

Umbilical Cord Blood TSH Levels in Term Neonates: A Screening Tool for Congenital Hypothyroidism

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This study was conducted to find normative values for thyroid stimulating hormone (TSH) in 1200 cord blood samples of term babies whose mothers were not on any thyroid medications. TSH was estimated within 24hrs by enzyme immunoassay. A full thyroid profile, viz, T3, T4, TSH, fT3 and fT4 was done at 7-10 days of age in all babies with cord TSH >20mIU/L. The mean, median and standard deviation for the TSH values for the cohort were 6.13 mIU/L, 5.8 mIU/L and 4.523 respectively. 22 babies with TSH values >20mIU/L were given repeat tests. Hypothyroidism was confirmed in two of these babies. We conclude that a cut off value of TSH >20mIU/L is adequate for neonatal thyroid screening in Indian settings.

Key words: Congenital hypothyroidism, Umbilical cord blood TSH.

CONGENITAL hypothyroidism (CH) is a major preventable cause of mental retardation. It has an incidence of 1 in 4000 births in various neonatal screening programs(1). Neonatal screening programs for detection of CH in neonatal period are widespread in the developed countries for the last three decades(2,3) and are fast gaining momentum in the developing world as well(4-7). 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(7,8). 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(7,8). Mixed cord blood samples for TSH values have compared well with filter paper samples

taken in the first few days of life(9,10). The Indian Academy of Pediatrics recommends the use of cord blood samples for screening for CH(11). Very few reports of cord blood values of TSH or T4 exist in Indian literature(12,13) and thus this study was carried out.

Subjects and Methods

The study was carried out from Jan 2000 to June 2004 in three hospitals in Kolkata. All consecutive deliveries conducted during this period were part of the study. Any one of the authors attended the deliveries as the attending neonatologist.

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 including both from the umbilical artery and vein was obtained. Babies who were born preterm (<37 wk) or weighed <2.5Kg or whose mothers were on any thyroid

medications were excluded.

Records of the mother's age, parity, thyroid status, race, residence, community, blood pressure, diabetes, use of iodine antiseptics on the mother prior to delivery *etc.* were kept. The type of medications/anesthesia given, anesthetic agents including doses used, duration of anesthesia given to the mother till birth of the baby, the type of antiseptics used on the mother were also noted. At birth, the baby was resuscitated and examined by the attending author and weight, sex, time to first cry, Apgar scores were noted. TSH was estimated within 24 hrs by enzyme immunoassay (Microwell TSH EIA) using kit provided by Syntron Bioresearch, Inc. One thousand two hundred samples of umbilical cord blood samples of as many neonates were examined. The mean, median, standard deviation, 1st, 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th centiles were determined. All babies wherein the cord TSH was found to be over 20mIU/L were visited at home at 7-10 days of age and fresh samples for T3, T4, TSH, fT3 and fT4 were taken.

Results

One thousand two hundred samples of cord blood were tested for TSH. Male: female ratio was 622:578 = 1.076:1. The birth weights ranged between 2.5 Kg to 4.3 Kg with an average of 2.84 Kg (*Table I*). Mean (SD) TSH was 6.48 (5.2) mIU/L in boys and 5.75(4.16) mIU/L in girls. *Table II* depicts the TSH values of the entire cohort. TSH values ranged from 0.8-101.2 mIU/L. TSH values corresponding to 3rd, 10th, 25th, 50th, 75th, 90th, 97th and 99th centile were 1.6, 2.5, 3.3, 5.8, 7.0, 9.0, 14.9, and 25.8 mIU/L, respectively. Twenty two infants (1.833%) were recalled for repeat complete thyroid profile. Two babies were finally proved to be hypothyroid after repeat confirmation. The cord TSH values in these

infants were 54 mIU/L and 101.2 mIU/L. There was no dropout amongst the babies approached for repeat testing.

Discussion

Screening for congenital hypothyroidism (CH) is widespread for the last two decades. We have not been able to implement it in India because of several factors, like cost, lack of reliable laboratories on a large scale, and nonavailability of baseline data in our population. Use of cord blood TSH as a screening tool is an attractive proposition because of its simplicity and accessibility. Fuse, *et al.*(9) had shown that mixed cord blood is a good sampling technique for screening for CH. Walfish(10) concluded that cord TSH had a better specificity and sensitivity as compared to cord or filter paper T4 at 3-5 days of age.

