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THYROXINE AND THYROTROPIN LEVELS IN CORD BLOOD SERA FROM SOUTH OF IRAN

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ABSTRACT

Birth is associated with significant changes in the hypothalamic-pituitary-thyroid axis and these changes complicate the proper assessment of thyroid function in neonates. Normal values for T_4 (thyroxine) and TSH (thyroid stimulating hormone) in cord blood are not well established. The present study was carried out on 4000 specimens of cord sera of both sexes in order to establish reliable reference values for these hormones. Our data imply that the level of T_4 in cord sera (mean± 1 SD: 10.99±2.46 μg/dL) is less than that of the neonatal period but is comparable to that of older infants. The concentration of TSH (mean ±1 SD: 7.09+4.54μU/mL) is comparable to the level expected in the first week of life but is higher than that of older infants. The values of T_4 and TSH obtained from cord blood of boys and girls did not show any statistically significant differences.

It is suggested that these values can be used as normal reference values for T_4 and TSH in cord blood.

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INTRODUCTION

To assess the effects of iodine deficiency on maternal and fetal thyroid functions, Medeiros and co-workers measured T_4, T_3, rT_3 and TSH in cord blood of newborns from goitrous mothers living in areas with chronic iodine deficiency in South America and compared their data with results of studies on infants from non-endemic areas of both North and South America. There were no significant differences among the various thyroid parameters in different groups of newborns studied.[1]

After Orinda et al. showed an inverse relationship between thyrotropin (TSH) concentration in cord blood and birth weight of normal newborn infants in Kenya, other investigators have suggested moderate iodine deficiency during the perinatal period in Kenya as a possibility.[2,3]

In 1984, Sava et al. studied thyroid function tests in newborns from three areas of Sicily with different iodine intake. Their studies indicate that in newborns from areas of iodine deficiency, there is a higher frequency of elevated TSH levels and low T_4 values than is found in areas where iodine intake is normal.

As the normal range of T_4 and TSH may vary according to the geographical region, it is advisable for each area to establish its own normal range.

In this paper we report the results of serum T_4 and TSH measurements in cord blood of newborns from Fars province, Southern Iran, which is an iodine deficient area.

MATERIALS AND METHODS

Four thousand consecutive cord blood samples from healthy full-term newborn babies following normal vaginal delivery were collected in order to determine reference values of T_4 and TSH. This study began in July 1990, covering five cities of Fars province, Southern Iran, namely

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Shiraz, Marvdasht, Jahrom, Kazeroon and Sepidan. 52% of the samples were from girls and the remaining 48% from boys.

Cord blood was obtained after an uncomplicated vaginal delivery and the umbilical cord was ligated from the placental side. After being separated by centrifugation, sera were stored in a central laboratory at -20°C until analysis.

Thyroid stimulating hormone was measured by immunoradiometric assay (Celltech Diagnostics, Slough, United Kingdom) with a normal reference range of 0.3 to 3.5 μU/L. Total serum T_4 was measured by radioimmunoassay (BYK Sangtec Diagnostic) with a normal adult trange of 4.5-12.0 μg/100 mL. The interassay and intraassay coefficients of variation for TSH and total T_4 were 4.5 and 4.2 percent, and 6.4 and 4.7 percent, respectively.

Student's t-test was used for statistical analysis of the data and variances from the means are indicated as standard deviations.

RESULTS

Serum T_4 concentration in cord sera ranged from 3.6 to 20 μg/dL with a mean value of 10.99 μg/dL. TSH concentration ranged from 0.77 to 24.91 μU/mL with a mean value of 7.09. Distribution of cord blood TSH concentration is shown in Fig. 2.

Based on the results obtained from this investigation, there is no statistically significant difference between the values of T_4 and TSH for boys and girls (Table I).

Values for T_4 were found to have a normal or Gaussian distribution as shown in Fig. 1, and that of TSH values had a skewed or chi-square distribution as shown in Fig 2.

DISCUSSION

Congenital hypothyroidism often causes irreversible mental retardation if thyroid hormone replacement therapy is not begun during the first few months of life.[5] Different screening programs have successfully helped in early diagnosis and treatment of congenital hypothyroidism. Although several investigators have meausred TSH and T_4 in cord and serum samples from both premature and term infants, every reference laboratory needs to establish its own normal values in order to validate its own data and technical expertise.[8,9,11-14]

Therefore it is important to have normal values for this age group to avoid misdiagnosis and incorrect treatment. The present study was undertaken to establish standard reference values for better evaluation of thyroid function in cord sera in Iran.

O'Halloran and associates reported T_3 resin-uptake and T_4 data for children of both sexes from birth to 3 years.[9] In their study T_3RU and total T_4 were measured in cord blood

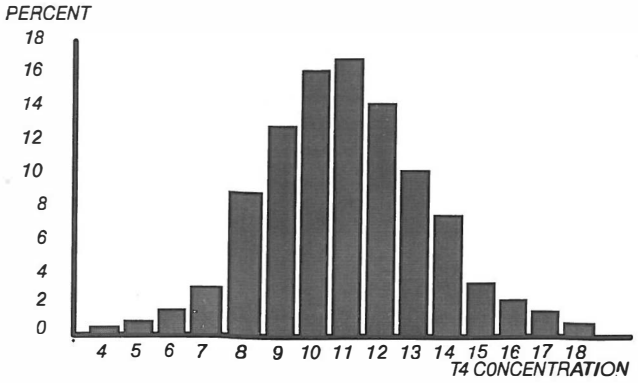

Fig. 1. Distribution of cord blood T_4 concentration.

