Thyroid dysfunction in hyperemesis gravidarum: a study in Turkish pregnant women

Hiperemezis gravidarumda tiroid disfonksiyonu: Türk gebelerde yapılan bir çalışma

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Abstract

Objective: In this study we investigate the possible relation of thyroid dysfunction and thyroid antibodies to hyperemesis gravidarum.

Material and Methods: Thirty-seven patients with hyperemesis gravidarum and 33 healthy controls have been included in this study.

Results: Thyroid dysfunction was significantly more common than in controls (38% vs 6%, p=0.002). Thyroglobulin antibodies were also significantly more common in patients with hyperemesis gravidarum than controls (54 IU/mL vs. 14 IU/mL, p=0.03).

Conclusion: Hyperemesis gravidarum can be a risk factor for postpartum thyroid dysfunction. Thyroid antibodies must be checked in the hyperemesis population in an endemic goitre region and/or iodine replacement regions. (J Turkish-German Gynecol Assoc 2011; 12: 140-3)

Key words: Hyperemesis gravidarum, thyroid function

Received: 26 March, 2011 **Accepted:** 13 May, 2011

Özet

Amaç: Bu çalışmadaki amacımız tiroid fonksiyon bozuklukları ve tiroid antikorları ile hiperemezis gravidarum arasındaki olası ilişkiyi araştırmaktı.

Gereç ve Yöntemler: Hiperemezis gravidarumu olan 37 hasta ve 33 sağlıklı kontrol gurubu çalışmada incelendi.

Bulgular: Tiroid disfonksiyon sıklığı hiperemezis gravidarumda kontrol grubuna göre anlamlı olarak daha fazla bulundu (%38'e %6, p=0.002). Anti-tiroglobulin düzeyleride anlamlı olarak kontrol grubundan daha yüksekti (54 IU/mL'e. 14 IU/mL, p=0.03).

Sonuçlar: Hiperemezis gravidarum postpartum tiroid fonksiyon bozuklukları için bir risk faktörü olabilir. Tiroid antikor düzeyleri de özellikle endemik guatr ve/veya iyot replasmanı yapılan bölgedeki gebelerde de mutlaka bakılmalıdır. (J Turkish-German Gynecol Assoc 2011; 12: 140-3)

Anahtar kelimeler: Hiperemezis gravidarum, tiroid fonksiyonu

Geliş Tarihi: 26 Mart 2011 **Kabul Tarihi:** 13 Mayıs 2011

Introduction

Hyperemesis gravidarum was defined as persistent vomiting accompanied by weight loss of at least 5% of pre- pregnancy body weight and/or ketonuria unrelated to other causes and requiring hospital admission for severe vomiting causing dehydration (1, 2). The pathogenesis of hyperemesis is unknown. Usually it is difficult to differentiate from the nausea and vomiting such as morning sickness from the HG, which affects 80% of pregnancies (3). Some hormonal changes determined in HG; elevated serum concentrations of estrogen and progesterone levels implicated in the pathogenesis of this disorder, serum human chorionic gonadotropin (hCG) concentration is higher in women with HG women also supports a possible etiologic role for this hormone. In addition, hCG has a thyroid-stimulating activity (4-6). Higher hCG levels in women with HG and a positive correlation between hCG levels and the severity of vomiting and degree of thyroid stimulation was established previously (7). Hyperthyroidism is possibly due to high serum concentrations of hCG which has a thyroid-stimulating activity (5). One study showed that low serum TSH concentrations are seen more often in women with HG than in normal pregnant women; TSH was suppressed in 60 percent of hyperemesis patients versus 9 percent of controls (8). In the literature there are insufficient studies which have investigated the thyroid antibodies in HG. In this study we investigate the possible relation of thyroid antibodies to hyperemesis gravidarum.

Method

Patients

Thirty-seven patients with hyperemesis gravidarum and 33 healthy controls have been evaluated in this study. We have chosen the control group as a gestational age matched control. The study protocol was approved by the Ankara Kecioren Education and Research Hospital. Written, informed consent was obtained from all patients which also adhered to the principles of the Helsinki Declaration. The study cohort has been selected from a gynecological outpatient population of a Research Hospital between June 2009 to May 2010.

