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Original Research Article

Cord blood spot thyroid stimulating hormone for screening of congenital hypothyroidism

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ABSTRACT

Background: Congenital hypothyroidism is one of the most common causes of mental retardation in pediatric age group. Screening for congenital hypothyroidism is one of most cost effective tools to prevent mental retardation among the general population. Umblical cord TSH estimation remains an easily available option for screening of congenital hypothyroidism. Aims and objectives was to estimate correlation between TSH obtained from cord blood TSH and heel prick TSH at 3rd day of life using blood spot. To estimate the predictability to rule out congenital hypothyroidism using cord blood spot TSH and to determine whether cord blood TSH can be advocated to screen congenital hypothyroidism.
Methods: Prospective study conducted in department of Neonatology, IOG, Egmore after obtaining consent from parents. The study was carried out in two phases. First phase, to establish correlation between cord blood spot TSH and heel prick TSH and to establish median cutoff point of TSH .Second phase, to establish cord blood spot TSH as screening method.
Results: The birth weights ranged between 2.5 to 4.3 kg. TSH values ranged from 2.0-33.3mlU/L. The mean value was 16.45mlU/L. A cutoff value of 20mlU/L was used for recall testing of complete thyroid profile (T3, T4 and TSH). Thirty six infants were recalled for repeating complete thyroid profile.
Conclusions: Congenital hypothyroidism (CH) is the one of the most common preventable causes of mental retardation which can be detected by measuring cord blood TSH .Cord blood TSH can be advocated in national public health program as a routine so that all babies can be tested before discharge thereby minimising interventions for the baby.

Keywords: Cord blood, Heel prick, Hypothyroidism, Thyroid stimulating hormone

INTRODUCTION

Congenital hypothyroidism is most common and effective preventable cause of mental retardation in infants, accounting for 90 % of hypothyroidism cases in infants. Screening for congenital hypothyroidism is widespread for the last two decades. Use of cord blood TSH as a screening tool has gained importance because of simplicity and accessibility. Walfish et al concluded that cord TSH had better specificity and sensitivity as compared to cord or filter paper T4 at 3-5 days of age.[1]

The present study was designed to estimate the level of TSH in cord blood as screening test of CH so that early intervention, follow up and counseling can be given.

METHODS

It is a Prospective cohort study conducted in Tertiary care hospital in Tamil Nadu - Institute of Obstetrics and Gynecology and Hospital for Women and Children, Madras Medical College, Chennai. Study period was from May 2017 to September 2017.

Inclusion criteria

All live newborns delivered during the study period.

Exclusion criteria

Newborns whose mother were on any thyroid medication, multiple order births, early preterm, newborns delivered outside the hospital

Prospective study conducted in department of neonatology, IOG, Egmore. All live newborns delivered during the study period were included in the study. The study was planned to be carried out in two phases.

In the first phase, the main purpose is to establish the correlation between cord blood spot TSH and heel prick TSH and to establish median cutoff point of TSH using cord blood to effectively screen congenital hypothyroidism in 100 neonates.

In the second phase, with power of 80% and alpha error of 0.5 with confidence interval of 95% an independent sample of 250 newborns were enrolled to estimate cord blood spot TSH to establish as a screening method to rule out congenital hypothyroidism.

Written consent for collection of blood was obtained from parents before study.

Anthropometric characteristics and blood samples were obtained at delivery room, immediately after delivery. Newborns will be distributed in the groups in study according the presence of SGA, AGA, or LGA.

Detailed information regarding mother's health was collected by direct medical history, physical examination and by reviewing their medical records.

2-3 ml of cord blood was collected in a sterile serum separating tubes immediately after birth of babies drawn from a 15 -20 cm length of umbilical cord while severing it at the time of birth of the baby. Blood was collected from heel prick by filter paper on day 3 of life.

SPSS (Version 21, IBM, USA) software was used for data analysis. The mean, median and standard deviation for TSH values of the cohort were calculated. Chi-square test was applied to see the significance of difference in mean TSH value of different groups.

