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RESEARCH ARTICLE
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FREQUENCY OF CONGENITAL HYPOTHYROIDISM IN NEWBORN AT TERTIARY CARE HOSPITAL

Dr Muhammad Fareeduddin[1], Dr Riffat Farrukh[2*], Dr Atika Sher[3], Dr Qamar Rizvi[4], Dr Syed Tariq Ali Adnan[5], Dr Shaheen Masood[6]

[1]Consultant Pediatrician, Indus Hospital, Karachi, Pakistan
[2*]Assistant Professor, Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan
[3]Assistant Professor, Liaquat National Hospital and Medical College, PakistanHamdard College of Medicine & Dentistry, Pakistan
[4]Hamdard College of Medicine & Dentistry, Pakistan
[5]Assistant Professor, CHS, KMDC, KMU, Pakistan
[6]Assistant Professor, Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan

***Corresponding author:** Dr Riffat Farrukh,
*Email: riffatfarrukh15@gmail.com

Abstract
Congenital hypothyroidism (CH) is a condition which presents at birth and causes severe developmental abnormalities if left undiagnosed/treated. The study reported the burden of Congenital hypothyroidism among neonates Department of paediatrics, Abbasi shaheed Hospital, Karachi in the duration from January, 2024 to June, 2024 and evaluated maternal and demographic risk factors. In the methodology Five hundred newborns were screened for CH using Thyroid-stimulating hormone (TSH) levels in a Cross-sectional study. There were three TSH level groups based on their levels: less than 10%, 11-20% and greater than 20%. Other data including criminal history, and patient s age, family history of thyroid diseases as well as gender and consanguinity were also collected and analyzed.
The overall prevalence, 2% was identified with CH which is same as that noted in other developing countries. Female newborns were much likely to have CH compared with male (about 60% vs. 40%). Further, being aged ≥ 35 years and having a positive family history of thyroid disease in the mother were found to be strong risk factors for CH.

Consequently, 20% of the cases were consanguineous.
The study an unexpectedly high prevalence of CH in the region underlining the necessity of having newborn screening programs as a routine to invite early diagnosis and intervention. This highlights the need for selective screening in particular among female infants, those with older maternal age or family history of thyroid conditions. We must broaden the scope of research to larger samples and multiple hospitals, for a better elucidation of molecular epidemiology in CH which might help to enhance maternal and newborn health outcomes.

Keywords: Congenital hypothyroidism, newborn screening, thyroid-stimulating hormone, maternal age, family history, gender, consanguinity.

Introduction

Congenital hypothyroidism (CH) is a major endocrine disorder that originates in an infant born with an underactive thyroid gland, characterized by reduced production of thyroid hormones. Hormones such as thyroxine (T4) and triiodothyronine (T3) (Pirahanchi et al., 2018), which are essential for normal growth in humans, especially of the central nervous system. This thyroid hormone is essential for myelination of the nervous system, formation of the skeletal system and metabolism in general during neonatal period. If left untreated or recognized late, CH can result in irreversible intellectual disability and/or developmental delays as well as growth failure (Srour et al., 2020), making it one of the most preventable causes of intellectual disabilities in children.

Thyroid hormones and neurodevelopment in the fetus, neonate If not recognized and treated early, CH can result in serious physical and mental health problems later during life than previously thought. The earlier the intervention, often thyroid hormone replacement therapy for CH is initiated; permanent complications are prevented and affected children to live a normal life as long as healthy. The prevalence of CH varies worldwide, ranging from 1 in 2,000 to more than 1 in 4,ooo newborns (Roth et al., 2018), nevertheless it can be higher particularly within populations characterized by a high rate of consanguinity and/or iodine deficiencies both factors strongly linked with thyroid gland development and function.

Congenital Hypothyroidism Pathogenesis

The two major types of congenital hypothyroidism are permanent and transient. The permanent form is either due to developmental failure of the thyroid gland (thyroid dysgenesis or agenesis, ectopy) that results in athyreosis, hypoplasia, hemiagenesis/hemidysplasia and associated structural abnormality including ion transport defects or a defect with normal morphogenesis characterizing dyshormonogenic goiter. Permanent CH is associated with dysgenesis (85%) and less commonly, dyshormonogenesis(10-15%) (Prabhu et al., 2018). The latter can result from maternal factors such as iodine deficiency or the presence of maternal blocking antibodies. It is self-limiting in the sense that this variety of CH may normalize over several weeks or months, but thyroid functions have to be monitored closely for normal growth.

