Newborn Screening for Congenital Hypothyroidism in India – Is OVERDUE

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Abstract

Newborn screening is an essential preventative public health program, and is the standard practice of care worldwide. India is yet to start any publicly funded program despite this having been established in many countries for over 50 years. The purpose of newborn screening is to reduce morbidity and mortality in the newborn. Detection must have a clear benefit for the baby and be cost effective when compared to the associated with delayed treatment. These criteria are clearly satisfied for screening a baby at birth for congenital hypothyroidism (CHT). Though systematic newborn screening for congenital hypothyroidism was introduced in the early 1970 in many countries, in India an estimated 10,000 babies are born with congenital hypothyroidism every year, yet there is no screening program for this. We present the details of our study, which reveals that CHT in India has a high incidence and is an URGENT high priority for public screening.

Keywords: Congenital hypothyroidism; Thyroid stimulating hormone; Time resolved fluorensimmuno assay

Introduction

Congenital Hypothyroidism is the most common preventable cause of mental handicap in the world. Neonatal screening programme with TSH for the same has been in place for last 5 decades in many countries. India has no such screening program so far. We undertook this study to see if we need to relook at this scenario.

Materials and Methods

All babies born at Cloudnine Hospitals, Bangalore, India were screened for Congenital Hypothyroidism during the period from Jan 2007 to Oct 2013 – accounting for nearly 19,800 samples.

Blood was collected from these babies between 36 to 48 hours along with other investigations, which were part of the hospital protocol. All babies born at Cloudnine & Fernandez were checked for discharge bilirubin, blood group and other screening disorders along with CHT. Parents were counseled on the need and benefits of screening and verbal consent was obtained prior to sample collection. For those who declined the test, despite the explanation about the importance of the screening, written consent was obtained as NON-CONSENT. Quantitative determination of Thyroid Stimulating Hormone (TSH) was carried out on dried filter paper blood by DELFIA Neonatal hTSH Time Resolved Fluorensimmuno Assay (TRFIA) kit of Perkin Elmer. TSH values up to 12 uU/ml of whole blood was taken as normal (as per international recommendations) and anything above 12 was taken as abnormal and the treating Pediatrician was informed to follow up and repeat the test.

Results

The screening used more than 12 uU/ml of whole blood as abnormal as per the nomogram considering the normal values for a baby of 36 hours of age. 32 of the 19,800 samples for CHT screening were positive, of which 19 samples contained a blood spot TSH concentration >100 uU/ml of whole blood, eight a TSH concentration between 50 and 100 uU/ml of whole blood, and five a concentration between 12 and 50 uU/ml of whole blood.

Once a result was reported as abnormal, the parents were notified of the results immediately by telephone and a repeat TSH along with T4 and T3 were checked as per our protocol to confirm the result. If any baby had NORMAL TSH, T4 and T3 results, no subsequent tests were done. If their TSH was high, the baby was subjected to radionuclide scan for thyroid.

Refusal to be screened accounted for less than 0.01% and once consented, there were no failures to collect samples. Even early discharge parents came the following day for the test. Follow up of the babies were 100% and no one was lost for follow up screening identified 32 babies with initial elevated TSH (0.16%). Of these 32, 8 babies had normal TSH on repeat testing. All these 9 babies had results of TSH that were less than 40 uU/ml of whole blood which probably accounted for our false positives (0.04%). Repeat testing included checking serum TSH, T4 and T3 levels. The remaining 24 were confirmed to have elevated TSH –19 of these 24 babies had congenital hypothyroidism with TSH levels ranging anywhere between 100 to 350 uU/ml of whole blood and had Congenital absence of thyroid gland confirmed by nuclear medicine scanning by Tc99m; and the remaining 5 of the 19 babies had an ectopic thyroid gland but had dyshormonogenesis confirmed by H131 perchlorate discharge test – their levels ranging from 45 to 100 uU/ml of whole blood. A Pediatric Endocrinologist followed up all babies. All the babies have improved with thyroxine supplementation and are doing well on follow up.
Discussion

In our cohort we have screened 19,800 babies to date by whole blood-spot TSH from samples collected between 36-48 hours of age and have identified 19 babies with CHT confirmed by absence of thyroid gland by nuclear medicine scan giving an incidence of 1:1042. An additional 5 babies were identified as having a normal technetium uptake on nuclear medicine scan, but having defective uptake of thyroxine (T4). One of these infants had clinical hypothyroidism that has resolved on follow up by 2 years and the other 3 are currently under follow up by a Pediatric Endocrinologist. 1 baby had Down syndrome. These 5 would NOT classify as CHT in the strict sense, since they had NORMAL thyroid gland and would resolve by few years’ time. Since these 5 were picked up by newborn screening only and otherwise could have been missed, if you consider them also, our incidence would be 1:825 for CHT. For a treatable disorder this is far too high – and surely reflects the tip of the iceberg.

