

# Thyroid Auto-antibodies in Goitrous Euthyroid Patients in Iraq

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## Abstract:

Thyroid auto-antibodies, especially anti-thyroglobulin antibodies (TgAb) and anti-thyroperoxidase antibodies (TPO) are present in positive titers in over 90% of auto-immune thyroiditis, but they are also present in positive titers in about 10-20% of the general population and females outnumber males.

Among the 112 patients with goiter, 99 were females (88.39%) and 13 were males (11.60%), with most of patients fall in the age range of 26-46years (60.68%).

Fine needle aspiration biopsy (F.N.A.) which was performed on 39 patients showed a colloid goiter in 79.48% of them..

Out of those 112 patients, 42 (37.5%) have a positive thyroid auto-antibody titer, while the other 70 (62.5%) have either a borderline or a negative titer ( p-value< 0.05).

Among the positive 42 (37.5%) patients, most of cases (64.2%) fall in the age range between 26-45, with female predominance (90.47% for females and 9.52% for males).

Mean titer of anti-thyroglobulin antibodies (anti-TgAb) was 577.88 i.u./mL and that for anti-thyroperoxidase antibodies (anti-TPOAb) was 203.21 i.u./ml ( p-value < 0.001) .

Among the normal 80 persons, 70 (87.5%) were females, and 10 (12.5%) were males. The auto-antibody test was positive in 18 persons (22.5%), 17 females and 1 male only.

**Key words:** Anti-thyroglobulin auto-antibodies (TgAb), anti-thyroperoxidase auto-antibodies (TPOAb), auto-immune thyroid disease (AITD).

## Introduction:

There are three principle thyroid auto-antigens to which thyroid auto-antibodies can develop, and these include the thyroperoxidase (TPO), thyroglobulin (Tg) and the thyroid stimulating hormone (TSH )receptor <sup>(1)</sup>. TSH receptor auto-antibodies (TRAb) are heterogeneous and may either mimic the action of TSH and cause hyperthyroidism, as observed in Grave's disease, or alternatively, antagonize the action of TSH and cause hypothyroidism. The presence of thyroperoxidase auto-antibodies (TPOAb) usually precedes the development of thyroid dysfunction. Some studies suggest that TPOAb may be cytotoxic to the thyroid<sup>(2,3)</sup>.

The pathologic role of thyroglobulin auto-antibodies (TgAb) remains unclear, but in iodide deficient areas, its measurement may be useful for detecting auto-immune thyroid disease (AITD) in patients with a nodular goiter, and for monitoring iodide therapy for endemic goiter.

TPOAb and/or TgAb are frequently present in the sera of patients with AITD <sup>(4)</sup>. The prevalence of thyroid auto-antibodies is increased in patients who have non-thyroid auto-immune disease such as type-1 diabetes and pernicious anemia <sup>(5)</sup>. The clinical significance of low

levels of thyroid auto-antibodies in euthyroid subjects is till unknown <sup>(6, 7)</sup>, however, longitudinal studies suggest that TPOAb may be a risk factor for future thyroid dysfunction, including postpartum thyroiditis (PPT), as well as the development of auto-immune complications from treatment by a number of therapeutic agents<sup>(8,9,10)</sup>. These include: amiodarone, interferon-alpha and lithium therapy <sup>(11, 12-15)</sup>. The use of thyroid auto-antibodies measurement for monitoring the treatment for AITD is generally not recommended <sup>(16)</sup>.

TgAb positive patients with differentiated thyroid carcinoma (DTC) who are rendered disease-free, typically become TgAb-negative within 1-4 years <sup>(17-19)</sup>. TgAb measurement does not appear to be a useful diagnostic test for AITD in areas of iodide deficiency <sup>(6, 20)</sup>. The following table represents the prevalence of thyroid auto-antibodies <sup>(7)</sup>.