Importance of Early Diagnosis

CH at birth is often asymptomatic and responds well to thyroxine replacement therapy, but unless newborn screening programs are in place the diagnosis may be delayed. Without screening, the majority of CH cases are not recognized until symptoms such as poor feeding, decreased activity, prolonged jaundice after birth or a large umbilical hernia develop typically within days to months from birth (Band et al., 2023). By the time you see a symptom, brain damage has occurred and is usually not reversible. Consequently, the implementation of newborn screening programs for CH represents one of the major breakthroughs in pediatric endocrinology. Screening for CH in the first days of life allow clinicians to start treatment with levothyroxine, a synthetic thyroid hormone that is fully effective as preventing almost all long-term consequences of the disease.

Congenital Hypothyroidism in Developing Countries

Although a number of pilot studies exist in developing nations, large scale newborn screening programs for CH are sparse due to limited resources and healthcare infrastructure along with competing demands on health budgets. CH is hitherto predominantly diagnosed late in regions where screening does not exist, when children miss developmental milestones or present with irreversible cognitive anomalies. This is further catalyzed by risk factors like iodine deficiency, which are more common in low and middle-income countries such as Pakistan (Wu et al., 2024). Thyroid hormone is produced by the thyroid and iodine has a critical role in its production, thus an inadequate supply during pregnancy can induce underfunction of this gland. Salt iodization programs have been launched in various countries to enhance the intake of this element among which, Pakistan is one such country where it remains a public health problem. As a result, there may be an increased

prevalence of thyroid disorders diagnosed at least in some cases as CH than in countries where iodine sufficiency is adequate (Vanderpump et al., 2019).

Literature review:

According to (Essazai et al., 2022) Determine frequency of the congenital hypothyroidism (CH) in newborn at tertiary care hospital. The Study design which is used in is Cross-sectional study. And the Place and Duration is the Department of Paediatrics, Unit-2, Bolan Medical College Hospital,Quetta, Pakistan from the January 2022 - June 2022. Neonates of both genders born with birth weight above 1500 grams having gestational age above 28 weeks, presenting between 3 to 5 days following birth were analyzed. At the time of enrollment, demographic characteristics of the neonates were noted and screening of CH was done. The CH was labeled asserum TSH ≥ 20mU/ml and T4 < 9 pmol/l. The Results of this during the study period, a total of 383 neonates as per inclusion/exclusion criteria were analyzed. There were 239 (62.4%) boys and 144 (37.6%) girls. The mean age was 3.87+0.843 days. The mean TSH level was 12.807+5.11 mU/ml (ranging 7 to 50 mU/ml). We noted that CH was found in 10 neonates (2.6%). The reported frequency of CH seems higher as compared to contemporary literature which raises the importance of CH screening programs at national level. The conclusion is the frequency of congenital hypothyroidism was 2.6% among newborns at a tertiary care hospital.

According to (Al-Qahtani et al., 2022) In human species congenital hypothyroidism (CH) is the commonest preventable cause of mental retardation. A clinician should be aware of its etiology, epidemiology, clinical presentation and management. As long as the visual late clinical findings is a predetermined mental retardation of advanced degree, and that diagnosis of it if not via newborn screening, how are decided during rare serious diseases in favor of a non-clinical base. These children should have definitive laboratory and radiologic diagnostic testing as soon as the neonatal screening test becomes positive. Its pathological approach, therapeutic and follow-up should be widespread knowledge for all pediatricians during their adolescence period, and later on to every generalist when these people eventually become adults in order to avoid brain damage and assure long-term clinical/biochemical euthyroidism. Given that congenital hypothyroidism is a disease deadly and depends on early diagnosis with appropriate diagnostic tools it also requires therapy early, early and controlled

According to (Rose et al., 2023) Congenital hypothyroidism (CH)Correlates with disabilities andCan be treated. Early and appropriate treatment because of the detection by universal newborn screening probably accounts for grossly normal neurocognitive outcomes significantly into adulthood. The NBS for hypothyroidism, however, has not yet been implemented in all the countries around the world. NBS is unavailable to 70 % of neonates globally.

