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Original Research

Clinical Characteristics and Pregnancy Outcomes of Thyrotoxicosis During Pregnancy: A Retrospective Observational Study

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Abstract

Objectives: Thyrotoxicosis during pregnancy may be associated with adverse maternal and foetal outcomes; however, data comparing overt and subclinical thyrotoxicosis are limited. This study aimed to evaluate clinical characteristics, management, and pregnancy outcomes, and to explore associations with the achievement of euthyroidism in pregnant women with thyrotoxicosis.
Methods: This retrospective study included 70 pregnant women diagnosed with thyrotoxicosis who presented to the outpatient clinics between 2022–2023. Patients were classified as having overt (n=34) or subclinical (n=36) thyrotoxicosis based on trimester-specific thyroid function tests. After excluding three patients with Graves' disease and one with a molar pregnancy, 31 overt and 35 subclinical gestational thyrotoxicosis patients were included in the analyses. Demographic features, clinical findings, biochemical parameters standardized as multiples of the upper limit of normal, treatment data, and pregnancy outcomes were obtained from medical records. Correlation analyses were performed to evaluate associations between gestational week and thyroid function tests.
Results: The mean age was 29.6±5.3 years, and the mean GW at diagnosis was 10.7±3.0, with no significant differences between groups. At diagnosis, TSH was lower and fT4/fT3 higher in overt thyrotoxicosis compared to subclinical cases ($p<0.05$). Euthyroidism was achieved at a mean of 17.1±4.0 weeks, without significant group differences. Prior antithyroid drug therapy had been initiated in 18.2% of patients, mainly with PTU, with similar doses and treatment durations between groups. Pregnancy outcomes were available for 42 patients; 13 experienced complications (oligohydramnios, preterm delivery, pre-eclampsia, gestational diabetes, and intrauterine foetal death). Complication rates did not differ between groups, although anti-TPO positivity was more frequent among patients with complications ($p=0.006$). Correlation analyses showed that earlier gestational age at diagnosis was associated with higher thyroid hormone levels, while later achievement of euthyroidism correlated with lower TSH and higher peak fT3.
Conclusion: Pregnancy outcomes were similar in overt and subclinical thyrotoxicosis. Gestational age at diagnosis was associated with thyroid hormone levels but not with maternal or foetal complications. Most patients achieved euthyroidism during pregnancy, and anti-TPO positivity was more common among those with pregnancy complications.
Keywords: Foetal goitre, gestational transient thyrotoxicosis, Graves' disease, hyperthyroidism, pregnancy outcomes, thyrotoxicosis

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The increased levels of human chorionic gonadotropin (hCG) during pregnancy, due to its structural similarity to thyroid-stimulating hormone (TSH), temporarily stimulate the thyroid gland, causing a slight increase in thyroid hormone concentrations and a corresponding decrease in TSH, especially during the first trimester.[1,2] This physiological adaptation during pregnancy becomes exaggerated in some pregnancies, resulting in gestational transient thyrotoxicosis (GTT). GTT occurs in approximately 2-11% of pregnancies, parallels the peak in hCG levels, and resolves spontaneously as hCG concentrations decline.[3,4] As thyroid function usually returns to normal without intervention, antithyroid drug therapy is not indicated, and treatment is limited to supportive care such as hydration, rest, and control of hyperemesis if present.[5,6]

In contrast, Graves' disease is the most common cause of pathologic hyperthyroidism in pregnancy, affecting approximately 0.05–0.2% of women.[2,7] Unlike GTT, Graves' disease is an autoimmune disorder characterized by thyroid-stimulating hormone receptor antibodies (TRAb) and often requires antithyroid drug therapy to maintain maternal euthyroidism while minimizing foetal risk.[2] Although Graves' disease is a well-known cause of thyrotoxicosis in pregnancy, the majority of cases encountered in routine clinical practice are related to transient gestational thyrotoxicosis.

