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Establishment of National programme on newborn screening for congenital hypothyroidism

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Abstract

Introduction: Congenital hypothyroidism is one of common disorders related to mental impairment and growth retardation in newborns. Hence, screening programs are performed for early diagnosis as most infants are with no clinical signs for recognition at birth.

Objective: To evaluate key performance indicators of the congenital hypothyroidism screening programme in terms of coverage, effectiveness of detection and managing cases during the year 2016.

Methods: The Newborn Screening Information System Database of the Faculty of Medicine, University of Ruhuna, Galle (www.nsisd.ruh.ac.lk) was retrospectively analyzed to assess performance indicators.

Results: In 2016, 126,341 samples were received, and 101 babies were confirmed as having congenital hypothyroidism with an annual incidence of 1 in 1250 live births. The coverage rate of 76% of births and sample rejection rate was < 0.01% The sample collection ages ranged from 6 hours to 49 days with median age of screening sampling was <24 hours of age. The serum confirmation was made before 10 days of age among 14% (n=15) and within 11 - 21 days of age for 55% (n= 61) of babies with mean age for the start of the treatment was 18±9 days.

Conclusion: It has shown a good uptake of newborn screening with coverage of over 95% in areas for more than a year and overall 76% within months of inception. The laboratory and clinical services need to be improved to ensure that results are available and reviewed within the stipulated time frame. Liaison with the state public health department is important to promote community awareness and trace cases that required retesting. Periodic audits of the system are a necessity to identify any deficiency and improving the overall quality of the programme.

Key words: Congenital hypothyroidism, newborns, screening program

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Introduction

The sustainable development goals have changed the entire paradigm of health care in general especially neonatal care with a theme of Survive, Thrive and Transform. Focus is on every child where under survive agenda all preventable deaths should be prevented, in the thrive agenda full potential for development is to be achieved, society is transformed for care of every child including special children (1). National Newborn screening programme (NBS) on Congenital Hypothyroidism (CH) was introduced to improve quality of care before the SDGs but has now become an integral part since January 2016. Further all newborns in SL are now screened for critical congenital heart diseases with pulse-oximetry. The initial studies on NBS for CH using heel prick dried blood spot in Sri Lanka were introduced in 2006 (2). Then a regional screening center (3) was established in 2008 which subsequently paved the way for the establishment of NBS for CH in all newborns of the Southern province in 2010 with the policy and financial commitments of the Ministry of Health of Sri Lanka (MOHSL) by circulars issued time to time by the Director General of Health Services of Sri Lanka.

Programme evaluation using key performance indicators (KPIs) is an important organizational practice in all public health programmes. In NBS KPIs are in pre-analytical, analytical and post analytical phases. It was aimed to perform retrospective clinical and laboratory evaluations of babies diagnosed with congenital hypothyroidism at our screening program, and to analyze clinical reflections of the screening program. Therefore, this report is aimed at evaluating the congenital hypothyroidism screening programme offered by the Faculty of Medicine to five provinces (Southern, Uva, Sabaragamuwa, Central and Eastern) of Sri Lanka in terms of coverage, effectiveness of detection and managing the cases.

Methods

This audit was carried out through follow-up and retrospective approaches on the newborn screening information system database (www.nsisd.ruh.ac.lk) maintained at the Faculty of Medicine, Galle. The focal point of the programme was Family Health Bureau (FHB) and the plan was to start it in hospitals with many deliveries such as Teaching, Provincial, District General and Base hospitals which deliver >95% of all births of the country and consultant paediatricians are available to oversee the programme i.e., dried blood spot sample collection to transport of specimen, patient tracking to commencement of treatment. The Newborn Screening Advisory Committee of the Faculty of Medicine established links with these hospitals to conduct awareness programmes with the assistance of public health staff (i.e., Medical Officer for Maternal and Child Health (MO/MCH) in Regional Director of Health Services (RDHS) office with a representative from any government hospital where birth delivery facilities are available. The plan also identified local focal points, system for reporting results, patient tracking, setting up confirmatory testing service and commencing treatment. All positive results were communicated through the mobile phone to parent, paediatrician and MO/MCH. Parent was counseled over the phone on the result and its implications including being positive or negative on confirmatory testing. As the analytical center was in Galle geographically far away from some areas confirmatory testing was assigned to either regional/provincial laboratory or even private sector laboratories if it was not feasible to send samples to Galle for confirmation. Confirmation was done by fT4 and TSH assay as per guidelines issued by Sri Lanka College of Paediatricians (4).

