

# A study of the relationship between thyroid autoantibodies and early missed abortion

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## Summary

**Objective:** The relationship between thyroid autoantibodies (TA) and early missed abortion remains unclear, and therefore, their relationship was investigated in this research. **Study Design:** One hundred cases of missed abortion women were selected as test group, and 100 early pregnant women were enrolled as control group. Thyroid peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb) were determined by electrochemiluminescence, the positive rates and levels of TPOAb and TgAb were compared, and their relationship with early missed abortion was analyzed by logistic regression analysis. **Results:** The results indicated that the positive rates of TPOAb and TgAb in the test group was much higher than the control group ( $p < 0.05$ ). The serum level of TPOAb in early missed abortion females was also higher than the control group ( $0.93 \pm 0.65$  vs.  $0.72 \pm 0.28$ ,  $p < 0.01$ ), while no significant differences for TgAb between the test group and normal controls ( $1.34 \pm 0.46$  vs.  $1.31 \pm 0.26$ ,  $p > 0.05$ ). According to the logistic analysis, the authors found that the positive rates of TPOAb in the test group was 4.129 times higher than that in the control group ( $p = 0.004$ ), and might be an independent risk factor for early missed abortion. **Conclusion:** In summary, the authors inferred that TA positive was related to early missed abortion, and TPOAb positive was an independent dangerous factor.

**Key words:** Missed abortion; Thyroid autoantibodies; Thyroid peroxidase antibody; Thyroglobulin antibody.

## Introduction

Missed abortion is a special type of spontaneous abortion with an incidence rate of 15-20% [1]. According to the statistics, the morbidity of missed abortion has been reported to be on the rise worldwide in the recent years [2]. In China, missed abortion represents a serious healthy problem which leads to the reduce quality of life for females [3]. It is generally considered that the causes and risk factors of missed abortion are complex. Some risk parameters have been identified, including abnormality of endocrine, abnormal infection, and some immunity factors [4,5]. Given the pain and damage caused by missed abortion, an increasing number of studies have been conducted to uncover the potential risk factors, which are closely correlated with the occurrence of missed abortion.

According to the results of previous studies, thyroid disorders are frequent in females at reproductive age [6]. Evidence indicated that the dysfunction of the thyroid in pregnant women contributed to various poor outcomes, such as miscarriage, fetal death, maternal post-partum thyroid disease, and premature birth [7, 8]. Thyroid disorders have been reported to be characteristics by the production of thyroid autoantibody (TA), which represents an common detection index of thyroid inflammation in clinical practices [9]. Thyroid autoantibody (TA), consisting of thyroid

peroxidase antibody (TPOAb) and thyroglobulin antibody (TgAb), have been found to be positive during the thyroid inflammation [10, 11]. Abundant studies have demonstrated that there was close association of TA with recurrent abortion [12, 13], indicating the crucial role of TA during the development of abortion. However, whether there was correlation between TA and missed abortion has been rarely reported till now.

In order to pave the way for prevention and treatment of early missed abortion, the present study was conducted to assess the relationship between TA and early missed abortion via evaluation of the serum levels of TPOAb and TgAb in females with early missed abortion.

## Materials and Methods

A total of 100 patients, who were diagnosed with early missed abortion in Gynecology Department of Qingdao Haici Medical Group from January 2013 to December 2014, were recruited in this study. In addition, there were age and gravidity matched 100 early pregnant females, who were randomly selected from the individuals receiving routine gynecological checkup in the hospital, to act as the control group. All the pregnant women were in accordance with the following inclusive criteria: 1) pregnancy equal or less than 12 weeks, 2) no history of thyroid diseases and other autoimmune diseases, 3) normal blood pressure and negative result of protein in urine, 4) normal fasting blood glucose, 5) without any severe clinical history, 6) normal levels of thyroid

stimulating hormone (TSH), and free thyroxine (FT4). The informed consents were signed from all the participants for the utilization of the clinical material.

Five mL fasting blood specimens were collected from cubital vein of all the participants and stored in the EDTA tubes for the next analyses. The content of TPOAb, TgAb, TSH, and FT4 in the blood samples were measured by electrochemiluminescence, which was carried out with a commercial kit and ran on an ACS180 system.

All statistical analyses were carried out by SPSS Version 13.0 software. The data used in the analyses were all expressed as mean  $\pm$  SD. The differences between the groups were analyzed with  $\chi^2$  test and *t*-test. To explore the relationship between TA and early missed abortion, logistic regression analysis was adopted to investigate the OR and 95% CI value for each of the parameter. Among all the analyses, differences were considered as statistically significant when the *p*-value of less than 0.05.

## Results

According to the electrochemiluminescence, the contents of TPOAb and TgAb were estimated in both early missed abortion patients and the normal controls. On the basis of the definition of TPOAb positive  $\geq 5.61$  IU/mL and TgAb positive  $\geq 4.11$  IU/mL, positive TA was identified in 21 (21%) early missed abortion patients (seven TPOAb positive cases, four TgAb positive cases, and ten both TPOAb and TgAb positive cases), which was significantly increased compared with the normal controls with nine (9%) TA positive cases (four TPOAb positive cases, two TgAb positive cases, and three both TPOAb and TgAb positive cases) ( $p < 0.05$ , Table 1).

