Section: Biochemistry

Original Research Article

ASSESSMENT OF CONGENITAL HYPOTHYROIDISM BY ESTIMATING CORD BLOOD TSH, SERUM TSH AND FT4 IN NEWBORNS

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Abstract

Background: Congenital hypothyroidism is a leading cause of mental retardation all over the globe as well as in India. To avoid such kind of morbidity, it is always better to perform a screening for cord blood TSH of all the neonates at least at the time of birth. So, this study was done to assess the cord blood TSH levels in neonates. **Aim & Objectives:** To assess cord blood TSH and subsequently serum TSH and fT4 levels in neonates. **Materials and Methods:** The present institution based cross sectional study was performed from January, 2019 to June, 2020 on 500 neonates in the Department of Biochemistry, COM&SDH, and Kamarhati. Cord blood TSH levels were analysed in all neonates and then subsequently serum TSH & fT4 were analysed in neonates having higher CBTSH levels and then those obtained data were analysed. **Results:** Total 500 children participated in this study among which 294(58.8%) were male. Out of 500, 309 (61.8%) children were from urban area and others from rural area. In urban children Muslims were majority (52.43%) where in case of rural children it was opposite i.e. 56.02% Hindu. 68.2 % children belonged from birth weight of 2.5-2.99 kg and 29.4% of children were from low birth weight group. Only 1.4 % children had TSH level more than 30 µIU/mL and 11.2% had TSH levels between 20.1-30.0 µIU/mL. 1.79% and 1.08% of infants of primi and multi gravid mothers had TSH level more than 30 µIU/mL respectively. In the present study, 1.27% and 1.87% had more CBTSH levels in normal delivery and caesarean sections respectively. Out of 156 neonates, having CBTSH values were more than10 µIU/mL, only 4 had increased serum TSH levels and decreased fT4 levels on day 3 and had confirmed congenital hypothyroidism. The incidence of congenital hypothyroidism was 0.8%. **Conclusion:** The incidence of congenital hypothyroidism in the present study is slightly higher. So, strictly assessment should be carried out to prevent further morbidity.

INTRODUCTION

Congenital Hypothyroidism is the one of the most common preventable cause of mental retardation all over the world as well as in India and with an incidence of 1:2500 to 1:2800 live births in India.[1,2] Clinical diagnosis is difficult at birth and the time of initiation of therapy is a critical determinant of outcome. In view of paramount importance of early diagnosis and treatment, various screening programs were initiated.

According to American Academy of paediatrics, more than 95% of newborn infants with congenital hypothyroidism have few clinical manifestations.[3,4] Though the Screening for congenital hypothyroidism will decrease the burden of mentally retarded children in the society but the method of screening is not uniform. Some countries use T4 while others prefer TSH as the tool since maternal diseases affecting placental dynamics influence T4 levels.[5,6] Few others use both T4 and TSH. Technically, using both T4 and TSH will be superior but would increase the cost of screening. Most of the countries have accepted TSH either through heel prick or through cord-blood as the screening method for congenital hypothyroidism. Cord blood collection of sample is preferred for its

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ease of collection of sample, more practical for mothers with short hospital stay following delivery and its utility as an indicator of the prevalence of iodine deficiency disorders.[7,8]

Cord blood TSH (CBTSH) estimation has the advantages of having 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.[9]

In most of the countries, blood samples are collected after 24 hours of life to evaluate CH but, the ideal timing of collection is betweendays 3 and 5 of life because a surge in neonatal TSH, and also fT4, occurs just after the birth and then subsidesto baseline over the next 24–72 hours.[10,11,12] So, another screening is advisable if the specimen wascollected just after the birthfor reducing the number of falsepositives. But, in India, mothers and their neonates are often get discharged from the hospital after 1 day of delivery , so second screening is not only difficult but also impossible due to different socioeconomic reasons. Therefore the first screening of cord blood TSH rather than second screening is used to detect CH for reducing the risk of mental retardation.

