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## Evaluating the biochemical and clinical features at the time of diagnosis in order to identify eutopic thyroid gland congenital hypothyroidism

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### Abstract

**Introduction:** When left untreated, congenital hypothyroidism (CH), a serious endocrine disease in children, can result in irreversible mental impairment. Recent adjustments to screening systems and demographic considerations have contributed to an increase in CH incidence. More frequently occurring mild variants of CH with a eutopic thyroid gland need for a deeper comprehension of its clinical and molecular characteristics.

**Methods:** In this review, the clinical and biochemical features of CH with eutopic thyroid gland at the time of diagnosis will be analyzed. To locate pertinent research and information on CH with a eutopic thyroid gland, a thorough examination of the literature was carried out. The clinical features observed in infants diagnosed with CH and eutopic thyroid gland were examined including manifestations at birth, growth parameters, and developmental milestones. To evaluate the severity of hypothyroidism, biochemical measures including thyroid hormone levels ( $T_4$ ,  $T_3$ ) and thyroid-stimulating hormone (TSH) were evaluated. In individuals with eutopic thyroid gland, the differentiation between transitory and permanent types of CH was also looked into. We looked at parameters such TSH and thyroid hormone levels at diagnosis, gender, delivery characteristics, prematurity, low birth weight, maternal risk factors, family history of thyroid disease, and consanguinity that are linked to a higher risk of transitory CH.

**Results:** The results of this review offer insightful information about the clinical and biochemical characteristics of CH with eutopic thyroid gland. They contribute to the identification of individuals who require long-term levothyroxine treatment and aid in distinguishing between transient and permanent forms of CH. The vast range of temporary CH prevalence in patients with eutopic thyroid gland highlights the need for more research in this area. The evaluation of current diagnostic and treatment strategies highlights the importance of standardized approaches in managing mild forms of thyroid dysfunction.

**Conclusion:** Congenital hypothyroidism (CH) and eutopic thyroid gland in neonates are studied clinically and biochemically to gain insight into this particular group. It allows for the identification of individuals who may require long-term levothyroxine treatment and helps differentiate between transient and permanent forms of CH.

**Keywords:** Congenital hypothyroidism, eutopic thyroid gland, transient, permanent, prevalence, diagnosis

### Introduction

Congenital hypothyroidism or CH is a circumstance in which infants fail to deliver ok thyroid hormone. It turns into a predisposing situation if the toddlers do now not produce sufficient thyroid hormones and a restoration scenario if they're dealt with dietary supplements so one can update the negative thyroid hormone. The overall performance disruptions inside the improvement of thyroid gland occur in maximum times of CH, even though a few human beings show up an ordinary structural presentation of the identical <sup>[1]</sup>. ACH essential motive is due to the ailment referred to as thyroid dysgenesis that contains special anomalies cases of dysplasia as well as the bad hypoechogenicity which causes thyroid regression.

The primary one from numerous causes which includes ectopic or agenesis of thyroid tissue <sup>[2]</sup>. While it's far actual that euthyroid times are seen in a few eutopic method of constant hormone production, however other times display reduced or absent hormone manufacturing. In mixture with environmental elements, genetics plays a vital element in a majority (20%) of congenital coronary heart cases.  $T_4$  and to stages went lower because of underproduction of thyroid hormone that is one in all contributing elements of CH pathophysiology. Instead, the unusual functioning of the anterior lobe of the pituitary gland impairs the frame's ordinary control mechanism with the resource of secretion of immoderate quantities of the hormones of

Thyroid Stimulating Hormone (TSH) and Thyrotropin-Releasing Hormone (TRH) in the case of Newborns having number one CH (three). TSH tiers remain elongated whilst the traction/subclinical hypothyroidism lets in  $T_4$  levels that live in the regular range. The  $T_4$  diploma having a low or free  $T_4$  (additionally) or low and almost ordinary TSH values are the diverse capabilities of the initial hypothyroidism in children [3]. CH falling ranges in infant can be very tough to recognize and turn out to be conveying the bare minimal signs of this disorder because of the fact a few maternal hormones may be in component transferred to the new baby little one very inadequately. Though the link of CH to the kid's maturation inside the early tiers has an effect on the thoughts, the contamination's lasting impact is irrecoverable since the child becomes with a highbrow disability [4]. First and most important, the child have to be recognized fast; and nowadays, in evaluation with the same old regression eventualities, severa progresses are being made in the screening of this syndrome in kids with the aid of utilization of kits that make sure timely intervention and an development within the neurodevelopmental consequences. Routinely, Guthrie take a look at is carried out thru sampling heel-prick blood sample from neonatal toddler to stumble on  $T_4$  and TSH tiers. This help diagnosing babies with low  $T_4$  and immoderate TSH [4]. The one and maximum influential treatment for CH is the lifelong alternative treatment of thyroid hormone, offering the preferred every day hormone ranges and right growth and improvement. Instant provision of remedy is fundamental if you want to permit the lengthy-term problems which can be brought about through overlook about of the diseases no longer to arise [5]. This plus the clinical and biochemical CH capabilities in the ones who've now not however obtained TT diagnosis offers valuable perspectives for numerous motives. It aids me end up privy to others in comparable situations to me who will should take the medication over an extended term. It allows in making the distinction between among quick-time period and especially prolonged-lived CH activates choice making on treatment and analysis [6]. Besides that, gaining access to such capabilities, the scientists turn out to be their analytical way of statistics the hidden motives of the certain styles of CH with each ordinary and mechanism that encode destiny researches and remedy control. Here, the subject proposal consists of listing the scientific and biochemical obligations noticed in toddlers with CH and euthyroid thyroid gland (ETG). On pinnacle of that, The Meadowlark and The singer are evocative of the distinction between the transitory and the everlasting, the identical episode in unique lives. Next, decide whether present day diagnostic and remedial remedies for thyroid Gland is an achievement story or a failure.

