

THE EVALUATION OF THYROID FUNCTION, ANTITHYROGLOBULINE ANTIBODY AND THYROID PEROXIDASE ANTIBODY IN CASE OF SPONTANEOUS ABORTION

By

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ABSTRACT

Background: Abortion is the interruption and/or termination of pregnancy, either spontaneously or intentionally, before the fetus develops sufficiently to survive. About 80% of abortions occur in the first 12 weeks of pregnancy. The underlying mechanism in about half of cases involves chromosomal abnormalities.

Objective: To evaluate the association between TSH, T3, T4, anti-thyroglobulin antibody and thyroid peroxidase antibody in women with spontaneous abortion.

Patients and methods: This study was conducted on 60 female patients in the age group of 21–35 years recruited from the outpatient and inpatient clinics of the Department of Obstetrics and Gynecology, Tanta University Hospital, this study period February 2019 to July 2020. Approval of the medical ethics committee and signing written informed consent. The levels of TSH, T3, T4, antithyroglobin antibody and thyroid peroxidase antibody were determined.

Results: There was no statistically significant relation between spontaneous abortion and TSH, T3, T4, anti-thyroglobulin antibody and thyroid peroxidase antibody.

Conclusion: No need to screen for subclinical hypothyroidism and thyroid autoimmunity in all pregnancy.

Keywords: Abortion, Thyroid function, Antithyroglobuline antibody, thyroid peroxidase antibody.

INTRODUCTION

Abortions may occur for many reasons, not all of which can be identified. Some of these causes include genetic, uterine, or hormonal abnormalities, reproductive tract infections, and tissue rejection. Most clinically apparent abortions (two-thirds to three-quarters in various studies) occur during the first trimester (*Francis, 2011*). About 30% to 40% of all fertilized eggs

abort, often before the woman knows she is pregnant (*Health and Services, 2012*).

Clinical investigation of pregnancy loss is sometimes initiated after two consecutive spontaneous abortions, especially when fetal heart activity has been identified before pregnancy losses, when the women are older than 35 years of age, or when the couple has had difficulty conceiving (*Fox-Lee and*

Schust, 2013). It affects approximately 1%–3% of couples who are trying to conceive (*Carrington et al., 2011*).

Several conditions are known to contribute to recurrent abortion, including parental chromosome abnormalities, structural uterine anomalies, and antiphospholipid syndrome (*Li et al., 2012*). However, the role played by autoimmune disorders in recurrent abortion is rather controversial. Thyroid dysfunction and thyroid autoimmunity are both associated with recurrent abortion (*Abalovich et al., 2010*).

Stagnaro-Green et al. (2011) found that the presence of thyroid peroxidase (TPO) or thyroglobulin antibodies in the first trimester of pregnancy is a risk factor for subsequent spontaneous pregnancy loss. These results were confirmed by other investigators. *Pratt et al. (2011)* studied the significance of the presence of thyroid antibodies before pregnancy in women with a history of habitual abortion and found these antibodies to increase the risk for yet another abortion significantly. Impaired maternal thyroid hormone availability may induce irreversible brain damage with consequent neurological abnormalities (*Walker et al., 2010*).

Allan et al. (2011) showed that TSH levels above 6 mU/l are significantly associated with a higher frequency of stillbirth. Both low and high TSH and Free T4 to be associated with abortion, fetal or neonatal death (child loss).

Autoimmune thyroid disorders are characterized by the presence of antithyroid antibodies, specifically antithyroglobulin and antithyroid peroxidase. Thyroglobulin is a molecule produced by the thyroid cells and stored in

thyroid colloid. The primary function of thyroglobulin is the storage and synthesis of thyroid hormones. Thyroid hormones (T3 and T4) are synthesized on thyroglobulin. Elevations in the serum concentration of this autoantibody may be identified in any condition that results in an abnormal or damaged thyroid follicular structure. Thyroid peroxidase is an enzyme responsible for iodination of tyrosine residues along with coupling of iodinated residues to form thyroid hormones. The role of TSH, the primary trophic hormone of the thyroid, is thyroid growth and development; therefore, thyroid cell activation stimulates thyroid hormone synthesis (*Li et al., 2019*).