Levothyroxine is the initial treatment of CH at 10 to 15 mcg/kg per day (Mateo et al., 2019). Treatment goals are to provide continuous euthyroidism with a thyroid-stimulating hormone level and free thyroxine concentration in the upper half of age-specific reference range during the first 3 years of life. Questions remain on how best to detect abnormal thyroid function and the appropriate treatment of selected population such as preterm or LGA infants, those with transient or mild CH, trisomy 21, central hypothyroidism (Rose et al., 2023).

Newborn screening alone would not significantly reduce the adverse results of CH in a young population. Managing CH as well as NBS, require timely diagnosis confirmation and interpretation of thyroid function testing (Rose et al., 2023), treatment and follow-up. Clinical implications: Even in apparently normal thyroid screening results, the presence of clinical symptoms should encourage physicians to investigate hypothyroidism However, in children with clinical symptoms and signs of hypothyroidism (eg., wide posterior fontanelle, macroglossia, umbilical hernia, prolonged jajsondication), we suggest to determine serum thyrotropin (TSH) and free thyroxine (FT4) concentration irrespective of NBS result.

Etiology of Congenital Hypothyroidism

CH can be separated into major categories including primary and central hypothyroidism. Primary CH is due to direct thyroid gland malfunction, and central CH is secondary to defective quantity of thyroid-stimulating hormone (TSH) resulting from pituitary or hypothalamic dysfunction.

There are two types of Primary Congenital Hypothyroidism, they are the following: thyroid dysgenesis, and thyroid dyshormonogenesis (Kostopoulouet al., 2021). Agenesis (absence), hypoplasia (underdevelopment) or ectopia (abnormal location of thyroid) grouped under the term as thyroid dysgenesis, is responsible for approximately 85% of CH cases. Dyshormonogenesis is used to define the alteration in thyroid hormone synthesis (Song et al., 2021), mostly by genetic mutations affecting hormonal production and explaining around 10–15% of CH cases.

Sometimes, it is only **transient congenital hypothyroidism** due to maternal iodine deficiency or intake of antithyroid drugs prior to pregnancy. Although self-limited in the majority, transient CH can progress to morbidity or even mortality if diagnosed late (clinical and subsequently laboratory) during the neonatal period.

Risk Factors for Congenital Hypothyroidism

There are few important factors that central to the development of congenital hypothyroidism:

Consanguinity:

Autosomal recessive mutations in genes involved in thyroid hormone synthesis or function can produce CH (Stoupa et al., 2021), which manifests as a genetic disorder that is more common where consanguinity is practiced,(occurring at high frequency among the population of such regions of the world including various parts of South Asia and the Middle East).

Iodine Deficiency:

As a result, iodine is an essential part of the thyroid hormone that your body produces. One of the most common risk factors for hypothyroidism and other thyroid dysfunctions is iodine deficiency. Congenital hypothyroidism is slightly more common in regions where iodine deficiency (such as certain parts of South Asia, Africa, and the Middle East) is usually the cause (Taylor et al., 2018). Salt iodization and other efforts globally have made headway in reducing the burden of iodine deficiency, that still is a huge issue in many parts of the developing world.

Maternal Autoimmune Diseases:

Maternal thyroid function has a direct influence on fetal thyroid status, and maternal autoantibodies to the transplacental ones (Huget-Penner et al., 2020). The antibodies in turn can cross the placenta and lead to suppression of fetal thyroid gland.

Environmental Factors:

Newborns with potentially contaminant-mediated exposure to thyroid gland uptake inhibitors (perchlorate, thiocyanate, nitrate) have been associated with thyroid dysfunction.

Clinical Manifestations of Congenital Hypothyroidism

Many newborns with CH are asymptomatic at birth, and thus detected by neonatal screening rather than clinical symptoms. Left untreated, you may develop symptoms a few weeks or months later that can include;

Prolonged jaundice
Poor feeding
Lethargy
Constipation
Large anterior fontanelle
Umbilical hernia
Macroglossia (increase in size of the tongue)
Low muscle tone (hypotonia)
Coarse facial features

If not treated by the end of the neonatal period, CH causes developmental delays, growth retardation and mental retardation. Screening programs are therefore potentially important for public health by enabling early diagnosis and treatment to eliminate such complications.

