International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2023; 7(3): 17-22
Received: 23-02-2023
Accepted: 26-03-2023

Dr. Gauri Bankapur
Post Graduate, Department of Obstetrics and Gynaecology Blde (Deemed to be University) Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Dr. Rajasri G Yaliwal
Department of Obstetrics and Gynaecology, Blde (Deemed to be University), Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Dr. Shailaja R Bidri
Department of Obstetrics and Gynaecology, Blde (Deemed to be University), Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Dr. Shreedevi S Kori
Department of Obstetrics and Gynaecology, Blde (Deemed to be University), Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Dr. Neelamma G Patil
Department of Obstetrics and Gynaecology, Blde (Deemed to be University), Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Dr. SS Kalyan Shettar
Department of Obstetrics and Gynaecology, Blde (Deemed to be University), Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Corresponding Author:
Dr. Gauri Bankapur
Post Graduate, Department of Obstetrics and Gynaecology Blde (Deemed to be University) Shri B.M. Patil Medical College and Hospital, Vijayapura, Karnataka, India

Effect of maternal hypothyroidism on obstetric and perinatal outcome, an observational study

Dr. Gauri Bankapur, Dr. Rajasri G Yaliwal, Dr. Shailaja R Bidri, Dr. Shreedevi S Kori, Dr. Neelamma G Patil and Dr. SS Kalyan Shettar

DOI: https://doi.org/10.33545/gynae.2023.v7.i3a.1344

Abstract
Objectives: Thyroid problems are one of the endocrine conditions that affect pregnant women most frequently. It is now widely acknowledged that both overt and subclinical thyroid problems can have a negative impact on obstetrical and neonatal outcomes. Surprisingly, there aren't many statistics from India regarding the prevalence of thyroid disease during pregnancy. The purpose of this study is to ascertain the frequency of thyroid dysfunction in pregnancy and how it affects both maternal and neonatal outcomes.
Materials and Methods: Thyroid stimulating hormone tests were performed on a total of 427 pregnant women to look for hypothyroidism. Thyroid peroxidase antibodies and free T4 were measured and classified as subclinical and overt hypothyroidism if the TSH (thyroid stimulating hormone) was greater than 3 IU/L. Low birth weight, fetal growth restriction, intrauterine death, and others like respiratory distress syndrome, cardiac arrest, hypoglycemic seizures were neonatal outcomes observed in our study and evaluated for statistical significance. Preterm births, abruption, oligohydramnios, rate of caesarean deliveries, gestational diabetes mellitus and hypertensive disorders of pregnancy were documented as obstetrical outcomes.
Results: Preterm births, abruption, and hypertensive disorders of pregnancy were discovered to be statistically significant obstetrical outcomes in our investigation. Clinically relevant factors included gestational diabetes, oligohydramnios, anemia and caesarean delivery frequency. In cases of maternal hypothyroidism, unfavourable neonatal outcomes such as foetal growth restriction, intrauterine mortality, cardiac arrest, and respiratory distress syndrome were found to be clinically significant.
Conclusion: According to the study's findings, maternal hypothyroidism has an impact on a number of variables. Specifically, placental abruption, hypertensive disorders of pregnancy, preterm deliveries, anemia, cardiac arrest, respiratory distress syndrome, and hypoglycemia seizures.

Keywords: Maternal hypothyroidism, obstetrical outcomes, thyroid peroxidase antibodies, thyroid gland, thyroid hormones, thyroid stimulating hormone

Introduction

The hormonal milieu of the thyroid gland will change dramatically throughout pregnancy, acting as a stress test for the thyroid during this time. During pregnancy, the gland undergoes a wide range of modifications that enable it adjust to the changing metabolic needs. The size of the gland grows, and thyroid hormone production rises as a result of these changes. This increase in hormone synthesis, in turn, results in a parallel increase in iodine requirement [1]. Numerous physiologic events lead to the alterations, which follow. Thyroid-binding globulin (TBG) shows a substantial estradiol-driven rise that peaks in the first trimester and plateaus in the second and third trimesters. This causes an increase in total T3 and T4 and a simultaneous decrease in free T3 and T4. Additionally, the TSH-Receptor is triggered by the action of human chorionic gonadotropin (hCG), whose beta subunit shares structural similarities with thyroid-stimulating hormone (TSH) and causes an increase in T3, T4, and a decrease in TSH during the first trimester. This effect continues through the first trimester. There are additional modifications in addition to these ones, such as a shift in the peripheral metabolism of thyroid hormones and an increase in renal iodine loss as a result of an increase in glomerular filtration rate.
In conclusion, these modifications cause a decline in TSH in the first trimester, a marginal decline in free T3 and T4, and a rise in total T3 and T4. Throughout pregnancy, the total T3 and T4 levels are elevated. After mid-pregnancy, TSH and free T3/T4 levels are likely to approach pre-pregnancy values [2]. Diabetes mellitus and thyroid problems are the two endocrinological conditions that affect women of reproductive age most frequently [3].

