

## Spontaneous abortion and anti-thyroid antibodies in mother's serum

Reza Maghsoudi<sup>1</sup>, Mahmoud Mirhosseini<sup>2,\*</sup>

<sup>1,2</sup> Shahrekord University of Medical Sciences, Shahrekord, Iran

\*Corresponding author, [Email: mirhosseini.m@skums.ac.ir](mailto:mirhosseini.m@skums.ac.ir)

**Background and Aim:** Spontaneous abortion is the most common pregnancy complication with no reasonable causes in most cases. Some research imply the role of anti-thyroid antibodies (e.g. anti TPO-Ab and anti TG-Ab) that can cause spontaneous abortion. In the present study, the association between abortion and presence of anti-thyroid antibodies in mother's serum was assessed. **Methods:** In this case control study, 102 women aged 15-45 years, who referred to Hajar hospital of Shahrekord or the clinic affiliated to Shahrekord University of Medical Sciences were selected. Out of 102 women, 51 who had had abortion selected as the cases and 51 pregnant women with gestational age less than 20 weeks were include as the controls. In order to assess anti-thyroid antibodies level, blood samples were taken from every participant with normal TSH level. Anti-thyroid peroxidase antibody (Anti-TPO-Ab)>50 IU/ml and anti-thyroglobulin antibody (Anti-TG-Abs)>75 IU/ml were defined as Positive. The obtained results were analyzed by means of t-test and  $\chi^2$ , using statistical SPSS software. **Results:** Out of 51 subjects, 18 had positive Anti-TPO-Ab, of which -10 were among the cases and 8 belonged to the controls. Out of 18 women with positive anti TG-Ab, 11 cases were in the control group and 7 were in the cases. The differences between the control group and the amounts of Anti-TPO-Abs ( $P=0.468$ ) and anti-TG-Abs ( $P=0.675$ ) were not significant. **Conclusion:** The results revealed that there is no association between abortion and presence of ant thyroid antibodies in mother's serum. Other abortion causes such as various kinds of infections and smoking might be involved which requires more research.

[Reza Maghsoudi, Mahmoud Mirhosseini. **Spontaneous abortion and anti-thyroid antibodies in mother's serum.** *Life Sci J* 2014;11(8s):41-44] (ISSN:1097-8135). <http://www.lifesciencesite.com>. 4

**Keywords:** Abortion, Anti-thyroid antibodies, Anti TPO-Ab, Anti TG-Ab

### Introduction

The thyroid gland produces two thyroid hormones that are associated with each other and named thyroxine ( $T_4$ ) and triiodothyronine ( $T_3$ ). These hormones have a crucial role in cell differentiation throughout the growth. Thyroid disorders in adults, often resulting in autoimmune processes. That stimulate excessive thyroid hormones, and or the gland destruction and decreased production of thyroid hormones (hypothyroidism) (1). Thyroid peroxidase (TPO) is an enzyme in the microsomal membrane of follicular cells of thyroid, which is involved in the biosynthesis of thyroid hormones (1, 2). Thyroglobulin (TG), is a large dimeric protein that is synthesized by thyroid follicular cells.  $T_3$  and  $T_4$  molecules after synthesis, stored in colloid space (follicular space) to form as a components of TG molecules, (1). Abnormalities in thyroid hormone synthesis, are considered as one of the rare cause of congenital hypothyroidism. Most of these disorders, are the cause of incidence of recessive mutation in TPO and or TG genes. Peroxidase thyroid antibodies (TPO Ab) and thyroglobulin antibodies (TG Ab) are also called anti-microsomal antibodies can be found In Hashimoto's thyroiditis, Graves' disease, postpartum thyroiditis and chronic thyroiditis painless (3). In fact, nearly all cases of Hashimoto's disease and Graves' disease have increased often in plasma