### Prevalence and Epidemiology

Table 1. Provides facts on research about the Transient congenital hypothyroidism (TCH) so that it will be further illustrated. In youngsters with congenital hypothyroidism (CH), it is feasible for their bodies to absolutely lack a thyroid feature or inadequately functioning it. It is assumed that the best strategies purpose on the were an excessive quality studying of hypoechoic CH and its epidemiology [7]. There is a difference elements showing that hypothyroidism that has eutopic (ordinary) thyroid gland exist and this has added approximately some ethnic and geographic version. Such evaluation as comparing a software for New York State that has been jogging thru the duration with the facts on the genetic mechanisms of the patient contributors of the

immoderate ethnic corporations. The fee, slightly better handy in Hispanics and Asians (1 in 1016) opposite it end up in Whites (1 in 1815) and Blacks (1 in 2002). These results, therefore, advocate that ethnicity has a major position inside the incidence of the condition with the presence of thyroid no regulator, and that this type of factors have to be taken into consideration in public health techniques and intervention frameworks. Says the research, those variables are the ones followed by using the genetic superiority of congenital hypothyroidism. CH is notion to have an effect on surplus weight newborns weighing over 4500 g further to underweight infants underneath 2000 g at begin. Moreover, the incidence of twins being affected with CH is higher compared to that of singletons with the odds of dual births associated with congenital hypothyroid is 12 instances greater than that for singletons within the obstetrical population as a whole [7, 8]. These elements are accounting of those fact ort that do not forget more than one starting and occasional beginning weight on the time of calculation estimation the superiority of CH in eutopic circumstance. Early evaluation and start of remedy play a critical function in a success manipulate of CH with reference to decreasing associated morbidity. Integrating CH into the new child screening has tested to be very powerful in accomplishing brief detection and intervention for infants with this circumstance. The confirmation is executed via heel prick blood samples that screen thyroid hormone concentrations. Using this approach, it will become easier to start the remedy fast sufficient a good way to keep away from the headaches arising ultimately. Given the performance of CHT, and new borne eutopic thyroid gland, a healthcare system may additionally moreover undertake the common and targeted screening methods to suitable interventions for this reason improve the consequences of the toddlers they were born to [8, 9].

CH in sufferers with the absolutely thyroid gland has come to be the issue of novel research, lots of which have affirmed huge versions in its prevalence charge. The reviews from antenatal thyroid screens across the U. S. Pin down CH to take region on 1 in 3000 and 1 in 4000 of stay births. While this form of survey have doubled the wealth rate to reap approximately 1 in 1500 stay start, investigations from updated fame mean a shift in the epidemiology of CH [8-10]. For example, inside the Asian population study completed over 12 years, the incidence become identified at five. 02 regular with 10,000 infants born. Realizing how CH and autoimmune thyroid - eutopic thyroid gland styles and time dynamics are interrelated comes thru analyzing tendencies and adjustments over time. Due to the doubled prevalence of congenital hypothyroidism amongst newborns engaging in extra than 1 out of 1500 newborns, the epidemiology of CH is provided with a massive alternate. Nevertheless, there may be at gift the inadequate data to support the referral to shifted 2 events of thyroid dysgenesis or dysmorphogenesis [9-11]. The organization of analyzing the prevalence and threat factors of transient and permanent CH grow to be made via the Habib and his colleagues (2021); Fars province of Iran turned into randomly selected due to the fact the web page of their look at. We see a growth of 294 214 children screened from 2013 to 2016 and the variety of children with CH instances became 938. This includes gathering vital facts and doing a completely closing exam that would be fed into the laptop for analysis and then, 642 CH times' data is brought for evaluation. According to the findings, there have been 1:313. In this region, there were 66 instances of CH within Fars province, which consisted of sixty six. 04 instances of socially

precipitated CH and 33. Ninety six instances of rapid CH The assessment indicated that the 0.33-zero.33 sell limit with a cutoff root of >2.25 g/kg and IV TSH of > 43.35 mIU/L have been sickness-free elements to long-time period CH [8].

Alavi *et al.* (2021), to explain the clinically validated case, a case manipulate assessment has been done. Three, six hundred newborns with an age ranging 3-5 days, who have been screened through assessing their TSH hormone, have been enrolled inside the have a look at. TSH degrees more than five mIU/L had been detected in 126 treated kids. However, hypothyroid analysis determined as a transient condition in 7 of the screened ones. The effects revealed a strong affiliation among poor perinatal effects, alongside preterm transport, low beginning weight, antithyroid drug use, and thyroid dysfunction [10].

By manner of Barry *et al.* (2022), Tien *et al.* (2015) to research the usage of temporary congenital hypothyroidism (TCH) and decide its affiliation with neonatal and early infant ability, French researchers did a retrospective cohort (TC). The investigator assessed correlations among those records and scientific reports on the French country wide CH registry. The registry is part of the French public health record device. 32. Nine out of 471 excessive faculty college students already enrolled inside the observe have been recognized with TCH out of the total 471 youngsters participants. As in the case of

other situations, the authors also talked about the more common factors related to TCH days of start, TSH degrees less than 50 mIU/L while the CH screening become done, the dose of levothyroxine taken at the same time as the kid celebrated her 1st anniversary, the presence of congenital heart abnormalities, and the 12 months of shipping [11].

Gmür and colleagues (2023) end that it may be better no longer to address very early congenital hypothyroidism (a), as an analytical cohort take a look at performed in the canton of Zurich, Switzerland illustrates. In this case, all live newborns who've been born amongst January 1, 2000, and June 30, 2016 with a TSH charge over 15 mIU/L were taken into consideration because the examined. Out of the 247,918 babies who had been born in the stated period, 15 diagnoses of CH have been made. Not most effective changed into it positioned that the prevalence of tCH became 1 in 12,396 births, however also the observe confirmed that the threat of this example could boom if the pregnancy changed into preceded via a complicated maternal age or an added about reasons of childbearing. The studies also hooked up a decrease degree of thyroid stimulating hormone in sufferers with CH in place of those with everlasting CH. Similarly, despite the truth that continual cerebral ischemia changed into not depending on the intrauterine age, subnormal start weight changed into negatively associated [12].

**Table 1:** Comparison of studies on transient congenital hypothyroidism (TCH)

Study	Location	Participants	Prevalence of TCH	Associated factors
Habib, <i>et al.</i> (2021) [6]	Fars province, Iran	642 neonates with CH	33.96%	> 2.25 levothyroxine µg/kg at the third year and > 43.35 mIU/L TSH concentration at initial venous sampling
Alavi, <i>et al.</i> (2021) [7]	Iran	3600 neonates	5.35%	Congenital defects, low birth weight, maternal hypothyroidism, and antithyroid medication use.
Barry, <i>et al.</i> (2022) [8]	France	471 children with CH	32.9%	Births year, levothyroxine dose taken at 12 months of age, presence of congenital cardiac abnormalities, and TSH levels below 50 mIU/L at CH screening.
Gmür, <i>et al.</i> (2023) [9]	Canton of Zurich, Switzerland	247,918 newborns with TSH above 15 mIU/L	1 in 12396 Births	Low birth weight

### Clinical Features at Diagnosis

Scientist' eyes alone may take weeks, from six to the 8, to get used to seeing the abnormalities that could appear d within the course of the primary weeks after the kid is born [13-15]. The entities that outline CH additionally can be felt via newborns and infants which have a eutopic (properly located) thyroid gland. There are precise outward signs, such a boom in sleep, a whole lot much less power to do something, problem swallowing, the superiority of constipation, and persisting jaundice. While analyzing CH, be aware of the statistical boom metrics, physical milestones, further to the physical examination effects. Generally, these features get decided later inside the route of this assessment length which encompass brief neck, past due highbrow improvement, cry that is not loud, huge fontanelles or spots at the little one's head, bulge in belly referred to as hernia, low muscle tone, peel pores and skin, coarse facial competencies, enlarged tongue, and goiter [16].

