

Analysing Maternal Thyroid Function and its Relationship to the Duration of the First Stage of Labour

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Received: 22-03-2023 / Revised: 25-04-2023 / Accepted: 23-05-2023

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Conflict of interest: Nil

Abstract

Objective: The typical course of labor is significantly influenced by the mother's thyroid function. It is yet uncertain if a mother's thyroid function impacts how long the initial stage of labor lasts. This study's objectives were to measure FT4, TSH, and TPOAb throughout pregnancy and to assess any potential effects they could have on the early stages of labor.

Method: Within a year, 150 pregnant women visiting Nalanda Medical College, Patna were found to have thyroid peroxidase antibody (TPOAb), thyroid-stimulating hormone (TSH), and free thyroxine (FT4) levels in their maternal blood. The length of the first stage of labor was examined concerning maternal thyroid function using a multiple linear regression model.

Results: The duration of the first stage of labor was shown to be inversely correlated with FT4 levels in the second and third trimesters ($\beta = -1.31$ h, 95% CI: -2.27, 0.31, $P < 0.02$; $\beta = -0.34$ h, 95% CI: -0.60, -0.11, $P < 0.02$). The length of the first stage of labor was shown to be positively correlated with TSH level in the third trimester ($\beta = 0.11$ h, 95% CI: 0.05, 0.17, $P < 0.002$). First-stage labor was significantly linked with TPOAb (IU/mL) per unit increase in the second and third trimesters ($\beta = 0.07$ h, 95% CI: 0.02, 0.13, $P = 0.01$; $\beta = 0.08$ h, 95% CI: 0.01, 0.14, $P = 0.02$).

Conclusion: These results imply that maternal FT4, TSH, and TPOAb may serve as significant indicators of the early stages of labor.

Keywords: Vaginal Births, Free Thyroxine, Thyroid-Stimulating Hormone, Thyroid Peroxidase Antibodies, And The Initial Stage Of Labor.

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Introduction

The health of mothers and their newborn children has suffered greatly as a result of excessive cesarean delivery rates. India has undertaken several local, regional, and governmental attempts to promote vaginal birth [1]. Even for those who had labor dystocia, the majority of pregnant women delivered vaginally even though the cesarean birth rate reached 34.9% in 2018 [2].

Three steps make up the natural labor process [Figure 1]. Regular contractions that cause the cervix to dilate and soften, shorten, and thin (effacement) mark the beginning of the first stage of labor. This enables the infant to enter the delivery canal. Of the three stages, the first is the longest. After the baby is born and before the placenta and membranes are released, the third stage of labor begins. The second

stage of labor lasts from the moment the cervix is fully dilated until the baby is born. The prolonged first stage of labor has been linked to a higher risk of cesarean

section, chorioamnionitis, hysterorrhexis, postpartum hemorrhage, and other unfavorable outcomes for mothers [3].

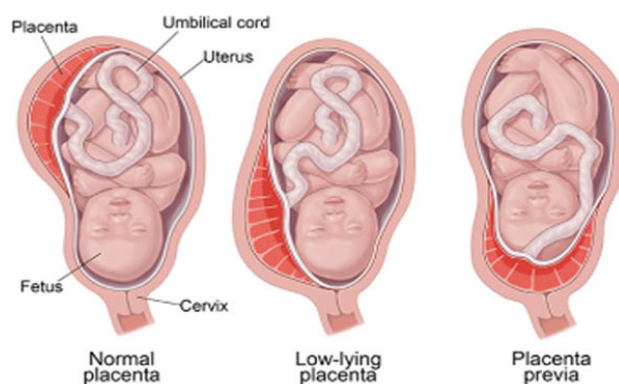


Figure 1: Stages of Natural Birth

More caution is warranted in light of mounting and convincing evidence that a protracted initial stage of labor may have detrimental effects on both mothers' and newborns' health [4]. Whether prenatal biological changes have an impact on the initial stage of labor is still not completely understood. Thyroid dysfunction is one of the most common endocrine problems during pregnancy, and current research reveals that maternal thyroid function, functioning as an important biological indicator throughout pregnancy, plays a key role in proper reproduction in numerous pathways [5]. Furthermore, it has been shown that maternal thyroid dysfunction is linked to poor pregnancy outcomes, including spontaneous abortion, premature delivery, and even infant death [6]. However, there is currently a dearth of epidemiological proof linking maternal thyroid function to the early stages of labor.

