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Comparison of Core Blood Parameters in Neonates Born to Hypothyroid Mothers and Euthyroid Mothers

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Abstract: Pregnancy-related Maternal thyroid dysfunction is a results of hypothyroidism, can have an effect on fetal improvement as well as on neonatal health. This study examines the cord blood parameters in neonates born to hypothyroid moms with those born to euthyroid mothers. This case-control study is a design of this research included sample size 60 participants: 30 born to hypothyroid mothers (15 diagnosed in the 1st trimester and 15 diagnosed in the 2nd trimester) and 30 neonates born to euthyroid mothers. Thyroid function tests, including thyrotrophic hormone (TSH), thyroxine (T4), triiodothyronine (T3), thyroxine-binding globulin (TBG), and thyroglobulin have measured. It indicates that neonates born to known as hypothyroid mothers exhibit irregularities in thyroid hormone levels which is characterized by evaluated higher TSH levels in 2nd trimester group than 1st trimester group and decreased the T4, T3, TBG, and thyroglobulin levels were also altered in neonates born to hypothyroid mothers. The control group of neonates from euthyroid mothers demonstrates that all levels are within an almost normal range. Maternal hypothyroidism, especially during the first and second trimesters, notably impacts neonatal thyroid hormone levels, increasing the likelihood of negative neonatal outcomes. Timely detection and proactive measures are essential to reducing these risks.

Keywords: Neonates Born, Hypothyroid Mothers, Euthyroid Mothers, Pregnancy, 1st trimester, 2nd trimester.

Introduction

Pregnancy-related maternal thyroid illness is prevalent; 2.5% to 2.5% of pregnancies result in hypothyroidism, and up to 5% in hyperthyroidism. Untreated overt thyroid illness increases the risk of obstetrical and labour difficulties, such as preterm birth, hypertensive disorders during pregnancy, and foetal losses. However, appropriate treatment can mitigate these risks. There is no agreement on the diagnosis or course of therapy for subclinical hypothyroidism during pregnancy since there is little information available on how well treatments work to prevent negative outcomes [1].

There is a correlation between low birth weight, intrauterine growth restriction, and hyperthyroidism. An increased risk of preterm delivery and pregnancy-related hypertension may influence these conditions, at least partially. Excessive thyroid hormone in the mother, even in the absence of hyperthyroidism symptoms (such as thyroid hormone resistance), negatively impacts fetal development by inducing a thyrotoxic and catabolic condition in the fetus [2].

Thyroid illness is a prevalent hormonal issue that specifically impacts women in their reproductive years and can have negative effects on their reproductive health and pregnancy outcomes. Gestational hyperthyroidism is rare, but gestational hypothyroidism is more prevalent and can result in neurodevelopmental impairments and maternal obstetric difficulties. Pregnancy can reveal hidden cases of hyperthyroidism and hypothyroidism, which are frequently managed and can lead to a successful pregnancy. Pregnancy can worsen thyroid-related physiological changes, as well as disrupt the function of the thyroid gland and the balance of thyroid hormones between the mother and fetus. Obstetric disorders, such as gestational trophoblastic illness or hyperemesis gravid arum, can also have an impact on thyroid function [3].

Thyroid dysfunction is the second most prevalent endocrine condition, occurring primarily in females of reproductive age, behind diabetes mellitus. The thyroid gland carries out several vital activities. Furthermore, these hormones make a significant contribution to the development of fetal brain cells [4].

Thyroid function is one biological state that is noticeably altered during pregnancy. Several factors contribute to these changes. The placenta secretes the hormone HCG (human chorionic gonadotropin), which is structurally similar to TSH (thyroid stimulating hormone) during pregnancy. Consequently, it activates the thyroid gland, which leads to a drop in TSH levels and an increase in the release of thyroid hormones (T3 and T4), especially during the first trimester [5].

Maternal steroid hormone levels and blood concentrations of thyroid-binding globulin (TBG) are subject to complicated variations throughout pregnancy. Total triiodothyronine (TT3) and thyroxine (TT4) levels rise throughout pregnancy, as does the amount of serum thyroxine-binding globulin (TBG). In the second and third trimesters, the concentrations of free T3 and free T4 decrease slightly. In the first trimester, TSH levels are lower than usual; in the second trimester, they return to normal. This process quickly reverts after birth, with blood TBG, T4, and T3 levels reaching pre-pregnancy levels in 4–6 weeks [6].

