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ORIGINAL ARTICLE

Thyroid Function in Mothers During the Process of Normal Delivery

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Marked changes in maternal thyroid activity occur in pregnancy and during labor. The present study investigates the effect of labor on thyroid function and the role of thyroid hormones during this process. Materials and Methods: Thyroid function was studied in 64 pregnant primigravida women. The study group comprised of 32 full term pregnant women scheduled for spontaneous vaginal delivery, while the control group included 32 pregnant women at around 32 weeks of gestation. Serum total T3 (TT3), total T4 (TT4) & thyrotropin (TSH) were estimated by high-sensitive radioimmunoassay. In the study group, blood samples were obtained during various phases of labor; Phase A: onset of labor; Phase B: within 2 hours of delivery of placenta and membranes and phase C: 24-48 hours after delivery (immediate puerperium). Results: Mean age of the study group was 23.46±3.07 years, and that of controls was 23±2.8 years. In Phase A, serum TT3 & TSH levels were significantly higher than in controls [1.479±0.52 vs 1.248±0.3 ng/mL & 3 (0.9-6.5) vs 1.2 (0.4-3) µIU/mL respectively; P< 0.05]. In Phase B, there were fall in levels of TT3, TT4, but TSH decreased significantly [1.8(0.6-6) vs 3 (0.9-6.5) µIU/mL; P< 0.05]. In Phase C, TT3 showed significant fall [1.117±0.39 vs 1.421±0.4 ng/mL; P< 0.05]. Conclusion: All the values of thyroid function test were within normal range in controls & study group in all phases. All alterations, the significant rise in TT3 in Phase A, and the fall in phase C and the significant rise in TSH in Phase A and the fall in Phase B, seen during labor seemed to be need based and was significantly influenced by stress present during labor.

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Introduction

Pregnancy & labor is accompanied by profound alterations in the thyroidal economy, resulting from a complex combination of factors specific to the pregnant state, which together concur to stimulate the maternal thyroid machinery [1]. Increased thyroidal stimulation, in turn, induces sequence of events leading to physiological adaptation of the thyroidal economy observed in healthy iodine-sufficient pregnant women[1].

Thyroid hormones triiodothyronine (T3) and thyroxin (T4) are one of the major catabolic hormones of our body. In the circulation, whole T4 originates from thyroid secretion but most T3 (80%) is produced extrathyroidally from T4 deiodination[2]. Formation of T3 from T4, secreted by the thyroid is the major pathway through which thyroid hormones exerts their effects[3].

Conversion of T4 to T3 may be influenced by various conditions and circulating T3 is a less reliable reflection of thyroid hormone production than T4.

Thyroid binding globulin (TBG) increases beginning early in the 1st trimester, and reaches its zenith at 20 weeks, stabilizing at approximately double baseline value for the remainder of the pregnancy;[4,5] in the 3rd trimester , there is high concentration of TBG under influence of increasing estrogen during pregnancy and altered glycation of TBG that inhibits its degradation[6]. This results in a marginal fall in free T3 (FT3) & free T4 (FT4) levels in the 3rd trimester, in iodine sufficient regions thus resulting in slight rise in serum thyroid stimulating hormone (TSH) levels near term1; hence in this trimester, there is increased level of TSH (due to fall in FT3 and FT4) despite of increase in total T3 (TT3) & total T4 (TT4) hormones[5,7,8].

At term, gestation is terminated by onset of labor or parturition. Parturition is very laborious process requiring high generation of pressure to deliver a baby and very often the mother is faced with sudden heavy bout of pain. To generate this pressure and to withstand this pain, there is heavy expenditure of energy by catabolic hormones.

Thyroid hormones have important metabolic and developmental functions. As thyroid hormones are important to maintain basal metabolic rate (BMR), they help to increase basal metabolic rate during pregnancy and various other stressful conditions[9-11].

These hormonal changes and metabolic demands occur not only in pregnancy, but also in labor and puerperium and result in profound alteration in the biochemical parameters of thyroid function. Important changes in thyroid economy during various trimesters of pregnancy have been studied extensively. However there is little information from India about thyroid economy during labor and role of these thyroid hormones in labor, and the data reported on thyroid function during labor and immediate puerperium vary.

Banovac K et al. reported that after delivery, serum TT3 and T4 fell transiently with a simultaneous increase in reverse T3, whereas serum TSH concentration showed no significant variation[12]. González-Jiménez reported that serum TSH levels showed a slight increment during gestation with a significant decrease ($p<0.01$) in the early postpartum period[13]. Ye X et al. found that serum TSH levels were at their highest levels after delivery[14]. The present study was hence undertaken to evaluate thyroid function during various stages of labor in healthy iodine-sufficient pregnant women.

