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TPO antibodies in pregnant and childbearing-aged women

Y.S. Jo, S.J. Kim

Department of Obstetrics and Gynecology, College of Medicine, The Catholic University of Korea, Seoul (Republic of Korea)

Summary

Purpose: The purpose of this study was to evaluate the prevalence of anti-thyroid peroxidase antibodies (TPO-Ab) in pregnant and childbearing-aged women in Korea. *Materials and Methods:* This was a retrospective study conducted in women tested for TSH and TPO-Ab at the present institution between January 2006 and January 2010. Data were collected from pregnant women and from women of childbearing age, defined as between 15 and 45 years with regular menstruation at health examination clinic. *Results:* A total of 349 pregnant and 358 non-pregnant women of childbearing age were enrolled. The prevalence of TPO-Ab in pregnant group was 19.7% (69 of 349), and in the non-pregnant group was 25.4% (91 of 358) ($p = 0.07$). TPO-Ab concentration in the pregnant group was significantly lower than that in the non-pregnancy group ($p = 0.008$). Among pregnant women in the first-trimester, TSH levels in TPO-Ab positive women were higher than that in TPO-Ab negative women with significance (2.59 ± 2.15 *vs*. 1.76 ± 1.62, $p = 0.047$). *Conclusions:* There is a higher rate of TPO-Ab positive pregnant women and women of childbearing age in Korea compared to other races.

Key words: Antiperoxidase antibodies (TPO-Ab); Thyroid-stimulating hormone TSH); Pregnancy; Korea.

Introduction

Autoimmune disorder of the thyroid is probably one of the most common autoimmune disorders in women of childbearing age. The prevalence of anti-thyroid peroxidase antibodies(TPO-Ab) has been shown to be about 10% by prospective studies [1, 2]. It has now been well established that women with asymptomatic autoimmune thyroid disorder are at risk of developing subclinical hypothyroidism during pregnancy [2]. It has been demonstrated that gestational subclinical hypothyroidism could have deleterious effects on the intellectual outcome of pregnancy in humans [3-5]. In the female, thyroid function exerts effects not only on the health of herself but also on her progenies. The purpose of this study was to evaluate thyroid function, the prevalence of TPO- Ab, and concentration of TPO-Ab in pregnant and childbearing-aged women in Korea.

Materials and Methods

This was a retrospective study conducted on women tested TSH and TPO-Ab at the present institution between January 2006 and January 2010. The study subjects were divided to two groups: one group of pregnant women and one group with non-pregnant women of childbearing age. Data were collected from pregnant women, and from women of childbearing age, defined between 15 and 45 years, with regular menstruation, at health examination clinic. Non-Korean and migrants were excluded. Obstetric and medical histories were collated from medical record review. The study excluded women with thyroid disorders, obesity (BMI > 25 kg/m2), diabetes, and autoimmune disorders. In the pregnant group, women with multiple gestations were excluded. The study was approved by the clinical study medical ethics committee at the present institution (XC10R1S10063V).

Serum TSH (reference range 0.17-4.05 mIU/l) was measured with an immunoanalyser. The analytical sensitivity was 0.025 mIU/L and the intra-assay coefficients of variation (CV) was 3.7%. TPO-Ab was determined by a radioimmunoassay (RIA) in calibrators and diluted patient sera are allowed to interact with 125I labeled TPO. The lower limits of detection and intra- and interassay coefficients of variation were, respectively, 0.03 u/mL, 2.7 and 8.2%. A TPO-Ab concentration above 0.3 u/mL was considered to be TPO-Ab positive.

All data are expressed as the means ± standard deviations (SD). SAS version 8 was used to perform statistical analysis. Statistical analysis was performed using the unpaired *t*-test and the chi-square test to determine differences in demographic, TPO-Ab positivity, and TPO-Ab concentration. Analysis of variance (ANOVA) was then used to identify statistically significant differences in TSH levels between the TPO-Ab positive and negative pregnant women by trimester. A $p < 0.05$ was considered statistically significant.

