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Hipotiroid Kongenital

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Abstract.

Congenital hypothyroidism (HK) is the most common congenital endocrine disorder in children and is the most common cause of preventable mental retardation. The disorder is caused by the absence of thyroid hormones in the womb and is not needed early can cause severe mental retardation. Clinical manifestations in neonates are not specific, but manifestations obtained after birth consist of gestational age > 42 weeks, BBL > 4kg jaundice > 3 days after birth, edema, umbilical hernia, macroglossia, acrocyanosis. The diagnosis can be made for thyroid screening. Thyroid screening in neonates is carried out before being discharged from the hospital, from the 2nd to 4th day of the baby's age, by checking TSH and T4 levels. The dose of the thyroxine hormone is adjusted to the baby's age and also the baby's body weight.

Keywords: *Congenital hypothyroidism; endocrine abnormalities and children.*

I. INTRODUCTION

Congenital hypothyroidism (CH) is the most common congenital endocrine disorder in neonates and represents a leading preventable cause of intellectual disability. This condition occurs due to insufficient or absent production of thyroid hormones since fetal life, which are essential for normal growth and neurodevelopment [1], [2]. Thyroid hormones, particularly thyroxine (T4) and triiodothyronine (T3), play a crucial role in the development of the central nervous system, including neuronal migration and myelination. Deficiency of these hormones during critical periods of brain development can result in irreversible neurological impairment if not treated promptly [3], [4]. The incidence of congenital hypothyroidism varies across countries but is generally reported at approximately 1:3000 to 1:4000 live births [1]. Higher incidence rates have been observed in Asian populations compared to other ethnic groups, with reported variations ranging from 1:1000 to 1:6467 births [3]. In Indonesia, national epidemiological data are still limited. However, hospital-based screening programs indicate a higher prevalence compared to global estimates. For example, screening conducted at RSUP Dr. Cipto Mangunkusumo identified 85 cases among 213,669 newborns, corresponding to an incidence of 1:2513 live births [5].

These findings highlight the importance of strengthening neonatal screening programs in Indonesia to detect cases early and reduce long-term complications. Etiologically, congenital hypothyroidism can be classified based on the site of dysfunction. Primary hypothyroidism accounts for the majority of cases and is most commonly caused by thyroid dysgenesis, which represents approximately 85% of cases [1], [6]. Thyroid dysgenesis includes agenesis, hypoplasia, and ectopic thyroid tissue. The remaining cases are mainly due to dyshormonogenesis, which involves defects in thyroid hormone synthesis [2], [6]. In addition, central or secondary hypothyroidism arises from dysfunction of the hypothalamus or pituitary gland, resulting in impaired secretion of thyroid-stimulating hormone (TSH). Other causes include peripheral resistance to thyroid hormone and transient hypothyroidism associated with maternal factors, such as iodine deficiency or exposure to antithyroid drugs during pregnancy [2], [7]. Clinical manifestations of congenital hypothyroidism in neonates are often subtle and nonspecific, especially during the first weeks of life. Early symptoms may include prolonged jaundice, lethargy, constipation, feeding difficulties, and hypothermia [7], [8]. Many infants appear clinically normal at birth, which makes diagnosis based solely on clinical signs challenging.

As the condition progresses without treatment, more characteristic features may develop, such as macroglossia, umbilical hernia, coarse facial features, and developmental delay [4], [9]. Delayed diagnosis is strongly associated with permanent intellectual disability and impaired physical growth. Given the

nonspecific presentation in early life, neonatal screening has become the cornerstone of early detection of congenital hypothyroidism. Screening using TSH measurement is the most sensitive method for detecting primary hypothyroidism and is recommended within 48 to 72 hours after birth to ensure optimal accuracy [6], [7]. Early diagnosis followed by prompt initiation of levothyroxine therapy, ideally before two weeks of age, is essential to prevent irreversible neurological damage and to ensure optimal growth and development [7], [10]. Therefore, congenital hypothyroidism represents a critical pediatric condition in which early detection and timely intervention play a decisive role in determining long-term outcomes.

