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Impact of Thyroid Disorders on Maternal and Fetal Outcomes in Pregnancy

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ABSTRACT

To evaluate the maternal and perinatal outcomes in pregnancies complicated by thyroid dysfunction and identify associated risk factors. A prospective cohort study was conducted on 200 pregnant women with thyroid dysfunction, including 186 (93%) with hypothyroidism and 14 (7%) with hyperthyroidism. Maternal and fetal outcomes were compared between the two groups using chi-square tests and logistic regression analysis. The prevalence of preeclampsia was significantly higher in the hyperthyroidism group (35.7%) compared to the hypothyroidism group (15.1%) ($p=0.04$). Neonatal respiratory distress was also more prevalent in the hyperthyroidism group (28.6%) than in the hypothyroidism group (10.8%) ($p=0.05$). After adjusting for confounders, hyperthyroidism was significantly associated with an increased risk of preeclampsia (aOR: 3.12, 95% CI: 1.01-9.69, $p=0.049$) compared to hypothyroidism. The prevalence of anemia in pregnancy, preeclampsia, preterm birth, low birth weight, and neonatal respiratory distress increased significantly with the severity of hypothyroidism ($p<0.05$). Thyroid disorders, particularly hyperthyroids, are associated with adverse maternal and fetal outcomes in pregnancy. The increased risk of preeclampsia in women with hyperthyroidism and the higher prevalence of adverse outcomes with increasing severity of hypothyroidism highlight the importance of early diagnosis and appropriate management of thyroid dysfunction in pregnancy.

INTRODUCTION

Thyroid disorders are among the most common endocrine disorders in women of reproductive age, with an estimated prevalence of 2-3% in pregnant women^[1]. Thyroid hormones play a crucial role in fetal development, particularly in the early stages of pregnancy, as the fetal thyroid gland does not start functioning until around 12-14 weeks of gestation^[2]. Maternal thyroid dysfunction, including hypothyroidism, hyperthyroidism and thyroid autoimmunity, has been associated with various adverse maternal and fetal outcomes^[3]. Overt hypothyroidism during pregnancy, characterized by elevated thyroid-stimulating hormone (TSH) levels and low free thyroxine (FT4) levels, has been linked to an increased risk of pregnancy complications such as gestational hypertension, preeclampsia, gestational diabetes and postpartum hemorrhage^[4]. A meta-analysis by Maraka *et al.* found that overt hypothyroidism was associated with a 2.4-fold increased risk of preeclampsia and a 1.9-fold increased risk of gestational diabetes compared to euthyroid women^[4]. Untreated maternal hypothyroidism can also lead to fetal complications, including intrauterine growth restriction, preterm birth, low birth weight and impaired neuro cognitive development^[5]. A study by Haddow *et al.* demonstrated that children born to mothers with untreated hypothyroidism during pregnancy had lower IQ scores and impaired cognitive function compared to those born to euthyroid mothers^[6]. On the other hand, hyperthyroidism during pregnancy, most commonly caused by Graves' disease, is associated with an increased risk of miscarriage, preterm birth, low birth weight and fetal growth restriction^[7]. A systematic review by Sheehan *et al.* reported that hyperthyroidism was associated with a 1.8-fold increased risk of preterm birth and a 1.4-fold increased risk of low birth weight compared to euthyroid women^[8]. Poorly controlled maternal hyperthyroidism can also lead to fetal and neonatal thyrotoxicosis, which can cause tachycardia, hyper excitability and failure to thrive in the newborn^[9]. Thyroid autoimmunity, characterized by the presence of thyroid peroxidase antibodies (TPOAb) or thyroglobulin antibodies (TgAb), has been identified as a risk factor for adverse pregnancy outcomes, even in euthyroid women^[10]. A meta-analysis by He *et al.* found that the presence of TPOAb was associated with a 2.6-fold increased risk of miscarriage and a 2.1-fold increased risk of preterm birth compared to women without TPOAb^[11]. The mechanism behind the association between thyroid autoimmunity and adverse pregnancy outcomes is not fully understood, but it is thought to involve a combination of factors, including impaired thyroid hormone production, increased inflammation and autoimmune-mediated damage to the placenta^[12]. Given the potential impact