Less frequent aetiologies include toxic multinodular goitre, toxic adenoma, thyroiditis, excessive thyroid hormone intake, and trophoblastic diseases such as hydatidiform mole or choriocarcinoma, which can cause markedly elevated hCG levels and significant thyrotoxicosis.[2,8] Distinguishing GTT from Graves' disease and other causes is critical, as treatment approaches and prognostic implications for maternal and foetal outcomes differ significantly.[7]

Although GTT is generally benign and self-limiting, inadequate control of overt thyrotoxicosis during pregnancy is associated with pregnancy loss, pregnancy-induced hypertension, pre-eclampsia, preterm birth, low birth weight, intrauterine growth retardation, stillbirth, thyroid storm, and maternal congestive heart failure.[5,9] Research on subclinical thyrotoxicosis and its impact on maternal and foetal outcomes may vary in terms of sample size, inclusion criteria, and study design. Evidence from a recent meta-analysis indicates that subclinical hyperthyroidism in pregnancy is not associated with adverse pregnancy outcomes.[10]

Studies comparing overt and subclinical thyrotoxicosis in pregnancy are limited.[9] In this retrospective study, we aimed to evaluate the aetiology, clinical characteristics, and management patterns of pregnant women without a prior history of thyroid disease who presented with thyrotoxicosis during pregnancy, and to compare antenatal follow-up, including whether euthyroidism was achieved and, if so, the gestational week at which it was attained, as well as maternal and foetal outcomes, between those with overt and subclinical thyrotoxicosis in the Eastern Anatolia region of Türkiye.

Methods

Patients and Data Collection

This retrospective study included pregnant women diagnosed with thyrotoxicosis who presented to the Endocrinology and Metabolism Clinics of University of Health Sciences, Van Training and Research and Sirnak State Hospital between 2022 and 2023. The study protocol was conducted in accordance with the Declaration of Helsinki and approved by the This study was approved by the Van Training and Research Hospital (Date: 04.26.2023, Decision no: 2023/09-09).

Patients were included if they met the following criteria: diagnosis of thyrotoxicosis during pregnancy, defined as TSH<0.1 mIU/mL in the first trimester, <0.2 mIU/mL in the second trimester, or <0.3 mIU/mL in the third trimester. Exclusion criteria were pre-existing hyperthyroidism before pregnancy and unavailable follow-up data.

Demographic and clinical data, including age, parity, smoking status, presence of hyperemesis gravidarum, and gestational week (GW) at the time of thyrotoxicosis diagnosis, were collected from medical records. Patients' use of antithyroid drugs before referral, including drug type, dosage, and duration of therapy, was noted from medical records. Biochemical parameters at the time of diagnosis were recorded, including TSH, free T4 (fT4), and free T3 (fT3) levels, and thyroid autoantibody status (TSI [thyroid-stimulating immunoglobulin], TRAb, anti-TPO [anti-thyroid peroxidase], anti-thyroglobulin [anti-Tg]). The peak thyroid hormone levels and nadir TSH values during follow-up were also documented. The achievement of euthyroidism during pregnancy (defined as normalization of TSH and free hormone levels according to trimester reference ranges) and the gestational week at which euthyroidism was achieved were recorded. Among 110 pregnant patients presenting with thyrotoxicosis, 70 were included in the study (6 had a prior history of Graves' disease, and 34 were lost to follow-up after the first trimester). Patient inclusion, exclusions, and final diagnoses are illustrated in Figure 1. Pregnancy outcomes, including maternal and foetal complications, were evaluated in 42 patients with complete available data.

The diagnosis of Graves' disease was made in patients with increased thyroid vascularity on Doppler ultrasound, TSI/TRAb positivity, or progressive elevations in thyroid hor-