The problems during pregnancy are linked to both overt and subclinical thyroid dysfunction in the mother, which can have long- and short-term effects on the mother and child. It appears that women with euthyroid autoimmune thyroid disease are more susceptible to these risks. Pregnant mothers with hypothyroidism are more likely to have gestational hypertension and low birth weight babies. Women who were already undergoing thyroid replacement therapy prior to pregnancy may require an increase in the dosage. One of the risks associated with spontaneous miscarriages in pregnant women with chronic autoimmune thyroiditis is higher. Women who test positive for thyroid-stimulating hormone (TSH) are almost three times more likely to deliver birth very prematurely [7].

When pregnant, patients with autoimmune thyroid disease are more likely to develop postpartum thyroiditis and thyroid insufficiency. Therefore, it is crucial to monitor their thyroid-stimulating hormone (TSH) levels throughout their pregnancy. Knowing the exact levels of TSH, free, and total thyroid hormones during each trimester is essential for accurate medication. The main cause of hyperthyroidism in pregnant women is Graves' disease, which has an incidence rate of about 0.2%. [8].

Previous research has established a link between maternal hypothyroidism and the need for neonates to be admitted to intensive care units. Additionally, reports link a higher incidence of respiratory distress syndrome to subclinical hypothyroidism. However, these studies did not assess the impact of other thyroid illnesses. Prior studies have lacked sufficient statistical power to assess the relationship between thyroid disorders and low birth weight at term or less prevalent neonatal outcomes [9].

Literature Review

Abraham, B. (2014) proved that the most effective method for detecting congenital hypothyroidism is to conduct universal testing on all newborns. Nonetheless, the levels of thyroid-stimulating hormone (TSH) in the umbilical cord blood may vary depending on a number of circumstances pertaining to the mother and child throughout the perinatal stage. The aim of this study is to assess the influence of perinatal variables on the differences in cord blood TSH levels between newborns delivered in a South Indian rural tertiary care hospital. They conducted cross-sectional research to measure the TSH levels in the cord blood of 430 term newborns during delivery. For those with abnormal levels, they took a follow-up TSH measurement on the third day following delivery. They examined the data statistically in light of maternal, paternal, and perinatal factors. CBTSH had a mean value of 12.88 mIU/mL. 25 of the 430 newborns, or 29.06% of the sample, had high CBTSH levels, the researchers discovered. Two infants had CBTSH levels that were 0.46%, less than 2.3 mIU/mL. Just 5 (3.94%) of the 127 newborns with abnormal CBTSH levels also had abnormal TSH estimates on the third day following delivery. Three neonates, or 2.67% of the total, had aberrant blood T4 levels in the same sample. CBTSH levels showed no discernible gender differences, although they did significantly rise with increasing infant gestational age ($p = 0.001$). Infants delivered to mothers with a history of hypothyroidism had significantly higher levels of CBTSH; these levels were linked to increasing maternal age ($p<0.001$). When they compared the prevalence of congenital hypothyroidism (3 in 430 infants) to worldwide and national criteria, they discovered a notable difference. This emphasizes the significance of maternal variables and the urgent need for universal screening.

Eng, L., et al. (2020) determined that thyroid hormones play a crucial role in growth and brain development during infancy and childhood. The newborn's hypothalamic-pituitary-thyroid axis develops and grows during pregnancy, with the fetus relying on the mother's thyroid hormones in the early stages of pregnancy. During the second trimester, the fetal thyroid gland starts to generate thyroid hormones, resulting in a decrease in need for external sources. This reduced dependency continues until delivery. Following delivery, the separation from the placenta and the shift in temperature conditions cause a rapid elevation in the new-born’s thyroid-stimulating hormone levels within a few

hours. This, in turn, leads to further rises in the concentrations of thyroxin and triiodothyronine. Preterm new-borns may have lower levels of thyroxin due to an underdeveloped hypothalamic-pituitary-thyroid axis at birth and premature cessation of maternal thyroid hormone transmission. Similarly, severe diseases unrelated to the thyroid gland may cause decreased thyroxin levels in neonates. New-borns of mothers with Graves' illness are susceptible to both hypothyroidism and hyperthyroidism due to the transmission of maternal autoantibodies and the use of antithyroid medicines. Understanding the typical development and functioning of the fetal and neonatal thyroid is critical when assessing thyroid problems in a newborn.