Methodology

It consisted of the research design, the population under study, how data were collected and an approach in assessing CH frequency among neonates at Department of paediatrics, Abbasi shaheed Hospital, Karachi in the duration from January, 2024 to June, 2024. This section is the key to ensuring that study is reproducible, transparent and more importantly makes your inferences robust which helps one judge its findings.

Research Design

For this purpose, a descriptive cross-sectional study was conducted in order to institute the frequency of congenital hypothyroidism among newborns at tertiary care hospital. A cross-sectional design is suitable for this study because it enables assessment of a large part of the newborn population by collecting data at only one time point. The descriptive design of the study permits quantification of newborns affected with CH, without any kind manipulation in variables or introducing an intervention.

Study Setting

An extensive data for annual deliveries is available at the neonatal unit of a tertiary care hospital situated in Pakistan where this study was conducted. Has access to proper diagnostic facilities eg neonatal screenings and caters for a mixed urban-rural population. The selection of a tertiary care hospital makes sure that this study includes the full spectrum from straightforward births to high risk pregnancies and complicated cases, which leads in an increased ratioof congenital conditions like hypothyroidism.

Study Population

The study population is newborn delivered at the tertiary care hospital during a specified period. The data include both male and female infants, no restrictions are made regarding having older siblings, birthweight or gestational age. Nevertheless, we impose a set of bespoke inclusion and exclusion criteria to guarantee the sample mirrors population statistics whilst maintaining that no bias be generated through selection.

Inclusion Criteria

Infants who were born alive at the hospital during this time may be included.

Infants whose parents give permission to be screened.

Full-term and preterm newborns.

Exclusion Criteria

Infants with severe congenital or fatal disease incompatible with the completion of screening.

Newborns whose parents do not give their consent for the study.

Sample Size and Sampling Method

The survey is administered on a convenience sampling basis and includes all low birthweight infants born during the study period. The choice of convenience sampling reflects how practical it is to find newborns in a hospital setting.

This disease is one of the commonest treatable causes of mental retardation, congenital hypothyroidism which has been estimated at 1:2,000-1:4,000 live births. Taking an incidence of 1 in 2,500 with a confidence level and margin of error at the usual 95% (there are other options), then sample size required to reach statistical power is calculated as below:

$$n = \frac{Z^2 \times \mathrm{P} \times (1 - \mathrm{P})}{E^2}$$

Where:

- n = sample size

- Z = Z-score corresponding to a 95% confidence level (1.96)
- P = expected prevalence (1/2,500 = 0.0004)
- E = margin of error (5% = 0.05)
- Plugging in those values, we estimate a sample of about 500 newborns. With the equally anticipated number of hospital deliveries, this period will permit inclusion in our sample at least 500 newborns.

Data Collection

- Newborn Screening For Congenital Hypothyroidism
- Neonatal screening for congenital hypothyroidism by doing blood sample to test TSH within 48–72 hours after birth. This screening is done by analyzing a heel-prick blood sample which has been collected on a filter paper card (Guthrie) in the laboratory of the hospital.
- Screening is with the thyroid-stimulating hormone (TSH) and one does not have to go further than that. Increased blood TSH levels hypothyroidism If the TSH level from initial testing is high, then a second blood test measuring serum free thyroxine (T4) levels is used to make this diagnosis.

Data Collection Tools

Demographic Data Form (height, weight, gestational age and birth order) will be obtained from medical records through a standard data collection form that contains other information on the gender of newborns to parents.

Test Results: Levels of TSH and, if necessary, T4 for each individual infant in the laboratory.

Parents or legal guardians give their written informed consent on a parental consent form in agreement of newborns' participation to the study. The consent form has all info regarding the study, the screening process, what are expected risks and that data will remain confidential.

Diagnostic Criteria

In this work, we will consider congenital hypothyroidism as:

A TSH level ≥ 20 mU/l in the dried blood spot (screening test)

T4 level is <10 µg/dL on the more specific follow-up serum test for confirmation.

Data Analysis

Analysis of the data was done by SPSS (statistical package for social science) version 24. We summarize demographic information and screening test results using descriptive statistics e.g., frequencies, percentages, means and standard deviations.

The primary outcome is the incidence of congenital hypothyroidism, expressed as a fraction defined by cases with CH and divided on all newborns screened. A 95% confidence interval is also calculated to give an idea about how precise the frequency estimate may be.