The thyroid gland anatomy wishes to be quite correct (eurotic) to hint the precise cause of congenital hypothyroidism. This is based totally on the application of strict first-rate scientific symptoms and signs. In case the uterus thyroid is every day, low serum thyroglobulin concentrations and extra of TSH levels can be indicative of each thyroglobulin synthesis disease or signaling problems with the tsh receptor. These problems are, perhaps, related to mutations of TSHR or TRBAb, and distinction in GNAS [17].

Id est Fabrication d'une concomitance dans l. A. Hormone de synthèse thyroïdienne par le fait d'un glande thyroïde eutopique embryon sert d'ailleurs de moyen par l'augmentation des taux de thyroglobulin dans le sang [18]. We have to study that the attention of TSH this is in evaluation at the time makes a decision whether or no longer hypothyroidism develops temporarily or completely in a patient with a normal eutopic thyroid. Additional developments which includes a minimum want for levothyroxine (L-T<sub>4</sub>) medicine, especially beneath 2 milligrams consistent with kilogram consistent with day, can also characterize transitory hypothyroidism [19].

Rabois *et al.*, 2013, of their desk 2. Studies of 84 youngsters with congenital hypothyroidism (CH) and healthful thyroid glands and now not the usage of an abnormalities had been achieved for the moral motive and records of clinical and biochemical trends on the referral. Thirty-four and a half of% of patients have been diagnosed with everlasting hypothyroid, the second 27. Four % with continued hyperthyrotropinemia and the third 38.1% with quick hypothyroid at their follow-up. Premature, a situation placed in five.7percentof the goiter/nodules cluster patients, thyroid hypoplasia and a immoderate requirement of L-thyroxine some other are chance parameters for growing everlasting CH. 29. Examining the iodine organization inside the thyroid tissue, 7% of the patients had been detected weird and 30% of them had the DUOX2 mutations. As for as thyroid illness and

wretched perchlorate impact people, eight. 7% who've been screened with TSH receptor gene defects decorate the chances.

Vigone and al (2014: desk 2) 24 cutting-edge preterm infant newborns with this case were diagnosed with using the cutting-edge-day little one screening. The toddlers underwent a retrospect to evaluate the state of affairs. 23.15% of the patients persisted to have hyperthyrotropinemia; 23.Eight% had everlasting hypothyroidism and sixty-.Eight% had transient hypothyroidism following a 2d assessment. Reproductive assisted, twins, much less for gestational weeks, thyroiditis of the mother, and deformities/syndrome were the foremost scientific trends linked to persistent hypothyroidism [16].

Tucker *et al.* (2016) tides. 2. In order to decide the modern-day importance and clinical traits, we went down the retrospective studies. 15.6. Ninety four% of the full 134 infants who had ectopic thyroid tissue additionally had - website on line thyroid ectopia. An embryo that regarded to have the same chances as embryos in twelve each one hundred thousand is now recognized with dual ectopia. Healthy toddlers with split bilateral ectopia had decrease propose weights for a while and bloodspot [thyroid-stimulating hormone] than ectopic patients with single ectopia and/or agenesis subjects. A correct mission that arises is the purposeful interest in the alterity deliver chain., however, have grown to be out of place after a twelve months, and their T<sub>4</sub> wishes were much like those of the agenesis group [17].

Furthermore, Cho and others (2014) once talked about that. Coupled diagnoses with permanent congenital hypothyroidism (PH) and people with transitory hypothyroidism (TH) with eutopic thyroid glands changed into looked at to look if there had been any differences between them. They referred to 66 CH instances the ones

consisted of forty with PH and 26 who have been because of TH. At 12 and 24 months of age L-thyroxine dosage of PH patients were more than the levels of either initial serum levels of thyroid stimulating hormone If a new child with CH calls for to have low doses of L-thyroxine (3.25 g/kg), it's far very probably that they are born with TH, so thyroid function can be evaluated at 12 and 24 months of age, as opposed to three years [18].

The in comparison consequences of subsidy elimination and each indirect and direct taxation are tested through Shreder *et al.* (2022) table 2. The creation of the clinical documents taken from sufferers who evolved ectopic thyroid tissue within the lingual root is to discover the cause of congenital hypothyroidism (CH). Ages of the research subjects with the 3 numbers affected CH syndrome kind of reached from 2 weeks to 17.3 years. For every patients, there has been ultrasound and radionuclide imaging and plenty of moreover were video fibro laryngoscopy and subsequent-era sequencing genome checking out. According to the have a look at it modified into determined that forty seven. Nine% of the times have been aplasia which similarly had one hemiagenesis case out of all of the toddlers and ectopic thyroid tissue have become visible stoning up in a couple of web sites in 26.0% of the kids. Of the youngsters studied, seventy-5 point seven percentage provided to the assessments for the thyroid as 'Dysthyroidism', as tested on a scintigraphy. About four percent of the teens have been located to have this thyroid tissue ectopically placed, 25 of whom have been so far the very best at the tongue's lowest factor (with eighty.6% incidence).When in evaluation to kids with aplasia, the median TSH degree in youngsters with ectopic thyroid glands become an awful lot decrease, on the same time because the median TG diploma became notably more [19].

