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THYROID STIMULATING HORMONE (TSH) LEVELS AND EARLY DETECTION OF CONGENITAL HYPERTHYROIDISM

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Abstract

Background: Hypothyroidism is a weakened thyroid gland function that produces abnormal thyroxine levels. Congenital Hyperthyroid screening uses the Thyroid Stimulating Hormone level test to measure newborn thyroid hormone levels. Objective: This study aims to assess TSH levels, early detection of congenital hyperthyroidism, and implementation of a screening program for congenital hyperthyroidism. Methods: This study reviewed the literature using PubMed's Congenital Hypothyroidism keyword. The study included Indonesian and English research publications on establishing the congenital hypothyroidism screening (CHS) program and the research location's CHS program from 2019-2023. 33 of 150 articles were described. Results: Most countries conduct congenital hypothyroidism screening programs in conjunction with screening for other diseases in newborns. Successful CHS can extend the life expectancy of patients. Conclusion: Laboratory screening tests in newborns are needed for immediate diagnosis and treatment, and an integrated congenital hypothyroidism screening program with T3, T4, and TSH levels must be implemented to reduce drug use.

Keywords: Congenital Hypothyroidism Screening, Early Detection, Newborns.

INTRODUCTION

Laboratory screening tests in newborns are needed for immediate diagnosis and treatment, and an integrated congenital hypothyroidism screening program with T3, T4, and TSH levels must be implemented to reduce drug use(Kurniawan 2020).

The Directorate General of Health Personnel, Directorate of Health Quality Improvement 2023 estimates that 1,500 of Indonesia's 4.4 million infants have Congenital Hypothyroidism. The Ministry of Health intensified CHS; in 2023, 1,202,953 newborn samples were collected in all health facilities. This is roughly 1000 times higher than in 2022, with an incidence rate of 1: 12,724 in Indonesia and 2.3% HK screening coverage. Despite falling short of the 4,452,717-baby objective, screening is rising.

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Congenital hypothyroidism is the most frequent endocrine condition and avoidable cause of intellectual disability worldwide. Due to lowered TSH screening cut-off time in newborn screening programs, milder HK in neonates has grown during the last several decades(Uthayaseelan et al. 2022).

Clinical characteristics Mild or asymptomatic hypothyroidism in babies will manifest in later months. The disorder is characterized by a lack of physical activity and an increase in the baby's sleep time. Symptoms of this condition include constipation, yellow skin and eyes, myxedema, wide fontanel, macroglasia, bloating, and other signs. If not addressed, growth retardation will become noticeable around 4-6 months of age. This condition causes intellectual disabilities and small height (Accogli et al. 2022). Hypothyroidism significantly affects cardiovascular, neurological, gastrointestinal, and metabolic functioning as thyroid hormones regulate nearly all organ systems(Yamakawa et al. 2021). Growth disorders are almost twice as common in hypo patients compared to normal people. Screening in newborns is one of the significant achievements in preventive medicine, and it has been integrated into the health system in many countries. (Yarahmadi et al. 2020). Detection of thyroid hormone deficiency in early life through CHS allows early treatment to prevent brain damage. Congenital thyroid hormone deficiency can be caused by impaired thyroid gland development or synthesis of thyroid hormones(Boelen et al. 2023).

Due to the risk of mortality in fetal and neonatal hyperthyroidism and medium- and long-term morbidity in hyper- and hypothyroidism, timely investigation, diagnosis, and treatment are necessary to restore normal thyroid function. 7. With a 5 million birth rate and 1:3000 incidence, more than 1600 kids will be born with congenital hypothyroidism each year(Shurbaji et al. 2023).

METHOD

A literature study searches Pubmed, Science Direct, and Google Scholar for 2019–2024 scientific articles. The study collected 1,180 Pubmed publications on congenital hypothyroidism, thyroid hormones, TSH, and newborn screening from 2019-2024. ScienceDirect discovered 13,487 articles, 35 open-access. Google Scholar discovered 37,200 items, 15,600 sorted by year. Specific article title searches yielded 32 journal articles. Multiple criteria were used to filter the data for completeness.