Chi-square tests are used to compare categorical variables (such as sex, birth weight and delivery mode) in neonates with CH versus normal thyroid status.

Independent t-tests are performed to compare differences in continuous variables (e.g., TSH and T4 levels) between groups.

The p-value < 0.05 means a significant result

Limitations of the Study

Although this study provides important incidence data for CH at a tertiary care hospital, there were several limitations to be considered:

The convenience sampling can work as a main factor for selection bias, and may not fully represent the general population.

The study is based on a single hospital, so it cannot be generalized to all areas.

The lack of data on follow-up for treatment success (since this paper only diagnoses CH) a further limitation.

Results

This study aimed to determine the frequency of congenital hypothyroidism (CH) in newborns at a tertiary care hospital. A total of 500 newborns were screened for CH using Thyroid Stimulating Hormone (TSH) levels. The results are presented below, including key demographic data and findings from the screening process.

1. Demographic Characteristics of the Study Population

The study included 500 newborns, with a gender distribution of 270 males (54%) and 230 females (46%).

The mean birth weight of the newborns was 3.15 kg (SD: 0.45), and the mean gestational age was 37 weeks (SD: 3.1).

Table 1: Demographic Characteristics of Newborns

Demographic Variable	Mean ± SD / Count (%)
Birth Weight (kg)	3.15 ± 0.45
Gestational Age (weeks)	37 ± 3.1
Gender	
Male	270 (54%)
Female	230 (46%)
Maternal Age (years)	29 ± 5.8
Consanguinity	
Yes	80 (16%)
No	420 (84%)
Family History of Thyroid Disorders	
Yes	35 (7%)
No	465 (93%)

2. Frequency of Congenital Hypothyroidism

Out of the 500 newborns screened, 10 newborns were diagnosed with congenital hypothyroidism based on elevated TSH levels (>20 μU/mL). The frequency of CH in this cohort was found to be 2%.

Table 2: Frequency of Congenital Hypothyroidism in Newborns

Parameter	Count (%)
Total Newborns Screened	500 (100%)
Newborns with Elevated TSH (>20 μU/mL)	10 (2%)
Confirmed Congenital Hypothyroidism	10 (2%)

3. TSH Levels in Newborns

The mean TSH level among all newborns screened was 10.35 μU/mL (SD: 5.75). Among the 10 confirmed cases of congenital hypothyroidism, the mean TSH level was significantly higher at 24.5 μU/mL (SD: 3.2).

Table 3: Thyroid Stimulating Hormone (TSH) Levels in Newborns

Group	Mean TSH Level (μU/mL) ± SD
All Newborns	10.35 ± 5.75
Newborns with CH	24.5 ± 3.2
Newborns without CH	9.65 ± 4.3

4. Distribution of CH by Gender

The gender distribution among the confirmed CH cases was slightly skewed towards females. Out of the 10 cases, 6 (60%) were female, and 4 (40%) were male.

Table 4: Gender Distribution in Confirmed CH Cases

Gender	Count (%)
Male	4 (40%)
Female	6 (60%)

5. Factors Associated with Congenital Hypothyroidism

Maternal age, consanguinity, and a family history of thyroid disorders were assessed as potential factors associated with the occurrence of CH. Among the 10 CH cases, 3 (30%) were born to mothers with a history of thyroid disorders, and 2 (20%) had consanguineous parents.

Table 5: Factors Associated with Congenital Hypothyroidism

Associated Factor	Cases with CH (n = 10) (%)	No CH (n = 490) (%)
Maternal Age > 35 years	2 (20%)	28 (5.7%)
Consanguinity	2 (20%)	78 (15.9%)
Family History of Thyroid Disorders	3 (30%)	32 (6.5%)

Discussion

The aim of this study was to evaluate the prevalence of congenital hypothyroidism (CH) in a target population, the newborns that attended at tertiary care hospital. There the CH preload was with 2% in a similar group of 500subset children. They are also reportedly associated with disease patterns of the noted condition in many areas except Eastern Africa where it has been found to be about one per 4000 births [3]. While the CH prevalence appeared to be higher or a similar frequency as in regions where this ethnic origin is prevalent, further corroboration cannot be provided. It is possible that this finding predominates in the region because of the population characteristics for which it provides care or maybe gene-environment interactions existing in that particular area.

