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Metrics from a Congenital Hypothyroidism Screening Program – A Tale of Unmet Challenges

Fatima Kanani[1)], Vikram Kumar[2)], Mamona Mushtaq[3)], Dua Sameer[3)], Syed Rehan Ali[2)]

[1)] Department of Chemical Pathology, Indus Hospital and Health Network, Karachi, Pakistan
[2)] Indus Hospital Research Center, Indus Hospital and Health Network, Karachi, Pakistan
[3)] Department of Paediatrics, Indus Hospital and Health Network, Karachi, Pakistan

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ABSTRACT

Background: Congenital hypothyroidism is one of the most common Inherited Metabolic Diseases for which newborn screening is recommended. A wide-scale program for this is lacking in our country. We undertook a study to retrospectively review our metrics from a regional project for newborn screening of Congenital Hypothyroidism including frequency of elevated neonatal Thyroid Stimulating Hormone (TSH), recall rate, rate of missed testing and turnaround time for results.
Subjects and Method: Retrospective data of neonates born between 13th July 2020 and 10th August 2021 was collected from electronic medical records. Dried blood spot specimens for TSH were collected from the umbilical cords for neonates born vaginally and by heel prick for those born by caesarian section and sent to the designated laboratory. Data was entered on Microsoft Excel and analyzed.
Results: A total of 4,037 babies were screened for neonatal TSH, 2149 males and 1888 females. The median (IQR) TSH level was 3.34 (2.09-5.30) µIU/mL. The TSH levels of ≥15 µIU/mL were noted in 95 newborns, out of which 31 newborns had values of ≥ 20 µIU/mL. There was a median (IQR) turnaround time of 14.00 (4.00-55.00) days for initial results accessibility to the clinician. The recall rate was 0.3%. Around 10% of the neonates were not screened and retesting was performed in 12 neonates with high TSH. Only one neonate was identified with persistently raised TSH and suppressed FT4.
Conclusion: Congenital Hypothyroidism was diagnosed in one out of 4037 neonates while 10% were not screened. Recall rate was low, 0.3%. The median turnaround time for reporting was 14 days. Increased awareness, strict monitoring, resource allocation, administrative support and follow-up are required for successful implementation of a CH screening program.

Keywords: congenital hypothyroidism, newborn screening program, inherited metabolic disease, thyroid stimulating hormone.

Correspondence:
Dr. Fatima Kanani. Department of Chemical Pathology, Indus Hospital and Health Network Plot C-76, Sector 31/5, Opposite Darussalam Society, Korangi Crossing, Karachi, Pakistan. Email: fatima.kanani@tih.org.pk, fatimakanani@hotmail.com.

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BACKGROUND

Despite being one of the most easily diagnosed and managed paediatric endocrine disorders, congenital hypothyroidism (CH) still remains a challenge in some parts of the world. Most cases of CH are primary. Thyroid dysgenesis makes up 80% of all primary cases of CH, while dyshormonogenesis contributes to the other 20% (Olney et al. 2010, Ahmad et al. 2017). Other possible causes are autoimmune thyroid disease in the fetus, fetal TSH receptor mutation, fetal thyroid tumors or maternal use of antithyroid medications (Olney et al. 2010).

CH can be either permanent or transient (Rastogi and LaFranchi 2010). The clinical features are often subtle and nonspecific resulting in delayed diagnosis in the absence of a neonatal screening program. These can include prolonged jaundice, sleepiness, inactivity, delayed passage of meconium, constipation, poor feeding, goiter, low birth weight and poor weight gain. CH impacts the neurodevelopment of the child, manifesting as decreased intelligence, gross and fine motor incoordination, speech disorders, attention deficit, and sensory neural deafness (Dayal and Prasad 2015). Before the introduction of Newborn Screening (NBS) programs in developed countries, about 25% of children diagnosed with CH experienced overt intellectual disability (Ahmad et al. 2017). Permanent CH requires life-long treatment and monitoring with thyroxine, which should be started immediately after diagnosis.

