Original Research Article

Screening of Congenital Hypothyroidism by cord blood T4-TSH a hospital based study

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Received: 01-10-2021 / Revised: 11-11-2021 / Accepted: 18-12-2021

Abstract

Background: Congenital hypothyroidism (CH) is the term applied to the hypothyroidism that is present at birth. It is a major preventable cause of mental retardation. **Objective:** to screen the congenital hypothyroidism cases by measuring T4-TSH values in cord blood sample among newborn patients of DR BHIM RAO AM Hospital of Raipur city (C.G.), India. **Materials and Methods:**The present Cross sectional observational Hospital based study was conducted in Pt. JNM Medical College, DR. BHIM RAO AMBEDKAR HOSPITAL, Raipur (C.G.) during study period April 2017-october 2017(6 months). Study was approved from institutional ethical committee.**Results:**Out of 500 babies 213 were females which constitute 42.6% & 278(57.6%) were males . 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. 266 (53.2) were delivered by Lscs& 234(46.8%) were delivered by NVD. Out of 500, 5 mothers(1%) had history of thyroid disorders. Mean age of mother is 24.11±3.16.mean weight of mother is 53.32±3.09.mean height of mother is 5.12±0.31.mean weight of baby is 2.77±0.45.mean length is 41.31±4.05.mean T4 is 6.61±2.32,TSH±2.76. Table 1

Conclusion- 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: Screening, Congenital hypothyroidism, Cord blood, T4-TSH

Introduction

Congenital hypothyroidism (CH) 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-foetal 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]

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Mixed cord blood samples forT4& TSH values have compared well with filter paper samplestaken in the first few days of life. [7,8] The Indian Academy of Pediatrics recommends the use of cord blood samples for screening for 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 costeffective, therefore, mostly TSH, and rarely T4 screening, is used around the world. [13]

TSH screening was shown to be more specific in the diagnosis ofcongenital 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 DR BHIM RAO AM Hospital of Raipur city (C.G.), India.

Materials & Methods

The present Cross sectional observational Hospital based study was conducted in Pt. JNM Medical College, DR. BHIM RAO AMBEDKAR HOSPITAL, Raipur (C.G.) during study period April 2017-october 2017(6 months). Study was approved from institutional ethical committee.

Inclusion Criteria: All term neonates born to mothers at Pt JNM medical college and Dr BHIM RAO AMBEDKAR Hospital, Raipur 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.

Methodology: After taking informed consent from all mothers were convinced to enroll their babies for the screening test to detect congenital hypothyroidism in their baby. Mothers' clinical details T4 regarding thyroid status, hormonal therapy, weight, BMI, and other chronic medical illnesses was recorded.At the birth – basic clinical details of the baby especially related to hypothroidism features like birth weight , tone, cry, Anterior Fontanelle size, congenital abnormality, feeding difficulty, vomiting, not passing stool/ abdominal distension, anemia, jaundice etc. were noted and entered on patient proforma. Blood sample from umbilical cord wascollected in sterile container drawn from placental side of the umbilical cord at the time of birth of the baby.After taking informed consent from the mother or the attendant, 3 ml of cord blood was collected within 1hour of delivery in plain vials. Serum analysis for T4, TSH was carried out. The parameters were measured by chemiluminescence, which is more sensitive and automated method.Although the concentration of TSH in the blood is extremely low, it is essential for the maintenance of normal thyroid function. The release of TSH is regulated by a TSH-releasing hormone (TRH) produced by the hypothalamus. The levels of TSH and TRH are inversely related to the level of thyroid hormone. When there is a high level of thyroid hormone in the blood, less TRH is released by the hypothalamus, so less TSH is secreted by the pituitary. The opposite action will occur when there is decreased thyroid hormone in the blood. This process is known as a negative feedback mechanism and responsible for maintaining the proper blood levels of these hormones.

Principle of the test: The T4, TSH CLIA test is based on the principle of a solid phase enzyme-linked immunosorbent assay. The assay system utilizes a specific monoclonal antibody directly against a distinct antigenic determinant on the intact TSH molecule. One monoclonal anti-TSH antibody is used for solid phase immobilization and another anti-TSH antibody is in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react simultaneously with the two antibodies, resulting in the T4, TSH molecules being sandwiched between the solid phase and enzyme-linked antibodies. After incubating for 60 minutes at 37°C, the wells are washed with Wash Solution to remove unbound labeled antibodies. Upon the addition of the substrate, the horseradish peroxidase activity bound on the wells is then assayed by a chemiluminescence reaction. The Related Light Unit (RLU) is directly proportional to the concentration of TSH in the test sample.

Statistical Analysis: Data was compiled in ms excel and checked for its completeness and correctness, then it was analysed. No. And percentage was calculated for qualitative data and mean and standard deviation was calculated for quantitative data. Histogram has prepared for Quantitative data.

Results

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. Out of 500 babies 213 were females which constitute 42.6% & 278(57.6%) were males 4. 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. 266 (53.2) were delivered by Lscs& 234(46.8%) were delivered by NVD. Out of 500 ,5 mothers(1%) had history of thyroid disorders.Out of 500 mothers, 13 had history of PIH which constituted 2.6%,3 mothers had history of APH which is o.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 oligohydroamnios& 2(0.4%)had history of sickling.Mean age of mother is 24.11±3.16.mean weight of mother is 53.32±3.09.mean height of mother is 5.12±0.31.mean weight of baby is 2.77±0.45.mean length is 41.31±4.05.mean T4 is 6.61±2.32, TSH ±2.76. Table 1

Table 1: 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

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 2

Table 2: 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

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

Table 3: 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

Table 4: Percentile of T4/TSH

Percentile	T4	TSH
2.5	3.4000	6.8000
97.5	12.6475	17.0000

Discussion

Congenital hypothyroidism often causes irreversible mental retardation if thyroid hormone replacement therapy is 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 andincorrect treatment.Net of study subjects 500 were participated in the study. 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 not written 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 are having value range between 0 to 10 mU/L.m. Nearly similar study from India where they found 85.75% patient having TSH level below less then 12mU/l. [17] 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 24.91mlU/L with a mean value of 7.09 which had higher values comparing to the present study. [19]

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. Currently, a large numberof 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. All of these factors make use of umbilical cord blood a practical alternative for thyroid screening purposes.(50) Interestingly, some countries revert to cord blood screening as the method of choice, when facing difficult patient recall for initial thyroid testing.

Conclusion

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.

Acknowledgment

I would like to express my profound gratitude to all the participants for their co-operation and for their immense faith they reposed in me and without whose willing cooperation, this work would not have seen the light of the day.

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Conflict of Interest: Nil
Source of support:Nil