JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S6

Updates in the Prevalence and Complications of Congenital Hypothyroidism in Saudi Arabia: Systematic Review

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Abstract

Background/ objectives: Clinical implications of congenital hypothyroidism (CH), such as brain problems, are mild and difficult to detect throughout infancy. They are detectable after treatment or prevention has failed. General neonatal screening is useful for detecting congenital hypothyroidism and commencing initial treatment. The purpose of this study is to compile current evidence on the prevalence and complications of CH in Saudi Arabia.

Methods: PubMed and EBSCO Information Services were chosen as the search databases for the publications used within the study, as they are high-quality sources.

Results: Our results included six studies with a total of 1,028,640 patients. The prevalence of CH among the Saudi population ranged from 0.01% to 0.12%. One study reported the prevalence of CH among the reported endocrinopathies to be 39.6%.

Conclusion: The prevalence of CH in Saudi Arabia was relatively high, owing primarily to the high number of consanguinity marriages. Thyroid disorders impact children of all ages, compromising their cognitive, physical, and behavioral development. To avoid complications, early diagnosis, and treatment, as well as continuous monitoring, are necessary. To reduce the complications of CH in children, screening, treatment, and follow-up measures must be done universally and consistently across the country in accordance with WHO and national guidelines.

Keywords; Congenital hypothyroidism; Thyroid disorders; Complications; Saudi Arabia; Systematic review.

Introduction

A lack of thyroid hormone present at birth is described as CH. A difficulty with thyroid development or thyroid hormone production (dysgenesis) is most frequent in thyroid birth hormone insufficiency. It is one of the main causes of avoidable mental delay in about 1:2,000 to 1:4,000 infants [1]. The published statistics show comparatively high incident CH in certain Arab nations, including Lebanon (1 in 1823), Bahrain (1 in 2967), Palestine (1 in 2133), Oman (1 in 2200), Saudi Arabia (1 in 2931), and Egypt with comparatively high occurrences of the CH in several Arab nations (Alexandria: 1 in 397412) [2].

CH is classified into permanent and transient forms, which in turn can be divided into primary, secondary, or peripheral etiologies. Thyroid dysgenesis accounts for 85% of permanent, primary CH, while inborn errors of thyroid hormone biosynthesis (dyshormonogeneses) account for 10-15% of cases [3]. Secondary or central CH may occur with isolated TSH deficiency, but more commonly, it is associated with congenital hypopituitarism. Transient CH most commonly occurs in preterm infants born in areas of endemic iodine deficiency. Babies in whom severe feto-maternal hypothyroidism was present in utero tend to be the most symptomatic at birth. Similarly, babies with athyreosis or a complete block in thyroid hormonogenesis tend to have more signs and symptoms at birth than infants with an ectopic thyroid, the most common cause of CH [4].

CH is common and can cause severe neurodevelopmental morbidity. The clinical manifestations are often subtle or not present at birth. Common symptoms include decreased activity and increased sleep, feeding difficulty, constipation, and prolonged jaundice. On examination,

common signs include myxedematous facies, large fontanels, macroglossia, a distended abdomen with umbilical hernia, and hypotonia [5].

Most newborns with CH have no or few clinical manifestations at birth. In countries with newborn screening programs in place, infants with CH are diagnosed after detection by screening tests .[6] There is an increased incidence of other congenital malformations in children with CH, particularly cardiac malformations, including septal defects, renal abnormalities, and the risk of neurodevelopmental disorders.[7]

Prompt diagnosis and treatment of CH is critical for the optimal neurodevelopmental outcome and require interprofessional communication and care coordination by newborn screen laboratories, primary care physicians, and pediatric endocrinologists are important .[8] Careful neurodevelopmental and neurosensory evaluations should be started early in life and repeated at important critical developmental phases, taking into account disease severity at diagnosis and providing appropriate interventions as required. Universal newborn screening is an important tool for detecting CH, but awareness of its limitations, repeated screening in high-risk infants, and a high index of clinical suspicion are needed to ensure that all affected infants are appropriately identified and treated.[9]

Study Objective

The study aims to summarize current evidence regarding the prevalence and complications of CH.