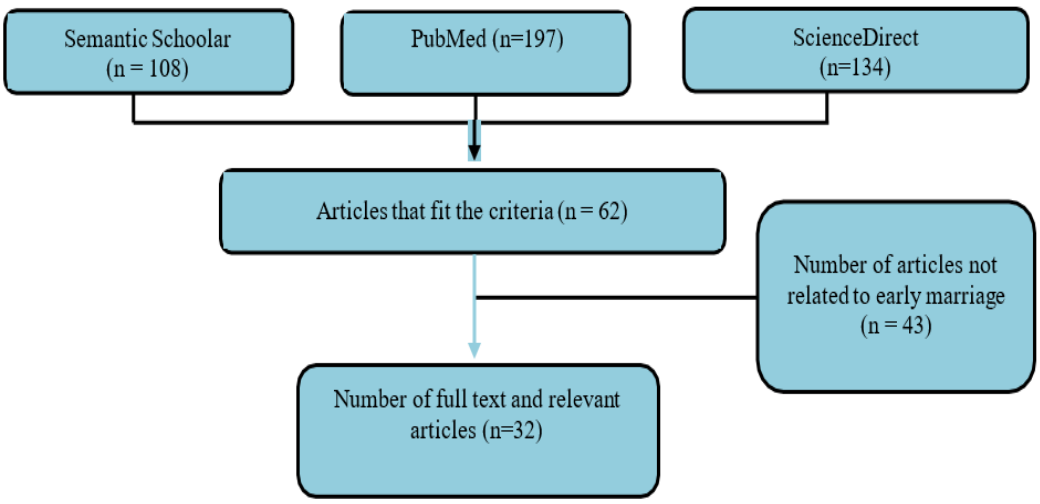

Figure 1: Literature Search Flowchart

Table 1: Research Result

No.	Name/Year/Journal	Research Title	Population/Sample	Methods	Results
1.	(Levaillant et al., 2022)published by Elsevier / 2022(Levaillant et al. 2022)	Neonatal screeningfor congenital hypothyroidism: time to lower theTSH threshold in France	measurement of thyroid-stimulating hormone (TSH) in whole driedblood sampleson filter paper ofnewborns in France	method (GSP, Genetic Screening Processor, Perkin Elmer)	Effect of decreasing France's day 3 TSH threshold from 17 mIU/L Canada 12mIU/L Belgium 12mIU/L Western Australia 12mIU/L New Zealand 12mIU/L Italy 6-12mIU/L UK 6-12, Greece 6- 8 France 17mIU/L Germany TSH: thyroid-stimulating hormone
2.	(Shurbaji et al., 2023)(Shurbaji et al. 2023)	High-sensitive detection and quantitation of thyroid-stimulating hormone (TSH) from capillary	102 fingersamples, venouspuncture whole blood, and serum samples	102 finger samples, venous puncture whole blood,and serum samples	Finecare showed high sensitivity [90.5% (69.6- 98.8)] and specificity [96.3% (89.6-99.2)] for the diagnosis of thyroidabnormalities (4.5 mIU/L).
3.	(González Martínez etal., 2022)(González Martínez et al. 2022)	Neonatal TSH as a marker of iodine nutrition status.Effect of maternal ioduria and thyroid function on neonatalTSH	Population330,560. Participants were selectedfrom the totalpregnant women who attended the initial visit to the midwife.	Longitudinal,observational, descriptive, and analyticstudies	Neonatal TSH levels are a good marker of iodine nutritional status, associated with an increased risk of neonatal TSH levels of more than 5 mIU/L.
4.	(Koohmanaee, Bakhshi, Pourkazem, et al., 2023)(Koohmanaee et al. 2023)	Diagnosis and Managementof Congenital Hypothyroidism: An Updated Overview	ISI Web of Sciences, Scopus, PubMed, andGoogle Scholardatabases 2000-2002	Retrospective cross-sectional studie are prospective or interventional.	Newborn screening, confirmatory assessment,accurate interpretation of thyroid function tests, prompt and therapeutic treatment
5.	(Kaluarachchi et al., 2019)(Kaluarachchi et al. 2019)	Thyroid-Stimulating Hormone Reference Ranges for PretermInfants	babies bornbetween 22 and 31 weeks of gestation from2012 to 2016 in Wisconsin.	Two groups (22-27 and 28-31weeks) and TSH percentiles were determined at birth	Differences in TSH levels increasing the frequency ofdiagnosis of congenital hypothyroidism are useful for defining the limits ofage-adjusted TSH newbornscreening for preterm infants.
6.	(Lakshminarayana et al., 2016)(Lakshminarayana et al. 2016)	Effect of maternal and neonatal factors on Cord Blood Thyroid Stimulating hormone	The study Included 979neonates (male = 506 and female = 473)	CBTSH levels	The prevalence rate of CBTSH level > 16.1 µIU/mL was significantlyhigher in neonates bornwith the help of vaginal delivery and normal delivery.
7.	(Kurniawan, 2020)(Kurniawan 2020)	Congenital Hypothyroidism: Incidence, Etiology and Laboratory Screening	Laboratory screening tests are done by taking blood From the newborn's heel and testing for TSH or T4, or both	Laboratory screening tests are done by taking blood From the newborn's heel and testing for TSH T4, or both.	TSH levels above 20 µU/mL are used as a cut-off that requires confirmatory testing using serum samples to confirm the diagnosis of congenital hypothyroidism.