MATERIALS AND METHODS

This Institution based cross sectional observational study was held from January, 2019 to June, 2020 for the duration of 6 months over total 500 neonates in the department of Biochemistry, COMSDH, Kamarhati. The study was approved by the institutional ethical committee. Written consent was obtained from all participants.

Samples were collected from apparently healthy mother without any complications during delivery.

Inclusion Criteria

All healthy neonates irrespective of gender.

Exclusion Criteria

1. Infants having congenital abnormalities.
2. Neonates requiring resuscitation at birth.
3. Mothers suffering from medical illness such as jaundice, Diabetes mellitus, malnutrition, kidney diseases.
4. Mothers suffering from anaemia of pregnancy, bad obstetrics history
5. Mothers suffering fromany active or chronic infection

Approximately 2.5 mL of cord blood taken from the neonates in plain vials and the centrifuged at 3000 R.P.M. and the separated serum was used for estimating TSH by electrochemiluminescence. A repeat Serum TSH estimation at 72 hours of life was carried out from all the neonates to diagnosis of congenital hypothyroidism. In this present study, the reference range of CBTSH used 1.3-10 µIU/mL, as per kit. The normal level of serum TSH and fT4 are 0.50-5.50 µIU/mL and 0.8- 2.0 ng/dL.[13]

The data were compiled in Excel sheet and analyzed in the SPSS software.

RESULTS

Total 500 children participated in this study among which 294(58.8%) were male and rest were female (Figure no -1). Out of 500, 309 (61.8%) children were from urban area and others from rural area. In urban children Muslims were majority (52.43%) where in case of rural children it was opposite i.e. 56.02% Hindu(Figure no-2).

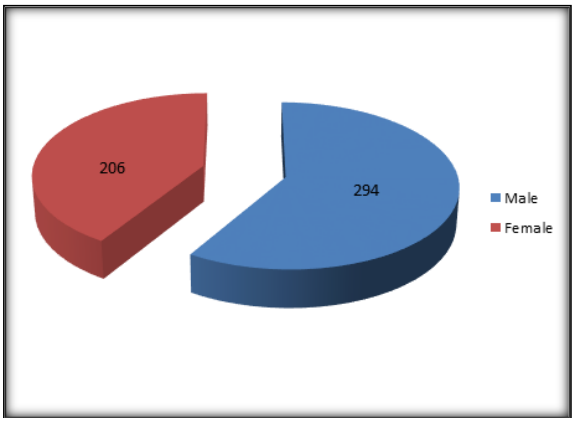

Figure 1: Distribution of children according to gender

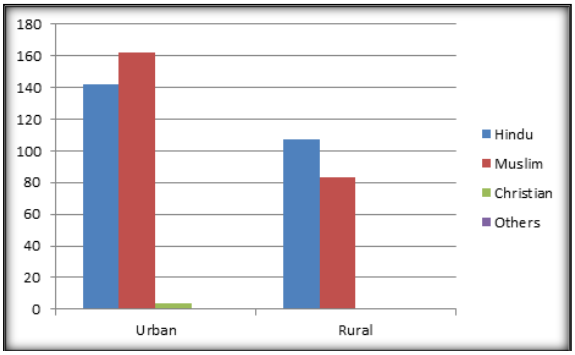

Figure 2: Distribution of children according to address and religion

Majority of children born from multi gravid mothers (55.4%).(Figure-3).