In our study, we performed CHT screening in babies at 36-48 hours of age, along with discharge bilirubin and blood group as a standard hospital policy. Bangalore being a cosmopolitan city-comprises of people from all over India. We had 40% of North Indians in our study and 60% South Indians in our study. (Any person from states of Karnataka, Andhra Pradesh, Kerala, Tamil Nadu were considered as South Indians and rest were considered as North Indians for study purpose). There was no significant difference in incidence among either north or south Indians.

The TSH was measured by TREFIA (DELFIA, Perkin Elmer) with a value greater than 12 mIU/L whole blood was reported as abnormal and requiring follow up. We had only 2 false positives, with an intermediate result in the range of 15 mIU/L whole blood. All confirmed CHT cases had TSH values greater than 80 mIU/L whole blood. These are acceptable performance metrics showing clear demarcation between false positive and positive result. In the 5 cases that had defective uptake, the TSH values were ranging from 45 to 80 mIU/L whole blood again indicating a clear demarcation.

Neonatal screening for CHT is an essential preventative public health program, which is the standard practice of care world-wide [1-4]. Newborn Screening for CHT is a well characterized disorder and systematic neonatal screening for congenital hypothyroidism was introduced in the early 1970 [5,6]. In India an estimated 10,000 babies are born with congenital hypothyroidism every year [7,8]. Recently, countries like Philippines and China too have commenced the screening because waiting for a symptomatic diagnosis of affected infants mean the baby will NEVER be normal [9-13].

Neonatal screening for CHT is performed by measuring Thyroid Stimulating Hormone (TSH) from a dried filter paper specimen (Guthrie Test). Some programs also include the measurement of thyroxine in order to increase the sensitivity of the screening test, but this comes at additional cost [11,12]. There are several methods used for the measurement of TSH from a 3mm whole blood filter paper that include Radio Immune Assay (RIA), Enzyme Immuno-Assay (ELISA), chemiluminiscence and Time Resolved Fluorenseimmuno Assay (TRFIA, DELFIA). The latter two methods have superior sensitivity and specificity, resulting in high accuracy and ease of interpretation of results. A clinician should be aware of the method used for the measurement of the hormone, as the reference range and the action limits for result interpretation critically depend on the method used and one method is NOT the same as the other.

The incidence of CHT has been reported to vary between 1:3000 to 1:5000 live births, in most parts of the world [8,10-12]. In India, the incidence of CHT is thought to be much higher although published reports have been limited and have been done prior to the availability of diagnostic methods such as nuclear scans for detection of thyroid gland which have increased the precision of the diagnosis [14-16]. Our present study clearly shows the incidence to be much higher – which may be due to multiple factors – with lots of hypothetical factors being considered like consanguinity being more common in India and also Iodine deficiency thought to be more common.

Pilot projects in India have been performed by the Indian Council of Medical Research (ICMR) and recommendations from the pilot projects are listed at http://www.icmrmetboninetindia.org for all health professionals to follow. Leaflets explaining CHT screening have been developed in many languages and are available to be downloaded for use.

Once a country decides to implement screening - then what & when to screen for? [17-19] Neonatal screening for CHT by measurement of TSH can be performed from either cord blood or whole blood collected onto filter paper at or near 48 hours of age. The use of cord blood limits the disorders that can be screened to CHT and G6PD whilst a sample collected at 48 hours enables the screening for a greater number of disorders including inborn errors of metabolism. In CHT the timing of sample collection for measuring TSH is critical since there is a surge of TSH soon after birth declining to near normal levels approaching 48 hours of age [4,11,12]. The reference range is significantly different depending on whether the TSH was measured on a sample taken from the umbilical cord, or soon after birth or at or 48 hours of age.