II. METHODS

Study Type and Design

This study applied a literature review design to systematically analyze existing evidence related to congenital hypothyroidism (CH) in neonates. The review focused on key aspects including epidemiology, diagnosis, screening, treatment, and long-term monitoring. A qualitative descriptive approach was used to synthesize findings from multiple sources and to provide a comprehensive understanding of CH as a preventable cause of intellectual disability. This approach is appropriate because CH involves well-established clinical guidelines and standardized management protocols that can be evaluated through existing literature rather than primary data collection. The design aimed to integrate theoretical knowledge and clinical practice recommendations in pediatric endocrinology. Emphasis was placed on early detection through neonatal screening and timely treatment with levothyroxine, as these factors strongly influence patient outcomes [7], [10].

The review also considered variations in incidence and clinical presentation across different populations, including data from Indonesia, to provide contextual relevance [5]. By using a structured literature review method, the study ensures that all relevant dimensions of CH are explored in a systematic and coherent manner. This design allows for the identification of consistent patterns in diagnosis and management, as well as gaps in implementation, particularly in developing countries. The approach also supports comparison between global recommendations and local practices. As CH is a condition where early intervention determines prognosis, reviewing established literature is essential to highlight best practices and improve clinical outcomes. Therefore, this study design provides a strong foundation for understanding the importance of early screening, accurate diagnosis, and continuous monitoring in managing congenital hypothyroidism [1], [2].

Data Sources and Search Strategy

Data for this literature review were obtained from a combination of national and international scientific sources. These included pediatric endocrinology textbooks, clinical practice guidelines, peer-reviewed journal articles, and official health reports. Key sources included publications from the Indonesian Pediatric Society (IDAI), Ministry of Health Indonesia, and international medical databases such as PubMed and institutional repositories [5], [7]. The selection of these sources ensured that the data used in this review were credible, relevant, and aligned with current clinical standards. The search strategy involved the use of specific keywords related to congenital hypothyroidism. These keywords included “congenital hypothyroidism,” “neonatal screening,” “TSH,” “free T4,” “levothyroxine therapy,” and “child development.” Boolean operators were used to refine search results and improve relevance.

Articles were selected based on their ability to provide information on epidemiology, clinical manifestations, diagnostic methods, and treatment protocols of CH. Priority was given to literature that discussed early diagnosis and screening, as these are critical components in preventing long-term complications such as intellectual disability [6], [8]. Studies that included data from Indonesia or similar populations were also emphasized to ensure contextual applicability. In addition, guidelines that outlined standardized management protocols were included to support evidence-based recommendations. The search process aimed to capture both classical and contemporary references to provide a balanced perspective. By combining multiple data sources and a structured search strategy, this review ensures comprehensive coverage of the topic and supports accurate synthesis of information related to congenital hypothyroidism [2], [7].

Study Selection Process

The study selection process was conducted in a structured and systematic manner to ensure that only relevant and high-quality literature was included in this review. Initially, all identified articles were screened based on their titles and abstracts. Articles that clearly addressed congenital hypothyroidism, particularly in neonatal populations, were selected for further evaluation. This initial screening helped eliminate irrelevant studies and reduced the number of articles for detailed review. Following the initial screening, full-text articles were assessed to determine their relevance and quality. Studies were evaluated based on their focus on key aspects of CH, including epidemiology, clinical features, diagnostic methods, and management strategies. Preference was given to studies that provided clear clinical data and practical recommendations.

Articles that discussed neonatal screening programs and treatment outcomes were considered highly relevant due to their direct impact on patient prognosis [7], [8]. The selection process also considered the credibility of the sources. Publications from recognized institutions, peer-reviewed journals, and established clinical guidelines were prioritized. Studies that lacked methodological clarity or did not provide sufficient clinical information were excluded. This ensured that the final selection consisted of reliable and evidence-based references. To maintain consistency, all selected studies were reviewed using the same criteria. This approach minimized bias and ensured that the data included in the review were relevant to the objectives of the study. By applying a systematic selection process, this review provides a focused and accurate synthesis of existing knowledge on congenital hypothyroidism [2].

