

Establishing a Newborn Screening Programme: A Success Story from a Low-Resource Setting

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ABSTRACT

The purpose of this communication was to assess the clinical effectiveness of a newborn screening (NBS) programme for congenital hypothyroidism (CH) in a tertiary care centre. This cross-sectional study was conducted from January 2019 to December 2023. Thyroid-stimulating hormone (TSH) on dried blood spot (DBS) specimens collected after 24 hours of birth with >10 mIU/L was further confirmed by testing serum TSH and FT4, and CH cases were referred to a paediatric endocrinologist for management. During the study period, coverage of NBS was tracked. Over a four-year period, 30,402 newborns were screened, with 96.2% coverage (total births-31610). Positive screening results (TSH>10 mIU/L) were found in 1.9% of neonates (n = 586), with confirmatory tests performed in 63.13% (n = 370) of these cases. CH was confirmed in 27 cases, with an incidence of 1:1126. This study demonstrated that NBS for CH was successfully implemented and highly effective. However, there is a need to further improve recall rates.

Key Words: Congenital hypothyroidism, Dried blood spot testing, Newborn screening, Clinical efficacy.

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Newborn screening (NBS) refers to an essential public health programme of biochemical testing, including testing, diagnosis, follow-up, treatment, education and evaluation for certain disorders, and symptoms of which are not apparent at birth.¹ Newborns are tested for specific disorders not symptomatically present at the time of birth, which, if remain untreated, can permanently impact the health of the baby. The signs and symptoms of many of these disorders are not apparent at birth, hence necessitating that testing is done for the early detection of the disorders included in the NBS programme.¹ The main goal of NBS programmes is to reduce morbidity and mortality and improve the health outcomes of newborns. Selection of disorder for inclusion in the NBS panel is generally done based on Wilson and Jungner (W and J) criteria, which includes disease burden, availability of cost-effective treatment, sensitive screening and confirmatory tests, appropriate treatments, and experts availability.¹

Prompt, efficient, and effective follow-up activities are crucial to ensure that newborns needing further testing are timely evaluated, receive indicated testing, and are promptly referred for subspecialty care and support services. Follow-ups of positive cases on NBS are means by which accountability of NBS programmes can be ensured.

Furthermore, outcome assessments are critical for tracking performance and improving the clinical effectiveness of an NBS programme.² CH is a disorder that, if screened for in every newborn, has a high benefit-to-risk ratio. A cost-effective treatment is available, it can lead to irreversible intellectual disability if not identified and treated within the first few weeks of birth. The incidence of primary CH in Pakistan ranges from 1:1000-1600.³ The aim of this study was to evaluate the clinical efficacy and performance of the NBS programme.

This study was conducted over a four-year period at the Biochemical Genetics Laboratory (BGL), Section of Clinical Chemistry, Pathology and Laboratory Medicine Department, in collaboration with the Paediatric and Child Health and Gynaecology and Obstetrics Departments. The study was carried out in accordance with the principles of the Helsinki Declaration between January and December 2022, and data were extracted from January 2019 to December 2022. An exemption was requested from the Institutional Review Board (ID# 2022-7346-20976) prior to the initiation of the study. The NBS programme policies and standard operating procedures were developed in line with the guidelines from the Clinical Laboratory Standards Institute (NBS01-A6) and standards from the College of American Pathologists. The NBS programme for CH based on DBS-TSH testing was initiated in January 2019 from one hospital and expanded to include four more hospitals in 2021.

The dried blood spot (DBS) samples were collected from newborns after 24 hours of birth and transported to the laboratory within 24 hours of collection, where they were checked for validity and stored at 4-8°C until analysis. Invalid specimens were rejected, and respective nurses were contacted to send in new specimens.

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Table I: Characteristics and results of the NBS for CH (2019 to 2022).