We set out to quantify FT4, TSH, and TPOAb throughout pregnancy to assess their possible influence on the first stage of labor because there is so little data on the connection between maternal thyroid function and the length of the first stage of labor. It would be very important to better understand the relationship between

thyroid dysfunction and unfavorable delivery outcomes if there was a correlation between maternal thyroid function and a longer first stage of labor.

Methods

Study Design: This prospective study was carried out Nalanda Medical College, Patna, within a year.

Methodology: The following information was taken from medical records provided by obstetricians: gestational age at delivery, maternal age, gestational ethnicity, marital status, medical insurance, parity, mode of delivery, type of labor, fetal positions, length of the first and second stages of labor, birth weight, and length, baby gender, Apgar score (1 min/5 min), and mode of delivery. Obstetricians identified pregnancy-related issues (such as thyroid dysfunction) by the recommended standards.

In the first trimester (13 gestational weeks), second trimester (13-26 gestational weeks), and third trimester (27 gestational weeks), maternal serum samples were taken, correspondingly.

During each trimester, the Architect system (Roche) was used to conduct electro-chemiluminescent microparticle immunoassays to measure the levels of

FT4, TSH, and TPOAb in the maternal serum. Serum FT4, TSH, and TPOAb had intra-assay coefficients of variation (CV) that were, respectively, 4.73, 4.16, and 6.33%. The TPOAb test has a detection limit of 10 IU/mL and a cut-off value of 1.74 IU/mL. TSH >5.16 mIU/L and FT4 12.90 pmol/L in the first trimester; TSH >5.21 mIU/L and FT4 9.80 pmol/L in the second trimester; and TSH >6.83 mIU/L and FT4 9.11 pmol/L in the third trimester are the diagnostic thresholds for gestational hypothyroidism. TSH >5.16 mIU/L with normal FT4 level in the first trimester; TSH >5.22 mIU/L with normal FT4 level in the second trimester; and TSH >6.83 mIU/L with normal FT4 level in the third trimester are the diagnostic thresholds for gestational subclinical hypothyroidism. TSH 0.04 mIU/L and FT4 >22.34 pmol/L in the first trimester; TSH 0.38 mIU/L and FT4 >17.25 pmol/L in the second trimester; and TSH 0.61 mIU/L and FT4 >15.70 pmol/L in the third trimester are the diagnostic thresholds for gestational hyperthyroidism.

Sample Size: 150 pregnant women were included in this study, based on inclusion and exclusion criteria.

Inclusion criteria: Women with vaginal delivery and were all not receiving treatment with thyroid hormone replacement or anti-thyroid medications.

Exclusion criteria: Women who did not have at least one thyroid function test or who were pregnant but lacked appropriate gestational age information were also eliminated. Participants who had type 1/2

diabetes, high blood pressure, subclinical hyperthyroidism, subclinical hypothyroidism, and other thyroid conditions before becoming pregnant.

Statistical analysis: For categorical variables, counts and percentages were used to characterize them, whereas mean and standard deviation, median, and interquartile range were used for continuous data. To enhance a normal distribution, the concentrations of FT4, TSH, and TPOAb were also ln-transformed. Models 2 and 3 were further adjusted for the type of labor, while Model 1 remained unadjusted. Model 2 was adjusted for potential confounders such as gestational age at delivery, parity, baby's gender, birth weight, gestational weeks when thyroid function indicators were measured in the mother, gestational hypertension, and diabetes. Additionally, a labor-stratified sensitivity analysis was done, either naturally occurring or created.

Results

Table 1 displays the characteristics of 150 pregnant women in total after their features were examined. The average age of pregnant women in this research was 29.12 years (standard deviation: 3.63). 76.44% of participants had health insurance, and 99.67% of them were married. Multiparae and spontaneous labor rates were respectively 72.81 and 64.00%. 49.38% of baby girls and 50.60% of boys were split equally. The average newborn weight was 3.36 kg (standard deviation: 0.36).