Inclusion and Exclusion Criteria

Clear inclusion and exclusion criteria were established to ensure that the literature included in this review was relevant, reliable, and aligned with the study objectives. Inclusion criteria focused on studies that discussed congenital hypothyroidism in neonates and infants, particularly those addressing diagnosis, screening, treatment, and monitoring. Articles published in English or Indonesian were included to ensure accessibility and relevance to both global and local contexts. Studies that provided epidemiological data, clinical guidelines, or evidence-based management strategies were also included [5], [7]. In addition, literature that emphasized early detection through neonatal screening was prioritized, as early diagnosis is critical in preventing long-term complications such as intellectual disability and growth retardation [6], [8].

Studies that included data from Indonesia or similar healthcare settings were considered important to provide contextual insight into the implementation of screening programs and treatment protocols. Exclusion criteria included studies that did not focus on neonatal or congenital hypothyroidism. Articles that discussed adult hypothyroidism or unrelated endocrine disorders were excluded. Case reports with limited generalizability were also excluded unless they provided significant clinical insights. Incomplete articles, outdated publications without relevance to current clinical practice, and studies lacking clear methodology were not included in the review. This selection framework ensured that only high-quality and relevant studies were included. By applying these criteria, the review maintains a strong focus on congenital hypothyroidism and provides accurate and clinically applicable information. This approach also enhances the reliability of the findings and supports evidence-based conclusions [2], [7].

Data Extraction and Summary Presentation

Data extraction was conducted systematically to ensure that all relevant information from selected studies was accurately captured. Key variables extracted included incidence rates, etiological factors, clinical manifestations, diagnostic criteria, treatment protocols, and monitoring strategies related to congenital hypothyroidism. Special attention was given to data describing neonatal screening methods and the effectiveness of early treatment with levothyroxine [7], [10]. The extracted data were organized into thematic categories to facilitate analysis and presentation. These categories included epidemiology, diagnosis, screening, management, and outcomes. Each category was analyzed separately to identify key findings and patterns across different studies. This structured approach allowed for a clear and logical presentation of information.

Narrative synthesis was used to present the findings. This method enabled the integration of data from multiple sources into a cohesive explanation. Tables and structured summaries were considered to support clarity, although the primary focus remained on descriptive analysis. Emphasis was placed on

explaining how early diagnosis and treatment influence long-term outcomes in children with CH [1], [2]. The summary presentation aimed to highlight consistent findings across studies while also identifying variations in clinical practice. By organizing data into clear themes, this review provides an accessible and comprehensive overview of congenital hypothyroidism. This approach supports clinicians and researchers in understanding key aspects of the disease and applying evidence-based practices in clinical settings [7].

Data Synthesis

Data synthesis was performed using a qualitative approach to integrate findings from multiple studies into a unified framework. The synthesis focused on identifying common themes and relationships between diagnosis, treatment, and outcomes of congenital hypothyroidism. This approach allowed for a comprehensive understanding of how early detection and intervention influence disease prognosis. The data were grouped into major thematic areas, including clinical presentation, laboratory diagnosis, screening strategies, treatment protocols, and long-term monitoring. Each theme was analyzed to identify patterns and consistencies across different studies. For example, findings consistently showed that early initiation of levothyroxine therapy significantly improves neurodevelopmental outcomes [7], [10].

Similarly, neonatal screening using TSH was identified as the most sensitive method for early detection [6], [7]. The synthesis also considered variations in practice across different regions, particularly in relation to screening implementation and access to treatment. Data from Indonesia highlighted the need for improved national screening programs to ensure early diagnosis [5]. Differences in incidence and clinical outcomes were also analyzed to provide a broader perspective. This qualitative synthesis enables integration of evidence without relying on statistical analysis. It provides a clear understanding of current knowledge and identifies areas that require further research. By combining findings from multiple sources, this review offers a comprehensive and evidence-based overview of congenital hypothyroidism, emphasizing the importance of early diagnosis and continuous monitoring [2], [7].

