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Fetomaternal Outcome in Maternal Hypothyroidism Complicating Pregnancies at Paropakar Maternity and Women's Hospital

Radhika Kunwar[1*], Sarmila Prajapati[1], Anamika Jha[1], Anupama Bhattarai[1], Umesh Bahadur Bogatee[2]

[1]Department of Obstetrics and Gynaecology, Paropakar Maternity and Women Hospital, Kathmandu, Nepal
[2]Kathmandu Model Hospital, Kathmandu, Nepal
Email: *Radhika312015@gmail.com

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Abstract

Background: Thyroid disorders are the most common endocrine disorders in pregnancy accounting for 10% of subclinical hypothyroidism in all pregnancies. Screening for hypothyroidism is essential in all pregnant women, especially in Nepal, a low-income region where women have an increased risk of developing iodine deficiency during pregnancy. Hence this study is to analyze fetomaternal outcomes in maternal hypothyroidism complicating pregnancies. **Methods:** This retrospective observational study was carried out at Paropakar Maternity and Women Hospital, a tertiary center located in Kathmandu, Nepal. The Subjects of this study were 330 antenatal women with a singleton pregnancy with hypothyroidism admitted for delivery in the obstetrics ward, and informed consent was obtained. Women were chosen irrespective of age, parity, residency, and socioeconomic status. Women with multiple pregnancies and any preexisting medical disorders including heart disease, diabetes, and hypertension were excluded. Routine hematological parameters and estimations of T3, T4, and thyroid stimulating hormone (TSH) were conducted. Patients with hypothyroidism were divided into overt and subclinical and were subsequently assessed for maternal and fetal complications. The occurrence of maternal outcomes and perinatal outcomes were recorded. **Result:** Out of 470 total hypothyroid cases, 330 were enrolled in the study and the remaining 140 were excluded. In our study, the incidence of hypothyroidism in pregnancy was 2.11% with 1.7% of subclinical hypothyroidism and 0.31% of overt hypothyroidism. The mean age of the patient was >30 years with 53.3% (n = 176) primigravida. Mostly 70.3% (n = 232) from rural areas. Pre-Eclampsia, gestational diabetes abruptio placenta, and postpartum hemorrhage were the adverse maternal outcome with a higher percentage of these in overt hypothyroidism which was statistically significant.

Concerning fetal outcome APGAR score <6 in 5 min, Intrauterine growth restriction (IUGR), NICU admission, neonatal Respiratory distress syndrome (RDS), Intrauterine fetal death (IUFD), and congenital anomaly were found with a higher percentage in overt hypothyroidism. **Conclusion:** Since the impact of hypothyroidism on fetomaternal morbidities have been identified so screening for hypothyroidism to be included as a routine screening test and should be treated accordingly to improve maternal and fetal outcome.

Keywords

Fetal Outcome, Maternal Outcome, Overt Hypothyroidism, Subclinical Hypothyroidism

1. Introduction

Thyroid disorders constitute one of the most common endocrine disorders in pregnancy and thyroid physiology plays a major role in pregnancy alteration in thyroid functions occurs due to increased thyrotropic effect of human chorionic gonadotropin (HCG), increased thyroid hormone binding globulin (TBG) concentration, and increased iodine clearance in the kidneys [1]. Fetus depends on maternal thyroid hormone for organogenesis, general growth, and development of a central nervous system since fetus synthesizes thyroid hormone only by the end of the first trimester [2] [3].

The prevalence of thyroid dysfunction is high in pregnant women, with subclinical dysfunction in 10% of pregnancies and overt in 2% - 3% of pregnancies [4]. Subclinical hypothyroidism occurs in 3% - 5% of pregnancies and overt hypothyroidism in 0.3% - 0.5% [5].

TSH level of 2.5 mIU/L in the first trimester and TSH level of 0.2 - 3 mIU/L in the second trimester and free thyroxine (FT4) as 12 - 30 pmol/l has been accepted according to the guideline of the American thyroid association published in 2011 for an accurate diagnosis and management of thyroid disease in pregnancy [6].

Various studies have shown that hypothyroidism in pregnancy leads to adverse maternal outcomes including anemia, gestational hypertension, gestational diabetes mellitus, placenta previa, placental abruption, premature rupture of membrane, premature delivery, LSCS delivery, and postpartum hemorrhage. Similarly, adverse perinatal outcomes including IUGR, LBW, fetal distress, prematurity, stillbirth, malformation, congenital hypothyroidism, neonatal thyrotoxicosis, and neurocognitive defects are also seen [7] [8].

With this background, this study aimed to find the fetomaternal outcome in pregnancy complicated by maternal hypothyroidism.

