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Research Article

Analysis of Congenital Hypothyroidism by cord blood T4-TSH: A Prospective study

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Abstract: Background: Congenital hypothyroidism (CH) 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 include defect in secretion of and action of thyrotropin (TSH) and action of thyrotropin releasing hormone and the action of triiodothyronine. Using umbilical cord blood to test for total thyroxine 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. 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.

Materials and methods: This is a Prospective, Observational and Cross-sectional study was conducted in the Department of Pediatrics, Arundathi Institute of Medical Sciences over a period of 1 year. All term neonates born to mothers and delivered during study period were included. Mothers' clinical details T4 regarding thyroid status, hormonal therapy, weight, BMI, and other chronic medical illnesses were recorded. At the birth – basic clinical details of the baby especially related to hypothyroidism 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 was collected in sterile container drawn from placental side of the umbilical cord at the time of birth of the baby.

Result: In table 1, male were 51 (56.66%) and females were 39 (43.4%). Male-female ratio was 1.15:1. In our study, least were above 40 weeks and maximum were belonging in the week of 37+1 to 38. The birth weights ranged between 2.5 and 4.5 kg, with an average birth weight of 2.82 kg. Mean (standard deviation) TSH value was 7.725 (8.99) among the study group. In our study depicts the TSH values of the entire cohort. TSH values ranged between 1.2 and 100 mIU/ml.

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. An elevated cord blood TSH value has been found in substantial numbers of babies. Male sex, mode of delivery and perinatal stress factors has a significant impact on CB-TSH levels. As various other factors can influence CB-TSH, its value should be interpreted with caution.

Keywords: Congenital hypothyroidism, Thyroid-stimulating hormone, Cord blood.

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1. 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 include 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 thyroxine 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]

Mixed cord blood samples for T4& TSH values have compared well with filter paper samples taken in the first few days of life. [6] The Indian Academy of Pediatrics recommends the use of cord blood samples for screening for congenital hypothyroidism. [7]

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. [8] Early diagnosis and therapy of congenital hypothyroidism improves the intellectual outcome and growth of the baby. [9,10] 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. [11]

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. [12] 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.

2. Material and methods

This is a Prospective, observational study and Conventional Routine dissection method.

Study Materials: 800 Embalmed human adult cadavers lower limb specimens. Adult lower limb specimens were obtained from the embalmed cadavers allotted for routine dissection to the first year MBBS students at the Department of Anatomy, Index Medical college.

Inclusion Criteria: Both right and left lower limbs were used from all 300 cadavers. Therefore, every right lower limb has a corresponding left lower limb.

Exclusion Criteria: Specimens where damage to piriformis or the sciatic nerve observed was excluded.

Documentation of the Variations: The parameters of the sciatic nerve and piriformis was measured for every cadaver in the sample group, regardless of whether a variation is present or not. Images were only taken of the lower limb if the specimens presenting anatomical variations. A Canon 600D 18.0-megapixel camera was used for capturing all the images. The lens has four-stop image stabilizer technology, which improves performance during low-light conditions, as can be expected in an artificially lighted dissection hall.

Statistical Analysis: For statistical analysis, a biostatistician, was consulted for quantitative and descriptive statistics of the study data. Statistical analysis was conducted with Statistica version 13.2

software. Comparisons were made between the left and right sides of the lower limbs, sex, and population groups.This Prospective, Observational and Cross-sectional study was conducted in the Department of Pediatrics, Arundathi Institute of Medical Sciences over a period of 1 year. Inclusion Criteria: All term neonates born to mothers and delivered during study period.

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

Methodology: Mother's clinical details T4 regarding thyroid status, hormonal therapy, weight, BMI, and other chronic medical illnesses were recorded. At the birth – basic clinical details of the baby especially related to hypothyroidism 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 was collected 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.

Statistical Analysis: Data was compiled in ms excel and checked for its completeness and correctness, and then it was analysed. Number and percentage was calculated for qualitative data and mean and standard deviation was calculated for quantitative data.

3. Results

Table 1. Gender of the baby

Gender	Frequency	Percentage
Male	51	56.66%
Female	39	43.34%

In table 1, male were 51 (56.66%) and female were 39 (43.4%).

Table 2. Gestational Age of Baby (in weeks)

Gestational Age (weeks)	Frequency	Percentage
37+1 to 38	38	42.22
38+1 to 39	32	35.55
39+1 to 40	19	21.11
Above 40	1	1.11

In table 2, least was above 40 weeks and maximum were belonging in the week of 37+1 to 38.

Table 3. Weight-wise distribution of the study group

Weight (kg)	Number of samples (%)
2.5-2.99	59 (65.5%)
3.00-3.49	27 (30%)
3.5-3.99	3 (3.3%)
4 and above	1 (1.1%)

The birth weights ranged between 2.5 and 4.5 kg, with an average birth weight of 2.82 kg [Table 3].

Table 4. Umbilical cord blood thyroid - stimulating hormone values (n=90)

Number of samples (mIU/ml)	Number of samples (%)
Below 10	74 (82.2%)
11-20	9 (10%)
21-50	5 (5.5%)
>50	2 (2.2%)

Mean (standard deviation) TSH value was 7.725 (8.99) among the study group. Table 4 depicts the TSH values of the entire cohort. TSH values ranged between 1.2 and 100 mIU/ml.

4. Discussion

Congenital hypothyroidism often causes irreversible mental retardation if thyroid hormone replacement therapy has not begun during the last 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. [13]

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. [14] Therefore, it is important to have population specic normal values for this age group to avoid misdiagnosis and incorrect treatment.

In our study 90 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. In our study we found that, out of 90 babies 82.2% had TSH value in the range of 0-10 mU/L & 10% 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 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. [15] And it was concluded that cord TSH had a better specificity and sensitivity as compared to cord or lter 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.

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. [16]

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. [17] All of these factors make use of umbilical cord blood a practical alternative for thyroid screening purposes. [18] Interestingly, some countries revert to cord blood screening as the method of choice, when facing difficult patient recall for initial thyroid testing. [19]

5. 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. Congenital hypothyroidism is a major preventable cause of mental retardation. In India, there is no screening programme for CH. An elevated cord blood TSH value has been found in substantial numbers of babies. Male sex, mode of delivery and perinatal stress factors have a significant impact on CB-TSH levels. As various other factors can influence CB-TSH, its value should be interpreted with caution.

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