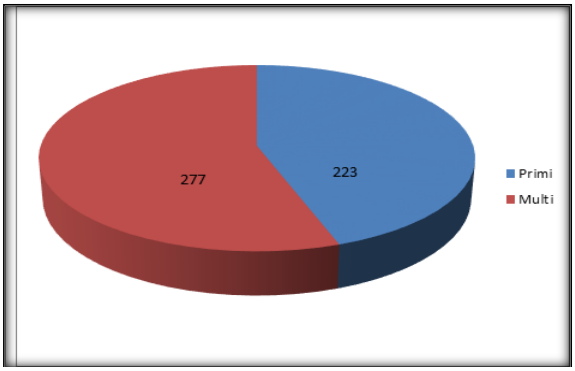

Figure 3: Distribution of children according to maternal gravida

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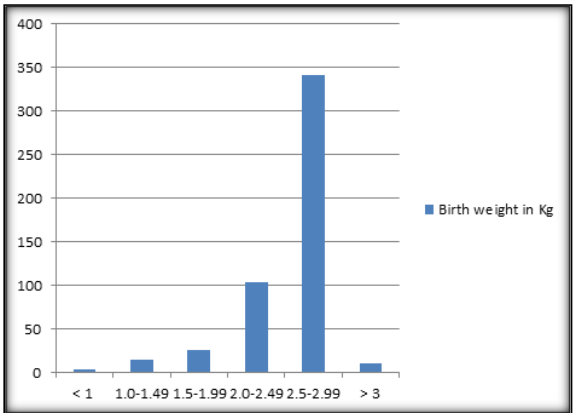

Figure 4: Distribution of children according to Birth weight

68.2 % children belonged from birth weight of 2.5-2.99 kg and 29.4% of children were from low birth weight group i.e. less than 2.5kg (Figure 4).

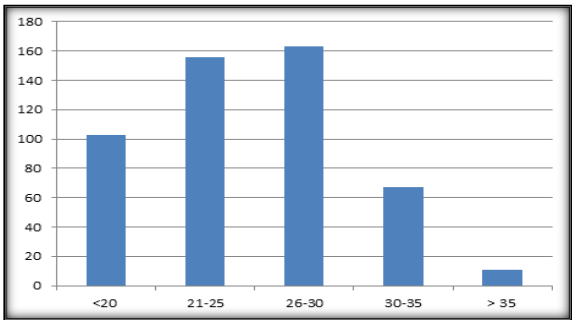

Figure 5: Distribution of children according to maternal age at birth

Majority of the children born belonged to maternal age group of 26-30 years (32.6%)(Figure 5).
Majority of the children born at term (77.4%)(Figure 6).

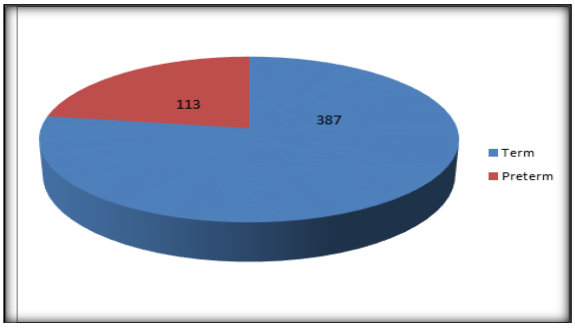

Figure 6: Distribution of children according to maturity

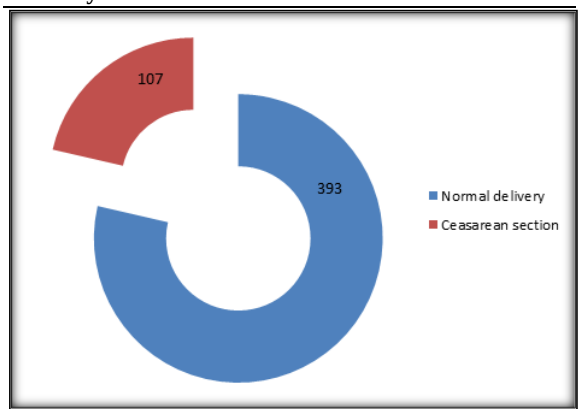

Figure 7: Distribution of children according to mode of delivery

Maximum i.e.78.6% children were born by normal delivery.