Table 1: Baseline characteristics of Pregnant women

Maternal Marriage Status	
Married	99.67%
Unmarried	0.28%
Divorced	0.02%
Gestational diabetes	
Yes	20.25%
No	79.73%
Gestational hypertension	
Normal	98.14%

Hypertension	1.03%
Preeclampsia	0.67%
Eclampsia	0.11%
Infant gender	
Boys	50.60%
Girls	49.38%
Parity	
Nulliparae	72.81%
Multiparae	27.21%
Gestational week (weeks)	39.82 ± 1.18
Birth weight (kg)	3.36 ± 0.36
Birth length (cm)	50.13 ± 1.12
Type of labor	
Spontaneous	64.00%
Induced	36.00%
Apgar 5 min	
≥ 7 min	99%
≤ 7 min	1%
Apgar 1 min	
≥ 7 min	99.04%
≤ 7 min	0.06%

The first and second phases of labor had median durations of 7.16 and 0.52 hours, respectively. After possible confounders were considered, it was shown that FT4 levels in the second and third trimesters were inversely correlated with the length of the first stage of labor ($\beta = -1.31$ h, 95% CI: 2-.27, -0.31, $P < 0.02$; $\beta = 0.34$ h, 95% CI: 0.60, 0.11, $P < 0.02$). The second trimester TSH level was found to be marginally negatively associated with the length of the first stage of labor ($\beta = 0.05$ h, 95% CI: -0.003, 0.11, $P < 0.06$), whereas the third trimester TSH level was found to be significantly positively associated with the length of the first stage of labor ($\beta = 0.11$ h, 95% CI: 0.05, 0.17, $P < 0.002$).

No statistically significant links between maternal FT4, TSH, and TPOAb levels in the first trimester and the length of the first stage of labor were found, though. After excluding cases of induced labor, a sensitivity analysis revealed that the relationships were strong. The analysis of high, medium, and low tertiles revealed consistent relationships between maternal FT4, TSH, and TPOAb levels and the

length of the first stage of labor, respectively.

To determine whether the correlations between maternal thyroid function markers and pregnancy outcomes persisted throughout the whole pregnancy, we averaged maternal FT4, TSH, and TPOAb concentrations over the three trimesters. Maternal FT4, TSH, and TPOAb levels showed significant correlations with the length of the first stage of labor after adjusting for possible confounders ($\beta = 0.63$ h, 95% CI: -1.11, -0.17, $P = 0.02$; $\beta = 0.07$ h, 95% CI: 0.01, 0.13, $P = 0.03$ and $\beta = 0.08$ h, 95% CI: 0.03, 0.14, $P < 0.002$). The length of the first stage of labor was significantly correlated with maternal FT4, TSH, and TPOAb levels, according to mixed linear models ($\beta = 0.33$ h, 95% CI: 0.53, 0.14, $P < 0.02$; $\beta = 0.06$ h, 95% CI: 0.01, 0.10, $P < 0.02$; and $\beta = 0.07$ h, 95% CI: 0.01, 0.13, $P < 0.002$).

Then, a sensitivity analysis was carried out after classifying people based on whether they had gestational thyroid disorders. In the first, second, and third trimesters,

respectively, 9.68%, 5.87%, and 11.57% of pregnant women had gestational thyroid disorders. After controlling for the same potential confounders, the analysis of pregnant women with normal thyroid function revealed that the duration of the first stage of labor was significantly correlated with the concentrations of FT4 (pmol/L) and TPOAb (IU/mL) in the second trimester by 0.67 h (95% CI: 1.03, 0.31, $P < 0.002$) and 0.08 h (95% CI: 0.01, 0.15, $P = 0.02$), respectively. The duration of the first stage of labor was significantly correlated with the concentrations of FT4 (pmol/L), TSH (mIU/L), and TPOAb (IU/mL) per unit increment in the third trimester by 0.65 h (95% CI: 1.01, 0.30, $P < 0.002$), 0.11 h (95% CI: 0.04, 0.20, $P < 0.02$), and 0.06 h (95% CI: 0.02, 0.13 $P = 0.02$), respectively.

The length of the first stage of labor was then evaluated for pregnant women with various gestational thyroid disorders. After adjusting for relevant confounders, subclinical hypothyroidism in the third trimester showed a substantially longer initial stage of labor than euthyroid women ($\beta = 0.31$ h, 95% CI: 0.002, 0.55, $P = 0.03$). The length of the first stage of labor was not, however, shown to be substantially correlated with any other form of thyroid impairment during pregnancy.

Then, stratifying them into subclinical hypothyroidism with positive TPOAb and subclinical hypothyroidism with negative TPOAb, primarily focused on maternal subclinical hypothyroidism in the third trimester. Maternal TSH levels showed a substantial positive correlation with the duration of the first stage of labor in pregnant women with subclinical hypothyroidism coupled without TPOAb. After adjusting for possible confounders, the first stage of labor lasted 2.43 (95% CI: 0.02, 4.85, $P = 0.03$) h longer for each unit rise of TSH (mIU/L).