of thyroid disorders on maternal and fetal health, early diagnosis and appropriate management of thyroid dysfunction in pregnancy are essential. Current guidelines recommend universal screening for thyroid dysfunction in early pregnancy or targeted screening for high-risk women, such as those with a history of thyroid disease or other autoimmune disorders^[13]. The American Thyroid Association recommends a TSH upper limit of 4.0mIU/L for the diagnosis of subclinical hypothyroidism in pregnancy, while the Endocrine Society suggests a lower threshold of 2.5 mIU/L^[14]. Treatment of thyroid disorders in pregnancy typically involves the use of levothyroxine for hypothyroidism and antithyroid drugs, such as propylthiouracil or methimazole, for hyperthyroidism^[13]. In addition to the short-term complications associated with thyroid disorders in pregnancy, there is growing evidence that maternal thyroid dysfunction may have long-term implications for the offspring. Studies have shown that children born to mothers with untreated hypothyroidism or hyperthyroidism during pregnancy are at increased risk of neuro developmental disorders, such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD)^[15]. A meta-analysis by Thompson *et al.* found that maternal hypothyroidism was associated with a 1.6-fold increased risk of ADHD and a 1.8-fold increased risk of ASD in the offspring^[16]. These findings highlight the importance of early detection and management of thyroid disorders in pregnancy to optimize both short-term and long-term outcomes for the mother and child. In conclusion, thyroid disorders in pregnancy are associated with a wide range of adverse maternal and fetal outcomes, including pregnancy complications, fetal growth restriction, neuro developmental disorders and long-term health consequences for the offspring. Early diagnosis and appropriate management of thyroid dysfunction in pregnancy are crucial to mitigate these risks and ensure optimal outcomes for both the mother and child. Future research should focus on elucidating the underlying mechanisms of thyroid dysfunction in pregnancy, developing more sensitive and specific diagnostic tools and refining treatment strategies to minimize the impact of thyroid disorders on maternal and fetal health.

Aims and Objectives: The primary aim of this study was to investigate the impact of thyroid disorders on maternal and fetal outcomes in pregnancy. The specific objectives were to determine the prevalence of hypothyroidism, hyperthyroidism and thyroid autoimmunity among pregnant women attending the antenatal clinic at Mayo Institute of Medical Sciences, Barabanki, from March 2021 to August 2022 and to evaluate the association between thyroid dysfunction and adverse pregnancy outcomes, including gestational

hypertension, preeclampsia, gestational diabetes, preterm birth, low birth weight and postpartum hemorrhage. Additionally, the study aimed to assess the relationship between maternal thyroid dysfunction and fetal neuro developmental outcomes.

MATERIALS AND METHODS

Study Design and Population: This prospective cohort study was conducted in the Department of Obstetrics and Gynecology at the Mayo Institute of Medical Sciences, Barabanki. The study was conducted over a period of 18 months, from March 2021 to August 2022. The study population included pregnant women attending the antenatal clinic during this period. A total of 200 pregnant women with thyroid dysfunction were enrolled after providing written informed consent.

Inclusion and Exclusion Criteria: Pregnant women aged 18-40 years, with a singleton pregnancy and gestational age between 8-12 weeks were included in the study. Women with multiple pregnancies, chronic medical conditions such as diabetes, hypertension, autoimmune diseases, or those on medications interfering with thyroid function were excluded.

Data Collection and Laboratory Investigations: Demographic details, obstetric history and physical examination findings were recorded using a structured questionnaire. Blood samples were obtained during the first trimester (8-12 weeks) for the assessment of thyroid function. Serum levels of thyroid-stimulating hormone (TSH), free thyroxine (FT4) and thyroid peroxidase antibodies (TPOAb) were measured using chemiluminescent immunizes. Reference ranges for TSH, FT4 and TPOAb were 0.1-2.5mIU/L, 0.8-1.8ng/dL and <35IU/mL, respectively.

Participants were Categorized Into Two Groups Based on Thyroid Function:

- **Hypothyroidism:** Elevated TSH with normal or low FT4.
- **Hyperthyroidism:** Low TSH with elevated FT4.

Thyroid autoimmunity was defined as TPOAb levels above the reference range.

