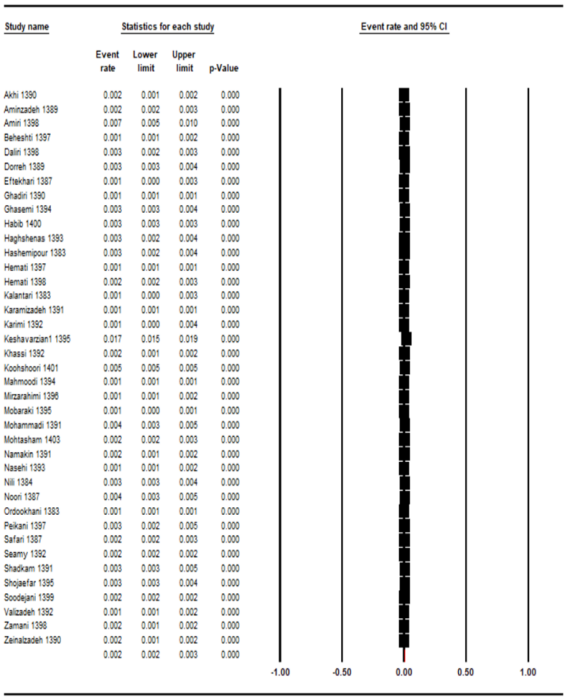


**Figure 2** Cumulative prevalence of congenital hypothyroidism in Iranian neonates based on a random-effects model

### Prevalence of Congenital Hypothyroidism in Female Neonates

Heterogeneity testing based on $I^2$ (92.37%) and significance level ($p < 0.05$) indicated substantial heterogeneity, requiring the use of a random-effects model. Seventeen studies involving 253,790 female neonates examined the prevalence. The prevalence was 3 per 1000 live births (95% CI: 0.002-0.004, $p < 0.05$) (Figure 4).

### Publication Bias Assessment

Publication bias was assessed using Egger's test. The non-significant result ($p > 0.05$) indicated no evidence of publication bias in the current study (Figure 5).

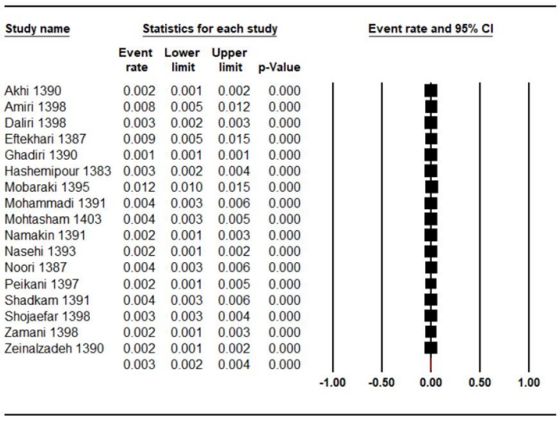


**Figure 3** Cumulative prevalence of congenital hypothyroidism in male neonates based on random-effects model

## 4 Discussion

This systematic review and meta-analysis aimed to determine the prevalence of congenital hypothyroidism in Iranian neonates. The findings revealed a prevalence of 2 cases per 1000 live births among Iranian neonates.

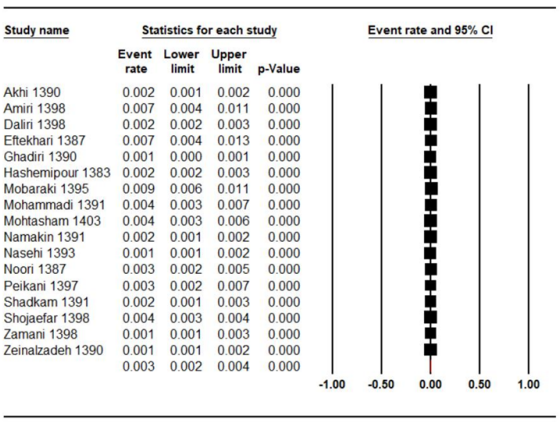


**Figure 4** Cumulative prevalence of congenital hypothyroidism in female neonates based on random-effects model

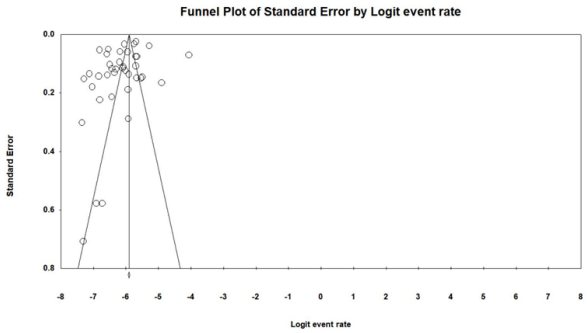


**Figure 5** Funnel plot of congenital hypothyroidism prevalence in Iranian neonates

Iran's national congenital hypothyroidism screening program achieves 99% coverage, ranking among the most successful health programs in the Eastern Mediterranean region.[54] Reported screening coverage rates included 99.7% in Fars province[55], 100% in Markazi province [56], 98.9% in Isfahan[23], and near-complete coverage (≈100%) in Mazandaran[3], East Azerbaijan[57], Kohgiluyeh and Boyer-Ahmad[58], and Hamadan[59].

