

Cord Blood versus Peripheral Venous Blood Sample of Thyroid Stimulating Hormone for Neonatal Thyroid Screening

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Abstract :

Background : Congenital hypothyroidism remains one of the most common preventable causes of mental retardation among children. There is limited data available on cut off criteria for defining congenital hypothyroidism in India and efficacy of cord blood TSH level to detect congenital hypothyroidism, hence this study is planned.

Aim : To study efficacy of cord blood TSH as a screening tool to detect congenital hypothyroidism and to define cut off level for cord blood TSH and peripheral venous blood TSH on 4th post natal day for screening congenital hypothyroidism.

Methods : This was hospital based cross-sectional observational study, carried out from July 2020 and January 2021. After enrolling live newborns >34 weeks of gestation, TSH assay was performed on cord blood and peripherally obtained venous blood on 4th postnatal day of life, results of which were compared using chi square test. P value < 0.05 was considered to be statistically significant. All babies with VBTSH >10 microU/ml were followed up with repeat serum TSH value after 2 weeks.

Results :Total 122 babies were enrolled in the study out of whom, only 7.38% babies had elevated CBTSH and only 0.8% had elevated VBTSH. There was positive correlation between CBTSH and VBTSH. Parameters like maturity of baby and birth weight were found to be statistically non significant with CBTSH & VBTSH.

Conclusion :Venous blood TSH value of > 10 mIU/mL on fourth postnatal day signifies congenital hypothyroidism. Cord blood TSH value of >20 mIU/mL can be safely used as a cutoff for the purpose of screening for congenital hypothyroidism in countries like India.

Key words :CBTSH (Cord Blood TSH), VBTSH (Venous Blood TSH), TSH (Thyroid Stimulating Hormone), CH (Congenital Hypothyroidism)

Introduction:The most common preventable cause of mental retardation among children is congenital hypothyroidism. There are various suggested strategies for thyroid hormone estimation at birth using cord blood or later in the neonatal period using venous blood.^{1,2,3,4} CBTSH sample is easy to collect, requires non-invasive technique and rates of follow-up loss is low as the results would be available before the discharge of mother. This allows early repeat sampling if needed, which is critical for early institution of treatment if necessary.⁵ But, as there is a TSH surge due to the stress of delivery at birth, it may lead to false positive result, which is main drawback of cord blood TSH screening.⁶ Most infants with CH do not show any signs or symptoms at birth, emphasizing the importance of screening programs in early detection of CH.^{7,8}

If CH remains untreated it may lead to a median IQ of nearly 80, with 40% below 70.⁹ There is no national screening programme for congenital hypothyroidism in India.¹⁰ In India, the incidence is 1:2500-2800 live births.¹¹ There has been an increase in case detection rates in the last 3 decades with current incidence rates between 1:1,400 to 1:2,800 newborn screened.¹² Indian data about the incidence of CH is scarce. At Wadia Hospital for Children in Mumbai showed an incidence rate of 1 in 2640.¹³

Ideally, universal screening for detection of congenital hypothyroidism should be done at 3–4 days but since babies get discharged early and there is no supportive follow-up system makes CBTSH, an important screening marker for detection of congenital hypothyroidism.¹⁴ Very few studies are available on cord blood TSH values in the Indian literature.^{15,16} There is limited data available on cut off criteria for defining congenital hypothyroidism in India and efficacy of cord blood TSH level to detect congenital hypothyroidism, hence this study is planned.

Methodology:

This hospital based, cross-sectional observational study was performed between July 2020 and January 2021 in pediatric department at Shalinitai Meghe Hospital & Research centre, Wanadongri in collaboration with Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi Meghe, Wardha, Maharashtra. Ethical clearance was sought for from institutional ethical committee before start of the study. Live newborns >34 weeks of gestation at birth were enrolled after taking informed consent from parent. A total volume of 5 ml of cord

blood was drawn for TSH assay from the maternal end of umbilical cord immediately after clamping. Another blood sample was collected on 4th day-of-life from peripheral vein.

Estimation of TSH was performed using ELISA method. Difference between the results obtained by 2 strategies was compared using chi square test. CBTSH value >20 microU/ml and VBTSH >10 microU/ml on 3rd postnatal day was the cut-off taken for screening congenital hypothyroidism. All babies with 3rd day TSH >10 microU/ml were followed up and TSH was repeated after 2 weeks. Other parameters like gestational age of baby, birth weight and sex of baby were also recorded.

Results :

Total 122 babies were enrolled in the study after applying inclusion exclusion criteria, out of which 64 (52.4%) were males and 58 (47.6%) were females. 89 (73%) babies were delivered by cesarean section and 33 (27%) were delivered vaginally. All babies underwent cord blood thyroid screening and venous blood thyroid screening on 4th postnatal day. The mean gestational age of enrolled babies was 38.81 weeks (SD = 1.573) and the mean birth weight was 2630 grams (SD = 453.116).

Out of 122 babies, only 6 (7.38%) babies had elevated CBTSH and only 1 (0.8%) baby had elevated VBTSH. Mean CBTSH was 7.16 uIU/ml (SD = 5.048) and mean VBTSH was 3.17 uIU/ml (SD = 1.994).

Table 1 : Table showing association between cord blood TSH and venous blood TSH

TSH value	Mean (uIU/ml)	SD	r value
CTSH	7.16	5.0477	0.6394
VTSH	3.17	1.994	

The above table shows that there is positive correlation between cord blood TSH and venous blood TSH with r value of 0.6394.