Feigl, S., et al. (2022) shown that there is a greater risk of autoimmune thyroiditis in women with polycystic ovarian syndrome (PCOS). Pregnancy complications and decreased fertility. This study aimed to determine whether thyroid parameters were comparable between women with and without PCOS and their term children, as well as whether there was any correlation between these characteristics and the group's perinatal outcome. This study was carried out utilizing a cross-sectional observational methodology at a single academic tertiary hospital in Austria. In total, 354 pregnant women without PCOS and 79 pregnant women with PCOS were included in the study. During delivery, blood samples were taken from the mother and the umbilical cord. At birth, the thyroid parameters of the mother and the infant were the main outcome measurements. The secondary outcome variables, which were integrated into a composite measure, were the rate of complications per mother and each infant. Thyroid dysfunction was more common in women with PCOS ($p < 0.001$). Women with polycystic ovarian syndrome (PCOS) had significantly lower levels of free triiodothyronine (fT3) after birth than women without PCOS ($p = 0.005$). Thyreoperoxidase antibody (TPO-AB) levels were considerably higher in PCOS women and their infants than non-PCOS women ($p = 0.001$). The incidence of hypothyroidism was significantly higher in women with higher TPO-AB levels ($p < 0.001$). The levels of free thyroxine, fT3, and TPO-AB were strongly positively correlated in both mothers and their infants. There were no appreciable differences in thyroid measures between moms and newborns, regardless of whether there were issues. The results of our study point to a common etiology for both thyroid dysfunction and autoimmunity in women with PCOS, as both disorders are more common in this population. They were unable to show a connection between thyroid markers and the complication rate.

Venugopalan, L., et al. (2021) showed an increase in both maternal and congenital hypothyroidism. They examine the causes and effects of hypothyroidism in babies born to hypothyroid mothers and present thyroid stimulating hormone testing results. The study included all pregnant mothers who visited our hospital. Group I included 249 term babies for hypothyroid women, and Group II included 2154 for euthyroid mothers. On day 3, all newborns in both groups received thyroid stimulating hormone through a heel puncture. Screen-positives in group II and all I babies had confirmatory venous testing. They followed guidelines for examination and therapy. The thyroid stimulating hormone levels for the two categories are shown. A significant correlation ($r = 0.7$, $P<0.05$) was found between the highest mother's thyroid stimulating hormone level and heel probe on day 3 for babies in group I. In groups I and II, confirmed illness rates were 4.3 and 0.6%, whereas positive screening test rates were 3.8 and 1.03% ($p<0.05$). Aetiological investigations revealed persistent (66.6%) and transitory (33.3%) hypothyroidism. Congenital hypothyroidism affects 4.3% of hypothyroid moms' babies. This condition has both temporary and permanent causes. A three-week venous test helps identify these infants' cases.

Van Trotsenburg, A. S. P. (2020) shown that thyroid hormone (TH) is essential for both fetuses and embryos to grow to their full potential. The placenta is the organ through which the mother releases TH throughout gestation; later in pregnancy, the fetal thyroid gland begins to contribute more often. Thyroid disorder in mothers can affect a child's or embryo's normal early development, result in TH levels that are either greater or lower than normal, and transmit to the fetus. Typically, autoimmune hypo- or hyperthyroidism, such as Graves' disease and Hashimoto's disease, causes maternal thyroid dysfunction. While TSHR antibody blocking may lead to autoimmune hypothyroidism in patients, TSHR antibody boosting causes autoimmune hyperthyroidism. Maternal TSHR Ab can cross the placenta starting in mid-gestation and result in either transient hyper- or hypothyroidism in the newborn. Antithyroid medications used for autoimmune hyperthyroidism have the potential to cause fetal and transient neonatal hypothyroidism during pregnancy through placenta crossing. This study offers helpful guidance for the clinical management of neonates delivered to mothers with thyroid dysfunction and focuses on the consequences of maternal hypo- and hyperthyroidism on the fetus and neonate.

Objective

In this research, the following objectives are mentioned below.

1. To assess thyroid function in cord blood of neonates born to hypothyroid mothers, and neonates born to euthyroid mothers.
2. To compare the results of the two groups.

Methodology

Study Design: Case control study.

Study Duration: 6 months.

