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Original Research Paper

Neonatology

SCREENING OF CONGENITAL HYPOTHYROIDISM BY CORD BLOOD T4-TSH - A HOSPITAL BASED PILOT STUDY

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ABSTRACT

Congenital hypothyroidism (CH) is the term applied to the hypothyroidism that is present at birth. It is a major preventable cause of mental retardation. It has an incidence of 1 in 4000 births in various neonatal screening programs. Cord blood remains a very practical alternative for screening purposes, and thus is the practice in some Asian countries.Early diagnosis and therapy of congenital hypothyroidism improves the intellectual outcome and growth of the baby.

Aim : Screening of congenital hypothyroidism by T4-TSH values on cord blood sample.

Objective :. To study prevalence of congenital hypothyroidism and Derive normative data of cord blood T4-TSH levels in our population

Material And Methods : A Cross sectional , observational, Hospital based study conducted in Lt LAM Medical College, Raigarh (C.G.) during April 2018 to october 2018(6 months).Total 500 neonates were included.Data was compiled in MS excel .Number and percentage was calculated for qualitative data and mean and standard deviation was calculated for quantitative data. Histogram was prepared for Quantitative data.

Result : Out of 500 babies, 62 (12.4%) were > 3kg,197 (39.4%) were <2.5 kg & 241(48.2%) between 2.6 to 3kg. 213 (42.6%) were females & 278(57.6%) were males. In our study, Out of 500 babies 24.8% had TSH value in the range of 0-10 mU/L & 75.2% between 10-20 mU/L. 266 (53.2) were delivered by LSCS & 234(46.8%) by NVD. Out of 500 mothers ,5(1%) had history of thyroid disorders, 13(2.6%) had PIH, 3(0.6%) had APH. No history of PPH in any mother.25 (5%)had PROM, 5 (1%) had oligohydramnios & 2(0.4%)had sickling . Mean age of mother was 24.11±3.16. Mean weight 53.32±3.09, Mean height 5.12±0.31.Mean weight of baby was 2.77±0.45, Mean length 41.31±4.05, Mean T4 was 6.61±2.32, TSH 12.43±2.76.

Conclusion: We conducted study for the duration of 6 months with profile of 500 patients , with no patient having congenital hypothyroidism. In the present study the reference intervals of TSH, T4 were tried to establish. The results obtained are 6.8 – 17 mIU/L for TSH, 3.4 – 12.64 ng/dL for T4.The present study, similar to other studies, suggests that TSH levels in cord blood might be a feasible alternative specimen for a congenital hypothyroidism screening program in those areas where neonatal blood is not easily attainable.

KEYWORDS : Congenital hypothyroidism , false-positive, oligohydramnios Thyroid-stimulating hormone,

INTRODUCTION

Congenital hypothyroidism (CH) is the term applied to the hypothyroidism that is present at birth. It is a major preventable cause of mental retardation. It has an incidence of 1 in 4000 births in various neonatal screening programs(1). It is usually caused by defects in the development of thyroid gland, which may be genetic or genetic defects in the synthesis of and secretion of thyroxine. Other causes includes defect in secretion of and action of thyrotropin(TSH) and action of thyrotropin releasing hormone and the action of triiodothyronine.(2) Using umbilical cord blood to test for total thyroxin has not been a popular newborn thyroid screening methodology. Concerns have been raised regarding false-negative test results and potential effects of maternal conditions and delivery on the interpretations of the results, as these may increase fetal thyroid-stimulating hormone (TSH) levels.(3)

Congenital hypothyroidism of any cause is difficult to recognize at birth or very soon thereafter, in part because it is mitigated to some extent in utero by maternal-fetal transfer of T4. If the therapy is not initiated very soon after birth, the result is irreversible damage to the developing brain.(4)

In most screening programs blood samples are collected at 5-6 days age, but with large number of babies being discharged early, cord blood samples are being used as well. In our country, it is very difficult to call back babies once discharged. Also, an effective social system whereby babies could be reached at home is practically non-existent. Thus cord blood remains a very practical alternative for screening purposes, and thus is the practice in some Asian countries.(5,6)