Material and Methods

The study was conducted between October 2009 and March 2010, in the Indira Gandhi Govt. Medical College, Nagpur, India. Subjects were from Nagpur region, an iodine sufficient area, based on data available from Urinary Iodine Excretion studies, conducted in the region[15]. The study group (n=32) comprised of young healthy, primigravida full term pregnant females, aged 18-32 (23.46±3.07) years who were in labor, admitted at the institution for delivery and expected to have spontaneous full term vaginal delivery. Thirty-two age matched (23±2.8years), normal healthy pregnants, primigrivida, attending ANC-OPD in the Obstetrics and Gynecology Department of the institution, made up the control group.

The protocol was approved by the institutional ethics committee and following selection of subjects, informed consent was obtained from them. Serum TT3, TT4 and serum TSH levels were assessed in both groups; to do this, 3ml of Blood was, in turn, drawn from the antecubital vein. Samples were collected with all aseptic precautions, using sterile needles and syringes in plain sterile bulb. In the controls, samples were obtained during their routine ANC-OPD visit, while in the study group, samples were taken on three occasions: Phase A (during

stage I of labor – from initiation of labor pains to full dilatation of cervix); phase B (2 hours after stage III of labor, i.e., after delivery of placenta & membranes) and phase C: (24-48 hours after delivery – immediate puerperium). Samples were kept undisturbed for 30 minutes and centrifuged at 3000rpm for 15 minutes. Serum was separated; we opted for use of monoclonal antibody in ELISA Test, which eliminates cross reactivity with other hormones. Quantitative determination of TT3 & TT4 concentration was carried out using ELISA. Quantitative deter-mination of TSH was carried out using streptavidin biotin technology, which is a solid phase sandwich ELISA method. Results of normal values obtained for healthy adults were follows: TT3: 0.52-1.85 ng/mL; TT4: 4.8-11.5 µg/dl, and serum TSH: 0.39-6.6 micro IU/mL.

Statistical Analysis

Results of TT3 and TT4 were reported as mean ± standard deviation and TSH was expressed as median and range. Statistical testing was done by unpaired student's 't-test' for comparing thyroid function between controls and study group, while paired 't-test' was used for comparing thyroid function in the study group during phases A, B, and C. Statistical significance was taken as $P<0.05$.

Results

Table 1 shows serum T3, T4 and TSH values in the control and study groups during phases A, B and C; all levels were within normal range. Table 2 compares serum TT3, TT4 &TSH levels among the various groups.

Table 1. Serum triiodothyronine, thyroxin and thyroid stimulating hormone levels in the control and study groups during three phases of labor

		Controls (n=32)	Study group (n=32)		
			Phase A	Phase B	Phase C
TT3 (ng/mL)	Mean	1.248	1.479	1.421	1.117
	s.d.	0.309	0.522	0.405	0.392
TT4 (µgm/dL)	Mean	10.115	9.815	9.196	9.709
	s.d.	1.08	2.746	2.31	2.390
TSH(µ IU/mL)	Median	1.2	3	1.8	2.45
	range	0.4-3	0.9-6.5	0.6-6	0.4-6.5

At onset of labor (Phase A) serum TT3 and TSH levels were significantly higher than those of controls at 32 weeks, while levels of TT4 were non significantly lower than those of controls. (Table 2).

Immediately after delivery (Phase B) the serum values of TT4 were significantly lower and TSH was significantly higher than those of controls at 32 weeks; however serum TT3 was non significantly higher than that of controls.

In the study group, values TT3 & TT4 returned to baseline, similar to those of the controls at 32 weeks in immediate puerperium (Phase C), while serum TSH level was significantly higher in puerperium than that of controls.

Table 2. Comparison and analysis of serum TT3, TT4 and TSH levels among various groups

		Control vs study group-phase A	Control vs study group-phase B	Control vs study group-phase C	Study group-phase A vs B	Study group-phase B vs C	Study group-phase A vs C
TT3	P-value	0.018*	0.06	0.07	0.22	5×10^{-6}	6.8×10^{-7}
TT4	P-value	0.28	0.02*	0.19	0.067	0.09	0.39
TSH	P-value	1.2×10^{-7}	0.005	8.9×10^{-5}	8.9×10^{-9}	0.07	0.052

* Numbers represent P value

Variation in thyroid hormone levels during various phases of labor

Variation in thyroid hormone levels during various phases of labor are shown in diagram 1. A comparison of thyroid function, during various phases of labor, showed that there was fall in serum TT3 from onset of labor (Phase A) to the period immediately after delivery (Phase B); then again a significant fall was seen in immediate puerperium (Phase C). Although no significant variation was observed in serum TT4 during the various phases of labor, a fall was seen in serum TT4 immediately after delivery (Phase B) and slight rise was observed in immediate puerperium (Phase C). In case of Serum TSH level, a significant fall was seen immediately after delivery (Phase B), and a non significant rise was observed in immediate puerperium (Phase C).

Discussion

For healthy pregnant women with iodine sufficiency, the challenge faced by the maternal thyroid gland is to adjust the hormonal output in order to achieve and thereafter maintain the new equilibrium state until term[1]. Many changes occur in thyroid function during the transition phase from the non–pregnant to the pregnant state, changes which stabilize by the end of 2nd trimester or the onset of the 3rd trimester[16.] We selected pregnant women at 32 weeks of gestation as a control group for assessing and comparing the changes that occur in thyroid function, to those seen in full term pregnant women undergoing spontaneous vaginal delivery.