Results

In total, 349 pregnant (pregnant group) and 358 non-pregnant women of childbearing age (non-pregnant group) were enrolled. The mean age at data collection was 33.35 ± 4.6 years in the pregnant group, and 36.06 ± 8.0 years in the non-pregnant group, respectively ($p < 0.001$). The parity was 0.87 ± 0.77 in the pregnant group, and 1.23 ± 0.9

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Table 1. — *Ethnic-related differences in prevalence of TPO-Ab.*

	Published Reports Relating incidence of TPO-Ab in women.											
	Negro *et al.* (2006) [1]	Benhadi *et al.* (2007) [14]				Hollowell *et al.* (2002) [13]			Debiève *et al.* (2009) [10]	Quinn *et al.* (2009) [15]	Present study	
Nation	Italy	The Netherlands			USA				Belgium	China	Korea	Korea
Race (n)	Caucasian (984)	Dutch (2475)	Surinam (277)	Turkish (162)	Moroccan (232)	White, non-Hispanic	Black non Hispanic	Mexican American	(784)	Chinese (251)	Korean (349)	Korean (358)
Subject	pregnant	pregnant				Non-pregnant			pregnant	Non-pregnant	pregnant	Non-pregnant women
Incidence of TPO-Ab (%)	11.7	5.5	15.6	17.5	15.6	15.6	6.4	14.7	9.5	17.5	19.7	25.4

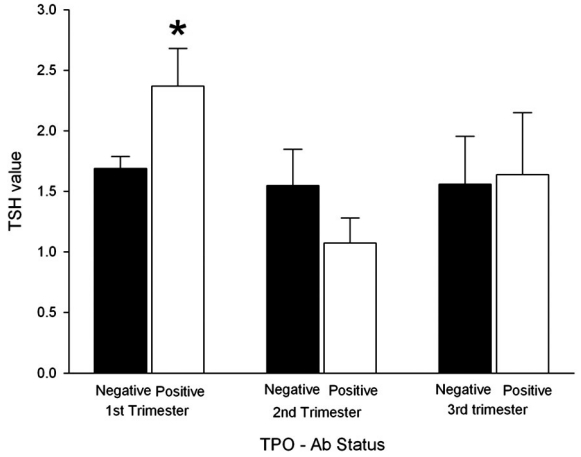

Figure 1. — TSH levels of TPO-Ab positive and negative pregnant women by trimester. Black and white bars represent TSH values in TPO-Ab negative and positive women in the pregnant (*$p < 0.05$).

in the non-pregnant group ($p < 0.001$). The mean gestational age at data collection in the pregnant group was 24.14 ± 11.58 weeks. The prevalence of TPO-Ab positivity in the pregnant group was 19.7% (69 of 349), and 25.4% (91 of 358) in the non-pregnant group. The prevalence of TPO-Ab in the pregnant group was lower than that in the non-pregnant group, but non-significantly (p = 0.07). There was no difference in the prevalence of TPO-Ab by age in the pregnant and non-pregnant groups. In the pregnant group, there was no difference in the prevalence of TPO-Ab by gestational age and trimester at data collection. The concentration of TPO-Ab in TPO-Ab (+) pregnant women (n=81) and TPO-Ab (+) non-pregnant women (n=117) were 2.54 ± 11.71 IU/ml and 5.93 ± 21.07 IU/ml, respectively. The concentration of TPO-Ab in the pregnant group was significantly lower than that in the non-pregnant group (p = 0.008). In the pregnant group, there was no difference in TPO-Ab concentration by age, parity, gestational age, and trimester. Also, in the non-pregnant group, difference in TPO-Ab concentration was not present by age and parity.

In the non-pregnant group, TSH level was comparable between TPO-Ab positive and negative women (4.77 ± 19.1 *vs*. 2.25 ± 1.2, p = 0.159). Also, in the pregnant group, TSH level was also comparable between TPO-Ab positive and negative women (1.98 ± 1.5 *vs*. 1.80 ± 1.39, p = 0.325). In the pregnant group, TSH levels were evaluated between TPO-Ab positive and negative women by trimester. In the first-trimester, TSH levels in TPO-Ab positive women were significantly higher than that in TPO-Ab negative women (2.59 ± 2.15 *vs*. 1.76 ± 1.62, p = 0.047). In the second- and third-trimester, TSH levels were comparable between TPO-Ab positive and negative women (Figure 1).

