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ORIGINAL ARTICLE

CORD BLOOD THYROID STIMULATING HORMONE LEVEL - AND THE INFLUENCE OF PERINATAL AND OTHER FACTORS ON IT

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ABSTRACT

Background: Thyroid hormone is essential for growth and development especially the brain. Deficiency of thyroid hormone i.e. congenital hypothyroidism (CH) is the commonest cause of preventable mental retardation. As it is difficult to diagnose CH with clinical symptoms at birth, most patients with CH are diagnosed by laboratory results. Early detection is important, either by Thyroid Stimulating Hormone (TSH) or T4 estimation or both by newborn screening. Cord blood TSH (CB-TSH) estimation has high sensitivity, but various maternal and perinatal factors affect the CB-TSH levels, which may interfere with the interpretation.

Aim: This study was done to find out the various maternal and perinatal factors affecting CB-TSH level.

Materials and Methods: A hospital-based cross-sectional study was conducted in the Department of Paediatrics, Obstetrics and Biochemistry of Medical College, Pune over a period of one and half year. Cord blood TSH level was estimated and the results were statistically analysed with respect to various maternal and perinatal factors. A TSH cut-off of >20 µIU/mL was considered as high.

Result: A total number of 726 newborns were enrolled in the study. The mean CB-TSH was 8.9 µIU/mL with 54 (7.5%) newborns having values more than 20 µIU/mL. CB-TSH was significantly raised in male babies, in first order neonates delivered by vaginal delivery. Neonates who had fetal distress or non-progress of labour had significantly higher CB-TSH than those who were delivered by elective caesarean section. Gestational age and birth weight of newborns did not have influence on CB-TSH.

Conclusion: About 7.5% newborns had elevated CB-TSH levels. Gender of the baby, perinatal stress factors and mode of delivery have significant relationship with the CB-TSH level. Hence, due consideration should be given to these factors while interpreting CB-TSH levels.

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KEYWORDS

TSH, Cord blood, congenital hypothyroidism.

Introduction

Early infancy is a critical period in which adequate levels of thyroid hormone are required for normal brain development. Deficiency of thyroid hormone during this period can cause neurological problems.[1] Clinical symptoms of congenital hypothyroidism (CH) are non-specific, hence it is difficult to diagnose during neonatal period, and most patients with CH can be diagnosed by laboratory results of TSH, T4, and T3 estimation. There are two main screening ways for CH: primary T4 testing (with backup TSH) or primary thyroid stimulating hormone (TSH) testing. In some states of USA, T4 estimation is done for screening while some US states screen T4 and TSH simultaneously[2], which may not be cost effective for developing countries like India. Primary TSH screen is more sensitive and specific for the diagnosis of primary CH compared to T4 screen[3]. Cord blood (CB) remains a very practical alternative for screening purpose as it is very difficult to call back babies once discharged. It is painless, usually not affected by neonatal surge. As most of the mothers are discharged early; Cord blood TSH (CB-TSH) to screen for CH is an effective strategy. However, it is not practical in all settings as round the clock trained personnel are needed and results may be affected by perinatal factors[4]. Moreover the cord sample cannot be used to screen for other metabolic disorders, as for their manifestation some feeding is required. Various maternal and perinatal factors are known to affect the CBTSH levels[5,6,7,8,9]. The aim of the present study was

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to determine the effect of various perinatal factors on cord TSH level.

