Are Thyroid Functions Effective in Pregnant Women with Hyperemesis Gravidarum?

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Abstract

Objective: This study aims to detect the role of thyroid hormones in the etiology of hyperemesis gravidarum (HG), which has apparent adverse effects on fetal and maternal outcomes.

Methods: In this study, we retrospectively evaluated 1634 term primiparous cases of single-birth deliveries (37–42 weeks of gestation) at the Koru Hospital Ankara between November 2012 and September 2014. Maternal age, existence of any treatment during pregnancy, the history of alcohol consumption before pregnancy, smoking habits, and newborn's gender were detected. The first-trimester HG cases and thyroid-stimulating hormone (TSH) and free tyroxine (fT4) levels were recorded.

Results: Compared with other two groups, the TSH level was lower in the HG group, while the fT4 level was higher. Despite this fact, no statistical significance was detected (p=0.06). Compared with other groups, maternal age was significantly lower in the group with HG and was thus statistically significant (p=0.01).

Conclusion: In HG pregnancies, the thyroid-metabolism-related disorders and maternal age should be kept in mind, and laboratory-clinical analyses and early diagnosing and treatment should be considered.

Keywords: Hyperemesis gravidarum, thyroid-stimulating hormone, free thyroxine

Hiperemezis Gravidarum olan Gebelerde Tiroid Fonksiyonları Etkili midir?

Öz

Amaç: Çalışmamızda, fetal ve maternal prognoz üzerine belirgin olumsuz etkisi olabilen Hiperemezis Gravidarum'un etyolojisinde tiroid hormonlarının rolünü bulmayı hedefledik.

Yöntemler: Çalışmamızda Kasım 2012-Eylül 2014 tarihleri arasında Koru Ankara Hastanesi'nde doğumu gerçekleştirilen 37-42 hafta aralığında, tekil, 1634 primipar olgu retrospektif olarak değerlendirildi. Olguların anne yaşı, yardımcı üreme tekniği ile gebe olup olmadığı, gebe kalmadan önceki alkol kullanım öyküsü, sigara kullanımı, yenidoğanın cinsiyeti tespit edildi. 1. Trimester'da tespit edilen HG vakaları ve 1. Trimestır'da ölçülen Tiroid Stimülan Hormon (TSH) ve serbest Tiroksin (sT4) değerleri kaydedildi.

Bulgular: TSH değerleri HG'u olan grupta diğer iki grup ile karşılaştırıldığında düşük, sT4 değeri ise yüksek bulunmasına rağmen istatistiksel anlamlılık tespit edilmedi (p=0,06). HG'u olan grup, diğer gruplar ile karşılaştırıldığında anne yaşı anlamlı olarak düşük bulundu ve istatistiksel olarak anlamlı tespit edildi (p=0,01).

Sonuç: HG tanısı alan gebelerde, tiroid metabolizması ile alakalı bozukluklar ve anne yaşı akılda tutulmalı, gerekli laboratuvar-klinik incelemeler ile erken tanı ve tedavi gözönünde bulundurulmalıdır.

Anahtar Sözcükler: Hiperemezis gravidarum, tiroid stimülan hormon, serbest tiroksin

Nausea and vomiting as the symptoms in pregnancy are reported in 50%–70% of cases with differing severity, generally beginning at weeks 6–8 and continuing throughout weeks 14–16 [1]. Hyperemesis gravidarum (HG) presents with a clinical picture of severe nausea and vomiting during pregnancy. Although its incidence varies across populations, HG occurs in 1%–2% of pregnancies [2]. Definitive criteria for diagnosing HG are not clear; however, the symptoms are severe nausea and vomiting, electrolyte abnormalities, the acid–base imbalance, dehydration, ketosis, keton-

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uria, and weight loss >5%. Renal and hepatic failure may also be included among the symptoms [3, 4].

The HG etiology is not clear. Hormonal changes in early pregnancy, certain metabolic disorders, psychosocial factors, motility disorders in the gastrointestinal system, and immunological factors are considered to be playing a part. Recently, the *helicobacter pylori* infection has also been added to these factors from an etiological point of view [5].

The HG diagnosis is made through an anamnesis, physical examination, and laboratory findings. Most diagnosed cases present with clinical conditions that need to be treated in hospital. The symptoms usually retreat before the end of the first trimester. Pregnant women who are malnourished, have electrolyte abnormalities, and have lost weight are at risk of encountering low-birth weight and intrauterine growth retardation. In most studies, it has also been reported that in addition to the negative effects for the fetus and the mother, the condition also impairs the quality of life and causes psychosocial problems [6].

