Comparison of Cord Blood Thyroid Stimulating Hormone with Thyroid Stimulating Hormone Levels from Venous Samples on 3rd Day of Life in Detecting Congenital Hypothyroidism in Newborn- A Retrospective Study

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ABSTRACT

BACKGROUND

Congenital Hypothyroidism (CH) is one of the most common disorders related to mental impairment and growth retardation in newborns. The main objective of screening is to detect and treat them early so as to prevent or minimize the neuropsychological damage which can be irreversible if the treatment is delayed beyond the first few weeks of life. In our institution, we do concomitant T4 and TSH after 48 hours of birth for screening. This study is aimed at assessing the usefulness of cord blood thyroid stimulating hormone (CBTSH) screening compared to TSH on 3rd postnatal day.

METHODS

A retrospective study was done in 272 term neonates at birth to analyse the cord blood TSH levels and TSH levels were tested for on 3rd postnatal day. The values were statistically analysed using Fisher's exact test.

RESULTS

272 babies were enrolled in the study. 17 (6.25%) babies had cord blood TSH above 20 mIU/ml and 11 (4.04%) babies had TSH values more than 10 mIU/ml in the 3rd day sample. The mean value of CBTSH was 9.68 microU/ml (SD +/-8.47) and that of 3rd day TSH was 3.76 microU/ml (SD +/- 3.17). 4 out of the 11 babies with elevated TSH levels on 3rd day was found to have congenital hypothyroidism on further follow up.

CONCLUSIONS

This study reveals a high proportion of congenital hypothyroidism when compared to national and international references, thus highlighting the need for universal screening. According to our study, cord blood TSH cannot substitute the 3rd day TSH for diagnosing congenital hypothyroidism.

KEY WORDS

Congenital Hypothyroidism, Cord Blood Thyroid Stimulating Hormone

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BACKGROUND

Congenital Hypothyroidism (CH) is one of the most common disorders related to mental impairment and growth retardation in newborns.^[1] Untreated CH has been shown to have a median IQ of approximately 80, with 40% below 70.^[2] The incidence of CH worldwide is 1:3000-4000 live births. In India, the incidence is 1:2500-2800 live births.^[3] Despite the significant role of thyroid hormones on multiple organ systems, especially the brain, most infants with CH appear normal at birth and show no signs, emphasizing the importance of screening programs in early detection of CH.^[4,5] The main objective of screening is to detect and treat them early so as to prevent or minimize the neuropsychological damage which can be irreversible if the treatment is delayed beyond the first few weeks of life.^[6] Various studies have been conducted to determine the effectiveness of cord blood TSH (CBTSH) in the detection of CH. The CBTSH estimation has the advantage of being easy to collect, non-invasive, and low rates of follow-up loss as the results would be available before the mother leaves the hospital. This enables repeat sampling if needed at the earliest, which is critical for early institution of treatment if necessary.^[7] But, the main drawback of cord blood TSH screening is that there is a TSH surge due to the stress of delivery at birth leading to false positive results. Therefore, most centres adopt concomitant TSH and T4 screening after 48 hours of birth. There are different strategies in NB screening for CH. Three approaches commonly used are

1. Primary Thyroid Stimulating Hormone (TSH), back up Tetraiodothyronine (T4).
2. Primary T4, back up TSH.
3. Concomitant T4 and TSH.^[8]

In our institution, we do concomitant T4 and TSH on 3rd day of life but some centres do a primary Cord Blood TSH screening and if abnormal confirm by a venous sampling after 48 hours of life before starting treatment. This study is aimed at the usefulness of cord blood thyroid stimulating hormone (TSH) screening compared to TSH after 48 hours as venous blood sampling is difficult to implement being an invasive procedure. We also wanted to find out the proportion of congenital hypothyroidism in normal term newborn babies in our hospital.