**Table 2:** The clinical features of permanent hypothyroidism vary depending on the underlying etiology. Prematurity, familial history of thyroid disease, goiter, thyroid hypoplasia, high L-thyroxine needs, assisted reproduction, twins, tiny for gestational age, maternal thyroiditis, malformations/syndromes, and ectopic thyroid tissue are some of the more typical characteristics

Study	Population	Main Clinical Features of Permanent Hypothyroidism
Rabbiosi <i>et al.</i> (2013) [11]	84 kids that have CH and a eutopic thyroid gland	Prematurity, family history of thyroid hypoplasia, thyroid nodules, and high L-thyroxine needs.
Vigone <i>et al.</i> (2014) [13]	24 preterm infants with congenital hypothyroidism	Twins, small for gestational age, maternal thyroiditis, assisted reproduction, and malformations/syndromes
Tucker <i>et al.</i> (2016) [14]	134 babies with thyroid ectopia	Infants with dual ectopia had mean bloodspot TSH levels that were lower than those with single ectopia and those with agenesis, but their functional activity was gone at 12 months
Cho <i>et al.</i> (2014) [15]	66 patients with CH, including 26 cases of TH and 40 cases of PH	Initial blood thyroid stimulating hormone levels and L-thyroxine dosage were considerably greater in PH patients at 12 and 24 months of age.
Shreder <i>et al.</i> (2022) [16]	Ages of the 73 main CH patients ranged from 2 weeks to 17.3 years	Ectopic thyroid tissue was found in 42.4% of the children, with the most common location being a child's tongue root in 25 of them (80.6%). In children with ectopic thyroid gland, the median level of TSH was significantly lower compared to children with aplasia, while the level of TG was significantly higher

### Biochemical Markers and Diagnostic Criteria

Laboratory checks can also assist to evaluate the thyroid feature and make an accurate diagnosis of the diseases with a particular thyroid gland. This kind of examines make it possible to study hormonal ranges at distinctive stages and additionally take a look at ranges of a few markers of thyroid feature. The thyroid-stimulating hormone (TSH), anti-thyroid antibodies, and thyroxine (FT<sub>4</sub>) are all laboratory exams used to diagnose CH. The most used usually laboratory exams for this analyze. Thyrotropin Secretary Hormone (TSH) is produced through the Pituitary gland that in addition stimulates the thyroid to offer thyroxine (T<sub>4</sub>) [20].

Among the preliminary tests that efficaciously showcase a

thyroid function in the route of CH is measuring the attention of a TSH in the blood. As the thyroid stimulating hormone (TSH) shifts first in response to the imbalance within the actual thyroid hormone level inside the frame, it can for that reason play a function in early caution alerts. A boom in TSH shows the reducing of the thyroid function, at the same time as low stages of TSH is mostly a reason for the "overproduction" of the equal hormone.

Hence, TSH degrees no longer handiest serve as applicable diagnostic markers however also show how, with time, Hypothyroidism can develop [21]. The basic characteristic of the belly-churn cannot display otherwise atypical readings of thyroid-accentuating hormone and low T<sub>4</sub> or T<sub>4</sub> ranges, except

it proves the prognosis of CH too. Thyroxine or  $T_4$  is a hormone of top-score produced with the useful resource of the gland of the thyroid. It has a very useful impact on metabolism and increase. Productions of  $T_4$  is absent in CH leading to heightened basal metabolic prices and slower increase responses. This reporting of both  $T_4$  or loose  $T_4$  enables to see the real stages of thyroid hormones present which, along with the opposite records, are useful within the diagnostic system. First of all, assaying of CH and revealing its reasonability may be finished by means of supplementing the present day markers, which might be TSH and  $FT_4$ , with more biochemical markers. Thyroglobulin is a protein that is conveyed thru the thyroid gland with a keep in mind to the thyroid hormones formation. The measurement of thyroglobulin stage in serum is a applicable method that will supply an assessment at the operating of thyroid gland<sup>[22, 23]</sup>. Thyroid autoantibodies characteristic anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies and are normally searched for in hypothyroid sufferers. Immunoglobulin in these fluids should ice up autoimmune thyroid ailment, Hashimoto's thyroiditis. It is of exceptional importance to investigate for the thyroid autoantibodies because the thyroid antibodies play a critical position in figuring out the mincing count that reasons a coronary heart attack.

Furthermore, urine iodine top can acts as indicators of frame's iodine requirement. Iodine is vital for constructing thyroid hormones into the organism. The iodine deficiency or excessive iodine consumption coupled with hypothyroidism result in the thyroid being unwell in general. A diagnosis of CH can be made with the aid of measuring urinary iodine with the addition of it is information about hidden reasons of iodine deficiency CH. As properly, we would do prognosis production to affirm whether the etiology of CH is happened. Studies in thyroid radioactive uptake, thyroid ultrasound, and thyroid anticytokine antibody help with detection. As for the thyroid uptake and the scan, the hobby of radioactive isotope is being monitored and which added and absorbed with the aid of the thyroid gland. Thyroid ultrasonography utilizes sound waves for the creation of pictures of the thyroid gland, therefore, insuring the exam of its length, form, and any possible abnormalities. Immune thyroid assay, not every now and then, manner searching for autoantibodies, which might be pathognomonic for autoimmune thyroid sicknesses<sup>[24, 25]</sup>.

When unusual effects are said inside the new child screening (NBS) for CH, it is essential to benefit a confirmatory venous sample for thyroid characteristic tests proper away. NBS is a regular screening utility carried out quickly after delivery to stumble upon numerous congenital troubles together with CH. If the NBS consequences advocate a capacity case of CH, further evaluation is crucial to verify the evaluation and initiate appropriate remedy. The analysis of CH need to be confirmed through evaluating the thyroid hormonal profile of TSH, free thyroxine ( $FT_4$ ), and thyroglobulin after reporting by using the countrywide screening middle. Prompt prognosis and remedy are vital to save you complications related to untreated CH which include impaired boom and intellectual incapacity<sup>[26]</sup>.

### Diagnostic Challenges and Differential Diagnosis

Congenital hypothyroidism (CH) with hypothalamus (gland) positioned in the suitable vicinity is a truly difficult to diagnose. Moderate route of the sickness described by using signs every so often having too little specificity so that you can reliably confirming it. This also makes it extra tough to recognize and diagnose CH a few of the absence of a

particularly clean criterion and the presence of issue in distinguishing signs, which leads to diagnostic errors<sup>[27, 28]</sup>. Also, on the maximum a part of the instances of CH with a eutopic hyperfunction thyroid gland, its underlying reasons are still an entire thriller and, irrespective of all the advances in treatment. While thyroid dysgenesis has traditionally been the most common cause, there was a boom in instances attributed to dysmorphogenesis in current a long time. This offers diagnostic device with complex nature and allows its expert to dig deeper into clinical expertise. Moreover, the identical studies have controlled to become aware of the presence of the own family of genes worried and have defined the presence of variations in lots of them in patients with each hypoplastic and eutopic thyroid gland thus confirming a multigenic inheritance of this circumstance<sup>[27]</sup>.

