Thyroid Function: Fetal-Maternal Relationship at Term

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Tamer Mungan, Kubilay Vicdan, Hakan Yalcin, Nilgun Turhan (Dr. Zekai Tahir Burak Women's Hospital, Ankara, Turkey.)

Abstract

The present study was undertaken to examine serum parameters of thyroid function at term in normal pregnant women and their normal fetuses. Paired sera from 56 mothers and their respective newborn infants' umbilical cord were obtained at parturation. Maternal and fetal TSH, PT4, T4, FT3 and T3 levels were measured and the differences between these two groups were analysed. The levels of fetal serum TSH (8.86±5.82 lu/ml) were significantly higher than maternal TSH levels (3.32±3.3 lu/mi) (P <0.001), but there was no significant difference between the fetal and maternal T4, FT4 and T3. On the other hand, cord FT3 levels (1.7±1.2 pg/dl) were significantly lower than maternal levels (2.7±1.4 pg/dl) (P<0.001) (JPMA 44:104, 1994).

Introduction

Until recently, fetal thyroid development has been based on histologic studies or blood samples obtained in early pregnancy at hysterotomy. Cordocentesis permits antenatal assessment of thyroid function in normal and abnormal fetuses. Moreover, it is also important to know thyroid hormone levels at term.The present study was undertaken to examine serum parameters of thyroid function at term in normal pregnant women and their normal fetuses.

Subjects and Methods

Fifty-six full term pregnant women were included in this study. There was no congenital anomaly in the study group. Fetal anemia and uteroplacental insufficiency symptoms were not present. All subjects had normal vaginal delivery. Paired sera from 56 mothers and their respective newborn infants' umbilical cord were obtained at parturation. Blood samples were collected in vacuum tubes and centrifugated immediately (2000 r/min for 10mm. The serum was kept at -20°C until assays were done. Serum free T4 (FT4), T4, free T3 (FL) and T3 levels were determined by radioimmunoassay using available kits (Amerlex M RA kits). Serum TSH was determined by Gama BCT TSH monoclonal antibody coated tube IRMA. Maternal and fetal TSH, FT4, T4, FT3 and T3 levels were measured and the differences between these two groups were analysed. Chi-square test and Mann-Whitney or Wilcoxon two sample tests were used for statistical analysis.

Results

Mean age and mean birth weight of mothers and new borns were 26.5±2.3 years and 3600±320g respectively. The mean TSH, T4, FL and FT3 and T3 values are shown in Table.

Table. Maternal and fetal TSH, T_4 FT_4, T_3 and FT_3 levels in term pregnancy.

	TSH (Iu/ml)	T_4 (micg/ml)	FT_4 (ng/ml)	T_3 (ng/ml)	FT_3 (pg/ml)
Maternal serum	3.32±3.39	12.27±4.08	1.05±0.29	1.70±0.48	2.72±1.43
Cord blood	8.86±5.84	10.67±3.39	1.33±0.24	0.38±0.15.	1.70±1.27
P*	<0.001	>0.05	>0.05	>0.05	<0.001
r**	0.32	-0.73	0.30	0.38	0.47

* = Student 't' test
** = Correlation analysis

The levels of fttal serum TSH (8.86±5.84 Iu/ml) were significantly higher than maternal TSH levels (3.32±3.39 Iu/ml) (P <0.001). No significant differences between the fetal and maternal T4, FT4 and T3 levels were noted. Cord FT3 levels
(1.7± 1.2 pg/dl) were significantly lower than maternal FT3 levels (2.72±1.43 pg/dl) (P <0.001).

Discussion

Fetal development is dependent on the placenta, which regulates substrate supply, provides excretory functions and synthesizes various polypeptide and steroid hormones that influence different aspects of maternal and fetal metabolism[1]. There are variations in placental thyroid hormone permeability between human and others species. Human placenta is permeable to thyrotropin releasing hormone (TRH) and there is evidence to suggest that it is also capable of TRH synthesis[2]. This extra hypothalamic TRH production thus leads to high levels of TRH in fetal serum. The placenta also produces polypeptide hor-. mones with thyrotropin- like bioactivity. These hormones achieve peak level at the end of the first trimester causing a transient increase in free thyroid hormone levels in maternal serum and transient sujpression of maternal TSH secretion[4]. However, they have little influence on fetal thyroid function. Fetal thyroid ontogenesis has been characterized in three phases: embryogenesis, hypothalamic maturation and development of hypothalamic-pituitary-thyroid system control[4]. Embryogenesis is largely completed by the 10th to 12th weeks of gestation. Hypothalamic maturation including the development of pituitary portal vascular system, begins at the 6th-7th weeks and is completed at 3Oth-35th weeks of gestation[5]. Maturation of cuntrol of thyroid hormone secretion is superimposed on progressive increase in the fetal serum thyroxine-binding globulin (TGB) concentration during the 10 to 35 weeks of gestation. Vyas et al.[6] have reported higher TSH and lower thyroid hormone levels in hypoxaemia growth retarded fetuses due to uteroplacental insufficiency. Increased serum TSH in IUGR fetuses may be due to pituitary stimulation by low thyroid hormones, increased catecholamines found in hypoxaemic growth retardation and increased brain perfusion[6]. Nicolaides et al.[7] have found higher TSH, 'free and total Tj-T4 levels when compared to control subjects in apemic fetuses due to red blood cell isoimmunization. On the other hand, the existence of thyroid dysfunction in chromosomally abnormal fetuses has recently been documented[8]. Because of these observations, IUGR fetuses, Rh isoimmunized fetuses and fetuses with congenital anomalies