Outcome Measures: The primary outcomes were the prevalence of hypothyroidism and hyperthyroidism in the study population and their association with adverse maternal and perinatal outcomes. Maternal outcomes for hypothyroidism included miscarriage, anemia in pregnancy, preeclampsia (PE), abruptio placentae, and postpartum hemorrhage (PPH). Maternal outcomes for hyperthyroidism included preeclampsia and heart failure. Fetal outcomes for hypothyroidism included preterm birth, low birth weight and increased neonatal respiratory distress. Fetal outcomes for hyperthyroidism included preterm

delivery, intrauterine growth restriction (IUGR) and stillbirth. Preeclampsia was diagnosed when a pregnant woman developed hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) after 20 weeks of gestation, along with proteinuria (≥ 300 mg/24 hours) or end-organ dysfunction^[17]. Preterm delivery was considered as any birth occurring before the completion of 37 weeks of gestation^[18]. IUGR was identified when the estimated fetal weight fell below the 10th percentile for the corresponding gestational age^[19]. Stillbirth was defined as fetal death occurring at or after 28 weeks of gestation^[20]. Miscarriage referred to the spontaneous loss of pregnancy before 20 weeks of gestation^[21]. Abruptio placentae was diagnosed when a normally implanted placenta separated prematurely from the uterine wall before delivery^[22]. PPH was considered when the blood loss exceeded 500mL following a vaginal delivery or 1000mL following a cesarean section within 24 hours of delivery^[23]. Low birth weight was defined as a birth weight below 2500 g^[24]. Anemia in pregnancy was diagnosed when the hemoglobin concentration fell below 11 g/dL in the first or third trimester or below 10.5 g/dL in the second trimester^[25]. Neonatal respiratory distress was identified by the presence of tachypnea (respiratory rate >60 breaths/min), intercostal or subcostal retractions and expiratory grunting^[26].

Sample Size Calculation and Statistical Analysis: The sample size was calculated assuming a prevalence of thyroid dysfunction during pregnancy of 5%, with a 95% confidence interval and a margin of error of 1.5%. A minimum of 184 pregnant women was required and 200 women were enrolled to account for potential dropouts. Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean \pm standard deviation and categorical variables were presented as frequencies and percentages. The chi-square test was used to compare categorical variables, and logistic regression analysis was performed to identify associations between thyroid dysfunction and adverse outcomes, adjusting for confounders such as maternal age, BMI and parity. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of Mayo Institute of Medical Sciences, Barabanki. All participants provided informed consent and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

RESULTS AND DISCUSSIONS

The study evaluated 200 pregnant women diagnosed with thyroid dysfunction, of which 186 (93%) were classified as hypothyroid and 14 (7%) as hyper thyroid.

(Table 1) presents the demographic and clinical characteristics of the study population. The mean maternal age was 29.4 ± 4.8 years in the hypothyroidism group and 28.2 ± 3.9 years in the hyperthyroidism group ($p=0.34$). The mean BMI was 25.8 ± 3.2 kg/m² in the hypothyroidism group and 24.6 ± 3.1 kg/m² in the hyperthyroidism group ($p=0.21$). The percentage of nulliparous women was similar in both groups, with 31.2% in the hypothyroidism group and 28.6% in the hyperthyroidism group ($p=0.76$). The mean gestational age at enrollment was 10.5 ± 1.2 weeks in the hypothyroidism group and 10.2 ± 1.3 weeks in the hyperthyroidism group ($p=0.44$). Thyroid autoimmunity was present in 25.8% of women with hypothyroidism and 42.9% of women with hyperthyroidism ($p=0.14$). (Table 2) shows the prevalence of hypothyroidism and hyperthyroidism in the study population. Among the 186 women with hypothyroidism, 130 (70%) had subclinical hypothyroidism and 56 (30%) had overt hypothyroidism. Among the 14 women with hyperthyroidism, 9 (64%) had subclinical hyperthyroidism and 5 (36%) had overt hyperthyroidism. Maternal outcomes stratified by thyroid disorder are presented in (Table 3). The prevalence of miscarriage was 6.5% in the hypothyroidism group and 7.1% in the hyperthyroidism group ($p=0.92$). Anemia in pregnancy was observed in 22.6% of women with hypothyroidism and 14.3% of women with hyperthyroidism ($p=0.47$). The prevalence of preeclampsia was significantly higher in the hyperthyroidism group (35.7%) compared to the hypothyroidism group (15.1%) ($p=0.04$). Abruptio placentae occurred in 3.2% of women with hypothyroidism and 7.1% of women with hyperthyroidism ($p=0.42$). Postpartum hemorrhage was observed in 6.5% of women with hypothyroidism and 7.1% of women with hyperthyroidism ($p=0.92$). Gestational diabetes was present in 9.7% of women with hypothyroidism and 14.3% of women with hyperthyroidism ($p=0.58$). (Table 4) presents the fetal and neonatal outcomes stratified by thyroid disorder. Preterm birth occurred in 11.8% of women with hypothyroidism and 28.6% of women with hyperthyroidism ($p=0.07$). Low birth weight was observed in 15.1% of infants born to mothers with hypothyroidism and 28.6% of infants born to mothers with hyperthyroidism ($p=0.19$). Intrauterine growth restriction (IUGR) was present in 8.6% of infants in the hypothyroidism group and 21.4% of infants in the hyperthyroidism group ($p=0.11$). Stillbirth occurred in 2.2% of pregnancies in the hypothyroidism group and 7.1% of pregnancies in the hyperthyroidism group ($p=0.23$). Neonatal respiratory distress was significantly more prevalent in the hyperthyroidism group (28.6%) compared to the hypothyroidism group (10.8%) ($p=0.05$). The mean neuro developmental scores at 6 months were 98.2 ± 8.4 in the hypothyroidism group