METHODS AND MATERIALS

Type of the study

Integrative Literature Review (ILR).

Exploratory research is included in this Integrative Literature Review (ILR). ILR is a method for gathering previously published studies with the goal of synthesizing evidence on a topic; it is widely used in the health sciences to find health-care methods and determine innovations, allowing for the application of evidence-based services, ensuring quality, and promoting patient safety. It comprises six steps that must be completed in order: Explanation of the study issue; inclusion and exclusion criteria; sample definition; evaluation of included studies; findings interpretation; and presentation of the ILR synthesis.

The papers that had the same goal as our study was reviewed in depth after searching and defining the sample. Following data collection, the information was grouped in a table, allowing the profile of the articles to be described and the main points to be highlighted.

PubMed and EBSCO Information Services were chosen as the search databases for the publications used within the study, as they are high-quality sources. PubMed is one of the largest digital libraries on the internet, developed by the National Center for Biotechnology Information (NCBI), which is a part of the United States National Library of Medicine. Topics concerning the prevalence and complications of CH were used in the making of the article. The founded articles were screened by titles and reviewing the abstracts.

Inclusion criteria:

The articles were selected based on their relevance to the project within the last 20 years, which should include one of the following topics; the prevalence of CH and complications of CH.

Exclusion criteria:

All other articles conducted more than 20 years ago do not have one of these topics as their primary end, or repeated studies and reviews studies were excluded.

STATISTICAL ANALYSIS

No software will be utilized to analyze the data. The data was extracted based on a specific form that contains (Title of the publication, author’s name, objective, summary, results, and outcomes). Double revision of each member’s outcomes was applied to ensure validity and minimize the mistakes.

During article selection, studies were doubled-reviewed, and their results were to assure that we enrolled the studies related to the objective of our study and to avoid or minimize errors in the results.

Results

Search results

A total of 655 study articles resulted from the systematic search, and 60 duplicates were deleted. Title and abstract screening were conducted on 595 studies, and 490 studies were excluded. 105 reports were sought for retrieval, and 25 articles were not retrieved. Finally, 80 studies were screened for full-text assessment; 53 were excluded for wrong study outcomes, and 21 for the wrong population type. Six eligible study articles were included in this ILR. A summary of the study selection process is presented in **Figure 1.**

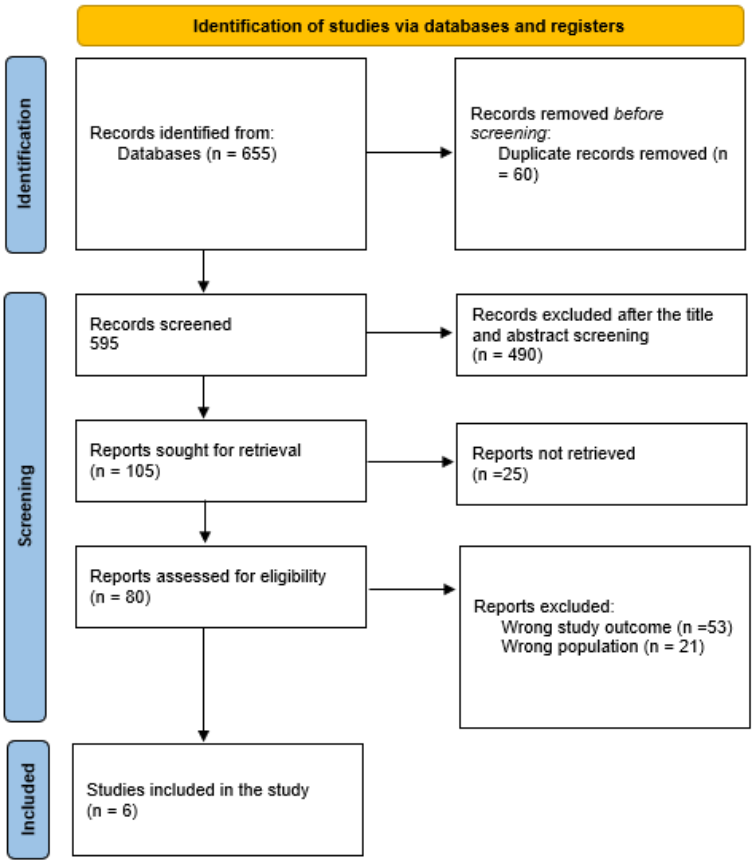

Figure (1): PRISMA flowchart summarizes the study selection process.

