

Original Article

Profile of umbilical cord blood TSH, T₄ and influence of perinatal factors on thyroid functions in Newborns

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Abstract

Background: Congenital Hypothyroidism, if not treated well in time, may be disastrous for growth and development of child, therefore early detection of congenital hypothyroidism is important, either by TSH or T₄, or both by newborn screening. Influence of several perinatal factors have to be considered while interpreting values of thyroid functions in newborns. The present study is to determine Umbilical cord blood TSH and T₄ profile in Newborns and to study influence of Perinatal factors on Umbilical cord blood TSH and T₄. **Methods:** Umbilical cord blood samples were collected for assessment of TSH and T₄ in 830 newborns. The influence of Perinatal factors such as gestational age, weight, sex, mode of delivery, Eclampsia, Ante partum haemorrhage, Birth Asphyxia, Premature rupture of membranes and maternal HIV status on the newborns TSH, T₄ were analyzed. **Results:** Mean TSH and T₄ levels between Pre term and Term and between Term and Post term was statistically significant. Whereas, only T₄ level between Preterm and Post term, was statistically significant. Mean TSH levels, when compared in babies with & without severe birth asphyxia was also statistically significant. Other perinatal factors did not affect cord TSH and T₄ levels, as it was not statistically significant. **Conclusion:** Perinatal factors have influence over values of Cord blood TSH and T₄ levels and a caution in their interpretation should be considered.

Key words: TSH (Thyroid stimulating hormone), CH (Congenital Hypothyroidism), APH (Ante Partum Hemorrhage).

Introduction

Congenital hypothyroidism is the commonest preventable cause of mental retardation and also thyroid disorders are most common among pediatric endocrinal problem². In regions where iodine deficiency is severe, Most babies with congenital hypothyroidism appear normal at birth and show minimal evidence of thyroid deficiency. Clinical diagnosis is made in only 10% children in the 1st month of life and 30% in the 1st three months, hence there is a high risk of delayed diagnosis based on clinical examination alone. Early diagnosis and therapy improves the intellectual outcome and growth of the baby. Therefore screening of newborns is justified to prevent complication like Congenital Hypothyroidism. Many countries of western world have their own screening programmes, where filter spot test for TSH and T₄ are performed in newborns at 4-5 days after birth. In our country no such programme exists at national level. It is very difficult to call back newborns for follow up once they are discharged and probably high turn over of delivery rates in tertiary hospitals, thus Cord blood sample is preferred for its ease, more practical for

short hospital stay following delivery and thus is a practice in some Asian countries^{3,4}. Fuse, et al⁵ had shown that mixed cord blood is a good sampling technique for screening for CH. Indian academy of pediatrics recommended the use of cord blood for screening of Congenital Hypothyroidism^{6,7}. However, using TSH alone for screening, though sensitivity is high but it has chances of high false positivity rates⁸. In addition Various perinatal factors such as gestational age, weight, sex, mode of delivery, Eclampsia, APH, Birth Asphyxia, PROM, HIV status, maternal age, etc. may influence cord blood TSH and T₄ levels^{7,9,10,11,12}. This study was performed to observe the influence of these perinatal factors and to decrease false positivity, both TSH and T₄ were included in our study and to compare the mean values of cord blood TSH & T₄ in relation to Gestational age and weight and to study the influence of perinatal factors on umbilical cord blood TSH & T₄.

Material and Methods

A prospective observational study,

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conducted in the Deptt. of pediatrics, Surat municipal institute of medical education and research (SMIMER), Surat for a period of one year. Study was approved by Institutional ethical committee. Consent for blood samples were obtained from parents of Newborns. It was based on the cord blood sample obtained during this period. Those newborns whose mothers were on antithyroid drugs or newborns with congenital anomalies, syndromic features or malformations, those delivered outside the institute were excluded from the study. Ten ml of mixed umbilical cord arterial and venous mixed blood in sterile plain vacuttes on the maternal side of cord, after ligation was carefully collected by attending resident doctor and was sent to the laboratory immediately. Serum was separated after centrifuging cord blood. Newborns were examined in detail after birth. Socio-demographic and other Data of both mothers and newborns were recorded and entered in pre-designed Performa. Factors included for comparison were, weight, gestational age, sex, Oxytocin, APH, Pre Eclampsia, HIV status of mother, Premature rupture of membranes and severe birth asphyxia. All newborns whose TSH report was found to be >20 MU/L and or T₄ <6.5 µg/dl were recalled after seven days for repeat TSH & T₄ estimation for confirmation of Congenital Hypothyroidism. These cut offs were also used by other studies^{2, 3, 7, 13, 14, 15, 16} and as per AIIMS protocol¹⁷ for diagnosing Congenital hypothyroidism. TSH and T₄ assay was performed by chemiluminometric technology by ADVITA Centaur CP TSH assay Kit manufactured by Siemens Health care diagnostics Inc. Assay range for TSH was 0.010 – 150 MU/L, whereas, it was 0.3 – 30 µg/dl for T₄ assay.