Robust NBS programs have been instrumental in facilitating early detection and eventual diagnosis of CH through confirmatory testing. State-level programs in developed countries have been largely successful in eradicating CH-associated intellectual disability, understood as IQ levels <70 (Dayal and Prasad 2015). The initiation of early treatment has ensured an excellent prognosis for normal neurodevelopment in children diagnosed with the condition (Ahmad et al. 2017).

CH has an estimated prevalence of 1:2,500 to 1:4,000 (Khokhar and Cheema 2021). Despite this global average, the incidence of congenital hypothyroidism varies across countries. Contributing factors to this are differences in socio-demographic make-up such as, age, race, ethnicity, sex, cultural prevalence of consanguineous marriages, differences in the testing strategies and methodologies as well as resource allocation to newborn screening worldwide (Ahmad et al. 2017, Mansoor 2020). In Pakistan, the earliest study into the condition, conducted at Aga Khan University Hospital (AKUH) in 1989, found the incidence to be 1:1000 – four times that of the global incidence at the time (Lakhani et al. 1989).

A 20-year audit of the congenital hypothyroidism screening program in the same institute in 2008 found the estimated incidence to be 1:1600 live births (Afroze et al. 2008). Approximately 70% of babies worldwide are not born in an area with an NBS program and hence are not detected and treated early. Wilson Jungner's defined criteria for screening of inherited diseases in a seminal article in 1968 (Wilson et al. 1968). Congenital hypothyroidism (CH) is one of the most common inherited metabolic diseases for which newborn screening is recommended according to these criteria. Where resource-rich countries have been able to execute national or state-level programs for newborn screening, efforts in the developing countries have been limited. This dearth of NBS programs poses a desperate challenge for developing countries with large populations and a higher disease burden (Dayal and Prasad 2015). Cost and lack of infrastructure are major constraint in

the establishment and implementation of a nationwide NBS program Mansoor states that in a resource-poor country such as Pakistan, governmental health priorities have retained their focus on infectious disease control and immunization programs as infectious diseases have a higher incidence in the country (Mansoor 2020).

A local project was initiated for CH screening and management in selected hospitals in 2019 in our region. Our institute participated in this project from July 2020 till August 2021. We decided to undertake a retrospective analysis of the following metrics for the project duration for our institution: frequency of elevated neonatal TSH, recall rate i.e. when patients returned for repeat testing, rate of missed testing and turnaround time for results in order to learn from the challenges and experience.

SUBJECTS AND METHOD

1. Study Design

The present retrospective study was conducted by Section of Chemical Pathology and Neonatal Unit at the Indus Hospital and Health Network. Data was collected for the entire project duration between 13th July 2020 and 10th August 2021.

2. Population and Sample

The deliveries during the studied period were considered. Specimen for TSH was generally collected from the umbilical cords for babies who were born by spontaneous vaginal delivery (SVD) and by heal prick at the time of discharge for babies who were born by caesarian section.

3. Study Variables

The variables include demographics, TSH levels, mode of delivery, and time taken for reporting.

4. Operational Definition of Variables

Demographics: Gender: Newborn's sex, recorded as male or female.

TSH Levels: Concentration of Thyroid-Stimulating Hormone in the newborn's blood, measured in µIU/mL.

Spontaneous Vaginal Delivery (SVD): Birth through the vaginal canal without surgical intervention.

Cesarean Section (C-section): Birth through an abdominal and uterine incision.

Time Taken for Reporting: Duration from sample collection to final report generation, measured in days.

Repeat Testing: TSH levels above 20 µIU/mL trigger repeat testing.

5. Study Instruments

Sampling was done on filter paper as dried blood spots and sent to a designated testing laboratory where the tests were performed by flourometric enzyme immunoassay (FEIA). Test request was generated by physicians at the time of baby's birth. The nursing team was responsible to draw the sample. A coordinator from the testing laboratory was responsible to transport the sample, share the reports, point out the raised results timely and ensure recall and collection of repeat samples. Repeat testing criteria was set at 20 µIU/mL.

