ANTITHYROID ANTIBODIES AND INFERTILITY IN WOMEN

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ABSTRACT

Background: Fecundity followed by pregnancy is the fundamental process to sustain life and require a close interplay between normally functioning and adapting endocrine and immune system **(1)**. Pregnancy represents one of the most significant areas of study for the immunobiologist **(2)**, the reasons for the success of gestation in both normal and abnormal pregnancies remain unclear because of the antigenically dissimilarity between the fetus and the mother **(3)**.

Patients and methods: This study included 180 females who were selectively collected and were suffering from infertility and 70 healthy fertile females as control group, that attending Al-Zahraa Teaching Maternity and Pediatrics hospital, and Al-Sader Teaching hospitals in Al-Najaf Al-Ashraf Governorate from November 2007 to June 2008. All the females were in their fertile age.

Results: The range of the women's age was between 18 years and 41 years with mean age of 27.1 years. In spite of the only slightly increased incidence of antithyroglobulin antibodies in the group of primary unexplained infertility (12.5%), there is significant raise in secondary unexplained infertile women (26.67%) compared to the fertile group (8.57%) as shown in table 3.16. Our results, however, show a highly significant correlation ($P < 0.005$) statistically.

Conclusions and recommendations: There was a significant correlation between women who are suffering from infertility and the presence of antithyroglobulin antibody in their serum whether they were suffering from thyroid diseases or not. So it is recommended to do an autoantibody survey particularly antithyroid antibody for females who are suffering from infertility specially those of unexplained type or those with failed therapy of unknown cause.

INTRODUCTION

Fecundity followed by pregnancy is the fundamental process to sustain life and require a close interplay between normally functioning and adapting endocrine and immune system **(1)**. Infertility is the inability of a couple to conceive after 1 year of unprotected intercourse **(4)**. Overall, frequent, unprotected intercourse results in conception for (50%) of couples within 3 months, for (75%) within 6 months, and for (90%) within 1 year **(5)**. Incidence of infertility is increasing, in part reflecting deferral of childbearing until women are older. Primary causes of infertility are sperm disorders (40% of couples), female factors (50%), and unidentified factors (10%). Inability to conceive often leads to feelings of frustration, anger, guilt, resentment, and inadequacy **(6).** Pregnancy represents one

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of the most significant areas of study for the immunobiologist **(2)**, the reasons for the success of gestation in both normal and abnormal pregnancies remain unclear because of the antigenically dissimilarity between the fetus and the mother **(3)**. Antibodies (proteins produced by the immune system that help to fight infections) are usually produced in response to the introduction of foreign substances into the body **(7)**. In some situations, the immune system may produce antibodies that act against integral parts of the body, causing inflammation and damage. This process is referred to as autoimmunity **(8)**. Autoimmune disorders are either general types (systemic autoimmune diseases) or a single organ or tissue is directly damaged by the autoimmune process (localized) **(9)**. However, the distinctions become blurred as the effect of localized autoimmune disorders frequently extends beyond the targeted tissues, indirectly affecting other body organs and systems **(10)**. The primary sites of modulation of the maternal response to the fetus are the uterus, regional lymphatic, and placental surface **(2)**. Antithyroid antibody can be associated with inflammation of the thyroid gland and affect its function. Antithyroglobulin and antimicrosomal antibodies are examples of antithyroid antibodies **(11, 12, 13)**. The incidence of thyroid autoantibodies in women with recurrent fetal loss, infertility or women who miscarried appears to be increased compared with controls of reproductive age without previous abortions **(14)**.

PATIENTS & METHODS

This study included 180 females who were selectively collected and were suffering from infertility and 70 healthy fertile females as control group, that attending Al-Zahraa Teaching Maternity and Pediatrics hospital, and Al-Sader Teaching hospitals in Al-Najaf Al-Ashraf Governorate from November 2007 to June 2008. All the females were in their fertile age. The females were divided into 4 groups as follows:

Group **A**: 80 patients with primary infertility of unexplained cause.

Group **B**: 70 patients with primary infertility of a known cause unrelated to the male.

Group **C**: 30 patients with secondary infertility of unexplained cause.

Group **D**: 70 healthy fertile females as control group.

A kit of indirect immunofluorescence test was used for the qualitative determination of antimicrosomal antibody (Mab), antithyroglobulin autoantibody (Tab) (EUROIMMUN, United Kingdom).

Mab reactivity	Evaluation
No reaction at 1:10	Negative. No antibodies against thyroid microsomes detected in the serum sample.
Positive reaction 1:10	Positive. Indication of autoimmune thyroid disease.
Tab reactivity	Evaluation
No reaction at 1:10	Negative. No antibodies against thyroglobulin detected in the serum sample.
Positive reaction 1:10	Positive. Indication of autoimmune thyroid disease.

The data were calculated and statistically tested according to chi- square distribution (X^2), where the P value was calculated **(15)**.

RESULTS

The range of the women's age was between 18 years and 41 years with mean age of 27.1 years. The mean age was 25.3 years for group A. A 27.4 years for group B. A 30 year for group C and a 26.2 years for the control group (D. The majority of cases were between the age of 25-34 years for all the studied groups representing 45.2% of the total number as shown in table 1.

Antithyroglobulin antibody.

Among whole study, in infertile cases an 18(12%) was positive. Group C is the major group 8(26.67%), then group A, 10(12.5%) respectively. Group B had no positive antithyroglobulin antibody while the control group has 6(8.57%) as shown in table 2.

Analysis of the distribution of cases of positive Tab among different age groups and the percentage to the total number in the each group in the study as were shown in table 3.

Antimicrosomal antibody.