Group	TSHRab (%)	hTGAb (%)	HTPOAb (%)
General population	0	5-20	8-27
Grave's disease	80-95	50-70	50-80
Auto-immune thyroiditis	10-20	80-90	90-100
Relatives of patients	0	40-50	40-50
Patients with type-1 diabetes	0	40	40
Pregnant women	0	14	14

As we can see in this table, the highest levels of TgAb and TPOAb are associated with auto-immune thyroiditis <sup>(5, 6)</sup>. In a study in Iraq, the prevalence of auto-immune associated hypothyroidism was 66% <sup>(21)</sup>. TSHRab= thyroid stimulating hormone antibodies , hTGAb=human thyroglobulin antibodies ,HTPOAb=human thyroperoxidase antibodies.

The present study was conducted to detect the titer of thyroperoxidase auto-antibodies (TPOAb) and the thyroglobulin auto-antibodies (TgAb) in goitrous euthyroid patients in Iraq, and also their level in normal persons with no evident endocrine problem.

## Patients and Methods:

This study was conducted in the Specialized Center for Endocrinology and Diabetes (SCED) in Baghdad over a period of 11 months, from March 2004 till February 2005. A total number of 112 goitrous, euthyroid patients were included in this study; their euthyroid state was confirmed, in addition to clinical examination, by hormonal assay of total T3, T4 and TSH.

Thyroid auto-antibody titers for both anti-Tg and anti-TPO were tested on all patients, using the enzyme-linked immunosorbent assay (ELISA) for the quantitative determination of antibodies against thyroglobulin REF-80502, and anti-TPO anti-REF.

The results were calculated according to the data supplied by the manufacturer as follows: *Positive*: if titer > 100 i.u./mL, *Borderline*: if titer = 60-100 i.u./mL and *Negative*: if titer <60 i.u./mL. Statistical analysis frequency distribution for selected variables was done. Statistical significance was done by Chi-square test and

P-values <0.05 were considered significant. In addition to that, eighty normal persons, with no evident endocrine abnormality, were tested quantitatively for anti-Tg and anti-TPO auto-antibodies for comparison and to see the auto-antibody titer among normal population.

Thyroid ultrasonic examination was performed for all patients. Fine needle aspiration biopsy (F.N.A) was performed on 39 patients. According to the state of goiter, the patients were divided into subgroups as follows: patients with diffused goiter, those with multinodular goiter, and lastly those with solitary thyroid nodule.

### Results:

Among the 112 patients with goiter, 99 were females (88.39%) and 13 were males (11.60%), with most of patients fall in the age range of 26-45years (60.68%). Family history was positive in 43.75% of cases and was negative in 56.25% (Table 1). Most patients (57.14%) have a duration of disease between 1 and 5 years (table 2).

Fine needle aspiration biopsy (F.N.A.) which was performed on 39 patients showed a colloid goiter in 79.48% of them (tables 3 and 4). Twenty-six patients (23.2%) have diffused solitary thyroid nodule as shown in table (4), which also shows the details of F.N.A. findings.

Out of those 112 patients, 42 (37.5%) have a positive thyroid auto-antibody titer, while the other 70 (62.5%) have either a borderline or a negative titer (table 5).

Among the positive 42 (37.5%) patients, most of cases (64.2%) fall in the age range between 26-45, with female predominance (90.47% for females and 9.52% for males).

Mean titer of anti-TgAb was 577.88 i.u./mL and that for anti-TPOAb was 203.21 i.u./mL. Most of the positive cases (57.14%) have a duration of thyroid enlargement between 1 and 5 years.

From these 42 positive cases, 13 (30.95%) have diffuse goiter, 15 (35.71%) have multinodular goiter ( M.N.G), and 14 (33.33%) have a solitary thyroid nodule. Among the patients with diffuse goiter, the auto-antibody titer was higher (for both anti-Tg and anti-TPO) than those with M.M.G. or solitary thyroid nodule. Borderline titer (60-100 i.u./mL) was present only for anti-TPOAb (5 cases, 12.5%). All titers of anti-TgAb were > 100 i.u./mL, while only 11 patients (27.5%) showed an anti-TPOAb titer > 100 i.u./mL.

