

Relation between anti-thyroid peroxidase antibody and recurrent pregnancy loss: A case control study

Case Study

Mohamed Sayed Ali¹, Rehab Mohamed Abdel Rahman¹, Nancy Samir Wahba², Mohamed Nabil Gaber³

¹Department of Obstetrics and Gynecology, ²Department of Clinical Pathology, Faculty of Medicine, Ain-Shams University, Cairo, ³Department of Obstetrics and Gynecology, Faculty of Medicine, Kafr El-Sheikh University, Egypt

ABSTRACT

Background: Thyroid dysfunction and autoimmunity are relatively common clinical scenario in women within reproductive age group and have been correlated and linked to a spectrum of adverse pregnancy outcomes such as recurrent miscarriage.

Aim: To investigate the correlation and linkage between anti-TPO antibody and recurrent miscarriage.

Materials and Methods: This case control observational research study was conducted on 90 pregnant female out which 45 with history of recurrent miscarriage were cases and 45 without such history were controls.

Results: The mean age of control group was 25.29 while it was 26.69 in cases group. The prevalence of anti-tpo antibody positivity in the study group was 18.8%.out of 90 pregnant female ;17 were positive for anti-tpo antibody. The prevalence of thyroid autoimmunity in pregnant women with recurrent abortion was (37.8%) while it was (0%) in the healthy group ($P=0.0$).

Conclusion: There was significant relationship between anti thyroid antibody positivity and recurrent miscarriage. Thyroid autoimmunity can be considered as risk marker for recurrent miscarriage.

Key Words: Anti-tpo antibody, pregnancy, recurrent miscarriage

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Corresponding Author: Mohamed Nabil Gaber, Department of Obstetrics and Gynecology, Faculty of Medicine, Kafr El-Sheikh University, Egypt, **Tel.:** 01149328772, **E-mail:** mn1838043@gmail.com

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INTRODUCTION

Miscarriage is defined as any spontaneous pregnancy loss before the capacity for fetus to survive extra uterine life. Recurrent miscarriage, defined as loss of three or more consecutive pregnancies affecting 1% of couples approaching conception. The etiology of recurrent spontaneous miscarriage involves anti-phospholipid Antibody syndrome, genetic, anatomical, and endocrinal factors. On the other hand around 50% of cases of recurrent miscarriage remain unexplained^[1].

Interestingly at molecular and cellular levels, a coordinated and integrated immunological interface between the maternal and the fetal systems is believed to have a cornerstone role in placental course of development besides embryonic survival and early pregnancy maintenance and stability^[2].

Actually, impairment of immunological maternal-fetal normal interaction could be the underlying cause of serious gestational issues and complications such as recurrent

miscarriage. Immunological factors have been estimated by various groups of researchers to be a contributory cause of pregnancy failures in at least 30% of clinically detected cases^[3].

Autoimmune thyroid disease is observed to the most frequent etiology of hypothyroidism issues revealed among women of reproductive age. Thyroid disorders have been long suspected to cause early pregnancy loss and other adverse pregnancy outcomes. Although the worst overt hypothyroidism is infrequent in pregnancy, subclinical hypothyroidism has an incidence of 2-3%^[4].

Autoimmune thyroid diseases are featured at molecular aspects by the existence anti-thyroid auto antibodies, particularly anti thyroid peroxidase (TPO-abs) and anti-thyroglobulin (TG-abs).Thyroid peroxidase (TPO) is a membrane-bound enzyme that catalyzes iodide oxidation and iodination of tyrosyl residues of thyroglobulin. Anti-TPO-antibody impact TPO, causing thyrocytes destruction and degeneration. Autoantibodies to TPO are frequent among euthyroid population and are correlated

to chief pregnancy course alterations influencing the maternal, fetal and/or neonatal pathophysiological status. Women with elevated antibody titer in early gestational period are frequently affected by postpartum thyroid dysfunction having its probable negative impact on future pregnancies^[5].

Women in euthyroid state but with thyroid autoimmunity are twofold liable to have spontaneous miscarriages since it triggers a generalized disordered immunological system activation, causing a raised estimated clinical risk of pathological progression to subclinical hypothyroid status besides the trans placental passage of Thyroid receptor blocking antibodies. Therefore subclinical hypothyroidism screening using anti-TPO antibodies could be required for cases with documented clinical history of recurrent miscarriage^[6].