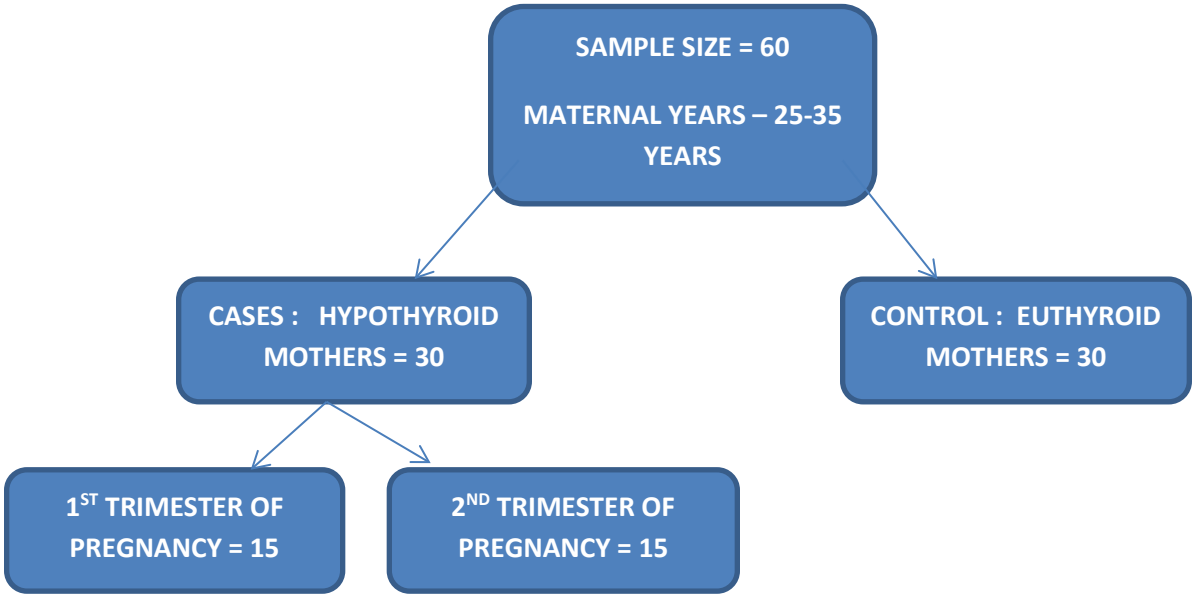
Sample Size: 60. (30 cases + 30 controls)

Study Site: OBG Department, Pediatrics Department and Central Clinical Laboratory (CCL), Mc-Gann Teaching Hospital, Shimoga, Karnataka India

Cases: - Neonates born to known hypothyroid mothers. (15 hypothyroid from 1st trimester + 15 hypothyroid from 2nd trimester of pregnancy)

Controls: - Neonates born to known euthyroid mothers.

Conceptual Framework



After taking consent from IEC and concerned patient attenders, cord blood samples will be taken from both groups. Thereafter, they will be sent to CCL for assessment of thyroid function tests. Thyrotrophic, thyroxin, triodothyronine, thyroxin-binding globulin and thyroglobulin will be measured.

All the measurements will be carried out by immunoassay (ELISA, micro particle enzyme immunoassay or chemiluminescence immunoassay).

Result

This study presents the results in a detailed manner. To adhere to the methodology, we can systematically organize the data into tables. Each table displays the percentage distribution of participants for thyroid parameters (TSH, T4, T3, TBG, and Tg) for both cases and controls, as described below.

Table 1: Thyrotrophic [TsH]

S NO.	CASE STUDY	THYROTROPHIC [TsH]	PERCENTAGE
1	1ST TRIMESTER HYPOTHYROID MOTHERS	5.00 mIU/L or more than that	46.66%
2	2ND TRIMESTER HYPOTHYROID MOTHERS	10 mIU/L or more than that	73.33%
CONTROL STUDY			
3	EUTHYROID	1.0 – 39.0 mIU/L	20%

According to the data presented in this table, it is evident that a significant percentage of mothers in their first trimester, specifically 46.66%, exhibit TSH levels of 5.00 mIU/L or higher, which is indicative of hypothyroidism. 73.33. In the second trimester, the TSH levels of mothers with hypothyroidism tend to be higher compared to the first trimester. Within the group of Euthyroid neonates, none of the individuals exhibited elevated TSH levels, suggesting that the TSH range is within the normal range.