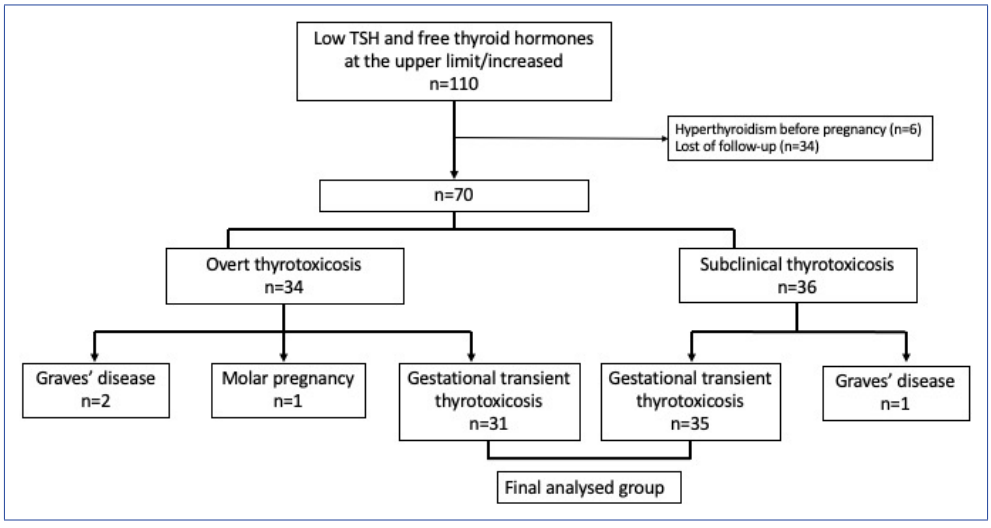

Figure 1. Flow chart of patient selection. Of 110 pregnant patients with thyrotoxicosis, 70 remained after applying exclusion criteria and loss to follow-up. These included 34 overt and 36 subclinical cases. After excluding 3 overt (1 molar pregnancy, 2 Graves) and 1 subclinical (Graves) cases, 31 overt and 35 subclinical GTT patients were included in the final analysis.

mone levels. Due to the absence of scintigraphy during pregnancy, definitive diagnosis of nodular hyperthyroidism was not possible. Patients with thyroid nodules were therefore classified based on clinical course, autoantibody status, and available pre-pregnancy thyroid function tests. Gestational transient thyrotoxicosis (GTT) was diagnosed in patients who developed symptoms during the first 16 weeks of pregnancy, were TSI/TRAb negative, had no significant Doppler vascularity, and showed a spontaneous decrease in thyroid hormone levels during follow-up.

As some laboratory parameters were measured using different assay kits, the results were standardized by expressing them as multiples of the upper limit of normal (×ULN), and these standardized values were used in the analyses. Due to the use of different assay kits, TRAb, TSI, anti-TPO, and anti-Tg results were reported qualitatively as positive or negative.

Statistical Analysis

All statistical analysis were performed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., USA). The normality of data distribution was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables were expressed as mean±standard deviation (SD) for normally distributed data and as median (interquartile range, IQR) for not normally distributed data. Categorical variables were presented as counts and percentages.

Comparisons between the overt thyrotoxicosis and subclinical thyrotoxicosis groups were performed using the Student t-test for variables showing a normal distribution and the Mann–Whitney U test for variables without a normal distribution. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Correlations between thyroid hormones and gestational age at diagnosis and gestational age at achievement of euthyroidism were analysed using Spearman's rank correlation coefficient for non-normally distributed data and Pearson's correlation coefficient for normally distributed data. A p-value <0.05 was considered statistically significant.

Results

A total of 70 pregnant women with thyrotoxicosis were included in the study; 34 had overt thyrotoxicosis, and 36 had subclinical thyrotoxicosis. A flow chart showing the distribution of patients is presented in Figure 1. Graves' disease was diagnosed in three patients, and one patient had a molar pregnancy. These cases were excluded from comparative analyses of overt and subclinical thyrotoxicosis due to their small number, while the remaining patients were included for descriptive clinical characterization. There were no patients with a definitive diagnosis of toxic nodular disease. After excluding Graves' disease and molar pregnancy cases, 31 patients with overt thyrotoxicosis and 35 patients with subclinical thyrotoxicosis were included in the analyses.

The demographic characteristics and baseline clinical features of the patients with gestational thyrotoxicosis are summarized in Table 1. The mean age of the cohort was 29.6±5.3 years, with no significant difference between overt and subclinical groups (29.2±5.7 vs. 29.9±5.0 years, p=0.625). Smoking was reported in 7% of patients, and the median gravida was 2 (IQR 1–3), with no significant differences between groups.

