Effect of thyroid peroxidase antibodies (TPO) on endometrium thickness (ET) - Ova size in infertile women in Kerbala a descriptive study

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Abstract

Infertility is a disease of the reproductive system defined by failure achieve a clinical pregnancy or inability of a couple to conceive naturally after 12 months or more regular intercourse without contraception. Thyroid dysfunction can lead to menstrual disturbance, anovulatory cycle and decreased fertility. Autoimmune thyroid diseases are the most common autoimmune conditions encountered in females in reproductive age characterized by presence of antibodies against some structures of thyroid gland such as thyroid peroxidase (TPO); which is the key thyroid enzyme catalyzing both the iodination and coupling reaction for the synthesis of thyroid hormone. Anti-TPO autoantibodies are present in approximately 90% of patients with autoimmune thyroid diseases.The study aimed to evaluate the role of thyroid antibodies in subfertility patients on ova size and endometrium thickness. The study was conducted during the period from March 2015 to September 2015 at Karbala Maternity Hospital, infertility unit, and some private clinics. This study included a total number of 92 women in the reproductive age; ranging between (15- 43) years; divided patients into: primary infertility included (56); while secondary infertility were (36) infertility females. The following parameter were measured for all study groups: anti-TPO using ELISA device .Additionally, ultrasound was done to measure the ova size and endometrial thickness. The results showed a significant difference between primary and secondary infertility in TPO, when relation between TPO with ova size and endometrial thickness there is a significant difference between TPO and ova size in abnormal TPO and a significant difference between TPO and ET in abnormal TPO in infertile women. There is a relation between ova size and TPO, anti-TPO may be used as a biochemical indicator of subclinical thyroid disorders and may help in assessment of thyroid function as a cause of infertility whether primary or secondary.

تأثير الأجسام المضادة بيروكسيديز الغدة الدرقية (TPO) على □مك بطانة الرحم (ET) - حجم البيوض في النساء المصابات بالعقم في كربلاء كدرا□ة وصفية

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الكلمات المفتاحية: العقم , بيروكسيديز الغده الدرقية

الخلاصة

العقم هو مرض يصيب الجهاز التناسلي التي يحددها فشل تحقيق الحمل السريري أو عدم قدرة الزوجين على الإنجاب بشكل طبيعي بعد 12 شهرا أو أكثر من الجماع العادي من دون استخدام وسائل منع الحمل. الخلل في الغدة الدرقية يمكن أن تؤدي إلى اضطراب الدورة الشهرية، دورة غياب الاباضة وانخفاض معدل الخصوبة. أمراض الغدة الدرقية المناعية هي الظروف المناعية التي كانت شائعة في الإناث في سن الإنجاب تتميز جود أجسام مضادة ضد بعض تراكيب الغدة الدرقية مثل البيروكسيديز (TPO)؛ وهو إنزيم رئيسي للغدة الدرقية يحفز كل من إضافة اليود واقتران التفاعل لتصنيع هرمون الغدة الدرقية. Anti-TPO موجود في حوالي 90٪ من المرضى الذين يعانون من أمراض الغدة الدرقية المناعية.

وهدفت الدراسة إلى تقييم دور الأجسام المضادة للغدة الدرقية في المرضى الذين يعانون من العقم على حجم البويضات وسمك بطانة الرحم. وقد أجريت الدراسة خلال الفترة من مارس 2015 إلى سبتمبر 2015 في مستشفى النسائية، وحدة العقم، وبعض العيادات الخاصة. وشملت هذه الدراسة عدد 92 امرأة في سن الإنجاب. تتراوح اعمارهم ما بين (15- 43) سنة. قسم المرضى الى العقم الأولي الذي يتضمن (56), بينما العقم الثانوي يتضمن (36) الإناث المصابات بالعقم تم قياس هرمون anti-TPO لجميع الفئات دراسة: باستخدام جهاز ELISA. بالإضافة إلى ذلك، تم إجراء الموجات فوق الصوتية لقياس حجم البويضات وسمك بطانة الرحم. وأظهرت النتائج وجود فرق كبير بين العقم الابتدائي والثانوي في TPO، توجد علاقه بين TPO مع حجم البويضات وسمك بطانة الرحم هناك فرق كبير بين TPO وحجم البويضات في TPO غير الطبيعي واختلاف كبيري كبير TPO وET في TPO غير طبيعي في النساء العقيمات.Anti-TPO يمكن أن تستخدم كمؤشر في الكيمياء الحيوية من اضطرابات الغدة الدرقية دون السريريه ويمكن أن تساعد في تقييم وظيفة الغدة الدرقية كسبب من العقم سواء الابتدائي أو الثانوي.