Women with antithyroid antibodies (ATA), face double risk of abortion as against women without them. Increased thyroglobulin and thyroid peroxidase auto-antibodies level show relationship to an increased abortion rate. About 31 percent of women experiencing recurrent spontaneous abortion (RSA) are positive to one or both antibodies (*Fröhlich and Wahl, 2017*).

The aim of this study was to evaluate the association between TSH, T3, T4, antithyroglobulin antibodies and Thyroid peroxidase antibody in women with spontaneous abortion.

PATIENTS AND METHODS

This study was conducted on 60 female patients in the age group of 21–35 years recruited from the outpatient and inpatient clinics of the Department of Obstetrics and Gynecology, Tanta University Hospital, this study period February 2019 to July 2020. Approval of the medical

ethics committee and signing a written informed consent.

Patients were divided in two equal groups:

- **Group A:** Pregnant women with normal pregnancy without history of abortion more than 12 weeks and below 20 weeks.
- **Group B:** Pregnant women aborting whatever any type of abortion more than 12 weeks and below 20 weeks.

Inclusion criteria:

Pregnant women with age between 21 to 35 years old, primigravidas or multigravidas, Gestational age above 12 weeks and below 20 weeks of gestation calculated according to last menstrual period (lmp) with an early ultrasound confirmation and euthyroid.

Exclusion criteria:

History of consanguinity, history of thyroid disease, history of major fetal abnormalities, history of pregnancy losses or fetal death above 20 weeks of gestation, women with chronic medical disorders, women with autoimmune disorders, women already on treatment for thyroid

dysfunction and women with history of cervical incompetence, bicornate uterus, uterine septum or any other uterine pathology.

All patients enrolled in the study were submitted to complete history taking, complete general examination, local examination of thyroid gland and ultrasonographic scanning. Laboratory investigations included: TSH, T3, T4 level, anti-thyroglobulin antibodies and thyroid peroxidase antibody.

Statistical analysis:

Analysis of data was done using Statistical Package for the Social Sciences version 22 (SPSS Inc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. In order to compare parametric quantitative variables between two groups, Mann-Whitney U test was performed. Qualitative variables were compared using chi-square (X²) test or Fisher's exact test when frequencies were below five. P value < 0.05 was considered significant.

RESULTS

In control group, the level of TSH was normal in 90% patients and abnormal in 0.33% patients with a mean value 3.85 ± 0.96 (μ IU/ml). In cases group, the level of TSH was normal in 86.7% patients and

abnormal in 10% patients with a mean value of 4.5 ± 1.75 (μ IU/ml). There was no statistically significant difference between the two groups regarding TSH level ($p=0.299$) (**Table 1**).

Table (1): Comparison between the two studied groups according to TSH

TSH \ Groups	Control (n = 30)		Cases (n = 30)		P-value
	No.	%	No.	%	
Normal (0.35-4.8 μ IU/ml)	27	90	25	83.3	0.299
Abnormal	1	3.3	3	10	
Min. – Max.	0.58-5		0.49– 9.0		0.081
Mean \pm SD.	3.85 \pm 0.96		4.5 \pm 1.75		
Median	3		4		

In control group, the level of T3 was normal in 90% patients and abnormal in 3.3% patients with a mean value 130.17 \pm 63.58 (ng/dl). In cases group, the level of T3 was normal in 86.7% patients and

abnormal in 6.7% patients with a mean value of 159.43 \pm 61.08 (ng/dl). There was no statistically significant difference between the two groups regarding T3 level (p=0.553) (Table 2).