8.	Shahin Yarahmadi, Nasrin Azhang, Bahram Nikkhoo, Khaled Rahmani. 2020(Yarahmadi et al. 2020)	Implementation and Achievements of the National Newborn Screening Program for Congenital Hypothyroidi sm in Iran.	For surveillance data registered at provincial and national levels.		Iran has demonstrated a successful CHS program for newborns, with an average incidence of 2.6/per 1000 live births.
9.	(Al Juraibah et al., 2019)(Al Juraibah et al. 2019)	Cord blood versus heel-stick sampling for measuring thyroid stimulating hormone for newborn screening Of congenital hypothyroidism	all babies born during the period May 2011 to May 2013. 17729 screened babies.	Comparative diagnostic accuracy of measurements from the umbilical cord And heel of infants	88 positive umbilical cord results (100% sensitivity, 99.6% specificity, with a recall rate of 0.04%) and 305 positive heel-stick results (100% sensitivity, 98.3% specificity, with a recall rate of 1.68%).
10.	(Knowles et al., 2018)(Knowles et al. 2018)	Newborn Screening for Primary Congenital Hypothyroidism: Estimating Test Performance at Different TSH Thresholds	629 newborns	blood TSH test thresholds of 6 mU/L and 8 mU/L, recommended at 10 mU/L	The performance of the screening program is good, but the TSH threshold of 8 mU/L appears to be higher than the current national standard (10 mU/L) and requires further evaluation.
11.	(Caiulo et al., 2021)(Caiulo et al. 2021)	Newborn Screening forCongenital Hypothyroidism: the Benefit of UsingDifferentia l TSH Cut-offs in a 2- Screen Program	119 Hypothyroid infants detected at the second screening in the Lombardy region of Italy, 2007 to 2014	Retrospective. December 2014, sampling time at the second screening was 15 ± 1 days of life	A lower TSH cut-off at the second examination may detect additional cases of hypothyroidism, and a second bTSH cut-off of 5.0 mU/L is appropriate for identifying premature newborns and infants with associated risk factors.
12.	(Wassie et al., 2019)(Wassie, Middleton, and Zhou 2019)	Agreement between markers of population iodine status in classifying the iodine status of populations:a systematic review	Studies assessing iodine status in populations using TSH markers	PubMed, Scopus, (CINAHL), Embase and PsycINFO until October 29, 2018.	TSH markers are more in line with goiter prevalence than MUIC when classifying the iodine status of a population.
13.	(Ali S. Alzahrani, et al. 2020)(Alzahrani et al. 2020)	Diagnosis and Management of Hypothyroidiin Gulf Cooperation Council (GCC)	The incidence of congenital hypothyroidism is 1:3450 newborns, although	PRISMA	In the Gulf countries of Saudi Arabia, hypothyroidism is under-diagnosed, and management approaches vary. There are no
		Countries	national prevalence data for congenital hypothyroidism are lacking,		guidelines for the diagnosis and management of hypothyroidism in these countries.