Discussion

Thyroid disease are four to five times more prevalent in women than in men, particularly during childbearing age [6]. The thyroid function of females exert effects not only on her health but also on her progeny. Fetal brain development is strongly dependent on adequate supply of thyroid hormone in the early stage of pregnancy, because fetal thyroid does not produce thyroxine until mid-gestation [7]. Not only hypothyroidism, but also subclinical hypothyroidism during pregnancy results in impaired fetal development [8, 9]. Women with asymptomatic autoimmune thyroid disorder are at risk of developing subclinical hypothyroidism during pregnancy [2]. Consequently, it has been suggested that replacement is recommended in TPO-Ab-positive patients with normal TSH and free T4 values during pregnancy to ensure adequate fetal development [10]. Studies on the change of thyroid function and autoantibody to thyroid according to pregnancy in women are not sufficient.

In the present study, pregnant women had a lower prevalence of TPO-Ab ($p = 0.07$) and lower TPO-Ab concentration ($p = 0.008$), compared to non-pregnant women. During pregnancy, autoimmunity is suppressed in patients with Grave's and Hashimoto's diseases [11]. Thyroid autoantibody titers fall during gestation in patients with Hashimoto's disease, only to rise sharply postpartum in association with a phase of acute T-cell-mediated thyroid cell destruction [12]. It may be concluded that autoimmunity suppression secondary to pregnancy may have contributed to the low positive rate and concentration of TPO-Ab in the present study. The mean age of the non-regnant group (36.06 ± 8.0 years) at data collection was higher than 33.35 ± 4.6 years in the pregnant group ($p < 0.001$). However, the prevalence and concentration of TPO-Ab do not differ with age [1, 2, 10].

In another study, it was concluded that in TPO-Ab positive pregnant women, the TSH level in the first trimester was significantly higher than TPO-Ab negative pregnant women, which implies the importance and the influence of TPO-Ab on the thyroid gland during early pregnancy [10]. In the present study, TSH levels in TPO-Ab positive pregnant women were higher than their TPO-Ab negative counterpart in the first-trimester with statistical significance ($p = 0.047$).

Ethnic-related differences in prevalence of TPO-Ab has been documented (Table 1). Non-pregnant female Caucasians (15.6%) and Mexican Americans (14.7%) have higher prevalence than Africans (6.4%) [13]. Ethnic-related differences in thyroid function and gestational adaptation may play a role in the extensively documented ethnic-related differences in short- and long-term perinatal outcome. Few data exist on ethnic differences of TPO-Ab in pregnancy [14]. The prevalence of TPO-Ab in four ethnic groups - Dutch, Surinam, Turkish, and Moroccan during pregnancy was comparable (about 6% in each). TPO-Ab concentration was also comparable between these ethnic groups [14]. An Italian prospective study has shown a 10% TPO-Ab prevalence in pregnancy [1]. Surprisingly, in the present study, the prevalence of TPO-Ab in pregnant group was 19.7%, and 25.4% in the non-pregnant, childbearing aged group. This is much higher than that of the existing studies (Table 1). Thus, reproductive and pregnant women in Korea may be highly susceptible to thyroid conditions that may influence both pregnancy and long-term perinatal outcome.

This is the first study which compares variation of TPO-Ab and TSH by pregnancy in healthy reproductive women without thyroid disease. Pregnant women had a lower prevalence of TPO-Ab and a lower TPO-Ab concentration, compared to non-pregnant women. It is thought that such results are due to autoimmunity suppression caused by pregnancy. However the present study has the limitations of being a small and retrospective study. For the elucidation of changes of the thyroid caused by pregnancy, a larger prospective study is required.

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Corresponding Author:
S.J. KIM, M.D., PhD
Department of Obstetrics and Gynecology
Bucheon St. Mary's Hospital
Sosa 2-dong, 420-717 Wonmi-gu, Bucheon-si
Kyungido (Republic of Korea)
e-mail: ksajin@catholic.ac.kr