Discussion

We conducted the first investigation of the relationships between maternal thyroid hormone level, autoimmune status, and the length of the first stage of labor based on population-based retrospective cohort research. Previous research suggested that abnormalities in maternal thyroid hormone (FT4 and TSH, for example) were linked to undesirable outcomes in children, such as low birth weight, premature birth, respiratory distress syndrome, epilepsy, attention deficit hyperactivity disorder, and autism spectrum disorder [7,8]. Additionally, thyroid autoimmunity (TAI) (such as TPOAb positive) has been shown to control how negatively the thyroid state affects labor and the growing fetus [9]. Our research revealed that maternal TSH and TPOAb were favorably correlated with the length of the first stage of labor, but FT4 was adversely correlated. The underlying processes are still unknown, although it has been demonstrated that TSH, which is controlled by FT4's negative feedback, may affect the release of oxytocin (OXT), which may lengthen labor [10,11].

Although there was a correlation between maternal TPOAb and the length of the first stage of labor, the study could not establish a cause-and-effect relationship, and the mechanisms were not clear. According to one theory, TPOAb might facilitate the iodization of tyrosine and its interaction with iodotyrosyl residues to produce free triiodothyronine and FT4, which would then control the release of OXT.

Notably, increased TSH, TPOAb, and lower FT4 levels in the third trimester were linked to labor's initial stage lasting longer. Despite a hardly significant link between TSH and the first stage of labor, similar correlations were seen in the second trimester. A similar pattern was also observed throughout the pregnancy. Interestingly, the connections mentioned above could not be verified during the first trimester. We hypothesized that this

phenomenon may have two possible causes. The sample size of pregnant women whose thyroid function was assessed in the first trimester was notable since it was substantially lower than those in the second and third trimesters, which likely reduced the statistical power and misled any inferences drawn. In contrast, even though the sample size was large enough to achieve greater statistical power, it may be the case that maternal thyroid function was not related to the length of the first stage of labor. The second and third trimesters were significantly closer to the labor process chronologically than the first trimester, and they likely contributed more to the length of labor, which caused a discrepancy between findings in the first trimester and throughout the whole pregnancy.

Maternal TPOAb may be a possible predictor of the duration of the first stage of labor, which is one of our unique discoveries. Under the effect of human chorionic gonadotropin, thyroid hormone fluctuated during pregnancy (23); however, TPOAb, the most prevalent thyroid autoantibody discovered in euthyroid people, remained comparatively steady. There were few randomized controlled trials of intervention treatment, despite previous research focusing on the increased risk of pregnancy problems (such as abortion and premature delivery) caused by maternal high TPOAb with normal thyroid hormone. There were no recommendations or contraindications for intervention treatment against maternal increased TPOAb with normal thyroid hormone in clinical practice [12,13]. Additionally, TPOAb was not thoroughly checked during the duration of the pregnancy. Our study's findings supported the need for pregnant women to undergo continuous TPOAb screening.

Another unexpected observation was that longer early stages of labor were related to greater TSH levels in pregnant women

with subclinical hypothyroidism mixed with TPOAb in the third trimester. Newborn neurological development was closely correlated with maternal thyroid function, and although the link between subclinical maternal hypothyroidism and poor fetal neurological development has not been conclusively shown [14], it is physiologically probable.

Additionally, we focused on the first stage of labor rather than the second stage because the former lasts longer, is more likely to be regulated by the endocrine and immune status of the mother, and is associated with poorer perinatal outcomes [15]. Additionally, forceps were commonly employed in the second stage of labor, which may have altered the duration of the second stage [16], and the assessment of the length of the second stage of labor was substantially influenced by subjective variables. The second stage of labor, however, deserves further consideration in future studies.

Limitation

The effects of all thyroid antibodies throughout pregnancy, including thyroglobulin antibodies and TSH receptor antibodies, on the labor process were not carefully measured and investigated. The power of the TPOAb model in the first trimester and labor process may be lower than that in the other trimesters as only pregnant women had their TPOAb measured in the first trimester.

Conclusion

We found that maternal FT4, TSH, and TPOAb levels were related to the length of the first stage of labor. For pregnant women with subclinical hypothyroidism combined with no TPOAb in the third trimester, a higher TSH level was related to a prolonged length of the first stage of labor. These data imply that maternal FT4, TSH, and TPOAb may serve as significant indicators of the early stages of labor.

Funding: No outside funding was used for this study.

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