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Paediatrics Section

Cord Blood TSH Level Variations in Newborn – Experience from A Rural Centre in Southern India

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ABSTRACT

Background: Universal screening of all neonates has for long been recognized as the most effective method to detect congenital hypothyroidism. However, various maternal as well as perinatal factors can influence the cord blood TSH levels.

Objectives: To evaluate the effect of perinatal factors on cord blood TSH level variations in neonates born in a rural tertiary care institution in South India.

Methods: A cross-sectional study was done in 430 term neonates at birth to analyse the cord blood TSH levels and a repeat TSH estimation was done on 3rd postnatal day for those having abnormal values. The values were statistically analysed with respect to maternal, paternal and perinatal parameters.

Results: The mean value of CBTSH was 12.88 mIU/mL. One hundred twenty five of the 430 neonates (29.06%) were found to have elevated CBTSH levels. Two babies (0.46%) had CBTSH levels below 2.3 mIU/mL. Repeat TSH estimation done on third postnatal day in the 127 babies who had abnormal CBTSH levels revealed only 5 (3.94%) babies had abnormal levels. Serum T4 levels done on the same sample showed abnormal values in 3 (2.67%) babies. CBTSH levels showed no gender varations but increased significantly with the gestational age of the baby (p=0.001). CBTSH levels increased with increasing maternal age (p<0.001) and were significantly higher in babies of mothers with history of hypothyroidism.

Conclusion: The incidence of congenital hypothyroidism was 3 in 430 babies, which was high compared to national and international references, highlighting the urgent need of universal screening giving importance to maternal factors also.

Keywords: Congenital hypothyroidism, Newborn screening

INTRODUCTION

Congenital Hypothyroidism (CH) is inadequate thyroid hormone production in the newborn infants and is one of the most common preventable causes of mental retardation. The worldwide incidence is 1:3000-4000 live births and the estimated incidence in India is 1:2500-2800 live births [1,2]. More than 95% of newborn infants with congenital hypothyroidism have few, if any clinical manifestations. In view of paramount importance of early diagnosis and treatment various screening programs have been initiated [3,4].

Cord blood TSH (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. Changes in TSH levels in response to T3 and T4 levels forms the basis of screening using CBTSH. However, various factors such as maternal age, gestational age, maternal illnesses during pregnancy, gender of the baby, perinatal insults etc. can influence the CBTSH levels [5,6].

Though neonatal screening for CH is being conducted all over India, most of these are being done at large urban hospitals and very little data is available among the rural population.

This study aims to evaluate the effect of maternal and perinatal factors on CBTSH level variations in neonates born in a rural tertiary care institution in Southern India.

METHODS

This cross-sectional study was conducted in the neonatology unit of Dr. SMCSI Medical College, Karakonam, Trivandrum, a tertiary care hospital in rural South Kerala,India over a period of six months from January 1st 2010 to June 30th 2010. Four hundred and thirty consecutive term neonates who were born during the study period were included in the study, after obtaining an informed consent from either of the parents. Preterm babies and babies with major congenital anomalies were excluded. Cord blood samples of all the babies born were collected and sent for CBTSH estimation. Blood samples were collected in a sterile container drawn from the umbilical vein with the help of a 5cc syringe, from 15-20 cm length of the umbilical cord severed at the time of birth of the baby. The sample was analysed within four hours of collection, using ELISA method (Sandwich Enzyme Linked Immunoassay using Bio-rad® QuantaseTM kit). Normal value as per this kit was 2.3 to 13.2 mIU/L, which was considered as a reliable parameter for the diagnosis of congenital hypothyroidism. Values more than 13.2 mIU/L were considered as abnormal.

On the third postnatal day, the investigator conducted a short questionnaire and physical examination of the newborns. Questionnaire comprised of details of mother, father, environmental factors and baby details which included gestational age, birth weight, sex and relevant clinical features suggestive of congenital hypothyroidism. CBTSH results were collected and those newborns with clinical features and/or elevated CBTSH level suggestive of congenital hypothyroidism were further evaluated with T4 and TSH values from babies' venous sample between 3-5 days of life. If these values were also abnormal, X-Ray of both knees were taken to assess the bone age for the presence of lower femoral epiphyseal ossification centre. Absence of lower femoral ossification centre is taken as a positive feature for congenital hypothyroidism. Those babies with abnormal TFT were started on treatment per the standard protocol.