Some risk factors affecting the development of HG are young maternal age, first pregnancy, multiple gestation, gestational trophoblastic disease, family history, HG history during previous pregnancies, an increased body mass index, and low socioeconomic level. There has also been found a negative correlation between HG and smoking and alcohol consumption [7].

Although some studies that included pregnant women diagnosed with HG have shown an increase of 40%–73% in the thyroxin (T4) level, labeling this situation as transient hyperthyroidism [8], neither the reason nor the effects of this elevation have been understood. It is considered to be caused by an increase in the human chorionic gonadotropin (hCG) level, or by thyrotropin receptors hypersensitive to hCG or an hCG variant increasing the thyroid stimulant hormone (TSH) stimulation. Pregnant women with a high level of thyroid hormone are found with thyrotoxicosis findings in hypothyroid picture developed in the society and antithyroid antibody are found to be negative [9, 10].

Our objective in this study is to find the role thyroid hormones play in the HG etiology, which is known to have an effect on the fetal and maternal morbidity.

Materials and Methods

In this study, we retrospectively evaluated 1634 term primiparous cases of single-birth deliveries (37–42 weeks of gestation) at the Koru hospital Ankara between November 2012 and September 2014. The study was approved by the Regional Ethical Board (protocol no. 29/09/2018-15). Because the study was retrospective, informed consent was not obtained. Maternal age, existence of any treatment during pregnancy, alcohol consumption history before pregnancy and smoking habits, and newborn's gender were detected. The first-trimester HG cases and TSH and free T4 (fT4) levels measured in the first trimester were recorded.

The retrospective study included three groups. The first group included 22 cases experiencing first-trimester nausea, vomiting, severe dehydration, ketosis, and electrolyte and acid–base imbalance paired with a loss ≥5% of body weight, and receiving a medical treatment in hospital; the second group consisted of 450 pregnancies with prescriptions for antiemetic drugs, receiving ambulatory treatment, and with complaints of nausea/vomiting, but without an acid–base imbalance and weight loss; and the third group included 1162 pregnancies without any note of HG presence. These three groups were compared based on the maternal age and TSH and fT4 values measured in the gender trimester. Also, the distribution according to factors of treatment pregnancy, a positive history of smoking before and during pregnancy, and the gender of the newborn were taken into account.

In the evaluation of thyroid functions, the range of TSH levels was determined as 0.1–2.5 mIU/L in the first trimester and 0.2–3.0 mIU/L in the second and third trimesters of pregnancy as normal reference values.

In determining the criteria for the presence of "treatment pregnancy," women who used any type of reproductive assisting methods (*in vitro* fertilization, intrauterine insemination, oral ovulation induction) were labeled as treatment pregnancy, whereas others were labeled as "spontaneous pregnancy." For the smokers or alcohol consumers, there was no distinction in terms of the time or duration: the patients were all categorized as users/nonusers.

After the collected data were transferred to the IT environment, they were analyzed using the SPSS 22.0 package program. To define the statistics percentage and average, SD values were used. Data were tested for normal distribution with the Kolmogorov–Smirnov test, using the one-way analysis of variance test for those appropriate with the normal distribution, and the Kruskal–Wallis test for those not appropriate for the normal distribution. A p-value <0.05 was accepted as statistically significant.

Results

A total of 1634 term births are shown in Table 1 according to the average value and ±SD and p-values of maternal age, TSH, fT4. The maternal age was found to be lower in a statistically significant manner in cases diagnosed with HG and receiving medical treatment in hospital (Group 1). The TSH values were found to be lower in Group 1 compared to two other groups,

Table 1. Comparison of Values of Maternal Age, TSH, and fT4

	Group 1 (n:22)	Group 2 (n:450)	Group 3 (n:1162)	p
Maternal age	26.2±5.3[a]	30±3.7	30.4±4.2	p=0.01*
TSH value (mIU/mL)	0.99±1.48	1.38±0.49	1.24±0.74	p=0.06˜
Free T4 value (pmol/L)	19.47±5.04	16.74±3.02	15.65±3.47	p=0.06˜

[a]p=0.02 for Group 2, p=0.03 for Group 3.

