

The relationship between preeclampsia and thyroid disorders and perinatal outcomes

Serhat Akcan^{1*}, Ahmet Nuri Danişman²

¹Mersin City Training and Research Hospital, Turkey

²Bayındır Healthcare Group, Turkey

Abstract

This study aimed to investigate changes in thyroid function tests among preeclamptic patients, explore the relationship between thyroid disorders and preeclampsia, and evaluate perinatal outcomes in these patients. This prospective study was conducted between February 8, 2010, and July 22, 2011, at Dr. Zekai Tahir Burak Women's Health Training and Research Hospital, involving 222 cases admitted between 24–42 weeks of gestation. The study group included 76 preeclamptic, 65 hypothyroid, and 21 hyperthyroid pregnant women hospitalized in our high-risk pregnancy unit. The control group comprised 74 healthy singleton pregnancies with no medical or obstetric complications, monitored in the delivery and labor unit. The preeclamptic group was further divided into mild and severe preeclampsia subgroups. At the onset of labor, 10 ml of venous blood was collected from all participants for hemogram (Hb, WBC, Plt), biochemistry (AST, ALT, BUN, creatinine), and thyroid function tests (fT3, fT4, TSH). Additionally, venous blood samples were collected from newborns admitted to the neonatal intensive care unit (NICU) for thyroid function testing (fT3, fT4, TSH). Heel-prick blood samples were also taken from newborns brought to the hospital's neonatal outpatient clinic between postpartum days 5–7 to analyze TSH levels. In the preeclampsia group, maternal fT3 and fT4 levels were significantly lower than those in the control group ($p < 0.01$). Although maternal TSH levels in the preeclampsia group were markedly higher than in the control group, this difference was not statistically significant. Within the preeclampsia group, TSH levels were higher in the severe subgroup compared to the mild subgroup, but again, the difference was not statistically significant ($p > 0.05$). Similarly, in preeclamptic patients, TSH levels were higher among those with birth weights below 2500 g and gestational age below 37 weeks compared to those above these thresholds, though these differences were also not statistically significant ($p > 0.05$). TSH levels were also higher in those with 1-minute Apgar scores below 7, compared to those with scores ≥ 7 , but this too lacked statistical significance ($p > 0.05$). Neonatal fT3 levels in the preeclampsia group were significantly lower than those in the thyroid disorder group ($p < 0.01$). Although not statistically significant, maternal TSH levels were notably higher and free thyroid hormone levels were significantly lower in preeclamptic patients compared to controls. These findings suggest the presence of "low T3 syndrome" and a biochemically hypothyroid profile in these patients. Maternal TSH levels, although not statistically significant, showed an inverse correlation with birth weight, gestational age, and Apgar score. Furthermore, TSH levels were higher in the severe preeclampsia group compared to the mild group, suggesting a potential relationship between maternal TSH levels and the severity of preeclampsia. We also observed "low T3 syndrome" in neonates born to preeclamptic mothers, which may be due to immaturity of the hypothalamic-pituitary-thyroid axis caused by premature birth. Although treatment of hypothyroid and hyperthyroid patients to achieve a euthyroid state improved outcomes such as miscarriage, low birth weight, and preterm birth, the incidence of preeclampsia remained higher than in the general population.

Keywords: Preeclampsia, Thyroid, FT3, FT4, TSH

1. Introduction

The incidence of preeclampsia varies by race, region, and country, but it occurs in approximately 7–10% of all pregnancies (1,2). Preeclampsia is among the leading causes of maternal and perinatal morbidity and mortality (2,3), accounting for approximately 17.6% of maternal deaths. Fetal complications include intrauterine growth restriction (IUGR), preterm birth, and perinatal asphyxia. Maternal complications can range from placental abruption, intracranial hemorrhage, liver failure, and renal failure to death (1).

Despite many years of clinical, biophysical, and biochemical research, the exact etiopathogenesis of

preeclampsia remains unknown. Therefore, there is currently no effective treatment for preeclampsia, and the only definitive management is induction of delivery (4). Various pharmacological and dietary interventions have been attempted to prevent preeclampsia; however, their efficacy has not been conclusively proven (5).

In this study, we aimed to investigate changes in thyroid function tests in preeclamptic patients, the relationship between thyroid disorders and preeclampsia, and the perinatal outcomes in these patients.

2. Materials and Methods

This prospective study was conducted on 222 cases

admitted between February 8, 2010, and July 22, 2011, to Dr. Zekai Tahir Burak Women's Health Training and Research Hospital between 24 and 42 weeks of gestation. The study group consisted of 76 preeclamptic, 65 hypothyroid, and 21 hyperthyroid pregnant women who were hospitalized in the high-risk pregnancy unit. The control group included 74 healthy singleton pregnancies with no medical or obstetric problems, monitored in the labor and delivery unit.

At the onset of labor, 10 ml of venous blood was collected from all participants. These samples were analyzed for hemogram (Hb, WBC, Plt), biochemical parameters (AST, ALT, BUN, creatinine), and thyroid function tests (FT3, FT4, TSH). Additionally, venous blood samples were obtained from neonates admitted to the neonatal intensive care unit for thyroid function testing (FT3, FT4, TSH). For neonates brought to the hospital's neonatal outpatient clinic on postpartum days 5–7, heel-prick blood samples were collected and analyzed for TSH using the Guthrie test.