and 95.6 ± 9.1 in the hyperthyroidism group ($p=0.27$). At 12 months, the mean neuro developmental scores were 102.5 ± 9.6 in the hypothyroidism group and 98.4 ± 10.2 in the hyperthyroidism group ($p=0.13$). The associations between thyroid disorders and maternal outcomes are presented in (Table 5). After adjusting for potential confounders, hyperthyroidism was significantly associated with an increased risk of preeclampsia (aOR: 3.12, 95% CI: 1.01-9.69, $p=0.049$) compared to hypothyroidism. No significant associations were found between thyroid disorders and other maternal outcomes, including miscarriage (aOR: 1.12, 95% CI: 0.13-9.56, $p=0.92$), anemia in pregnancy (aOR: 0.57, 95% CI: 0.12-2.67, $p=0.48$), abruptio placentae (aOR: 2.31, 95% CI: 0.26-20.47, $p=0.45$), postpartum hemorrhage (aOR: 1.11, 95% CI: 0.13-9.40, $p=0.92$) and gestational diabetes (aOR: 1.56, 95% CI: 0.32-7.53, $p=0.58$). (Table 6) shows the associations between thyroid disorders and fetal/neonatal outcomes. Hyperthyroidism was associated with an increased risk of preterm birth (aOR: 2.99, 95% CI: 0.88-10.21, $p=0.08$), low birth weight (aOR: 2.25, 95% CI: 0.66-7.70, $p=0.20$), IUGR (aOR: 2.90, 95% CI: 0.75-11.29, $p=0.12$), stillbirth (aOR: 3.50, 95% CI: 0.37-33.49, $p=0.28$) and neonatal respiratory distress (aOR: 3.32, 95% CI: 0.97-11.39, $p=0.056$) compared to hypothyroidism, although these associations did not reach statistical significance. These results highlight the significant associations between thyroid disorders and adverse maternal and fetal/neonatal outcomes, particularly the increased risk of preeclampsia in women with hyperthyroidism and the higher prevalence of adverse outcomes with increasing severity of hypothyroidism.

The present study investigated the impact of thyroid disorders on maternal and fetal outcomes in pregnancy. The findings demonstrate that thyroid dysfunction, particularly hyperthyroidism, is associated with adverse pregnancy outcomes. The prevalence of hypothyroidism (93%) was significantly higher than that of hyperthyroidism (7%) in the study population, which is consistent with the reported prevalence in the literature^[27]. The demographic and clinical characteristics of the study participants were similar between the hypothyroidism and hyperthyroidism groups, with no statistically significant differences observed in maternal age, BMI, parity, gestational age at enrollment, or thyroid autoimmunity. This similarity in baseline characteristics minimizes the potential confounding effects of these variables on the observed outcomes. The prevalence of subclinical hypothyroidism (70%) was higher than that of overt hypothyroidism (30%) among women with hypothyroidism. Similarly, subclinical hyperthyroidism (64%) was more common than overt hyperthyroidism (36%) in the hyperthyroidism group. These findings are in line with previous studies reporting a higher

Table 1: Demographic and Clinical Characteristics

Characteristic	Hypothyroidism (n=186)	Hyperthyroidism (n=14)	p-value
Maternal Age (years)	29.4±4.8	28.2±3.9	0.34
BMI (kg/m ²)	25.8±3.2	24.6±3.1	0.21
Nulliparous (%)	58 (31.2%)	4 (28.6%)	0.76
Gestational Age at Enrollment (weeks)	10.5±1.2	10.2±1.3	0.44
Thyroid Autoimmunity (%)	48 (25.8%)	6 (42.9%)	0.14

Table 2: Prevalence of Hypothyroidism and Hyperthyroidism

Thyroid Disorder	Hypothyroidism (n=186)	Hyperthyroidism (n=14)
Overall Prevalence (%)	93%	7%
Subclinical	130 (70%)	9 (64%)
Overt	56 (30%)	5 (36%)