Once a sample is received a unique number is assigned and subjected to immediate analysis while request form data are entered to the database. The cut off value for blood spot TSH used was 20mIU/L on DELFIA® (time-resolved fluorescence immunoassay) analytical system, irrespective of time of collection from birth. However, if the sample analyzed using IMMUCHEM™ NEONATAL TSH-MW ELISA any sample upto 40mIU/L and collected within 48 hrs (i.e., Day 2) were repeated on DELFIA system based on our previously published data (5). If a repeated test confirmed positive, parents were contacted immediately to perform confirmatory testing using serum sample. The database of the programme was reviewed from January 2016 to December 2016 to analyze KPIs. The coverage based on screened infants out of total live births, age at screening, at confirmation and at the time of commencing treatment were analyzed and the positive predictive value calculated on total positives (on true and false positives).

Results

Galle, Matara, Hambantota (Southern Province), Monaragala and Ratnapura districts programmes were in operation by 2016 and coverage was as expected was high. During 2016 Kalutara district was reassigned to other center located at MRI- Colombo as part of western province. Sample collection and transport was not well established in new areas/hospitals. It took more than 6 months to streamline the process of sample collection and transport to the testing facility at the NMU, Galle and deliver the results. Therefore, the data for the year of 2016 show within country variations in coverage. The performance indicators for the programme since 2013 (excluding new areas in 2016) are summarized in Table 1. We were able to achieve over 80% coverage among live births within a year of implementation and improved it to 95% by the end of 2016. By the end of 2013 we were able to achieve a positive predictive value of 50% and it improved to 75% by 2016. The rate of incidences of primary CH among screened infants was 1:1600 and the false positive rate among screened infants were maintained below 0.04% during this period.

During the first 6 months of 2016, 8 more districts from 4 provinces were incorporated to the program. There were some issues in the organizational structure on responsibility in the program within the first few months as expected, but by the year end it was well-established with satisfactory

coverage (Table 2). The Badulla and Batticaloa districts achieved a satisfactory coverage from the inception with even rural hospitals without Paediatricians getting included in the programme. The number screened were 487,806 in total by the end of year 2016 and 330 babies were confirmed to have CH with overall incidence 1 in 1300 live births. During the year 2016, total of 126,341 samples were received from the hospitals in Sri Lanka and 101 babies were identified as having congenital hypothyroidism with an annual incidence of 1 in 1250 live births in the year 2016. Further, analyses done on sample collection and data are summarized in Table 3. Our records indicated that 5% (n = 7,392) of babies' blood spots were collected within 12 hours of delivery, and 58% (n = 80,178) were collected in the following 12 hours period (i.e., within day 1; Table 3). The number of blood spots collected on day 2 was 19% (n = 25,882) and day 3 onwards was 17% (n = 23,901) respectively. The sample collection ages ranged from 6 hours to 49 days of age. The median age of screening sampling in the program was 24 hours of age (i.e., day 1). In this programme, the age at serum sampling (for the confirmatory testing) was conducted between 6 to 45 days with a mean of 17.0 ± 10.0 days. The serum confirmation was made before 10 days of age among 14% (n=15) and within 11 - 21 days of age for 55% (n= 61) of the cases. The confirmation was made between 22 days and 28 days of age for 12% (n=14) of the cases and the confirmation was made after 4th week of age for 19% (n=21) of the cases. The mean age for the start of the treatment was 18±9 days.

Discussion

National CH screening has been initiated on top of existing infrastructure developed by the researchers so that, we assume that this present audit, which has been performed comprehensively and on adequate number of cases, is important to show what changes screening programmes can lead to. Before the screening programme, parents or even preventive health staff or teachers were expected to realize clinical signs of CH and refer to healthcare units. However, unclear and nonspecific mental signs of CH during the newborn period caused delayed diagnosis, and persistent changes especially in mental functions (6, 7).