III. RESULT AND DISCUSSION

Clinical Presentation and Diagnostic Challenges

Congenital hypothyroidism (CH) presents a major diagnostic challenge due to its nonspecific clinical manifestations during the early neonatal period. Most infants appear normal at birth, and symptoms typically develop gradually within the first weeks of life. In neonates up to 8 weeks of age, clinical signs are often subtle and easily overlooked. Common early symptoms include prolonged jaundice, lethargy, constipation, decreased feeding, and cold or dry skin [7], [8]. In some cases, pallor may also be observed, although this is not a specific finding. These early manifestations are frequently misinterpreted as normal neonatal variations, which contributes to delayed diagnosis. As the condition progresses without treatment, more characteristic clinical features begin to appear. These include macroglossia, umbilical hernia, coarse facial features, hypotonia, and developmental delay [4], [9]. Infants may also exhibit hypothermia, respiratory distress, and abdominal distension. Over time, untreated CH leads to severe growth retardation and permanent intellectual disability. This progression reflects the critical role of thyroid hormones in brain development, particularly in neuronal migration and myelination [3].

Medical history plays an important role in early suspicion of CH. Clinicians should assess family history of thyroid disorders, maternal health during pregnancy, use of antithyroid medications, and exposure to radiation [6]. Maternal iodine deficiency or autoimmune conditions may also contribute to transient forms of CH. However, reliance on clinical symptoms and history alone is insufficient for diagnosis due to the variability and subtlety of early signs. The difficulty in early clinical recognition underscores the importance of neonatal screening programs. Without systematic screening, many cases remain undiagnosed until symptoms become severe and irreversible damage has occurred. Therefore, early identification through laboratory screening is essential to prevent long-term complications. This highlights that CH is not only a clinical condition but also a public health concern that requires structured early detection strategies [1], [2].

Laboratory Diagnosis and Neonatal Screening

Laboratory evaluation is the cornerstone of diagnosing congenital hypothyroidism, as clinical findings alone are not reliable in early life. The primary diagnostic tests include measurement of serum thyroid-stimulating hormone (TSH) and free thyroxine (FT4), interpreted using age-specific reference ranges [7]. Neonatal screening programs predominantly rely on TSH measurement due to its high sensitivity in detecting primary hypothyroidism. Elevated TSH levels indicate impaired thyroid hormone production and stimulate further diagnostic evaluation. Timing of screening is critical to ensure accuracy. The optimal window for neonatal screening is between 48 and 72 hours after birth [7]. Screening conducted before 48 hours may yield false-positive results due to the physiological TSH surge that occurs shortly after birth. This surge is a normal adaptive response and can lead to misinterpretation if testing is performed too early.

Therefore, adherence to proper screening timing is essential to minimize diagnostic errors.

A TSH level ≥ 20 mU/L on screening requires confirmation with serum testing before initiating therapy. If serum FT4 is low, treatment should begin immediately without delay [7]. In cases where TSH is elevated but FT4 remains within the normal range, further evaluation is necessary. These cases may represent subclinical hypothyroidism or transient conditions, and repeat testing or referral to a pediatric endocrinologist is recommended. Neonatal screening has proven to be highly effective in early detection of CH. It allows identification of affected infants before the onset of clinical symptoms, thereby preventing irreversible neurological damage. In Indonesia, screening data indicate a higher prevalence compared to global estimates, highlighting the importance of expanding screening coverage nationwide [5]. Early detection through laboratory screening is essential to ensure timely treatment and optimal developmental outcomes.

Management and Therapeutic Intervention

The management of congenital hypothyroidism focuses on early initiation of thyroid hormone replacement therapy to prevent irreversible neurological damage. Levothyroxine (L-T4) is the treatment of choice and should be started as soon as the diagnosis is confirmed, ideally before the infant reaches two weeks of age [7], [10]. Early initiation of therapy is strongly associated with improved cognitive and physical outcomes, while delayed treatment increases the risk of permanent intellectual disability. Levothyroxine is administered orally, and proper administration is essential to ensure optimal absorption. Tablets can be crushed and mixed with water to facilitate administration in infants. However, it should not be given together with substances such as soy, iron, or calcium, as these can interfere with drug absorption [7]. Consistency in the timing and method of administration is important to maintain stable hormone levels.