AIM OF THE WORK

The study aimed to investigate the correlation and linkage between anti-thyroid peroxidase antibody and recurrent miscarriage.

PATIENTS AND METHODS

This case control observational research study conducted in Ain-Shams University Maternity Hospital on 90 pregnant women. The research study subjects were recruited from Ain-Shams Maternity Hospital Obstetric out-patient clinics. They have been categorized into two research groups : study research group involving 45 women with history of recurrent pregnancy loss recruited from recurrent miscarriage outpatient clinic of Ain-Shams University Maternity Hospital. Control research group including 45 women without any history of pregnancy loss recruited from those attended obstetric outpatient clinic.

Inclusive research criteria for the study group involved pregnant women with history of three or more spontaneous, consecutive miscarriage ≤ 22 weeks.

Inclusive research criteria for the control research group involved age-matched control group of pregnant women with normal obstetric history without a history of miscarriage, stillbirth, intrauterine growth restriction and preeclampsia and at least one term pregnancy.

Exclusive research criteria implemented for both research groups involved presence of uterine abnormalities revealed by sonography or HSG or hysteroscopy (e.g. septate uterus, bicornuate, Asherman syndrome and fibroid uterus), autoimmune disease

(e.g. antiphospholipid antibody syndrome). Endocrinal disease e.g uncontrolled diabetes mellitus, overt thyroid disease, polycystic ovary syndrome, hyperprolactinemia, abnormal karyotyping of both parents. The two groups have been compared and contrasted as regards anti-thyroid peroxidase antibody. Anti-thyroid peroxidase antibody assay done by ELISA technique at central lab, El-Demerdash Hospital.

STATISTICAL ANALYSIS:

Research Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative research data were presented as mean, standard deviations and ranges when their distribution found parametric and median with inter-quartile range (IQR) when their distribution found non-parametric. Also qualitative research variables were presented as number and percentages.

The comparison between research groups as regards qualitative research data was conducted using Chi-square test. The comparative analysis between two independent research groups with quantitative research data and parametric distribution was performed using independent t-test. The comparison between two independent research groups with quantitative research data and non-parametric pattern of distribution have been performed using Mann-Whitney test. The comparative analysis between more than two research groups with quantitative research data and parametric distribution pattern was conducted using One Way ANOVA test.

The comparison between more than two research groups with quantitative research data and non-parametric distribution pattern was conducted using Kruskal Wallis test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same groups. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05 .

RESULTS

Table 1 shows that the prevalence of thyroid autoimmunity in pregnant women with recurrent abortion was (37.8%) while it was (0%) in the healthy group .

Table 2 shows that there was no correlation between age and thyroid antibody positivity.

Table 1: Comparison between results of anti TPO in both groups

Anti TPO	Control group	Cases group	Test value	P-value	Sig.
	No. = 45	No. = 45			
Median (IQR)	5 (0 – 10)	25 (10 – 110)	-5.555≠	0.000	HS
Range	0 – 20	0 – 340			
Negative	45 (100.0%)	28 (62.2%)	20.959*	0.000	HS
Weak positive	0 (0.0%)	3 (6.7%)			
Positive	0 (0.0%)	14 (31.1%)			

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P-value > 0.05: Non significant; *P-value* < 0.05: Significant; *P-value* < 0.01: Highly significant

*: Chi-square test; ≠: Mann-Whitney test

Table 2: Relation between anti Tpo and age in study group

Age	Anti TPO			Test value•	P-value	Sig.
	Negative	Weak positive	Positive			
	No. = 28	No. = 3	No. = 14			
Mean ± SD	26.07 ± 3.37	27.33 ± 6.81	27.79 ± 2.22	1.305	0.282	NS
Range	21 – 34	22 – 35	24 – 31			

P-value > 0.05: Non significant; *P-value* < 0.05: Significant; *P-value* < 0.01: Highly significant

•: One Way ANOVA test

DISCUSSION

Miscarriage is defined as any pregnancy ending spontaneously prior the fetal ability to survive extra uterine life. Recurrent miscarriage, defined as loss of 3 or more consecutive pregnancies before 22 gestational weeks^[7]. Recurrent miscarriage is a very crucial public health issue. Besides the psychological trauma to the mother and the family, it is interrelated to maternal morbidity and mortality clinical consequences^[8]. This serious obstetric clinical scenario impacts around 1-5% of pregnant women^[9].