The mean gestational week (GW) at diagnosis was 10.7±3.0, with no significant difference between overt and subclinical groups (10.4±2.6 vs. 10.9±3.3 GW, p=0.494). Hyperemesis gravidarum was present in 17.1% of patients (16.1% vs. 17.1%, p=0.912). Thyroid nodules were detected in 37.3% of patients (34.5% vs. 40%, p=0.433), and increased thyroid blood flow on Doppler ultrasonography was observed in 28.6% of those evaluated (33.3% vs. 22.7%, p=0.311). Anti-TPO and anti-Tg antibody positivity were not different between groups (p=0.658 and 0.489) (Table 1).

Anti-thyroid drug treatment had been initiated by the primary care provider or the internal medicine department before referral in 18.2% of patients, with no significant difference between groups. In the overt thyrotoxicosis group, one patient had previously received methimazole (MMZ) for 8 weeks at a dose of 10mg, while all other patients had been treated with propylthiouracil (PTU) prior to referral. The median ATD dose was 100mg/day (50-112.5) for subclinical and 100mg/day (100-125) for overt thyrotoxicosis, with no significant difference between groups (p=0.686).

Table 1. Demographic characteristics, clinical features, laboratory findings, and pregnancy outcomes of the patients with overt and subclinical thyrotoxicosis

	All patients (n=66)	Patients with overt thyrotoxicosis (n=31)	Patients with subclinical thyrotoxicosis (n=35)	p
Age (years) mean±SD	29.6±5.3	29.2±5.7	29.9±5.0	0.625
Smoking, (n) %	4 (7.0)	2 (6.5)	2 (5.7)	1.000
Gravida median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.432
Initial evaluation				
GW at diagnosis mean±SD	10.7±3.0	10.4±2.6	10.9±3.3	0.494
Presence of hyperemesis gravidarum, n (%)	12 (17.1)	5 (16.1)	6 (17.1)	0.912
Presence of thyroid nodule, n (%)	22 (37.3)	10 (34.5)	12 (40)	0.433
Increased thyroid blood flow on Doppler US (n=49) n (%)	14 (28.6)	9 (33.3)	5 (22.7)	0.311
Anti-TPO positivity n (%)	4 (6)	2 (6.5)	2 (5.7)	0.658
Anti-Tg positivity (n=47) n (%)	1 (3)	1 (3.8)	0	0.489
Prior anti-thyroid drug initiation n (%)	12 (18.2)	6 (19.4)	6 (17.1)	0.533
TSH at diagnosis (mUI/mL) median (IQR)	0.016 (0.006-0.033)	0.01 (0.005-0.023)	0.022 (0.008-0.05)	**0.017**
fT4 at diagnosis (xULN) median (IQR)	0.95 (0.81-1.17)	1.16 (1.01-1.29)	0.85 (0.73-0.94)	**<0.001**
fT3 at diagnosis (xULN) median (IQR)	0.97 (0.82-1.13)	1.1 (1.01-1.18)	0.86 (0.80-0.96)	**<0.001**
Follow-up evaluation				
Nadir TSH (mUI/mL) median (IQR)	0.011 (0.005-0.032)	0.008 (0.005-0.022)	0.024 (0.008-0.046)	**0.011**
Peak fT4 (xULN) median (IQR)	1.00 (0.86-1.30)	1.16 (1.00-1.32)	0.89 (0.75-0.95)	**0.001**
Peak fT3 (xULN) median (IQR)	1.00 (0.83-1.18)	1.1 (1.02-1.19)	0.86 (0.82-0.95)	**0.002**
TSH in the last trimester (mUI/mL) median (IQR)	0.69 (0.4-1.00)	0.64 (0.4-0.98)	0.74 (0.3-1.05)	0.957
Euthyroidism achieved during pregnancy n (%)	64 (91.4)	31 (91.2)	33 (91.7)	0.942
GW when euthyroidism was achieved mean ± SD	17.1±4.0	17.9±3.6	16.3±4.2	0.095
GW at delivery (n=42) median (IQR)	39 (38-40)	39 (38-40)	38 (37-39)	0.058
Cesarian delivery rate (n=42) n (%)	19 (45.2)	8 (33.3)	11 (61.1)	0.070

Data are presented as mean±SD or median (IQR) unless otherwise specified. Bold p-values indicate statistical significance (p<0.05). SD: Standard deviation; IQR: interquartile range; GW: Gestational week; US: Ultrasonography; Anti-TPO: Anti–thyroid peroxidase antibody; Anti-Tg: Anti-thyroglobulin antibody; TSH: Thyroid-stimulating hormone; fT4: Free thyroxine; fT3: Free triiodothyronine; ULN: Upper limit of normal.