	2019	2020	2021	2022
Demography				
Live births	5,162	5,760	5,532	15,156
Screened children	4,830	5,220	5,196	13,447
Coverage (%)	93.6	90.6	93.9	88.7
Screening				
Screen positives (%)	52	148 (2.5)	171 (3.3)	215 (1.42)
Recall success rate (%)	25 (48%)	94 (63.5%)	132 (77%)	119 (55%)
Confirmed children with CH	6	5	7	9

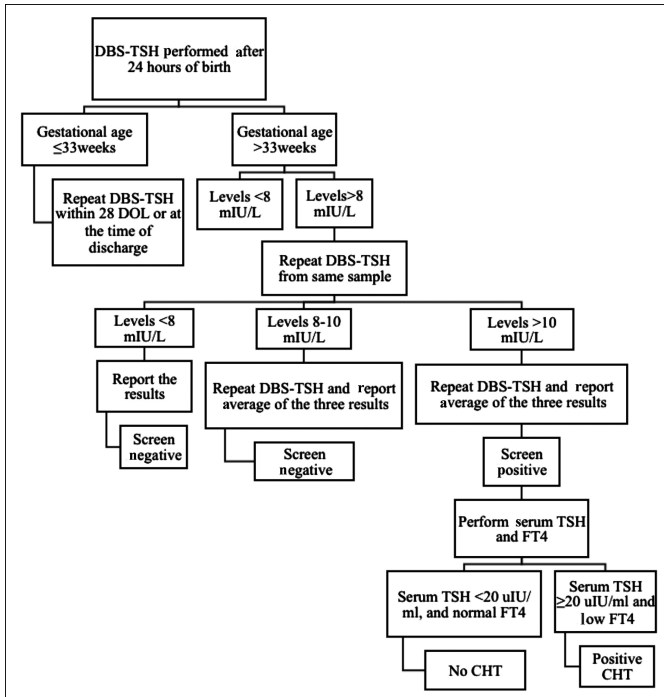


Figure 1: The diagnostic algorithm of the CH-NBS programme.

Babies were also included if they were screened after 28 days of life. Thyroid-stimulating hormone (TSH) was measured using Lab Systems Diagnostic Fluorometric enzyme immunoassay kits on a Varioskan™ LUX multimode microplate reader.

After consulting with a neonatal endocrinologist, the positive screen cut-off for DBS-TSH was set at 10 mIU/L. Diagnostic algorithm is shown in Figure 1. Positive screen newborns were recalled for confirmatory test, serum TSH, and free thyroxine (FT4). The CH was confirmed if serum TSH was ≥ 20 uIU/ml along with low FT4, and thyroxine replacement therapy was initiated. For programme evaluation, an NBS programme committee, including pathologists, neonatologist, paediatric endocrinologists, and NBS lab in charge - was established with the aim to monitor and evaluate the programme.

Data were entered and analysed using Microsoft Excel. Frequency and percentages were generated for gender, while mean and standard deviation (SD) with interquartile ranges (Q1-Q3) were calculated for quantitative parameters.

A total of 30,402 neonates were screened between 2019 and 2022, with a mean sample collection age of 48 ± 12 hours; 47% (n = 14,288) were boys. In 2019, the average length of stay in five hospitals was 36.2 hours, ranging from 30-44 hours. Table I shows the demographic and clinical characteristics of the newborns who were screened. The total NBS coverage over a three-year period was 96.2% (n = 30,402 / 31,610). Positive screening results (DBS-TSH levels >10 mIU/L) were obtained for 1.9% (n = 586) of the specimens, and 100% were communicated within 24 hours of analysis. Recall rate for confirmatory testing was 63.13% (n = 370 / 586), and of these, 27 were proven to have CH, accounting for 7.3% (n = 27 / 370) of the total tested for serum TSH. The incidence of CH was 1:1126 in this cohort.