Results

A total of 830 newborns were enrolled in the study out of which 290 (34.9%) were pre terms, 380 were terms (45.78) and 160 (19.22) were post terms. In the preterm 207 were AGA and 83 were SGA. In term 268 (70.52) were AGA and 112 were SGA (29.47). In post term neonates 100 were AGA and 60 were SGA. Observed Range of TSH was 1.04-150 Mu/L in preterm, 1.09 – 162 Mu/L in Term and 1.04 – 20.98 Mu/L in Post Term respectively. Observed Range of T₄ was 4-28 µg/dl, 2-25 µg/dl and 9-28 µg/dl in pre term, term and post term respectively. Percentile Umbilical cord blood TSH (mu/l) and T₄(µg/dl) values according to Gestational Ages is mentioned in Table-1.

On comparing, Mean TSH and T₄ levels among Pre-term, Term and Post term newborns it was found that mean TSH levels between Pre term and Term newborns was statistically highly significant ($p < 0.001$) whereas, T₄ levels were also statistically significant ($p < 0.05$). Table-2

Mean TSH levels between Term and Post term newborns was found statistically significant ($p < 0.05$) whereas, T₄ levels were statistically highly significant ($p < 0.001$). However, mean TSH levels between Pre-term and Post term newborns was not significant, ($p > 0.05$) whereas, T₄ levels were statistically significant ($p < 0.05$). Mean TSH and T₄ levels when compared among intra preterm groups (28.30 wks, 31-33 wks, 34-36 wks), Preterm AGA and Preterm SGA, Term AGA and Term SGA, Post term AGA and Post term SGA, between different birth weight groups (1 kg, 1-2 kg, 2-3 kg, >3 kg), vaginal and LSCS mode of delivery, male and female, with or without Oxytocin, presence or absence of Pre Eclampsia, APH and without APH, with and without PROM, HIV status of mother, Maternal age was not significant ($p > 0.05$). However Mean TSH levels, when compared between babies with severe birth asphyxia (both preterm and term) to babies without birth asphyxia (both preterm and term) was statistically significant ($p < 0.05$) Table-3, mean T₄ levels were not affected in the Birth Asphyxia group. However, when T₄ levels were compared in Post terms with and without severe birth asphyxia it was statistically significant ($p < 0.05$), though mean TSH levels remained unaffected in Post terms. Two newborns continued to have high level of TSH (>150) and low level of T₄ <6.5 µg/dl at one week during this study with pre stated cut off levels of TSH and T₄. The characteristics of these newborns were recorded Table -4.

Gestational Age	TSH 3 rd	TSH 97 th	TSH 99 th	T ₄ 3 rd	T ₄ 97 th	T ₄ 99 th
Preterm	2.68	18.48	24.74	6.83	21	25
Term	3.21	22.64	29.59	4	20	22
Post term	2.05	17.54	18.96	7	23	24

Table-1: Percentile Umbilical cord blood TSH (mu/l) and T₄(µg/dl) values according to Gestational Age

Discussion

Although several Studies with Thyroid functions in newborns have been conducted, the exact incidence of congenital hypothyroidism in India is not known². Data from various studies conducted show different incidences of congenital hypothyroidism varying from 1:248 to 1:2800 (including north east India).^{3, 13, 14, 18}. Studies have been conducted with and its influence of perinatal factors on Cord blood TSH with paradoxical and different results in different studies. In our study term newborns had increased levels of cord blood TSH as compared to

