Spontaneus Abortion and Thyroid Functions

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Abstract

Background and Objective: To investigate thyroid functions as an etyologic factor in spontaneous abortions.

Methods: We performed thyroid function tests in 60 patients having spontaneous abortion without any known etiology between 5 to 20 weeks of gestation and compared them with these of 40 pregnant women of same gestational weeks and known to reach term and had a healthy labor.

Conclusions: There may be subclinical hypothyroidism in spontaneous abortion group and this may be responsible from some of the spontaneous abortions.

Keywords: Pregnancy, abortion, thyroid, T4, TSH.

Spontan abortus ve tiroit fonksiyonları

Amaç: Spontan abortus etyolojisinde tiroit fonksiyonlarının yerini araştırmak.

Yöntem: 5-20 gebelik haftalarında spontan abortus yapan ve abortus etyolojisi bilinmeyen 60 hastanın tiroit fonksiyonları,aynı gebelik haftalarında bulunan ve daha sonra miada ulaşarak sağlıklı doğum yapan 40 gebenin tiroit fonksiyonları ile karşılaştırıldı.

Bulgular: Spontan abortus yapan grubun hem total T3,T4 hem de serbest T3 ve serbest T4 seviyeleri miada ulaşan gruptan anlamlı olarak düşük,TSH değeri ise anlamlı olarak yüksekti.

Sonuç: Abortus grubunda klinik olmasa bile subklinik hipotiroitizm mevcut olabilir ve bu da spontan abortusların bir bölümünden sorumludur.

Anahtar Sözcükler: Gebelik, abortus, tiroit, T4, TSH.

Introduction

Diagnosis of thyroid diseases in pregnancy becomes difficult due to some physiological changes that remind hyperthyroidism. During pregnancy, requirements of thyroid hormone and iodine are increased.[1,2] Synthesis of thyroid binding globulin (TBG) is raised in pregnancy with estrogen effect, resulting in elevated total T3 (TT3) and total T4 (TT4) levels. Increase in total fractions through the end of pregnancy leads to decrease in free fractions, which in turn results in stimulation of TSH and consequently enlargement of the thyroid gland.[3,4] Renal loss of iodine as a result of increased glomerular filtration is increased in pregnancy . Fetus takes up only thyroid from the mother for thyroid hormone synthesis; daily iodine requirement of a pregnant woman is 200 mg. 5 T hyroid is also stimulated by the human chorionic

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gonadotropin (hCG). Therefore, in the first trimester where hCG rapidly increases, TSH can decrease while FT3 and FT4 can increase. The hCG values are at peak at gestational week 10 whereas TSH is at lowest level. When hCG is reduced to its stable value as the pregnancy advances, TSH levels are increased, establishing a new balance. The temporary increase in FT4 disappears during the second trimester.[6,7] TBG continues to increase by the gestational week 20, and thus total thyroid hormones continue to increase by that period, but free fractions remain unchanged in their new balanced status following the first trimester.[1,3,6] Fetal hormone synthesis is initiated at gestational week 10 by means of TSH secretion from fetal hypophysis, and it is maintained at lower levels until the gestational week 20 while the synthesis is facilitated from that week, sustaining the increase until the end of pregnancy.[5,6,8]

The prevalence of hyperthyroidism is 0.05-0.02% in pregnancy. The most valuable tests in diagnosis are determination of TSH reduction and FT4 increase. However, as previously indicated, a 20% reduction can be observed physiologically in TSH during the first trimester. Graves disease is the most common cause of hyperthyroid in pregnant women. Other causes may include subacute thyroiditis, toxic nodular goiter and toxic solitary nodules.[9,10] The most common maternal complications observed in hyperthyroid are abortus, premature delivery, abruptio placentae, preeclampsia, congestive hearth failure and hyperemesis gravidarum while most common fetal complications are neonatal tyrotoxicosis, intrauterine growth retardation, prematurity, stillbirth and congenital anomalies.[1,9,11,12]

Prevalence of permanent hypothyroidism in pregnancy is 0.11% while its temporary (sub-clinic) prevalence is 0.19%. The most common cause of hypothyroidism in pregnancy is Hashimoto thyroiditis or disorders treated by thyroid ablation due to tyrotoxicosis (tyroidectomy or radioactive iodine treatment).[3,8,13] The most valuable diagnostic tests are assessments of FT4 and TSH. Diagnosis for primary hypothyroidism is made by lower FT4 and higher TSH levels. The maternal complications reported with hypothyroidism include abortus, premature delivery, hypertensive problems and postpartum bleeding, and the most severe complication is congestive heart failure while fetal complications are congenital anomalies, lower birthweight, stillbirth, prematurity and mental retardation.[14,15]

We evaluated the presence of thyroid function disorder in the etiology of spontaneous abortus by comparing the thyroid functions of women whose pregnancy resulted in spontaneous abortus with those of normal pregnant women.