Characteristics of the included studies

Table 1 includes the clinical and sociodemographic characteristics of the studies. Our results included thirteen studies with a total of 1,028,640 patients. Three studies were conducted in Riyadh [13-15], one in Dammam [10], one in Bisha [11], one in Arar [12], and one in Jeddah [15]. Five studies were retrospective in nature [10, 12-15], and one was a cross-sectional study [11].

The prevalence of CH among the Saudi population ranged from 0.01% [14] to 0.12 [11]. **Al-Qahtani *et al.*** [10] reported the prevalence of CH among the reported endocrinopathies to be [39.6%]. Inherited diseases are widespread in Saudi society due to high consanguinity marriages. The thyroid condition spectrum is very comparable to the findings from both local and international studies. Thyroid problems affect children of all ages, affecting their cognitive, physical, and behavioral development. To avoid complications, early diagnosis and treatment, as well as constant monitoring, are required [10, 11, 15]. An effective neonatal screening program allows for early detection, which leads to quick treatment of CH and prevention of long-term neurocognitive impairment [15].

Table (1): Clinical and sociodemographic characteristics of the included studies.

Study	City	Study design	Participants	Age range	Females (%)	Prevalence (%)	Risk factors and main outcomes	ROBIN-I
Al-Qahtani et al., [10]	Dammam	Retrospective	148	1-16 (y)	64.2	39.6	Apart from inherited problems, which are widespread in Saudi society due to high consanguinity marriages, the thyroid disorder spectrum is highly comparable to the local and international findings. Thyroid diseases affect children of all ages, varying their intellectual, physical, and behavioral development. This necessitates early diagnosis and treatment and continuous follow-up to avoid complications.	Moderate
Abbas et al., [11]	Bisha	Cross-sectional	2501	2-4 (w)	47.7	0.12	Thyroid hormone insufficiency at birth is usually caused by the thyroid gland's maldevelopment (dysgenesis) or biosynthesis problems (dyshormonogenesis). These conditions cause primary, secondary, or central hypothyroidism at birth, resulting in TSH insufficiency.	Moderate
Alenazi et al., [12]	Arar	Retrospective	18989	NM	NM	0.03	NM	High
Mohamed et al., [13]	Riyadh	Retrospective	56632	> 23 (w)	NM	0.03	NM	Moderate
Alfadhel et al., [14]	Riyadh	Retrospective	775000	NM	NM	0.01	NM	

								High
Al Shaikh et al., [15]	Riyadh and Jeddah	Retrospective	175,370	9 (y), (median)	53.5	0.04	Because of consanguinity, the incidence of dyshormonogenesis in CH is higher than in the rest of the world (34.5% vs. 20%). An effective neonatal screening program allows for early detection, which leads to quick treatment of CH and prevention of long-term neurocognitive impairment.	Moderate

Discussion

In this ILR, we are studying the prevalence and possible complications of CH among the Saudi population. We found that the prevalence of CH among the Saudi population ranged from 0.01% to 0.12 [11, 14]. **Al-Qahtani *et al.*** [10] reported the prevalence of congenital hypothyroidism among the reported endocrinopathies to be 39.6%. Inherited diseases are widespread in Saudi society due to high consanguinity marriages [10].

A higher frequency (85%) of consanguineous marriage in some Saudi areas, such as Najran, compared to the rest of the Kingdom (55%) was found [16], with the recessive inheritance of enzyme abnormalities in thyroxine synthesis postulated as the source of this high occurrence in Saudi Arabia [16]. Other locations in Saudi Arabia reported CH occurrences ranging from 1 in 2500 to 1 in 3500 [17]. These figures are equivalent to the global prevalence of CHT [18].