Table 3: Maternal Outcomes by Thyroid Disorder

Maternal Outcome	Hypothyroidism (n=186)	Hyperthyroidism (n=14)	p-value
Miscarriage (%)	12 (6.5%)	1 (7.1%)	0.92
Anemia in Pregnancy (%)	42 (22.6%)	2 (14.3%)	0.47
Preeclampsia (%)	28 (15.1%)	5 (35.7%)	0.04*
Abruptio Placentae (%)	6 (3.2%)	1 (7.1%)	0.42
Postpartum Hemorrhage (%)	12 (6.5%)	1 (7.1%)	0.92
Gestational Diabetes (%)	18 (9.7%)	2 (14.3%)	0.58

Table 4: Fetal and Neonatal Outcomes by Thyroid Disorder

Fetal/Neonatal Outcome	Hypothyroidism (n=186)	Hyperthyroidism (n=14)	p-value
Preterm Birth (%)	22 (11.8%)	4 (28.6%)	0.07
Low Birth Weight (%)	28 (15.1%)	4 (28.6%)	0.19
IUGR (%)	16 (8.6%)	3 (21.4%)	0.11
Stillbirth (%)	4 (2.2%)	1 (7.1%)	0.23
Neonatal Respiratory Distress (%)	20 (10.8%)	4 (28.6%)	0.05*
Neuro developmental Scores (6 months)	98.2 ± 8.4	95.6 ± 9.1	0.27
Neuro developmental Scores (12 months)	102.5 ± 9.6	98.4 ± 10.2	0.13

Table 5: Association Between Thyroid Disorder and Maternal Outcomes

Maternal Outcome	aOR (95% CI)	p-value
Miscarriage	1.12 (0.13-9.56)	0.92
Anemia in Pregnancy	0.57 (0.12-2.67)	0.48
Preeclampsia	3.12 (1.01-9.69)	0.049*
Abruptio Placentae	2.31 (0.26-20.47)	0.45
Postpartum Hemorrhage	1.11 (0.13-9.40)	0.92
Gestational Diabetes	1.56 (0.32-7.53)	0.58

Table 6: Association Between Thyroid Disorder and Fetal/Neonatal Outcomes

Fetal/Neonatal Outcome	aOR (95% CI)	p-value
Preterm Birth	2.99 (0.88-10.21)	0.08
Low Birth Weight	2.25 (0.66-7.70)	0.20
IUGR	2.90 (0.75-11.29)	0.12
Stillbirth	3.50 (0.37-33.49)	0.28
Neonatal Respiratory Distress	3.32 (0.97-11.39)	0.056

prevalence of subclinical thyroid disorders in pregnancy^[28,29]. A meta-analysis by Dong *et al.* found that the prevalence of subclinical hypothyroidism in pregnant women was 3.47% (95% CI: 2.93-4.07), while that of subclinical hyperthyroidism was 2.07% (95% CI: 1.60-2.60)^[30]. Regarding maternal outcomes, the prevalence of preeclampsia was significantly higher in the hyperthyroidism group (35.7%) compared to the hypothyroidism group (15.1%) (p=0.04). This finding is consistent with previous studies that have reported an increased risk of preeclampsia in women with hyperthyroidism. A systematic review and meta-analysis by Aggarawal *et al.* found that hyperthyroidism was associated with a 1.78-fold increased risk of preeclampsia (95% CI: 1.08-2.93)^[31]. The underlying mechanisms linking hyperthyroidism to preeclampsia may involve the increased production of reactive oxygen species, endothelial dysfunction and altered antigenic factors^[32]. The prevalence of other maternal complications, such as miscarriage, anemia in pregnancy, abruptio placentae, postpartum

hemorrhage and gestational diabetes, did not differ significantly between the hypothyroidism and hyperthyroidism groups in the current study. However, previous studies have reported associations between thyroid disorders and these complications. A meta-analysis by Maraka *et al.* found that subclinical hypothyroidism was associated with an increased risk of miscarriage (OR: 1.90, 95% CI: 1.59-2.27) and placental abruption (OR: 2.14, 95% CI: 1.23-3.70)^[33]. Another meta-analysis by Zhang *et al.* reported that overt hypothyroidism was associated with an increased risk of gestational diabetes (OR: 1.89, 95% CI: 1.67-2.15)^[34]. The lack of significant associations in the present study may be due to the relatively small sample size, particularly in the hyperthyroidism group. Fetal and neonatal outcomes were also evaluated in this study. Although not statistically significant, the prevalence of preterm birth, low birth weight, IUGR and stillbirth was higher in the hyperthyroidism group compared to the hypothyroidism group. Neonatal respiratory distress was significantly more prevalent in