Median treatment duration was 4 weeks (2.3-9.5) in subclinical and 5 weeks (2-9) in overt thyrotoxicosis (p=1.000).

At diagnosis, the median TSH level in patients with overt thyrotoxicosis was significantly lower compared to the subclinical group (0.01 vs. 0.023mIU/ , p=0.017), while the median fT4 and fT3 levels were significantly higher in the overt group (1.16 vs. 0.85×ULN, p<0.001; 1.1 vs. 0.86×ULN, p<0.001; respectively). During follow-up, nadir TSH levels were lower in the overt thyrotoxicosis group compared to the subclinical thyrotoxicosis group, and the peak fT4 and fT3 levels were higher (Table 1). The mean gestational age at which euthyroidism was achieved was 17.1±4.0 weeks, and there was no significant difference between the groups (17.9±3.6 and 16.3±4.2 weeks, p=0.095). The gestational week at which euthyroidism was achieved was compared between patients with (17.91±4.89) and without (16.88±3.80) prior ATD use. There was no difference regarding prior ATD use (p=0.222).

One patient underwent uterine evacuation by suction curettage at 13 weeks due to a molar pregnancy. Foetal goitre (n=1) and neonatal transient hypothyroidism (n=1) were seen in patients with Graves' disease. These patients were excluded from analysis. Pregnancy outcomes were evaluated in 42 patients (Table 2). Thirteen patients experienced at least one pregnancy complication, while 29 patients had an uncomplicated pregnancy. Complications such as oligohydramnios (n=4), preterm delivery (n=3), premature rupture of membranes (n=2), pre-eclampsia (n=1), gestational diabetes (n=2), abortus (n=1), intrauterine foetal death (n=1), and intrauterine growth restriction (n=1) were observed. There was no statistically significant difference between the overt and subclinical thyrotoxicosis groups in terms of maternal or foetal complications (Table 2). The median gestational age at delivery in the 42 patients who completed their pregnancies was 39 weeks (IQR 38-40). There was no significant difference between overt and subclinical thyrotoxicosis (p=0.058). Caesarean delivery was performed in 45.2% of patients (respectively; 33.3% vs. 61.1%, p=0.070).

The mean age was similar between patients with pregnancy-related complications and those without complications (28.62±5.09 vs. 28.67±5.01 years, p=0.488). The mean GW at diagnosis was 11.77±2.83 in pregnancies with complications and 10.14±2.08 in those without (p=0.079). Among the four anti-TPO-positive patients, pregnancy outcomes were available for three, all of whom experienced pregnancy-related complications. Anti-TPO positivity was therefore significantly more common in patients with complications compared to those without (respectively; 100% vs. 0, p=0.006). Among the 12 patients who had used ATDs, pregnancy outcomes were available for 8. The rate of prior initiation of ATD did not differ significantly between the two groups (25% vs. 75%, p=1.000). There was no difference between the groups in terms of smoking history and the presence of hyperemesis gravidarum (7.7% vs. 10%, p=0.652, and 7.7% vs. 20%, p=0.412, respectively). TSH and free thyroid hormone levels did not differ between those who developed complications and those who did not.

Correlation analyses are presented in Table 3. Gestational week (GW) at diagnosis was positively correlated with GW when euthyroidism was achieved (CC=0.406, p=0.001) and negatively correlated with thyroid hormone levels, including fT3 (CC=-0.273, p=0.029) at diagnosis and peak fT4 (CC=-0.297, p=0.031). GW when euthyroidism was achieved showed negative correlations with TSH at diagnosis (CC=-0.292, p=0.021), nadir TSH (CC=-0.354, p=0.011), and TSH in the last trimester (CC=-0.662, p<0.001), whereas it was positively correlated with peak fT3 (CC=0.295, p=0.046).