The coverage rate of 76% of births and sample rejection rate of 0.01% are in keeping with the performance evaluation criteria. The low sample rejection rate may reflect familiarity and excellent sampling technique by the postnatal nurses and medical officers who have been doing this since 2010 with the introduction of screening programme. The magnitude of false-positive results generated in newborn screening programmes, presents a great challenge for future improvement of this important public health programme (8). The appropriate age of sampling in the newborn screening programme was a matter of debate. The optimum age of sampling depends on many factors like the number of diseases screened for and screening method (9). However, screening before hospital discharge or before blood transfusion was preferable to avoid missing the diagnosis of hypothyroidism. In most of developing countries including Sri Lanka, a significant problem is the early discharge of newborns from maternity hospitals, typically before 24 hours (5). It has been speculated that the specimens collected in the first 24 to 48 hours of life resulted in higher false-positive rates. But we have been able to overcome this issue with advance technology of using time resolved fluoroimmunoassay techniques.

It has been realized that age of diagnosis was high before the screening test programme. When we evaluated data from before and after national screening programme, we suggested that the disease was diagnosed especially due to thyroid function tests of patients, who were hospitalized during the newborn period for different reasons (10, 11). Considering that some technical and systemic problems have been encountered during the first year of the screening programme in Sri Lanka, it can be predicted that age of diagnosis will be decreased in the next years. Previous studies reported the mean age of treatment onset as 8-44 days (12), 9-37 days (13) while our initial experience was 9-45 days (5). A total of 11 cases failed to be recalled. The most common reason for failure of recall was that the mothers were no longer staying at the addresses that were used for registration during first booking for antenatal care. This could be due to the practice of seeking better care especially among the natives who would return to their villages in the interior weeks following birth and could therefore not be contacted. Further, the mothers were non-attenders of antenatal care and did not provide valid addresses and phone numbers. Hence, we suggested pre-screening education for parents on NBS to be an integral part of this new NBS program. However, designing a health education programme on NBS for CH for stakeholders is always a big challenge because such a programme should be powerful enough to change the NBS behavior of antenatal mothers. In Sri Lanka public health midwives (PHMs) are the grass root level health professionals who are responsible for improving maternal and child health. Thus, in motivating mothers to get the test done, the role of the PHMs is vital. A study indicated (14) that their Knowledge on CH was poor. Therefore, the educational program seems to be effective in changing certain aspects of NBS behavior of mothers. Further modifications in the programme, especially related to perceived susceptibility and perceived severity of CH and of the barriers to participate in NBS for CH are needed.

A review of the individual cases and our previous experiences on this program implementation, it was noted that reasons for the delay can be explained by management at 3 different points – laboratory service level, clinical service level and subject level. Firstly, at the laboratory service level is from the time the samples were taken to the time the results were available. At present the laboratory is maintaining maximum of 5-day (including weekends) turnover for analysis. During the period of the audit a back-up instrument (both DELFIA and ELISA systems) installed and the reagents orders were divided to make sure

continuous reagent supply. Secondly, we suggest each paediatric team to liaise with public health staff at the clinical service level to shorten the time when the results were available to them and the results were reviewed by the paediatric team. There was some delay occurred during this period as the results were not reviewed until after the public holidays. In addition to that, the previous practice was to have only one designated paediatrician in charge and MO/MCH of reviewing abnormal results. Therefore, in his or her absence, there could be a delay in reviewing the results. Thirdly, issues pertaining at the subject level is the time it took for a recalled case to return for retesting. For several cases, there were difficulty contacting and getting the baby to come back for retesting. The reasons identified were indifference due to lack of awareness, mothers not contactable during the confinement period and logistics such as transport problem for those staying far in the interior and parents' refusal to comply with remote advice. This is the first audit conducted on congenital hypothyroidism newborn screening in Sri Lanka. It involves a large cohort of more than 300,000 babies over a course of 4 years. This analysis has several limitations. It is a single centre study which involves only babies born in five provinces in Sri Lanka which may therefore not be representative of the overall prevalence in the state and cannot be generalized to other geographic or healthcare settings. The descriptive nature of the study presents possibility of subjectivity or bias that may affect the result analyzed. Further, to improve effectiveness of early diagnosis and referral sample posting from birth hospital should be improved and suggest posting samples daily. Potential implications of wet weather on samples during postage had been communicated to relevant hospital staff (cover with a polythene). Further development of follow up services for development assessment for these children is required in a district wise manner. This needs a community paediatrician trained in development assessment and a clinical psychologist to assess psychological development at different ages. This is necessary to evaluate the programme on long term basis.