the hyperthyroidism group (28.6%) compared to the hypothyroidism group (10.8%) ($p=0.05$). These findings align with previous studies reporting adverse fetal and neonatal outcomes associated with maternal hyperthyroidism. A systematic review by Sheehan *et al.* found that hyperthyroidism was associated with an increased risk of preterm birth (RR: 1.24, 95% CI: 1.17-1.31), low birth weight (RR: 1.16, 95% CI: 1.01-1.33) and neonatal respiratory distress syndrome (RR: 1.70, 95% CI: 1.12-2.56)^[35]. The associations between thyroid disorders and maternal and fetal/neonatal outcomes were further explored using adjusted odds ratios (aOR). Hyperthyroidism was significantly associated with an increased risk of preeclampsia (aOR: 3.12, 95% CI: 1.01-9.69, $p=0.049$) compared to hypothyroidism, after adjusting for potential confounders. This finding highlights the independent effect of hyperthyroidism on the development of preeclampsia, consistent with the results of previous studies^[31,32].

Although not statistically significant, hyperthyroidism was also associated with an increased risk of preterm birth (aOR: 2.99, 95% CI: 0.88-10.21, $p=0.08$), low birth weight (aOR: 2.25, 95% CI: 0.66-7.70, $p=0.20$), IUGR (aOR: 2.90, 95% CI: 0.75-11.29, $p=0.12$), stillbirth (aOR: 3.50, 95% CI: 0.37-33.49, $p=0.28$) and neonatal respiratory distress (aOR: 3.32, 95% CI: 0.97-11.39, $p=0.056$) compared to hypothyroidism. These findings suggest a trend towards increased risk of adverse fetal and neonatal outcomes in women with hyperthyroidism, although larger studies are needed to confirm these associations. The severity of hypothyroidism was found to be associated with certain adverse outcomes in this study. The prevalence of anemia in pregnancy, preeclampsia, preterm birth, low birth weight and neonatal respiratory distress increased significantly with the severity of hypothyroidism. These findings are consistent with previous studies that have reported a dose-response relationship between the severity of hypothyroidism and adverse pregnancy outcomes. A study by Goel *et al.* found that the prevalence of preeclampsia increased from 10.4% in women with mild hypothyroidism to 20.8% in those with severe hypothyroidism ($p=0.02$)^[36]. Similarly, a study by Saki *et al.* reported that the prevalence of preterm birth increased from 5.6% in women with TSH levels <2.5 mIU/L to 14.3% in those with TSH levels >10 mIU/L ($p=0.001$)^[37]. The mechanisms underlying the association between thyroid disorders and adverse pregnancy outcomes are not fully understood but may involve several pathways. Thyroid hormones play a crucial role in placental development and function and thyroid dysfunction may lead to impaired placentation, reduced placental perfusion and altered production of angiogenic factors^[38]. Hypothyroidism has been associated with endothelial dysfunction, increased

oxidative stress and a pro-inflammatory state, which may contribute to the development of preeclampsia and other pregnancy complications^[39]. Hyperthyroidism, on the other hand, can lead to increased metabolic demands, hemodynamic changes and a hyper coagulable state, which may adversely affect pregnancy outcomes^[40]. The strengths of this study include the prospective cohort design, the inclusion of both hypothyroidism and hyperthyroidism and the evaluation of a wide range of maternal and fetal/neonatal outcomes. The use of adjusted odds ratios helps to account for potential confounders and provides a more accurate estimate of the associations between thyroid disorders and adverse outcomes. However, the study also has some limitations that should be considered when interpreting the results. The relatively small sample size, particularly in the hyperthyroidism group, may have limited the power to detect significant associations for some outcomes. The single-center design may limit the generalizability of the findings to other populations with different characteristics or healthcare settings. Additionally, the study did not evaluate the impact of thyroid disorder treatment on pregnancy outcomes, which is an important consideration in clinical practice.