Methods

The study group included 60 patients who presented to the clinic with complaints of vaginal bleeding, pelvic pain and tissue discharge, and diagnosed with spontaneous abortus at gestational weeks 5-20 while the control group consisted of 40 pregnant women who were at the same gestational weeks and then reached term and gave birth. Serum total T3 (TT3), total T4 (TT4), TSH, free T3 (FT3), free T4 (FT4) were studied in both groups. Diagnostic criteria for spontaneous abortus were uterine bleeding, presence of cervical dilatation, pelvic pain associated with uterine contraction, tissue discharge (complete or partial moles), damaged or absent pregnancy pouch in vaginal ultrasonography (thickened and irregular endometrium), absence of fetal cardiac activity or presence of placental detachment and hematoma. No restriction was imposed on age, parity and gravida in the pregnant women. The patients with metabolic or endocrinologic disorders were excluded. Cases that may effect the uteroplacental circulation such as ones with multiple pregnancy, genital organ anomaly, uterine myoma, advanced malnourishment, exposure to toxic substances, diabetes, hypertension, autoimmune disease and infection (TORCH) were also excluded. Patients in each group underwent a thorough physical and thyroid gland examination. Demographic characteristics of patients were determined by means of anamnesis. The gestational ages based on the start of the last menstruation period were confirmed by measurements of gestational pouch and crown-rump length. TT3, TT4, FT3, and FT4 measurements were carried out by chemiluminescence systems (ACS: 180+A Chiron Diagnostics, USA). And, TSH measurements were done by two-site sandwich immunoassay, automated chemiluminescence system, again using the direct chemiluminescence technology. Statistical analyses were performed by SPSS 10.0. Thyroid function tests of both groups were compared by Student-t test.

Results

No significant difference was found between the abortus group and the control group in the parameters such as age, parity, gravida and gestational age (p>0.05). The mean age was 24.38±3.34 years in the abortus group, and 24.14±4.66 years in the control group. TT4 values were 9.93±1.28 µgr/dl in the abortus group, and 11.39±1.41 µgr/dl in the control group where the TT4 value in the abortus group was very significantly lower (p<0.001) (Table 1). FT3 values were 3.22±0.82 pgr/ml and 4.19±1.14 pg/ml in the abortus group and control group respectively, and FT3 was significantly lower in the abortus group (p<0.001). The mean FT4 values were 1.11±0.31 ng/dl and 1.45±0.69 ng/dl in the study and control groups, respectively, and again in the abortus group FT4 value was found significantly lower than the value in the control group. When TSH values were compared, the mean values were 1.80±1.18 mIU/dl and 0.97±1.45 mIU/dl in the abortus and control groups, respectively, and TSH was significantly higher in the study group (p<0.05). TT3 values in the abortus and control groups were 2.61±0.51 ng/ml and 2.88±0.48 ng/ml, respectively, and there was a statistically significant difference between two groups (p<0.05).

Tablo 1. Comparison of thyroid function tests in spontaneous abortus and control groups.

	TSH (mIU/dl)	TT4 (µg/dl)	TT3 (ng/dl)	FT4 (ng/ml)	FT3 (pg/ml)
Abortus Group	1.80±1.18	9.93±1.28	2.61±0.51	1.11±0.31	3.22±0.82
Control Group	0.97±1.45	11.39±1.41	2.88±0.48	1.45±0.69	4.19±1.14
P	P<0.05	P<0.001	P<0.05	P<0.001	P<0.001

Discussion

In spite of many studies available regarding the physiological changes in the thyroid during pregnancy, it is uncertain if functional disorders of the thyroid play a role in the etiology of spontaneous abortus.6 Maruo et al. proposed that maternal thyroid hormone levels are one of the endocrine factors responsible from the abortus threat. They reported that 32 patients diagnosed with abortus threat had higher FT3 and FT4 levels compared to 21 pregnant women at the same gestational week, and TSH level was indifferent.[16] Ross et al. indicated that functional disorders of the thyroid is not effective in the outcomes of miscarriage.[17]

In three different studies, Pratt, Bussen and Singh found out that the thyroid autoantibody levels were higher in women with recurrent miscarriages during the first trimester than in the normal pregnant women.[18,19,20] It was suggested that those autoantibodies, which can also be higher in the euthyroid patients, may produce a threat for miscarriage in the subsequent pregnancy. In a prospective study by Rushworth et al., it was concluded that thyroid antibodies are not associated with spontaneous abortus,[21] which was also supported by Esplin et al.[22] As it can be seen from these studies, the role played by neither thyroid hormone levels (total hormone or free fraction) nor thyroid autoantibody levels in the etiology of spontaneous abortus and/or recurrent abortus is clear. However, we evaluated only the thyroid function tests, as there is a tendency in recent prospective studies to emphasize that thyroid autoantibodies are not responsible from spontaneous abortus.

Lower TT3, TT4, FT3, FT4 levels and higher TSH values we obtained in the spontaneous abortus group are an indication of the presence of a hypothyroidic situation in this group. It may lead to slowing down in the necessary synthesis and oxidation procedures, resulting in termination of the pregnancy. Thus, there are several publications indicating that ratio of spontaneous abortus rises two-fold in women with hypothyroid.[3,5,6,8] Again Matsua et al.[32] showed that FT3 and FT4 values of women whose pregnancy was terminated by abortus were significantly lower than those with a healthy continuation of pregnancy in thyroid function tests performed following the clinic diagnosis of abortus imminence, which is parallel to our findings.[16] All of these studies including our study indicate the frequency of subclinic hypothyroidism in pregnancy and its association with spontaneous abortus.

Subclinic hypotyroidism can be evaluated in two different groups where TSH is always higher than 10 mIu/L and lower than 10 mIu/L. There is a consensus regarding that subclinic hypothyroidism should be treated with thyroxine in the subgroup with higher TSH.[23] Particularly pregnancy and/or thyroid peroxidase antibody positive cases require immediate treatment. In the subgroup with TSH lower than 10 mIu/L, no consen-

sus exits regarding the treatment. Need for treatment in this group of pregnancies can be clarified by further studies.[23,24]

Conclusion

Thyroid function disorders play a role in the etiology of at least some part of spontaneous abortus and/or recurrent abortus, and based on our results spontaneous abortus seems more associated with subclinic hypothyroidism. Therefore, TSH levels should be measured as a routine screening test in all pregnancies.

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