2. Methods

This was a retrospective observational study conducted at Paropakar Maternity

and Women's Hospital (PMWH), Thapathali, Kathmandu from July 2020 to April 2021. Institutional approval was taken for the study (60/1692).

All singleton pregnant women with hypothyroidism delivered at the institution during the study duration were included. Molar pregnancy, hyperthyroid pregnant women, multiple gestations, women with diagnosed chronic hypertension, diabetes mellitus, and previous bad obstetric history with a known underlying cause were excluded from the study. The Sample size was calculated by the prevalence method for hypothyroidism in pregnancy.

Pregnant women in their antenatal visit were screened with TSH, free T3, and free T4 levels with additional TPO antibody when required. As per the ATA, guideline women were categorized as having overt hypothyroidism TSH > 3 mIU/L with a low FT4 or a TSH ≥ 10 mIU/L irrespective of FT4 levels, subclinical hypothyroidism (TSH of 3-10 MIU/L and a normal FT4 levels), normal (TSH of 0.2 to 3 mIU/L and FT4 of 11.84 ± 3.86).

Data were recorded in a predesigned pro forma. Obstetric outcomes and perinatal outcomes were noted for hypothyroid mothers including the mode of delivery, and postpartum hemorrhage. Neonatal assessment with APGAR score, birth weight, and presence of congenital anomalies was also noted. Chi-square test and Fisher exact test were applied for data analysis and statistically analyzed using SPSS. P-value of < 0.05 was regarded as statistically significant. The ethical clearance was taken from the Institutional Review Committee (IRC) of Paropakar Maternity and Women's Hospital before starting the study.

3. Results

A total of 470 cases of hypothyroidism were admitted for delivery, among which only 330 were enrolled for the study, and the remaining 140 cases were excluded. Total population delivered were 22200 in 1 year. So the prevalence is calculated as follows:

$$\frac{\text{No of patient with hypothyroidism in 1 year}/470}{\text{Total number of population delivered in 1 year}/22200}$$

So the prevalence of hypothyroidism in pregnancy was 2.11% of total deliveries with 1.7% of subclinical and 0.31% of overt hypothyroidism.

In present study most of the cases belonged to age group >30 years 57.9% (n = 191), followed by 20 - 29 years 36.4 % (n = 120) and less than 20 years 5.8% (n = 19). Similarly, 70.3% (n = 232) of the cases were from rural areas and 29.7% (n = 98) of the cases were from urban areas. Primigravida constituted 53.3% (n = 176) of the cases, followed by multigravida-2 (27.9%), multigravida-3 (13%) and multigravida −4 (5.8%). A regular menstrual cycle was found in 59.1% (n = 195) of the cases whereas 40.9% (135) had an irregular cycle.

In the present study, 85.8% (n = 283) had subclinical hypothyroidism and 14.2% (n = 47) had overt hypothyroidism. The mean TSH levels in these subgroups were 4.654 and 5.99 respectively (**Table 1**).

Table 1. Thyroid profile inference and mean TSH Levels.

Hypothyroid	Frequency (n = 330)	Percent (%)	Mean TSH level
Overt	47	14.2	5.997 m IU/L
Subclinical	283	85.8	4.6547 m IU/L
Total	330	100	

Table 2. Maternal adverse outcomes seen with hypothyroidism in study participants.

Maternal association	Hypothyroidism		P value
	Overt N = 47	Subclinical N = 283	
Pre-eclampsia	12 (25.5%)	27 (9.5%)	**0.004**
Gestational Diabetes (GDM)	12 (25.5%)	26 (9.1%)	**0.003**
Abruptio placentae	2 (4.2%)	5 (1.7%)	0.26
Postpartum hemorrhage (PPH)	7 (14.8%)	8 (2.8%)	**0.002**

Preeclampsia, Gestational Diabetes Mellitus, Abruptio placenta, and Postpartum Hemorrhage were the adverse maternal outcomes found in hypothyroid mothers with a higher percentage of these in overt hypothyroidism (Table 2).

Instrumental delivery was performed in 6.3% of participants with overt and 2.1% with subclinical hypothyroidism. Cesarean delivery was performed for 53.1% of overt and 46.2% of subclinical hypothyroid participants, indicating a higher cesarean rate in these women.

Preterm delivery 29.7% were observed in overt hypothyroidism while 11.2% was observed in subclinical hypothyroidism which was statistically significant (Table 3).

Table 3. Gestational age at delivery.

Gestational age at delivery	Hypothyroid		P value
	Overt N = 47	Subclinical N = 283	
28 to 34 weeks	4 (8.5%)	4 (1.4%)	**0.001**
34 - 36 weeks 6 days	10 (21.2%)	28 (9.8%)	
Term	33 (70.2%)	251 (88.6%)	

Hypothyroid mothers were also found to have adverse perinatal outcomes including congenital anomaly, IUFD, IUGR, NICU admissions, neonatal respiratory distress syndrome (RDS), and a low APGAR at 6 minutes of life (Table 4).