Our study finding on prevalence of CH is concordant to some studies conducted at few developing countries like India and Pakistan which report a rangeof 1.8% to 2.5%. These studies underscore the critical nature of newborn screening programs in areas where these may be prevalent due to insufficiency of dietary iodine or genetic factors. In contrast to this several nationwide studies conducted in western countries for example regions of united states (public health initial screening program) and Europe have shown the prevalence to be around 1:3000-4000 births as they contribute to a lower number of the population cohort detected due to well implemented public health strategies, community programs and also good nutritional Iodine and this seems to be consistent with other part of developing word that iodine sufficiency is major contribution factor. The results of this study similarly corroborate what other scholars have argued that the increased prevalence recorded in the current study could be as a result of variations in geographical coverage and delivery care services, other environmental and maternal health factors that increase susceptibility to congenital hypothyroidism.

Moreover, we have also documented that females are more commonly to be involved (60% of cases) than males (40% of cases), and this agrees with other observations on the autism-congenital hypothyroidism female predominance. These are for example, was brought into notice by the population based study of Rastogi and LaFranchi in which also expressed same views that hypothyroid females tends to have more thyroid dysgenesis than males which is most common type of CH. This gender bias has been recognized for some time, but the biological reason for this was unclear. But hormonal and genetic factors appear to be involved. Our study accentuates the notion that female neonates may be at higher potentiality for CH compared with male newborns and targets the strict compliance to follow up and screening policies.

Combined with maternal factors such as higher maternal age and family history thyroid disease accounted for a greater risk of CH. In our study, we observed that 20% of CH cases occur in infants born to mothers aged ≥ 35 years and 30% have a family history for thyroid disorders. Again, Similar results were reported by others who demonstrated the strong influence of maternal age and family history on CH. A research done by Aoplané has also showed that CH babies born to such families from malignant were indeed a large level Pontiac Disting family history of thyroid disease in relation to severity parlanceurovisionerre (education). Outside star Chile Associated tog Evans Public Pool Research Society Campbell Althought, only a minimal relationship of Cohesion of Consanguinity with CH was revealed (of 20% of total CH cases) in the current study this has been made in some other studies particularly among Middle Eastern countries, where marriages are consanguineous, and

it seens to predispose affected children to an autosomal recessive disease such as Congenital Hypothyroidism (CH).

We agree that in area where this disease is high prevalent and obligatory congenital hypothyroidism screening of newborn infants should be implemented early and systematically. Our study confirms earlier findings and elucidates the extent to which indigenous peoples as well as the maternal attributes contributed to CH prevalence. Further studies are required to probe deeper into the determinants responsible for regional disparities in CH and well-defined CH screening approaches should be executed across various geographies. However, it will be important to only expand the focus of additional research to test more hospitals that differ by scale in case we are really seeking a comprehensive picture of congenital hypothyroidism epidemiology.

Conclusion

The study was conducted to analyze the prevalence of Congenital Hypothyroidism (CH) in a group of newborns at tertiary care hospital and found that 2 % out of 500 infants were CH cases. These estimates were close to findings in other countries like India (1.8%) and Pakistan (2.5%) where, CH is common. Whereas prevalence rates of less than 1% are reported in developed countries such as the United States and European regions due to stringent neonatal screening programs and iodine-rich diet for the mother. Results of our study indicate the necessity for an enhanced and prompt screening system in high CH prevalence regions, to expedite diagnosis and intervention.

CH was diagnosed in 60% of the female new-borns, and in 40% of males (this finding correlates with data from other research that indicates a greater vulnerability to CH among girl new-borns). Older maternal age and a family history of thyroid disorders were also associated with a higher CH risk. These poorer outcomes highlight the need for focused screening in high-risk populations, such as female infants, older mothers and persons with a family history of thyroid disorders.

Although such studies are useful in documenting the developmental patterns of CH prevalence and risk factors, its results also underscore a need for more expansive study. Action should be taken immediately, such as broadening screening programs and increasing awareness especially in underdeveloped healthcare infrastructure localities to control the problem of CH. Larger samples and more diverse populations in future studies would help to identify genetic or environmental factors that drive regional gap of CH prevalence. This can help healthcare systems to detect early and intervene in a timely manner with newborns who are at risk for congenital hypothyroidism.

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