Comparison of Mean TSH & T ₄ Levels between Preterm and Term Newborns			
Maturity	Preterm n= 290	Term n=380	p value
Mean TSH (Mu/L)	7.51±4.54	9.15±5.41	0.001
Mean T ₄ (µg/dl)	10.90±4.26	11.81±4.00	0.035
Comparison of Mean TSH & T ₄ Levels between Term and Post term Newborns			
Maturity	Term n= 380	Post term n=160	p value
Mean TSH (Mu/L)	9.15±5.41	7.02±4.57	0.026
Mean T ₄ (µg/dl)	11.81±4.00	13.56± 3.93	0.0002
Comparison of Mean TSH & T ₄ Levels between Preterm and Post term Newborns			
Maturity	Preterm n= 290	Post term n=160	p value
Mean TSH (Mu/L)	7.51±4.54	7.02±4.57	0.985
Mean T ₄ (µg/dl)	10.90±4.26	13.56± 3.93	0.011

Table - 2: Comparison of Mean TSH & T₄ Levels among Pre-term, Term and Post term.

Gestational Age	Severe Birth Asphyxia	No Birth Asphyxia	p value
Pre term	n=9	n=100	
Mean TSH (Mu/L)	7.51±4.54	5.47± 2.12	0.023
Mean T ₄ (µg/dl)	13.22 ± 6.41	11.81± 4.00	0.323
Term	n=13	n=150	
Mean TSH (Mu/L)	18.57± 10.48	9.22±5.51	0.037
Mean T ₄ (µg/dl)	11.30±3.98	10.90±4.26	0.729
Post term	n=12	n=100	
Mean TSH (Mu/L)	7.57±4.37	7.52±4.57	0.973
Mean T ₄ (µg/dl)	11.41± 2.02	13.56±4.93	0.014

Table -3: Effect of Severe Birth Asphyxia on of Mean TSH and T₄ Cord blood levels in Preterm, Term and Post term newborns.

preterms, whereas, Desai et al¹⁸ had increased levels of TSH in preterm rather than in term newborns whereas, Gupta⁷, Kim⁹ and Armanian¹² did not find any influence of gestational age on it. In our study and in Gupta⁷, Kim⁹, Armanian¹², Feleke¹⁹ Cord blood TSH was not influenced by birth weight but in Desai et al¹⁸ cord TSH levels fell with increase in weight of newborns. Mode of delivery did not influence Cord blood TSH and T₄ levels in our as well as in Fuse et al⁵, Seth¹⁰, studies, while in Herbtzman²⁰ cesarean section had lower TSH values than vaginal mode of delivery, Tehrani²¹ had higher values of TSH in cesarean group, whereas in Gupta et al⁷, Kim⁹, Armanian¹² and Mehmat et al²² vaginal mode had higher Cord TSH than cesarean section mode of delivery.

Features and Investigations	Case1	Case2
Maturity	Preterm	Preterm
Perinatal Factors	APH	Pre-Eclampsia
Sex	F	F
Birth weight	1410 gm	2250 gm
Prolonged Jaundice	Yes	No
Constipation	No	No
Lethargy	Yes	No
Dry Skin	No	No
Cord Blood TSH	>150 Mu/L	>150 Mu/L
Cord Blood T ₄	4.6 µg/dl	05 µg/dl
TSH Day ₇	>150 Mu/L	>150 Mu/L
T ₄ Day ₇	01 µg/dl	02 µg/dl

Table-4: Characteristics of Congenital Hypothyroidism Patients

Pre eclampsia had no influence on cord blood TSH in our as well as, Laura et al²³ studies, whereas, TSH level was more in Pre Eclampsia group in Kim¹² and ChanY et al²⁴ and studies. Birth Asphyxia had significant influence on Cord TSH as the levels were increased as compared to normal newborns in our study, Gupta⁷, Kim⁹, Seth¹⁰ and Armanian¹². H.I.V. status of mother did not influence Cord TSH either in our as well as in Herbtzman study²⁰. Thus there were varying results in different studies considering the influence of perinatal factors on thyroid functions in newborns. On follow up of newborns after 7 days, we found two preterm newborns who had raised Serum TSH and low T₄, corresponding to their upper and lower limits, however further follow up and treatment could not be started as free T₄ is recommended before starting treatment and the patients were lost to follow up.

Conclusion: Various perinatal factors can influence Umbilical cord TSH and T₄ levels. As there are different results in different studies regarding effect of perinatal factors on Umbilical Cord blood TSH & T₄, further studies are needed. The values of Umbilical cord TSH and T₄ should be interpreted with caution for screening, as there may be influence of perinatal factors.

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