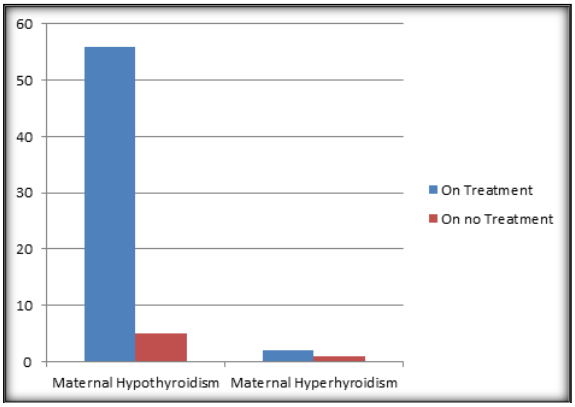

Figure 8: Distribution of children according to maternal thyroid function status

Out of 500 mothers, 61 had hypothyroidism and 91.8% were on treatment. Only 3 mothers had hyperthyroidism and out of 3, 2 were on treatment(Figure 7).

Table 1: Distribution of children according to cord blood TSH levels

Cord Blood TSH (µIU/mL)	No of children
Below 1.3	3(0.6%)
1.3- 10.0 (Normal)	341(68.2%)
10.1-20.0	93(18.6%)
20.1-30.0	56(11.2%)
>30	7(1.4%)
Total	500

From Table no 1, it is revealed thet only 1.4 % children had TSH level more than 30mIU/ml and 11.2% had TSH levels between 20.1-30.0 mIU/ml.(Table no -1).

Table 2: Distribution of children according to different parameters with their cord blood TSH levels

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Characteristics	Cord Blood TSH value in µIU/mL					
	<1.3	1.3 -10.0	10.1-20.0	20.1-30.0	>30	Total
Gender						
Male	2	197	58	33	4	294
Female	1	144	35	23	3	206
Habitant						
Urban	2	199	64	40	4	309
Rural	1	142	29	16	3	191
Religion						
Hindu	1	162	55	28	3	249
Muslim	2	173	38	28	4	245
Christian	-	5	-	-	-	5
Others	-	1	-	-	-	1
Gravida						
Primi	2	164	32	21	4	223
Multi	1	177	61	35	3	277
Birth Weight in kg						
<1	1	1	1	-	-	3
1.0-1.49	1	10	1	1	2	15
1.5-1.99	1	17	3	3	2	26
2.0-2.49	-	70	26	6	1	103
2.5-2.99	-	238	59	44	1	342
>3.0	-	5	3	2	1	11
Maternal Age (yrs)						
<20	1	59	20	21	2	103
21-25	1	114	14	25	2	156
26-30	-	117	44	2	-	163
31-35	-	45	13	7	2	67
>35	1	6	2	1	1	11
Gestational age						
Pre term	1	64	21	21	6	113
Term	2	277	72	35	1	387
Mode of delivery						
Normal delivery	2	285	65	36	5	393
Caesarean section	1	56	28	20	2	107
Maternal Hypothyroidism						
On medication	-	43	7	5	1	56
Not on medication	-	-	1	2	3	5
Maternal Hyperthyroidism						
On medication	-	2	-	-	-	2
Not on medication	-	1	-	-	--	1

From Table 2, we can observe the distribution of children according to different parameters with their cord blood TSH levels(Table 2).

The mean CBTSH value was 9.987 ± 0.654 µIU/mL. The male and female neonates had almost same mean CBTSH values, 9.087 ± 0.435 µIU/mL and 9.134 ± 0.876 µIU/mL respectively. Neonates from urban area had more mean CBTSH value (10.976 ±0.453 µIU/mL) than the neonates from rural areas (7.986 ± 0.876 µIU/mL). In case term neonates the mean CBTSH was 7.067 ± 0.321 µIU/mL where in preterm neonates it was 13.876 ± 0.653 mIU/ml. The neonates born through normal delivery had mean CBTSH level 12.013 ± 0.456 µIU/mL, where it was 7.988 ± 0.876 µIU/mL in case of caesarean section.