During pregnancy, subclinical hypothyroidism (SCH) is the most prevalent thyroid disorder [4]. While Indian research have showed a greater prevalence of up to 13 percent, according to western data, the prevalence of hypothyroidism in pregnancy is only about 2.5%. [5]. Subclinical hypothyroidism is characterised by a high TSH level but a normal T4 level. SCH is frequent during pregnancy and especially so in regions where iodine insufficiency is chronic. Anti-TPO antibodies are the second most common cause after iodine deficiency [6].

The majority of thyroid dysfunctions are curable, but if they are not properly diagnosed and controlled, they may have negative effects on the mother and foetus. Preterm labour, placental abruption, and postpartum haemorrhage are some of the poor maternal outcomes linked to hypothyroidism [7].

During the first 12 weeks of pregnancy, the developing foetus solely relies on maternal thyroid hormones; but, after that point, the foetal thyroid gland begins to produce hormones (8). Poor foetal outcomes, such as low birth weight, foetal growth restriction, stillbirths, neonatal fatalities, neonatal hyperbilirubinemia, and perinatal mortality, can result from maternal SCH [7]. A higher risk of intellectual and motor developmental delays, attention deficit hyperactivity disorder, and language, vision, and hearing impairment is also linked to maternal SCH [9].

There is a gap in the research on the prevalence of maternal hypothyroidism in this region of the country as well as the impact of hypothyroidism on foetal and maternal outcomes. In order to determine how maternal hypothyroidism affects obstetrical and perinatal outcomes, this study was conducted.

Materials and Methods

This observational study was carried out in the Department of Obstetrics and Gynaecology at BLDE (deemed to be University) Shri B.M. Patil's Medical College, Hospital and Research Centre, Vijayapura, Karnataka, India from December 2020 to April 2022, in which total 427 cases who met inclusion criteria were enrolled following clearance from the institutional ethics committee (IEC NO- 09/2021) and registered in CTRI trial approved by GOI (CTRI NO- CTRI/2021/09/036518). Written and informed consent was obtained from all participants. Out of 800 pregnant women, 435 women met inclusion criteria and thyroid stimulating hormone test sent for all 435 pregnant women and thyroid stimulation hormone value was more than 0.1 in 427 women and rest 8 were having levels <0.1 were excluded for further assessment. Among 427 pregnant women who had thyroid stimulating hormone (TSH) levels >3micro-IU/LITRE were considered as hypothyroid and free T4 and thyroid peroxidase antibodies were sent to further classify them as subclinical and overt hypothyroid and their effects on various factors have been studied. The Preterm births, oligohydramnios, postpartum haemorrhage, and hypertensive disorders of pregnancy were documented as adverse obstetrical outcomes and fetal growth restriction, intrauterine deaths, cardiac arrest, hypoglycemic seizures, respiratory distress and neonatal hyperbilirubinemia as adverse neonatal outcomes

On the third day after delivery, thyroid stimulating hormone (TSH) levels were checked in the newborn to check for neonatal hypothyroidism. No additional tests were run on the mother.

Inclusion criteria of the study

- Pregnant women with a known case of hypothyroidism
- Women who Develop Hypothyroidism During Pregnancy
- All pregnant women beyond the 28-week get admitted to the labour ward.

Exclusion criteria of the study

- Patients have undergone radioiodine therapy
- Patients have undergone a partial thyroidectomy.
- Multifetal gestation

Materials and Methods

Sample Size

The study will involve all expectant mothers who are past the 28-week mark in gestation.

The study would need a sample size of 427 [5] if it were assumed that 13% of the population's subjects have the factor of interest.

for calculating the predicted proportion with an accuracy of 5% absolute and a confidence level of 98%.

N = Z2p*q/d2 was the formula used.

Where does the z=z statistic fall within the significance threshold?

d2 is the absolute error.

P is the proportional rate.

q= 100-p

Statistical Analysis

The collected data will be entered into an Excel document, where statistical analysis for the social sciences will be done (version 20), and the findings will be displayed using graphs, counts and percentages, a mean (or median), SD, and other metrics.

For comparing regularly distributed continuous variables between two groups, an independent t-test will be used; for variables that are not normally distributed, Mann-Whitney u tests will be employed.

SPS version 20 was used for data analysis. To compare categorical variables, the chi-square test will be utilised, and a p-value of 0.05 was used to determine statistical significance.

Results and Observations

The majority of mothers were between the ages of 20 and 24 years (49.8%) and there were more multigravida (58.07%), with gravida 2 being the most common

The prevalence of subclinical and overt hypothyroidism were 25.7% and 18.9% respectively

The prevalence of various hypothyroidisms is explained in the table (1) and graph below.

