

Comparison of TSH and Anti TPO Levels in Giving Birth Pregnant Women and Pregnant Women with Aborted Fetus in the First Trimester of Pregnancy

Arezoo Golizadeh, Zahra Raoofi

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Abstract

Introduction: Thyroid disease affects 2-3% of pregnant women and is associated with undesirable pregnancy outcomes. Thyroid antibodies in euthyroid women are associated with a significant risk of forgetfulness, abortion, preterm birth, and postpartum maternal euthyroidism. Hence, present study was conducted to evaluate the different levels of TSH and Anti TPO in the two groups of giving birth pregnant women and pregnant women with aborted fetus. **Methodology:** This cross-sectional study was conducted comparatively between 2016 and 2017 years. A total of 156 pregnant women at gestational age of 8 to 14 weeks were divided into two groups of pregnant women who were giving birth and pregnant women with aborted fetus and their TSH and Anti TPO levels were measured and compared. Data on participants were collected and then were analyzed using SPSS, version 21, software. **Results:** The mean age of participants was 28.9 years. This study revealed that with increasing TSH, the frequency of abortion increased significantly ($P = 0.012$). It also revealed that with increasing TSH level, the frequency of pregnant women with Anti TPO was significantly higher than normal ($P = 0.006$). Results showed that frequency of abortion increased with increasing anti TPO ($P = 0.00$). **Conclusion:** Positive anti TPO Ab may result in abortion in the first trimester of pregnancy.

Key words: Pregnant women, Abortion, TSH, Anti Tpo

Introduction

Physiological changes during pregnancy increase the production of thyroid hormones from the thyroid gland by 100-40% to meet the needs of the mother and fetus. In this regard, a number of pregnancy-induced changes occur in the thyroid. Anatomically, the thyroid gland is moderately enlarged during pregnancy as a result of glandular hyperplasia and increased vascularity (Krassas et al., 2010; Abalovich et al., 2007). Thyroid disorders have been suspected as possible causes of premature abortion and other undesirable pregnancy outcomes since old days. Severe iodine deficiency, which is not prevalent in developed countries, has been associated with increased rates of abortion (Krassas et al., 2010; Thangaratinam et al., 2011). Thyroid disease is one of the most important diseases in women and affects about 2-3% of pregnant women. It leaves undesirable pregnancy outcomes (Fitzpatrick and Russell, 2010). Thyroid disorders are classified into two types of clinical hyperthyroidism/hypothyroidism (subclinical) and autoimmune disorders. Hyperthyroidism is found in 0.1-0.4% of pregnant women. It is caused mainly due to Graves' disease (Bahn et al., 2011). Graves' disease during pregnancy is associated with abortion, preeclampsia, preterm labor, placental contraction, and fetal hyperthyroidism (Earl et al., 2010). The clinical hypothyroidism prevalence in pregnant women is also 0.3-0.5%. Hypothyroidism in women of gestational age is often caused by autoimmune thyroiditis and Hashimoto's disease. Hypothyroidism during pregnancy is associated with abortion, placental contraction, neonatal intensive care unit (NICU) and lower information scores (Abalovich et al., 2007). Thyroid autoimmunity is defined as the presence of thyroid antibody against thyroperoxidase (TPO-Ab) and / or thyroglobulin (Tg-Ab) in combination with normal thyroid function or euthyroid status. Its prevalence in women of gestational age has been reported about 8 to 14 percent (Krassas et al., 2010). The presence of thyroid antibodies in euthyroid women is associated with a significant risk of forgetfulness, abortion, preterm birth, and postpartum maternal euthyroidism (Thangaratinam et al., 2011). Women with thyroid autoimmunity who are euthyroid in the first stage of pregnancy are at the risk of hypothyroidism during pregnancy, which must be monitored (Stagnaro-Green et al., 2011). There are adequate research suggesting that subclinical hypothyroidism with $TSH > 4$ is associated with abortion, but there is not adequate research on $TSH: 2.5-4$. The biggest risk of hypothyroidism during pregnancy is delaying the neonate's growth and mental retardation after birth. Fetus is completely dependent on mother in terms of thyroid hormone during pregnancy until the thyroid gland begins its function. This does not happen earlier than week 2 of pregnancy. Hence, maternal hypothyroidism in the first 6 months of pregnancy can leave

Arezoo Golizadeh

MD, Department of obstetrics and gynecology, Iran University of Medical Sciences, Tehran, Iran.

Zahra Raoofi*

Assistant professor, Department of obstetrics and gynecology, Iran University of Medical Sciences, Tehran, Iran.