All patients underwent obstetric ultrasound evaluation prior to delivery. During the ultrasound examination, Biparietal Diameter (BPD), Abdominal Circumference (AC), and Femur Length (FL) measurements were obtained to estimate gestational age and fetal weight.

Data recorded included maternal age, gravida, parity, abortion history, last menstrual period, gestational age at delivery, mode of delivery, neonatal birth weight, gender, and Apgar scores. The preeclamptic, hypothyroid, hyperthyroid, and control groups were compared in terms of hemogram, biochemical parameters, thyroid function tests, and obstetric outcomes. Preeclamptic patients were further subdivided into two groups: mild and severe preeclampsia.

Statistical analysis was performed using SPSS version 14.0. In addition to descriptive statistical methods (frequency, percentage, mean, standard deviation), the Pearson Chi-square test was used for comparison of categorical variables. For comparisons of continuous variables between two groups, the Independent Samples t-test was used when the data were normally distributed. Results were evaluated at

a 95% confidence interval, and a p-value of <0.05 was considered statistically significant.

3. Results

Table 1. Distribution of the preeclampsia, thyroid disorder, and control groups

		Preeclampsia			Total
		No	Mild	Severe	
Thyroid Disease	No Disease	74	14	48	136
	Hypothyroidism	54	2	9	65
	Hyperthyroidism	18	1	2	21
Total		146	17	59	222

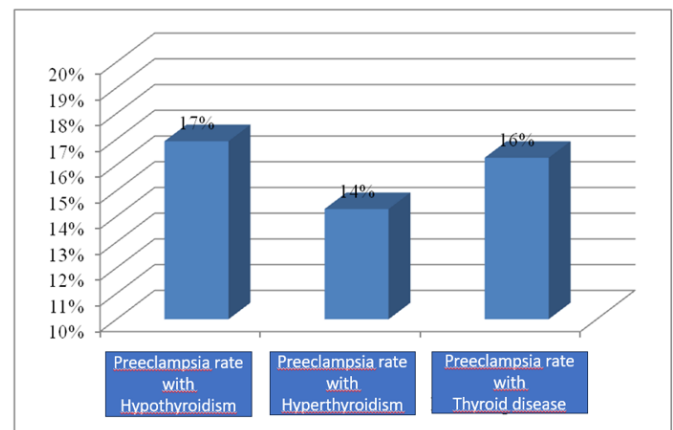


Figure 1. Rates of preeclampsia in hypothyroidism, hyperthyroidism, and thyroid disorders

In the preeclampsia group, the mean maternal age and parity were significantly higher compared to the control group ($p < 0.01$). Gestational age, birth weight, and Apgar scores (1st and 5th minute) were significantly lower in the preeclampsia group compared to the control group ($p < 0.01$).

The mean maternal FT3 and FT4 levels were significantly lower in the preeclampsia group than in the control group ($p < 0.01$). Although the mean maternal TSH level in the preeclampsia group was notably higher than in the control group, the difference was not statistically significant ($p > 0.05$).

The rate of vaginal delivery was significantly lower in the preeclampsia group compared to the control group ($p < 0.01$), while the rate of cesarean delivery was significantly higher ($p < 0.01$). Perinatal

mortality was also significantly higher in the preeclampsia group ($p < 0.05$). In addition, the need for neonatal intensive care was significantly increased in the preeclampsia group ($p < 0.01$). The rate of Small for Gestational Age (SGA) and Intrauterine Growth Restriction (IUGR) was also significantly higher in the preeclampsia group compared to the control group ($p < 0.01$).

Table 2. Comparison of maternal thyroid function tests between the preeclampsia and control groups

	Control (n=74)		Preeclampsia (n=62)		p
	Ort	Ss	Ort	Ss	
Maternal FT3	2.9	0.3	2.7	0.4	0.001**
Maternal FT4	1.1	0.2	1.0	0.2	0.005**
Maternal TSH	2.7	3.3	3.7	4.6	0.181

* $p < 0.05$ ** $p < 0.01$

In the hypothyroidism group, the mean maternal age and parity were significantly higher compared to the control group ($p < 0.01$). The rate of vaginal delivery

was significantly lower ($p < 0.05$), and the rate of cesarean delivery was significantly higher than in the control group ($p < 0.05$). Interestingly, the rate of small for gestational age (SGA) and intrauterine growth restriction (IUGR) was significantly lower in the hypothyroidism group compared to the control group ($p < 0.05$).

In the preeclampsia + thyroid disorder group, both mean birth weight and gestational age were significantly lower than in the control group ($p < 0.05$). Rates of cesarean delivery, perinatal mortality, and need for neonatal intensive care were significantly higher in this group compared to controls ($p < 0.01$).

When comparing the preeclampsia group and the preeclampsia + thyroid disorder group, no statistically significant difference was found in terms of perinatal outcomes ($p > 0.05$).