Among the whole study in infertile women a 38(25.33%) women were positive. Group C is the major group8(26.67%), then group A 16(20%)and B 14(20%) equally. The control 7(8.57%) as in table 4.

Analysis of the distribution of cases of positive Mab among different age groups and the percentage to the total number in the each group in the study as were shown in table 5.

DISCUSSION

Although reproductive technologies have improved rapidly during the last decade, but still 15% of female infertility is of unknown causes **(16)** and even with the presence of specialized centers for assisted reproduction, we can only achieve a pregnancy rate per cycle of about 25%, which leaves many infertile couples seeking medical help childless, regardless of the costs invested and efforts made. Several factors have been identified as causing the infertility in women such as patient's age, duration and causes of infertility **(17)**. Infertility and reproductive impairment can, therefore, be related to abnormalities in the endocrine or immune system, or both **(18).** This case_ control study sought to determine the association between antithyroid antibodies (antithyroglobulin antibody, antimicrosomal antibody) positivity and female infertility (primary, secondary), also to determine the effect of some medical condition on female infertility. The data showed that there were a recognized percentage of positive antithyroid antibodies, and anticardiolipin antibody among different groups of the study. In the study inspite of the only slightly increased incidence of antithyroglobulin antibodies in the group of primary unexplained infertility (12.5%), there is significant raise in secondary unexplained infertile women (26.67%) compared to the fertile group (8.57%) as shown in table 3.16. Our results, however, show a highly significant correlation ($P < 0.005$) statistically. These results are in agreement with **van Voorhis** and **Stovall** in **1997 (19)**. They observed the presence of thyroglobulin antibody in infertile patients. In the study, the incidence of elevated thyroglobulin antibody in healthy fertile group of women is considerably lower (8.57%) than has been reported by **(18)** for United States population (10.4 %). This agrees with the studies of **Wilson, 1975, Rousseve *et al*., 1996, Kutteh *et al*., 1999 , and Petta, 2007 (11, 20, 21,22)** that

have investigated the prevalence of thyroid autoimmunity in women with infertility, they found the prevalence of thyroid autoimmunity is significantly higher among infertile women than among fertile women, especially among those whose infertility is caused by endometriosis or ovarian dysfunction **(23, 24, 25)**. This may be a consequence of subclinically altered thyroid status in some of our women which could have been missed, since no thyroid function related hormones were determined. There are studies showing that the presence of antithyroid antibodies in 32 % women with abortions points to their possible role in early reproductive failure **(26, 27)**. The prevalence of thyroid autoimmunity is 5–10-fold higher among women than men, probably because of a combination of genetic factors, estrogen-related effects and chromosome X abnormalities **(28; 29)**. Thyroid autoimmunity is the most common autoimmune disorder, affecting 5–20% of women in the childbearing period. thyroid autoimmunity is also the main cause of thyroid dysfunction, even though thyroid autoimmunity can be present without hormonal dysfunction **(1)**. Systematic screening for thyroid disorders in pregnant women remains controversial but might be advantageous in women at high risk, particularly infertile women **(1)**. The different incidence of elevated values for antithyroid antibody in the infertile groups in this study as compared to that reported for cases of recurrent abortions mentioned previously, could also reflect the physiological differences between fertilization/implantation problem studied, and the later maintenance of established pregnancy **(26)**.

TABLES

Table 1: Age distribution (years) among the study groups

group / Age	Group A		Group B		Group C		Group D		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
15- 24	32	40	23	32.86	9	30	25	35.71	89	35.6
25- 34	37	46.25	33	47.14	14	46.67	29	41.43	113	45.2
=>35	11	13.75	14	20	7	23.33	16	22.86	48	19.2
Total	80	100	70	100	30	100	70	100	250	100

Table 2: The relationship of antithyroglobulin antibody in the study groups

Tab / Groups	Positive antithyroglobulin antibody		Negative antithyroglobulin antibody		Total	
	No.	%	No.	%	No.	%
group A	10	12.5	70	87.5	80	100
group B	0	0	70	100	70	100
group C	8	26.67	22	73.33	30	100
Group D	6	8.57	64	91.43	70	100
Total	24	9.6	226	90.4	250	100

X^2= 18.36 df= 3 $P < 0.005$

Table 3: Distribution of cases with positive antithyroglobulin autoantibody (Tab) according to the age

Age / Group	15- 24		25- 34		= >35		Total
	No.	%	No.	%	No.	%	No.
GroupA	5	15.63	4	10.81	1	9.09	10
GroupB	0	0	0	0	0	0	0
GroupC	2	22.22	3	21.43	3	42.86	8
GroupD	2	8	2	6.9	2	12.5	6
Total	9	10.11	9	7.96	6	12.5	24

X^2= 3.17 df= 6 $P > 0.05$

Table 4: The relationship of antimicrosomal antibody in the study groups

Mab / Groups	Positive antimicrosomal antibody		Negative antimicrosomal antibody		Total	
	No.	%	No.	%	No.	%
Group A	16	20	64	80	80	100
Group B	14	20	56	80	70	100
Group C	8	26.67	22	73.33	30	100
Group D	7	10	63	90	70	100
Total	45	18	205	82	250	100

X^2= 4.97 df= 3 $P > 0.05$

Table 5: Distribution of cases with positive antimicrosomal antibody (Mab) according to the age

Age / Group	15- 24		25- 34		35-44		Total
	No.	%	No.	%	No.	%	No.
Group A	6	18.75	6	16.22	4	36.36	16
Group B	7	30.34	5	15.15	2	14.29	14
Group C	2	22.22	3	21.43	3	42.86	8
Group D	2	8	3	10.34	2	12.5	7
Total	17	19.1	17	15.04	11	22.92	45

X^2= 2.32 df= 6 $P > 0.05$

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