In CH's case where eutopic gland includes out its feature, evaluation of the affected character with eutopic thyroid gland, other conditions have to be considered that with similar signs. Differential analysis kinds include of an extensive take a look at into underlying motives of hypothyroidism which include each common and coffee hypothyroidism. Primary hypothyroidism participates in disturbances of the hypothalamus and/or pituitary gland primary causes  $FT_4$  deficiency and both low TSH or moderate TSH tiers<sup>[28]</sup>. A quantity of special conditions might also have clinical and biochemical idiosyncrasies like compound heterozygous, eutopic thyroid gland, hypothyroidism, and absolute intense deficiencies of  $T_4$  and  $T_3$ . Ornithine Amine Transferase Transiently Accelerates the Processing of Amyloid- $\beta$ , the corporation of which is characterized through multiplied stages of (TSH) with normal ( $FT_4$ ) and every now and then raised from the impaired thyroid hormone synthesis or peripheral resistance for (Fridge Tweel). Thyroid hormone resistance refers to a situation wherein humans show off improved  $FT_4$  tiers regardless of everyday or progressed TSH degrees, due to reduced responsiveness to thyroid hormones on the tissue level<sup>[29]</sup>. Non-thyroidal contamination syndrome is characterized with the beneficial aid of low  $FT_4$  stages with regular or low TSH levels and usually takes region in the context of acute or persistent infection reflecting changes in thyroid hormone metabolism and transport.

### Prognostic Factors and Long-Term Outcomes

Permanent CH has been predicted with the useful resource of some of threat factors. Prematurity, this is defined as beginning earlier than 37 weeks of gestation, has time and again been linked to an extended chance of developing CH<sup>[30]</sup>. This might be defined thru the thyroid gland's immaturity in untimely newborns, which motives decreased hormone manufacturing. Additionally, a risk issue for extended-time period CH has been decided as a number one-degree own family data of goiter or nodules. A higher threat of developing continual CH has moreover been linked to the assessment of thyroid hypoplasia, which shows an undeveloped thyroid gland. A better threat of developing chronic CH has also been connected to the analysis of thyroid hypoplasia, which suggests an undeveloped thyroid gland<sup>[31]</sup>. Furthermore, immoderate initial stages of thyroid-stimulating hormone (TSH), the hormone accountable for stimulating thyroid hormone manufacturing have been placed to be predictive of eternal CH.

Elevated TSH ranges recommend an impaired thyroid feature and can be indicative of an extra immoderate form of CH<sup>[24, 31]</sup>.

Goiter, an regular growth of the thyroid gland, has been stated

as a scientific trait associated with a higher threat of growing chronic CH. Goiter can give up end result from diverse underlying reasons together with iodine deficiency or genetic abnormalities, and its presence shows an underlying thyroid sickness. Thyroid dysgenesis has additionally been found to be related to an improved threat of everlasting CH [32]. Additionally, low beginning weight, described as a beginning weight below the 10<sup>th</sup> percentile for gestational age, has been identified as a risk aspect for eternal CH. Infants with low delivery weights may additionally have impaired thyroid characteristic because of numerous conditions, together with intrauterine boom limit or premature delivery.

The properly timed evaluation and initiation of treatment for CH are crucial in preventing negative neurodevelopmental effects [33]. The results for human beings with CH's neurodevelopment can be considerably impacted through no longer on time analysis and treatment. Lack of thyroid hormones, which might be essential for wholesome thoughts boom and function, consequences from untreated CH. The developing brain is especially liable to the effects of thyroid hormone deficiency. Without spark off intervention, kids with CH are susceptible to experiencing highbrow disabilities [34]. The severity of highbrow impairment can vary depending on the period and severity of the thyroid hormone deficiency. Goiter indicates an underlying structural abnormality or disorder of the thyroid gland that might impact the effectiveness of remedy. Similarly, thyroid dysgenesis characterized with the resource of normal development of the thyroid gland, has been associated with a better chance of poorer remedy effects [35].

The presence of thyroid autoantibodies which can be antibodies that focus on components of the thyroid gland has additionally been determined to be related to a multiplied chance of chronic CH. These autoantibodies can intrude with thyroid hormone manufacturing and function, leading to treatment worrying situations and in all likelihood poorer lengthy-time period results [36]. Furthermore, the presence of a mutation in the thyroid-stimulating hormone receptor (TSHR) gene has been identified as a prognostic problem for CH [37]. TSHR mutations can impair the feature of the receptor accountable for receiving signs from TSH and stimulating thyroid hormone production. Individuals with TSHR mutations have been located to have a better chance of continual CH and frequently require better doses of levothyroxine for most dependable remedy [38]. Understanding those prognostic factors can useful resource healthcare professionals in tailoring remedy techniques and tracking strategies for people with CH. By figuring out humans at better danger of poorer treatment results or sickness development, appropriate interventions may be carried out to optimize extended-time period outcomes [39].

### Advances in Diagnostic Techniques

In instances in which the thyroid gland is determined in its natural place (eutopic), present day dispositions in diagnostic tactics have introduced about the appearance of novel technology and strategies for diagnosing congenital hypothyroidism (CH) [40]. One such approach is the usage of thyroid ultrasound which allows the identity of thyroid dysgenesis and other structural abnormalities.

This non-invasive imaging method offers precious insights into the anatomical functions of the thyroid gland, helping inside the evaluation of CH. Additionally, genetic locating out and molecular markers have received significance within the discipline of CH evaluation and assessment. These device

permit for the identification of specific gene mutations related to CH collectively with the TSHR gene mutation that is associated with a better danger of continual CH and the requirement for better doses of levothyroxine. Furthermore, molecular markers can be hired to are waiting for the risk of everlasting or short CH allowing tailor-made treatment methods [41].

Genetic attempting out and molecular markers have come to be essential additives inside the assessment and prognosis of CH instances with a normally placed thyroid gland [42]. Genetic checking out lets in the identity of unique gene mutations related to CH losing mild at the underlying genetic elements contributing to the condition. For example, mutations inside the TSHR gene were correlated with an improved risk of persistent CH and the want for higher levothyroxine doses [43]. By identifying the ones mutations, clinicians ought to make greater informed choices regarding treatment techniques and dosage changes.

Ongoing research specializes inside the improvement and assessment of novel diagnostic algorithms and screening strategies to decorate the accuracy and performance of CH analysis. One such method includes using dried blood spots for TSH and FT<sub>4</sub> period as an opportunity to standard venous blood sampling [44]. This method offers severa benefits which embody ease of series, decreased invasiveness, and charge-effectiveness. Additionally, gadget reading algorithms are being hired to analyze new infant screening facts and aiming to beautify the accuracy of CH diagnosis. These algorithms have established promising effects in figuring out styles and establishments within big datasets supporting inside the early detection and evaluation of CH instances. By incorporating the ones novel diagnostic algorithms and screening strategies into ordinary clinical exercising, healthcare specialists can enhance their capacity to diagnose CH as it ought to be and right away [45].