Table 2: Thyroxin [T4]

S NO.	CASE STUDY	THYROXIN (T4)	PERCENTAGE
1	1ST TRIMESTER HYPOTHYROID MOTHERS	<4 µg/dl	53.33%
2	2ND TRIMESTER HYPOTHYROID MOTHERS	<4 µg/dl	66.66%
CONTROL STUDY			
3	EUTHYROID	8-15 µg/dl	10%

According to the data presented in Table 2, a significant percentage of mothers in their first trimester who have hypothyroidism show low Tg levels of less than 4 ug/dl, which indicates hypothyroidism. We have observed that mothers with hypothyroidism tend to have lower Tg levels during the second trimester compared to the first trimester. This could be an indication of a more severe level of hypothyroidism. Among the neonates in the control group, 10 percent displayed elevated Tg levels, suggesting that the Tg range is within the normal range.

Table 3: Triodothyronine [T3]

S NO.	CASE STUDY	TRIODOTHYRONINE [T3]	PERCENTAGE
1	1ST TRIMESTER HYPOTHYROID MOTHERS	<99 ng/dL	60%
2	2ND TRIMESTER HYPOTHYROID MOTHERS	<99 ng/dL	80%
CONTROL STUDY			
3	EUTHYROID	Nil…	Nil

According to the data presented in Table 3, a significant proportion of mothers in their first trimester who have hypothyroidism exhibit T3 levels of <99 ng/dl or higher. 73.33. In the second trimester, the T3 levels of mothers with

hypothyroidism tend to be lower compared to the first trimester. In the control group of euthyroid neonates, none of the individuals had elevated T3 levels, suggesting that the T3 range is within the normal range.

Table 4: Thyroxin-Binding Globulin [tbg]

S NO.	CASE STUDY	THYROXIN-BINDING GLOBULIN [TBG]	PERCENTAGE
1	1ST TRIMESTER HYPOTHYROID MOTHERS	>39 mg/L	40%
2	2ND TRIMESTER HYPOTHYROID MOTHERS	>39 mg/L	66.66%
CONTROL STUDY			
3	EUTHYROID	nil	nil

Table 4 shows that 40% of mothers with hypothyroidism in their first trimester have TbG levels of >39 mg/L or higher, indicating the presence of hypothyroidism. A significant percentage of mothers with hypothyroidism experience higher levels of TbG during the second trimester compared to the first trimester. In the control group of euthyroid mothers, none of the individuals showed elevated levels, suggesting that the TbG range is within normal limits.

Table 5: Thyroglobulin [Tg]

S NO.	CASE STUDY	THYROGLOBULIN [TG]	PERCENTAGE
1	1ST TRIMESTER HYPOTHYROID MOTHERS	>45 ng/mL	66.66%
2	2ND TRIMESTER HYPOTHYROID MOTHERS	>45 ng/mL	80%
CONTROL STUDY			
3	EUTHYROID	50 ng/mL	0%

According to the data in Table 5, a significant percentage of mothers in their first trimester who have hypothyroidism show Tg levels of over 45 ng/mL, which is an indication of the condition. A significant number of pregnant women in their second trimester who have hypothyroidism show elevated levels of Tg compared to the first trimester, suggesting a more severe form of the condition. The control group of neonates Euthyroid mothers showed elevated Tg levels at 50 ng/ml, indicating that the range of Tg levels falls within the normal range.

Conclusion

The findings are primarily observed during the 2nd trimester of pregnancies affected by hypothyroidism, which poses considerable risks and complications for both the mother and the infant. Unmanaged hypothyroidism in pregnancy may result in a range of negative consequences. Also this research suggested that children born to women experiencing severe, untreated hypothyroidism during pregnancy displayed lower IQ scores and impaired psychomotor development. With proper management, frequently involving increased thyroid hormone levels, mothers experiencing hypothyroidism can give birth to healthy, unaffected infants.

Hence, the results demonstrate a notable impact of maternal hypothyroidism on the thyroid function of newborns, especially in mothers during the first and second trimesters of pregnancy. The results indicate that neonates born to mothers with hypothyroidism exhibit irregularities in thyroid hormone levels, characterized by elevated Thyrotrophic (TSH), decreased Thyroxin (T4), Triiodothyronine (T3), and heightened levels of Thyroglobulin (Tg) and Thyroxin-Binding Globulin (TBG). The control group of neonates from euthyroid mothers demonstrates that all levels are within an almost normal range. This research emphasizes the essential importance of early identification and intervention for maternal hypothyroidism to mitigate the risks associated with thyroid-related complications in infants. It is essential for pregnant women undergoing thyroid hormone therapy to undergo regular blood tests throughout their pregnancy, as their requirements may vary.

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