Table 4. Perinatal outcome in hypothyroid mothers.

Perinatal outcome	Hypothyroidism		P value
	Overt N = 47	Subclinical N = 283	
Congenital anomaly	6 (12.7%)	2 (0.7%)	**0.001**
IUFD	5 (10.6%)	6 (2.1%)	**0.011**
IUGR	15 (31.9%)	33 (11.6%)	**0.001**
NICU admission	13 (27.6%)	27 (9.5%)	**0.001**
Neonatal RDS	5 (10.6%)	16 (5.6%)	0.198
Apgar score <6 in 5 minute	18 (38.2%)	55 (19.4%)	**0.005**

Neonatal weight of <2.5 kg was found in 42.5% and 19.7% of women with overt and subclinical hypothyroidism respectively reaching a statistical significance with a P-value of 0.001. Among participants with overt hypothyroidism, a birthweight of 2.6 - 3.5 kg was seen in 53.1% and 3.6 - 4.5 kg in 4.2%. Similarly, with subclinical hypothyroidism, the birthweight was 2.6 - 3.5 kg in 63.6% and 3.6 - 4.5 kg in 16.6%.

4. Discussion

Hypothyroidism in pregnancy can be masked under certain physiological changes from the pregnancy itself like weight gain, muscle cramps, constipation, or fatigue emphasizing the importance of screening with the thyroid function test. Our study consisted of 330 antenatal patients undergoing screening for thyroid dysfunction. The incidence of hypothyroidism among the study population was 1.7% for subclinical and 0.31% for overt hypothyroidism. Similar to our study, Shrestha A *et al*. had an incidence of 1.9% for hypothyroidism in pregnancy [9].

The majority of the patients in the present study were above 30 yrs age (51.3%) with a mean age of 28.9 years, which was also observed in a study done by kalpesh *et al*. that showed increased maternal age associated with thyroid dysfunction [10]. The majority belonged to rural areas (70.3%) whereas urban areas accounted for 29.7%. Overt Hypothyroidism had a higher incidence compared to subclinical hypothyroidism for preeclampsia (11.8%), gestational diabetes melli-

tus (11.5%), and postpartum hemorrhage (4.5%). Endo T *et al*. showed that hypothyroidism can lead to hypertension [11]. Similarly, Wolfberg et al concluded that women who were treated for hypothyroidism were more likely to have chronic hypertension and increased risk for preeclampsia [12]. However, our study had a much higher incidence compared to their study (4.3%). Although another study by Cleary Goldman and colleagues documented a greater risk of GDM with overt hypothyroid and no such association with SCH [13].

In the study by Casey et al, the risk for placental abruption in hypothyroidism was increased by 3 times, while preterm birth was increased two-fold. [14] Our study had 7 cases (2%) of placental abruption and preterm delivery was seen in 13.9%.

Although the incidence of IUGR was 2.9% as per the study by Shrestha A *et al*., our study had a higher overall incidence of 14.5% with 31.9% among the population who had overt hypothyroidism [9]. Similar to our study Ohashi *et al*. reported IUGR in 25% of pregnancies involving maternal thyroid disorder [15]. This could be due to thyroid hormone which is responsible for the metabolism along with fetal weight. Similarly, hypothyroid mothers in our study showed an adverse effect on perinatal outcomes including IUFD (3.3%), NICU admissions (12.1%), and APGAR score of less than six at five minutes (22.1%). Shrestha A *et al*. also studied a low APGAR of 11.3% in their study [9]. Congenital anomaly was noted in 2.4% hypothyroid study population in our study. Su and colleagues also reported malformation in a fetus (1 case of circulatory system and 2 cases of musculoskeletal system) mainly in women with overt hypothyroid [16]. However, the study by Casey et al suggested that maternal thyroid disorder was not associated with an increased rate of fetal malformation [14].

More studies with larger sample sizes and longer duration of study should also be done for more targeted research.

5. Conclusion

Undiagnosed and untreated hypothyroidism in pregnancy can lead to adverse maternal and fetal outcomes with increased risk of preeclampsia, gestational diabetes mellitus, preterm birth, postpartum hemorrhage, IUFD, IUGR, poor APGAR score, and NICU admissions. In endemic iodine deficient countries like Nepal, screening with TSH during pregnancy can diagnose and ultimately reduce the adverse outcomes associated with hypothyroidism with early treatment.

Conflicts of Interest

The authors declare no conflicts of interest.

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