Data entry was done in an Excel sheet and analysis was done using SPSS for Windows version 16. Chi-square test was used to test the significance of the associations and Pearson's correlation test to assess the correlations. A p-value of <0.05 was defined as significant.

RESULTS

Total number of babies born at Dr. SMCSI Medical College and Hospital, Karakonam, India, Trivandrum during the study period was 456, of which 430 babies who satisfied the inclusion criteria were enrolled in the study. The profile of subjects included in the study is shown in [Table/Fig-1].

The mean value of TSH was 12.88 mIU/dL. Of the 430 neonates studied, there were more females than males. The male to female ratio was 1:1.07. Mean birth weight of the neonates was 2.77kg.

The cord TSH levels from 2.3 to 13.2 mIU/mL was taken as normal and the number of babies with values above and below these levels is shown in [Table/Fig-2].

Characteristic	Number (n)	Percentage (%)
Maternal Age (years)		
18-25	190	44.19
26-35	235	54.65
Above 35	5	1.16
Obstetric Score		
Primi	197	45.81
Multi	233	54.19
Antenatal complications		
No	400	93.02
Yes	30	6.98
Pregnancy Induced hypertension	21	79.07
Gestational Diabetis Mellitus	9	20.93
Maternal Hypothyroidism		
No	422	98.13
Yes	8	1.86
Maternal hypothyroidism on treatment		
No	6	75.0
Yes	2	25.0
Anti thyroid drug intake in mother		
No	430	100
Yes	0	00.00
History of maternal Goiter		
No	430	100.00
Yes	0	00.00
H/O paternal thyroid disease		
No	429	99.76
Yes	1	0.23
Environmental Factors		
Coastal	8	1.86
Rural	420	97.67
Urban	2	0.47
Gestational Age of Baby (in weeks)		
37+1 to 38 wks	184	42.79
38+1 to 39 wks	138	32.09
39+1 to 40 wks	106	24.65
Above 40 wks	2	0.47
Birth Weight of the baby (kg)		
Below 2.500	3	0.70
2.501-3.000	245	56.98
3.001-3.500	180	41.9
3.501-4.000	2	0.47
Gender of the baby		
Male	208	48.37%
Female	222	51.62%

[Table/Fig-1]: Profile of subjects included in the study

Repeat TSH and T4 estimation were done on peripheral blood sample taken on the third postnatal day in the 127 babies who had abnormal CBTSH levels and the results are shown in [Table/Fig-3].

Out of the 127 babies evaluated for suspected hypothyroidism, the male to female ratio was 1:1.35 (53:74), showing a female predominance. CBTSH levels were found to increase with increasing maternal age ($p<0.001$). There was no significant difference in the CBTSH levels between male and female babies ($p=0.814$). It was also found that the CBTSH levels increased significantly with the gestational age of the baby ($p=0.001$). The CBTSH levels were significantly higher in babies of mothers with hypothyroidism ($p=0.001$) [Table/Fig-4].

DISCUSSION

Congenital hypothyroidism is one of the major and most common preventable causes of mental retardation. Universal screening of all neonates has for long been recognized as the most effective method to prevent the severe developmental and physical morbidities associated with congenital hypothyroidism [7]. Different centres use different tools for screening such as cord blood TSH alone, serum T4 levels alone or both T4 and TSH levels.

CBTSH mIU/mL	n	Percentage
Below 2.3	2	0.46
2.3- 13.2 (Normal)	303	70.46
13.3-20.0	84	19.53
20.1-30.0	35	8.14
30.1-40.0	6	1.39
Total	430	100.00

[Table/Fig-2]: Cord blood TSH level

Rpt. TSH	n	Percentage
Normal	122	96.06
Abnormal	5	3.94
S.T4		
Normal	124	97.63
Abnormal	3	2.67