So, titers for both auto-antibodies were high in only 11 patients (27.5%) as shown in table (6). Details of auto-antibody test in the other 70 patients are shown in table (7). Among the normal 80 persons, 70 (87.5%) were females, and 10 (12.5%) were males. The auto-antibody test was positive in 18 persons (22.5%), 17 females and 1 male with details shown in tables (8 and 9).

Table (10) shows the comparison between the number of positive cases among patients and normal persons (37.5% and 22.5% respectively).

**Table (1):** Age, gender and family history distribution among the total number of patients and the positive cases.

Cases		Age (Years)						Family history	
		15-25	26-35	36-45	46-55	56-65	>65	Positive	Negative
Total Cases	♀ 99(88.39%)	20	35	27	11	5	1	45	54
	♂ 13(11.6%)	6	3	3	1	---	---	4	9
	Total 112	26 (23.2%)	38 (33.9%)	30 (26.73%)	12 (10.71%)	5 (4.46%)	1 (0.89%)	49 (43.75%)	63 (56.25%)
Positive Cases	♀ 38(90.47%)	8	13	11	4	2	---	18	20
	♂ 4(9.52%)	1	2	1	---	---	---	1	3
	Total 42	9 (21.42%)	15 (35.7%)	12 (28.5%)	4 (9.52%)	2 (4.76%)	---	19 (45.23%)	23 (54.76%)
P-values		> 0.1						> 0.1	

**Table (2):** The duration of the disease among the total number of patients and the positive cases.

Cases	< 1 year	1-5 years	6-10 years	> 10 years
Total 112 (100%)	26 (23.21%)	64 (57.14%)	12 (10.71%)	10 (8.92%)
Positive Cases 42(37.5%)	10 (23.8%)	24 (57.14%)	6 (14.25%)	2 (4.75%)

**Table (3):** The details of number of patients on whom fine needle aspiration biopsy(F.N.A)supposed to be done among the total number of patients and the positive cases.

Cases	Done	Difficult	Refused
Total 112 (100%)	39 (34.82%)	37 (33.0%)	36 (32.14%)
Positive	18	14	10

Cases 42 (37.5%)	(42.8%)	(33.33%)	(23.9%)
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**Table (4):** The types of goiter and F.N.A. findings among the total number of patients and the positive cases.

Cases	Type of Goiter			F.N.A. Findings			
	Diffused	M.N.G.	Solitary	Colloid goiter	Hypercellular goiter	Foamy pigmented macrophages	Chronic thyroiditis
Total Cases 112 (100%)	26 (23.2%)	46 (41.0%)	40 (35.7%)	31 (79.48%)	5 (12.82%)	2 (5.11%)	1 (2.5%)
Positive Cases 42 (37.5%)	13 (30.95%)	15 (35.71%)	14 (33.33%)	12 (66.66%)	3 (16.66%)	2 (11.11%)	1 (5.55%)
P-values	>0.1			>0.1			

F.N.A=fine needle aspiration biopsy, M.N.G=multinodular goiter

**Table (5):** The auto-antibody status.

Positive cases	Borderline negative	Total	P-value
42 (37.5%)	70 (62.5%)	112 (100%)	<0.05

**Table (6):** The details of mean auto-antibody levels in positive cases (i.u./mL).

Cases	Antibody type	Diffused goiter	M.N.G.	Solitary nodule	Total mean	P-value
Positive (42)	TgAb	68.5.66 (13)	620.72 (15)	367.28 (14)	577.88 (42)	<0.001
	TPOAb	274.75 (2)	154.41 (6)	207.46 (3)	203.21 (11)	

M.N.G=multinodular goiter

**Table (7):** The auto-antibody status among the other 70 cases.

Antibody type	Titer (i.u./mL)		Total	P-value
TgAb	< 60	60-100	70 (100%)	<0.001
	26 (37.14%)	44 (62.85%)		
TPOAb	63 (90%)	7 (10%)	70 (100%)	