were excluded from this series. The secretion of TSH and thyroid hormones is minimal until mid-gestation[1]. At this time fetal thyroid gland iodine uptake and serum T4 concentrations begin to rise[4,9]. TSH is also present in the 12 weeks old fetus and rapidly increases thereafter, with levels parallel to levels of Ft. The TSH level is higher in the fetus than in mother and at term the fetal value is more than twice that found in the mother. At term, cord blood TSH levels were found to be 8.5±0.7 micU/ml[10]. In this study, cord blood TSH levels were significantly higher than maternal serum TSH levels (P< 0.00 1). This hypersecretion of TSH, within the first minute of life, may be due to the sudden drop in fetal body temperature after birth. Exposure of the fetus to the extrauterine environment evokes an acute pituitary TSH release that stimulates a prolonged release of thyroid hormones. Sçrum TSH levels make a peak 30 min. after birth and rapidly increase in the first 24 hours after birth. T4 is detectable in the fetal serum by the 12th week of gestation. Thereafter, both the total T4 and FT4 increase linearly in relation to the gestational age. At term the T4 reaches a level of 12±4.0 micg/dl in the umbilical cord serum, which is 10% to 20% lower than the corresponding value in maternal serum. In human infants with thyroid agenesis or a total organification defect, the average cord serum T4 levels is about 4 micg/dl, whereas the normal mean level is about 11 icg/dl11. In our study, cord blood T4 concentrations were found to be 10.67±3.39 micU/ml and maternal serum levels were 12.27±4.08 micU/ml. These results were similar to the findings of Abuid et al.[10]. The FT4 level in the cord blood was equal to or higher than that in the maternal blood. Serum total and free T4 levels gradually increase to peak levels at the first 24 to 36 hours and then slowly decrease over the first week of life. Thyroid hormones undergo several types of biochemical transformation in tissue. These include deiodination, side-chain metabolism and conjugation (with sulfate or glucuronide). Monodeiodination of the thyroid hormones is the most important pathway of thyroid hormone metabolism. Several enzyme activities are involved in this monodeiodination: two types of outer-ring monodeiodinase (type I and II) activity and an inner-ring iodothyronine monodeiodinase (type III). Type I deiodinase, predominantly expressed in liver and kidney is inhibited by propyithiouracil (PTU) and stimulated by thyroid hormone. Type II deiodinase activity, predominantly located in brain, pituitary and brown adipose tissues is insensitive to PTU and inhibited by thyroid hormone. Type I activity in liver, kidney and perhaps muscle probably accounts for most of the peripheral deiodination of T4. The type II deiodinase probably plays an important role in providing intracellular T3 to those tissues that are dependent on T3 during fetal life, whereas the activity of the type I enzyme which provides increased serum T3 levels, increases only during the final weeks of gestation and during postnatal life. Type III deiodinase is present in fetal liver, brain, skin and placenta. This enzyme catalyzes the conversion of T4 to T3 and to 3,3'-diiodothyronine. Studies of the ontogenesis of this enzyme system in rodents and sheep have shown a predominance of type III enzyme activity in the fetal period[1]. In the fetus, T4 is metabolized predominantly to reverse T3, rather than to T3. The T3 and FT3 levels in the cord blood have been shown to be 30% to 50% of the maternal concentrations at term. In this study cord blood and maternal serum T3 levels were found to be
0.38±0.15 ng/ml and 1.7±0.48 ng/ml respectively. On the other hand FT3 levels were 1.7±1.27 pg/rnl and 2.72±1.43 pg/ml respectively. There was a significant difference in TSH and free T3 levels between maternal and fetal cord blood at parturation (P <0.001).

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