*Email: drarezoofi@yahoo.com

undesirable effects on fetus health. Most mothers become aware of their pregnancy after a long period of three months, imposing irreparable harms to the born child. Thus, mothers should take the necessary steps to diagnose and treat their thyroid disease before pregnancy (Alan, 2012). The aim of this research was to evaluate the level of TSH and to determine the positive or negative Anti Tpo in giving birth pregnant women and pregnant women with aborted fetus in the first trimester of pregnancy.

Methodology

This study was a cross-sectional study conducted on 156 pregnant women during 2016-2017 years. Out of them, 72 were pregnant women referred to the prenatal clinic of Shahid Akbarabad Hospital and 84 were pregnant women with 2 ultrasound scans showing no FHR who referred to the Shahid Akbar Abadi gynecology ward. Inclusion criteria of this study were pregnant women aged 15 to 45 years, gestational age of 8-14 weeks and exclusion criteria included the history of thyroid disease (hypothyroidism, hyperthyroidism, thyroid nodule, thyroid cancer, and thyroidectomy), diabetes, and hyperthyroidism, autoimmune disorders such as lupus, history of alcohol consumption and smoking, and history of recurrent abortions. After obtaining written consent of the participants, questionnaires including information on age, weight, height, number of pregnancies, gestational age and history of disease were completed. Then, 5 ml of venous blood was taken to measure thyroid hormones and anti-thyroid antibodies. Thyroid hormone was measured by IRMA method and thyroid antibody was measured by ELISA method. Normal pregnant women were followed up to 20 weeks and 82 patients with missed abortion confirmed by two ultrasound scans suggesting no FHR below 12-week gestation age were compared with 76 pregnant women with positive FHR up to 14-week gestational age to evaluate TSH and Anti Tpo levels. Based on lab kits, Anti TPO above 60 U / ML was considered high and abnormal. All data were collected in a checklist including gestational age, disease age, gravidity of disease history, BMI, TSH, and Anti tpo. Then, the data were analyzed in predetermined forms using SPSS, version 21, software.

Results

A total of 216 patients were examined in this study, out of which 5 were excluded due to the lack of tests, 23 were excluded due to iodopholic use, 1 was excluded due to runoff at 18 weeks, and 2 were excluded due to twin pregnancy. 86.9% of the subjects had no history of disease, but the rest of the participants (n=19, 13.1%) had hypertension, diabetes, a history of thyroid disorders and autoimmune disease, so they were excluded from the study. Additionally, 36.6% (n=53) reported a history of non-thyroid surgery. The mean age of participants in this study was obtained 26.42 years at normal pregnancy and 28.27 at abortion. The youngest participant was 15 years of old and the oldest was 45 years of old. Participants in this study were divided into two groups of less than 35 and equal or greater than 35 and they were compared. The mean age of participants in above 35 years group was 37.3 years in the normal pregnancy and 37.9 years in the abortion group, and the mean age of participants in below 35 years group was 25.2 years in the normal group and 25.4 years in the abortion group. The investigated pregnant mothers of this study had gestational age of 8 to 14 weeks.

Out of them, 35.5% experienced first pregnancy, 42.1% experienced second pregnancy, 13.1% experienced third pregnancy, 6.9% experienced fourth pregnancy and 1.4% experienced fifth pregnancy. In the giving birth group, 95.9% did not have a history of abortion and 4.1% reported one history abortion without a cause, and in the abortion group, 95.4% did not have a history of abortion and 4.6% had one history abortion. No significant difference was found between two groups in terms of previous history of abortion. None of the participants had a history of alcohol consumption and smoking, PID and uterine anomaly and cervical insufficiency. With regard to BMI, 63% were normal, 19% were overweight, 10% were underweight and 8% were obese. In the group aged above 35 years, 54.8% (n = 84) had forgotten abortion and 45.2% (n = 72) had positive FHR pregnancy. In the group aged below 35 years, pregnant women with abortion had the highest Anti TPO value of 268 U / ml and the lowest value of 1 U / ml, and in the child giving pregnancy group, its highest level was 159 U / ml and its lowest value was 1u / ml. At the age group of 35 years and over, in pregnant women with abortion, the highest Anti TPO level was 248 U / ml and the lowest TPO level was 1 U / ml. At the age group below 35 years, in pregnant women with abortion, the highest TSH was 4.8 mu / l and the lowest value was 0.5 mu / l, and in the giving birth group, the highest was 4.02 mu / l and the lowest was 0.5 mu / l. At the age group of 35 years and over, in pregnant women with abortion, the highest TSH value was 4.9 mu / l and the lowest value was 0.5 mu / l, and in the giving birth group, the highest was 4.09 and the lowest was 0.5u / ml. With regard to anti-TPO antibody level, 82.5% of the participants (n=128) were in the normal range (less than 60) and the rest (n=26) were above the normal range. In the statistical analysis of Anti TPO Ab level in the participants, the skewness statistic was found to be 0.216, which was smaller than +1, so it can be stated that the data had a normal distribution. Table 1 shows the demographic characteristics of the abortion and giving birth groups at the age group of below 35 years. Table 2 shows the demographic characteristics of the abortion and giving birth pregnancy groups at the age group of over 35 years.