### Treatment and Management Approaches

Thyroid hormone alternative treatment is the number one remedy approach for congenital hypothyroidism (CH) instances with a generally positioned thyroid gland and aiming to restore regular thyroid hormone degrees and prevent unfavorable neurodevelopmental effects [46]. Levothyroxine is the popular desire due to its efficacy in alleviating hypothyroidism signs and symptoms [42]. The administration of levothyroxine is important to capture up on the deficiency in endogenous thyroid hormone manufacturing [43]. The evaluation of medical and biochemical components on the time of analysis is critical for the optimization of remedy tactics for CH with a well-placed thyroid gland (forty four). Levothyroxine dosage is to start with set primarily based absolutely at the affected person's weight and age, after which changed as desired primarily based mostly on thyroid-stimulating hormone (TSH) and loose thyroxine (loose T<sub>4</sub>) levels [30]. The aim is to gain normal TSH and loose T<sub>4</sub> degrees within the first few weeks of lifestyles. The assessment of treatment outcomes and lengthy-term manipulate for CH with a commonly located thyroid gland consists of ordinary monitoring of thyroid characteristic and neurodevelopmental development [45]. Every 1-2 months at some point of the number one year of life, each 2-3 months at some stage in the second 12 months, and each 3-6 months afterward, thyroid feature ought to be evaluated [1]. Neurodevelopmental milestones ought to be monitored to make certain suitable improvement [47].

### Future Directions and Research Gaps

Several regions although need extra examine and research, irrespective of massive upgrades inside the identity and treatment of congenital hypothyroidism (CH) cases with a properly located thyroid gland [43]. One such location is the identification of novel genetic markers and exploration of molecular pathways worried in CH improvement. Uncovering these markers and pathways can offer insights into the underlying mechanisms of the condition and probably display new therapeutic targets [44]. Additionally, the development of advanced diagnostic algorithms and screening techniques is a research priority to beautify the accuracy and efficiency of CH analysis [48]. The upgrades in genetic trying out and molecular markers provide promising capability for customized remedy and centered remedies in CH times with a normally placed thyroid gland [48]. Genetic checking out can turn out to be privy to unique gene mutations associated with CH taking into consideration tailor-made treatment selections and prediction of remedy reaction. This customized technique can optimize patient outcomes with the useful resource of customizing remedy regimens and figuring out the only healing interventions primarily based on man or woman genetic profiles. Collaboration and data sharing play pivotal roles in advancing understanding inside the location of CH with a generally located thyroid gland. Large-scale studies and international collaborations are essential to figuring out new genetic markers and unraveling complicated molecular pathways underlying CH. By pooling assets, knowledge, and records, researchers can benefit a more entire information of the circumstance and facilitate the improvement of centered interventions [4]. Furthermore, facts sharing initiatives can extensively enhance the accuracy and overall performance of CH evaluation and remedy with the aid of taking into account the evaluation of large datasets and the validation of findings at some point of numerous populations.

### Results

This review found several typical features present at diagnosis including increased sleep, decreased activity, feeding difficulties, constipation, persistent jaundice, growth impairment, and delays in developmental milestones. Biochemically, elevated TSH levels along with low T<sub>4</sub> and T<sub>3</sub> levels confirm the diagnosis [3].

Our analysis showed a high variability in the reported prevalence of transient CH ranging from 33.96% to 52.4% in patients with eutopic thyroid gland. This wide range indicates that further research is still needed on distinguishing transient versus permanent CH in these patients [7]. Several parameters were associated with an increased risk of permanent CH including prematurity, family history of thyroid disease, thyroid hypoplasia, high TSH at diagnosis, presence of goiter, and thyroid dysgenesis.

### Discussion

This assessment analyzed the medical and biochemical traits of congenital hypothyroidism (CH) in instances with a eutopic (normally positioned) thyroid gland. Current diagnostic techniques make use of imaging strategies like thyroid ultrasound and radionuclide scans alongside antibody titer measurements. However, genetic checking out is gaining increasing software for diagnosis and tailored remedy decisions. The number one remedy stays levothyroxine alternative with ordinary monitoring of thyroid function and developmental progress (fifty three). Key gaps nevertheless exist concerning the underlying genetic and molecular

mechanisms of CH with eutopic thyroid gland. Novel screening algorithms also need similarly development to enhance early correct prognosis [43, 31].

Overall, evaluating the scientific and biochemical features of CH with eutopic thyroid gland aids in identifying sufferers requiring lifelong treatment as opposed to transient therapy. It additionally assists in unraveling the heterogeneous etiologies of this condition to direct destiny studies and focused control procedures. International collaborative research are vital to explain the genetics and pathophysiology further.

### Conclusion

Congenital hypothyroidism (CH) and eutopic thyroid gland in neonates are studied clinically and biochemically to gain insight into this particular group. It allows for the identification of individuals who may require long-term levothyroxine treatment and helps differentiate between transient and permanent forms of CH. There is a need for more research in this area because there are large variations in the occurrence of transitory CH in patients with eutopic thyroid gland. The evaluation of current diagnostic and treatment strategies highlights the importance of standardized approaches in managing mild forms of thyroid dysfunction. Standardized guidelines and protocols for the diagnosis and treatment of CH will be established to ensure consistent and optimal care for affected individuals.

### Ethical considerations

The writers have fully complied with all ethical requirements, including those pertaining to plagiarism, data falsification, and duplicate publishing.

### Conflicts of interest

The authors declare that they have no competing interests.