In the severe preeclampsia subgroup, the mean maternal TSH level was noticeably higher than in the mild preeclampsia subgroup, although the difference was not statistically significant ($p > 0.05$).

Table 3. Distribution of maternal thyroid function tests according to severity in preeclampsia cases

	Mild Preeclampsia (n=13)		Severe Preeclampsia (n=45)		p
	Ort	Ss	Ort	Ss	
Maternal FT3	2.758	0.317	2.672	0.455	0.531
Maternal FT4	0.966	0.194	0.965	0.199	0.984
Maternal TSH	2.578	1.485	3.974	5.112	0.338

4. Discussion

Although the physiological changes in thyroid function throughout normal pregnancy have been well studied, there are limited studies investigating the alterations in thyroid function among preeclamptic pregnancies and their potential fetal effects.

In pregnancies complicated by preeclampsia-eclampsia, decreased TBG (thyroxine-binding globulin) levels lead to reduced T4 concentrations (6). Since the majority of T3 is generated through peripheral conversion of T4, a decrease in T4 is expected to result in a subsequent decrease in T3

levels (7). Furthermore, the liver and kidneys — the primary organs involved in the peripheral conversion of T4 to T3 — are also affected in preeclampsia, which may contribute to the reduction in T3 concentrations (8).

In our study, we evaluated thyroid function test alterations in preeclamptic pregnancies based on maternal FT3, FT4, and TSH measurements.

According to our findings, the mean maternal FT3 and FT4 levels in the preeclampsia group were significantly lower compared to the control group ($p < 0.01$). While the mean maternal TSH level was notably higher in the preeclampsia group, this

difference did not reach statistical significance ($p > 0.05$). Likewise, the mean maternal TSH level was higher in the severe preeclampsia subgroup compared to the mild subgroup, although this difference was also not statistically significant ($p > 0.05$). Several other studies have reported similar findings to ours.

A condition referred to as "low T3 syndrome", characterized by reduced T3 levels, has been documented in preeclamptic pregnancies, and several publications suggest that this syndrome may be a feature of preeclampsia itself (9).

Lao et al. found that FT4, TT4, and TBG concentrations were significantly lower in preeclamptic women compared to normotensive pregnant women in the third trimester, while TSH levels were significantly higher (10,11).

Similarly, Larijani et al. reported significantly lower FT3 and FT4 levels and significantly higher TSH levels in women with severe preeclampsia compared to controls (12).

Başbuğ M. et al. also found that FT3, FT4, TT3, and TT4 levels were significantly decreased in the preeclamptic group, whereas TSH levels were significantly elevated. They suggested that the increase in TSH levels was associated with the severity of preeclampsia (13).

Our study included a relatively larger sample size, and we also found significantly lower FT3 and FT4 levels in the preeclampsia group compared to controls ($p < 0.01$). Although TSH levels were noticeably elevated, the difference was not statistically significant.

On the other hand, Qublan et al. compared 27 women with severe preeclampsia to 26 normal pregnancies and found no significant differences in maternal FT3, FT4, or TSH levels. They concluded that thyroid function does not significantly change in severe preeclampsia and is not associated with disease severity (14).

The reduction in FT3 and TT3 levels observed in preeclamptic patients resembles that seen in severe systemic illnesses and malnutrition. In such cases,

impaired peripheral conversion of T4 to T3 results in decreased serum FT3 and TT3 levels. Since the liver and kidneys are the main sites for this conversion, their dysfunction in preeclampsia and eclampsia may explain the lower T3 concentrations reported in these conditions (15,16).

Kaya E. et al. suggested that in toxemia, increased loss of protein-bound hormones due to proteinuria could lead to a decrease in maternal TT3 and TT4 levels, depending on the severity of the disease (17).

Vojvodik et al. reported preeclampsia incidences of 26.8% in hypothyroidism and 26% in hyperthyroidism, proposing that thyroid disorders may be a risk factor for the development of preeclampsia (18).

In conclusion, untreated hypothyroidism and hyperthyroidism are associated with serious pregnancy complications, most commonly including preeclampsia, IUGR, preterm birth, and anemia.

5. Conclusion

As a result of this study, we found that although the differences were not statistically significant, maternal TSH levels were markedly higher, and free thyroid hormone levels (FT3, FT4) were significantly lower in preeclamptic patients compared to the control group. These findings suggest the presence of "low T3 syndrome" in these patients, indicating a biochemical state resembling hypothyroidism.

Furthermore, although not statistically significant, maternal TSH levels showed an inverse correlation with birth weight, gestational age, and Apgar scores. In the severe preeclampsia group, maternal TSH levels were noticeably higher than in the mild group, suggesting a possible association between TSH levels and disease severity.

We also observed low T3 levels in the neonates of preeclamptic mothers. We hypothesize that this may be due to the immaturity of the hypothalamic-pituitary-thyroid axis in premature newborns rather than primary thyroid dysfunction.

Despite effective treatment of hypothyroidism and hyperthyroidism achieving a euthyroid state and

thereby improving outcomes such as miscarriage rate, low birth weight, preterm birth, and other perinatal complications, we concluded that the incidence of preeclampsia remains higher in these populations compared to the general obstetric population.

6. References

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