Mixed cord blood samples for T4& TSH values have compared well with filter paper samples taken in the first few days of life(7,8). The Indian Academy of Pediatrics recommends the use of cord blood samples for screening of congenital hypothyroidism.(9)

The clinical manifestations of congenital hypothyroidism are often subtle or not present at birth. Common symptoms include decreased activity and increased sleep, feeding difficulties, constipation, and prolonged jaundice. On examination, common signs include myxedematous facies, large fontanels, macroglossia, distended abdomen with umbilical hernias, and hypotonia.(10)

Early diagnosis and therapy of congenital hypothyroidism improves the intellectual outcome and growth of the baby. In a study carried out earlier for congenital hypothyroidism, the mean intelligence quotient (IQ) of children with congenital hypothyroidism was 76. Specific cognitive defects were found even in those children who had normal IQs. Studies have shown that if therapy for congenital hypothyroidism is started before 3 months of age, the mean IQ is 89. If it is delayed the IQ drops to 70 between 3 months and 6 months and is as low as 54 after 6 months of postnatal life.(11)

The first congenital hypothyroidism (CH)screening was performed by Dussault, in Quebec-Canada in 1972. They detected 7 hypothyroid infants among 47 000 newborns during a 3-year period.(11,12)

Walfish reported in the Lancet that cord blood TSH measurements had greater sensitivity and specificity as compared to cord blood T4 and spot blood (collected on 3 to 4 day old newborns) T4 results and that both false positives and costs were higher in the T4 method. This same author also suggested routine T4 supplemented by TSH estimation be used in mass screening. Although more sensitive, screening by T4 and TSH together is not cost effective, therefore, mostly TSH, and rarely T4 screening, is used around the world.(13)

TSH screening was shown to be more specific in the diagnosis of congenital hypothyroidism (CH), while T4 screening was more

sensitive in detecting newborns with rare hypothalamic-pituitary hypothyroidism but less specific with a high frequency of false positives mainly in low birth weight and premature babies(14). With this background, the present study was conducted to screen the congenital hypothyroidism cases by measuring T4-TSH values in cord blood sample among newborn patients of Lt LAMMC, Raigarh (C.G.), India.

AIM

Screening of congenital hypothyroidism by T4-TSH values on cord blood sample.

OBJECTIVE OF THE STUDY

1. To study prevalence of congenital hypothyroidism
2. Derive normative data of cord blood T4-TSH levels in our population

Material and methods

Study Design : It was a Cross sectional , observational, Hospital based study.

Study Setting: Study was conducted in Lt LAM Medical College, Raigarh (C.G.)

Duration of study: Study was conducted during April 2018 to october 2018(6 months).

Study size - Total 500 neonates were included in the study.

Inclusion Criteria - All term neonates born to mothers at Lt LAM Medical College, Raigarh (C.G.) and delivered during study period .

Exclusion criteria: Babies whose cord blood sample could not be collected/preserved, pre term ,very low birth , baby admitted in NICU.

Ethical approval- Study was approved from institutional ethical committee.

Statistical Analysis

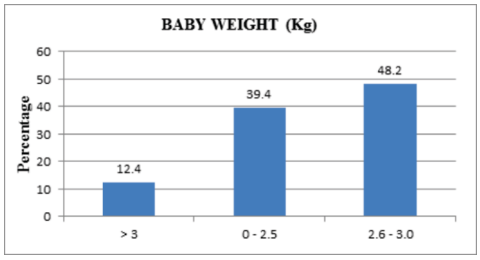
Data was compiled in MS excel and checked for its completeness and correctness, then it was analysed. Number and percentage was calculated for qualitative data and mean and standard deviation was calculated for quantitative data. Histogram was prepared for Quantitative data.