Nutrients are stored in early pregnancy to meet the feto-placental and maternal demands of late gestation, labor and lactation. During pregnancy the demand of thyroid hormones increases to about 30-50 %, an increase the thyroid has to cope with [17].There is biochemical evidence of functional stimulation of the thyroid, such as an elevation in serum thyroglobulin levels, preferential T3 secretion, increased T3/T4 ratio and slight increases in basal TSH at delivery[18,19]. The TT3 level may rise at the onset of labor to stimulate metabolism, and to metabolize these stored nutrients to meet extreme high energy demands faced during labor. In labor, a state of physical and mental stress, there is a heavy expenditure of energy, which is provided by metabolism of nutrients. The concentration of T3, one of the main catabolic hormones, may increase at the onset of labor; hence the elevation in levels of serum TT3 during labor may be to adjust internal environment of mother to meet the additional requirements imposed during labor by increased metabolic demands, indicating that a significant rise in serum TT3 at onset of labor may be a physiological adaptation enabling energy during high metabolic needs. Despite T4 being the main hormone secreted by thyroid gland, it is biologically less active than T3. As already mentioned, there occurs near term a preferential secretion of T3 by the thyroid, and a raised T3/T4 ratio and also because of inner deiodenase activity of placenta[20-24]; T4 is converted to rT3 or T3 resulting in increased turnover of T4 and a state of relative hypothyroxenemia; hence

there is fall in total serum T4 level at the term[25]; T4 acts as precursor of T3, the major active form of the thyroid hormone, about 80% of which is produced in the body is derived extrathyroidally from T4 deiodination[3,26].Thus magnitude of stress, energy expenditure during labor, perineal injury, blood loss, and physiological status of mother are the factors that change the mother's metabolism rate, which may be responsible for variation of T4 during different phases of labor; T4 level is equilibrated in circulation on a manufacture and expenditure basis.

Levels of serum TT3 and T4 decline immediately after delivery, the fall being significant only in the case of TT3. Levels of the serum thyroid hormone are determined not only by their synthesis/secretion but also by their metabolism[27]. Fall in thyroid hormone levels (TT3 and TT4) during this period may be due to expenditure of these hormones to produce large amount of energy which is required during any normal delivery. Like in other stressful situations, delivery influences peripheral T4 metabolism, causing increased conversion of T4 to rT3 rather than to T3, resulting in a fall in both TT3 and TT4 during delivery; this finding is in accordance with that of Banovac K, who observed a transient fall in free and TT3 and T4 immediately after delivery[12] Variations in TT3 and TT4 seem to be need based.

Serum TT3 level shows a significant decline in immediate puerperium, in which period, all metabolic and hormonal changes begin to revert back to the pre-pregnant state, and serum TT3 levels, which increased during pregnancy, now start to decline in puerperium, to reach their pre pregnancy values. Thus normalization of thyroid function begins to start in puerperal period[19].

In the third trimester there is high concentration of TBG[7]; T3, and especially T4, which mainly binds to TBG, results in decline in FT3 and FT4 levels in this trimester,[14,16,28] and thereby a rise in serum TSH levels near term,[14,16,29] (in the last trimester of the gestation period), resembling those of a slight thyroid insufficiency[16]. This might be the reason behind the significant rise in serum TSH levels during delivery, in all 3 phases, when compared to the controls at 32 weeks.

Immediately after delivery, a fall was seen in serum TSH level, which may be due to stress. The whole process of labor is stressful, at onset of labor (stage I of labor) the stress is due to pain caused by uterine contractions and stretching of the cervix; stage II is more stressful because of increased painful uterine contraction to generate high intrauterine pressure, trauma to cervix and perineal laceration during delivery of the baby; again exhaustion and bleeding associated with expulsion of placenta make stage III stressful; in Phase B, immediately after stage III, stress continues because the mother is still exhausted, and there is continuing pain due to the trauma to the cervix, blood loss and perineal laceration during delivery. In the puerperal period, or Phase C, there is fall in the stress levels, as observed in our study, immediately after delivery or phase B, a more stressful phase. Stress has inhibitory effect on thyrotropin releasing hormone (TRH) secretion, [30] and hence a decline in TRH secretion results in a fall in serum TSH level immediately after delivery. Various emotional reactions can also affect the output of TRH and TSH and therefore indirectly affect the secretion of thyroid hormones. Excitement and anxiety-conditions that greatly stimulate the sympathetic nervous system, cause an acute decrease in TSH secretion[31]. The body responds to stress by releasing adrenalin and non-adrenalin and glucocorticoid, which also inhibits TSH secretion;[30] this may be the reason behind the significant decline in serum TSH immediately after delivery, and its recovery in immediate puerperium, when stress decreases[13]. Results of thyroid function tests should be cautiously interpreted

considering physiological variat-ions during pregnancy, labor and puerperium.

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