Methods & Materials

This prospective study was carried out in maternal and neonatal care unit of Bhausaheb Sardesai Talegaon Rural Hospital (BSTRH), Pune from November 2016 to April 2018. The study was approved by the hospital ethics committee. An informed consent was obtained from either of the parents. Antenatal and intra-partum information was noted from mother's medical record. The live newborns delivered in BSTRH in whom parents gave consent during study period were included in the study. Newborns whose mother were on any thyroid medication and newborns delivered with congenital anomalies were excluded from the study. Two-three ml of cord blood was collected in a sterile serum separating tubes immediately after birth of the baby from the incised umbilical cord while severing it at the time of birth. The sample collected was sent to laboratory for testing for TSH. At birth baby was examined. Weight and sex of the baby was noted. Babies were considered to have low birth weight (LBW) if birth weight was <2.5 kg and normal birth weight if weight was >2.5kg. Gestational age was determined by maternal menstrual history. According to gestation by dates, all newborns were classified as preterm if gestational age was <37 weeks and term babies if gestational age was >37 weeks. Fetal distress was detected by non-assuring foetal heart tracing on intra-partum monitoring, thick meconium stained amniotic fluid and/or very low APGAR score at birth requiring resuscitative measures. TSH was measured by Chemiluminescence Immunoassay (CLIA) method. A TSH cut-off of >20 µIU/mL was considered as high.[10] High CB-TSH levels could not be confirmed with dried blood spot test after 72 hours of birth due to the cost constraints.

Statistical Analysis: The data were entered in Excel sheet and percentages of various outcome measures were calculated using SPSS for Windows version 12. Z-test was applied to see the significance of difference in mean CB-TSH value of different groups and a p value of <0.05 was defined as significant.

Table 1. Demographic data of newborns with high and normal TSH.

Variables	Newborns with Normal TSH (%)	Newborns with TSH > 20 µIU/mL (%)
Gender		
Male	384 (57.1%)	17 (31.5%)
Female	288 (42.9%)	37 (68.5%)
Gestational Age		
Preterms	127 (18.9%)	16 (29.6%)
Full terms	545 (81.1%)	38 (70.4%)
Birth Weight		
Low Birth Weight	155 (23.1 %)	14 (25.9%)
Normal Birth Weight	517 (76.9 %)	40 (74.1%)
Birth order		
1st baby	243 (36.2 %)	32 (59.3%)
2nd or later baby	429 (63.8 %)	22 (40.7%)
Mode of Delivery		
Normal Vaginal Delivery	349 (51.9 %)	30 (55.6%)
Assisted Vaginal Delivery	16 (2.5 %)	02 (3.6%)
Elective Caesarean Section	44 (6.5 %)	03 (5.6%)
Emergency Caesarean Section	263 (39.1 %)	19 (35.2%)
Dysphagia	-	1 (1.5%)
Fetal distress	63 (9.4 %)	22 (40.7%)

Results

A total number of 726 newborns were enrolled in the study. Mean CB-TSH was 8.9 µIU/mL and the CB-TSH values ranged between 0.06 - 55.57 µIU/mL. Fifty-four

Table 2. Comparison of CB-TSH levels according to various demographic parameters.

Parameters	Mean ± SD	p value
Gender		
Males	9.9 ± 8.3	0.0001
Females	7.6 ± 5.6	
Gestational Age		
Preterm	9.5 ± 8.7	0.317
Term	8.7 ± 6.9	
Birth Weight		
Low Birth Weight	9.4 ± 8.6	0.36
Normal Birth Weight	8.7 ± 6.9	
Birth order		
1st baby	9.4 ± 8.2	0.132
2nd or later baby	8.5 ± 6.7	
Foetal Distress -		
Yes	13.3 ± 11.7	0.0001
No	8.3 ± 6.7	
Mode of Delivery		
Vaginal Delivery Normal / Assisted	9.3 ± 7.6	0.84
Elective/ Emergency LSCS	8.5 ± 6.8	
Elective LSCS	6.6 ± 4.5	0.00024
Vaginal Deliveries & Emergency LSCS	9.1 ± 7.5	
Elective LSCS	6.6 ± 4.5	0.00427
Emergency LSCS	8.7 ± 7.2	
Normal Vaginal Delivery in Primi-para mother	10.4 ± 8.3	0.0003
Normal Vaginal Delivery in Multipara mother	8.7 ± 7.6	

