ORIGINAL RESEARCH

A study on thyroid hormone levels in cord blood

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ABSTRACT
Neonatal screening programs for detection of CH in neonatal period are widespread in the developed countries for the last three decades and are fast gaining momentum in the developing world as well. In most screening programs for CH, blood samples are collected at 5 - 6 days of life. Because of large number of babies being discharged early, cord blood samples are being used as an alternative. Blood samples were collected in a sterile container drawn from a 15-20 cm length of the umbilical cord incised while severing it at the time of birth of the baby. Thus, a mixed cord blood sample (1.5 ml) including both from the umbilical artery and vein was obtained. The level of thyroid hormones in the cord blood samples of the 1550 neonates of this study were T3: 72.69±13.12 (ng/dl): T4: 9.01±2.227 (µg/dl) and TSH: 8.64±6.195 (mIU/l).
Key words: Thyroid hormone levels, cord blood, newbornscreening

INTRODUCTION

Newbornscreening commenced in 1960s with the work of Dr. Robert Guthrie, a researcher in the USA. He used filter paper for collecting blood specimens to detect phenylketonuria (PKU), an inborn error of metabolism causing severe mental retardation with bacterial inhibition assay (BIA) method. Few years later, it was suggested that small amounts of blood or serum extracted from filter paper punches as small as 3mm for detecting other biochemical markers of debilitating conditions, would be of sufficient sensitivity and specificity to allow expansion of the screening process for conditions such as CH, congenital adrenal hyperplasia (CAH), sickle cell diseases, etc.[1]

Neonatal screening programs for detection of CH in neonatal period are widespread in the developed countries for the last three decades and are fast gaining momentum in the developing world as well. In most screening programs for CH, blood samples are collected at 5 - 6 days of life. Because of large number of babies being discharged early, cord blood samples are being used as an alternative. In developing countries, the limitation of follow up remains, i.e., to call back babies once discharged. Cord blood samples for TSH values have compared well with filter paper samples taken in the first few days of life.

Klein *et al.*, (1974), showed that serum measurements of thyroid hormones (T_4 - TSH) in cord blood could detect hypothyroidism in the neonatal period.[2] Walfish PG (1976) and Fuse Y (1991) *et al*.,suggested that mixed cord blood samples for TSH values had compared well with blood samples taken in the first few days of life.[3]

Walfish*et al*.,(1976), in their study involving evaluation of three thyroid-function screening tests for detecting neonatal hypothyroidism in Toronto had screened cord blood for T4 and TSH by radioimmunoassay and blood of infants 3 to 5 days of life with the filter - paper T4 method and concluded that cord TSH as an initial screening test had a higher specificity and sensitivity for the diagnosis of primary hypothyroidism. In order to avoid the impracticably high recall rate and false-positive incidence resulting from an initial T4 screening test, and to reduce the estimated follow-up recall to less than 0-2% of the screened infant population, it is recommended that infants with low T4 be selected for a supplementary TSH screening test.[4]

Walfish*et al*.,(1979), in their study involving regional screening programme to detect neonatal hypothyroidism in Toronto used initial cord blood T4 determinations with supplemental TSH and T3 resin uptake measurements, and detected an incidence of thyroid abnormalities to be 1 / 3,000 births. 1,15,000 infants had severe primary hypothyroidism. None of

the hypothyroid infants had been suspected of CH clinically before the screening. Retrospectively only a few babies had signs of hypothyroidism. To avoid missing affected cases, supplemental TSH and T3 resin uptake (T3U) determinations were required on 8-12% of the population screened initially with a T4 test. With an initial T4 and supplementary TSH and T3U testing on cord blood serum, recalls to exclude primary hypothyroidism were reduced to 0-16% of the screened population. The incidence of abnormalities detected in this cord blood screening programme was comparable with that reported by others using neonatal dried blood screening methods, indicating that cord blood screening can be effective provided the appropriate recall criteria and transport conditions are used. But for several practical reasons, neonatal dried blood methods are recommended as the screening test of choice for surveying large populations over extensive geographical areas.[5]

Desai *et al*.,(1987), screened 12,407 newborns for CH using cord blood TSH measurement. The incidence was found to be 1 in 2481. 2.8% babies were called for retesting. In 1994, the same group screened 25,244 neonates at 24-94 hours and measured filter paper T4. The babies recalled were 18.91%. The incidence was 1: 2804. This screening missed 3 out of 9 babies despite a high recall. Considering this high incidence of CH, availability of low cost therapy and a screening test like TSH, is highly desirable to start a screening program nationwide to prevent the most preventable cause of mental subnormality.[6]

METHODOLOGY

STUDY DESIGN

Prospective comparative study conducted over a period of 20 months.