**Table (8):** The gender and auto-antibody status among the normal persons.

Gender (n=80)	Positive Ab Titer	Borderline Titer	Negative Titer	P-value
♀	17 (21.25%)	TgAb 18 TPOAb 4	TgAb 20 TPOAb 11	>0.1
♂	1 (1.25%)	TgAb 4 TPOAb 2	TgAb 2 TPOAb 1	
Total	18 (22.5%)	TgAb 22 TPOAb 6	TgAb 22 TPOAb 12	

Ab=antibody

**Table (9):** The details of age, gender and auto-antibody among normal persons with positive titers.

Gender (n=80)	Age	Number	TgAb	TPOAb
♀	25-45	50 (71.41%)	6 (8.5%)	8 (11.41%)
	46-60	15 (21.42%)	2 (2.85%)	10 (14.28%)
	>60	5 (7.14%)	1 (1.42%)	1 (1.42%)
	Total	70 (100%)	9 (12.77%)	19 (27.11%)
♂	25-45	8 (80%)	---	1 (10%)
	46-60	2 (20%)	---	---
	Total	10 (100%)	---	1 (10%)
	P-values	>0.5	>0.5	>0.5

TgAb=thyroglobulin antibody, TPOAb-thyroperoxidase antibody

**Table (10):** Comparison between the number of positive cases among patients and normal persons with gender correlation

Cases	Total number	Titer		Gender	
		Positive	Borderline or negative	Female	Male
Patients	112 (100%)	42 (37.5%)	70 (26.5%)	38 (33.9%)	4 (3.57%)
Normal Persons	80 (100%)	18 (22.5%)	62 (77.5%)	17 (21.25%)	1 (1.25%)
P-values		P<0.05		P>0.5	

### Discussion:

The clinical utility of thyroglobulin antibodies(TgAb) and thyropoxidase antibodies (TPOAb) can be summarized in the following <sup>(7)</sup>:

1. Establishment of disease etiology such as Hshimoto's thyroiditis, and also their measurement allows the generation of data on the prevalence of auto-immune thyroid disease(AITD)within the patient's family.
2. Prediction of disease onset; like in subclinical hypothyroidism, when there is 5% per year chance of progress to overt hypothyroidism when antibody test is positive.
3. Thyroid nodule and unnecessary surgery: auto-immune thyroiditis in a nodular gender or particularly a hard prominent nodule with no malignancy on fine needle aspirayion biopsy( F.N.A).
4. Risk analysis for postpartum thyroid disease (PPTD). More than 33% of women with positive TPOAb titer early in pregnancy develop some forms of PPTD.
5. Thyroid disease screening in associated auto-immune conditions, for example patients with type-1 diabetes are at particular risk, and the presence of thyroid auto-antibodies is helpful in selecting patients for monitoring of thyroid function.

In this study it had been found that among 112 patients with goiter who are in a euthyroid state, the auto-antibody titer was positive in 42 patients (37.5%), and the mean titer for thyroglobulin antibodies ( TgAb) was higher for those with diffuse goiter (685.66 i.u./mL) who constituted 30.95%, coming next are those with multinodular goiter ( M.N.G )(620.72 i.u./mL) who constituted 35.71%, and lowest in those with solitary nodule (367.28 i.u./mL) who constituted 33.33%. while the titer of TPOAb was lower in all groups although it was higher in those with diffused goiter (274.77 i.u./mL), comes next those with solitary nodule (207.46 i.u./mL), and then those with M.N.G. (154.41 i.u./mL). These

patients are at risk of having hypothyroidism in future <sup>(21)</sup>.

