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Neonatal screening for congenital hypothyroidism using cord blood thyroid stimulating hormone.

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Abstract

This study was done to find the effectiveness of cord blood thyroid stimulating hormone (TSH) as a screening tool for congenital hypothyroidism (CH) in a rural teaching hospital. A total of 785 healthy term neonates were screened at birth with cord blood TSH. Elevated TSH of > 20mIU/L was noted in 22 neonates (2.8%). Six of these 22 neonates recalled had elevated TSH and low fT4 on retesting. Follow up of these neonates revealed transient CH in 5 of them and permanent CH in one. The incidence of CH in our study was 1:785.

Keywords: Congenital hypothyroidism, cord blood thyroid stimulating hormone.

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Introduction

Newborn screening for congenital hypothyroidism (CH) is routinely done in developed countries, while in developing countries a routine screening program for CH is not yet universal. Children with CH are being missed at birth and are often diagnosed late in infancy and sometimes even later. Hence we undertook to study the usefulness of cord blood thyroid stimulating hormone (TSH) screening in our set up as heelprick filter paper assay on day four is difficult to implement due to logistic reasons (early discharge and poor follow up).

Material and Methods

All term deliveries by normal vaginal delivery or Caesarean delivery in our hospital from June 2010 to Nov 2012 (2 years 6 months) were taken for the study. Preterm neonates (less than 37 completed weeks), birth asphyxia or any illness requiring immediate NICU admission were excluded. Mixed cord blood was taken within 5 minutes of delivery and sent for TSH analysis. TSH analysis was done by Microplate Enzyme Immunoassay. A cut off value of 20mIU/L was taken for initial screening of congenital hypothyroidism. For those with elevated TSH values a repeat venous sample for fT4 and TSH was done after 72 hours of life.Patients discharged earlier were recalled by telephonic recall and mail.

Results

A total of 861 neonates were born over the period of 2 years and 6 months (Jun 2010 – Nov 2012).We excluded 76 neonates from the study because of prematurity and NICU admissions for respiratory distress and birth asphyxia. Of the 785 neonates included in the study 376 were males and 409 were females. Elevated cord blood TSH of more than 20mIU/L was noted in 22neonates (2.8%). TSH levels were within the borderline category (10 – 20mIU/L) in 107 neonates (13.6%). Cord blood TSH less than 10mIU/L was noted in 656 neonates (83.6%) [Fig: 1].

Eight of the 22 neonates with elevated cord blood TSH levels were resampled on day four during hospital stay. The remaining 15 neonates were recalled by telephone/mail and venous samples taken from day 7 to day 16 of life. The recall rate as a result of abnormal values was 2.8%.

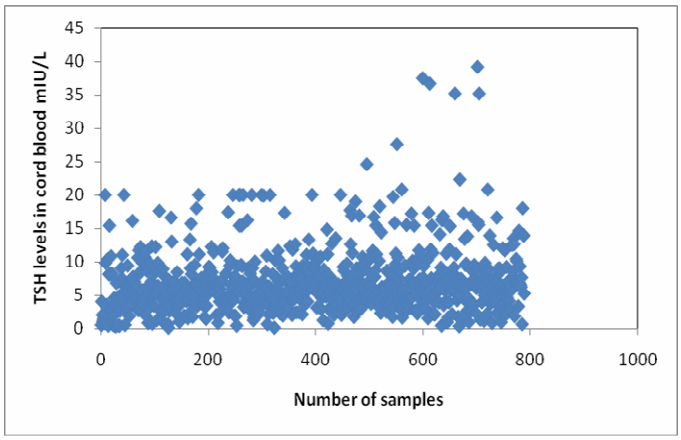

Figure 1. *Scatter plot of distribution of cord blood TSH levels*

The mean cord blood TSH level was 6.9±4.8mIU/L.There was no difference in the mean cord blood TSH level between males (7.0±4.9mIU/L) and females (6.8±4.7m IU/L). Six of the 22 recalled neonates had elevated TSH and low fT4 on retesting. Radioisotope thyroid scan and ultrasound of the thyroids could not be done in any of these neonates. All the 6 neonates were started on levothyroxine and were followed up. At two years only one child was found to have permanent CH with persistent elevation of TSH (44.2mIU/L) and low fT4 (0.8ng/dl). The rate of congenital hypothyroidism in our study was 1:785.