Table2 :Table showing association between cord blood TSH and maturity of baby

CBTSH level (uIU/ml)	Full term baby	Preterm baby	Total	χ^2	P
Normal CBTSH	101	15	116	0.069	0.39
Elevated CBTSH	5	1	6		
Total	106	16	122		

The above table shows that out of total subjects (n= 122), only 6 babies had elevated cord blood TSH, out of which 5 babies were full term babies and only 1 baby was preterm baby. This was found to be statistically non significant by applying chi square test with P value of 0.39.

Table 3 :Table showing association between venous blood TSH and maturity of baby

VBTS (uIU/ml)	Full term baby	Preterm Baby	Total	χ^2	P
Normal VBTS	105	16	121	0.15	0.34
Elevated VBTS	1	0	1		
Total	106	16	122		

The above table shows that out of total subjects (n= 122), only 1 baby had elevated venous blood TSH, who was full term baby. This was found to be statistically non significant by applying chi square test with P value of 0.39.

Table 4 :Table showing association between birth weight and cord blood TSH

CBTS level (uIU/ml)	LBW (wt< 2.5 kg)	Normal weight	Total	χ^2	P
Normal CBTS	47	69	116	1.36	0.122
Elevated CBTS	1	5	6		
Total	48	74	122		

The above table shows that out of total subjects (n= 122), only 48 babies had low birth weight, out of which only 1 baby had elevated cord blood TSH. This was found to be statistically non significant by applying chi square test with P value of 0.122.

Table 5 : Table showing association between birth weight and venous blood TSH

VBTS level (uIU/ml)	LBW (wt< 2.5 kg)	Normal weight	Total	χ^2	P
Normal VBTS	47	74	121	1.55	0.10
Elevated VBTS	1	0	1		
Total	48	74	122		

The above table shows that out of total subjects, only 48 babies had low birth weight, out of which only 1 baby had elevated venous blood TSH. This was found to be statistically non significant by applying chi square test with P value of 0.55.

The observed positive correlation between cord blood TSH and venous blood TSH appears to be independent of perinatal factors such as birth weight of baby and maturity of baby which are known to interfere with the thyroid status in newborns

Discussion :

Cord blood remains a good sampling technique for screening of CH all over the world. As there are dramatic changes in TSH and thyroid hormone levels at birth and in the first month after birth, screening for CH gets complicated.¹⁷ The magnitude of these hormonal changes differ as per the maturity of baby, birth weight, which makes single measurements difficult to interpret without appropriate local cut offs.¹⁸

Rose Tresa George et al retrospectively compared CBTSH with VBTSH on 3rd day of life to detect CH in Newborn in 2020 at Government Medical College, Ernakulam, Kerala, India.¹⁹ They found that 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). In our study, mean Cord Blood TSH was 7.16 uIU/ml (SD +/- 5.0477) and mean venous blood TSH was 3.17 uIU/ml (SD +/- 1.994) whereas, Rashmi et al in 2007 studied the influence of perinatal factors on cord blood (CB) TSH levels on 1590 infants and found that the mean TSH level in the study group was 10.6 +/- 6.7 microU/ml.²⁰ Gupta et al. also studied the influence of perinatal factors on cord blood TSH levels. The median CBTSH was 8.75 microIU/mL (IQR = 6.475 -12.82).²¹

In our study, the mean gestational age was 38.81 weeks with SD of 1.57. There was no association between cord blood TSH and gestational age of baby. Rashmi, Seth A et al also found that there was positive correlation between TSH-heel prick and TSH-cord blood, which was independent of perinatal factors such as birth weight, gestational age and mode of delivery, which are known to alter the thyroid status in newborns.²⁰

The incidence of high cord blood TSH (CBTSH > 20 microU/ml) was 4.91 % in our study. In the study done by Rose Tresa George et al, the Cord blood TSH was found to be > 20 microU/ml in 6.25 % babies.¹⁹ Whereas the incidence of high cord blood TSH was 11.45% in the study done by Gupta A et al²¹. In the study done by V. Ilamaram, R. Rathisharmila et al, elevated TSH greater than 20 mIU/L was found in 2.8%.²² A study by Rose Tresa George et al showed a significant difference between CBTSH and 3rd day TSH. As per their study, cord blood TSH cannot substitute the 3rd day TSH values for diagnosing congenital hypothyroidism.¹⁹

The proportion of congenital hypothyroidism in the study done by Rose Tresa George et al was 4 in 272 which is remarkably elevated when compared to the national incidence of 1:2500-2800 live births.¹⁹ Similar result was seen in the study done by Sunil Raj et al in a rural tertiary care in South Kerala where the incidence was 3 in 430.²³ In our study, the incidence of congenital hypothyroidism was 1 in 122, which is very high comparatively, so screening for CH is the need of the hour.

Conclusions :

- Though CBTSH value can be falsely elevated due to the stress of delivery at birth, CBTSH > 20 uIU/ml can be safely used as a cutoff for the purpose of screening for

congenital hypothyroidism in countries like India where resource constraints is a major issue and the earliest possible discharge of newborn is the current practice.

- Venous blood TSH value of > 10 uIU/ml on fourth postnatal day signifies congenital hypothyroidism.

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