The auto-antibody titer was positive in 18 normal persons (22.5%) out of 80, as it was found in other studies <sup>(7, 22, 23)</sup>. Those persons with positive titer might be, also, at risk of developing hypothyroidism in future. A similar study on school children and adolescents was performed in Saudi Arabia few years ago which showed positive TgAb test in 7.1% of school children and adolescents, while TPOAg were observed in 14.3% of school children especially young females where the prevalence reached 21.5% <sup>(24)</sup>. Among the other 70 patients (62.5%) out of 112 patients, 51 patients (72.84%) have borderline titer, 44 (62.85%) for TgAb, and 7 (10%) for TPOAb. This borderline titer should be taken into consideration, as low titers might be of significance regarding the development of auto-immune thyroid disease(AITD) in future <sup>(7-10)</sup>.

In conclusion, the tests for thyroid auto-antibodies in patients with goiter even in an euthyroid state is important, in order to detect those with thyroiditis and for the possible appearance of hypothyroidism in future. Also the test for thyroid auto-antibodies could eliminate the need for unnecessary surgery, and fine needle aspiration biopsy (F.N.A) is of great help in this regard. The test for antibodies is also important for the families of patients with positive titers, in order to follow then for the possible development of AITD.

In this study, the auto-antibody titer was positive in 42 patients (37.5%) out of 112. The measurement of thyroid auto-antibodies in normal persons is coasty and not practical, but we have to do it at least for those persons who have a strong family history of auto-immune thyroid disease. In this study, the titer was positive in 18 normal persons (22.5%) out of a total of 80, which is still within the international range, with female predominance.

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# الأجسام المضادة ذاتية المنشأ لدى المرضى العراقيين المصابين بتضخم الغدة الدرقية ذات الإفراز الطبيعي

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## الملخص:

ان المرضى الذين لديهم مستويات عالية من الاجسام المضادة وعددهم ٤٢ (٣٧,٥%) تتراوح اعمار معظمهم بين ٢٦-٤٥ سنة واكثرهم من الاناث (٩٠,٤٨% اناث ، ٩,٥٢% ذكور).

ان متوسط مستوى الاجسام المضادة ل Thyroglobulin كان ٥٧٧,٨٨ وحدة عالمية لكل ملي لتر من الدم في حين كان ٢٠٣,٢١ وحدة لكل ملي لتر بالنسبة للاجسام المضادة ل Thyroperoxidase ( $p<0.001$ ). ضمن مجموعة السيطرة البالغ عددهم ثمانين (٨٠) كان اكثرهم من الاناث (٧٠) انثى (٨٧,٥%) في حين كان عدد الذكور عشرة (١٠) ذكور (١٢,٥%).

كانت مستويات الاجسام المضادة مرتفعة لدى ١٨ شخصا (٢٢,٥%) بضمنها ١٧ انثى وذكر واحد.

ان الاجسام المضادة للدرقية ذاتية المنشأ وخاصة المضادة ل Thyroglobulin وتلك المضادة ل ((ثايروبيروكسيداز)) موجودة بمستويات عالية لدى اكثر من ٩٠% من المصابين بالتهاب الغدة الدرقية المناعي ذاتي المنشأ، لكن هذه الاجسام موجودة ايضا بمستويات عالية عند حوالي (١٠-٢٠%) من عامة الناس وخاصة لدى النساء.

من مجموع ١١٢ مريضا كان عدد الاناث ٩٩ (٨٨,٣٩%) وعدد الذكور ١٣ (١١,٦٠%) ومعظم المرضى تتراوح اعمارهم بين ٢٦-٤٥ سنة (٦٠,٦٨%)، ان خزعة الدرقية التي تم انجامها على ٣٩ مريضا اظهرت ان ٧٩,٤٨% منهم كان لديهم تضخم الدرقية الغرواني colloid goitre من مجموع ١١٢ مريضا تحت الدراسة كان ٤٢ منهم (٣٧,٥%) لديهم مستويات عالية من الاجسام المضادة للدرقية ذاتية المنشأ في حين ان الباقي وهم ٧٠ مريضا (٦٢,٥%) كانت مستويات الاجسام المضادة لديهم سالبة او ذات مستويات واطنة ( $p<0.05$ ).