Out of 156 neonates, having CBTSH values were more than10 µIU/mL, only 4 had increased serum TSH levels and decreased fT4 levels on day 3 and had confirmed congenital hypothyroidism. That 4 neonates had the following serum TSH & fT4 levels at 72 hrs of birth- 10.259 µIU/mL & 0.654 ng/dL, 23.256 µIU/mL & 0.326 ng/dl ,21.012 µIU/mL & 0.364 ng/dl and 19.146 µIU/mL & 0.414 ng/dl.

DISCUSSION

As congenital hypothyroidism is one of the major cause of mental retardation, universal screening of all the newborn is an effective as well as essential method.[14] Some studies used only TSH or fT4 alone or both TSH &fT4 in combined.The reference ranges of cord blood TSH levels are different in different studies. In the present study, the reference ranges of cord blood TSH i.e. 1.3-10 µIU/mL. So, we considered cord blood TSH value more than10 µIU/mL is to be abnormal. From 10.1 to 20 µIU/mL is considered borderline and more than more than 20 µIU/mL is considered abnormal.

In the present study, 93 neonates had border line i.e. CBTSH values 10.1-20 µIU/mL and 63 neonates had TSH values more than 20 µIU/mL. Out of 63, 7 neonates had CBTSH values more than 30 µIU/mL.1.79% and 1.08% of infants of primi and multi gravid mothers had TSH level more than 30mIU/ml respectively. Out of 163 neonates, only 4 had hypothyroidism i.e. increased serum TSH levels and decreased fT4 levels on day 3, on repeat serum TSH and fT4 estimation on day 3. So, the incidence of congenital hypothyroidism was 0.8%.

In a study by Gupta A et al, the median CB-TSH was 8.75 µIU/mL (IQR = 6.475 – 12.82) with 11.5%

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neonates having values more than 20. CB TSH was significantly raised in first order neonates (P <0.01) and in babies delivered by assisted vaginal delivery and normal delivery (P <0.01). But, they found neonates who had fetal distress or non-progress of labour had significantly higher CB TSH than those who were delivered by elective caesarean section.[15] In the present study, 1.27% and 1.87% developed CH in normal delivery and caesarean sections respectively.

In a study by Raj S et al,the mean value of CBTSH was 12.88 μIU/mL. One hundred twenty five of the 430 neonates (29.06%) were found to have elevated CBTSH levels. CBTSH levels showed no gender variations but increased significantly with the gestational age of the baby (p=0.001).[9] CBTSH levels increased with increasing maternal age (p<0.001) and were significantly higher in babies of mothers with history of hypothyroidism.[6,9,16] But in the present study we got opposite result.

In another study,a total of 96,015 newborn infants were screened in the period from January 1990 to December 2007. Twenty-six cases of primary congenital hypothyroidism, six cases of transient hypothyroidism and 13 cases of central hypothyroidism were detected. This method of screening resulted in 100% sensitivity and 98% specificity.[17]

In a study by Seth A et al, 130 neonates were enrolled. The mean (range) gestational age and birth weight was 38.16 weeks (28-42 weeks) and 2600 g (800-4500 g), respectively. The comparison between TSH from cord blood and TSH from heel prick blood on 4th to 7th day of life was done. There was no statistically significant difference observed in mean TSH values. The TSH from heel prick blood increased with increasing TSH from cord blood with a positive correlation coefficient of 0.87.[16,18]

CONCLUSION

Congenital hypothyroidism is a major preventable cause of mental retardation. To prevent mental retardation, the estimation of cord blood TSH is a must thing. If the any chance of getting second time screening, that should be considered as a golden opportunity to reduce the number of false positives.

Limitations

1. Only one follow up done. Repeated assessment should be done.
2. Lack of time, fund& manpower.

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