RESEARCH

NEWBORN SCREENING FOR CONGENITAL HYPOTHYROIDISM USING CORD BLOOD TSH AND VARIATIONS IN CORD BLOOD TSH WITH MATERNAL AND NEONATAL FACTORS: STUDY FROM RURAL CENTRE IN CHATTISHGARH, INDIA

Renu Kale[1], Medha Bhagwat[1], Chitranjan Nayak[2], Kiran Akhade[3]

[1]Associate Professor, Department of Pediatrics RIMS, Raipur, Chattisgarh, India
[2]Assistant Professor, Department of Pediatrics RIMS, Raipur, Chattisgarh, India
[3]Associate Professor, Department of Community Medicine, RIMS, Raipur Chattisgarh, India

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Corresponding Author:
Dr. Renu Kale,
Email: kalerenu65@rediffmail.com
ORCID: 0000-0002-3507-8444

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Abstract

Background: Congenital Hypothyroidism is most common cause of treatable mental retardation. Universal screening is now recognised tool for screening in newbornsworld wide. In India screening is optional, leading to increased prevalence of Congenital hypothyroidism. Maternal and neonatal factors are known to influence Cordblood TSH (CBTSH). The objective was to estimate the prevalence of Congenital hypothyroidism in rural population of Raipur Chattishgarh and to evaluate maternal and neonatal factors affecting CBTSH. **Materials and Methods:** Prospective cross-sectional study was conducted in 300 neonates. CBTSH values were assessed and correlation with maternal and neonatal factors was done. Repeat TSH was done on day 3-5 of life in newborn with high CBTSH values. **Result:** Mean CBTSH value was 8.68IU/ml. Values above 13.1IU/ml was found in 24 (8%) babies .3 babies had values below 1IU/ml. Repeat TSH was done on day 3-5 of life. 23 newborns had normal values, 1 baby had high TSH values, and treatment was started as per standard protocol. Mean CBTSH values were higher in postterm newborns of10.77IU/ml (23%) ,male gender had higher CBTSH values as compared to females. **Conclusion:** The prevalence of Congenital Hypothyroidism was estimated to be 1: 300. High prevalence reflects the need for Universal screening of newborns.

INTRODUCTION

Congenital Hypothyroidism is most common cause of preventable mental retardation in neonates. The incidence of congenital hypothyroidism is approximately 1:2000 to 1:4000 newborns worldwide.[1,2] Incidence in India is 1: 2500 – 1:2800 live births.[1,2,3] Clinical manifestation of hypothyroidism in newborns are subtle, or not present at birth. Early diagnosis and treatment are of paramount importance to prevent mental retardation.

Countries with neonatal screening ensures early diagnosis and treatment and prevents mental retardation. In India screening for congenital hypothyroidism is limited to metropolitan cities and there is no uniform policy or methodology for screening.

Cord blood TSH (CBTSH) is an easy and noninvasive method of collection of blood and results are available before mother leaves the hospital. This ensures repeat sampling in infants with high TSH and early institution of therapy with laevothyroxin.

Neonatal screening methods use either cord blood TSH or sample from heel prick on day 3 of life. Values obtained of TSH from heel prick and from cord blood are comparable.[4]

Maternal and perinatal factors influence cord blood TSH and there are very few studies from India, comparing the effects of these factors on CBTSH.

Incidence of CH in central India is 3.1:1000 which is very high.[5] This study was done at RIMS medical college which is situated in rural area of Raipur, to estimate prevalence of congenital hypothyroidism, and find various neonatal and maternal factors which can affect cord blood TSH.

Prevalence of congenital hypothyroidism in India has shown great variations according to region from where study has been done. Study from Uttar Pradesh had prevalence of 1:122,[6] Kochi in south India had prevalence of 2.1:100,[7] and AIIMS New Delhi between 2007 -2012 a pan India study reported incidence of 1:1172, with higher incidence in south Indian population.[8]

Studies from central India especially Chhattisgarh with high rural population are few .This study was rural based , and was done to estimate prevalence of

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CH using cord blood TSH .The study was also used to evaluate association between CBTSH and various maternal and neonatal factors. Maternal factors evaluated were (mode of delivery, gravida, parity, age, presence of Antenatal hypothyroidism) on level of Cord Blood TSH. Neonatal factors (maturity, birthweight, mode of delivery, gender and parity) and its effect on Cord blood TSH were evaluated .

MATERIALS AND METHODS

This prospective cross-sectional study was conducted in Department of Pediatrics at Raipur Institute of Medical Sciences Raipur. Study was conducted between June 2021-December 2021 (6months) among newborns delivered at RIMS Hospital after due permission from hospital ethics committee.

Sample Size: Total number of deliveries during June 2021 -December 2021 was 413 .300 newborns were included in the study.