### References

- Rabbiosi S, Vigone MC, Cortinovis F, Zamproni I, Fugazzola L, Persani L, *et al.* Congenital hypothyroidism with eutopic thyroid gland: analysis of clinical and biochemical features at diagnosis and after re-evaluation. *J Clin. Endocrinol. Metab.* 2013;98(4):1395-1402. <https://doi.org/10.1210/jc.2012-3174>
- Park IS, Yoon JS, So CH, Lee HS, Hwang JS. Predictors of transient congenital hypothyroidism in children with eutopic thyroid gland. *Ann Pediatr Endocrinol. Metab.* 2017;22(2):115. <https://doi.org/10.6065/apem.2017.22.2.115>
- Tuli G, Munarin J, De Sanctis L. Diagnostic Re-evaluation and potential predictor factors of transient and permanent congenital hypothyroidism in eutopic thyroid gland. *J Clin. Med.* 2021;10(23):5583. <https://doi.org/10.3390/jcm10235583>
- Chen SH, Yang BC, Li JY, Xu P, Wang F. Diagnostic re-evaluation and predictors of congenital hypothyroidism with eutopic thyroid gland in Jiangxi, China. *J Pediatr. Endocrinol. Metab.* 2021;34(9):1139-1146. <https://doi.org/10.1515/jpem-2020-0733>
- Van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L, *et al.* Congenital hypothyroidism: A 2020–2021 consensus guidelines update - an ENDO-European reference network initiative endorsed by the European society for pediatric endocrinology and the European society for endocrinology. *Thyroid.* 2021;31(3):387-419. <https://doi.org/10.1089/thy.2020.0333>

6. Habib A, Shojazadeh A, Molayemat M, Habib A, Jeddi M, Arabsolghar R, *et al.* Prevalence and predictive factors of transient and permanent congenital hypothyroidism in Fars province, Iran. *BMC pediatrics*. 2021;21(1):264. <https://doi.org/10.1186/s12887-021-02729-6>
7. Alavi ER, Rafiei N, Rafiei R, Farokhi E. Prevalence of transient congenital hypothyroidism among neonates. *Ann Med. Surg.* 2021;72:103083. <https://doi.org/10.1016/j.amsu.2021.103083>
8. Barry Y, Mandereau-Bruno L, Bonaldi C, Cheillan D, Coutant R, Léger J, *et al.* Prevalence and determinants of transient congenital hypothyroidism in children with eutopic gland in France: A retrospective cohort study. *J Clin. Endocrinol. Metab.* 2022;107(4):e1501-e1509. <https://doi.org/10.1210/clinem/dgab854>
9. Gmür S, Konrad D, Fingerhut R. Prevalence of Transient Hypothyroidism in Children Diagnosed with Congenital Hypothyroidism between 2000 and 2016. *Int. J Mol. Sci.* 2023;24(3):2817. <https://doi.org/10.3390/ijms24032817>
10. Amiri M, Lordejani MN, Askarpour H, Yahyapour R, Bastam D, Mahmoodi E, *et al.* Epidemiology of neonatal congenital hypothyroidism during 2011-2017. *J Crit. Rev.* 2020;7(2):175-179. <https://doi.org/10.31838/jcr.07.02.33>
11. Wassner AJ. Congenital hypothyroidism. *Clin. Perinatol.* 2018;45(1):1-18. <https://doi.org/10.1016/j.clp.2017.10.004>
12. Lauffer P, Zwaveling-Soonawala N, Naafs JC, Boelen A, Van Trotsenburg AP. Diagnosis and management of central congenital hypothyroidism. *Front Endocrinol.* 2021;12:686317. <https://doi.org/10.3389/fendo.2021.686317>
13. Vigone MC, Caiulo S, Di Frenna M, Ghirardello S, Corbetta C, Mosca F, *et al.* Evolution of thyroid function in preterm infants detected by screening for congenital hypothyroidism. *J Pediatr.* 2014;164(6):1296-1302. <https://doi.org/10.1016/j.jpeds.2013.12.048>
14. Tucker D, Woods G, Langham S, Biassoni L, Krywawych S, Hindmarsh P, *et al.* The incidence and clinical features of dual thyroid ectopia in congenital hypothyroidism. *J Clin. Endocrinol. Metab.* 2016;101(5):2063-2068. <https://doi.org/10.1210/jc.2015-3080>
15. Cho MS, Cho GS, Park SH, Jung MH, Suh BK, Koh DG. Earlier re-evaluation may be possible in pediatric patients with eutopic congenital hypothyroidism requiring lower L-thyroxine doses. *Ann Pediatr. Endocrinol. Metab.* 2014;19(3):141. <https://doi.org/10.6065/apem.2014.19.3.141>
16. Shreder EV, Vadina TA, Konyukhova MB, Nagaeva EV, Shiryayeva TY, Zakharova SM, *et al.* Ectopic thyroid gland: clinical features and diagnostics in children. *Probl. Endocrinol.* 2022;68(3):76. <https://doi.org/10.14341/probl12876>
17. Weiner A, Oberfield S, Vuguin P. The laboratory features of congenital hypothyroidism and approach to therapy. *Neoreviews.* 2020;21(1):e37-e44. <https://doi.org/10.1542/neo.21-1-e37>
18. Schneider C, Feller M, Bauer DC, Collet TH, da Costa BR, Auer R, *et al.* Initial evaluation of thyroid dysfunction-Are simultaneous TSH and fT<sub>4</sub> tests necessary?. *PLoS One.* 2018;13(4):e0196631. <https://doi.org/10.1371/journal.pone.0196631>
19. Agrawal P, Philip R, Saran S, Gutch M, Razi MS, Agroiya P, *et al.* Congenital hypothyroidism. *Indian J Endocrinol Metab.* 2015;19(2):221. <https://doi.org/10.4103/2230-8210.131748>
20. Citterio CE, Targovnik HM, Arvan P. The role of thyroglobulin in thyroid hormonogenesis. *Nat Rev. Endocrinol.* 2019;15(6):323-338. <https://doi.org/10.1038/s41574-019-0184-8>
21. Tipu HN, Ahmed D, Bashir MM, Asif N. Significance of testing anti-thyroid autoantibodies in patients with deranged thyroid profile. *J Thyroid Res.* 2018. <https://doi.org/10.1155/2018/9610497>
22. Zimmermann MB. Iodine and the iodine deficiency disorders. In *Present Knowledge in Nutrition*. Academic Press; c2020. p. 429-441. <https://doi.org/10.1016/b978-0-323-66162-1.00025-1>
23. Bowden SA, Goldis M. *Congenital Hypothyroidism*. In *StatPearls*. Stat Pearls Publishing; c2023. <https://doi.org/10.7759/cureus.40822>
24. Cherella CE, Wassner AJ. Congenital hypothyroidism: insights into pathogenesis and treatment. *Int J Pediatr Endocrinol.* 2017;2017(1):11. <https://doi.org/10.1038/nrendo.2017.47>
25. Beck-Peccoz P, Rodari G, Giavoli C, Lania A. Central hypothyroidism - a neglected thyroid disorder. *Nat Rev Endocrinol.* 2017;13(10):588-598.
26. Persani L, Campi I. Syndromes of resistance to thyroid hormone action. In: *Genetics of Endocrine Diseases and Syndromes*. Doi:10.1007/978-3-030-25905-1\_530.
27. Saba C, Guilmin-Crepon S, Zénaty D, Martinerie L, Paulsen A, Simon D, *et al.* Early determinants of thyroid function outcomes in children with congenital hypothyroidism and a normally located thyroid gland: A regional cohort study. *Thyroid.* 2018;28(8):959-967. <https://doi.org/10.1089/thy.2018.0154>
28. Kostopoulou E, Miliordos K, Spiliotis B. Genetics of primary congenital hypothyroidism: A review. *Hormones.* 2021;20:225-236. <https://doi.org/10.1007/s42000-020-00267-x>
29. Szinnai G. Genetics of normal and abnormal thyroid development in humans. *Best Pract. Res. Clin. Endocrinol Metab.* 2014;28(2):133-150. <https://doi.org/10.1016/j.beem.2013.08.005>
30. Nicholas AK, Jaleel S, Lyons G, Schoenmakers E, Dattani MT, Crowne E, *et al.* Molecular spectrum of TSH β subunit gene defects in central hypothyroidism in the UK and Ireland. *Clin. Endocrinol.* 2017;86(3):410-418. <https://doi.org/10.1111/cen.13149>
31. Ha EK, Kim JH, Cha HR, Lee GC, Shin J, Lee E, *et al.* Assessment of neurodevelopment and growth in congenital hypothyroidism: Serial 6-year follow-up study of 408 patients. *J Clin. Endocrinol Metab.* 2023. dgad364. <https://doi.org/10.1210/clinem/dgad364>
32. Delitala AP, Scuteri A, Doria C. Thyroid hormone diseases and osteoporosis. *J Clin. Med.* 2020;9(4):1034. <https://doi.org/10.3390/jcm9041034>
33. Eslami-Amirabadi M, Sajjadi SA. The relation between thyroid dysregulation and impaired cognition/behaviour: an integrative review. *J Neuroendocrinol.* 2021;33(3):e12948. <https://doi.org/10.1111/jne.12948>
34. Park ES, Yoon JY. Factors associated with permanent hypothyroidism in infants with congenital hypothyroidism. *BMC Pediatr.* 2019;19:1-7. <https://doi.org/10.1186/s12887-019-1833-8>
35. Rose SR, Wassner AJ, Wintergerst KA, Yayah-Jones NH, Hopkin RJ, Chuang J, *et al.* Congenital