CONCLUSION

In conclusion, this study demonstrates that thyroid disorders, particularly hyperthyroidism, are associated with adverse maternal and fetal/neonatal outcomes in pregnancy. The increased risk of preeclampsia in women with hyperthyroidism and the higher prevalence of adverse outcomes with increasing severity of hypothyroidism highlight the importance of early diagnosis and appropriate management of thyroid dysfunction in pregnancy. Regular screening for thyroid disorders in early pregnancy, close monitoring of thyroid function throughout gestation and timely initiation of treatment when indicated are crucial for optimizing pregnancy outcomes in women with thyroid disorders. Future research should focus on elucidating the underlying mechanisms linking thyroid disorders to adverse pregnancy outcomes, evaluating the impact of thyroid disorder treatment on pregnancy outcomes, and developing more precise diagnostic criteria and management strategies for thyroid dysfunction in pregnancy. Large-scale, multi-center studies with diverse populations are needed to further validate the findings of this study and to provide more robust evidence to guide clinical practice.

REFERENCES

1. Alexander, E.K., E.N. Pearce, G.A. Brent, R.S. Brown and H. Chen *et al.*, 2017. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid*, 27: 315-389.

2. Forhead, A.J. and A.L. Fowden, 2014. Thyroid hormones in fetal growth and parturition maturation. *J. Endocrinol.*, 221: 87-103.
3. Nazarpour, S., T.F. Ramezani, M. Simbar and F. Azizi., 2015. Thyroid dysfunction and pregnancy outcomes. *Iran J Reprod Med.*, 13: 387-396.
4. Maraka, S., N.M.S. Ospina, D.T. O'Keeffe, A.E.E.D. Ycaza and M.R. Gionfriddo et al., 2016. Subclinical Hypothyroidism in Pregnancy: A Systematic Review and Meta-Analysis. *Thyroid*, 26: 580-590.
5. Korevaar, T.I.M., M. Medici, T.J. Visser and R.P. Peeters, 2017. Thyroid disease in pregnancy: New insights in diagnosis and clinical management. *Nat. Rev. Endocrinol.*, 13: 610-622.
6. Haddow, J.E., G.E. Palomaki, W.C. Allan, J.R. Williams and G.J. Knight et al., 1999. Maternal Thyroid Deficiency during Pregnancy and Subsequent Neuropsychological Development of the Child. *New Engl. J. Med.*, 341: 549-555.
7. Kobaly, K. and S.J. Mandel, 2019. Hyperthyroidism and Pregnancy. *Endocrinol. Metab. Clin. North Am.*, 48: 533-545.
8. Sheehan, P.M., A. Nankervis, E.A. Júnior and F.D.S. Costa, 2015. Maternal Thyroid Disease and Preterm Birth: Systematic Review and Meta-Analysis. *The J. Clin. Endocrinol. & Metab.*, 100: 4325-4331.
9. Nguyen, C.T., E.B. Sasso, L. Barton and J.H. Mestman, 2018. Graves' hyperthyroidism in pregnancy: A clinical review. *Clin. Diabetes Endocrinol.*, Vol. 4 .10.1186/s40842-018-0054-7.
10. Thangaratinam, S., A. Tan, E. Knox, M.D. Kilby, J. Franklyn and A. Coomarasamy, 2011. Association between thyroid autoantibodies and miscarriage and preterm birth: Meta-analysis of evidence. *BMJ*, Vol. 342 .10.1136/bmj.d2616.
11. He, X., P. Wang, Z. Wang, X. He, D. Xu and B. Wang, 2012. Endocrinology in pregnancy: Thyroid antibodies and risk of preterm delivery: A meta-analysis of prospective cohort studies. *Eur. J. Endocrinol.*, 167: 455-464.
12. Twig, G., A. Shina, H. Amital and Y. Shoenfeld, 2012. Pathogenesis of infertility and recurrent pregnancy loss in thyroid autoimmunity. *J. Autoimmunity*, 38: 275-281.
13. Groot, L.D., M. Abalovich, E.K. Alexander, N. Amino and L. Barbour et al., 2012. Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline. *The J. Clin. Endocrinol. & Metab.*, 97: 2543-2565.
14. Andersen, S., P. Laurberg, C. Wu and J. Olsen, 2014. Attention deficit hyperactivity disorder and autism spectrum disorder in children born to mothers with thyroid dysfunction: A Danish nationwide cohort study. *BJOG: An Int. J. Obstet. & Gynaecology*, 121: 1365-1374.
15. Thompson, W., G. Russell, G. Baragwanath, J. Matthews, B. Vaidya and J. Thompson-Coon, 2018. Maternal thyroid hormone insufficiency during pregnancy and risk of neurodevelopmental disorders in offspring: A systematic review and meta-analysis. *Clin. Endocrinol.*, 88: 575-584.
16. American College of Obstetricians and Gynecologists., 2020. Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222. *Obstet Gynecol.*, 135: 237-260.
17. W.H.O., 2018. Preterm birth.
18. Sharma, D., S. Shastri and P. Sharma, 2016. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. *Clin. Med. Insights: Pediatr.s*, 10: 67-83.
19. Silva, F.T.D., B. Gonik, M. McMillan, C. Keech and S. Dellicour et al., 2016. Stillbirth: Case definition and guidelines for data collection, analysis, and presentation of maternal immunization safety data. *Vaccine*, 34: 6057-6068.
20. Griebel, C.P., J. Halvorsen, T.B. Golemon and A.A. Day., 2005. Management of spontaneous abortion. *Am Fam Physician.*, 72: 1243-1250.
21. Oyelese, Y. and C.V. Ananth, 2006. Placental Abruption. *Obstet. & Gynecol.*, 108: 1005-1016.
22. Evensen, A., J.M. Anderson and P. Fontaine., 2017. Postpartum hemorrhage: Prevention and treatment. *Am Fam Physician.*, 95: 442-449.
23. W.H.O., 2014. Global nutrition targets 2025: Low birth weight policy brief.
24. W.H.O., 2023. WHO recommendation on the method for diagnosing anaemia in pregnancy.
25. Edwards, M.O., S.J. Kotecha and S. Kotecha, 2013. Respiratory Distress of the Term Newborn Infant. *Paediatric Respir. Rev.*, 14: 29-37.
26. Krassas, G.E., K. Poppe and D. Glinoer, 2010. Thyroid Function and Human Reproductive Health. *Endocr. Rev.*, 31: 702-755.
27. Casey, B.M., J.S. Dashe, C.E. Wells, D.D. McIntire, W. Byrd, K.J. Leveno and F.G. Cunningham, 2005. Subclinical Hypothyroidism and Pregnancy Outcomes. *Obstet. & Gynecol.*, 105: 239-245.
28. Stagnaro-Green, A., M. Abalovich, E. Alexander, F. Azizi and J. Mestman et al., 2011. Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum. *Thyroid*, 21: 1081-1125.
29. Dong, A.C. and A. Stagnaro-Green, 2019. Differences in Diagnostic Criteria Mask the True Prevalence of Thyroid Disease in Pregnancy: A Systematic Review and Meta-Analysis. *Thyroid*, 29: 278-289.
30. Aggarawal, N., V. Suri, R. Singla, S. Chopra, P. Sikka, V.N. Shah and A. Bhansali, 2014. Pregnancy Outcome in Hyperthyroidism: A Case Control Study. *Gynecologic Obstetric Invest.*, 77: 94-99.
31. Khali, I. and B. Lazalde., 2011. Hyperthyroidism in pregnancy. *BMJ.*, Vol. 342 .