Our results show that only 7.5% (90 cases) samples showed a cord blood TSH value of >10 mIU/L. This is comparable to figures from Ethiopia(14). Our mean value was 6.13 ± 5.29 mIU/L, while Feleke, *et al.*(5) observed value of 9.6 ± 7.8 mIU/L in 4206 newborns. Our 97th & 99th percentile were 14.98 & 25.8 mIU/L respectively, whereas Mekennon *et al.*(14) found a 97.8th percentile as 15.4 mIU/L and Kung, *et al.*(15) have quoted a 95th percentile of 16 mIU/L. However, our TSH values were somewhat lower than found by Khadilkar, *et al.*(13) who, in a study of 203 neonates found a mean cord TSH value of 12.3

TABLE I— Weight Wise Distribution of Samples for TSH Estimation.

Weight	No of samples (%)
2.5-2.99Kg	645(53.75%)
3-3.49Kg	324(27%)
3.5-3.99Kg	178(14.83%)
4Kg & above	53(4.42%)

TABLE II—*Umbilical Cord Blood TSH levels.*

Cord TSH level (mIU/L)	No of samples n=1200 (%ages)
Below 4	367 (30.58%)
4- 7.99	630 (52.5%)
8-11.99	153 (12.75%)
12-15.99	21 (1.75%)
16-19.99	7 (0.58%)
20-24.99	9 (0.75%)
25-29.99	2 (0.17%)
30-34.99	2 (0.17%)
35-39.99	3 (0.25%)
40-44.99	1 (0.08%)
45-49.99	3 (0.25%)
50-99.99	1 (0.08%)
above 100	1 (0.08%)

The details of the 13 samples > 25 mIU/L were 25.8, 27.9, 34, 34.2, 35, 35.9, 38.1, 43, 45, 45, 46, 54 and 101.2 (all in mIU/L).

± 4.9 mIU/L Our recall rate for repeat testing was 22 out of 1200 *ie* 1.83%, which compared well with of the large study of Wu *et al.*(7) whose large cohort of 11,000 neonates had a recall rate of 2.27%. Normal cord TSH values show a wide range of 1-38.9 mIU/L(16), and we had used a cut-off of 20 mIU/L, but had we opted for a higher cut-off of 25, 30 or 40 for recall purposes, our recall rates would have fallen to 1.08%, 0.91% or 0.42% respectively. A 5-year prospective study from Thailand(17) used a cut-off value of 30 to begin with and had a recall rate of 1.1% in a large sample size of 35,390 neonates. They subsequently modified their recall policy and raised the cut-off value to 40 leading to a fall in recall rate to 0.43%. However, considering our annual birth rate of about 25 million, a recall rate of close to 2% may envisage calling back almost 500,000 newborns for full thyroid profile. Higher cut-

off values of cord TSH for recall purposes and thus a lower recall rate will vastly improve the economic and practical logistics in any widely organized public health program particularly so in our country.

We had two babies with CH out of a cohort of 1200 giving an incidence of 1 in 600, which is much higher than the world figure of 1 in 4000(1), but other Indian data too have quoted higher incidences as 1 in 248(12) and 1 in 1700(18) and a recent Iranian study found an incidence of 1 in 914(8). Probably geographic and ethnic differences are responsible and of course, this cohort of 1200 samples is too small to assess incidence.

Our figures have shown a comparable trend as with the normative data for cord blood TSH values as reported by various workers across the globe. We conclude that we may safely use the widely used cutoff cord blood TSH value of >20 mIU/ml for purposes of recall for retesting, though from logistic angles a cutoff value of >30 or >40 may be used. Still even larger population-based studies may be done to achieve more credible guidelines, more so to gauge the incidence and epidemiology of CH in our country.

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Key Messages

- Indian normative data for cord blood TSH are comparative with those elsewhere
- Babies with cord blood TSH values >20 mIU/L may be recalled for full thyroid profile when they are >7 days old.

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