14.	Stephen T. Wang, Sam Pizzolato, Helen P. Demshar 1998(Wang, Pizzolato, and Demshar 1998)	(Diagnostic Effectiveness of TSH Screening and T4 with Secondary TSH Screening for Newborn Congenital Hypothyroidism. n.d.)	2,198 cases of normal Hypothyroid and 117 cases of abnormal hypothyroid were evaluated using Wallac Delfia neonatal TSH and neonatal T4	Delfia neonatal TSH kit (1244-032) and neonatal thyroxine (T4) kit (A065-110)	From the precision, accuracy, and frequency distribution studies, Wallac neonatal T4 and TSH kits are suitable for newborn Hypothyroid screening.
15.	(Fingerhut, 2021)(Fingerhut 2021)	Newborn Screening for Congenital Hypothyroidism - Clinical Evaluation and Comparison of Two Different Test Kits for the Determinationof TSH in Dried Blood Samples on Two Different Platforms	Of the 472 samples, 66 were from newborns with confirmed hypothyroidism. In addition, in total, 36 were measured on the LDx/NS2400 platform.	TSH was measured from 3.2 mm punch of the DBS withtwo different test kits	Both tests have a good correlation. With the LDx/NS2400 platform, However, the difference between the two results from the mean was within ±2 SD, up to 30 mU/L, and only for values above 50 mU/L did the difference become larger.
16.	(Yarahmadi et al., 2020)(Yarahmadi et al. 2020)	A Success Story: Review of the Implementation and Achievements of the National Newborn Screening Program for Congenital Hypothyroidism in Iran	By the end of 2017, 1,501,624 neonates were screened, 40,773 of whom were diagnosed with hypothyroidism	Structure, process, key indicators, and achievements over 15 years of Congenital diagnosis and treatment in Iran.	Primary TSH measurement with determination of reserve thyroxine (T4) in infants with elevated TSH levels is used as a screening strategy in Iran.
17.	(Rachel West, 2020)(West et al. 2020)	Newborn Screening TSH Values Less than 15 mIU/L Are Not Associated With Long-Term Hypothyroidism or Cognitive Impairment	newborns with TSH levels of 8 to 14 mIU/L blood, ages 6.9 to 12.6 years at screening	Thyroid function tests (serum TSH And free thyroxine)	The mean newborn TSH mTSHe level was 10.1 mIU/L blood and 2.4 mIU/L at assessment (range, 0.8-7.0 mIU/L, serum). Higher newborn TSH levels in the mTSH group correlate with lower full-scale IQ scores
18.	(Antonio Delgado Juan Robles Bauza A et al., n.d. 2021)(Delgado et al. 2021)	Challenges in Screening for congenital hypothyroidism: Optimization of thyrotropin cut-off values (Challenges in screening for congenital	A retrospective observational study at Son Espases Universitari Hospital screening newborns with a population of	Biochemical data were obtained from the laboratory information system GestLab (Indra, Spain);	A total of 72,133 newborns were screened for CH. Different TSH cut-off values that trigger further actions (test repetition, new sample request, confirmatory test) were evaluated and optimized in terms of diagnostic performance.
		hypothyroidism: Optimization of thyrotropin cut-off values)	approximately 1,200,000.		

19.	(Zdraveska N, Kocova M, Nicholas AK, Anastasovska V and Schoenmakers N.2020)(Zdraveska et al. 2020)	Genetics of Gland- in-situ or Hypoplastic Congenital Hypothyroidin Macedonia	Neonate screeningis done to detect iodine coverage and hypothyroidism.	SLR	Macedonia is continuously conducting NBS, the barriers to the implementation of the CHS program in Macedonia are not mentioned in this article.
20.	(Paul van Trotsenburg at al, 2021)(Van Trotsenburg et al. 2021)	Congenital Hypothyroidism: A 2020-2021 Consensus Guidelines Update by the European Society for Pediatric Endocrinology Initiative	Twenty-two participants from the ENDO- ERN network, thyroid Major Thematic Group, including ENDO-ERN patient association representatives.	comprehensive literature research using PudMed	This update of the consensus guidelines on CH recommends worldwide neonatal screening and appropriate diagnosis-including genetics to assess the causes of primary and central hypothyroidism.
21.	(Koohmanaee, Bakhshi, & Pourkazem, 2023)(Koohmanaee et al. 2023)	Diagnosisand Managementof Congenital Hypothyroidism	etiology, epidemiology, manifestations, diagnosis,and management of congenital hypothyroidism	ISI Web of Sciences, Scopus, PubMed, and Google Scholar databases	Newborn screening, confirmatory assessment, accurate interpretation of thyroid function tests, prompt and therapeutic treatment.
22.	(Spiekerkoetter U, Krude H:. 2022)(Krude and Spiekerkötter 2022)	Target diseases for neonatal screening inGermany-challenges for treatment and long-term care	Neonatal screeningin Germany currently covers 19 diseases, 13 of which are metabolic diseases.	Systematic Literature Review and PRISMA	Germany is working to improve and minimize the effects of therapy, This article does not list the barriers to the CHS program in Germany.
23.	(Anita Boelen, Nitash Zwaveling-Soonawala, Annemieke C Heijboer, ASPaulvan Trotsenburg. 2023)(Boelen et al. 2023)	Neonatal screening for primary and central congenital hypothyroidis m: is it time? to go Dutch?.	Detection of primary congenital hypothyroid, with a positive predictive value (PPV) of 55%.	Systematic Literature Review	The innovative newborn baseline detection program (NBS) has increased the incidence of congenital hypothyroid detection to 1:16,404 examinations. NBS includes T4-reflex, TSH reflex, and T3. This is an effective three-step approach, but the difference in PPV between T4-based NBS and TSH-based NBS is very large.
24.	(Lee, 2016)(Lee 2016)	Perinatal factors Associated with Neonatal thyroid-stimulating	Medical records of 705 healthy infants born through normal	neonatal screening test with free thyroxine (FT4) and17	Kes: Neonatal TSH levels in normal, healthy newborns are associated with several factors. Acute stress during labor may
		the hormone in normal newborns	Labor was examined	hydroxyproges terone (17OHP) levels.	Affect neonatal TSH levels in the early neonatal period
25.	(Li, Abby A. et al., 2019)(Li et al. 2019)	Practical considerations for the assessment of the progression	The OECD and EPA guideline studieshave slightly different	Samples were collected from a limited practical guide.	1. test sensitivity varies within and between methodologies; 2.laboratoriesgenerally