To compare the different TA levels between early missed abortion patients and early pregnant females, the raw data was transformed with logarithmic and analyzed by *t*-test. From the results of the analysis, which are all listed in Table 2, the serum levels of TPOAb was significantly higher in missed abortion patients compared with that in the normal controls ( $0.93 \pm 0.65$  vs.  $0.72 \pm 0.28$ ,  $p < 0.01$ ). However, no significance was found between the TgAb levels in missed abortion group with that in the normal group ( $1.34 \pm 0.46$  vs.  $1.31 \pm 0.26$ ,  $p > 0.05$ ).

In order to confirm whether serum levels of TA was correlated with early missed abortion, the relationships between early missed abortion with TPOAb and TgAb levels were analyzed by logistic analysis. From analysis results, the TPOAb levels were found to be 4.129 times higher in missed abortion group than that in the normal controls ( $p = 0.004$ ). Thus, the present authors considered that positive TPOAb served as an independent risk factor for early missed abortion patients (OR=4.129, 95% CI=1.502-12.072).

## Discussion

As already known, Tg represents a crucial protein secreted by the follicular cells of thyroid [14]. TPO, an important factor involved in thyroid hormones production,

Table 1. — The positive rates of TPOAb and TgAb.

Group	TPOAb positive rate (%)	TgAb positive rate (%)
Test group (n=100)	17	14
Normal group (n=100)	7	5
$\chi^2$ value	4.736	4.709
<i>p</i> value	<0.05	<0.05

Table 2. — Serum levels of TPOAb and TgAb.

Group	lg (TPOAb)	lg (TgAb)
Test group (n=100)	$0.93 \pm 0.65$	$1.34 \pm 0.46$
Normal group (n=100)	$0.72 \pm 0.28$	$1.31 \pm 0.26$
<i>t</i> value	5.932	1.522
<i>p</i> value	<0.01	<0.05

plays as a primary autoantigen in various autoimmune thyroid diseases [15, 16]. Thus, it is of great importance for Tg and TPO during the secretion and production of thyroid hormones. TA includes autoantibodies against TPO and Tg, is considered as one of the most prominent indicator of thyroid inflammation, and can be identified in some females (10-20%) at reproductive age [17, 18]. Therefore, the positive TAs are closely correlated with activation of autoimmune progression. Based on the statistics, thyroid disorders have been detected in lots women at childbearing age [19]. Evidence demonstrated that the dysfunction of thyroid during pregnancy, such as TA positive, has been involved in a wide of poor outcomes, including miscarriage, fetal death, pre-term birth, impaired neuropsychological development in the child, and maternal post-partum thyroid disease [20-22]. For example, TAs have been evaluated by Stefanie *et al.* in patients with recurrent spontaneous abortion (RSA) and have indicated to be correlated with the increased incidence of RSA [23]. The study by Liu *et al.* also demonstrated that the risk of miscarriage was increased in women with thyroid autoimmunity [24]. The data in these studies indicate the significance of involvement of TAs with poor outcomes of women during pregnancy.

Missed abortion represents a kind of pregnancy in which fetal demise occurs without any external intervention. The uterus usually is not working to support conception in females with missed abortion [25]. Data in the previous research has demonstrated that some factors were involved in the occurrence of missed abortion, such as abnormalities of uterus, parental chromosomal abnormalities, endocrinological disorders, hereditary thrombophilia, immunological factors, and environmental and nutritional factors [26, 27]. Although abundant studies on missed abortion have been performed, the report regarding the role of TA acting in missed abortion has been limited until now. It was therefore the purpose of this study, which was to un-

cover the association between TA and early missed abortion in females with this disease.

In the present study, 100 early missed abortion patients and paired normal pregnant females were recruited in our research. The serum contents of TAs (TPOAb and TgAb) were measured by electrochemiluminescence in missed abortion women and normal controls. The analysis results showed that the positive rates of TPOAb and TgAb were all elevated in the test group than those in the normal pregnant controls (both  $p < 0.05$ ). This result indicates that positive TA might serve as a potential risk factor for missed abortion. In addition, the levels of TPOAb and TgAb were also compared between the two groups. According to  $t$ -test analysis, the serum levels of TPOAb were found to be significantly increased in missed abortion patients compared with the normal controls ( $p < 0.01$ ), which was in accordance with the results in other poor outcomes during pregnancy [13, 28], that demonstrated higher TgAb and TPOAb levels in recurrent miscarriage females than those in the controls women. However, no significant differences of TgAb levels were detected between the missed abortion females and normal pregnant women ( $p > 0.05$ ). Given the significant increased positive TA in missed abortion patients, the relationship between TA and missed abortion was explored in the current study through logistic regression analysis. The result of this assay indicated that TPOAb was an independent risk factor for females with early missed abortion and that positive TA was also closely correlated to it.

Despite the evidence provided from the present study in that TA appears to be correlated with missed abortion, the molecular mechanism that TA plays in the progression of missed abortion remains unclear. Based on the data in the studies by Monteleone *et al.* [29] and Negro *et al.* [30], it is considered that although no abnormality of thyroid was observed in early pregnant women with positive TPOAb, the dysfunction of the thyroid would be subsequently performed along with the gestational ages. The levels of TSH have been found to be increased and FT4 has decreased, which might lead to miscarriage or premature birth. To clarify the potential molecular mechanisms for TA involved in the missed abortion, more focused efforts should be carried out in further studies.

In conclusion, the data in this study revealed that there was a close relationship between TA and missed abortion. In addition, TPOAb could serve as an independent risk factor for missed abortion. Thus, the detection of serum TSH, FT4, and TPOAb is necessary for women before or after pregnancy.

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