Inclusion criteria: All newborns above 32 weeks of gestation were included in the study.

Exclusion criteria: Preterm neonates below 32 weeks were excluded, Neonates with major congenital malformations, Neonates needing NICU admission, and parents who refused consent.

Study tools: An informed written consent was taken from parents. Proforma was filled which contained all maternal information (age of mother, gravida, parity, mode of delivery, antenatal hypothyroidism, any history of medication) Neonatal information was taken after birth (maturity, gender, mode of delivery, number of siblings).

Blood samples were collected from 15 -20 cc of umbilical cord severed at time of birth of baby. 5cc sample was collected from umbilical vein in sterile container and sent for CBTSH estimation. CBTSH estimation was done by Chemiluminescence technique using Siemens Adiva Centaur TSH kit. Normal values according to kit were 0.1-13.2 µlU/ml. All values above 13.2µIU/mlwere considered abnormal. All neonates with CBTSH values above 13.2 IU/ml, were clinically assessed, maternal history was reviewed, and venous sample was sent on day 3-5 of life for free T3 and T4 and TSH. Values of free T3, T4, TSH of newborns which were in range of diagnosis of Congenital Hypothyroidism were again reassessed clinically for evidence of hypothyroidism, maternal history was reviewed for antenatal hypothyroidism. Newborn was then started on L-thyroxine according to weight. Infant was asked to come for follow up at 1, 3 and 6 months. Data was entered in Excel sheet and SPSS 16 was used for data analysis. Chi square test was used to test the association of various maternal and neonatal parameters with CBTSH. Multiple regression analysis was done for prediction of CBTSH based on birth order, gestational age, gender, mode of delivery, parity, maternal age and birth weight. A p value< 0.05 was taken as statistically significant. Study was approved by hospitals ethics committee.

RESULTS

Total of 413 babies were delivered at RIIMS Medical College, located in rural area of Raipur Chattishgarh during study period June 2021 to December 2021. 300 newborns were included in the study, who fulfilled all the variables of study parameters. The clinical profile of subjects according to neonatal and maternal parameters are summarized in [Table 1].

Table 1: Profile of Subjects with Mean TSH

Parameters	Number of Subjects	%	Mean TSH	Standard Deviation	p-value
All Subjects	300	100	8.68	6.01	
Birth Order					
First	91	30.3	9.32	7.62	p=0.786
Second	145	48.3	8.45	4.90	
Third or more	64	21.4	8.28	5.73	
Gestational age					
<32	1	0.33	9.90		p=0.627
32-36	52	17.33	8.90	6.13	
37-41	224	74.67	8.41	5.59	
>42	23	7.67	10.77	9.04	
Gender					
Male	152	50.7	9.08	7.11	p=.271
Female	148	49.3	8.27	4.61	
Delivery					
Normal	82	27.3	8.03	5.11	p=.320
LSCS	218	72.7	8.92	6.31	
Parity					
Primi	86	28.7	9.48	7.81	p=0.274
Multi	214	71.3	8.35	5.10	
Mothers age					
Less than 25	194	64.7	8.61	5.74	p=0..586
More than 25	106	35.4	8.80	6.50	
Birth weight					

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1.5-2.5 kg	117	38.3	8.55	3.36	p=0.918
2.6-4.0kg	183	61.7	8.76	7.19	

The mean value of CBTSH was 8.68µ IU/ml mean range of 0.74 -49.41µIU/ml. The mean CBTSH was highest in postterm neonates of 10.77µIU/ml. Male gender had higher CBTSH as compared to females (9.08 versus 8.27 µIU/ml. LSCS delivered newborns had raised CBTSH.
Effect of maternal and neonatal factors were assessed on CBTSH and the same are given in [Table 2].

Table 2: Effect of Maternal and Neonatal Factors on TSH

Parameters	**CBTSH**			**Total**	**P (Chi Square test) TSH levels with Maternal and Neonatal factors**
	<1-13.1N	**>13.1n(%)**	**<1n**		
All Subjects	273(91%)	24 (8%)	3(1%)	300	
Birth Order					
First	84	7 (7.69)	0	91	p=0.641
Second	128	15 (10.34)	2	145	
Third or more	61	2 (3.12)	1	64	
Gestational age					
<32	1	0	0	1	p=0.01
32-36	47	5 (9.61)	0	52	
37-41	206	16 (7.14)	2	224	
>42	19	3 (13.04)	1	23	
Gender					
Male	137	13(8.55)	2	152	p=0.980
Female	136	11(7.43)	1	148	
Delivery					
Normal	81	1(1.21)	0	82	p=0.01
LSCS	192	23(10.55)	3	218	
Parity					
Primi	78	8 (9.30)	0	86	p=0.860
Multi	195	16 (7.47)	3	214	
Mothers age					
Less than 25	176	17(8.76)	1	194	p=0.79
More than 25	97	7(6.60)	2	106	
Birth weight					
1.5-2.5 kg	109	08(6.95)	0	117	p=0.661
2.6-4.0kg	169	16 (8.64)	3	183	