		of thyroid toxicity:	recommendations for TH and TSH measurements		achieve a fairly sensitive TH quantization level,
26.	(SM Park,VKK Chatterjee, 2020)(Park and Chatterjee 2005)	Genetics of congenital hypothyroidism	Genetic aspects of primary congenital hypothyroidism.	TSH receptor-relatedgenes in congenital hypothyroidism	Congenital hypothyroidism is a common neonatal problem that is easily detected and treated, hence the success of national neonatal screening programs.
27.	(Sumreena Mansoor. 2020)(Mansoor 2020)	Trends of congenital hypothyroidism and inborn errors of Metabolismin Pakistan.	Neonate screening (NBS) is performed for all metabolic diseases, including congenital hypothyroidism	Systematic Literature Review	Congenital hypothyroid NBS is being developed at multiple hospitals, however, epidemiological data is lacking, indicating the CHS program is not yet optimized.
28.	(grace mengqin ge, et.al 2020)(Ge et al. 2020)	Maternal Thyroid Dysfunction During Pregnancy and the Risk of Adverse Outcomes in the Offspring	Reviewers extract data on research characteristics and results	Estimates were pooled to 95% confidence (CI). The I^2 test was applied to assess heterogeneity.	29 eligible articles Concentration disorder and maternal hypothyroidism association with increased risk of ADHD
29.	(Vikas Yadav et al., 2021)(Yadav et al. 2021)	Prevalenceof Hypothyroidism in Pregnant Women in India: A Meta-Analysisof Observational Studies	Metanalysis of the prevalence of hypothyroidism in pregnant women in India	Meta-analysis according to PRISMA guidelines and registered in PROSPERO data base.	The prevalence of subclinical and overt hypothyroidism was 9.51% (95% CI: 7.48-12.04, 198%) and 2.74% (95% CI: 2.08-3.58, 1^2=94%), respectively.
30.	(Octavius, G.S.; Daleni, V.A.; Sagala, Y.D.S. 2023)(Octavius, Daleni, and Sagala 2023)	An Insight into Indonesia's Challenges in Implementing Newborn Screening Programs and Their Future Implications.	Indonesia is targeting 463,000 screened samples, or 10% of the total sample of all newborns.	-	By 2022, the Ministry of Health is accelerating the NBS program for congenital hypothyroidism with 11 referral laboratories.
31.	(Stine Linding Andersena Stig Andersen. 2020)(Andersen and Andersen 2020)	Turning to Thyroid Disease in Pregnant Women	Hypothyroid pregnant women	Observational study	The consequences of under-treating maternal thyroid disease in pregnancy can be fatal.
32.	(Rose Susan R et al., 2023)(Rose et al. 2023)	Congenital Hypothyroidism: Screeningand Management	population screeningis carried out cost-effectively by public health laboratories	Dried blood spots (DBS) for NBS were obtained by appropriate collection.	In most infants affected by Congenital Hypothyroidism, this is a permanent abnormality in TH synthesis.
33.	(Minamitani, K. Newborn Screening for Congenital Hypothyroidism in Japan. 2021)(Minamitani 2021)	Newborn Screening for Congenital Hypothyroidism in Japan.	Among CH patients,46% had life insurance.	Laboratory newborn CH detection for testing	The rise in incidence may be attributed to a rise in mild patients due to the lowered screening limit for TSH levels.

RESULT

Hypothyroidism is common in the Arabian Gulf, with different treatments. Congenital hypothyroidism is common in Saudi Arabia, with 10% in primary care and 13-35% in women. Insufficient national hypothyroidism prevalence 18. Pakistan has only used the CHS program in hospitals since 1987. Test results show no SOPs or incidence rates. The CHS initiative has failed to solve Pakistan's congenital hypothyroid condition(Mansoor 2020).

Iranian newborn screening began in 2004 to detect early congenital hypothyroid diseases. Of 1,501,624 neonates examined in 2017, 40,773 were found with congenital hypothyroidism and treated according to Iran's recommendations. More than 95% of Iranian babies use CHS(Yarahmadi et al. 2020).

Due to delayed TSH elevation detection, Japan has recommended re-examining premature neonates and newborns with low birth weight at four weeks or 2500 g since 1987. True hepatitis B incidence has risen to 1:2500, likely due to a lower TSH screening cut-off and more preterm or low birth weight neonates (Minamitani 2021).

