Relation between Anti-thyroid Peroxidase Antibody and Recurrent Pregnancy Loss: A Case Control Study

Thesis

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Mohamed Nabil

List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
AACE	*American Association of Clinical Endocrinologists*
AITD	*Autoimmune Thyroid Disease*
ALT	*Alanine Aminotransferase*
Anti-TPO-Ab	*Anti- Thyroid Peroxidase-Antibody*
AST	*Aspartate Aminotransferase*
ATA	*American Thyroid Association*
ATDs	*Antithyroid Drugs*
DIT	*Di-Iodotyrosine*
ER	*Estrogen Receptor*
ESHRE	*European Society of Human Reproduction and Embryology*
GD	*Graves' Disease*
HCG	*Human Chorionic Gonadotropin*
HLA	*Human Leukocyte Antigen*
HSG	*Hystero-Salpingography*
HSV	*Herpes Simplex Virus*
IUS	*Intrauterine Synichea*
IVF	*In Vitro Fertilization*
LPD	*Luteal Phase Defect*
MIT	*Mono-Iodotyrosine*
MTHFR	*Methylene Tetra-Hydro-Folate Reductase*
OH	*Overt Hypothyroidism*
PCOS	*Polycystic Ovarian Syndrome*
PGD	*Pre-Implantation Genetic Diagnosis*
PPTD	*Postpartum Thyroid Dysfunction*
PR	*Progesterone*
PTU	*Propylthiouracil*

List of Abbreviations (Cont...)

Abb.	Full term
RCT	*Randomized Control Trial*
RM	*Recurrent Miscarriage*
RPL	*Recurrent Pregnancy Loss*
SH	*Subclinical Hypothyroidism*
T3	*Triiodothyronine*
T4	*Tetraiodothyronine (Thyroxin)*
TBG	*Thyroxin Binding Globulins*
TES	*Endocrine Society*
Tg	*Thyroglobulin*
TPO	*Thyroid Peroxidase*
TPO-abs	*Antithyroid Antibodies, Specifically anti Thyroid Peroxidase*
TRAb	*TSH Receptor Antibody*
TSH	*Thyroid Stimulating Hormone*

ABSTRACT

Background: Thyroid dysfunction and autoimmunity are relatively common in women of reproductive age group and has been associated with various adverse pregnancy outcomes such as recurrent. **The aim of this study** was to find out association between anti-tpo antibody and recurrent miscarriage. **Patient and Methods:** This case control observational study was carried out 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**.**

Keywords: Anti-tpo antibody, Pregnancy, Recurrent Miscarriage.

INTRODUCTION

Miscarriage is defined as any pregnancy ending spontaneously prior the fetus can survive. Recurrent miscarriage, defined as loss of three or more consecutive pregnancies affecting 1% of couples trying to conceive. The etiology of recurrent spontaneous miscarriage includes anti-phospholipids antibody syndrome, genetic factors, anatomical factors, endocrinal factors, immunological factors and inherited thrombophillic defects However about 50% of cases of recurrent miscarriage remains still unexplained ***(Green-top Guidelines no.17, April 2011).***

In this context, a proper immunological interaction between the mother and the fetus is believed to play a role in placental development as well as in embryo survival and in the maintenance of early pregnancy ***(Kwak-Kim et al., 2010).***

In fact, an altered maternal–fetal immunological dialogue may be responsible for serious gestational complications including recurrent miscarriage. It has been estimated that immunological factors could be involved as a contributory cause of pregnancy failures in at least 30% of the cases ***(Baek et al., 2007).***

Autoimmune thyroid disease (AITD) is by far the most frequent cause of Hypothyroidism in 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% ***(Poppe et al., 2008).***

Autoimmune thyroid diseases are characterized by the presence of antithyroid antibodies, specifically anti thyroid peroxidase (TPO-abs) and anti-thyroglobulin (TG-abs).

Thyroid peroxidase (TPO), is a membrane-bound enzyme, which catalyzes iodide oxidation and iodination of tyrosyl residues of thyroglobulin. Anti-TPO-antibody (anti-TPO-Ab) can react with TPO, leading to the destruction of thyrocytes. Autoantibodies to TPO are common in the euthyroid population and are associated with major alterations in the course of pregnancy affecting the mother, fetus, and/or neonate. Women with high antibody titer in early pregnancy are commonly affected with postpartum thyroid dysfunction (PPTD) with its potential impact on future pregnancies ***(Bhattacharyya et al., 2015).***

Women in euthyroid state but with thyroid autoimmunity are twice likely to experience spontaneous miscarriages as it probably represents a generalized activation of immune system, or there is an increased risk of progression to subclinical hypothyroidism or probably due to transplacental transfer of

thyroid receptor blocking antibodies. Hence screening for subclinical hypothyroidism and thereby anti-tpo antibody might be required for patients with history of recurrent miscarriage. The present study was carried out to find out relation between anti-tpo antibody and recurrent miscarriage ***(Faussett et al., 2000).***

AIM OF THE WORK

The aim of the present work is to assess the association between anti-thyroid peroxidase antibody and recurrent miscarriage.

Research question

In women with recurrent miscarriage is there any association with anti-thyroid peroxidase antibody?

Research hypothesis

In women with recurrent miscarriage an association with antithyroid peroxidase antibody may be present.

Chapter 1
RECURRENT MISCARRIAGE

Background

Recurrent miscarriage (RM) is one of the most prevalent reproductive problems faced by couples ***(Ghafourian et al., 2014).***

A history of three or more consecutive spontaneous miscarriages occurs in 0.5 - 3% of women reproductive age ***(Tomsu et al., 2002).***

The incidence of two miscarriages is 2-4 %and the incidence of three consecutive losses is less than 1% ***(Prummel and Wiersinga, 2004).***

This recurrent loss of pregnancy is often distressing for the patients and frustrating for physicians. In most cases, the cause is not apparent and often requires intensive and expensive clinical and laboratory investigations, despite which there is still a limited understanding of RM ***(Tomsu et al., 2002).***

Definition:

The term 'miscarriage' is applied to many complications of early pregnancy and it is important to be clear on terminology. A pregnancy loss that occurs after a positive urinary human chorionic gonadotropin (HCG) or a raised serum

B-HCG but before ultrasound or histological verification is defined as a 'biochemical loss'. In general, this occur before 6 weeks of gestation. The term clinical miscarriage is used when ultrasound examination or histological evidence has confirmed that an intrauterine pregnancy has existed. Clinical miscarriages may be subdivided into early clinical pregnancy losses (before gestational week 12) and late clinical pregnancy losses (gestational weeks 12 to 21). There is no consensus on the number of pregnancy losses needed to fulfill the criteria for recurrent miscarriage (RM), but European Society of Human Reproduction and Embryology (ESHRE) guidelines define RM as three or more consecutive pregnancy losses before 22 weeks of gestation ***(Larsen et al., 2013).***

Spontaneous miscarriage is a common gynecological condition creating an emotional crisis for the family, and around half of spontaneous miscarriages occurs in the first trimester ***(Jaleel and Khan, 2013).***

Spontaneous pregnancy loss is a surprisingly common occurrence with approximately 15% of all clinically recognized pregnancies resulting in pregnancy failure. Recurrent pregnancy loss (RPL) has been inconsistently defined. When defined as 3 consecutive pregnancy losses prior to 22 weeks from the last menstrual period, it affects approximately 1% to 2% of women ***(Ford and Schust, 2009).***