Table 1. Comparison of demographic characteristics of two groups of abortion and giving birth pregnancy at the age group below 35 years

	Missed Abortion	giving birth pregnancy	P Value
Age (year)	25.2	25.4	0.31
BMI(Kg/m2)	26.78	26.02	0.28

Gravidity	1.4	1.8	0.9
Mean gestational age	10.7	10.9	0.15
History of previous abortion	0 (95.4%) 1 (4.6%)	0 (95.9%) 1 (4.1%)	0.18
Folic acid intake in pregnancy	87.5%	94.3%	0.09

Table 2. Comparison of demographic characteristics of two groups of abortion and giving birth pregnancy in age group of 35 years and over

	Missed Abortion	giving birth pregnancy	P Value
Age (year)	37.3	37.9	0.12
BMI(Kg/m ²)	26.81	26.85	0.3
Gravidity	1.7	1.8	0.21
Mean gestational age	10.4	10.9	0.9
History of previous abortion	0 (96.2%) 1 (3.8%)	0 (95.9%) 1 (4.9%)	0.15
Folic acid intake in pregnancy	83.4%	83.06%	0.2

Table 3 shows the results of this study on the frequency of giving birth pregnancy and missed abortion at different TSH levels in two groups of abortion and giving birth pregnancy at the age group of below 35 years and Table 4 shows the results of this study on the frequency of giving birth pregnancy and missed abortion at different TSH levels in two groups of abortion and giving birth pregnancy at the age group of 35 years.

Table 3. Frequency of giving birth pregnancy and missed abortion at different TSH levels of abortion and giving birth pregnancy at age group of below 35 years

	TSH 0.5 – 1.5 mIU/L	TSH 1.5 – 2.5 mIU/L	TSH 2.5 – 3.5 mIU/L	TSH 3.5 – 4.5 mIU/L	TSH 4.5≥ mIU/L	Mean TSH	sd	Total
Missed Abortion	9	23	14	12	4	2.67	±1.19	60
	15%	38%	23%	20%	6%			
Normal Pregnancy	22	16	12	5	1	1.99	±1.09	56
	36%	28%	21%	8%	1%			
OR	1	1.17	1.82	1.8	1.92			
P Value	0.06	0.01	0.04	0.02	0.005	0.00		

Table 4. Frequency of giving birth pregnancy and missed abortion at different TSH levels of abortion and giving birth pregnancy at the age group of above 35 years

	TSH 0.5 – 1.5 mIU/L	TSH 1.5 – 2.5 mIU/L	TSH 2.5 – 3.5 mIU/L	TSH 3.5 – 4.5 mIU/L	TSH 4.5≥ mIU/L	Mean TSH	sd	Total
Missed Abortion	3	7	7	5	3	2.55	1.10	25
	18.5%	41%	21%	18%	9%			
Normal Pregnancy	4	5	4	2	1	2.83	1.24	16
	36%	27%	22%	7%	3%			
OR	1.09	1.2	1.89	1.24	1.9			
P Value	0.09	0.21	0.49	0.08	0.04	0.29		

Chi-square test was used to test the hypothesis stated on the relationship between TSH and the frequency of abortion and frequency of giving birth pregnancy in women aged below 35 years. Results analysis revealed that P value was 0.001. Therefore, the null hypothesis was rejected and there was a relationship between the TSH level and the incidence of forgotten abortion. The results revealed that the mean TSH was higher in pregnant women with abortion than that in women with giving birth pregnancy (1.8 Mu / 1 versus 2.03) (p