In the current study, 30,402 newborns were screened, with an average coverage of 96.2% over four years. Parents were responsible for all testing, follow-ups, and treatment costs. Hence, to curtail the cost incurred to the newborn's family, single test strategy was followed for screening. Screening coverage reported by this study was adequate and comparable to that of many other countries that provide government-sponsored mandatory NBS.⁴ Guidelines recommend that TSH samples be collected after 24 hours of birth, while the ideal time for specimen collection is between 48-72 hours of birth. The timing of sample collection is critical because false results can occur due to physiological neonatal TSH surges in the early hours of birth (within 24 hours of birth) and the immaturity of the hypothalamic-pituitary-thyroid axis in premature newborns.

The recall rate for positive screens in this study was 1.9% (n = 586 / 30,402), which is comparable to other established NBS programmes in North America and Europe.⁵ Only two-thirds of the screen-positive newborns were tested for the confirmatory test, serum TSH, in the current study. This could be due to the fact that these newborns were monitored in other hospitals, as well as the parents' lack of knowledge about the significance of this disorder. Hence they do not come back for the confirmatory testing. This study is comparable to the local literature reported from Pakistan, which reports a higher prevalence of CH, with estimated incidence ranging from 1:250-1,600.³ Similarly, studies from neighbouring country India have revealed the incidence of CH to be higher in this region than the rest of the world.⁶ These findings indicate that NBS for CH should be initiated in Pakistan, and the availability of low-cost diagnostic and

treatment options makes it an ideal disorder for launching NBS services.

The current study had some limitations, including the lack of follow-up on all positive screens, so an accurate positive predictive value for the DBS-TSH could not be calculated.

This is the first study to report the results of an NBS programme from Pakistan; it demonstrates that the NBS for CH was successfully implemented and quite effective; however, further improvement of recall rates is required. The prevalence of CH was higher than in other developed countries, compelling policymakers, healthcare professionals, and government officials to devise strategies to extend NBS coverage to the entire country.

ETHICAL APPROVAL:

The study was carried out in accordance with the principles of the Helsinki Declaration. An exemption from the Institutional Review Board (ID# 2022-7346-20976) was requested prior to the initiation of the study.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

HM: Conceived the idea, conducted the project, collected data, analysed and wrote the initial draft of the manuscript. LJ, SA, KNH, SK: Reviewed the manuscript critically for important intellectual content.

AHK: Supervised the project and reviewed the manuscript. All authors approved the final version of the manuscript to be published.

REFERENCES

1. Watson MS, Puryear MAL, Howell RR. The progress and future of US newborn screening. *Int J Neonatal Screening* 2022; **8(3)**:41. doi: 10.3390/ijns8030041.
2. Mutze U, Garbade SF, Gramer G, Lindner M, Freisinger P, Grunert SC, et al. Long-term outcomes of individuals with metabolic diseases identified through newborn screening. *Pediatr* 2020; **146(5)**:e20200444. doi: 10.1542/peds.2020-0444.
3. Majid H, Jafri L, Khan N, Khan AH. Establishing a nationwide newborn screening programme for congenital hypothyroidism: A systematic review. *Pak J Pathol* 2022; **33(3)**: 104-8. doi: 10.55629/pakjpathol.v33i3.715.
4. Majid H, Jafri L, Ahmed S, Humayun K, Kirmani S, Ali N, et al. Perspective on newborn screening (NBS): Evidence sharing on conditions to be included in NBS in Pakistan. *J Pak Med Assoc* 2022; **72(3)**:526-31. doi: 10.47391/JPMA.01181.
5. Mehran L, Khalili D, Yarahmadi S, Amouzegar A, Mojarrad M, Ajang N, et al. Worldwide recall rate in newborn screening programmes for congenital hypothyroidism. *Int J Endocrinol Metabol* 2017; **15(3)**:e55451. doi: 10.5812/ijem.55451.
6. Kumar KR, Agrawal A. Neonatal screening for congenital hypothyroidism in India. *Indian J Child Health* 2017; **4(4)**:462. doi: 10.32677/IJCH.2017.v04.i04.001.

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