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REVIEW ARTICLES

A clinical review of early assessment for congenital hypothyroidism in newborns

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Abstract
Congenital hypothyroidism is a critical factor associated with stunting, as thyroid hormone deficiencies can impair growth starting in utero. Children with thyroid disorders, including conditions like hypoparathyroidism, often experience growth retardation due to congenital abnormalities and growth hormone deficiencies. For neonates, a lack of thyroid hormones can lead to long-term impacts, such as physical and mental disabilities, neurological disorders, and stunted growth. Early detection of congenital hypothyroidism is, therefore, essential and is typically part of newborn screening aimed at identifying congenital abnormalities. Implementing early screening protocols can diagnose and treat congenital hypothyroidism promptly, mitigating risks such as stunting and enabling better health outcomes for children. This literature review examines methods of early detection for congenital hypothyroidism across various global contexts. Three databases—PubMed, ScienceDirect, and Google Scholar—were searched using a systematic literature review approach, yielding five eligible studies with a combined study population of 920.441 newborns. These studies involved screenings for T4, TSH, 17-OHP, and G-6-PD, identifying hypothyroidism in 2.530 (27%) cases. Screening involved blood samples taken from the umbilical cord or heel within 48 to 72 hours after birth. Understanding early detection procedures for congenital hypothyroidism is essential for nurses, as it enables them to engage in early intervention and provide effective nursing care for affected infants. Early involvement can help prevent the adverse, long-term effects associated with congenital hypothyroidism, improving quality of life and supporting healthy growth trajectories for children at risk.

Keywords: Congenital hypothyroidism; literature review; nursing assessment; paediatric nursing; prevention

Introduction

Congenital Hypothyroidism (CH) is a condition present at birth where the thyroid gland is underactive, leading to insufficient production of thyroid hormones crucial for growth and development (van Trotsenburg et al., 2021). The thyroid gland, located in the neck, produces hormones that regulate metabolism, energy levels, and support brain development (Rastogi & LaFranchi, 2010). In infants with CH, the lack of these hormones can lead to developmental delays, growth impairment, and intellectual disabilities if left untreated (Cherella & Wassner, 2017). Causes of CH can include a missing or underdeveloped thyroid gland (thyroid dysgenesis), genetic defects that impair hormone production, or less commonly, maternal antibodies that interfere with the infant's thyroid function (Lauffer, Zwaveling-Soonawala, Naafs, Boelen, & van Trotsenburg, 2021). The diagnosis of CH often occurs through newborn screening, which measures levels of thyroid-stimulating hormone (TSH) in the blood (Stoupa, Kariyawasam, Polak, & Carré, 2022). Elevated TSH levels indicate low thyroid hormone production, prompting further testing to confirm the condition. Early detection is critical, as initiating hormone replacement therapy, typically with levothyroxine, within the first few weeks of life can prevent many complications (Weiner, Oberfield, & Vuguin, 2020). Regular follow-up is essential to monitor growth and hormone levels, ensuring the child's development proceeds normally (Rose et al., 2023). Thanks to effective newborn screening programs and early treatment, children with CH can generally lead healthy lives with normal cognitive and physical development.

A common endocrine condition in infants, CH affects roughly 1 in 2000 to 4000 live births (Chen, Lee, Lee, Lai, & Huang, 2013). The incidence of CH is rising in Western nations, according to several epidemiologic research (Liu et al., 2023). CH is closely related to stunting, as hypothyroidism can be a contributing factor that affects growth and development starting in the womb (Uthayaseelan et al., 2022). Children who experience thyroid disorders, such as hypoparathyroidism, experience growth retardation due to congenital anomalies after birth and growth hormone deficiency (Nazari et al., 2021). Thyroid hormones are essential for children's growth, and damage to their production

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(Parathyroid Hormone-related Protein) can cause deficiencies in thyroid hormone, vitamin D, and calcium absorption. In children, calcium deficiency can reduce the number of osteoclasts and osteoblasts, adversely affecting bone growth, tooth eruption patterns and stunting (Lin et al., 2022; Cornelia, Tedjosasongko, Dewi, & Ayuningtyas, 2022). Most newborns with CH may appear normal and lack specific physical symptoms, making clinical detection challenging. Therefore, early detection in neonates is crucial to determine whether a baby has CH. Thyroid hormone deficiency in neonates can lead to long-term impacts, including physical disabilities, mental disabilities, nerve disorders, and stunted growth (Ford & LaFranchi, 2014; Hashemipour, Rabbani, Rad, & Dalili, 2023). Early detection of CH allows treatment to start within two weeks after birth, preventing intellectual disability, developmental issues, and growth problems (Kumari et al., 2023).