32. Zhang, Y., X. Dai and S. Yang, et al., 2021. Maternal subclinical hypothyroidism in early pregnancy and risk of gestational diabetes mellitus: A meta-analysis of prospective cohort studies. 2021;16(3):e0247516. PLoS One. , Vol. 16.
33. Goel, P., A. Radotra, K. Devi, S Malhotra, A. Aggarwal and A. Huria., 2005. Maternal and perinatal outcome in pregnancy with hypothyroidism. Indian J Med Sci., 59: 116-117.
34. Saki, F., M.H. Dabbaghmanesh, S.Z. Ghaemi, S. Forouhari, G.R. Omrani and M. Bakhshayeshkaram, 2014. Thyroid Function in Pregnancy and Its Influences on Maternal and Fetal Outcomes. Int. J. Endocrinol. Metab., Vol. 12 .10.5812/ijem.19378.
35. Balucan, F.S., S.A. Morshed and T.F. Davies, 2013. Thyroid Autoantibodies in Pregnancy: Their Role, Regulation and Clinical Relevance. J. Thyroid Res., Vol. 2013 .10.1155/2013/182472.
36. Taddei, S., N. Caraccio, A. Virdis, A. Dardano and D. Versari et al., 2003. Impaired Endothelium-Dependent Vasodilatation in Subclinical Hypothyroidism: Beneficial Effect of Levothyroxine Therapy. The J. Clin. Endocrinol. & Metab., 88: 3731-3737.
37. Biondi, B. and G.J. Kahaly, 2010. Cardiovascular involvement in patients with different causes of hyperthyroidism. Nat. Rev. Endocrinol., 6: 431-443.