Parental education plays a crucial role in ensuring adherence to treatment, as long-term therapy is often required. Treatment decisions are based on laboratory findings. Immediate therapy is indicated in cases with low FT4 levels, regardless of TSH levels. If TSH levels exceed 20 mU/L, treatment should be initiated even if FT4 remains normal [7]. For borderline cases with moderately elevated TSH, further evaluation or repeat testing is recommended before initiating therapy. This approach helps avoid overtreatment while ensuring that affected infants receive timely care. In addition to pharmacological treatment, iodine supplementation may be considered in cases related to iodine deficiency, although it does not address sporadic CH [2]. Overall, effective management requires a combination of early diagnosis, appropriate dosing, and consistent follow-up. Early and adequate treatment significantly reduces morbidity and allows children with CH to achieve normal growth and development [1], [2].

Monitoring and Long-Term Outcomes

Long-term monitoring is essential in the management of congenital hypothyroidism to ensure optimal growth, neurodevelopment, and biochemical control. The primary goal of treatment is to maintain a euthyroid state, which is achieved by keeping serum TSH and FT4 levels within the normal range [4], [7]. Regular monitoring allows clinicians to adjust levothyroxine dosage according to the child's growth and metabolic needs. Monitoring should begin shortly after initiation of therapy. Thyroid function tests are recommended at 2 and 4 weeks after treatment initiation, followed by regular intervals during infancy and childhood. During the first six months of life, monitoring should be conducted every 1-2 months. From 6 months to 3 years, evaluations are performed every 3-4 months, and thereafter every 6-12 months [7]. More frequent monitoring is required if there are concerns about treatment adherence or dosage changes.

In addition to biochemical monitoring, assessment of growth parameters, cognitive development, hearing function, and bone age is necessary. Thyroid hormone deficiency can affect multiple organ systems, and comprehensive evaluation ensures early detection of developmental delays [4], [9]. Early-treated children generally achieve normal intellectual outcomes, while delayed treatment is associated with permanent deficits. At around 3 years of age, reevaluation is recommended to determine whether CH is permanent or transient. This involves temporary discontinuation of therapy under medical supervision and reassessment of thyroid function [7]. Permanent cases require lifelong treatment, while transient cases may not. Overall, consistent monitoring and early intervention are key determinants of prognosis. Effective follow-up ensures that children with CH can achieve optimal physical and cognitive development, highlighting the importance of long-term care strategies [1], [7].

IV. CONCLUSION

4 Congenital hypothyroidism is the most common congenital endocrine disorder in neonates and remains a major preventable cause of intellectual disability. The condition originates from insufficient thyroid hormone production during critical periods of fetal and early neonatal development, which directly affects brain maturation and physical growth. If not identified and treated early, it leads to irreversible neurological damage and long-term developmental impairment. Early clinical detection of congenital hypothyroidism is challenging because initial symptoms are often subtle and nonspecific. Many affected infants appear normal at birth, and early signs such as prolonged jaundice, lethargy, constipation, and feeding difficulties are frequently overlooked. This limitation highlights the critical role of neonatal screening as the primary strategy for early identification. Screening performed within the appropriate time window allows detection before clinical manifestations become evident, ensuring timely intervention.

Prompt initiation of levothyroxine therapy is the cornerstone of management and should begin as early as possible to prevent permanent neurological damage. Early and adequate treatment supports normal growth and cognitive development, allowing affected children to reach their developmental potential. Consistent drug administration and strong parental adherence are essential to maintain therapeutic effectiveness. Long-term management requires regular monitoring of thyroid function, growth parameters, and neurodevelopmental progress. Continuous follow-up enables appropriate dose adjustments and early detection of potential complications. Reevaluation during early childhood is also necessary to distinguish between permanent and transient forms of the disease, which determines the duration of therapy. In conclusion, congenital hypothyroidism is a critical pediatric condition where outcomes are highly dependent on early detection and timely treatment. Strengthening neonatal screening programs, improving clinical awareness, and ensuring access to appropriate therapy are key strategies to reduce long-term morbidity and improve quality of life in affected children..

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