SOURCE OF DATA

1550 neonates born in hospitals.

INCLUSION CRITERIA

- Neonates whose parents gave consent for the blood sampling.
- Term neonates with birth weight more than 2kg.

EXCLUSION CRITERIA

- Neonates discharged before day 3 of life.
- Neonates born to hypothyroid mother.
- Neonates admitted to NICU.
- Preterm and low birth weight neonates.

METHOD OF COLLECTION OF BLOOD SAMPLE

Blood samples were collected in a sterile container drawn from a 15-20 cm length of the umbilical cord incised while severing it at the time of birth of the baby.

Thus, a mixed cord blood sample (1.5 ml) including both from the umbilical artery and vein was obtained.

T3, T4 and TSH were estimated by competitive immunoassay by using VITROS Total T3 and T4 Reagent Pack and the VITROS Immunodiagnostic Products TSH30 Reagent Pack.

The following details of the neonates included in the study were recorded on the proforma.

- Maternal address, maternal age, parity, thyroid status of the mothers.
- At birth, sex and weight of the neonates.
- Gestational age (was assessed by new modified Ballard scoring system).
- Informed oral and written consent were taken from the parents.

Categorisation of thyroid function status to suspect CH in cord blood and on day 3 of life:

- LowT4.
- High TSH.
- Normal T4 High TSH.
- Low T4 High TSH.
- Low T4 Normal TSH.

A level <6.2 µg/dl was considered as the cut - off value for T4 in cord blood and day 3 venous blood samples for screening CH.

A level of >20 mlU/L was considered as the cut - off value for High TSH in cord blood and day 3 venous blood sample for screening CH.

The thyroid hormone T3 is not taken into account as a screening tool for screening CH, because of variation in values due to peripheral conversion of T4 to T3.

RESULTS

Table 1:Distribution of Baseline Characteristics Included in the Study (n=1550)

Characteristics		Mean ± SD
Maternal age		25.01±3.74
Parity	Primi	828 (53.4%)
	Multi	722 (46.6%)
Mode of delivery	Normal	991 (63.9%)
	LSCS	559 (36.1%)
Sex	Male	675 (43.5%)
	Female	875 (56.5%)
Birth weight (kg)		2.75 ± 0.40
Cord blood	T3 (ng/dl)	72.69 ± 13.12
	T4 (µg/dl)	9.01 ± 2.227
	TSH (miu/L)	8.64 ± 6.195

	T4 (µg/dl)	11.55 ± 3.596
	TSH (miu/L)	2.98 ± 2.191

A total of 1550 neonates were enrolled in the study.
Mean maternal age of 1550 neonates enrolled in the study was 25.01±3.74 years.828 (53.4%) neonates were born to primi mothers and 722 (46.6%) were born to multi gravdia mothers.All neonates were term.991 (63.9%) neonates were delivered by normal delivery, 559 (36.1%) were delivered by caesarean section. 675 (43.5%) were males and 875 (56.5%) were females.mean value of T3, T4 and TSH in cord blood was 72.69±13.12 ng/dl, 9.01±2.227 µg/dl and 8.64±6.195 mIU/l respectively.

Table 2: Maternal Age

Maternal age	Frequency	Percentage
<20	181	11.7
21 - 25	738	47.6
26 - 30	494	31.9
31 - 35	123	7.9
36 - 40	14	0.9
Total	1550	100.0

Of the 1550 neonates, 181 (11.7%) were born tomothers aged between 19-20 years, 738 (47.6%) were born to mothers aged between 21-25 years, 494 (31.9%) were born to mothers aged between 26-30 years, 123 (7.9%) were born to mother aged 31-35 years and 14 (0.9%) were born to mothers aged 36-40 years.
The mean maternal age distribution was 25.01±3.74 years.

Table 3:Parity

Parity	Frequency	Percentage
Primigravida	828	53.4
Multigravida	722	46.6
Total	1550	100.0

Of the 1550 neonates, 828 (53.4%) were born to primi mothers and 722 (46.6%) were born to multi gravida mothers.

Table 4: Mode of Delivery

Mode of delivery	Frequency	Percentage
Normal Vaginal delivery	991	63.9
LSCS	559	36.1
Total	1550	100.0

Of the 1550 neonates 991 (63.9%) neonates were delivered by normal delivery, 559 (36.1%) were delivered by caesarean section.