concentration of TPO Ab (4). Autoimmune thyroid disease can be easily diagnosed by measurement of TPO and TG antibodies in Circulation. About 5 to 15% of euthyroid women and 2% of euthyroid men have thyroid antibodies. These individuals are at high risk in terms of dysfunction of thyroid (1). If TPO Ab test be positive it is an indicative of autoimmune thyroid disease (5). The Usage of each way and means to terminate a pregnancy before the fetus can be survive, is called abortion. This definition in National Center for Vital Statistics and the World Health Organization, is provided to this form: to termination of pregnancy before the twentieth week of pregnancy (which is calculated from the first day of the last normal menstrual) and or fetal giving birth with weight of under 500 grams (6). Early abortion, is termination of pregnancy before the 12 week of pregnancy and late abortion is between weeks of 12 to 20 week (7). Spontaneous abortion is the most common single abortion. Variety of clinical spontaneous abortion include: threatened abortion, inevitable abortion, missed abortion, recurrent abortion, incomplete abortion, septic abortion, and subclinical spontaneous abortion (6, 7). More than 80% of abortions occur in the first 12 weeks, which are at least 50% of abortions due to chromosomal abnormalities. Other causes of spontaneous abortion are maternal infections, endocrine disorders such as

hypothyroidism, diabetes mellitus, luteal phase dysfunction, autoimmune factors, such as: anti-phospholipid antibodies, usage drugs and environmental factors such as smoking, alcohol consumption, caffeine, radiation, contraceptives drugs, uterine anomalies such as cervical incompetence and uterine leiomyomas and physical trauma, cardiac and renal disease, and also blood disease (6, 8, 9). As noted above, hypothyroidism is one of the causes of spontaneous abortion, but the evidence shows that even in euthyroid patients, the presence of thyroid antibodies can lead to abortion, even the recurrent type. The mechanism of this association is unclear. However, these antibodies could be a sign of a more general trend of autoimmune, although the approval or rejection of the relation of thyroid antibodies and abortion, conflicting theories have been proposed, but the simple preventive methods, namely the T4 hormone administration can decrease the number of abortions in the presence of a significant relationship between abortion and levels of thyroid antibodies. So, the researcher wants to examine this relationship, once again.

#### Methods

The present study was an analytical study of case – control named as double-blind (laboratory and analysis). After obtaining the approval of the Ethics Committee of the medical sciences university of Shahrekord, the project was conducted in 2012 in Chaharmahal & Bakhtiari province. In this study, among patients with spontaneous abortion (first abortion or with a history of abortion), referred to a university-affiliated clinic or women section of Gynecologic Hajar Hospital of Shahrekord, in age range of 15 to 45 years, 51 patient from eligible cases, were selected as the case group; also, 51 cases of pregnant women with gestational age less than 20 weeks and no previous abortion and referring to the Clinic, were selected as the control group, and according to age, body mass index, gestational age and the number of pregnancy, were matched with case group. Patients with non-spontaneous abortion and patients treated with thyroid medication

(levothyroxine, Methimazole and propyl tio urasil), according to information had obtained from the questionnaires and tests, were excluded from study. After completion of the questionnaires and consent by the patient, on the day of abortion, from each sample, 5 ml blood was taken for measurement of TSH concentrations. Abnormal serum TSH range (normal range, according to experimental kit was considered 4Mu/l – 0.3), indicated the hyperthyroidism or hypothyroidism, and these patients were excluded from the study and were replaced with other qualified patients. In case of normal amounts of serum TSH, (mean, patients be euthyroid) anti-thyroid antibody concentrations, (mean, anti TPO-Ab and anti TG-Ab) measured in serum and at the end, the evaluation of the amounts of antibody concentration specified that, whether there is a relationship between the concentration of antibodies and incidence of spontaneous abortion, or not? All samples were tested by a qualified expert performed with one type of kit. Kits available for the study of thyroid antibodies including: anti TPO-Ab kit and anti TG-Ab kit that is used with ELISA method. The sensitivity of these kits is 95% and the specificity of them is 98%. According to laboratory kit, levels of anti TPO-Ab and anti TG-Ab was 50 IU/ml and 75 IU/ml respectively, and was considered positive. The data have collected, then entering them into the SPSS statistical software (13.5 version). The data were analyzed with uses of dependent groups T-test and X2 test.