[Table/Fig-3]: Repeat TSH and T4 levels

Characteristic	CBTSH level						p-value
Baby Gender	<2.3	2.3 -13.2	13.3-20.0	20.1-30.0	30.1-40.0	Total	
Male	1	149	44	20	4	218	0.814
Female	1	154	40	15	2	212	
Total	2	303	84	35	6	430	
Maternal Age (yrs)							
18-25	0	133	40	15	2	190	0.001
25-35	1	169	43	18	4	235	
Above 35	1	1	1	2	0	5	
Total	2	303	84	35	6	430	
Gestational age of baby (wk)							
37 + 1 to 38	1	146	20	14	3	184	0.001
38+ 1 to 34	0	102	19	15	2	138	
39 +1 to 40	0	55	45	5	1	106	
> 40	1	0	0	1	0	3	
Total	2	303	84	35	6	430	
Environmental Factors							
Coastal	0	3	1	2	2	8	0.001
Rural	1	299	83	33	4	420	
Urban	1	1	0	0	0	2	
Total	2	303	84	35	6	430	

[Table/Fig-4]: Factors associated with cord blood TSH level variations

Various studies have used different cut-offs for CBTSH levels, ranging from 20-90 mIU/mL. We used the cut –off value for cord blood TSH as per the kit which is a lower cut-off value. Devi AR and Noushad et al., [8], has taken the following range for comparison - CBTSH value < 10μ/ml as normal,10-20 μU/ml as borderline and > 20 μU/ml as abnormal. Recently,another study from India by Gurjit Kaur et al., [9] from Chandigarh has taken 9μU/ml as the TSH cut-off value. Ruth V Mikelsaar et al., [10] from Estonia have taken the TSH cut –off value for neonatal screening as 12 μU/ml,which is a still lower cut-off value as compared to our study. The re-testing rate for our study i.e. 31.9% was very high as compared to other studies, which was only 7.5 % by Manglik et al., [7] from India and 8.8% by Mekennon Y et al., [11] from Ethiopia.

In our study, of the 127 babies re-evaluated, 5 babies had repeat TSH values abnormal. On further evaluation, three were confirmed as congenital hypothyroidism with serum T4 and TSH values along with radiograph (X-Ray both Knees), and were started on treatment as per treatment protocol. The incidence in present study was 3 in 430 which is very high compared to the estimated incidence in India of 1:2500-2800 live births. Other studies such as Manglik et al., :2 in 1200 [7], Rasul et al., [12]:1.5 in 1000 from Bangladesh, Urvi Sanghvi et al., [13] :1 in 1000 from India, Ordookhani A et al., [14] with 1 in 914 from Iran are the ones with incidence closest to the present study.

Various studies have shown correlation between CBTSH levels and factors such as baby gender, birth weight, mode of delivery, maternal age etc [6,15-17]. In our study, we found that there is a correlation between maternal age and CBTSH with babies of mothers of older age groups having higher CBTSH levels. There was no significant difference in CBTSH levels between male and female babies, similar to the observation of Amit Gupta et al., [18]. The CBTSH levels were also found to increase with increasing gestational age, unlike authors who found a negative correlation between gestational age and CBTSH levels [19].

LIMITATIONS

To have more conclusive evidence for our findings we need to evaluate more number of babies from the rural population as well as include other maternal and perinatal parameters in the analysis.

CONCLUSION

In this study, the incidence of congenital hypothyroidism was 3 in 430 babies, which was very high compared to national and international references, indicating an urgent need for adopting universal screening of all neonates for congenital hypothyroidism, especially in the rural setting. Maternal age, maternal hypothyroidism and gestational age of the babies were found to significantly influence the CBTSH levels. A knowledge of these factors is important for reliable interpretation of the measured values and any rise in TSH should be seen in the light of these.

RECOMMENDATIONS

This study, having been conducted in a rural population shows that the incidence of congenital hypothyroidism may be much higher in the rural setup as compared to the overall national prevelance. This indicates the need for urgent initiation of screening in rural areas and peripheral centres and more over a credible national universal screening program for the whole country.

As several factors can influence the CBTSH levels, knowledge of these factors is important for reliable interpretation of the measured values and any rise in TSH should be seen in the light of these. This will help to avoid unnecessary repeat evaluations, thereby saving on cost as well as the need to subject the newborn to invasive tests.

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