Introduction

Infertility is defined as failure to achieve a clinical pregnancy or inability of a couple to conceive naturally after 12 months or more of regular unprotected sexual intercourse [1]. Problems with fertilisation arise mainly from either structural problems in the Fallopian tube or uterus or problems releasing eggs. Infertility may be caused by blockage of the Fallopian tube due to malformations, infections such as chlamydia and/or scar tissue. For example, endometriosis can cause infertility with the growth of endometrial tissue in the Fallopian tubes and/or around the ovaries. Endometriosis is usually more common in women in their mid-twenties and older, especially when postponed childbirth has taken place [2].

Thyroid hormones have profound effects on reproduction and pregnancy. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin (PRL) levels, and sex hormone imbalances. Therefore, normal thyroid function is necessary for fertility, Autoimmune thyroid diseases (AITD); are the most common autoimmune conditions encountered in females in reproductive age characterized by presence of antibodies against to some structure of thyroid gland such as thyroglobulin (TG), thyroid peroxsidase (TPO) and thyroid microsomale (TM). Excessive immune response which is usually 5-10 times more in females stimulates organ specific or non-specific auto-immunity. Organ specific ATA occurring against TG damages thyroid follicle tissue, ATA occurring against TPO impedes iodination of tyrosine. Non-specific antibodies occur as a result of stimulation of T cells against specific thyroid molecules and subsequently effecting B cells. Abnormal immune response effects release of cytokines. There are studies reporting a significant and high correlation between ATA and endometriosis. Suggestion the [3] have reported endometriosis was nearly 2 times more compared to control group (25% vs 14%). Similarly, in patients with polycystic ovarian disease ATA positivity was significantly higher compared to control group. [4] Even association of this antibody positivity with premature ovarian insufficiency was also suggested.

Endometrial thickening is defined as an endometrium of > 5 mm discovered on ultrasound, many studies were done about affecting factors on endometrial thickness in infertile women, over the years, but the results is still unclear [5]. Researchers suggest effect of age, etiology of infertility and factors such as dominant follicle number on endometrial thickness [6]. Some factors such as women age, infertility etiology, drug protocol, estradiol levels, previous injuries to endometrium, were supposed as important affecting factors with endometrial growth [7].The processes leading to ovulation, fertilization, and implantation of the fertilized ovum are complex and not clear. Ovulation results from an interplay between the hypothalamus, ovary, pituitary and endometrium. The ovary has two roles: the first is the endocrine function of producing

oestrogen and progesterone to prepare the endometrium to receive the fertilized ovum. The second, which is related, is gametogenesis and ovulation.

Development of the ovarian follicle occurs in response to stimulation from the pituitary gland. The hypothalamus and pituitary are intimately associated. Together they regulate ovarian structure and function throughout the menstrual cycle. The hypothalamus produces gonadotropin releasing hormone (GnRH) in a pulsatile fashion and this in turn stimulates production of the gonadotropins follicular stimulating hormone (FSH) and luteinizing hormone (LH) [8].

The female body produces outward signs that can be easily recognized at the time of ovulation. The two main signs are thinning of the cervical mucus and a slight elevation in body temperature. The menstrual (uterine) cycle is a series of changes in the endometrium (lining) of the uterus. Each month, the endometrium is prepared for the potential arrival of a fertilized ovum that will develop in the uterus. If an ovum is not fertilized, the outer portion of the endometrium sheds off.