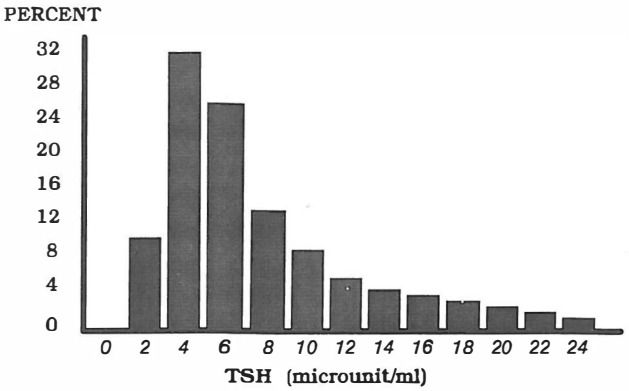

Fig. 2. Distribution of cord blood TSH concentration.

Table I: T_4 and TSH values in cord sera of boys and girls (n=4000).

T_4, TSH	mean±SD boys	mean±SD girls	P-value
T_4 (μg/dL)	11.05±2.57	11.15±2.35	0.03
TSH (μU/mL)	8.15±7.28	8.01±7.51	0.07

of 64 infants. Total T_4 ranged from 7.3 to 15.3 μg/dL (mean 11.3).

Czernichow et al.[10] measured TSH and T_4 in cord blood of 20 normal newborns. The TSH and T_4 levels ranged from 2.1 - 10.7μU/mL (mean± S.D: 5.5±2.5) and 7.8-19.7 μg/dL (mean±SD: 12.6 ±4.0), respectively.

The present data show that T_4 level in cord sera is comparable to T_4 levels reported by O'Halloran and associates,[9] but the values are higher than those reported by Czernichow et al.[10] TSH level is also higher in the present study than that of Czernichow's study.

Czernichow et al. demonstrated that TSH concentration in maternal sera is lower than that of cord samples.[10] It seems likely that the TSH measured at birth in cord samples is a true reflection of the fetal environment and is only fetal in

origin.[10]

It is assumed that high T_4 levels in cord sera are due to increased thyroxine binding globulin (TBG) secondary to estrogenic effects from the mother.[9]

Our data, similar to those of other investigators, show that T_4 and TSH values in cord sera differ from those of adults.[6]

Penny et al. measured cord serum thyroxine and TSH levels of 101 infants (50 males and 51 females). Similar to our data, they concluded that levels in females and males did not differ significantly.[12, 13] They also concluded that serum TSH and T_4 levels did not correlate with birth weight. The result of the study of Mitsuda et al. which examined the relation between TSH concentration in cord blood and birth weight[14] was comparable to that previously reported by Penny et al.

Miyamoto et al. measured the cord serum levels of TSH in 922 neonates delivered by mothers who had no thyroid disorder, to evaluate the influence of mode of delivery on the fetal pituitary-thyroid axis.[15] The mean cord serum TSH level in neonates delivered by vacuum extraction was 16.3±10.0μU/mL (n=30), which was significantly higher than the level following normal vaginal delivery (9.5 ±6.0 μU/mL, n=6222, $p<0.005$). The mean cord serum TSH level following elective cesarean section was 6.5±3.1 μU/mL (n=79), and this was significantly lower than after normal vaginal delivery.

For evaluating the effect of perinatal factors on TSH and thyroxine levels in cord blood, Fuse et al. measured the concentration of these hormones in cord blood of 124 healthy term neonates.[16] 88 infants were born by normal vaginal delivery, 25 were delivered by vacuum extraction and 11 by cesarean section. There was no significant difference among the three infant groups concerning mean TSH levels. Birth weight, the infant's sex and duration of labor had no effect on cord serum TSH and free thyroid hormone levels in the neonates born by normal vaginal delivery.

Basarir et al. studied the cord blood levels of TSH in 56 mature and healthy newborns. TSH levels observed in their study is comparable to our results.[17]

To assess the possible effects of chronic iodine deficiency on maternal and fetal thyroid function, Medeiros et al. measured T_4, T_3, rT_3 and TSH in cord blood of infants born in areas with mild to severe iodine deficiency and areas with no iodine deficiency in South and North America.[1] Their results showed no differences among the various thyroid parameters in the groups of newborns studied.[1] Our findings are consistent with Medeiros' report, although some investigators have reached different conclusions on the basis of their studies.[4]

The present study, similar to other reports, [14-17] suggests that TSH levels in cord blood might be a feasible alternative specimen for a TSH screening program in countries where neonatal blood is not easily attainable.

Considering the sample size (4000) in the present study, these data can be used as standard reference values for neonatal screening concerning congenital hypothyroidism, the importance of which cannot be over-emphasized.

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