The 2014 systematic review and meta-analysis by Visani et al.[60] In Iran, a congenital hypothyroidism prevalence of 2 per 1000 live births was reported, consistent with our findings, indicating stable prevalence rates over the past decade in Iran. Globally, prevalence varies substantially (range: 1:2000 to 1:4000 live births) due to geographic, genetic, and environmental factors, with some regions reporting much higher rates.[61]

The 2023 systematic review by Liu et al.[10] reported a global prevalence of 4.25 cases per 1,000 live births, with the highest incidence in the Eastern Mediterranean region (2.48 times higher than in Europe). Our findings demonstrate lower prevalence rates in Iran compared to global estimates. Liu et al. found an increasing global prevalence from 1969 to 2020, potentially reflecting the expansion of neonatal screening programs and lower diagnostic thresholds for thyroid-stimulating hormone.

A 2023 Chinese study by Yao et al.[62] documented significant incidence increases from 2012 to 2019 (4.0 to 5.7 cases per 1000 live births). The variation between Iran and other countries may reflect differential screening implementation, where pre-screening incidence was low, but regional/national screening programs increased detected cases through improved diagnostic sensitivity.[63] Barry et al.'s 2016 French study [64] reported a prevalence of 2.8 per 1000 live births.

Multiple factors potentially contribute to the increased prevalence of congenital hypothyroidism. Studies indicate numerous risk factors, including: advanced maternal age, maternal thyroid disorders, gestational diabetes, anxiety, medication use during pregnancy, radiation exposure, family history of thyroid disease, low birth weight, fetal macrosomia, preterm birth, multiple pregnancies, and congenital anomalies. [65, 66]

A 2022 Indian study by Anne et al. [67] reported prevalence rates of 0.9 per 1000 screened neonates in non-endemic areas, 0.7 in endemic areas, 50 cases per 1000 neonates born to mothers with thyroid disorders, and 14 in preterm neonates. These findings indicate higher prevalence rates among Iranian neonates relative to their Indian counterparts. In contrast, a Pakistani study by Ahmad et al.[68] reported a prevalence of 4 per 1,000 live births, indicating higher rates than those in Iran. This discrepancy may reflect Iran's more comprehensive national screening program.

A US-based study (Waller et al.[69]) revealed a two-fold higher prevalence in low-birth-weight neonates compared to normal weight neonates, with rates 33% lower among Black neonates compared to White neonates. A 2021 study by Minamitani[70] In Japan, a prevalence of 4 per 10,000 live births was reported, with doubled rates attributable to enhanced detection of mild cases through lower TSH screening thresholds and higher numbers of at-risk preterm/low birth weight neonates.

Our analysis revealed a comparable prevalence between male and female Iranian neonates (3 per 1,000 live births), which is higher than the overall prevalence (2 per 1,000). This divergence may stem from differing sample sizes (17 gender-specific versus 39 overall studies) or variations in screening methods and diagnostic sensitivity. Some gender-specific studies may have been conducted in high-prevalence regions or used lower TSH diagnostic thresholds, warranting further investigation.

While Rezaeian et al.[70] proposed female sex as a potential risk factor, though our study found no gender difference. Soodjani et al.[50] similarly, reported equal prevalence in Iranian male and female neonates, consistent with our findings, while another study also found no gender difference.[71]

Our findings underscore the need for nationwide implementation of neonatal screening across Iran.

Early detection of congenital hypothyroidism through systematic screening can substantially mitigate long-term complications from untreated cases. The American Academy of Medicine advocates for universal neonatal screening to identify affected infants before clinical manifestations occur. While Iran has established neonatal screening initiatives, their implementation remains inconsistent across regions, particularly in resource-limited areas that lack adequate screening infrastructure or follow-up care. Expanding screening accessibility is paramount to ensure comprehensive neonatal evaluation. Public health initiatives should prioritize education for parents and healthcare providers regarding the importance of screening. Concurrently, maternal health programs must emphasize adequate iodine nutrition during pregnancy, given its established role in preventing congenital hypothyroidism.

Several limitations warrant acknowledgment: regional disparities across Iran's diverse provinces, seasonal variations in data collection, inconsistent TSH diagnostic thresholds (with studies using various cutoffs, including> 10 mIU/L or ≥ 10 mIU/L), and the potential confounding effects of socioeconomic factors and maternal age on disease prevalence.

## 5 Conclusion

This systematic review reveals important epidemiological patterns while highlighting several knowledge gaps that require further investigation. Longitudinal outcome studies could elucidate the effectiveness of early intervention protocols. Genetic research may identify population-specific susceptibility factors to guide targeted screening. Environmental studies should investigate potential endocrine disruptors that contribute to disease etiology. Regional comparative analyses could reveal location-specific risk factors that influence prevalence variations. Such investigations would substantially advance our understanding of congenital hypothyroidism in the Iranian context.

## Declarations

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**Authors' Contributions**
Conceptualization and project administration: Saeed Khorramnia and Zia Navidi; Literature searching: Babak Shekarchi, Mojgan Mohajeri Iravani, Mohammad Teymurizadeh; Data extraction and quality assessment: Ali Sarkoohi, Seyed Hamid Pakzad Moghadam, Romina Golpayegani; Investigation: Akbar Haji Ghasemalian, Ebadallah Shiri Malekabad; Data Analysis: Saeed Khorramnia and Zia Navidi; Writing - original draft: Zia Navidi; Writing - review & editing: all of the authors.

**Availability of Data and Materials**
Data are available online for the included studies.[15-53]

**Conflict of Interest**
The authors declare no conflicts of interest.

**Consent for Publication**
All authors have read and approved the final manuscript and provided their consent for publication.

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**Ethical Considerations**
Not applicable.

**Artificial Intelligence Disclosure**
The authors confirm that no artificial intelligence (AI) tools were used in the preparation of this manuscript.



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