METHODS

This is a retrospective study done in the Department of Neonatology, Government Medical College, Ernakulam over a period of 3 months. Institutional Ethical Committee clearance was obtained prior to starting the study. The study included all term newborn babies with birth weight $\geq$ 1500 grams delivered in our hospital from February 1st 2016 to January 31st 2017 whose cord blood samples were done for TSH estimation as part of another study done in the department analysing "maternal risk factors and cord blood TSH levels". Term babies referred from other institutions, babies born to mothers with thyroid disease, babies with severe birth asphyxia, syndromic babies, babies with congenital malformations, those with antenatally detected CNS malformations, term babies with birth weight <1500 grams

and preterm babies were excluded from the study. The relevant data was collected from medical records department, GMC EKM using a pretested Performa.

Study Procedure

All babies were enrolled after obtaining informed parental consent in writing. Information was collected from the neonatal database recorded in Neonatal ICU. Data was entered into a proforma which included socio-demographic details of the mothers, details of antenatal period and delivery including date and time of birth, gestational age, birth weight, sex of the baby and type of delivery. Baby's weight was measured using digital weighing machine within 1st hour of birth. Apgar scoring was done at 1 and 5 minutes by skilled residents. In addition to taking cord blood required to do blood grouping which is routinely done at our institution, an extra 2 mL of blood was taken for TSH assay from the maternal end of umbilical cord immediately after clamping. The sample was transported to the laboratory within 1 hour in room temperature. Estimation of TSH was performed using immunoradiometric assay. The routine screening for congenital hypothyroidism was done for all babies on 3rd postnatal day with Total T4 and TSH values. CBTSH value >20 microU/ml and TSH >10 microU/ml on 3rd postnatal day was the cut-off taken for screening congenital hypothyroidism.^[9] All babies with 3rd day TSH >10 microU/ml were followed up and TSH was repeated after 2 weeks.

Definitions of Relevant Major Variables

1. Term – Gestational age more than 37 completed weeks.
2. AGA – Birth weight more than or equal to 2500 grams.
3. GDM – Gestational Diabetes Mellitus. Carbohydrate intolerance of variable severity first diagnosed during pregnancy.
4. Gestational hypertension - Those mothers who were diagnosed to have hypertension without proteinuria after 20 weeks of gestation.
5. CTG (Cardiotocography) - Measuring fetal heart rate and uterine contractions antepartum for monitoring fetal distress.

Statistical Analysis

The data was recorded in the proforma, numerically coded and entered in Microsoft Excel spread sheet. Difference between the cord blood TSH and 3rd day TSH was analysed categorically using Fisher's exact test.

RESULTS

Of the 272 babies included in the study, 148 (54.4%) were males and 124 (45.6%) were females (Fig.1). The mean birth weight of the study population was 2763.47 grams (SD +/- 531.30). 35.7% of babies had birth weight between 2500 to 3000 grams (Table 1). 10.3% of the mothers had gestational hypertension and 8.5% mothers had gestational diabetes mellitus. 111 babies were born by emergency LSCS and 93 babies were born by normal spontaneous vaginal delivery. 40 babies (14.7%) had fetal distress (Table 2). The mean TSH of cord blood sample was 9.68 microU/ml (SD +/- 8.47) and that

of the 3rd day sample was 3.76 microU/ml (SD +/- 3.17). The mean total T4 on 3rd postnatal day was 14.44 (SD +/- 8.27).

Cord blood TSH was found to be >20 microU/ml in 17 (6.25%) babies and 3rd day TSH was >10 microU/ml in 11 (4.04%) babies. Of the 17 babies with abnormal cord blood TSH, only 4 babies were detected to have abnormal TSH values on 3rd day (Table 3). Abnormal values on screening was found in 11 (4.05%) out of 272 babies in the study based on the 3rd day TSH and T4 values. Among those 11 babies, 7 babies had normal CBTSH. 11 babies with abnormal screening tests were recalled and tested after 2 weeks, where 4 babies (36.4%) had persistently elevated TSH and low TT4. On applying Fisher's exact test, a statistically significant difference (P value=0.003) was found between the values of cord blood and 3rd day blood TSH sample.