RESULTS

TABLE NO. 1. BACKGROUND CHARACTERISTIC OF SUBJECT

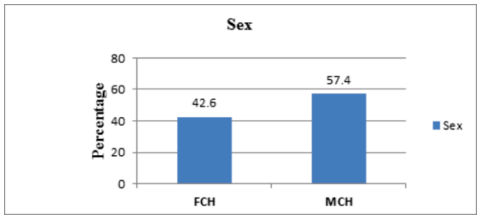
Variable		No.	%
Sex	Female	213	42.6
	Male	287	57.4
PIH	NO	487	97.4
	YES	13	2.6
PPH	NO	500	100
APH	NO	497	99.4
	YES	3	0.6
PROM	NO	475	95
	YES	25	5
MOTHER THYROID STATUS	NO	495	99
	YES	5	1
OTHER ILLNESS	NO	493	98.6
	OLIGOHYDROMINOS	5	1
	SICKLING	2	0.4
DRUG H/O	NO	500	100
BABY H/O (AF)	OPEN	500	100
SYSTEMIC EXAM (CVS)	NO	500	100
SYSTEMIC EXAM (RS)	NO	500	100
SYSTEMIC EXAM (PA)	NO	500	100
SYSTEMIC EXAM (CNS)	NO	500	100
BABY H/O (BABY WT) (Kg)	> 3	62	12.4
	1.5 - 2.5	197	39.4
	2.5 - 3.0	241	48.2
LAB FINDING (TSH)mIU/L	0 – 10	124	24.8
	10.1 – 20	376	75.2
NVD/LSCS	LSCS	266	53.2
	NVD	234	46.8

Figure-1. DISTRIBUTION SUBJECT ACCORDING TO BIRTH WEIGHT



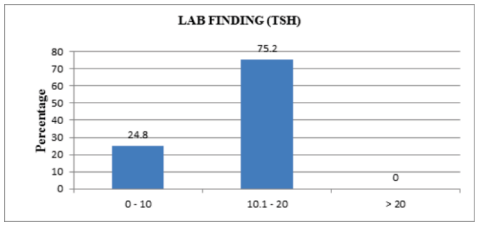
62 babies (12.4%) were of weight more than 3kg,197 (39.4%) were less than 2.5 kg & 241(48.2%) were between 2.6 to 3kg.

Figure-2. DISTRIBUTION OF SUBJECT ACCORDING TO SEX



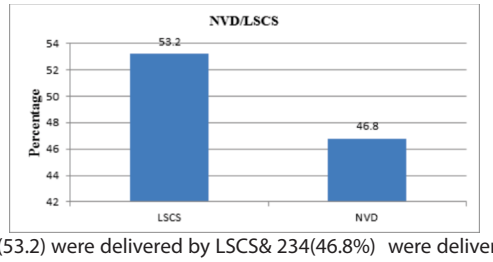
Out of 500 babies 213 were females which constitute 42.6% & 278(57.6%) were males

Figure 3 DISTRIBUTION SUBJECT ACCORDING TO TSH LEVEL



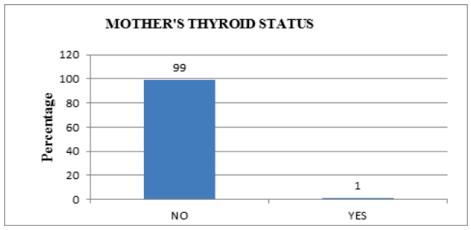
found that , Out of 500 babies 24.8% had TSH value in the range of 0-10 mU/L & 75.2% had TSH level between 10-20 mU/L.

Figure. 4 DISTRIBUTION OF SUBJECT ACCORDING TO NVD/LSCS



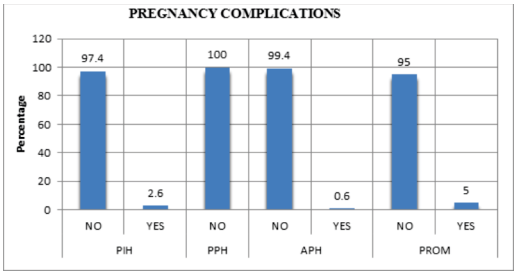
266 (53.2) were delivered by LSCS& 234(46.8%) were delivered by NVD.

Figure No.5 DISTRIBUTION OF SUBJECT ACCORDING TO MOTHER'S THYROID STATUS



Out of 500 ,5 mothers(1%) had history of thyroid disorder

Figure 6. DISTRIBUTION OF SUBJECT ACCORDING TO MOTHERS PREGNANCY COMPLICATION



Out of 500 mothers, 13 had history of PIH which constituted 2.6%,3 mothers had history of APH which is 0.6% of population. No history of PPH was seen in any mothers.25 mothers (5%)had history of PROM, 5 mothers (1%) had history of oligohydramnios & 2(0.4%)had history of sickling .