The patient in whom foetal goitre was detected had Graves' disease with 70-fold increased TSI levels and free thyroid

Table 2. Comparison of pregnancy outcomes between overt and subclinical thyrotoxicosis

	All patients (n=42)	Patients with overt thyrotoxicosis (n=24)	Patients with subclinical thyrotoxicosis (n=18)	p
Patients with pregnancy complications, n (%)	13 (28.6)	6 (25)	7 (38.9)	0.335
Oligohydramnios	4 (9.5)	2 (8.3)	2 (11.1)	NS
Prematurity	3 (7.1)	1 (4.2)	2 (11.1)	NS
Premature rupture of membranes	2 (4.8)	1 (4.2)	1 (5.6)	NS
Preeclampsia	1 (2.3)	0	1 (5.6)	NS
Gestational diabetes	2 (4.8)	1 (4.2)	1 (5.6)	NS
Abortus	1 (2.4)	1 (4.2)	0	NS
Intrauterine foetal death	1 (2.4)	1 (4.2)	0	NS
Intrauterine growth retardation	1 (2.4)	1 (4.2)	0	NS

Data are presented as mean±SD or median (IQR) unless otherwise specified. SD: Standard deviation; IQR: Interquartile range; GW: Gestational week.

Table 3. Correlations of gestational week at diagnosis and gestational week at achievement of euthyroidism with thyroid function parameters in patients with gestational transient thyrotoxicosis

	GW at diagnosis	GW when euthyroidism was achieved
GW at diagnosis	-	**p=0.001; CC: 0.406**
GW when euthyroidism was achieved	**p=0.001; CC: 0.406**	-
TSH at diagnosis	p=0.958; CC: 0.007	**p=0.021; CC: -0.292**
fT4 at diagnosis (xULN)	p=0.052; CC: -0.244	p=0.142; CC: 0.189
fT3 at diagnosis (xULN)	**p=0.029; CC: -0.273**	p=0.227; CC: 0.158
Nadir TSH	p=0.756; CC: -0.043	**p=0.011; CC: -0.354**
Peak fT4 (xULN)	**p=0.031; CC: -0.297**	p=0.310; CC: 0.148
Peak fT3 (xULN)	p=0.081; CC: -0.249	**p=0.046; CC: 0.295**
TSH in the last trimester	p=0.187; CC: -0.210	**p<0.001; CC: -0.662**
GW at delivery	p=0.786; CC: -0.043	p=0.867; CC: -0.028

Bold p-values indicate statistical significance (p<0.05). Abbreviations: GW: Gestational week; TSH: Thyroid-stimulating hormone; fT4: Free thyroxine; fT3: free triiodothyronine; ULN: Upper limit of normal; CC: correlation coefficient.

hormone concentrations approximately five times above the ULN. The patient was initiated on antithyroid therapy and followed regularly during pregnancy. However, the patient discontinued scheduled follow-up on her own for nearly two months, and at her return visit at 28 weeks of gestation, a decline in free T4 levels was noted. A detailed foetal ultrasound revealed foetal goitre. With close monitoring, free T4 levels improved, foetal goitre regressed, and a healthy baby was delivered at 38 weeks. The baby developed transient thyrotoxicosis in the neonatal period and required short-term, low-dose antithyroid treatment.

The patient whose baby had neonatal transient hypothyroidism had 4.5-fold increased TSI levels and thyroid hormone levels three times above the ULN at the time of diagnosis. The mother was treated with low-dose PTU from the 9th to the 17th week of pregnancy, and treatment was discontinued when free T4 remained at the upper limit of normal. The infant developed transient neonatal hypothyroidism. The mother required antithyroid treatment one month after delivery.

Discussion

Thyrotoxicosis in pregnancy is a heterogeneous clinical condition with a wide range of aetiologies and biochemical severity levels. In this study, we compared pregnancy outcomes between pregnant women with overt and subclinical thyrotoxicosis and found that, despite significant differences in thyroid hormone levels, pregnancy outcomes were similar between the two groups. These findings suggest that biochemical classification alone may not adequately reflect the complexity of pregnancy risks associated with thyrotoxicosis.