Table (2): Comparison between the two studied groups according to T3

T3 \ Groups	Control (n = 30)		Cases (n = 30)		P-value
	No.	%	No.	%	
Normal (90-190ng/dl)	27	90	26	86.7	0.553
Abnormal	1	3.3	2	6.7	
Min. – Max.	88 – 197		81 – 189		0.074
Mean \pm SD.	130.17 \pm 63.58		159.43 \pm 61.08		
Median	145		156		

In control group, the level of T4 was normal in 90% patients and abnormal in 3.3% patients with a mean value 9.39 \pm 3.72 (ng/dl). In cases group, the level of T4 was normal in 86.7% patients and

abnormal in 6.7% patients with a mean value of 10.71 \pm 3.85 (ng/dl). There was no statistically significant difference between the two groups regarding T4 level (p=0.553) (Table 3).

Table (3): Comparison between the two studied groups according to T4 .

T4 \ Groups	Control (n = 30)		Cases (n = 30)		P-value
	No.	%	No.	%	
Normal (4-12ng/dl)	27	90	26	86.7	0.553
Abnormal	1	3.3	2	6.7	
Min. – Max.	2.3 – 11.6		3.2 – 11.6		0.182
Mean \pm SD.	7.39 \pm 3.72		8.71 \pm 3.85		
Median	10.3		10.55		

In control group, the level of antithyroglobulin auto antibodies was normal in 86.7% patients and abnormal in 6.7% patients with a mean value of 32.62 ± 61.03 (IU/ml). In cases group the level of antithyroglobulin auto antibodies was normal in 73.3% patients and abnormal in

20% patients with a mean value of 77.67 ± 130.87 (IU/ml). There was no statistically significant difference between the two groups regarding antithyroglobulin auto antibodies level ($p=0.127$) (Table 4).

Table (4): Comparison between the two studied groups according to antithyroglobulin

Antithyroglobulin	Control (n = 30)		Cases (n = 30)		P-value
	No.	%	No.	%	
Normal (up to 115 IU/ml)	26	86.7	22	73.3	0.127
Abnormal	2	6.7	6	20	
Min. – Max.	10.9 – 301		10.3 – 406		0.105
Mean \pm SD.	32.62 ± 61.03		77.67 ± 130.87		
Median	14.3		12.85		

In control group, the level of thyroid peroxidase auto antibodies was normal in 86.7% patients and abnormal in 6.7% patients with a mean value of 24.36 ± 52.21 (IU/ml). In cases group the level of thyroid peroxidase auto antibodies was

normal in 73.3% patients and abnormal in 20% patients with a mean value of 28.65 ± 53.19 (IU/ml). There was no statistically significant difference between the two groups regarding thyroid peroxidase autoantibodies level ($p=0.127$) (Table 5).

Table (5): Comparison between the two studied groups according to thyroid peroxidase

Thyropoxidase	Control (n = 30)		Cases (n = 30)		P-value
	No.	%	No.	%	
Normal (up to 35 IU/ml)	26	86.7	22	73.3	0.127
Abnormal	2	6.7	6	20	
Min. – Max.	2.5 – 298		2.1 – 298		0.760
Mean \pm SD.	24.36 ± 52.21		28.65 ± 53.19		
Median	13.1		12.35		

DISCUSSION

We found that 10% of cases had abnormal TSH level. On the other hand, 3.3% of control group had abnormal TSH level. There was no significant difference in the TSH level in the two groups. 6.7% of cases had abnormal T3 level. On the

other hand, 3.3% of control group had abnormal T3 level. There was no significant difference in the T3 level in the two groups. 6.7% of cases had abnormal T4 level. On the other hand and 3.3% of control group had abnormal T4 level. There was no significant difference between the two groups.

We found that 20% of cases were positive for antithyroglobulin antibodies and 6.7% of control group were positive. No significant difference between the two groups. 20% of cases were positive for thyroid peroxidase antibodies. 6.7% of control groups no significant difference two groups.