*the analysis of variance test

˜the Kruskal–Wallis test

TSH: thyroid-stimulating hormone; mIU/mL: mili International Unit per milliliter; pmol/L: picomoles per liter

Table 2. Distribution of the Three Groups According to Treatment Pregnancy, Alcohol and Tobacco Consumption, and Gender of the Newborn

	Group 1 n (%)*	Group 2 n (%)*	Group 3 n (%)*
Treatment pregnancy	16 (72.7)	57 (12.6)	98 (8.4)
Alcohol consumption	0	0	2 (3.1)
Smoking	2 (9.1)	1 (0.1)	24 (2)
Newborn's gender			
female	16 (72.7)	255 (56.6)	501 (43.1)
male	6 (27.3)	195 (43.4)	661 (56.9)
Total	22 (100)	450 (100)	1162 (100)

*column percentage

whereas the fT4 were found to be higher. The difference in these values is not statistically significant.

The distribution with regard to criteria such as treatment pregnancy, the history of alcohol consumption prior to conception, the history of smoking before and during pregnancy, and newborn's gender is presented in Table 2. The frequency of treatment pregnancy was found to be significantly higher among the cases with HG and receiving medical treatment at hospital (Group 1) compared to the two other groups (72.7%). Alcohol consumption was found to be similar in all three groups. Smoking as the percentage was found to be higher in Group 1 compared to other two groups (9.1%). Although the distribution of newborn's gender was found to be similar in Groups 2 and 3, the cases with HG and receiving medical treatment at hospital (Group 1) were found to give birth to a higher ratio of girls to boys (72.7%).

Discussion

Changes in the thyroid functions occur during pregnancy mostly during the first trimester. Many clinical studies including pregnant women with HG comparing TSH and fT4 levels retrospectively have shown that the changes in the thyroid functions may play a role in the etiology and have a significant effect on the severity of the illness. These studies have not clearly shown how the changes in the thyroid function could result in such a picture [11]. Although the reason is not completely understood, it is believed that hCG plays the main role in the pathogenesis, and many clinical studies support the claim that hCG has thyrotrophic activity [12]. It has been argued that during the early pregnancy period, hCG acts like a TSH, causing gestational nausea and vomiting. Both structurally and in terms of the receptors they connect to, TSH and hCG show a similar activity [13].

Mori et al. [14] and Tareen et al. [15] showed that an increased level of hCG reduces the TSH level and increases fT4, and once the fT4 and TSH levels return to normal levels, the symptoms reduce.

Rodien et al. [16] showed that an increase in hCG levels also increases the thyrotrophic activity. Deruelle et al. [17] in their study detected biochemical hypothyroidism in 22 patients out of 33 (66.7%) and stated that the severity of hyperemesis changed directly with the level of the hyperthyroidism. In our study, Group 1 patients with HG compared to the other two groups

were found to have lower TSH values and higher fT4 values. Although the results of our study are consistent with literature, the results were not found to be statistically significant (p=0.06). We believe that this is due to a small number of the HG group patients in our study.

Fejzo et al. [18] in showed that one of the risk factor in HG could be treatment pregnancy and that this might be caused by high levels of hCG and high serum estradiol. Our study's findings are supporting this result with treatment pregnancy rates (72.7%) in Group 1 being higher than in other two groups.

Depue et al. [19] detected a negative correlation between smoking and HG. In our study, the smoking ratio was found to be higher in Group 1 diagnosed with HG (9.1%) than the other groups. However, this could be because our study did not account for the smoking duration and frequency, but only distinguished between the smoker and nonsmoker categories.

Derbent et al. [20] found the maternal age to be lower in patients with HG compared to the control group (p=0.01). Also, compared to the control group, it was found that the ratio of girls born was higher (71%) in patients with HG. In our study, the maternal age of patients with HG was found to be significantly less compared to other groups (p=0.01), and although the newborn's gender distribution in Groups 2 and 3 was similar, the patients with HG being medically treated at hospital (Group 1) were found to have a higher rate of girls (72.7%). These results were found to be consistent with the literature.

Hyperemesis gravidarum poses an important problem in pregnancy with effects on both the newborn and the mother in terms of morbidity. Thyroid functions play a significant role in HG etiology along with anamnesis information. Therefore, we have concluded that it would be a positive step toward monitoring the negative antenatal stage by investigating in detail the etiological reasons researched in our study in the anamnesis of patients with HG, as well as ensuring thyroid function tests are administered in the early period.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Koru Hospital (29/09/2018-15).

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

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