RESULTS

Table 1 shows 20-25 years (68.5%) were the predominant age group, primi mothers were most common. Normal vaginal delivery was the common mode of delivery and literate mothers were more common. Table 2 shows birth weight 2.5 to 2.99 kg were more predominant in this study. Table 3 shows males were predominant in this study.

Table 1: Maternal demographic factors.

		Numbers	Percentage
Age	20-25 years	240	68.5%
	26-30 yrs	70	20%
	>30 yrs	40	11.5%
Residence	Urban	280	80%
	Rural	70	20%
Gravida	Primi	270	77.1%
	Multi	80	22.9%
Type of delivery	Labour natural	220	62.8%
	LSCS	130	37.2%
Education status	Literate	220	62.8%
	Illiterate	130	37.2%

Table 2: Birth weight distribution.

Weight	No. of samples	%
2.5 to 2.99 kg	145	41.5
3 to 3.49 kg	105	30
3.5 to 3.99 kg	65	18.5
4.0 kg and above	35	10

Table 3: Gender wise distribution.

Gender	Number	N (%)
Male	234	66.8%
Female	116	33.2%

In table 4 Term neonates predominate in our study. In table 5 ,100 neonates were included in phase I of 50 each in Cord blood TSH and Heel prick TSH and p value was 0.044 and was stastically significant .Median value in cord blood TSH was 16.2 mIU/ML and heel prick TSH was 16.7 mIU/ML in phase I of our study. Mean Value of 16.45 mIU /ml was arrived from cord blood and heel prick TSH and was used as cut off to rule out congenital hypothyroidism using cord blood TSH in phase II.

Table 4: Distribution according to gestational age.

	Number	N (%)
Term	242	69.1%
Late Preterm	108	30.9%

Table 5: TSH collected from cord blood and heel prick (phase I).

TSH(mIU/ml)	Cord blood TSH	Heel prick TSH
<4	6	21
4 to 7.99	10	6
8 to 11.99	6	9
12 to 15.99	5	3
16 to 19.99	7	3
20 to 24.99	7	1
25 to 27.99	2	2
28 to 31.99	3	2
32 to 35.99	4	3
Total	50	50

Table 6: Cord blood TSH collected at time of birth (phase II).

TSH values (mIU/ml)	Cord blood TSH (mIU/ml)
<4	115
4 to 7.99	43
8 to 11.99	30
12 to 15.99	24
16 to 19.99	19
20 to 24.99	6
25 to 27.99	5
28 to 31.99	7
32 to 35.99	2

Table 6 shows, 250 neonates were subjected to cord blood TSH. Mean cord blood TSH values collected at time of birth 3rd,25th,50th,75th,90th,95th centiles were 2.4,4.5,5.5,7.5,13.1 and 20.4 respectively . Median value was 16.5mIU/ml.

Table 7 shows sensitivity 50%, specificity 89.94%, positive predictive value 2.78% and negative predictive value 99.68% ,thus cord blood TSH was effective in ruling out congenital hypothyroidism .36 neonates were recalled for repeat thyroid profile. One baby was finally proved to be hypothyroid after repeat confirmation. The cord TSH value in that neonate was 26.3mlU/L.

Table 7: Sensitivity, specificity, positive predictive and negative predictive value of cord blood TSH.

	Value	95% CI
Sensitivity	50 %	1.26% to 98.74%
Specificity	89.94 %	86.29% to 92.89%
Positive predictive value	2.78 %	0.69% to 10.58%
Negative predictive value	99.68%	98.74% to 99.92%

DISCUSSION

This study is only one of a few that have compared the efficacy of cord blood and heel-prick TSH samples for detecting cases of Congenital Hypothyroidism (CH). In our study we have arrived median value using cord blood TSH and heel prick TSH and this value was used to screen congenital hypothyroidism using cord blood TSH.