Birth Weight Range (in Grams)	Frequency	Percentage
1501-2000	25	9.2
2001-2500	59	21.7
2501-3000	97	35.7
3001-3500	73	26.8
3501-4000	14	5.1
4001-4500	4	1.5

Table 1. Birth Weight

Gestational Hypertension	Frequency	Percent
No	244	89.7
Yes	28	10.3
Total	272	98.9
Gestational diabetes	Frequency	Percent
No	249	91.5
Yes	23	8.5
Total	272	100
Type of Delivery	Frequency	Percent
Spontaneous Vaginal delivery	93	34.2
Induced Vaginal delivery	12	4.4
Instrumental vaginal delivery	2	0.7
Elective LSCS	54	19.9
Emergency LSCS	111	40.8
Total	272	100
Fetal Distress	Frequency	Percent
Yes	40	14.7
No	232	85.3
Total	272	100

Table 2. Antenatal and Perinatal Details

Blood Sample Type	Elevated TSH	Normal TSH	Total	p value
Cord Blood	17 (6.25%)	255 (93.75%)	272	0.003
3 rd Day sample	11 (4.05%)	261 (95.95%)	272	

Table 3. Comparison of Congenital Hypothyroidism Based on Cord Blood and 3rd Day TSH Values

DISCUSSION

Congenital Hypothyroidism (CH) is one of the most common disorders related to mental impairment and growth retardation in newborns.^[1] Untreated CH has been shown to have a median IQ of approximately 80, with 40% below 70.^[2] Our study was aimed at comparing cord blood TSH and 3rd day TSH and the efficacy of CBTSH as screening tool for detecting

congenital hypothyroidism. The CBTSH estimation has the advantages of being easy to collect, non-invasive, and low rates of follow-up loss as the results would be available before the mother leaves the hospital, enabling repeat sampling if needed at the earliest, which is critical for early institution of treatment if necessary.^[7] But, the main drawback of cord blood TSH screening is that there is a TSH surge due to the stress of delivery at birth leading to false positive results.

The mean TSH of cord blood sample was 9.68 microU/ml (SD +/- 8.47) and that of the 3rd day sample was 3.76 microU/ml (SD +/- 3.17). The mean total T4 on 3rd postnatal day was 14.44 (SD +/- 8.27). Our mean TSH values were similar to the findings of Rashmi et al in 2007.^[10] Cord blood TSH was found to be > 20 microU/ml in 17 (6.25%) babies in our study which is comparable to the study by Gupta A, Srivastava S & Bhatnagar A in 2014.^[11] In Indian setup, cord blood TSH value of >20 μ U/mL is seen as safe cut off for recall^[12]. The 3rd day TSH was >10 microU/ml in 11 (4.04%) babies. Of the 17 babies with abnormal cord blood TSH, only 4 babies were detected to have abnormal TSH values on 3rd day (Table 3).

Abnormal values on screening was found in 11 (4.05%) out of 272 babies in the study based on the 3rd day TSH and T4 values. Among those 11 babies, 7 babies had normal CBTSH who would have had a delayed diagnosis if CBTSH alone was used as the screening test. On statistical analysis, there was significant difference between the values of CBTSH and 3rd day TSH. All the babies with abnormal screening tests were recalled and tested after 1 week where 4 babies had persistently elevated TSH and later diagnosed as congenital hypothyroidism. The proportion of congenital hypothyroidism in present study is 4 in 272 which is remarkably elevated when compared to the national incidence of 1:2500-2800 live births.^[3] Similar result was seen in the study done by Sunil Raj et al in a rural tertiary care in South Kerala.^[13]

CONCLUSIONS

The incidence of congenital hypothyroidism was high compared to national and international references, thus highlighting the urgent need for universal screening. Our study showed a significant difference between CBTSH and 3rd day TSH. As per our study, cord blood TSH cannot substitute the 3rd day TSH values for diagnosing congenital hypothyroidism. A large study population and a multicentric study with uniform cut off values may be recommended for evaluating the efficacy of CBTSH as screening test for diagnosing congenital hypothyroidism.

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