CH can be prevented through early detection and treatment, with newborn screening serving as a vital tool for identifying congenital hypothyroidism. This screening is a cost-effective strategy that can yield significant health improvements, particularly in countries with limited resources. Various screening strategies for CH exist worldwide, reflecting the diversity of screening programs. However, the primary examination for CH screening involves measuring TSH and T4 levels (Hashemipour et al., 2023). Newborn screening for CH through TSH and T4 measurements is a nationally established program in many countries, including Indonesia, Japan, Bangladesh, and the Netherlands (Lauffer, Zwaveling-Soonawala, Naafs, Boelen, & van Trotsenburg, 2021; Nagasaki et al., 2023; Hashemipour et al., 2023). Early assessment for CH is crucial because timely detection and intervention can significantly mitigate the long-term consequences associated with this condition. CH is often asymptomatic at birth, with affected infants appearing normal and showing no immediate signs of thyroid hormone deficiency. However, if left undiagnosed and untreated, CH can lead to severe complications, including intellectual disabilities, growth retardation, and other neurodevelopmental issues. The first few weeks of life are critical for brain development, and thyroid hormones are essential for proper neuronal growth and maturation. Early screening allows for the initiation of treatment—typically involving thyroid hormone replacement therapy—within the first two weeks of life, which can prevent or minimize cognitive impairments and promote healthy physical development. Moreover, early assessment is not only beneficial for the individual child but also has broader public health implications. Implementing routine newborn screening for CH can lead to improved health outcomes across populations, reducing the incidence of preventable disabilities. Screening programs can be cost-effective, as they identify cases that would otherwise go unnoticed until significant developmental delays have occurred. Countries that have adopted systematic screening protocols for CH report better overall health outcomes for children, demonstrating the effectiveness of early detection in preventing long-term complications. Conducting a literature review on this topic is essential to consolidate existing research, identify gaps in knowledge, and highlight best practices in screening methodologies. This review will provide valuable insights for healthcare providers and policymakers, guiding them in enhancing early detection strategies and improving health outcomes for children at risk of congenital hypothyroidism.

Method

This study employs a literature review to explore the early detection of congenital hypothyroidism conducted in various countries around the world. A literature review is essential because it synthesizes existing research on a specific topic, providing a comprehensive overview of current knowledge, methodologies, and findings (Leite, Padilha, & Cecatti, 2019). Critically analyzing and summarizing relevant studies identifies gaps in the literature, highlights trends and patterns, and establishes a theoretical framework for further research (Parker & Sikora, 2022). It also helps researchers understand the context of their work, guiding them in formulating research questions and hypotheses while ensuring that their study builds on and contributes to the existing body of knowledge (Silva et al., 2022). The literature search utilized three databases: PubMed, ScienceDirect, and Google Scholar. The selection of PubMed, ScienceDirect, and Google Scholar for the literature review is based on their comprehensive coverage and credibility in the field of medical and scientific research. PubMed is a premier database for biomedical literature, providing access to a vast repository of peer-reviewed articles and clinical studies, which is crucial for understanding health-related topics like congenital hypothyroidism. ScienceDirect offers a wide range of scientific and technical research articles, making it an excellent resource for original research and reviews in various disciplines. Google Scholar complements these databases by allowing broader searches across multiple disciplines and sources, including theses, books, and conference papers. Together, these databases ensure a robust and diverse collection of high-quality literature, facilitating a thorough exploration of early detection methods for congenital hypothyroidism.

The keywords used for the search were "Congenital Hypothyroidism," "Newborn," and "Early Detection." The selected articles focused on original research published in English between 2021 and 2024, with the inclusion criteria specifying that the subjects must be newborns who underwent congenital hypothyroidism screening. Articles examining

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early detection of hypothyroidism in infants older than one month were excluded based on the exclusion criteria. Data extraction was performed on all identified articles, focusing on the following parameters: first author, year of publication, research location, study objectives, population, implementation methods, early detection of congenital hypothyroidism, and screening results.