(7.5%) neonates had CB-TSH values >20 μIU/mL of which 5 (0.7%) had values >40μIU/mL. Demographic data of all newborns with normal TSH and TSH >20 μIU/mL is depicted in table 1. CB-TSH levels as per various demographic data are depicted in table 2. Total 143 (19.7%) newborns were preterm and 583 (80.3%) were term newborns and 169 (23.28%) newborns were LBW and 557 (76.72%) had normal birth weight. The mean birth weight was 2.8 ± 0.43 kg. Fetal distress was present in 85 (11.7%) newborns. Mode of delivery was vaginal in 397 (54.68%) babies and 329 (45.32%) were delivered by lower segment caesarean section (LSCS).

Discussion

Congenital Hypothyroidism (CH) being preventable cause of mental retardation, it has been accepted now that the screening for CH will decrease the burden of mentally retarded children in society. Many Western countries and some of the Asian countries have established screening programmes.[2,11] In India an attempt has been made to screen neonates at various centres in 2007 by ICMR[12], but national programme does not exist at present. The method of screening is also not uniform. Various cut-offs have been used in different studies[13,14,15], but it has been accepted to take cut-off of >20 μIU/mL for recall.

Studies have been conducted using cord blood TSH and the influence of perinatal and other factors on CB-TSH with paradoxical and different results. In our study conducted under setting of hospital attached to Medical College in rural area, we found that 7.44% of all samples had values more than 20 μIU/mL. A comparable result has been reported.[16] Mean cord blood TSH in our study was 8.88 μIU/mL and standard deviation was 7.3. TSH ranging from 6.13 to 10 μIU/mL have been reported.[17,18] The mean CB-TSH was higher than 10 μIU/mL in some studies.[19,20] In our study male: female ratio was 1.23:1. We found male newborns had significantly higher levels than female. Similar observation has been reported.[9,21] However, some studies did not find any significant differences in mean TSH level according to sex.[7,8,22,23,24,25] It has been observed that mean CB-TSH was higher in preterm babies, low birth weight newborns and babies born of 1st order but the difference was not significant. Many previous studies have reported that TSH levels increase with increasing gestational age[6,24,25]; however, higher TSH levels in preterm than in term babies has been reported[7] and several other studies have reported no difference in TSH levels according to gestational age.[8,23] Although some studies have reported that low birth weight is related to high TSH levels[7,24], we did not find any association between birth weight and TSH level, in line with two previous reports.[21,23] Therefore, the relationship between TSH level and gestational age or birth weight seems to be different according to the study population and the mechanisms for the same are poorly understood.

Infants with foetal distress or prolonged second stage of labour had significantly higher Cord Blood TSH levels. Similar observation has been reported.[6,7] As far as mode of deliveries was concerned the newborns delivered by elective Caesarean Section had significantly lower mean levels of CB-TSH as compared to in those delivered by vaginal delivery or emergency LSCS. This difference can be explained on the basis a surge in catecholamine secretion during the process of parturition and this can be more in asphyxiated newborns and in vaginally delivered newborns compared to those born by elective caesarean section.[26,27] In contrast, two studies have shown no difference in neonatal TSH level according to mode of delivery.[7,28] Observed higher value of CB-TSH in primiparous mother delivered vaginally may be due to relatively more difficult labor associated with a first delivery compared to subsequent deliveries could increase TSH levels. It is in line with the previous reports.[7,9,21,22] Thus there were varying results in different studies as far as the influence of perinatal and other factors on CB-TSH levels. The newborns with elevated CB-TSH could not be investigated further due to the high cost of free T4 estimation and the patients were lost to follow up.

Conclusion

Congenital hypothyroidism (CH) is a major preventable cause of mental retardation. In India, there is no screening programme for CH. An elevated cord blood TSH value has been found in substantial numbers of babies. Male sex, mode of delivery and perinatal stress factors has a significant impact on CB-TSH levels. As various other factors can influence CB-TSH, its value should be interpreted with caution.

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.

Compliance with Ethical Standards

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Conflict of Interest: None

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