6. Data Analyze

The descriptive statistics were calculated via IBM SPSS Statistics 24.

7. Research Ethics

The study was performed after getting exemption from the Institutional Review Board (IHHN_IRB_2022_02_008). Data anonymity and confidentiality was maintained throughout the work.

RESULTS

There were a total of 4037 babies born during the studied time frame. The population comprised of 1888 (46.77%) females and 2149 (53.23%) males. 2041 (51%) neonates were delivered vaginally, while 1987 (49%) through C-Section (Figure 1).

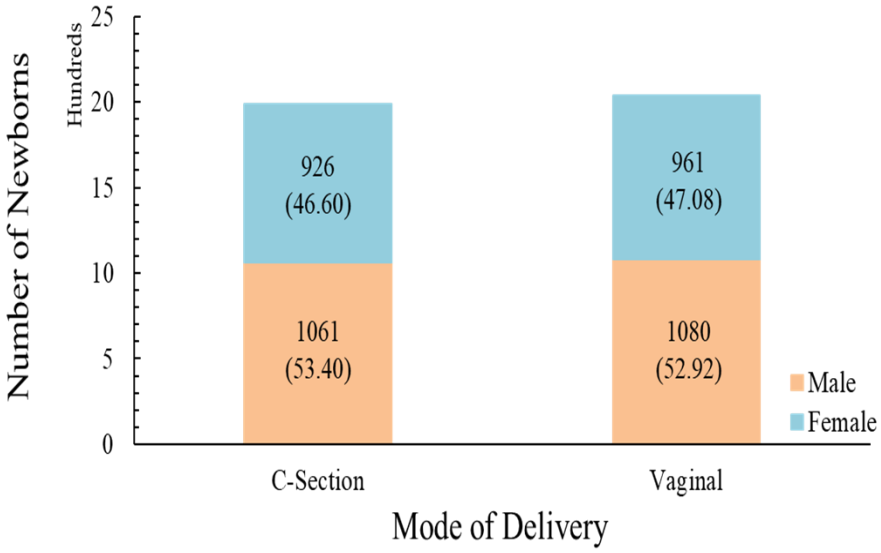

Figure 1: Distribution of newborns based on the mode of delivery and gender

The mode of delivery was not mentioned in nine records. Neonatal TSH was performed in 3618 (89.62%) neonates, comprising 1913 (52.88%) males and 1705 (47.13%) females. The median value recorded was 3.34 (2.09-5.30) µIU/mL with minimum and maximum TSH levels as 1.18 and 75.00 µIU/mL respectively. Values of 15 µIU/mL and above were recorded for a total of 95 newborns, out of which 31 newborns had values of 20 µIU/mL or greater. The detailed description in different categories based on sample type (Figure 2)