Germany screens newborns for 19 hereditary illnesses, 13 of which are metabolic. These targeted disorders affect 1 in 1,300 babies. Early identification and treatment improve development and often lead to a normal life25. Netherlands uses the T4-TSH-TBG test to diagnose. Early discovery of central HK is expected to enhance clinical outcomes and care for individuals with multiple pituitary hormone deficits; however, NBS detection is debatable(Boelen et al. 2023).

Healthcare centers in Mekodonia piloted CHS in newborns for five years. Since 2018, written consent from patients and/or next of kin has been required for CHS. Additional clinical follow-up measurements are taken. The average hospital screening coverage was 97.03% (Bolognani et al. 2021). Studies show that incidence is crucial for early detection of congenital hyperthyroidism, with accuracy determining recovery and life expectancy. Successful CHS programs achieve over 95% success, with countries developing risk reduction programs for treatment.

DISCUSSION

Healthcare innovation in newborn congenital hypothyroid screening is needed to prevent baby mortality and growth and development issues, including mental impairment. The newborn screening program is part of the child health program, which recognizes that healthy children are the foundation of great human resources and works to improve child health. Indonesia's Ministry of Health mandates Congenital Hypothyroid Screening (CHS) to treat congenital hypothyroid diseases.(Boelen et al. 2023).

Only CHS is committed to NBS in Indonesia. HK NBS is funded by municipal revenue and spending and health operating budgets. There are conflicts when the government believes screening funds are sufficient while health centers only meet 50% of the CHS target. The Ministry of Health now requires newborn CHS acceleration in 2020 and 2021. The MOH advanced HK NBS with 11 reference laboratories in 2022. They tested 463,000 babies, 10%. However, only 99,263 samples (21.4%) were examined against the initial objective by 2022.(Koohmanaee et al. 2023),(Octavius, Daleni, and Sagala 2023).

Infants born at ≤32 weeks gestation or very low weight <1,500 g are at risk of hypothyroidism. Given the risk of false negative results at screening and the possibility of thyroid dysfunction, it is recommended to repeat analytical determinations at 2 weeks, 4 weeks, when the child's weight reaches 1,500 g, or at hospital discharge(Mirnia et al. 2022). Clinical and subclinical hypothyroidism during pregnancy increases the risk of preterm labor by 4.4 times(Yang et al. 2018).

Differences in TSH levels by gestational age category may explain the increased frequency of diagnosis of congenital hypothyroidism in preterm infants. These data are useful for defining the limits of age-adjusted TSH newborn screening for preterm infants. Neonatal TSH levels are a good marker for iodine nutritional status, and maternal iodine deficiency is associated with an increased risk of neonatal TSH levels of more than 5 mIU/L(González Martínez et al. 2022).

From the precision, accuracy, tggdsu` and frequency distribution studies, Wallac neonatal T4 and TSH kits are suitable for newborn Hypothyroid screening. Evaluation of diagnostic accuracy on Wallac neonatal TSH kit for newborn CH screening by ROC analysis showed excellent results(Wang, Pizzolato, and Demshar 1998). A TSH level above 20 µU/mL is used as a cut-off that requires confirmatory testing using serum samples to confirm the diagnosis of congenital hypothyroidism. Once the diagnosis is made, immediate treatment and laboratory monitoring are required for a better outcome(Kurniawan 2020).

A negative connection was discovered between TSH and postnatal sample time. Vacuum-assisted twins and neonates had greater TSH than controls. Neonatal TSH was unrelated to birth weight, gestational age, maternal age, and membrane rupture time. No significant variation in TSH levels by gender, Apgar score, inducement of labor, maternal illness, or medication.(Lee 2016). Cord blood TSH hormone monitoring is simple and non-invasive. Umbilical cord blood samples are accessible and non-invasive, and they reduce blood sampling loss, as infants from day 3 to day 7 often have difficulty because the patient has already been discharged from the hospital. The results are readily available before the mother leaves the hospital, allowing re-sampling if needed at the earliest possible time (Lakshminarayana et al. 2016).

Larger populations have more labs, like Russia's 78. Many European countries have one or two labs. One European lab can examine 100-20,000 newborns. NBS in Indonesia requires roughly 225 laboratories in 2021 with 4,496,383 infants(Octavius, Daleni, and Sagala 2023).

CONCLUSION

This research review advises measuring neonates' TSH levels with cord blood serum, heel blood, and venous blood serum. Congenital hypothyroidism patients need laboratory screening tests for prompt diagnosis, treatment, and drug usage risk reduction. The addition of congenital hypothyroidism screening programs to T3, T4, and TSH levels will increase addiction coverage.