In our study, subclinical hypothyroidism was most frequently observed (25.7 percent).

Table 1: Prevalence of hypothyroidism among pregnant women in late gestation

Types	Number of patients	Percentage
No hypothyroid	236	55.2
Overt hypothyroid	81	18.9
Subclinical hypothyroid	110	25.7
Total	427	100.0

Maternal outcomes

It is demonstrated that both overt and subclinical hypothyroidism have a statistically significant impact on preterm births (p value 0.003)

According to our research, late preterm, which is defined as between 34 +0/7 and 37 +6/7, is the most common.

Table 2: Effect of maternal hypothyroidism on anemia

	Anemia							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi Square Value	P (Significance)
	N	%	N	%	N	%	2.503	0.286
Yes	94	39.8	45	55.5	47	42.7		
No	142	60.2	36	44.5	63	57.3		
Total	236	100	81	100	110	100		
Statistically insignificant								

Table 3: Need for cesarean delivery in maternal hypothyroidism

	Cesarean Section							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi-Square Value	P (Significance)
	N	%	N	%	N	%	1.898	0.755
Yes	58	24.6	26	32.1	36	32.7		
No	178	75.4	55	67.9	74	67.3		
Total	236	100	81	100	110	100		
Statistically insignificant								

The multigravida with a history of previous caesarean deliveries who chooses to have another one is the most typical of these.

Table 4: Effect of maternal hypothyroidism on gestational dm

	Gestational DM							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		CHI-Square Value	P (Significance)
	N	%	N	%	N	%	1.303	0.521
Yes	4	1.7	0	0	1	0.9		
No	232	98.3	81	100	109	99.1		
Total	236	100	81	100	110	100		
Statistically insignificant								

There was only one patient with gestational diabetes in the subclinical hypothyroidism group.

Table 5: Effect of maternal hypothyroidism on oligohydramnios

	Oligohydramnios							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi- Square Value	P (Significance)
	N	%	N	%	N	%	3.621	0.164
Yes	27	11.4	16	19.7	27	24.5		
No	209	88.6	65	80.2	83	75.5		
Total	236	100	81	100	110	100		
Statistically insignificant								

Subclinical hypothyroid group had more oligohydramnios than overt thyroid group

Neonatal Outcomes

Fetal growth limitation has been impacted by foetal hypothyroidism, both subclinical and overt.

Despite the clinical difference, no statistically significant difference was discovered by the chi square test.

Table 6: Effect of maternal hypothyroidism on fetal growth restriction

	Fetal Growth Restriction							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi-Square Value	P (Significance)
	N	%	N	%	N	%	0.054	0.973
Yes	35	14.8	23	28.4	27	24.5		
No	201	85.2	58	71.6	83	75.5		
Total	236	100	81	100	110	100		
Statistically insignificant								

Table 7: Effect of maternal hypothyroidism on intrauterine death

	Intrauterine Death							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi-Square Value	P (Significance)
	N	%	N	%	N	%	5.306	0.070
Yes	6	2.5	6	7.9	16	14.5		
No	230	97.5	75	92.1	94	85.5		
Total	236	100	81	100	110	100		
Statistically insignificant								

The correlation between intrauterine death and overt hypothyroidism and subclinical hypothyroidism is positive.

And in our research, preterm patients accounted for the majority of the deaths, which is statistically insignificant (p value > 0.05).

Table 8: Effect on of maternal hypothyroidism low birth weight

	Low Birth Weight							
	No Hypothyroid		Overt Hypothyroid		Subclinical Hypothyroid		Chi-Square Value	P (Significance)
	N	%	N	%	N	%	5.609	0.061
Yes	67	28.4	30	37	43	39.1		
No	169	71.6	51	63	67	60.9		
Total	236	100	81	100	110	100		
Statistically insignificant								

Both subclinical and overt hypothyroidism have affected low birth weightThe most prevalent weight range, 1500–2000 grams, accounts for 18.9% of those between 2000–2500 grams (8.4%) 1000-1500 (very LBW) – 6%, 500-1000 (extremely LBW)- 1.7%

Table 9: Effect of maternal hypothyroidism on other factors

Any Others, Specify								
	No hypothyroid		Overt hypothyroid		Subclinical hypothyroid		Chi-Square Value	P (Significance)
	N	%	N	%	N	%	34.852	0.010
Hypoxic ischemic encephelopathy	1	0.4	1	1.2	0	0		
Meconium aspiration syndrome	2	0.8	1	1.2	1	0.9		
Respiratory distress syndrome	4	1.7	1	1.2	4	3.6		
Hypoglycemic seizures	0	0	0	0	1	0.9		
Meningitis	0	0	1	1.2	0	0		
Birth asphyxia	0	0	2	2.5	0	0		
Cardiac arrest	0	0	1	1.2	0	0		
Cleft lip	0	0	1	1.2	0	0		
Pneumonia	0	0	0	0	1	0.9		
None	229	97.1	73	90.3	103	93.7		
Total	236	100	81	100	110	100		
Statistically significant								

The effects of maternal hypothyroidism on additional new born problems are depicted in this graph and chart.