Clinical Assessment

Hyperemesis gravidarum, defined as persistent vomiting accompanied by weight loss of at least 5% of pre- pregnancy

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doi:10.5152/jtgga.2011.33

body weight and/or ketonuria unrelated to other causes and requiring hospital admission for severe vomiting causing dehydration (2). The control group did not have any symptoms or only mild nausea without vomiting. Patients or controls with molar pregnancy, multiparity, coronary heart disease, diabetes, hypertension or any chronic disease using medication were not included in the study. Fasting (8 hours) blood samples were taken in the morning from each patient and were centrifuged for 5 min at 3.000 g and stored at -80°C until the time of analysis. Blood glucose, serum creatinine, blood urea nitrogen, aspartate and alanine aminotransferases, sodium, potassium and calcium electrolytes were measured using an automatic analyzer (Konelab 60i, Thermo Scientific, Finland). Serum thyroid stimulating hormone and free thyroid hormones were analyzed by UniCel DxI 800 Access Immunoassay System (Beckman Coulter, USA). Complete blood counts were measured using a Coulter LH 500 hematology analyzer (Beckman Coulter, USA).
Thyroglobulin antibody (Anti-Tg) and thyroperoxidase antibody (TPO-Ab) Liason analyzer systems manufacturered by Diasosin, STILLWATER, MN 55082, USA were used.
Ultrasound exams were performed by the same radiologist blinded to the clinical characteristics of the patients.
Patients admitted to the hospital were intravenously hydrated followed by reintroduction of oral intake. Dehydration was supplemented with appropriate electrolytes, vitamins and metoclopramide (5 to 10 mg) as needed. Normal values of hormones were; TSH (0.3-4.2 mIU/L), fT3 (2.2-4.2pg/mL), fT4 (0.65-1.7 ng/mL), Thyroglobulin antibody/antiTG (5-100 IU/mL) and thyroperoxidase antibody/TPO-Ab (1.16 IU/mL). Upper limits of the reference values were accepted as positive.
Thyroid dysfunctions were defined as (5, 8);

- Lower TSH values with or without abnormal thyroid antibodies and/or free thyroid hormone levels.
- Higher TSH values with or without abnormal thyroid antibodies and/or free thyroid hormone levels.

Statistical analysis
Shapiro-Wilk test was used to identify the data distribution. Normally distributed data were presented as mean (SD) for baseline and descriptive statistics, and median and interquartile range for non-normally distributed data. Data with normal distribution were analyzed using unpaired t test. Mann-Whitney U test was used for analyzing abnormally distributed data. Positive and negative values were compared by chi-square test. All *P* values were calculated as two-tailed. $p < 0.05$ was set as statistically significant. SPSS 15.0 was used for statistical calculations (SPSS Inc., Chicago, IL, USA).

Results

Baseline clinical and laboratory characteristics of the patients and controls are presented in Table 1. Groups were similar in age, weight, gestational week, hemoglobin, creatinine and glucose levels. No patients or controls had any other systemic disease or any medication. The hyponatremia frequency in HG group was 24% which was significantly higher than the 3% of hyponatremia in the control group ($p=0.005$). AST levels were significantly elevated in the HG group compared to the controls (18±7.5 u/L versus 17±3 u/L, p:0.01). ALT levels were also significantly higher in the HG group than the controls (18±14 u/L versus 14±4 u/L, $p=0.04$). Also the HG group had lower levels of TSH, p values were 0.03. HG patients had significantly higher

Table 1. Baseline clinical and laboratory characteristics of 37 patients with hyperemesis gravidarum, dysmenorrhea and 33 healthy pregnant controls

	Patients (n=37)	Controls (n=33)	p
Age, years	25.4(±5.2)	25.3(±4.5)	0.36
Gestation, week	9.7(±2.2)	10(±2.2)	0.73
Weight, kg	63(±11)	62(±9)	0.34
Creatine	0.65(±0.1)	0.61(±0.1)	0.74
Hgb, g/dL	12(±0.9)	11.7(±1)	0.33
Plt, x 10 3μL	234(±67)	226(±48)	0.056
Glucose, mg/dL	85(±8)	86(±8)	0.75
BUN, mg/100 ml	20(±6.3)	16(±3.3)	0.005
AST, u/L	18(±7.5)	17(±3)	0.01
ALT, u/L	18(±14)	14(±4)	0.04
Sodium, mEq/L	135(±2.7)	136(±1.7)	0.005
Potassium, mEq/L	3.9(±0.3)	3.7(±0.2)	0.9
TSH, mIU/l	0.95(±0.56)	1.4(±1.15)	0.03
fT3, pg/mL	2.86(±0.46)	2.6(±0.3)	0.07
fT4, ng/mL AntiTg, IU/mL, IR	1.07(±0.3)	0.89(±0.17)	0.02