#### Results

The mean age of the study group, was  $28.27 \pm 6.6$  and in control group was  $28.19 \pm 5.2$ . Body mass index in case group with average of  $24.13 \pm 3.9$  and in control group was  $24.21 \pm 4.2$ . The number of pregnancies in the study group with a mean  $2.19 \pm 1.11$  and in control group was  $1.88 \pm 1.25$  and according to t-student test, there is no significant difference between control and case group ( $p < 0.05$ ) (table 1). The number of anti TPO-Ab in case group with average of  $38.45 \pm 48.4$  and the counts of anti TG-Ab in control group with mean was  $327.3 \pm 35.7$  (Table 1).

Table 1: Comparison of age, body mass index, number of pregnancy, and antibody titers in both groups

Variables	Control (N=51)	Case (n=51)	P
Age	28.20±5.20	28.30±6.60	0.948
The number of pregnancies	1.90±1.25	2.20±1.10	0.186
BMI	24.20±4.20	24.10±3.90	0.924
Anti TPO-Ab	32.30±35.70	38.40±48.40	0.468
Anti TG-Ab	55.10±46.10	60.80±84.10	0.675

From 102 studied patients, 18 patients (17.6%) have positive anti TPO-Ab or with level of antibody, were more than 50 IU/ml that 10 cases of them belonged to 51 patient in case group (19.6%) and 8 cases belonged to 51

patient in control group(15.7%). As well, 18 cases from 102 cases (17.6%), have positive anti TG-Ab or with level , higher than 75 IU/ml which the 7 cases (13.7%) belonged to case group and 11 cases (21.6%) belonged to control group. With using X2 test, there was no significant difference between the counts of anti TPO-Ab and anti TG-Ab ( $p>0.05$ ) (table-2).

Table 2: Comparison of frequency of positive cases in the two study groups

Variables	Groups	Positive	Negative	OR	p
anti TPO-Ab	Case	10 (19.60)	41 (80.40)	0.763	0.398
	Control	8 (15.70)	43 (84.30)		
Anti TG-Ab	Case	7 (13.70)	44 (86.30)	1.72	0.218
	Control	11 (21.60)	40 (78.40)		

## Discussion

The results showed that, there was no significant relationship between the levels of anti TPO-Ab and anti TG-Ab of mother and fetus ( $p>0.05$ ). The results of this study with the studies of Esplin, Pratt, Roye-Green and Muller were consistent (4,10,12); also Lejeune and colleague in their study with the aim of evaluate the correlation of abnormal abortion and asymptomatic abnormality such as thyroid autoantibodies, reached the conclusion that high titers of anti-thyroglobulin antibodies and anti-thyroperoxidase, is associated with an increase in the number of abortions(13). Despite the above studies, researchers believe that the presence of thyroid antibodies influencing abortion, but studies of Pratt and Colleagues showed that the prevalence of thyroid antibodies in women with recurrent miscarriage, did not have a significant increase compared with the control group (10). Research on 50 women with recurrent abortion found that, there was no significant difference between presence of thyroid autoantibodies in groups with habitual abortions and with the control group (11). Wilson & colleagues were done their study with the aim of finding the correlation between anti- thyroid antibody and abortion, they found that, during pregnancy, the activity and titer of antibodies against thyroid, in women who had a miscarriage is significantly higher than women who completed the pregnancy, and thus autoimmune plays a role in recurrent spontaneous abortion. But Kutteh with study on 700 women, observed that, the presence of anti-thyroid antibodies, have an association with high risk of abortion (14). However, in this study and other studies, women was considered with a history of two or more of recurrent abortion, from this view, is different with this study (15-17). The study was conducted by Kaprara, showed a significant relationship between anti- thyroid antibodies and increased rate of abortion, however, patients with high titers of thyroid autoantibodies, in comparison of patient with low titer, had not more abortions (18). According to Popp, existence of autoimmune thyroiditis, is not associated with the implantation of eggs, but the risk of miscarriage increases basically