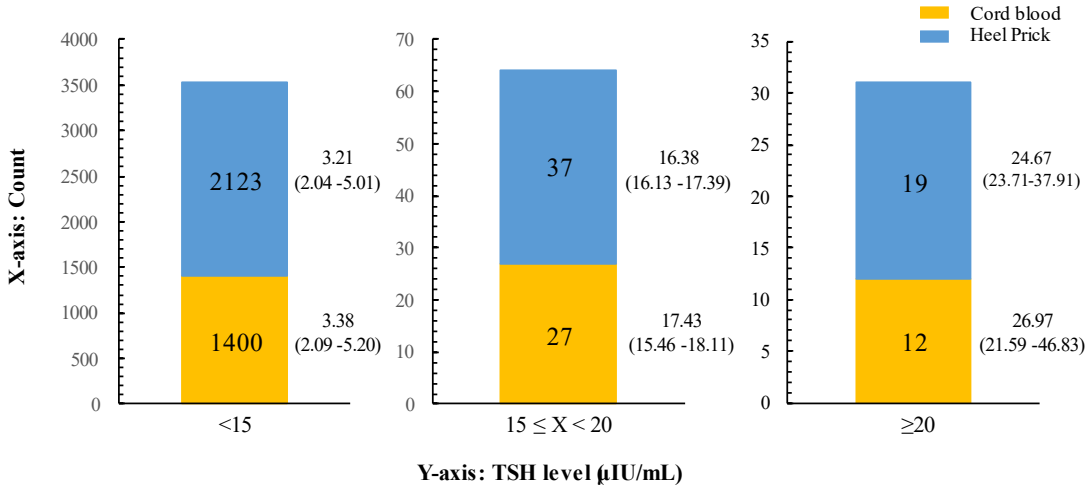

Figure 2: Division of studied population based on specimen type used and observed TSH levels

Only 12 of these patients were recalled for repeat testing, which is 0.3% of total neonatal TSH performed during the study period. One neonate was identified who had a persistently raised TSH with suppressed FT4 and was started on thyroxine for congenital hypothyroidism.

There were 419 or 10% of neonates who were not screened for CH, breakdown of which is mentioned in Table 1.

Table 1. Neonates missed TSH test

Neonates not screened for CH (n=419)	Males 236 (56.46%)	Females 183 (43.54%)
TSH requested but no records of sample collection n=14 (3.34%)	6 (42.86%)	8 (57.14%)
Record of sample collection exists but TSH not reported n=158 (37.70%)	84 (53.17%)	74 (46.84%)
No neonatal TSH test requested n=246 (58.85%)	146 (59.35%)	100 (40.65%)
Sample rejected n=1 (0.2%)	-	1

Time taken for various steps in result delivery (n=3618) is given in Table 2, showing a median (IQR) time of 14 (4-55) days from sample collection to availability of result to clinician.

Table 2. Time taken for reporting

Time Cut offs	Median (IQR)	Min	Max
Request to Sample collection (Days)	0.00 (0.00-1.00)	0	67
Sample collection to confirmation of collection in software (Days)	0.00 (0.00-1.00)	0	144
Sample collection to reporting (Days)	10.00 (7.00-15.00)	2	135
Time taken from initial result generation till accessibility to clinician (Days)	14.00 (4.00-55.00)	0	133

DISCUSSION

We observed the screening neonatal TSH values to be less than 15 µIU/mL in 97.3% of the babies born in our institute. There were a total of 31 neonates who had an initial TSH value of greater than 20 µIU/mL. Eventually, only one out the entire cohort of 4037 neonates was confirmed to have CH by repeat TSH and FT4 tests. A study conducted on 430 term neonates in rural India(Raj et al. 2014) revealed raised cord blood TSH in 127 babies at birth of which 3 were subsequently proved to have congenital hypothyroidism on repeat TSH on third postnatal day and serum thyroxine on the initial sample. As mentioned before, a study from Pakistan revealed a prevalence of 1 in 1600 newborns through a retrospective audit over ten months (Afroze et al. 2008), while an earlier study from the same institute demonstrated an incidence of 1 in 1000 (Lakhani et al. 1989).

Screening and diagnostic mechanisms for congenital hypothyroidism have varied across global NBS programs. Afroze in discussing the 2008 audit of the CH screening program laid out the strategy used for CH screening (Afroze et al. 2008). It included sending a TSH test for every newborn at the hospital. If elevated, a repeat TSH test was conducted. Upon confirmation of elevated TSH, follow-up T4 and TSH tests were performed. The patient was then referred to a paediatric endocrinologist if the TSH was high and T4 was low. The protocol decided for Indus Hospital and Health Network was screening all neonates with TSH and performing a confirmatory TSH and Free Thyroxine (FT4) for positively screened patients.