Discussion

Congenital hypothyroidism (CH) is one of the most common preventable causes of mental retardation. The worldwide incidence is 1:3000 live births [1] and the estimated incidence in India is 1:2500-2800 live births [2]. The incidence across Indian states varies with reports from North India (Chandigarh) 1:3400 [3], Southern India (Kochi) 1:500 [4], and Eastern part of the country 1:600 [5].As a national newborn screening program is still not being universally implemented, a treatable cause of mental retardation like CH is being missed and cases are being diagnosed quite late. In one study from New Delhi, nearly one third of children with hypothyroidism diagnosed after 5 years had CH, with a mean age of 86.6±35.3 mo. (range 60-216 mo.) at presentation [6].

Screening for CH can be done by estimation of TSH, T4 or both on heel prick filter paper card between 2 and 5 days of age.Many newborn screening programs in North America and Europe measure levels of T4, followed by measurement of TSH when T4 is low. Other neonatal screening programs in North America, Europe, Japan, Australia, and New Zealand are based on a primary measurement of TSH [1].The advantage of primary T4 over TSH screening is that hypothalamic or pituitary hypothyroidism, hypothyroxinemia and thyroid binding globulin deficiency will be missed by primary TSH method. When T4 is checked first milder /subclinical cases of CH will be missed as T4 is initially normal with elevated TSH due to the initial surge during labor. Concomitant measurement of T4 and TSH is the most sensitive approach but incurs a higher cost [7].

Alternately cord blood can be used for screening of CH in situations of early discharge before 3 days. The use of cord blood TSH for CH screening has been validated by numerous studies. Mixed cord blood samples for TSH values have compared well with heel prick filter paper samples taken in the first few days of life [8]. Cord blood TSH has been found to be more sensitive than cord blood T4 [9].

A cut off of TSH greater than 20mIU/L has been validated for suspecting CH [10]. When TSH is used as a primary screening tool values above 3% of the most elevated values are retested and rescreened with T4 to lower the rate of false positives (especially when TSH is collected early during the period of TSH surge). In this study the 95th percentile of cord blood TSH was 16.8mIU/L and the 97th percentile of cord blood TSH was 19.9mIU/L which is almost the same as the standard cut off value of 20mIU/L used for retesting. In a study from North America TSH level in cord blood samples was less than 20mIU/L in 85% and higher than 60 in 0.04% of the cases [11].

Our study found elevated TSH greater than 20mIU/L in 22 out of 785 cases. Thus there was a medical recall rate of 2.8%. Gupta et al reported an elevated cord blood TSH rate of 11.5% [12].

Even though we had 6 infants (out of 22 recalled) with persistently elevated TSH and low T4 on retesting only one child was found to have permanent hypothyroidism on follow up at 2 years. An apparent incidence of CH in 1 in 785 live born neonates is unusually high when compared to the available literature from India [3-5].

The higher recall rate could be explained by undetected iodine deficiency in the population and other causes of transient hypothyroidism like prenatal or postnatal iodine excess, maternal hyperthyroidism, antithyroid drugs in mother, use of dopamine and steroids, maternal thyroid stimulating antibody receptor antibodies, dual oxidase 2 (DUOX 2) mutations, isolated hyperthyrotropinemia and hypothyroxinemia of prematurity (low TSH) [13].

Conclusion

Cord blood TSH screening in our institute has been effective as a screening tool. Given the convenience of cord blood sampling and the logistics of early discharge, cord blood TSH screening program will be continued in our set up.

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