(19). Bahrami Sharif study showed that the significant difference between two groups with studied thyroid antibodies, (a group which her recent pregnancy up to 20 weeks lead to abortion and the group that their pregnancy continued after 20 weeks), and abnormal amounts of antibodies, are in a group which their pregnancy lead to abortion but had not any relation with their previous abortion (20). In Afshar study there is no correlation between anti TPO-Ab and abortion, in women with recurrent abortion, so he said the assessment of the antiTPO in patient with history of recurrent spontaneous abortion is not useful (21). Moravej came to the conclusion that anti-thyroglobulin antibodies, have not direct effect on organs such as the placenta and decidual or ovary in patients with autoimmune thyroiditis that have recurrent abortion (22). Mavragani showed that, in women with autoimmune disorder, the loss of recurrent pregnancy, independently associated with the presence of thyroglobulin antibodies (23). Also Soltan Gharaei reported that, levels of anti TG5>500 in women with recurrent abortion, is twice higher than control group but the levels of anti TPO-Ab have not a significant difference (24).

## Conclusion

In accordance with the present findings, existence of anti-thyroid antibodies in the mother's blood, is not associated with abortion. It is recommended that, since the several factors are effective in causing abortion (such as genetic factors, diabetes mellitus, maternal infection, autoimmune diseases like lupus and environmental factors such as smoking and alcohol, etc.), these factors should be considered in other studies.

## Acknowledgement

This article was obtained from a PhD students thesis with number of 908, thereby the authors thanked from all those who helped us in this study, particularly, Deputy of university of medical sciences that accepts the found of the project, and staff of the ward of Gynecologic Hajar Hospital.