Value of >13.1µIU/ml was higher in second born child as compared to first and second born. CBTSH of > 13.1µIU/ml was higher in newborns between 37 – 41 weeks of gestation. Maternal factors which had effect on CBTSH were mode of delivery, with higher CBTSH in newborns born by LSCS delivery. Newborn of multiparous women had higher CBTSH values . Age of mother also had effect on CBTSH ,with higher values recorded in neonates with maternal age less than 25 years.
The values of newborn with repeat TSH, T3 and T4 values.

Table 3: Repeat TSH

	Total	**Normal**	**Abnormal**	**Percentage**
Repeat TSH	24	23	01	4.16%
Values			T3 =115.13ng/dl T4 =15.2µg/dl TSH = 21.71mIU/L	

DISCUSSION

Congenital Hypothyroidism (CH) is inadequate thyroid hormone production in newborn infants. It can occur because of anatomic defect in the gland, an inborn error of thyroid metabolism or iodine deficiency. CH is most common neonatal endocrine disorder leading to preventable cause of mental retardation. The Cord blood TSH (CBTSH) estimation is easy to collect, non-invasive and with low rates of loss to follow up ,as results are available before mother is discharged from the hospital, and enables repeat sampling where CBTSH is high and early institution of therapy.

This study was done to estimate prevalence of CH in Raipur (rural region), along with maternal and neonatal factors which affect CBTS. The morbidity from CH can be reduced to minimum by early diagnosis and treatment. Initial screening using CBTSH is quick and non-invasive method of screening.
In our study mean CBTSH level was 8.68µIU/ml, which was comparable to other studies where mean TSH ranged from 6.13µIU/ml – 10 µIU/ml.[9,10,11] The mean CBTSH was higher than 10µIU/ml in few studies.[12,13,14] CBTSH levels were higher in our study in infants delivered by cesarean section(LSCS) 8.92 µIU/ml as compared to those born by normal vaginal delivery 8.03 µIU/ml,but the

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values were not found to be statistically significant. This was in variation with other studies where CBTSH was significantly raised in neonates delivered by assisted vaginal delivery as compared to LSCS delivery.[11,15,16]

The effect of gender on CBTSH was not found to be significant in our study, but few studies have shown significant variation with gender and insignificant in others.[11,13,14,15,16]

CBTSH was found to be to be higher in first born as compared to as compared to second and third born, but was not statically significant which was similar to other studies.[11,16]

Birth weight had varying effect on CBTSH but variation was not statistically significant and compared with other studies.[13,16]

Term babies were found to have higher CBTSH as compared to preterm and post term neonates which was different from other studies where preterm had higher CBTSH than term but did not have statistically significant effect on CBTSH and findings correlated with other studies.[11] In our study newborns delivered to mothers less than 25 year had higher CBTSH which was different from other studies where CBTSH had increasing trend with increasing age.[14] CBTSH values ranging from 10 -20 µIU/ml have been used in various studies.[9,11,12] In our study kit value of 1-13.01 µIU/ml was used as there were no normative data available from local population. Many previous studies have also used cut off values based on kits used for analysis.

In our study kit values of < 1µIU/ml and >13.01µIU/ml were considered abnormal. Values above 13.01µIU/ml were seen in 24 (8%) neonates. Repeat TSH, free T3. freeT4, samples were sent on day 3 to day 5 of life from peripheral venous sample, and neonate with abnormal value was started on L-thyroxine and baby is on regular followup.

1 newborn was confirmed to have CH from sample of 300 newborns delivered in period of June to December. Our results estimated Prevalence of 3:1000 were comparable with study done from Central India (5) where 4(3.1/1000) were diagnosed with CH. High prevalence of CH has been reported from other parts of India with reported prevalence of 3: 430, 1: 476, 1:700 1:280 #.[14,17]

CONCLUSION

CBTSH is an easy, non-invasive method of estimation of TSH .It is a good screening tool, and ensures early institution of therapy. Variation in CBTSH were found with birthweight, and gender of newborn and parity of mother. Higher values were found in LSCS deliveries, which may be due to higher incidence of emergency cesarian section in the institute.

Limitations

This study was done at single center in rural area and is not representative of entire rural population. A large multicentric study from local region and state is required to estimate true prevalence of CH. Chattishgarh being largely tribal population and has high incidence of Sickle cell anemia, and does this also effects values of CBTSH ,is not known

A national protocol for screening for CH is need of the hour, as CH is preventable cause of mental retardation

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