The significant prevalence of CH in the Saudi population, we believe, underscores the need for a neonatal screening program. Although the TSH levels in the six confirmed CHT cases in the current study were greater than 60 mIU/L, we would be mindful of changing the cut-off value from 30 to 60 mIU/L, as some false-negative instances may be overlooked. Furthermore, we discovered that sensitivity and specificity were equivalent, so we will continue to use the lower cut-off number and collect more data to determine a more appropriate figure [19].

We found that thyroid problems affect children of all ages, affecting their cognitive, physical, and behavioral development. To avoid complications, early diagnosis and treatment, as well as constant monitoring, are required [10, 11, 15]. CH is one of the most prevalent and predictable causes of mental retardation in children, and early detection and treatment can save lives. Clinical effects of congenital hypothyroidism, such as brain dysfunction and injury and nerve growth retardation, are modest and unnoticeable in infancy, only becoming apparent when it is too late for treatment or prevention. As a result, general newborn screening is helpful in detecting congenital hypothyroidism and commencing early therapy [20].

Most hypothyroid infants are normal at birth and show no indications of the condition. However, follow-up studies in these patients show that, in addition to recognized neurological complications such as mental retardation, developmental problems (poor motor coordination, imbalance), eye aberrations, and learning obstacles, delays in diagnosis and treatment may result in stunted development and short stature [21, 22].

Previous research has mostly focused on the primary indicators of children's growth, such as height and weight, and has not addressed developmental difficulties. **Faizi *et al.*** compared the growth status of children with hypothyroidism diagnosed in the congenital hypothyroidism screening program in Isfahan to that of healthy children in the same age group in research. They measured and reported height, weight, and head circumference for case and control groups in their study. The results demonstrated that the range of these indicators in affected children was substantially different from healthy children at the start of diagnosis. Still, the condition in head size reduced to less than 3% of normal head circumference at the age of 3, and height gradually reduced to 3% and 9% of normal height in girls and boys, respectively. However, the weight index difference was still greater than 3% of normal weight in both sexes. As a result, it may be inferred that kids with congenital hypothyroidism experienced growth abnormalities that improved during follow-ups [22].

Mental and developmental retardation caused by CH can only be avoided with quick treatment and close monitoring throughout childhood and adolescence. The treatment should begin as soon as the diagnosis is confirmed via NBS or a follow-up blood test. Treatment should begin within the first two weeks of infancy to ensure appropriate neurodevelopment [24].

Our study demonstrated that the effective neonatal screening program allows for early detection, which leads to quick treatment of CH and prevention of long-term neurocognitive impairment [15]. Screening programs for CH have been established in Canada, the United States, portions of Mexico, Western Europe, Japan, Australia, and New Zealand, and they are in the process of being developed in many other countries throughout Eastern Europe, Asia, South America, and Africa. It is estimated that 25 percent of the world's 127 million births are screened for CH [23].

Saudi Arabia is one of the countries with a significantly higher incidence of CH (1:500) [25]. In 1989, the Ministry of Health began a countrywide screening program. Although the majority of newborns in the Kingdom are born in hospitals, most mothers and babies are discharged within 24 hours following birth. TSH in cord blood was agreed upon as a primary screening test by the CH screening advisory group [16].

Conclusion

The prevalence of CH in Saudi Arabia was relatively high, mostly due to the high rate of consanguinity marriages. Thyroid conditions affect children of all ages, affecting their cognitive, physical, and behavioral development. To avoid complications, early diagnosis and treatment, as well as constant monitoring, are required. To decrease the complications of CH in afflicted children, screening, treatment, and follow-up procedures must be implemented universally and coherently across the country in accordance with WHO and national guidelines.

Following the establishment of the diagnosis, immediate therapy is required. Frequent monitoring can help to avoid overtreatment or undertreatment. TSH is a highly sensitive test; however, further research is needed to establish the cutoff and eliminate false positives. Additional research is also required to identify temporary cases. Families and carers require extensive counseling on diagnosis, drug administration methods, compliance, and the implications of inadequate treatment.

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