**References**

1. Jameson JL, Weetman AP. Disorders of the thyroid gland. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine*. 17th ed. Mc Graw-Hill: 2008. 2: pp:2224-9.
2. Wilson R, Ling H, MacLean MA, Mooney J, Kinnane D, McKillop JH, et al. Thyroid antibody titer and avidity in patients with recurrent miscarriage. *Fertil Steril*. 1999; 71(3): 558-61.
3. Novak B. *Novak's Gynecology*. Translated by: Kazemzade S, Khatibi SN, Monajemi A, Rahimzade P. Tehran: Noore Danesh publication. 14th ed: 2003. pp: 117-261.
4. Esplin MS, Branch DW, Silver R, Stagnaro-Green A. Thyroid autoantibodies are not associated with recurrent pregnancy loss. *Am J Obstet Gynecol*. 1998; 179(6 Pt 1):1583-6.
5. Herman-Bonert VS. The thyroid gland in Cecil essentials of medicine. In: Andreoli TE, Carpenter CC, Griggs RC, Benjamin IJ. *Cecil essentials of medicine*, 7th ed. Philadelphia: Elsevier Saunders: 2007. pp 649.
6. Antepartum, Abortion. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Kouse DJ, Spong CY. *Williams Obstetrics*, 23rd ed. Mc Graw Hill: 2010. pp: 215-65.
7. Mukherjee GG, Chakravarty S, Pal B, et al. *Current Obstetrics & Gynecology*, Translated by: Habibinia A. Tehran: Chehr Publication: 1994. pp: 69-72.
8. Fox-Le L, Schust DJ. Reproductive endocrinology, recurrent pregnancy loss. In: Berek JS. *Berek & Novak's Gynecology*. 14th ed. Philadelphia: Lippincott Williams & Wilkins: 2007. 2: pp 1277-300.
9. Ryan KJ, Berkowitz RS, Barbieri RL, Kistner RW. *Kistner's Gynecology Principles & Practice*, Translated by: Ghazijahani B. Tehran: Esharat Publication: 1995. pp: 315-326.
10. Pratt D, Novontny M, Kaberlein G, Dudkiewicz A, Gleicher N. Antithyroid antibodies and the association with non-organ-specific antibodies in recurrent pregnancy loss. *Am J Obstet Gynecol*. 1993; 168(3 Pt 1): 837-41.
11. Roye-Green K, Frederrick J, Wharfe G, Choo-Kang E, DaCosta V, Fletcher H, et al. Anti-phospholipid and other autoantibodies in a cohort of habitual aborters and healthy multiparous women in Jamaica. *Hum Antibodies*. 2011; 20(1-2): 1-5.
12. Muller AF, Verhoeff A, Mantel MJ, Berghouf A. Thyroid autoimmunity and abortion: a prospective study in women undergoing in vitro fertilization. *Fertil Steril*. 1999; 71(1): 30-34.
13. Lejeune B, Grun JP, de Nayer P, Servais G, Glinoe D. Antithyroid antibodies underlying thyroid abnormalities and miscarriage or pregnancy induced hypertension. *Br J Obstet Gynaecol*. 1994; 101(5): 461-462.
14. Kutteh WH, Yetman DL, Carr AC, Beck LA, Scott RT. Increased prevalence of antithyroid antibodies identified in women with recurrent pregnancy loss but not in women undergoing assisted reproduction. *Fertil Steril*. 1999; 71(5): 843-8.
15. Stagnaro-Green A, Glinoe D. Thyroid autoimmunity and the risk of miscarriage. *Best Pract Res Clin En*. 2004; 18(2): 167-181.
16. Pratt DE, Kaberlein G, Dudkiewicz A, Karande V, Gleicher N. The association of antithyroid antibodies in euthyroid nonpregnant women with recurrent first trimester abortions in the next pregnancy. *Fertil Steril*. 1993; 60(6): 1001-5.
17. Bussen S, Steck T. Thyroid autoantibodies in euthyroid non-pregnant woman with recurrent spontaneous abortions. *Hum Reprod*. 1995; 10(11): 2938-40.
18. Kaprara A, Krassas GE. Thyroid autoantibody and miscarriage. *Hormones*. 2008; 7(4): 294-302.
19. Poppe K, Velkeniers B, Glinoe D. The role of thyroid autoimmunity in fertility and pregnancy. *Nat Clin Pract Endocrinol Metab*. 2008; 4(7): 394-405.
20. Bahrami Sharif M, Hoseini MS. Evaluation of antithyroid antibodies in aborting people from Obstetrics Clinic of Mahdieh Hospital at Shaheed Beheshti university. *Sci J Hamdan Univ Med Sci*. 2009; 16(2): 27-32.
21. Ashrafi M, Salman Yazdi R, Madani T, Bazrafshan A. Anti-thyroid peroxidase and risk of recurrent spontaneous abortion. *Fertil Steril*. 2007; 1(2): 113-116.
22. Moravej A, jeddi-tehrani M, Salek-moghaddam AR, Dokouhaki P, Ghods R, Rabbani H, et al. Evaluation of thyroglobulin expression in murine reproductive organs during pregnancy. *Am j reprod immunol*. 2010; 64(2): 97-103.
23. Mavragani CP, Ioannidis JPA, Tzioufas AG, Hantoumi IE, Moutsopoulos HM. Recurrent pregnancy loss and autoantibody profile in autoimmune diseases. *Rheumatology (Oxford)*. 1999; 38(12): 1228-33.
24. Soltanghorae H, Arefi S, Mohammadzadeh A, Taheri A, Zeraati H, Hashemi SB, et al. Thyroid autoantibody in euthyroid women with recurrent abortions and infertility. *Iran J Reprod Med*. 2010; 8(4): 153-6.

5/2/2014