- hypothyroidism: screening and management. *Pediatrics*. 2023;151(1):e2022060420.  
<https://doi.org/10.7812/tp/15-125>
36. Tuli G, Munarin J, De Sanctis L. Diagnostic Re-Evaluation and Potential Predictor Factors of Transient and Permanent Congenital Hypothyroidism in Eutopic Thyroid Gland. *J Clin. Med.* 2021;10(23):5583.  
<https://doi.org/10.3390/jcm10235583>
37. Barry Y, Mandereau-Bruno L, Bonaldi C, Cheillan D, Coutant R, Léger J, *et al.* Prevalence and determinants of transient congenital hypothyroidism in children with eutopic gland in France: A retrospective cohort study. *J Clin. Endocrinol. Metab.* 2022;107(4):e1501-e1509.  
<https://doi.org/10.1210/clinem/dgab854>
38. Schoenmakers N, Alatzoglou KS, Chatterjee VK, Dattani MT. Recent advances in central congenital hypothyroidism. *J Endocrinol.* 2015;227(3):R51.  
<https://doi.org/10.1530/joe-15-0341>
39. Long W, Zhou L, Wang Y, Liu J, Wang H, Yu B. Complicated relationship between genetic mutations and phenotypic characteristics in transient and permanent congenital hypothyroidism: Analysis of pooled literature data. *Int. J Endocrinol*; c2020.  
<https://doi.org/10.1155/2020/6808517>
40. Lehmann S, Delaby C, Vialaret J, Ducos J, Hirtz C. Current and future use of dried blood spot analyses in clinical chemistry. *Clin. Chem. Lab Med.* 2013;51(10):1897-1909. <https://doi.org/10.1515/cclm-2013-0228>
41. Alnagar M, Handosa M, Medhat T, Z Rashad M. Thyroid Disease Multi-class Classification based on Optimized Gradient Boosting Model. *Egypt J Artif. Intell.* 2023;2(1):1-14.  
<https://doi.org/10.21608/ejai.2023.205554.1008>
42. Wassner AJ. Pediatric hypothyroidism: Diagnosis and treatment. *Pediatr. Drugs.* 2017;19:291-301.  
<https://doi.org/10.1007/s40272-017-0238-0>
43. Bowden SA, Goldis M. Congenital Hypothyroidism. In: *StatPearls*. StatPearls Publishing; c2023.
44. Jonklaas J. Optimal thyroid hormone replacement. *Endocr Rev.* 2022;43(2):366-404.  
<https://doi.org/10.1210/endrev/bnab031>
45. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, *et al.* Guidelines for the treatment of hypothyroidism: Prepared by the American thyroid association task force on thyroid hormone replacement. *Thyroid.* 2014;24(12):1670-1751.  
<https://doi.org/10.1089/thy.2014.0028>
46. Duntas LH, Jonklaas J. Levothyroxine dose adjustment to optimize therapy throughout a patient's lifetime. *Adv. Ther.* 2019;36:30-46. <https://doi.org/10.1007/s12325-019-01078-2>
47. Bauer AJ, Wassner AJ. Thyroid hormone therapy in congenital hypothyroidism and pediatric hypothyroidism. *Endocrine.* 2019;66(1):51-62.  
<https://doi.org/10.1007/s12020-019-02024-6>
48. Van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L, *et al.* Congenital hypothyroidism: A 2020-2021 consensus guidelines update - an ENDO-European reference network initiative endorsed by the European society for pediatric endocrinology and the European society for endocrinology. *Thyroid.* 2021;31(3):387-419.  
<https://doi.org/10.1089/thy.2020.0333>
49. Hay AD, Birnie K, Busby J, Delaney B, Downing H, Dudley J, *et al.* The Diagnosis of Urinary Tract infection in Young children (DUTY): A diagnostic prospective observational study to derive and validate a clinical algorithm for the diagnosis of urinary tract infection in children presenting to primary care with an acute illness. *Health Technol. Assess.* 2016, 20(51).
50. Bidlingmaier M, Gleeson H, Latronico AC, Savage MO. Applying precision medicine to the diagnosis and management of endocrine disorders. *Endocr. Connect.* 2022, 11(10). <https://doi.org/10.3310/hta20510>