In agreement with this study, *Pratt et al. (2011)* determined that 31% of the cases were positive compared to 19% of controls. The correlation was statistically non-significant.

Esplin et al. (2011) stated that 29.3% of the cases and 37% of control had positive result for both with no statistically significant difference.

Muller et al. (2010) a prospective study observed that pregnancy occurred in 48% of the antibody-positive women and in 28% of the antibody-negative women. Among those who became pregnant, miscarriage occurred in 33% of TPO antibody-positive women and in 19% of TPO antibody-negative women. The TSH level was abnormal (<0.2 microIU/mL) in only one of the TPO antibody-positive women who miscarried. There was no statistically significant difference.

In disagreement with this study, *Bussan et al. (2010)* in a case control study done on 28 euthyroid non-pregnant habitual aborters were analyzed for thyroglobulin (TG), thyroid peroxidase antibodies (TPO) and multigravida without previous abortions or endocrine dysfunctions served as controls. 39% with recurrent spontaneous miscarriage, but only 7% controls demonstrated positive titers of TG, TPO, or both antibodies.

In contrary to this study, *Dendrinios et al. (2011)* in a case control study done on women with history of recurrent abortion and fertile women were tested with a chemiluminescence immunoassay. Results were compared using the chi-squared test. There was a higher frequency of antithyroglobulin auto antibodies in women with recurrent abortion compared to controls (37% versus 13%).

The current study found that adverse pregnancy outcomes levels are higher in patients with thyroid dysfunction, than normal control group, but this difference was not statistically significant.

CONCLUSION

There was no significant relation between spontaneous abortion and TSH, T3, T4, anti-thyroglobulin antibody and thyroid peroxidase antibody. Therefore, no need to screen for subclinical hypothyroidism and thyroid autoimmunity in all pregnancy.

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تقييم وظائف الغدة الدرقية والأجسام المضادة للثيروجلوبيولين والأجسام بيروكسيديز الغدة الدرقية المضادة في حالات الاجهاض التلقائي

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خلفية البحث: يعتبر الاجهاض من اشد الاشياء المحبطة والصعبة فى مجال الطب الانجابى لان السبب فى كثير من الاحيان يكون غير معروف. وتعتبر المناعة الذاتية من احد العوامل المرتبط مباشرة مع اسباب العقم وحدث الاجهاض المتكرر بصورة خاصة.

الهدف من البحث: دراسة الأجسام المضادة للغدة الدرقية بدورها المناعى والهرمونى وتأثيرها على وظيفة هذه الغدة لتكون احد العوامل المؤثرة فى حدوث الاجهاض التلقائي.

المريضات وطرق البحث: تم دراسة عينة مكونة من ٦٠ امرأة حامل الذين حضروا إلى قسم التوليد و أمراض النساء بمستشفى دمنهور التعليمي ,ومقسمة الى مجموعتين متساويتين ليس لديهن أي تاريخ مرضي للإجهاض من قبل والمجموعة الثانية تعانين من إجهاض فعلي دون النظر لنوع الإجهاض. وقد تم قياس نسبة هرمونات الغدة الدرقية والأجسام المضادة للثيروجلوبيولين والأجسام المضادة لبيروكسيديز الغدة الدرقية.

نتائج البحث: لا توجد علاقة ذات دلالة إحصائية بين الاجهاض التلقائي وهرمونات الغدة الدرقية والأجسام المضادة للثايروجلوبين والأجسام المضادة لبيروكسيدز الغدة الدرقية.

الإستنتاج: لا توجد هناك علاقة ذات دلالة احصائية بين الاجهاض والتلقائي هرمونات الغدة الدرقية والأجسام المضادة للثايروجلوبين والأجسام المضادة لبيروكسيدز الغدة الدرقية لدى السيدات الحوامل.

الكلمات الدالة : الإجهاد - وظائف الغدة الدرقية - الأجسام المضادة للثايروجلوبولين - الأجسام المضادة للبيروكسيدز فى الغدة الدرقية .