Table-2. Quantitative analysis of basic variables [Age, Anthropometry & Thyroid profile]

	Mean	S.D.
Age of mother	24.11	3.16
Weight of mother (kg)	53.32	3.09
Height of mother (feet)	5.12	0.31
Baby wt (kg)	2.77	0.45
Baby height (centimeter)	41.31	4.05
Lab finding (T4) baby	6.61	2.32
Lab finding (TSH) baby	12.43	2.76

Mean age of mother was 24.11±3.16. Mean weight of mother was 53.32±3.09. Mean height of mother was 5.12±0.31.Mean weight of baby was 2.77±0.45. Mean length was 41.31±4.05. Mean T4 was 6.61±2.32,TSH12.43±2.76.

Table-3.Umbilical cord blood TSH Level of study subjects

Cord TSH Level(mIUL)	No. of samples n = 500
Below 4	0
4 - 7.99	18
8 - 11.99	173
12 - 15.99	241
16 - 19.99	68

Out of 500 babies maximum241 were in range 12-15.99,followed by 173 in the Range of 8 to 11.99.no one had TSH below 4.

Table-4. Quantitative analysis and Histogram of T4 & TSH Hormone

Statistics			
		T4	TSH
Mean		6.6089	12.4275
Std. Error of Mean		0.10367	0.12349
Median		6.0000	12.5000
Std. Deviation		2.31819	2.76139
Skewness		1.520	-.214
Std. Error of Skewness		.109	.109
Kurtosis		2.947	-.630
Std. Error of Kurtosis		.218	.218
Minimum		3.10	4.90
Maximum		18.40	18.30
Percentiles	2.5	3.4000	6.8000
	10	4.6000	8.7000
	20	5.0000	9.8000
	30	5.2000	10.8000
	40	5.6000	12.0000
	50	6.0000	12.5000
	60	6.4000	13.4000
	70	7.0400	14.0000
	80	8.1800	15.0000
	90	9.6900	16.0000
	97.5	12.6475	17.0000

Mean TSH 12.4 2 +_2.76, Mean T4 6.6+_2.318

TABLE-5. Percentile of T4/TSH

Percentile	T4	TSH
2.5	3.4000	6.8000
97.5	12.6475	17.0000

Figure-7 .Histogram of T4 Hormone with Mean+ SD

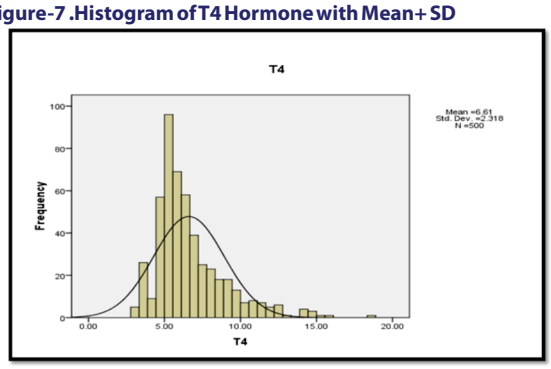
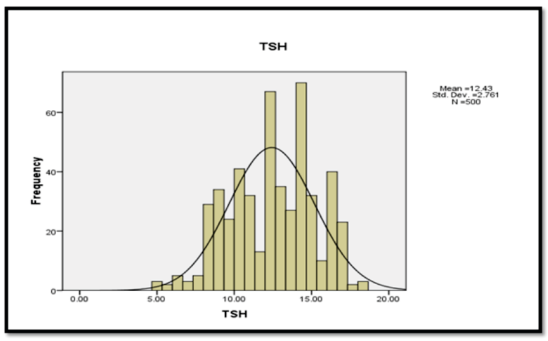


Figure-8. Histogram of TSH Hormone with Mean+ SD



DISCUSSION

Congenital hypothyroidism often causes irreversible mental retardation if thyroid hormone replacement therapy has not begun during the first few months of life. The successful introduction of screening in the 1970's has enabled North America, Europe, to a limited extent Asia, Latin America and a few African countries to combat the ill effects of Congenital hypothyroidism and saved lives. Those screening programs have successfully helped in early diagnosis and treatment of congenital hypothyroidism (15).