Results

The literature search yielded a total of 26 articles from PubMed, 6 articles from ScienceDirect, and 152 articles from Google Scholar, resulting in 184 articles across the three databases. Subsequently, a screening process was conducted, evaluating the articles based on their format (text, full text, or abstract), publication year, and journal reputation. This screening revealed that 61 articles were either only available as abstracts or published in non-reputable journals, leaving 123 articles for further evaluation. From the 123 articles, an assessment of the research methods was performed, resulting in 35 articles being deemed eligible, while 88 articles were excluded. Among the 35 articles, 20 were excluded because they did not address early detection of CH, ultimately leaving 5 articles that were appropriate and utilized in this literature review **(Table 1)**.

The subjects of the studies were neonates born in hospitals across various regions, including India, Australia, Bangladesh, and Italy. The population sizes for the studies were as follows: 100 neonates in India, 346.849 in Australia, 500.000 in Bangladesh, and 73.000 in Italy. The implementation methods for newborn screening for thyroid disorders involved two approaches: collecting umbilical cord blood at the time of delivery and taking blood samples from the heel 48 to 72 hours after birth. To facilitate the early detection of congenital hypothyroidism, several examinations were conducted, including T4, β-TSH, glucose-6-phosphate dehydrogenase (G-6-PD), 17-hydroxyprogesterone (17-OHP), FT3, FT4, and parallel serum TSH examination (sTSH). The results of the congenital hypothyroidism screening revealed decreased T4 concentrations, indicating low total T4 levels in CH babies, who exhibited symptoms of moderate to severe hypothyroidism. In the TSH examination, a decrease in the β-TSH threshold was noted, with the majority of diagnosed cases occurring in premature infants. In the G-6-PD examination, among 369 neonates, one male baby showed increased TSH levels, while six male babies had elevated 17-OHP levels. In the FT3, FT4, and TSH examinations conducted on 500.000 samples, 274 samples exhibited low TSH values, suggesting that female babies were at a higher risk for congenital hypothyroidism. In the β-TSH, sTSH, and FT4 examinations, it was found that 119 babies were diagnosed with congenital hypothyroidism during the first examination, and the second examination revealed low β-TSH values in these cases.

Discussion

The literature review indicates that CH screening is performed on neonates to facilitate early detection and immediate treatment of thyroid disorders. During the neonatal period, thyroid hormones are crucial for brain development; thus, early detection of hypothyroidism can prevent long-term complications. In many cases, clinical symptoms of CH are not apparent at birth, making laboratory examinations essential for identifying the condition before further symptoms arise (Léger et al., 2014). Screening neonates is a logical approach, as it is a cost-effective strategy that maximizes health benefits, particularly in resource-limited countries (Hashemipour et al., 2023). The method for early detection of congenital hypothyroidism involves collecting umbilical cord blood and heel blood samples (Rathod, Pradhan, Lekharu, Vala, & Kulshrestha, 2024). Umbilical cord blood samples are taken immediately after birth, allowing for the early detection of thyroid disorders. This procedure is critical because the newborn's brain remains highly sensitive to thyroid hormone levels right after birth. Collecting blood from the umbilical cord is a non-invasive procedure that minimizes discomfort for the infant, as the cord has already been cut. Additionally, the umbilical cord contains an adequate blood volume for various laboratory tests, including TSH and T4 levels, ensuring accurate results. The immediate examination of umbilical cord blood samples enhances time efficiency, facilitating faster diagnosis and treatment (Nagasaki et al., 2023). In addition to umbilical cord blood sampling, heel blood samples are also collected, which has become a standard practice in neonatal screening programs due to its practicality and effectiveness (Rathod, Pradhan, Lekharu, Vala, & Kulshrestha, 2024). The heel is an accessible location for obtaining capillary blood samples, as its skin is thin and rich in blood vessels, allowing for sufficient blood collection. Heel blood sampling is generally safe and non-invasive, making it easy for trained personnel, such as nurses, to perform without complications (Nagasaki et al., 2023). According to the review, blood sampling is ideally conducted within 48 to 72 hours after birth (Caiulo et al., 2021). TSH levels typically increase in the first 24 hours of life in response to environmental changes. Therefore, performing the TSH examination between 48 to 72 hours after birth ensures more stable and accurate results (Nagasaki et al., 2023).

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Table 1. Studies highlighted early detection of CH.