Thyroid disorders have been long suspected to cause early pregnancy loss and other adverse pregnancy outcomes. Although the worst overt hypothyroidism is infrequent in pregnancy, subclinical hypothyroidism has an incidence of 2-3%^[4].

In the current research study, the investigators aimed to investigate and observe the correlation and linkage between recurrent miscarriage and anti-TPO positivity.

A cohort of 90 pregnant females were recruited from outpatient clinic of Ain-Shams University Maternity Hospital, in which 45 females had prior history of recurrent abortion and 45 females had no history of recurrent abortion. Both research groups recruited were analytically compared as regards anti TPO positivity, age, parity and gravidity

The mean age of control group was 25.29 while it was 26.69 in cases group, which shows no significant different between each groups.

There was no relation between anti TPO-antibody positivity and the age of study subjects.

There was statistically significant positive correlation found between anti TPO level and number of abortion while no statistically significant relation found with parity.

In this study, 18.9 % of pregnant females were anti-TPO positive, finding similar with the literature which stated thyroid antibody positivity in 5-15% of the women during reproductive age group^[11].

The prevalence of thyroid autoimmunity has been observed to be greater in pregnant females having a medical history of recurrent abortion in comparison and contrast to healthy pregnant control population.

The prevalence of thyroid autoimmunity in pregnant women with recurrent abortion

was (37.8%) whereas it was (0%) in the control research group (P value =0.0).

A previous clinical research trial previously performed by Jaiswal and Bag^[10] it was observed by research data analysis that the thyroid autoimmunity prevalence is higher in cases having a past history of recurrent miscarriage than the research control population.

Another research study priory performed by Mena *et al.* in 2016 have shown a statistical significant rise in miscarriage rate within the first gestational trimester in conjunction to the TPO Ab presence of elevated titers.

In 2015, another research study by Bhattacharyya *et al.* research team of investigators^[6] revealed and displayed a TPO Ab prevalence of 11.34% and statistically significant correlation was observed between TPO Ab positivity and miscarriage rate^[14].

In 2006, Ghafoor *et al.*^[12] investigated 1500 Pakistani females for thyroid peroxidase antibodies and thyroid function tests during gestation. Cases were followed up all the way through the gestational period to observe the clinical outcome of pregnancy. Thyroid antibody positive women, represented 11.2% of the cohort, had a spontaneous miscarriage rate of 36.3% as compared to 1.8% in antibody negative women (P value <.01). A significantly higher prematurity rate was additionally revealed and displayed among the research study findings (26.8% versus 8.0%) (P value <.01) in antibody positive females. All 1500 recruited study subjects on clinical and investigational basis were euthyroid.

A research meta-analysis performed by Prummel and Wiersinga research team of investigators^[13], have shown that TPO Ab positivity is linked and correlated to a doubled clinical estimated risk of miscarriage.

Similarly, the current research study have shown in harmony with previously performed studies that there is a statistically significantly greater prevalence as regards recurrent miscarriage rate among anti-TPO positive pregnant females.

CONCLUSION

There have been a statistically significant correlation between anti thyroid antibody elevated titers and recurrent miscarriage. Thyroid autoimmunity could be considered as a clinical risk factor for recurrent miscarriage. Screening of anti-

thyroid peroxidase antibody is should be considered in recurrent miscarriage cases. However to verify and confirm the current research study findings future research studies should be multicentric in nature considering racial, ethnic and BMI differences that could impact the investigational results of thyroid anti-TPO. Management course using levothyroxine could aid in risk reduction of recurrent miscarriage in clinical scenarios with positive anti thyroid peroxidase anti body testing however again this issue of concern should be confirmed on larger sample sizes and in multicentric fashion to aid in future clinical guidelines application in management of those category of cases.

CONFLICT OF INTEREST

There are no conflicts of interests.

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