Material and Methods

The study is cross-sectional, The study was conducted during the period from March 2015 to September 2015 at Karbala Maternity Hospital The study consisted of a total number of 92 infertility women in the reproductive age, This group subdivided into two subgroups : primary infertility (number =56), secondary infertility (number= 36 their age range was between (15-43) years. The sample of our study is patient selected from attending the infertile unit at Karbala Maternity teaching Hospital, and from private clinics, all patient given consent to be candidate for this study , history taking and examination done in Karbala fertile unite by a gynecologist and data records in questionnaire, Measurement of height and weight for each patient was done to calculate their body mass index(BMI), a pelvic ultrasound was done by the specialist Radiologist for checking the reproductive system and measurement of follicle(ova size) at pre ovulation time of the menstrual period. About 5 ml of venous blood samples were collected from selected patients suffering from infertility during 2nd-5th day of the menstrual cycle to measurement of TPO. The blood was put in plane tube. Each specimen of blood was allowed to clot, centrifuged for five minutes and then serum was separated and put Eppindorff tubes. The sample stored at -20 ºC till analyzed. All samples were kept frozen in fridge hospital. Then the samples were analyzed by ELISA device in Imam Hussein Teaching Hospital.

On pre ovulation day according to the length of cycle ultrasound was done by radiologist to determine these ova size and Endometrium thickness (ET) measurements.

the frozen serum samples were brought to room temperature and tested for positively to auto-antibodies (anti TPO) in infertile group using a commercially available enzyme linked immune- absorbent assay Kit (ELISA).

Statistical analysis was carried out using SPSS version 22 in which we use paired -sample T-test, significant difference for the measurement of data. We set p- value <0.05 as significant.

Results

Data showed of thyroid peroxidase in primary and secondary infertility by using mean and SEM. The results shows a significant difference (p=<0.05) in TPO in serum of primary and secondary infertility and no significant difference in ET and ova size. The result shows in table (1).

Table (1): thyroid peroxidase, ovarian follicular size and endometrium thickness in infertile group

Subject	Type of infertility	Mean ±SEM	p-value
TPO	**Primary**	0.99± 13.37	**<0.05**
	Secondary	5.54± 27.39	
ET	**Primary**	7.241 ± 0.2464	>0.05
	Secondary	7.625 ± 0.3282	
Ova size	**Primary**	13.55 ± 0.7883	>0.05
	Secondary	15.70 ± 1.046	

There is an association between TPO and ova size in abnormal TPO result shows a significant difference but no significant association in normal TPO.

There is an association between TPO and ET in abnormal TPO result shows a significant difference but no significant association in normal TPO.

Table (2): association between thyroid test with ova size and ET

ameters	**pe**	**an± SEM**	**value**
O and ova size	**rmal**	41± 1.609	05
	normal	.77± 54.72	**05**
O and ET	**rmal**	88± 4.232	05
	normal	.41±54.7	**05**

Discussion

Thyroid autoantibodies (Ab) that react with key proteins in the thyroid, such as thyroid peroxidase (TPO) or thyroglobulin (Tg), can induce a chronic lymphocytic thyroiditis that ultimately results in destruction and loss of thyroid function. Regarding the type or cause of infertility, data of the current study found that there is significant difference in serum levels of TPO between primary and secondary infertility. These results might be explained by age variation between women with primary and secondary. Nevertheless, there is a paucity of researches in this field. But some previous studies comparing between patient and control in infertile women with TPO [9]. One study in Iraq in 30 infertile patients found that there was a significantly higher level of TPO in the infertility group.

We investigated the association between thyroid function, ova size and ET. Results show there is a significant difference between ova size with TPO,

Regarding ET, results show significant difference between ET with TPO, In order to explain these findings, it is likely that it is a part of the hormonal control mechanism related to the pituitary-thyroid and pituitary-ovarian axes interrelations. However, the exact mechanism of the association between thyroid antibodies and infertility is not clear. It is of interest that there is an increase in infertility in women with endometriosis [10] which is known to have natural killer

cell depression, as well as decreased activity and cytotoxicity against autologous endometrium, [11] and [12] have shown impaired cellular and humoral response in women with unexplained infertility. The demonstration of antithyroid antibodies in ovarian follicles [13].

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