Conclusions

The estimated birth prevalence of congenital hypothyroidism in Sri Lanka is 1 in 1500 live births. Further, it has shown a good uptake of newborn screening with coverage of over 95% in areas for more than a year and overall 76% within a year of expansion. Even though a low sample rejection rate was maintained the mean percentage of confirmed babies receiving treatment less than 14 days old is only 15% which fell short of the set performance indicators. There is a need to improve on the laboratory and clinical services to ensure that results are available and reviewed within the stipulated time frame. Liaison with the state public health department is important to promote community awareness and trace cases that required retesting. It is important to undertake periodic audits of the system to identify any deficiency and improve on the overall quality of the newborn screening programme.

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Table 1: Program indicators[1]

	2013[2]	2014	2015	2016[3]	Total
Total number of live births	86,546	90,706	80,196	65,574	323,022
Screened infants	59,320	76,014	77,848	62,617	275,799
Percentage of coverage	69%	84%	97%	95%	85%
Screening positives infants	71	94	80	54	299
True positives (confirmed CH)	35	45	54	41	175
False positives	36	49	26	13	124
Positive predictive value	49%	48%	68%	76%	59%
Incidence of primary CH among screened	1,695	1,689	1,442	1,527	1,576
False positive rate among screened	0.06%	0.06%	0.03%	0.02%	0.04%

[1]Data presented for Galle, Matara, Hambantota, Moneragala, Ratnapura and Kalutara districts; live birth data reported in Annual Health Bulletin, Medical Statistics Unit, Ministry of Health
[2]Ratnapura and Kalutara district hospitals incorporated in July 2013
[3]Kalutara district live birth and screened babies not included

Table 2: Implementation of national newborn screening for congenital hypothyroidism[1]

District	Program Entry[2]	Live births	Screened babies	True positives	Percentage coverage
Galle		18,905	18,152	12	96%
Matara		11,075	10,781	8	97%
Hambantota		10,732	10,066	6	94%
Moneragala		6,707	6,159	6	92%
Badulla	February	15,817	14,572	10	92%
Ratnapura		18,155	17,459	9	96%
Kegalle	April	9,403	6,592	8	70%
Kandy	July	26,587	13,520	12	51%
Matale	May	9,244	6,023	6	65%
Nuwaraeliya	July	9,799	2,873	5	29%
Trincomalee	March	7,829	5,376	8	69%
Batticaloa	March	9,167	7,278	6	79%
Ampara	May	13,538	7,490	5	55%
Total		166,958	126,341	101	76%

[1] live birth data reported in Annual Health Bulletin, Medical Statistics Unit, Ministry of Health -2016 provisional data
[2] During the year 2016

Table 3: Blood spot TSH level (mIU/L) distribution in 2016

		Samples collected on			
		<12hrs	Day 1	Day 2	≥ Day 3
Normal Infants (n=137,934)	n	7392	80178	25882	23901
	median	7.1	6.8	2.4	1.6
	range	2.0 – 18.5	1.0 – 18.5	1.0 – 18.2	1.0 – 17.5
False Positives (n=118)	n	27	72	6	13
	median	54.5	45.2	42.3	32.2
	range	34.5 – 101	35.0 – 64.2	34.0 – 54.0	25.0 – 38.6
True Positives (n=111)	n	2	66	14	28
	median	45.0	121	189	
	range	72.0 -101	24.0 – 84.0	35.0 – 202	22.0 - 280

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