value: 0.001). However, at the age group of 35 years and over, this difference in mean TSH was not significant between the two groups (p value: 0.29). Moreover, at age group below 35 years, chi-square test was used to evaluate the relationship between Anti TPO Ab and the frequency of abortion. The results revealed that 23.4% had Anti TPO higher than normal in the abortion group, while 13% had Anti TPO higher than normal in normal pregnancy group. P value was calculated as 0.002 in the analysis. Thus, the null hypothesis was rejected and there was a relationship between the Anti TPO Ab level and the incidence of forgotten abortion. Given the normal distribution of Anti TPO Ab, T-test was used to examine the relationship between Anti TPO Ab and Abortion level and frequency of abortion. The mean Anti TPO Ab in women who did not have an abortion was 9.99 with a standard deviation of 33.15. This mean was 35.73 with a standard deviation of 52.34 in women with forgotten abortion. At the age group of 35 years and over, the chi-square test was used to examine the relationship between Anti TPO Ab and the frequency of abortion. The results of analysis showed that P value in pregnant women with Anti TPO Ab was above 0.05. Hence, the null hypothesis was accepted and there was no relationship between the Anti TPO Ab level and the incidence of forgotten abortion.

Due to normal distribution of Anti TPO Ab, T-test was used to examine the relationship between Anti TPO Ab level and frequency of abortion. Mean anti TPO Ab in non-abortion women was obtained 32.4 with a standard deviation of 31.05. This mean was obtained 84.43 with a standard deviation of 42.34 in women with forgotten abortion. Chi-square test was used to examine the relationship between TSH and frequency of Anti TPO. The results revealed that 18.5% of the samples had Anti TPO higher than normal. In these women, TSH (3.8) was significantly higher than that (2.4) of samples with normal Anti TPO. P value was calculated 0.006 that was less than 0.05, so the null hypothesis was rejected and there was a difference and relationship between TSH level and Anti TPO Ab level. Due to normal distribution of Anti TPO Ab, One way ANOVA test was used to examine the relationship between Anti TPO Ab level and the TSH level. The mean Anti TPO Ab in subjects with 0.5-1.5 TSH was 7.31 with a standard deviation of 8.68 and the mean Anti TPO Ab in subjects with 1.5-2.5 TSH was 24.88 with a deviation 51.60, the mean Anti TPO Ab in subjects with 2.5-3.5 TSH was 23.75 with a standard deviation of 38.36, the mean Anti TPO Ab in subjects with 3.5-4.5 TSH was 47.37 with a standard deviation 59.99, and the mean Anti TPO Ab in subjects with above 4.5 was 87.00 with a standard deviation of 102.17.

Discussion

The present study's results revealed that there was a relationship between TSH and abortion. It means that an increase in TSH had an effect on the frequency of abortion in the first trimester of pregnancy. In a similar study conducted by Negro in 2010, the results showed that abortion frequency in the group with higher TSH was significantly higher (Negro et al., 2010), which was consistent with current study. Moreover, the results of this study revealed a correlation between Anti TPO Ab and different TSH groups (0.5-1.5, 1.5-2.5, 2.5-3.5, 3.5-4.5, and above 4.5). In fact, with increasing Anti TPO Ab, TSH also increased. In a study conducted by Ghoreyshian in 2006 in Yazd on 2425 patients, a relationship was observed between increased TSH and positive anti TPO. The results of the present study showed that positive Anti TPO Ab was associated with abortion frequency. In fact, Anti TPO Ab was associated with an increased risk of abortion and reduced chance of a live birth. The study conducted by Grossman in 2016 on 118 patients with a history of abortion also found that women with a history of abortion had higher anti-TPO levels, which was in line with the present study. The results of the present study were in line with the results of the studies conducted by Sangdamrang, Mina, and Maray. Additionally, the research conducted by Unan et al. (2017) and Lukaszuk (2015) achieved results contrary to those of the current study. They concluded that positive or negative Anti TPO Ab had no effect on successful pregnancy. Further studies are needed to know if Anti TPO Ab affects the incidence of abortion and successful pregnancy, but the results of the current study may be due to the biochemical effects of Anti TPO Ab on the fetus. This effect may be due to maternal race, fetal genetic structure, or the direct teratogenic effect of this substance. Anti TPO Ab may have receptors on fetal germ cells and may prevent cell division by binding to these receptors. It may be also due the fact that this antibody has an effect on the mechanism of fetal growth that prevents this growth and leads to abortion by lack of fetal development.

Conclusion

The results of this study revealed that at the age group of 35 years and above, abortion rate increased significantly with increasing TSH level from 1.5 to 0.5 to 1.5. However, there was no significant increase in age over 35 years, which means that other factors are involved in abortion at the age of above 35 years. There was also a significant increase in anti-TPO abortion at the age of below 35 years, but no significant increase was observed at ages of above 35 years. Abortion at the age of 35 years and above, especially if associated with an increase in Anti TPO, showed significant increase in abortion than normal Anti TPO, and at age of 35 years, if TSH was above 2.5, Anti TPO would be above the normal and abortion would increase significantly.

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