No	Authors, years	Participants and method	Parameters assessment	Finding
1	Rathod, Pradhan, Lekharu, Vala, & Kulshrestha, 2024	100 neonates (50 males and 50 females) were assessed for thyroid status after excluding those born of known hypothyroid mothers or having a history of distress. Cord blood was collected at the time of delivery, and dried blood spots (DBS) from heel prick at 72 hours were collected and TSH was compared.	Newborn screening and T4 examination for primary CH.	Decreased T4 concentration, Low total T4, CH infants show symptoms of moderate to severe hypothyroidism.
2	Yu et al., 2023	NBS data of 346.849 infants born in NSW/ACT, Australia from 1 November, 2016-1 March, 2020 inclusive were analyzed. A clinical audit was conducted on infants with a preliminary diagnosis of CH born between 1 January, 2016-1 December, 2020 inclusive.	b-TSH examination	Clinically relevant CH was detected using the lowered threshold, albeit at the cost of an eight-fold increase in recall rate.
3	Kumari et al., 2023	A screening program was conducted at a tertiary care hospital for 1 year at All India Institute of Medical Sciences (AIIMS), Patna.	Blood levels of glucose-6-phosphate dehydrogenase (G-6-PD), 17-hydroxyprogesterone (17-OHP) and thyroid-stimulating hormone (TSH).	Congenital adrenal hyperplasia (CAH) is the most prevalent disorder followed by CH in the population.
4	Al Azim et al., 2024	A thorough screening program was launched in Bangladesh from July 2018 to June 2022, gathering over 500.000 samples from infants.	FT3, FT4, dan TSH examination.	274 samples were found to have TSH values of more than 20 U/mL.
5	Caiulo et al., 2021	Maternal and neonatal clinical features were analyzed for 119 CH babies detected in the Lombardy region of Italy, 2007 to 2014.	Blood samples are collected 49 to 120 hours after birth, Infants with bTSH 10-20 mU/L undergo a second examination by taking blood spots for parallel serum TSH (sTSH) and free thyroxine (FT4) examination.	Lower TSH cutoff at the second screening can detect additional cases of CH. A second bTSH cutoff of 5.0 mU/L is appropriate for identifying preterm newborns and babies with associated risk factors.

Sampling too early, such as within the first 24 hours, may yield inaccurate results due to elevated TSH levels, leading to false positives. The review also found that CH screening involves examining T4, TSH, β-TSH, G-6-PD, and 17-OHP (Kumari et al., 2023). These examinations have become standard for diagnosing CH. The T4 test helps detect hypothyroidism that may not be evident through TSH levels, as T4 is the primary thyroid hormone produced by the thyroid gland. The TSH test is crucial for assessing thyroid function; elevated TSH levels indicate that the thyroid gland is not

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functioning properly. In newborns, increased TSH levels signal potential issues with thyroid hormone production, making this examination vital for detecting CH. The Blood Spot TSH (β-TSH) test, taken from heel blood samples, is a quicker and easier method for screening CH compared to serum blood tests.

Additionally, the examination for G-6-PD aims to identify early G-6-PD deficiency, which can lead to severe hemolytic crises if left undetected. G-6-PD is an essential enzyme in the pentose phosphate pathway that protects red blood cells from oxidative damage (Ford & LaFranchi, 2014; Léger et al., 2014). The 17-OHP test is also included in the screening process. It detects CAH, a genetic condition affecting adrenal hormone production. Early detection of CAH is crucial, as it can lead to hormonal imbalances and serious health issues in newborns, including adrenal crises and genital development abnormalities. Some studies suggest that simultaneous testing for multiple disorders—such as T4, TSH, 17-OHP, and G-6-PD—can facilitate early detection of various conditions, enhancing the likelihood of healthy development for the infant (Ford & LaFranchi, 2014; Léger et al., 2014; Minamitani, 2021). The literature review revealed that out of 920.441 newborns examined, 2.530 babies (27%) were found to have thyroid disorders. Hypothyroidism can result from issues with the pituitary or hypothalamus, leading to reduced stimulation of the thyroid gland to produce T3 and T4. Such problems may arise from central nervous system disorders or genetic mutations that affect pituitary development. Prematurity can also contribute to hypothyroidism due to the immaturity of the endocrine system, including the thyroid gland. Other causes include the Syndrome of Inappropriate TSH Secretion (SITS), where newborns exhibit low T4 and TSH levels due to regulatory issues in the pituitary gland. This condition may be associated with prenatal developmental disorders or birth-related injuries. Non-Thyroidal Illness, a severe systemic disease such as sepsis or respiratory failure, can also lead to thyroid dysfunction in newborns. In some cases, transient congenital hypothyroidism occurs due to maternal factors, such as thyroid antibodies from mothers with Graves' disease or excessive iodine intake during pregnancy, which can trigger the condition (Klosinska, Kaczynska, & Ben-Skowronek, 2022; Lauffer, Zwaveling-Soonawala, Naafs, Boelen, & van Trotsenburg, 2021; Léger et al., 2014).