Pilot screening programs for CH were developed in Quebec, Canada, and Pittsburgh, Pennsylvania 2, in 1974 and have now been established in Western countries. Certainly the main objective of screening is the eradication of mental retardation caused due to congenital hypothyroidism. In addition to the profound clinical benefit, it has been estimated that the cost of screening for CH using cord blood TSH is much lower than the cost of diagnosing CH at an older age. Many studies have been published comparing heel-stick TSH testing and T4, but relatively little research has been conducted of TSH testing on cord blood samples.[3-5]

Regional differences in CH incidence are suggesting to be more likely to be due to iodine deficiency than to ethnic affiliation. In fact, the CH incidence is lower in countries where the iodine supply is sufficient (e.g. USA 1:4000, Japan 1:5000, Taiwan 1:5700) than in those were iodine supply is deficient Italy, Turkey 1: 2400. Unfortunately, iodine deficiency is still prevalent in large part of the world; including our country which is characterized by a moderate-mild iodine deficiency.

Total 100 neonates were included in phase I of 50 each in Cord blood TSH and Heel prick TSH .Median value in cord blood TSH was 16.2mIU/ML and heel prick TSH was 16.7mIU/ML (p value 0.044 statstically significant). Value of 16.45Miu /ml was used as cut off to rule out congenital hypothyroidism using cord blood TSH. In our study mean TSH values ranged from 2-33.3mlU/L Mean cord blood TSH values collected at time of birth corresponding to 3rd,25th,50th,75th,90th,95th centiles were 2.4,4.5,5.5,7.5,13.1 and 20.4 respectively . Median value was 16.5mIU/ml.

Thirty six infants were recalled for repeat complete thyroid profile. One baby was finally proved to be hypothyroid after repeat confirmation. The cord TSH value in that infant was 26.3mlU/L and it proved significant.

Results show that 38.8% (52 cases) samples showed a cord blood TSH value of >10mlU/L. This is less to figures from a study in Ethiopia.[6] Our mean value was 16.2 mlU/L in cord blood TSH and heel prick TSH was 16.47 Miu/L, while Feleke et al observed value of 9.6mIU/L in 4206 newborns.[7] However, our TSH values were somewhat similar to that found by Khadilkar et al who, in a study of 203 neonates found a mean cord TSH of 12.3mlU/L.[8] Arunkumar et al who study in 1200 neonates found a mean TSH value 6.13mIU/L which is lower compared to this study.[9]

Using cord blood TSH as a tool for screening for CH disorders is still important, especially in developing countries like India where the current practice is to discharge the child as earliest as possible as it is difficult to get the newborn back to do the test in the hospital and to minimize the number of false positive samples and avoid unwanted parental anxiety as their baby needs retesting.[10] It avoids unnecessary pricking the newborn.

Both cord and heel-stick testing are highly sensitive; cord TSH was superior to capillary dried blood from heel stick in terms of a lower recall rate, which was clearly due to sampling at an early age. Cord blood TSH had specificity of 89.94%, negative predictive value 99.68% in our study thus establishing cord blood TSH can be used to screen congenital hypothyroidism effectively.

Cord blood TSH can be used as a screening modality to screen congenital hypothyroidism rather than heel prick TSH and it can be advocated as public health program particularly in our country so that unnecessary interventions can be avoided.

Few limitations of the study was that study did not take into account premature babies with delayed TSH surges; such cases can be easily missed by TSH screening

CONCLUSION

Congenital hypothyroidism (CH) is the one of the most common preventable causes of mental retardation which can be detected by measuring the level of cord blood TSH. It can be conclude that we may safely use the widely used cutoff cord blood TSH values of >20 mlU/ml for purposes of recall for retesting. Thus cord blood TSH can be advocated as routine in national public health program so that all babies can be tested before discharge thereby minimising interventions for the baby and missing cases of congenital hypothyroidism

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Ethical approval: The study was approved by the Institutional Ethics Committee

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