References

1) Accogli, Andrea et al. 2022. “Diagnostic Approach to Macrocephaly in Children.” *Frontiers in Pediatrics* 9(January).

2) Alzahrani, Ali S. et al. 2020. “Diagnosis and Management of Hypothyroidism in Gulf Cooperation Council (GCC) Countries.” *Advances in Therapy* 37(7): 3097–3111.

3) Andersen, Stine Linding, and Stig Andersen. 2020. “Turning to Thyroid Disease in Pregnant Women.” *European Thyroid Journal* 9(5): 225–33.

4) Boelen, Anita, Nitash Zwaveling-Soonawala, Annemieke C. Heijboer, and A. S.Paul van Trotsenburg. 2023. “Neonatal Screening for Primary and Central Congenital Hypothyroidism: Is It Time to Go Dutch?” *European Thyroid Journal* 12(4).

5) Bolognani, Marco et al. 2021. “Development of a Perinatal Palliative Care Model at a Level II Perinatal Center Supported by a Pediatric Palliative Care Network.” *Frontiers in Pediatrics* 8(January): 1–5.

6) Caiulo, Silvana et al. 2021. “Newborn Screening for Congenital Hypothyroidism: The Benefit of Using Differential TSH Cutoffs in a 2-Screen Program.” *Journal of Clinical Endocrinology and Metabolism* 106(1): E338–49.

7) Dahir, Kathryn et al. 2022. “Health Care Transition from Pediatric- to Adult-Focused Care in X-Linked Hypophosphatemia: Expert Consensus.” *Journal of Clinical Endocrinology and Metabolism* 107(3): 599–613.

8) Delgado, Jose Antonio et al. 2021. “Challenges in Screening for Congenital Hypothyroidism: Optimization of Thyrotropin Cut-off Values.” *Clinica Chimica Acta* 512(June 2020): 20–25.

9) Fingerhut, Ralph. 2021. “Newborn Screening for Congenital Hypothyroidism-Clinical Evaluation and Comparison of Two Different Test Kits for the Determination of Tsh in Dried Blood Samples on Two Different Platforms.” *International Journal of Neonatal Screening* 7(3).

10) Ge, Grace Mengqin et al. 2020. “Maternal Thyroid Dysfunction during Pregnancy and the Risk of Adverse Outcomes in the Offspring: A Systematic Review and Meta-Analysis.” *Journal of Clinical Endocrinology and Metabolism* 105(12): 3821–41.

11) González Martínez, Silvia et al. 2022. “Neonatal TSH as a Marker of Iodine Nutrition Status. Effect of Maternal Ioduria and Thyroid Function on Neonatal TSH.” *Anales de Pediatria* 97(6): 375–82.

12) Al Juraibah, Fahad, Ali Alothaim, Wafa Al Eyaid, and Angham Nasser AlMutair. 2019. “Cord Blood versus Heel-Stick Sampling for Measuring Thyroid Stimulating Hormone for Newborn Screening of Congenital Hypothyroidism.” *Annals of Saudi Medicine* 39(5): 291–94.

13) Kaluarachchi, Dinushan C. et al. 2019. “Thyroid-Stimulating Hormone Reference Ranges for Preterm Infants.” *Pediatrics* 144(2).

14) Knowles, Rachel L. et al. 2018. “Newborn Screening for Primary Congenital Hypothyroidism: Estimating Test Performance at Different Tsh Thresholds.” *Journal of Clinical Endocrinology and Metabolism* 103(10): 3720–28.

15) Koohmanaee, Shahin, Arash Bakhshi, Shayan Pourkazem, and Behrang Motamed. 2023. “Diagnosis and Management of Congenital Hypothyroidism: An Updated Overview.” *Journal of Comprehensive Pediatrics* 14(4): 1–13.

16) Krude, Heiko, and Ute Spiekerkötter. 2022. “Zielkrankheiten Des Neugeborenenscreenings in Deutschland : Herausforderungen an Therapie Und Langzeitbetreuung.” *Deutsches Arzteblatt International* 119(17): 306–16.

17) Kurniawan, Liong Boy. 2020. “Congenital Hypothyroidism: Incidence, Etiology and Laboratory Screening.” *Indonesian Journal of Clinical Pathology and Medical Laboratory* 26(3): 375–80.

18) Lakshminarayana, Sheetal, Nidhish Sadanandan, A. Mehaboob, and Lakshminarayana Gopaliah. 2016. “Effect of Maternal and Neonatal Factors on Cord Blood Thyroid Stimulating Hormone.” *Indian Journal of Endocrinology and Metabolism* 20(3): 317–23.