The recall rate for TSH was defined as when the patients returned for repeat

testing. This is varied in literature and ranges from 0.01 to 13.3%(Mehran et al. 2017) depending on the criteria selected. Our recall rate was 0.3%, which is on the low end. Some of the reasons for the poor recall rate could be that babies were discharged before receiving results as it took a median of 14 days from specimen collection to availability of results to the clinician. During the first two months of the project, the process of informing critical results to the clinical team was not stream-lined. The flow was then established. Critical results, categorized as greater than or equal to 20μIU/-mL, were informed by the laboratory to the clinical team, who then informed the parents for re-testing. The reasons for poor show up for re-testing could be that as this was a screening test, the neonates did not have any gross presenting clinical features to suggest CH resulting in poor parental compliance. Another contributing factor was lack of public awareness.

The ratio of false positive to confirmed CH in most screening programs is 3:1 or 2:1 (Desai 2012). Prompt evaluation is required for neonates screened positive to prevent complications. Majority of the programs use cord blood TSH for NBS. The use of cord blood TSH has improved the implementation of screening for CH. Globally, 25% of live born babies undergo CH screening, majority of whom are from developing countries (Desai 2012). Most NBS programs use filter paper to test for initial TSH after 48 hours of birth. Earlier testing can result in false positive because of TSH surge, unless specimen is taken from placental side of umbilical cord. Our protocol for testing was to use cord blood specimen in neonates discharged within 6 -24 hours of birth and heel prick specimen at 48-72 hours for those having more than 48 hours of hospital stay.

The median cord blood TSH values in newborns has been reported as 7.30 to 8.75 μIU/mL (Gupta et al. 2014, Nasheeda et al. 2018). A single cut-off of 20 μIU/mL was kept for all patients. Similar cut-off has been used in several studies, although higher cut-offs have also been proposed for cord blood to minimize false positives and increase specificity (Nasheeda et al. 2018, Paul et al. 2021).

Our analysis showed that there was a significant time gap between the request and result availability to the clinician. Many neonates were lost to follow-up and never showed up in the out-patient clinics. Various factors such as delay in specimen collection or confirmation in the software, delay in processing the results by the testing laboratory, delay in result transmission, connectivity incompatibility between the host and testing labs, lack of proper monitoring, logistics as well as financial constraints accounted for this.

Although this is a single center study focusing purely on births within a tertiary care hospital, the situation on ground has multitudes of other challenges. In Pakistan, around 65% of deliveries take place at home (Demographic 2008). There is no system in place to track all newborns at the time of delivery. For any successful newborn screening program, these home-born newborns have to be included. Formation of an administrative health network structure for tracking the newborns, sample collection, reporting, repeat testing of borderline and high results and streamlining management will be mandatory for a successful implementation of any national level program for NBS.

The study had certain limitations. All data was retrieved from the electronic medical records. Due to the small sample size, no estimation can be made on the true frequency of hypothyroidism. Clinical details or follow-ups on low birth weight or preterm infants were not considered in this study. In

conclusion, CH was diagnosed in only one neonate out of 4,037 babies in the study, with around 10% of neonates not screened. This low incidence rate, while valuable in assessing the effectiveness of the screening program, underscores the challenges in its implementation. The recall rate of 0.3% was notably low, possibly due to delays in receiving results, averaging 14 days from testing to availability—along with logistical barriers such as insufficient follow-up and lack of parental awareness. Furthermore, a significant number of neonates were lost to follow-up, indicating that more robust mechanisms are required for tracking and informing families, especially in regions where home deliveries are common. These findings emphasize the need for a more organized and resource-supported health network to ensure the sustainability of CH screening programs, particularly at a national level. Streamlining communication between testing laboratories, clinicians, and parents, as well as improving awareness and accessibility, are crucial steps in enhancing the effectiveness of neonatal screening for congenital hypothyroidism.

AUTHOR CONTRIBUTION

Fatima Kanani contributed to the study design, data retrieval, drafting, and final review. Vikram Kumar provided a critical review. Mamona Mushtaq was involved in data retrieval, data analysis, and the critical review. Dua Sameer contributed to data retrieval and critical review. Syed Rehan Ali was responsible for study design and critical review.