These all were affected by overt and subclinical hypothyroidism and determined to be clinically significant (p value>0.05) using the chi square test.

Discussion

The current observational study was conducted at Vijayapura's B. M. Patil Medical College and Research Institute. The screening method involved 427 pregnant women who were in their third trimester and arrived at the labour and delivery units to give birth. Each woman's thyroid stimulating hormone (TSH) levels were examined, and if TSH was greater than 3 microIU/liter, free T4 (FT4) and thyroid peroxidase (TPO) antibodies were tested to determine the prevalence of overt, subclinical hypothyroidism and its consequences on obstetrical outcomes.

Comparision between Prevalence of overt and subclinical hypothyroidism with other studies

In our study, the prevalence of overt hypothyroidism is 18.9%, but Sahu *et al*. survey.'s [10] found only 4.56 percent, which is 13% lower than our study's prevalence.

The prevalence of overt hypothyroidism in the other study by Weiping Teng *et al*. [11], Tuija Mannisto *et al*. [12], and Stagnaro *et al*. [13] conducted in China, North Finland and Washington D C respectively is substantially lower than in our study at <1%, 1.3 percent, and 0.4 percent, respectively.

Our study found that 25.7 percent of participants had subclinical hypothyroidism, which is similar to the 23 percent found in the survey conducted by Casey BM *et al*. [14].

The prevalence of subclinical hypothyroidism was quite low in the other studies by Sahu *et al*. [10], Tuiha Mannisto *et al*. [12], and Weiping *et al*. [11], coming in at 6.47 percent, 3.5 percent, and 3.5 percent, respectively.

Effect of maternal hypothyroidism on obstetrical and neonatal outcomes in our study

In our study, the effects of both overt and subclinical maternal hypothyroidism on

- Obstetrical outcomes like hypertensive disorders of pregnancy, abruption, preterm deliveries found to be significant
- Others like oligohydramnios, rate od caesarean deliveries and gestational diabetes found to be clinically significant
- Neonatal outcomes like respiratory distress, meconium aspiration and rate of cardiac arrest found to be clinically significant

Effect of maternal hypothyroidism on obstetrical and neonatal outcomes in other studies

- In Bangalore, Karnataka, 96 of 100 individuals in an observational study by Sreelatha *et al*. (15) had subclinical hypothyroidism. Preterm labours (3.1%), oligohydramnios (16.67%), caesarean births (22.9%), postpartum haemorrhage, anaemia (4.20%), pregnancy-induced hypertension (14.7%), gestational diabetes mellitus (4.2%), and miscarriages (2.1%) are all linked to thyroid deficit during pregnancy (63 percent).
- In a research by Leung *et al*. (16) that was similar to ours, the incidence of PE in patients with overt hypothyroidism was 22%, that of LBW in those with overt hypothyroidism was 22%, and that of subclinical hypothyroid patients was 15%.

- Pre-eclampsia, preterm births, and foetal growth restriction are more common in Sahu MT *et al*. study's [10], which was conducted in Lucknow, Uttar Pradesh, than in our study, at 20.7 percent, 4.7 percent, and 13.8 percent for overt hypothyroidism, and 9.8 percent, 10.3 percent, and 2.4 percent for subclinical hypothyroidism, respectively.
- According to Kattah *et al*. [17], subclinical hypothyroidism and pregnant hypertension are related since these individuals' blood pressure readings were normalised when they were diagnosed with gestational hypertension and treated with levothyroxine.
- Numerous studies [18-29] have found a correlation between SCH and a higher risk of adverse pregnancy and newborn outcomes. Preterm births (13.5 percent), gestational hypertension (11%), pre-eclampsia (6%) abruptio placenta (4%) caesarean delivery (27%) low birth weight (8.5 percent), low Apgar score (0.7 percent), and neonatal death (0.5 percent).

Conclusion
In our study, thyroid issues, including overt and subclinical hypothyroidism, are highly common. We recommend routine thyroid monitoring for all pregnant women, particularly in the third trimester, in order to predict adverse obstetrical outcomes and provide appropriate therapy.

Conflict of Interest
Not available

Financial Support
Not available

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How to Cite This Article
Bankapur G, Yaliwal RG, Bidri SR, Kori SS, Patil NG, Kalyan SSS. Effect of maternal hypothyroidism on obstetric and perinatal outcome, An observational study. International Journal of Clinical Obstetrics and Gynaecology. 2023;7(3):17-22.