19) Lee, Seong Yong. 2016. “Perinatal Factors Associated with Neonatal Thyroid-Stimulating Hormone in Normal Newborns.” *Annals of Pediatric Endocrinology and Metabolism* 21(4): 206–11.

20) Levaillant, L. et al. 2022. “Neonatal Screening for Congenital Hypothyroidism: Time to Lower the TSH Threshold in France.” *Archives de Pediatrie* 29(4): 253–57.

21) Li, Abby A. et al. 2019. “Practical Considerations for Developmental Thyroid Toxicity Assessments: What’s Working, What’s Not, and How Can We Do Better?” *Regulatory Toxicology and Pharmacology* 106(December 2018): 111–36.

22) Mansoor, Sumreena. 2020. “Trends of Congenital Hypothyroidism and Inborn Errors of Metabolism in Pakistan.” *Orphanet Journal of Rare Diseases* 15(1): 1–10.

23) Minamitani, Kanshi. 2021. “Newborn Screening for Congenital Hypothyroidism in Japan.” *International Journal of Neonatal Screening* 7(3).

24) Mirnia, Kayvan et al. 2022. “A Suggested Screening Method for Hypothyroidism in Very Preterm and/or Very Low Birth Weight Neonates.” *Revista Paulista de Pediatria* 40: 1–9.

25) Octavius, Gilbert Sterling, Vamela Adman Daleni, and Yulita Delfia Sari Sagala. 2023. “An Insight into Indonesia’s Challenges in Implementing Newborn Screening Programs and Their Future Implications.” *Children* 10(7): 1–13.

26) Park, S. M., and V. K.K. Chatterjee. 2005. “Genetics of Congenital Hypothyroidism.” *Journal of Medical Genetics* 42(5): 379–89.

27) Rose, Susan R. et al. 2023. “Congenital Hypothyroidism: Screening and Management.” *Pediatrics* 151(1): 1–10.

28) Shurbaji, Samar et al. 2023. “High-Sensitive Detection and Quantitation of Thyroid-Stimulating Hormone (TSH) from Capillary/Fingerstick and Venepuncture Whole-Blood Using Fluorescence-Based Rapid Lateral Flow Immunoassay (LFIA).” *Heliyon* 9(10): e20589.

29) Van Trotsenburg, Paul et al. 2021. “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* 31(3): 387–419.

30) Uthayaseelan, Kivonika et al. 2022. “Congenital Anomalies in Infant With Congenital Hypothyroidism: A Review of Pathogenesis, Diagnostic Options, and Management Protocols.” *Cureus* 14(5): 1–9.

31) Wang, Stephen T., Sam Pizzolato, and Helen P. Demshar. 1998. “Diagnostic Effectiveness of TSH Screening and of T4 with Secondary TSH Screening for Newborn Congenital Hypothyroidism.” *Clinica Chimica Acta* 274(2): 151–58.

32) Wassie, Molla Mesele, Philippa Middleton, and Shao Jia Zhou. 2019. “Agreement between Markers of Population Iodine Status in Classifying Iodine Status of Populations: A Systematic Review.” *American Journal of Clinical Nutrition* 110(4): 949–58.

33) West, Rachel et al. 2020. “Newborn Screening TSH Values Less than 15 MIU/L Are Not Associated with Long-Term Hypothyroidism or Cognitive Impairment.” *Journal of Clinical Endocrinology and Metabolism* 105(9): E3329–38.

34) Yadav, Vikas et al. 2021. “Prevalence of Hypothyroidism in Pregnant Women in India: A Meta-Analysis of Observational Studies.” *Journal of Thyroid Research* 2021.

35) Yamakawa, Hiroyuki et al. 2021. “Thyroid Hormone Plays an Important Role in Cardiac Function: From Bench to Bedside.” *Frontiers in Physiology* 12(October): 1–14.

36) Yang, Jin et al. 2018. “Associations of Maternal Iodine Status and Thyroid Function with Adverse Pregnancy Outcomes in Henan Province of China.” *Journal of Trace Elements in Medicine and Biology* 47(December 2017): 104–10.

37) Yarahmadi, Shahin, Nasrin Azhang, Bahram Nikkhoo, and Khaled Rahmani. 2020. “A Success Story: Review of the Implementation and Achievements of the National Newborn Screening Program for Congenital Hypothyroidism in Iran.” *International Journal of Endocrinology and Metabolism* 18(2).

38) Zdraveska, Nikolina et al. 2020. “Genetics of Gland-in-Situ or Hypoplastic Congenital Hypothyroidism in Macedonia.” *Frontiers in Endocrinology* 11(July): 1–10.