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CONFLICT OF INTEREST

There are no conflicts of interests to declare.

REFERENCES

Afroze B, Humayun KN, Qadir MJ(2008). Newborn screening in Pakistan—lessons from a hospital-based congenital hypothyroidism screening programme. Ann Acad Med Singap. , 37(12 Suppl):114-3.

Ahmad N, Irfan A, Al Saedi S AJ (2017). Congenital hypothyroidism: Screening, diagnosis, management, and outcome. J Clin Neonatol. 6(2):64-70. doi: 10.4103/jcn.JCN_5_17

Dayal D and Prasad RJ (2015). Congenital hypothyroidism: current perspectives. Res Rep Endocr. 5(5):91-102. doi.org/-10.2147/RRED.S56402

Demographic P (2008). Health Survey 2006. Islamabad, Pakistan, National Institute of Population Studies and Macro International Inc; National Institute of Population Studies (NIPS) and Macro International

Desai MP (2012). Congenital hypothyroidism: Screening dilemma. Indian J Endocrinol Metab. 16(Suppl 2):S153. doi: 10.4103/2230-8210.104027

Gupta A, Srivastava S, and Bhatnagar AJIp (2014). Cord blood thyroid stimulating hormone level—interpretation in light of perinatal factors. Indian Pediatr. 51:32-6. doi: 10.1007/s13312-014-0330-2

Khokhar AR and Cheema AM (2021). Higher frequency of congenital hypothyroidism among newborns, District Dera Ghazi Khan-Punjab, Pakistan: A case control study. Pak J Med Sci. 37(5):1419-24. doi: 10.12-669/pjms.37.5.4086

Lakhani M, Khurshid M, Naqvi SH, Akber M (1989). Neonatal screening for congenital hypothyroidism in Pakistan. J Pak Med Assoc.39:282-4

Mansoor S J (2020). Trends of congenital hypothyroidism and inborn errors of metabolism in Pakistan. Orphanet J Rare Dis., 15(1):1-10. doi: 10.1186/s13-023-020-01602-6.

Mehran L, Khalili D, Yarahmadi S, Amouzegar A, Mojarrad M, Ajang N, Azizi F (2017). Worldwide recall rate in newborn screening programs for congenital hypothyroidism. Int J Endocrinol Metab 15(3), e55451. doi: 10.5812/-ijem.55451.

Nasheeda CM, Philip P, Shenoy RD, Shetty S (2018). Diagnostic utility of cord blood thyroid stimulating hormone in congenital hypothyroidism in the era of expanded newborn screening. Indian J Clin Biochem. 33(4):461-6. doi: 10.1007/s12291-017-0697-7.

Olney RS, Grosse SD, Vogt RF (2010). Prevalence of congenital hypothyroidism—current trends and future directions: workshop summary. Pediatrics. 125(Supplement 2):S31-S36. doi: 10.1542/peds.2009-1975C

Paul PG, Rebekah G, Korula S, Kumar M, Bondu JD, Palany R, Simon A, et al. (2021). Optimizing cord blood thyroid stimulating hormone cutoff for screening of congenital hypothyroidism—experience from screening 164,000 newborns in a Tertiary Hospital in India. Indian J Endocrinol Metab. 25(4):348-53. doi: 10.4103/ijem.ijem-_220_21.

Raj S, Baburaj S, George J, Abraham B, Singh S (2014). Cord Blood TSH Level Variations in Newborn - Experience from A Rural Centre in Southern India. J Clin Diagn Res. 8(7):Pc18-20. doi: 10.7860/JCDR/2014/9058.4603

Rastogi MV and LaFranchi SHJ (2010). Congenital hypothyroidism. Orphanet J Rare Dis. 5(1):1-22.

Wilson JMG, Jungner G,Organization WH (1968). Principles and practice of screening for disease.