Consistent with previous reports, gestational thyrotoxicosis (GTT) constituted the most common aetiology in our cohort, while Graves' disease was identified in a smaller group of patients (4.3%).[5,11] This aetiological distribution is consistent with the physiological role of human chorionic gonadotropin in early pregnancy, and distinguishing transient, hCG-mediated thyrotoxicosis from Graves' disease is crucial due to differing treatment approaches.[5] A clinically important observation in our study was that a proportion of patients, particularly those later classified as GTT, had been started on antithyroid drugs prior to endocrinology consultation and before a definitive etiological evaluation. Given that most cases of GTT are self-limiting and not associated with adverse outcomes, unnecessary antithyroid drug exposure during pregnancy may carry avoidable foetal risks, including hypothyroidism and goitre.[12,13] Our findings support current recommendations emphasising the need for a clear aetiological diagnosis before initiating antithyroid treatment.

As expected, patients with overt thyrotoxicosis exhibited higher free thyroid hormone levels and lower TSH concentrations than those with subclinical disease, both at diagnosis and during follow-up. An inverse relationship was observed between gestational age at diagnosis and free thyroid hormone levels, indicating that more pronounced biochemical thyrotoxicosis tends to be detected earlier in the first trimester of pregnancy. This finding is consistent with the physiological effect of hCG in early pregnancy.[1,5] Interestingly, no significant difference was observed between the groups with respect to hyperemesis gravidarum; however, this finding should be interpreted with caution, as the limited sample size may have reduced the ability

to detect a true association. Furthermore, the gestational week at which euthyroidism was achieved was associated with the degree of maternal TSH suppression and fT3 levels. However, thyroid hormone levels, gestational age at diagnosis, or achievement of euthyroidism did not show a significant association with pregnancy complications. The rates of euthyroidism achieved during pregnancy, gestational age at delivery, caesarean section rates, and maternal and foetal complications were similar between overt and subclinical thyrotoxicosis. Considered together, these findings suggest that thyroid hormone dynamics may be related to the biochemical and temporal characteristics of thyrotoxicosis during pregnancy but do not allow definitive conclusions to be drawn regarding their effects on clinical pregnancy outcomes.

In the present cohort, pregnancy complications were observed in approximately one-third of patients with thyrotoxicosis, with no statistically significant differences between overt and subclinical forms. Importantly, individual obstetric complications, including prematurity, preeclampsia, gestational diabetes, oligohydramnios, and pregnancy loss, occurred at low frequencies and were comparable between groups. These findings are consistent with previous studies indicating that gestational transient thyrotoxicosis (GTT) and mild thyrotoxic states are not associated with a substantial increase in major adverse pregnancy outcomes compared with euthyroid pregnancies. In a large population-based case–control study, GTT was not linked to increased risks of preeclampsia, pregnancy-induced hypertension, placental abruption, low birth weight, or perinatal mortality. However, a slightly shorter gestational duration was observed in affected pregnancies.[14]

The relatively high overall complication rate observed in our study may be explained by the inclusion of conditions such as oligohydramnios and gestational diabetes, which are not consistently categorized as major adverse outcomes in all population-based cohorts. While these conditions are clinically relevant, they are often variably reported or excluded from composite outcome measures in previous studies, potentially leading to lower reported overall complication rates.[3,14,15] The absence of significant differences between overt and subclinical thyrotoxicosis in our cohort further supports existing evidence suggesting that transient or mild biochemical thyroid hormone excess has a limited impact on pregnancy outcomes, in contrast to sustained or poorly controlled hyperthyroidism.[3,16] Overall, these findings support the notion that overt and subclinical gestational thyrotoxicosis are associated with broadly similar and generally favourable pregnancy outcomes.

Oligohydramnios and gestational diabetes are adverse pregnancy outcomes that have been less emphasized in previous studies of pregnancies complicated by thyrotoxicosis. Previous studies have reported that oligohydramnios may occur in pregnancies complicated by thyrotoxicosis, particularly in Graves' disease.[17,18] In addition, recent Mendelian randomisation studies have suggested a potential association between thyrotoxicosis and an increased risk of gestational diabetes.[19] However, it should be noted that both oligohydramnios and gestational diabetes are common obstetric conditions with multifactorial aetiologies, arising from the interplay of placental function, maternal metabolic status, and population-specific factors rather than excessive thyroid hormone alone.[20,21] Overall, the inclusion of common obstetric conditions such as oligohydramnios and gestational diabetes in the composite outcome may partially explain the higher complication rates observed in our study.