Table 5:Gender of Neonate

Gender	Frequency	Percentage
Male	675	43.5
Female	875	56.5
Total	1550	100.0

Of the 1550 neonates, 675 (43.5%) were males and 875 (56.5%) were females.

Table 6: Birth Weight (kg)

Birth Weight (Kg)	Frequency	Percentage
< 2.5	339	21.9
2.5 - 3	925	59.7
3.1 - 3.5	223	14.4

> 3.5	63	4.1
Total	1550	100.0

Out of 1550 neonates, 339 (21.9%) weighed between 2-2.5 kg, 925 (59.7%) weighed between 2.5-3 kg, 223 (14.4%) weighed between 3.1-3.5 kg and 63 (4.1%) weighed more than 3.5 kg.
The mean birth weight is 2.75±0.40 kg.

The level of thyroid hormones in the cord blood samples of the 1550 neonates of this study were T3: 72.69±13.12 (ng/dl): T4: 9.01±2.227 (µg/dl) and TSH: 8.64±6.195 (mIU/l).

Table 7:Cord Blood Levels of T3, T4 and TSH in the Neonates of this Study (n=1550)

Thyroid profile	Min – Max	Mean ± SD
T3 (ng/dl)	35.0 – 108.0	72.69 ± 13.12
T4 (µg/dl)	6.21 – 20.6	9.01 ± 2.227
TSH (mIU/l)	1.04 – 34.5	8.64 ± 6.195

DISCUSSION

Of the 1550neonates studied, the male to female ratio in the present study is 0.77. Mean birth weight of neonates present in the study was 2.75± 0.40 kg which is similar to Mangli*et al*.,(2005) study.[7]
The mean cord blood T3 value is72.69 ± 13.12 ng/dl, day 3 T3 value is 82.40 ± 11.76 ng/dl. Cord blood T4 is 9.01 ± 2.227 µg/dl while day 3 T4 is 11.55 ± 3.596µg/dl.Mean cord blood TSH is 8.64 ± 6.195 mlU/L while day 3 TSH value is 2.98 ±2.191 mlU/L. The 'p' value was found to be <0.001 for T3, T4 and TSH valuesbetween cord blood and day 3 venous sample, which is highly statistically significant. In this study we found that cord blood T3 and T4 is less compared to that of day 3 T3 and T4. There is a steady increase in T3 and T4 from day 0 to day 3. While cord blood TSH value is higher compared to that of day 3 values and this decline in TSH value on day 3 is due to the surge in T3 and T4 that occurs in the postnatal period.[8]
During the initial hours after birth 3-6 fold increase occurs in circulating T3 and T4 coincident with an increase in serum TSH. The initial increase in circulating thyroid hormone levels largely result from increase hormone secretion from the thyroid gland. A postnatal increase in serum catecholamine concentration occurs at the time of parturition and thyroid gland is adrenergically innervated. Stimulation of thyroid adrenergic receptor may augment TSH induced changes in the T3, T4 ratio. Thyroid Binding Globulin (TBG) concentration remains relatively constant throughout the newborn period, Free T3 and T4 rise abruptly after birth. The decrease in TSH that followsduring 72-96 hours after birth results from feedback inhibition by T3.[8]
The mean cord blood TSH value in the present study was 8.64 ± 6.195 mlU/L. In astudy done in Ethiopia TSH was measured from cord blood of 1207 consecutivenewborn screening by Immunoradiometric Assay (IRMA). Majority of the newborn screening had TSH values <10 mIU/L, and the study concluded that the cord blood is practical and apparently simple to collect and can be put in to practice for large scale programme such as CH where hospital discharge is within 24 hours of delivery.[9]
The mean value of cord T4 in the present study was 9.01 ± 2.227 µg/dl. Retrospective study conducted by Hardy *et al*.,(2008), found that 13 infants had CH and in 6 of these cord blood T4 was low and in 7 of them cord blood T4 was normal. Cord FT4 identified infants were found to have severe CH and hence the study concluded that cord TSH was more sensitive than Cord FT4 in screening.[10]

CONCLUSION

- The mean value of T3, T4 and TSH was72.69 ± 13.12 (ng/dl), 9.01 ± 2.227 (ug/dl) and 8.64 ± 6.195 (mIU/L) respectively in cord blood.
- Out of 1550 neonates, 339 (21.9%) weighed between 2-2.4 kg, 925 (59.7%) weighed between 2.5-3.0 kg, 223 (14.4%) weighed between 3.1-3.5 kg and 63 (4.1%) weighed between >3.5 kg. The mean birth weight is 2.75 ± 0.40 kg.

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