The role of pediatric nursing in this context is critical. Pediatric nurses are essential in the screening process, as they are trained to perform blood sampling procedures safely and effectively. They play a vital role in educating parents about the importance of newborn screening and the implications of thyroid disorders (Miculan, Turner, & Paes, 1993). Pediatric nurses also monitor the neonates for any signs of complications and provide support for families navigating the diagnosis and treatment of congenital hypothyroidism. Facilitating early intervention and ensuring that follow-up care contribute significantly to improving health outcomes for affected infants (Pulungan et al., 2024). The role of government in public health, particularly regarding congenital hypothyroidism screening, is crucial for establishing and implementing comprehensive screening programs. Governments are responsible for creating policies that mandate newborn screening, ensuring access to testing and treatment across all regions, especially in underserved areas. They allocate funding for screening initiatives, provide training for healthcare professionals, and promote public awareness campaigns to educate parents about the importance of early detection. Additionally, governments monitor and evaluate screening programs to maintain quality standards and improve health outcomes for newborns, ultimately aiming to reduce the incidence of preventable health complications related to thyroid disorders.

When parents learn that their baby has congenital hypothyroidism, the first step is to seek immediate medical advice and establish a treatment plan with a pediatric endocrinologist. Early intervention is critical, as timely treatment can prevent intellectual disabilities and developmental delays associated with untreated hypothyroidism. Parents should ensure that their baby begins hormone replacement therapy, typically with synthetic thyroxine (levothyroxine), as soon as possible. Regular monitoring of thyroid hormone levels through blood tests is essential to adjust medication dosages and ensure that the baby's thyroid function remains within the normal range. Parents should maintain open communication with healthcare providers, attend all follow-up appointments, and keep a detailed record of their baby's medication schedule and any observed symptoms or side effects. In addition to medical management, parents should educate themselves about congenital hypothyroidism and its implications for their child's development. Understanding the condition enables parents to advocate for their child's needs effectively, including special educational services if necessary. They should also foster a supportive environment that encourages developmental milestones by engaging in stimulating activities suitable for their baby's age. Connecting with support groups or organizations dedicated to congenital hypothyroidism can provide valuable resources and emotional support, helping parents navigate the challenges associated with the condition. Being proactive and informed can play a pivotal role in their child's health and well-being, ensuring they receive the best possible care and opportunities for healthy development.

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Conclusion

Early assessment and screening for CH in newborns are critical for preventing long-term developmental complications associated with untreated hypothyroidism. The implementation of universal newborn screening programs has significantly improved early detection rates, allowing for timely intervention through hormone replacement therapy. Despite these advancements, challenges remain, including variations in screening practices, access to healthcare, and the need for continuous monitoring of thyroid function in affected infants. The evidence underscores the importance of early diagnosis and consistent management to ensure optimal health outcomes for newborns diagnosed with CH. Future research should focus on several key areas to enhance the understanding and management of congenital hypothyroidism. Firstly, studies should investigate the long-term developmental outcomes of infants diagnosed with CH through early screening, including cognitive, physical, and psychosocial development. Additionally, research should explore the effectiveness of different screening methods, such as the use of dried blood spots versus serum samples, to optimize detection rates. It is also essential to examine the barriers to access and adherence to follow-up care in diverse populations, particularly in low-resource settings. Finally, investigating the genetic and environmental factors contributing to the incidence of CH could provide insights for preventive strategies and tailored interventions.

Author's declaration

The authors made substantial contributions to the conception and design of the study and are responsible for data analysis, interpretation, and discussion of results. For manuscript preparation, all authors read and approved the final version of this article.

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Availability of data and materials

All data are available from the authors.

Competing interests

The authors declare no competing interest.

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Authors' insight

Key points

- Early assessment and screening for CH in newborns are critical in paediatric nursing practice
- Understanding the condition enables parents to advocate for their child's needs effectively
- Research should explore the effectiveness of different screening methods

Emerging nursing avenues

- What are the key benefits of implementing universal newborn screening programs for congenital hypothyroidism?
- How do they impact long-term developmental outcomes in affected infants?
- What challenges do healthcare providers face in ensuring timely and accurate screening for congenital hypothyroidism?

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