Use of cord blood TSH or combined with T4 as a screening tool is an attractive preposition because of its simplicity and accessibility. Although several investigators have measured TSH and T4 in cord and serum samples from term infants, every reference laboratory needs to establish its own normal values in order to validate its own data and technical expertise. Population-specific reference intervals are an important prerequisite for interpreting thyroid hormone measurements. In addition to that, the clinical value of TSH, free thyroxine and free triiodothyronine analysis depends on the reference intervals with which they are compared (16). Therefore, it is important to have population specific normal values for this age group to avoid misdiagnosis and incorrect treatment.

In our study 500 subjects were participated. The demographic data, which are the maternal age, birth weight, gestational age and gender of the newborn, were obtained from the hospital records and interview of the mothers. Mothers age was concentrated around the age of 19 - 28 years with mean values 24.11± SD years. Since there was no evidence about the age of the mothers, there is a probability to found biased data which have an effect on the test of association of maternal age with other variables. 62 babies (12.4%)

were of weight more than 3kg,197 (39.4%) were less than 2.5 kg & 241(48.2%) were between 2.6 to 3kg in the present study .

The conventional 95th percentile reference limits (2.5th to 97th centile) the method was used to determine the reference ranges of TSH values of the cord blood. in our study T4 & TSH 2.5 percentile(3.4000 & 6.8000) & 97.5 percentile(12.6475 &17.0000) has Prior the establishing of the reference intervals the data was tested for normal distribution. In our study we found that , Out of 500 babies 24.8% had TSH value in the range of 0-10 mU/L & 75.2% had TSH level from 10-20 mU/L.

The TSH results of the whole participants have shown a comparable trend as with the normative data for cord blood TSH values as reported by various studies across the globe. 75.2 % of the cord blood results were having value range between 0 to 10 mU/L.m. Nearly similar study from India (17) where they found 85.75% patient having TSH level below less then 12mU/l.

Many studies reported that cord blood TSH can be used as a screening tool for congenital hypothyroidism from all over the world. A study from Japan had shown that mixed cord blood is a good sampling technique for screening for Congenital hypothyroidism (18). And it was concluded that cord TSH had a better specificity and sensitivity as compared to cord or filter paper T4 at 3-5 days of age. A study from Iran shows the reference range of TSH Concentration ranged from 0.77 to 24.91mIU/L with a mean value of 7.09 (19) which had higher values comparing to the present study.

Many hospitals perform newborn screening at 5–6 days of age, and the reference values reflect this postnatal age. In term healthy newborns, there is an initial physiologic surge of TSH (up to 60 mIU/L within 30 minutes of delivery), followed by a rapid decline over the first five days of life to 10 mIU/L.(20)

Currently, a large number of healthy term newborns are discharged early (before 48 hours of age). Thyroid screening during this time is associated with an increasing number of false-positive results, due to this neonatal TSH surge. In addition, it is difficult to call back infants for thyroid testing once discharged.(21)

All of these factors make use of umbilical cord blood a practical alternative for thyroid screening purposes.(22) Interestingly, some countries revert to cord blood screening as the method of choice, when facing difficult patient recall for initial thyroid testing.(23,24)

Summary and Conclusion

We conducted study for the duration of 6 months with profile of 500 patients , with no patient with congenital hypothyroidism.

In the present study the reference intervals of TSH and T4 were tried to establish. The results obtained are 6.8 – 17 mIU/L for TSH, 3.4 – 12.64 ng/dL for T4.

The present study, similar to other studies, suggests that TSH levels in cord blood might be a feasible alternative specimen for a congenital hypothyroidism screening program in those areas where neonatal blood is not easily attainable.

Limitation of study

1. The current study was conducted on 500 study subjects due to limitation of resources. The further study should be expanded on a sufficient large scale to get the more valid results.
2. The Further in-depth analysis should be done regarding association of T4 & TSH level with other background characteristics so that we can use this data for future planning.

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