Thyroid autoimmunity has emerged as a significant factor associated with pregnancy complications in our cohort. Anti-thyroid peroxidase (anti-TPO) antibody positivity was more prevalent among patients who developed complications. To explain the adverse effect of thyroid autoimmunity on pregnancy outcomes, various mechanisms have been proposed, including immune-mediated placental dysfunction, altered trophoblast invasion, and a proinflammatory cytokine environment.[22-25] These mechanisms may operate independently of thyroid hormone concentrations, potentially explaining why anti-TPO positivity was associated with complications even in patients with subclinical disease.

Foetal goitre and transient neonatal thyroid dysfunction were observed in two patients complicated by Graves' disease; however, the limited sample size precludes definitive conclusions. The other Graves' disease patient did not develop complications. These findings are consistent with previous reports indicating that neonatal thyroid dysfunction is primarily related to transplacental transfer of TSH receptor antibodies rather than thyroid hormone excess.[26-27] Overall, these observations highlight the need for careful antenatal and neonatal monitoring in pregnancies complicated by Graves' disease.[28] Therefore, while our observations support the biological possibility of autoimmune-mediated foetal and neonatal thyroid involvement, they should be interpreted with caution due to the limited sample size.

An additional consideration is the geographical context of the study. Most available studies about thyrotoxicosis in pregnancy originate from Western populations, and data from iodine-deficient or mildly iodine-sufficient regions

remain scarce. In Türkiye, regional differences in iodine status persist despite the nationwide salt iodization program. Studies from Eastern Anatolia have demonstrated that pregnant women often have suboptimal urinary iodine concentrations, reflecting mild iodine deficiency.[29,30] Our cohort was derived from a region known to be affected by iodine deficiency. Iodine deficiency has been associated with altered thyroidal adaptation during pregnancy and may predispose to both thyroid dysfunction and adverse obstetric outcomes.[31,32] The relatively high rate of pregnancy complications observed in our study may reflect underlying regional characteristics influencing maternal and perinatal outcomes, in addition to thyrotoxicosis.

The inability to assess iodine status represents an important limitation of our study. Urinary iodine concentration was not routinely measured, precluding direct evaluation of iodine deficiency and its potential interaction with thyrotoxicosis and pregnancy outcomes. Consequently, it was not possible to disentangle the relative contributions of thyroid dysfunction and environmental iodine deficiency. Additional limitations include the retrospective design, relatively small sample size, and the absence of a control group, all of which restrict causal inference. Furthermore, the heterogeneity of treatment in terms of dosage and duration in patients who received unnecessary treatment in the early stages may also have affected biochemical control and pregnancy outcomes. Pregnancy outcome data were incomplete for some patients. Also, thyroid autoantibodies were assessed qualitatively rather than quantitatively. Furthermore, the retrospective nature of the study may have resulted in missing data.

The strengths of this study include its real-world setting, detailed biochemical assessment, and comprehensive evaluation of maternal and foetal outcomes. Expressing thyroid hormone levels as multiples of the upper limit of normal allowed for standardized comparisons across different assays.

Conclusion

In conclusion, our findings suggest that overt and subclinical thyrotoxicosis during pregnancy were associated with broadly similar maternal and foetal outcomes in our cohort, despite evident biochemical differences. Pregnancy-related complications were observed in both groups, indicating that subclinical thyrotoxicosis should not be assumed to be uniformly benign, particularly in the presence of thyroid autoimmunity. Careful etiological evaluation, avoidance of unnecessary antithyroid therapy, and consideration of thyroid autoimmunity remain important aspects of the clinical assessment of thyrotoxicosis during pregnancy.

Disclosures

Ethics Committee Approval: This study was approved by the Van Training and Research Hospital (Date: 04.26.2023, Decision no: 2023/09-09).

Informed Consent: All patients were informed about the study, and written informed consent was obtained.

Conflict of Interest: None declared.

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