Dr Gurjit Kaur et al. from Chandigarh has screened newborns for 3 common disorders in India: congenital hypothyroidism, congenital adrenal hyperplasia and G6PD deficiency and reported it is worthwhile for these 3 disorders [14].

From our study, there is no doubt that CHT screening fits into the criteria of the diseases that need to be screened in India as the incidence in our study of nearly 1:1000 is far too high and should not be ignored [20]. Also with the globalization of the world with recent trends in immigration and emigration, it is not a problem for India alone as a baby born in India can land up in any part of the world and it could be a burden for that country too. Congenital Hypothyroidism is such an important Public Preventive Program of International significance and the whole world is looking at India as to why they are not screening still as a country?

The International Society of Newborn Screening (ISNS) with its abundant data should take initiatives to make CHT screening mandatory through the government of India and SAVE our children from needless mental retardation. We hope this study provides the impetus required.

References:

1. Kishore Kumar R, Nagar N (2007) Challenges in implementation of universal neonatal screening in India, NNF, Pune, India.

2. Verma IC, Bijarnia S (2002) The burden of genetic disorders in India and a framework for community control. Community Genet 5: 192-196.
3. Rama Devi AR, Naushad SM (2004) Newborn screening in India. Indian J Pediatr 71: 157-160.

4. Harris R, Sawaya GF, Moyer VA, Calonge N (2011) Reconsidering the criteria for evaluating proposed screening programs: reflections from 4 current and former members of the U.S. Preventive Services Task Force. Epidemiol Rev 33: 20-35.

5. Desai MP, Upadhye P, Colaco MP, Mehre M, Naik SP, et al. (1994) Neonatal screening for congenital hypothyroidism using the filter paper thyroxine technique. Indian J Med Res 100: 36-42.

6. Wilson JMG, Junger G (1968) Principles and practice of screening for disease. Geneva: World Health Organization 26-7

7. Desai MP, Colaco MP, Algaonkar AR, Mahadik CV, Vas FE, et al. (1987) Neonatal screening for congenital hypothyroidism in a developing country: problems and strategies. Indian J Pediatr 54: 571-581.

8. American Academy of Pediatrics (1992) Committee on Genetics: Issues in newborn screening. Pediatrics 89: 345-349.

9. Amar HSS (1997) Screening for congenital hypothyroidism in Southeast Asia. J Paediatr Obstet Gynaecol1:5-9

10. Low LC, Lin HJ, Cheung PT, Lee FT, Chu SY, et al. (1986) Screening for congenital hypothyroidism in Hong Kong. Aust Paediatr J 22: 53-56.

11. American Academy of Pediatrics AAP Section on Endocrinology and Committee on Genetics, and American Thyroid Association Committee on Public Health (1993) Newborn screening for congenital hypothyroidism: recommended guidelines. Pediatrics 91: 1203-1209.

12. Lafranchi S (2004) Hypothyroidism In: Nelson textbook of pediatrics, (17thedtn) Saunders, Philadelphia

13. Padilla CD, Therrell BL (2007) Newborn screening in the Asia Pacific region. J Inherit Metab Dis 30: 490-506.

14. Desai MP (1997) Disorders of thyroid gland in India. Indian J Pediatr 64: 11-20.

15. Kochupillai N (1992) Neonatal hypothyroidism in India. Mt Sinai J Med 59: 111-115.

16. American Academy of Pediatrics, Rose SR; Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS; Public Health Committee, Lawson Wilkins Pediatric Endocrine Society, et al. (2006) Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics 117: 2290-2303.

17. Kaur G, Srivastav J, Jain S, Chawla D, Chavan BS, et al. (2010) Preliminary report on neonatal screening for Congenital Hypothyroidism, Congenital Adrenal Hyperplasia and Glucose-6-Phosphate Dehydrogenase Deficiency: A Chandigarh Experience. Indian J Pediatr 77: 969 – 973.

18. Dutta R (2005) ICMR to conduct first nationwide newborn screening for genetic disorders. Express healthcare Management.

19. Kapoor S, Kabra M (2010) Newborn screening in India: current perspectives. Indian Pediatr 47: 219-224.

20. Toublanc JE (1999) Guidelines for neonatal screening programs for congenital hypothyroidism. Working Group for Neonatal Screening in Paediatric Endocrinology of the European Society for Paediatric Endocrinology. Acta Paediatr Suppl 88: 13-14.