Table 2. Thyroid Dysfunctions in HG and control group

	Decreased TSH (<0.3mıu/L)	Positive AntiTG (>100IU/mL)	Positive TPO-Ab (>16IU/mL)	p value (Chi-Square)
Hyperemesis (n:37)	3(8%)	9(24%)	2(5.5%)	
Control (n:33)	0	0	2(6%)	
Total (n:70)	3	9	4	0.002

levels of freeT4, but all values were within the normal reference range of our laboratory. AntiTG titers were significantly higher than controls in the HG group (54 IU/mL vs. 14 IU/mL, p=0.03) but TPO-Ab were not. In the HG group 9 (24%), patients had positive antiTG but thecontrol group did not (p=0.007). There was no significant difference between the two groups of TPO-Ab (p=0.9). Lower TSH with normal free thyroid hormone level was determined in 3 patients in the HG group. Neither hyperthyroid nor hypothyroid pregnant women had clinical symptoms so they were not given any antithyroid medication. When we evaluate the all thyroid dysfunctions (*only lower TSH with normal freeT3/T4, positive TPO-Ab with negative anti-Tg and positive anti-Tg with negative TPO-Ab)* 14 (38%) patients in the HG group and 2 (6%) in the control group (p=0.002) are also presented in Table 2. In patients who had thyroid dysfunction, thyroid stimulating antibodies were negative. There is no correlation between the anti TG, TPO-Ab, TSH, freeT3 and free T4. All the study population had normal thyroid on physical examination.

Discussion

Results from this study showed for the first time that thyroglobulin antibody concentrations are significantly higher in the HG group compared to healthy pregnant controls. Also hyperemetic pregnant women had significantly higher (38% vs. 6%, p: 0.002) thyroid dysfunctions than controls.

Thyroid functions change in pregnancy, especially within the first trimester, in general because of estrogen-induced increases in serum thyroxine-binding globulin (TBG) levels and human chorionic gonadotropin (hCG) induced increases in thyroid hormone synthesis and release (9). Most prospective studies which compared TSH and T4 levels of HG patients with the controls showed significantly lower levels of TSH and significantly higher levels of T4 titers. Also there is a relationship between hyperthyroidism and severity of HG but the exact role is not yet known (10, 11). In our study, we found 8% subclinical hyperthyroidism but there was no correlation between the TSH and HG severity. These rates are lower than previous studies carried out in other populations. Also we found hyponatremia and elevated ALT/AST significantly different, but at lower rates than the previous studies. However, this is one of several studies carried out on the Turkish pregnant population.

The prevalence of anti-thyroid antibodies (ATA) has been reported as 15-20% in normal pregnant women, and anti TPO antibodies were found to have a significant association with recurrent miscarriage. Therefore, the prognostic value of ATA remains uncertain (12, 13). Our control group had only 6% ATA but the HG group had 30% ATA. Pearce et al found that 12.4% elevated TPO-Ab in pregnant which was higher than our study population for TPO-Ab (9). The presence of measurable maternal thyroid antibodies can be a risk factor for postpartum thyroiditis, miscarriage and premature birth. In fact, findings from a recent study suggest that treatment of TPO-Ab–positive euthyroid women with levothyroxine results in improved obstetric outcomes (9, 14-17). Propylthiouracil can provide relief of symptoms of HG. In our population hyperemesis gravidarum can be a risk factor for postpartum thyroid hyperemesis, so it should be suggested that the thyroid antibodies should be checked in the HG population in an endemic goiter region and/or iodine replacement regions like Turkey.

In this study we did not follow up the pregnant patients after delivery so we could not report the pregnancy outcomes of HG patients.

In conclusion, this is the first study of Turkish HG women in whom a significantly elevated percentage of thyroid dysfunction, especially thyroglobulin antibodies, compared to controls was found.

Conflict of interest

No conflict of interest was declared by the authors.

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